

# 150 ANOS PARA 118 ELEMENTOS **A TABELA PERIÓDICA**

### **XXVI ENCONTRO NACIONAL**

### DA SOCIEDADE PORTUGUESA DE QUÍMICA

### 24, 25 E 26 DE JULHO DE 2019 FACULDADE DE CIÊNCIAS DA UNIVERSIDADE DO PORTO



ANO INTERNACIONAL DA TABELA PERIÓDICA





XXVI ENCONTRO NACIONAL DA SOCIEDADE PORTUGUESA DE QUÍMICA

## 150 ANOS PARA 118 ELEMENTOS – A TABELA PERIÓDICA

Livro de Resumos

24, 25 e 26 de julho de 2019

Faculdade de Ciências – Universidade do Porto

#### Titulo

Livro de resumos do XXVI Encontro Nacional da Sociedade Portuguesa de Química

#### Editores

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O presente livro foi produzido a partir dos trabalhos submetidos diretamente pelos autores. Foram apenas introduzidas pequenas alterações de edição que de modo algum modificaram os conteúdos científicos. O modelo final de impressão foi estabelecido para o XXVI Encontro Nacional da Sociedade Portuguesa de Química de acordo com as normas divulgadas publicamente nos anúncios do evento. A responsabilidade dos conteúdos científicos é dos respetivos autores.

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#### Prefácio

2019 é um ano muito especial para a química e para os químicos, pois um pouco por todo o mundo estão em curso várias ações concertadas sobre a química e os seus principais atores.

É um ano pleno de efemérides que apelam à centralidade da química em vários planos distintos, sendo o maior destaque a proclamação da Assembleia Geral da Nações Unidas, de 2019 como o Ano Internacional da Tabela Periódica dos Elementos estabelecida por Dimitri Mendeleiev em 1869.

A Sociedade Portuguesa de Química (SPQ) e o seu Encontro Nacional associam-se a esta comemoração para celebrar a sua XXVI edição que decorrerá na Universidade do Porto, Faculdade de Ciências, de 24-26 de julho de 2019, com o Alto Patrocínio de sua Excelência o Presidente da República, o Professor Doutor Marcelo Rebelo de Sousa.

A química é verdadeiramente excecional no seu todo e mais do que a ciência da transformação, é a ciência do engenho e da imaginação. E a Tabela Periódica contém toda a química possível e conhecida, sendo mesmo fonte inspiradora para as artes e letras, desde "II Sistema Periodico" (1975) de Primo Levi nomeado pela Royal Institution of Great Britain, como o melhor livro de ciência de sempre, até ao recentemente publicado "O Bairro da Tabela Periódica" (2019) do Professor Manuel João Monte, cujo o lançamento ocorreu sob a égide da Universidade do Porto e da SPQ e que também celebramos neste encontro.

O programa do XXVI Encontro Nacional da SPQ com o mote "150 Anos para 118 Elementos – A Tabela Periódica", foi composto de modo a integrar as diferentes contribuições da química que se faz em Portugal e ao mesmo tempo endereçar os desafios que se nos colocam no âmbito dos Objetivos de Desenvolvimento Sustentável e das suas metas. O Encontro Nacional inclui uma lição do Prémio Ferreira da Silva, oito lições plenárias generalistas de nível excecional, uma conferência da Medalha Vicente Seabra, 16 keynotes, 48 comunicações orais e sessões para exibição dos mais de 290 painéis submetidos. Todas estas contribuições estão agrupadas em torno de três temas agregadores: A Tabela Periódica e os Elementos da Vida (saúde, alimentação e ambiente); A Tabela Periódica Luminescente (materiais, energia e nanotecnologia); A Tabela Periódica na Sala de Aula (comunicação, cultura e ensino).

Num ano em que também se celebra o papel das mulheres na química, marcado pela realização de um pequeno almoço global das mulheres em torno da Tabela Periódica (ocorrido a 12 de fevereiro) é uma feliz coincidência que ambos os prémios SPQ contemplem, pela primeira vez em simultâneo, duas químicas a todos os níveis excecionais.

Contamos, que seja qual for o suporte, em que agora consulta este documento, ele constitua uma referência merecedora de ser guardada como lembrança do seu contributo, porque é para si que organizamos mais este XXVI Encontro Nacional da SPQ.

Os Editores

#### **APOIO INSTITUCIONAL**

COM O ALTO PATROCÍNIO DE SUA EXCELÊNCIA UNDER THE HIGH PATRONAGE OF THE PRESIDENT OF THE PORTUGUESE REPUBLIC







### PLATINA





### OURO



Keeping life in mind.

### PRATA

















# PROGRAMA CIENTÍFICO



IX

Horas		4ª feira (24)			5ª feira (25)			6ª feira (26)		
0046				AFS 9h00-9h45	<b>PL3 - Muno Maulide</b> (UVienna - AT)		AFS 9h00-9h45 F	PL6 - Henry Schaefer (UC&B - USA)		
		EN I KEGA DA DOCUMEN I AÇAO		AFS 9h45-10h40	Medalha Vicente de Seabra 2018 <b>Mara G. Freire (U A)</b>		AFS : 9h45 - 10h40 KN9 INuno Mateus (FCUP) COC13 II illian Barros (IPB)	A1: 9h45 - 10h40 KN10 ILuisa Maia (UNL) COC14 I Filina Marcelo /I MI )	S1 : 9h45 - 10h40 KN11 I Marcela Segundo (FFUP) COC 15 I Marce da Sika (FCTI INI	
10h30	ø	SESSÃO DE ABERTURA (10h30-11h3	(30)	Pausa p	X Café e Discussão de Painéis (10h40 - 11	145 min)	Pausa p/ Ca	0001411 lipa valceo (04L) afé e Discussão de Painéis (10h45 - 1	11 hds min)	
11h30	AFS 11130-12040	Premio Ferreira da Silva 2018 Marta José Calhorda (FCUL)		AFS:11145-12140 KN41 Vania André (IST) COC4 Paula Gomas (FCUP)	A1 : 11IM5 - 12M0 ECGGE IRcardo Maa (Uson, FR) COC5 INargarda Comes (Uson, FR) COC6 IMargarda Comes (Uson, FR)	S1 : 11h45 -12h40 KN5 I Armando Silvestre (UA) COC21 I Fernando Nunes (UTAD)	AFS : 11h45 - 12h40 KN12 I Lisete Sika (C, UK) COC16 I José Câmara (UMad)	<u>A1: 11h45 - 12h40</u> KN131 Beatriz Royo (UNL, ITQB) COC17 Nuno Xavier (FCUL)	<u>81 : 11h45 - 12h40</u> KN14 I Verónica Bermudez (UTAD) COC 18 I Eduardo Marques (FCUP)	
12h40		Almoço (12h40 -14h00)			Almoço (12140 - 14400)			Almoço (12h40 - 14h00)		
14h00 14h15	AFS 14h00-14h15 AFS 14h15-15h00 PL	Christopher Brett (IUPAC) 'L1 - Martyn Poliakoff (U. Nottingham, L	UK)	AFS 14h00-14h45 PL4 - Edu	<b>ardo Fernadez-Megia</b> (USantiago de Com	postela, ES)	AFS 14h00-14h45	PL7 - Cristina Freire (FCUP)		
				AFS:14h45-16h40	A1:14h45-16h35	<b>S1</b> : 14h45 - 16h35	<b>AFS</b> : 14h45 - 15h55	A1 : 14h45 - 15h55	S1:14h45-15h55 GJQ	
15h00	AFS:15h00-16h55 KNI1 ICristing Matrix (ISED)	A1:15h00 - 16h45 KN2 II uis Belchior Sector (ECUID)	S1:15h00 - 16h50 KN31 Inão P. André (I Minho)	KN6 I Luisa Martins (IST-UL)	KN7 I Luis Mafra (UA)	KN8 I Cláudia Silva (FEUP)	KN151 Alberto Pais (FCTUC)	KN16 I Marta Pinero (FCTUC)	COC22   João Borges (UA)	
	COC1 I M <sup>a</sup> Lurdes Cristiano (UAIg)	CO4   Luis Branco (FCTUNL)	COC3 Dosé Moura (FCTUNL)	COC9 I Nuno Moura (UA) COC10 I Pedro Paulo (IST-UL)	COC11 I Andreia Valente (FCUL) CO16 I Adrià Gil-Mestres (FCUL)	COC 12 I Vania Calisto (UA) CO20 I Carlos Baleizão (IST-UL)	COC19   António Parola (FCTUNL, PT) CO24   Filipe Santos (UTAD)	COC201 Luisa Ferreira (FCTUNL)	COC241 Monica Santos (FEUP)	
	COC2 I lola F. Duarte (UA) CO1   José Tavares (FCT-UNL) CO2  Hélio Albuquerque (UA)	CO5   João Avó (IST-UL) CO6   Paulo Martinho (FCUL) CO7   Carina Crucho (IST-UL)	CO9   Sérgio Rodrigues (UC) CO10   Natércia Teixeira (FCUP) CO11   José Araújo (FCUP)	CO13  João Rodrigues (UA) CO 14   Diana Resende (FFUP) CO 15   Ana Fernandes (FEUP)	CO17   Beatriz Gomes (FFUP) CO 18   Roberto Russo (FFUL) CO19   Cláudia Braga (FFUL)	CO 21   Eliana da Silva (FEUP) CO22   Richard Gomes (IUA) CO23   Ricardo Sendão (FCUP)	AFS 15h55-16h40 PL	. <b>8 - Nicola Armaroli</b> (CNR. Bologna, I	Ē	
17h00	CO3   Nuno Alves (FCT-UC) Pausa p/ 0	COB   Luis Silva (FCUP) Caté e Discussão de Painéis (16h55 - :	CO12   Fernanda Carvalho (IST-UL) - 17h45 min)	Pausa p	)/ Café e Discussão de Painéis (16h40 - 17	7h15 min)	AFS 16h40-17h50 Entreg: Prof. João Monte   Dra.	a de Prémios e Sessão de Encerrar . Ana Rita Almeida   Livro "O Bairro Festa de Despedida	mento · da Tabela Periódica"	
	AFS 17h45-18h30	PL2 - Zita Martins (IST-UL, PT)		AFS 17h15-18h00	PL5 - João Carlos Lima (FCTUNL)					
		PORTO de Honra			Reunião SPQ					
20h00				Jant	ar do Encontro   Restaurante Casa da M	lúsica				
	DI - Dionáriae									٦ <sup>-</sup>

PL - Plenárias KN - Keynotes COC - Comunicações Orais Convidadas CO - Comunicações Orais

#### 09:00 - 10:30 Registo

#### Auditório Ferreira da Silva (AFS)

**10:30 - 11:30** Cerimónia de Abertura Dr. Pedro Nuno Teixeira, Presidência da República - Consultor da Casa Civil para a

Ciência e o Ensino Superior Prof. Sousa Pereira, Reitor da Universidade do Porto Prof. Ana Cristina Freire, Diretora da FCUP Prof. Artur Silva, Presidente da SPQ Dr. Raúl Moreira, Diretor de Filatelia dos CTT (Philatelic Issuance of the International Year of the Periodic Table: 1st Day Stamp) Prof. José Ferreira Gomes, Comissário Nacional para o AITP Prof. Vitor Freitas, Organizador do XXVI EN SPQ

#### Auditório Ferreira da Silva | Chair: Artur Silva (Presidente SPQ, UA, PT)

11:30 - 12:40 Prémio Ferreira da Silva | Maria José Calhorda (FCUL, PT)

Pilgrimages in the Periodic Table

12:40 - 14:00 Almoço

AFS | Chair: Ana Isabel Ricardo (FCTUNL, PT)

14:00 - 14:15 Christopher Brett, IUPAC (FCTUC, PT)

14:15 - 15:00 PL1 | Martyn Poliakoff (U. Nottingham, UK)

Mendeleev's Gift to Education (and to me)

#### AFS | Chair: Pedro Gois (FFUL, PT)

15:00	KN1   Cristina Matos (ISEP, PT)
	REWATER- Sustainable and safe water management in agriculture: increasing the efficiency of water reuse for crop growth while protecting ecosystems, services and citizens' welfare
15:30	COC1   Maria Lurdes Cristiano (UAlg, PT)
	Selective photochemistry of 5-aminotetrazole derivatives; effect of the saccharyl moiety on the photostability
15:50	COC2   Iola Duarte (UA, PT)
	Modulation of macrophage metabolism by phytochemicals and biomaterials: insights from metabolomics
16:10	CO1   José Tavares (FCTUNL, PT)
	Nanoimmunoassays – Metal nanoparticles for sensitivity and Antibodies for specificity
16:25	CO2   Hélio Albuquerque (UA, PT)
	Modulating protein aggregation in cell models using modified steroids
16:40	CO3   Nuno Alves (FCTUNL, PT)
	Understanding the mechanism of action of a new spiro- $\beta$ -lactam with dual anti-HIV and anti-Plasmodium activity using in silico target fishing
16:55 - 17:45	Pausa p/ Café e Discussão de Painéis (Sessão 1)

#### Auditório Ferreira da Silva | Chair: Adelino Galvão (IST-UL, PT)

#### 17:45 – 18:30 PL2 | Zita Martins (IST – UL, PT)

The origin and evolution of organic matter in the solar system - interstellar ices, comets and primitive carbonaceous meteorites

#### 18:30 – 19:30 PORTO de Honra

#### A1 | Chair: Luis Carlos (UA, PT)

15:00	KN2   Luís Belchior (FCUP, PT)
	Nanostructuration effect on the physical chemical properties of ionic liquids
15:30	CO4   Luís Branco (FCTUNL, PT)
	Metal based Ionic Systems for Sustainability
15:50	CO5   João Avó (IST-UL, PT)
	Delayed Fluorescence Materials for Imaging Applications
16:10	CO6   Paulo Martinho (FCUL, PT)
	The thermosalient effect in Fe(III) salen spin labile complexes
16:25	CO7   Carina Crucho (IST-UL, PT)
	Enzyme-responsive silica nanocapsules
16:40	CO8   Luís Silva (FCUP, PT)
	Porous Metal-Organic Framework based materials for sustainable catalytic application
16:55 - 17:45	Pausa p/ Café e Discussão de Painéis (Sessão 1)

#### S1 | Chair: Mariette Pereira (UC, PT)

15:00	KN3   João Paulo André (UM, PT)
	Poções e Paixões na Sala de Aula
15:30	COC3   José Moura (FCTUNL, PT)
	Building Artificial Enzymes Using the Metals of the Periodic Table
15:50	CO9   Sérgio Rodrigues (FCTUC, PT)
	Periodic Table and Theoretical and Computational Chemistry: a lesser- known link
16:10	CO10   Natércia Teixeira (FCUP, PT)
	Study of five iberian medieval iron-gall inks obtained through the use of historically accurate reconstructions
16:25	CO11   Fernanda Carvalho (IST-UL, PT)
	Design and synthesis of silver camphorimine compounds with high antimicrobial activity
16:40	CO12   José Araújo (FCUP, PT)
	"Química ao pé da letra": das raízes etimológicas às oportunidades de multidisciplinaridade e divulgação científica
16:55 - 17:45	Pausa p/ Café e Discussão de Painéis (Sessão 1)

#### AFS | Chair: Augusto Tomé (UA)

09:00 - 09:45 PL3 | Nuno Maulide (Vienna University, AT)

The beautiful simplicity of rearrangements: methodology and total synthesis

#### AFS | Chairs: Joaquim Faria (VP SPQ, FEUP) / João Rocha (CICECO, UA)

09:45 – 10:40 Medalha Vicente de Seabra 2018 | Mara G. Freire (UA)

Water, Ionic Liquids and Salts: From the salting-out phenomenon to the formation of aqueous two-phase systems

10:40 - 11:45 Pausa p/ Café e Discussão de Painéis (Sessão 2)

#### AFS | Chair: Fernanda Proença (UM, PT)

11:45	KN4   Vánia André (IST-UL, PT)
	Antibiotics' coordination frameworks: a new perspective towards improved properties and activity
12:15	COC4   Paula Gomes (FCUP, PT)

12:45 - 14:00 Almoço

#### A1 | Chairs: Nuno Maulide/Nuno Candeias/Muna Sidarius

Group of Expatriate Chemists (GEC/GQE)

11:45	COC5   Ricardo Mata (U. Gottingen, DE)
	Structured proton wires – a design principle for biochemical regulation
12:05	COC6   Margarida Gomes (U.Lyon, FR)
	Chemistry or free volume? Porous liquids for gas absorption
12:25	COC7   Pedro Costa (KAUST, SA)
	Alkaline Oxidation of Carbon Materials for Elemental Analysis
12.45 - 14.00	Almosa

#### S1 | Chair: José Câmara (UMad, PT)

11:45	KN5   Armando Silvestre (UA, PT)
	Nanocellulose fibers: biobased masterpieces for the development of sustainable functional materials
12:15	COC21   Fernando Nunes (UTAD, PT)
	As melanoidinas. O que são, como se formam e para que servem?
12.45 - 14.00	Almoco

#### AFS | Chair: Matilde Marques (IST-UL, PT)

#### 14:00 – 14:45 PL4 | Eduardo Fernandes-Megia (U. Santiago de Compostela, ES)

Dendritic Nanostructures for Biomedical Applications

#### AFS | Chair: Teresa Pinho e Melo (UC, PT)

14:45	KN6   Luísa Martins (IST-UL, PT)
	Alkanes or $CO_2$ to added value commodities - the role of C-scorpionate catalysts
15:15	COC9   Nuno Moura (UA, PT)
	Synthesis and emerging applications of $\beta$ -functionalized porphyrin derivatives bearing N-heterocycles
15:35	COC10   Pedro Paulo (IST-UL, PT)
	Single-Molecule Fluorescence from Porphyrins Enabled by Gold Nanodimer Antennas
15:55	CO13   João Rodrigues (UA, PT)
	Bioactive chitosan-on-chitosan multilayered assemblies for biomedicine
16:10	CO14   Diana Resende (FFUP, PT)
	Synthesis and Biological Evaluation of Nature-Inspired Indole-Containing Alkaloids
16:25	CO15   Ana Fernandes (FEUP, PT)
	Morphological Modifications on Carbon Nitride for Enhanced Selectivity Towards the Synthesis of p-Anisaldehyde
16:40 - 17:15	Pausa p/ Café e Discussão de Painéis (Sessão 3)

#### AFS | Chair: Sérgio Seixas de Melo (UC, PT)

17:15 – 18:00 PL5 | João Carlos Lima (FCTUNL – U. Lisbon, PT)

Aurophilic Luminescent Hydrogels

18:00 - 19:00 Reunião SPQ

20:00 Jantar do Encontro | Restaurante Casa da Música

Inclui a performance: "When science becomes an art"

#### A1 | Chair: Eduardo Marques (FCUP, PT)

14:45	KN7   Luís Mafra (UA, PT)
	Understanding the mechanism of CO2 chemisorption on amine-modified porous adsorbent solid surfaces for gas capture applications
15:15	COC11   Andreia Valente (FCUL, PT)
	Fighting metastatic cancers with ruthenium cyclopentadienyl compounds
15:35	CO16   Adrià Gil-Mestres (FCUL, PT)
	Use of Phenanthroline Derivatives in Chemotherapy Treatments for Cancer and as Alternative Therapeutics in the Era of Antibiotic Resistance: Interaction with DNA and Modulation of the Efficiency
15:55	CO17   Beatriz Gomes (FFUL, PT)
	H <sub>2</sub> S-diclofenac vs. diclofenac: effects on membrane lipids
16:10	CO18   Roberto Russo (FFUL, PT)
	3HQs as Boronic Acid Hotspots for site-selective formation of iminoboronates
16:25	CO19   Cláudia Braga (FFUL, PT)
	Triazene-based prodrugs for selective targeting of hypoxic solid tumors
16.40 - 17.15	Pausa n/ Café e Discussão de Painéis (Sessão 3)

#### S1 | Chair: Jorge Marques (UC, PT)

14:45	KN8   Cláudia Silva (FEUP, PT)
	Metal-free photocatalysis: a great step toward sustainability
15:15	COC12   Vânia Calisto (UA, PT)
	Development and application of waste-derived carbon materials for improving wastewater treatments
15:35	CO20   Carlos Baleizão (FC-UL, PT)
	Chasing Boron: Optical Detection and Scavenging Materials for Wastewater Remediation
15:55	CO21   Eliana da Silva (FEUP, PT)
	Remarkable Solar-Driven H <sub>2</sub> Production from Polymeric Carbon Nitride Doped with Carbon and with Distorted Structure
16:10	CO22   J. Richard Gomes (UA, PT)
	A computational study on the water splitting reaction by Mxenes
16:25	CO23   Ricardo Sendão (FCUP, PT)
	Insight into the Interaction between Fluorescent Carbon Dots and Molecular By-Products of their Synthesis

#### 16:40 - 17:15 Pausa p/ Café e Discussão de Painéis (Sessão 3)

#### AFS | Chair: Maria José Calhorda (FCUL, PT)

09:00 - 09:45 PL6 | Henry Schaefer (U. California at Berkeley - USA)

A Brief History of Quantum Chemistry and Computers

#### AFS | Chair: Cristina Matos (ISEP, PT)

#### 09:45 – 10:15 KN9 | Nuno Mateus (FCUP, PT)

Exploring the colour and bioactivity of anthocyanin derivatives

#### 10:15 - 10:45 COC13 | Lilian Barros (IPB, PT)

Recuperação de antocianinas de biorresíduos de Ficus carica L. e Prunus spinosa L.: propriedades corantes e bioativas

#### 10:45 - 11:45 Pausa p/ Café e Discussão de Painéis (Sessão 4)

#### AFS | Chair: Marco Silva (FCTUNL, PT)

11:45	KN12   Lisete Silva (IC, UK)
	The biochemical principles and applications of carbohydrate microarrays
12:15	COC16   José Câmara (UMad, PT)
	Foodomics platforms - new avenues to investigate food quality, traceability and bioactivity
12:40 - 14:00	Almoço

#### A1 | Chair: Celso Reis (I3S, PT)

09:45	KN10   Luísa Maia (UNL, PT)
	Life with Molybdenum

10:15	COC14   Filipa Marcelo (UNL, PT)
	Decoding Glycan-Lectin Interactions in Cancer

#### 10:45 - 11:45 Pausa p/ Café e Discussão de Painéis (Sessão 4)

#### A1 | Chair: Clara Magalhães (UA, PT)

11:45	KN13   Beatriz Royo (ITQB UNL, PT)
	Manganese: The Black Swan
12:15	COC17   Nuno Xavier (FCUL, PT)
	Dodecyl-containing Azide and Glucuronamide-based Nucleosides as Promising Anticancer Lead Molecules for Circumventing Chemotherapy Resistance
12:40 - 14:00	Almoço

#### S1 | Chair: Armando Silvestre (UA, PT)

09:45	KN11   Marcela Segundo (FFUP, PT)
	Greener analytical methods through miniaturization and automation
10:15	COC15   Marco da Silva (FCTUNL, PT)
	Multidimensional GC: Reality, alternative or just a separative extravagancy

#### 10:45 - 11:45 Pausa p/ Café e Discussão de Painéis (Sessão 4)

#### S1 | Chair: Marcela Segundo (FFUP, PT)

11:45	KN14   Verónica Bermudez (UTAD, PT)
	Solutions for improving energy efficiency in buildings
12:15	COC18   Eduardo Marques (FCUP, PT)
	Versatile biocompatible vesicles based on cationic/anionic surfactants: from rational design to biomolecular delivery
12:40 - 14:00	Almoço

#### AFS | Chair: Mário Simões (UA, PT)

14:00 - 14:45	PL7   Cristina Freire (FCUP, PT)
	Catalysis: the successful marriage between Carbon and other Elements in the Periodic Table
AFS   Chair: Pa	ula Gomes (FCUP, PT)
14:45	KN15   Alberto Canelas Pais (FCTUC, PT)
	Polyelectrolyte interaction, confinement and adsorption
15:20	COC19   António Parola (FCTUNL, PT)
	Photoswitching Supramolecular Host-Guest Systems
15:40	CO24   Filipe Santos (UTAD, PT)
	On Chondroitin Sulfate/ Citric Acid Electrolytes as a New Electrolyte Material
AFS   Chair: Vie	ctor Freitas (FCUP, PT)
15:55 – 16:40	PL8   Nicola Armaroli (CNR – Bologna, IT)
	Photoactive systems for solar energy conversion, luminescence and catalysis
16:40 - 17:30	Entrega de Prémios e Sessão de Encerramento

Prof. Joaquim Faria, Vice-Presidente da SPQ

Prof. José Ferreira Gomes, Comissário Nacional para o AITP

Prof. Victor Freitas, Organizador do XXVI EN SPQ

#### 17:30 – 17:50 Prof. João Monte | Dra. Ana Rita Almeida

Leitura encenada de alguns excertos do Livro "O Bairro da Tabela Periódica"

#### 17:50 Festa de Despedida

#### A1 | Chair: Verónica Bermudez (UTAD, PT)

14:45	KN16	Marta Piñero	(FCTUC, PT)
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Sustainable Synthesis of Tetrapyrrolic Macrocycles

15:20	COC20   Luisa Ferreira (FCTUNL, PT)
	Design, production and evaluation of a task specific cellulose-based

Design, production and evaluation of a task specific cellulose-b polymer for wine stabilization

#### S1 | Chair: Lillian Barros (IPB, PT)

Young Chemists Group (YCG/GJQ)

14:45	COC22   João Borges (UA, PT)
	Supramolecular engineering of modular ECM-like functional nanobiomaterials to instruct cell behavior
15:20	COC23   Filipe Reis (IPB, PT)
	Desenvolvimento de formulações cosmecêuticas a partir de extratos obtidos de cogumelos
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	Anticancer Drugs: a Growing Environmental Threat

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# PRÉMIO FERREIRA DA SILVA



# Pilgrimages in the Periodic Table / Peregrinações na Tabela Periódica

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All the chemists use The Periodic Table in their activity. It enters their life at a relatively early stage of their chemical education, becoming part of it forever. For many years, periodic tables were available in paper, sometimes in plastic, now they are electronic. They were static, now they are interactive. They appeared in very different sizes, from the large ones which used to hang in the walls of many chemistry lecture halls, to the A4 classic that many of us use, to the pocket size. The number of elements has been growing since the 63 present in Mendeleev's periodic table in 1869. The following one made the cover of an Inorganic Chemistry textbook. It has been described in ref.1.



How many of the elements do we know well? Even if we dedicated most of our chemical life to one element, do we know it really well? And when we think that we did not explore most of the periodic table are we right?

I'll try to follow the research I performed since I was an undergraduate until today going over the periodic table and highlighting the elements which challenged me. My favorite element? Molybdenum!

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# MEDALHA VICENTE DE SEABRA



#### MVdS

# Water, Ionic Liquids and Salts: From the salting-out phenomenon to the formation of aqueous two-phase systems

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lonic liquids (ILs) have received relevant attention to be applied in a broad range of applications, with a significant fraction of the reported works focusing on their use in separation processes from aqueous media. In this field, a large interest has been placed in hydrophobic ILs due to their immiscibility with water and ability to create biphasic (liquid-liquid) systems. However, these tend to be more toxic and of higher cost, rendering the use of water-soluble (hydrophilic) ILs as a more appropriate choice. Although these ILs are water-soluble, aqueous two-phase systems can be created by combining them with inorganic or other organic salts with salting-out characteristics. These aqueous two-phase systems, if properly designed, are sustainable and biocompatible separation strategies due to their high water content [1-2]. Nevertheless, the design of these systems as effective separation processes requires a better understanding of the molecular-level mechanisms ruling the liquid-liquid phase behavior and salting-out and salting-in phenomena of salts over ILs in aqueous media.

In this work, our contributions over the past years toward a comprehensive understanding of the molecular-level mechanisms ruling the formation of two-phase systems constituted by water, ILs and salts will be overviewed. These findings are based on a large set of experimental liquid-liquid and spectroscopic data and modeling results. It will be shown how salting-out inducing ions (high charge density) and salting-in inducing ions (low charge density) act through different mechanisms. Based on the acquired knowledge, a large set of water-rich biphasic and multiphasic systems have been further designed, most of the times with the required characteristics to carry out target separations of added-value compounds. This understanding on the molecular-level mechanisms also allowed the design of switchable systems (thermoreversible and pH-driven), which can act as integrated production-separation platforms. Some examples of most recent advances in this field will be shown.

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# LIÇÕES Plenárias



#### PL1

### Mendeleev's Gift to Education (and to me)

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2019 has been declared the International Year of the Periodic Table in celebration of the 150th anniversary of Dmitri Mendeleev's first publication of his Periodic Table.<sup>1</sup> The purpose of this lecture is to demonstrate that Mendeleev's genius was to create something that anyone can use as a highly flexible framework for expressing their chemical ideas. I shall do this by giving examples of a whole variety of periodic tables ranging from one of the oldest surviving examples of periodic table intended to be shown in a lecture theatre<sup>2</sup> to the periodic table recently devised specifically by the European Chemical Society (EuChemS) for the IYPT, highlighting some of the elements which are becoming scarce.<sup>3</sup> I shall also highlight how the Periodic Table has impacted my own career and research including the use of niobium catalysts,<sup>4</sup> searching for a better process for making terephthalic acid<sup>5</sup> and a lower cost manufacturing process for the anti-malarial drug artemisinin<sup>6</sup> as well as mentioning our own contribution to the debate about designs of the periodic table.<sup>7</sup>

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# The origin and evolution of organic matter in the solar system - interstellar ices, comets and primitive carbonaceous meteorites

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The Solar System was formed 4.568 billion years ago with the collapse of a dense cloud of interstellar gas and dust, which served as the building blocks of future asteroids and comets. The photo- and thermo-processing of organic matter in interstellar ice grains in the pre-accretion stage was followed by incorporation into asteroids and comets, and then processed by aqueous alteration<sup>1</sup> (i.e., increasing aqueous alteration means the melting of ices in asteroids and comets, mostly likely due to the heating from the decay of short-lived radionuclides such as <sup>26</sup>Al)<sup>2</sup>. Meteorites are fragments from the asteroid belt. A class of primitive meteorites named carbonaceous meteorites contain 3-5wt% of organic carbon, present as insoluble organic matter (IOM)<sup>3</sup>, and as soluble organic compounds (SOM), including carboxylic acids, amino and diamino acids, sulfonic and phosphonic acids, purines and pyrimidines, sugar-related compounds, and hydrocarbons, among others<sup>4</sup>. The analysis of the soluble organic inventory present in these primitive meteorites, and comparison with the one present in interstellar icy grains helps to establish the chemical reactions of the early solar system. Our team has analysed the amino acid content of one of the least aqueously altered CM chondrites (named the Paris meteorite)<sup>5</sup> and of laboratory organic residues, which are analogues of the organic material formed in interstellar icy grains<sup>6</sup>. In this talk I will show that the interstellar ice evolution is one of the sources of organic matter in the Solar System.

Comets are also another primitive body of our solar system that provides information about the origin and evolution of the primordial organic matter. Amino acid precursors (e.g. ammonia, methanol and carbonyl compounds) have been detected in comets, e.g. Halley, Hyakutake, Tempel-1, and Hale–Bopp<sup>7</sup>. In addition, space missions that have visited comets showed that these contained several organic molecules: e.g., comet Wild-2 contained glycine, and comet 67P/Churyumov-Gerasimenko alcohols, carbonyls, amines, nitriles, amides, isocyanates, the polymer polyoxymethylene, phosphorus and glycine<sup>8</sup>. Furthermore, our team has experimentally tested that the hypervelocity impact-shock of a typical comet ice mixture synthesises amino acids<sup>9</sup>. Indeed, the impacts of comets onto planetary rocky surfaces generates enough energy to produce several  $\alpha$ -amino acids<sup>9</sup>.

The analysis of the soluble organic matter present in primitive planetary bodies (i.e., interstellar ices, comets and primitive carbonaceous meteorites) provides a window into the formation of our solar system, and into the origin and chemical evolution of prebiotic matter, that may have been incorporated later into the first living organisms of our planet.

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# The beautiful simplicity of rearrangements: methodology and total synthesis

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The turn of the century brought about a pressing need for new, efficient and clean strategies for the chemical synthesis of biorelevant compounds. Our group has studied the use of various molecular rearrangements and atom-economical transformations as particularly appealing means towards the streamlined synthesis of complex small molecule targets.

In this lecture, we will present an overview of our research in these areas focusing on the chemistries of sulfonium salts, keteniminium ions and small strained rings, and how they provide efficient solutions for the discovery of unusual reactivity or concise total synthesis.<sup>1,2,3</sup>

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#### PL4

### **Dendritic Nanostructures for Biomedical Applications**

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Dendrimers and PEG-dendritic block copolymers constitute interesting polymeric nanostructures in the biomedical field.<sup>1</sup> Their multivalent nature and ability to tune their solubility and self-assembly properties in solution make them interesting building blocks for the engineering of biocompatible drug delivery and diagnostic nanosystems. With this aim, our research group has developed the GATG (Gallic Acid-Triethylene Glycol) dendritic family.<sup>2</sup> Thanks to the presence of terminal azides, GATG dendrimers can be easily functionalized with biologically relevant ligands like cations/anions, carbohydrates, metal chelates, peptides and small proteins. The resulting functionalized materials afford interesting tools in the study of biological processes,<sup>3</sup> diagnosis,<sup>4</sup> and drug & gene delivery applications.<sup>5</sup> In this presentation, the preparation of this family of dendrimers and some bioapplications will be shown.



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### Aurophilic Luminescent Hydrogels

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Metallogels are a subject of study in the last few years.<sup>[1]</sup> The reason for the growth of interest stems from the availability and the diversity of metal-ligand coordination that could readily induce or control the self-assembly process of the gel formation and thereby influence the gel properties, as a difference with what occurs in organic gels. Organometallic Au(I) complexes present the additional advantage to use both classical supramolecular interactions (e.g.  $\pi$ - $\pi$  stacking or hydrogen bonding) together with the establishment of Au(I)···Au(I) bonds (aurophilic interactions), which are particularly strong. Furthermore, these complexes exhibit interesting emissive properties that usually are modulated by the presence of the aurophilic interactions, display sup-picosecond intersystem crossing rate constants<sup>[2]</sup> and can display thermally assisted delayed fluorescence (TADF) with short luminescence decay times and a high PL quantum efficiency<sup>[3]</sup>, important properties for OLED emitters.

We have reported on the formation of luminescent Au(I) hydrogels based on water soluble organometallic alkynyl complexes where aurophilic intermolecular interactions are involved on the gelation process.<sup>[4-8]</sup> Slight modifications on the chemical structure can induce significant changes on the supramolecular assemblies leading to hydrogels, rods or vesicles (Figure 1).



Figure 1: AFM image showing the hierarchical self-assembly from vesicles to fibers and bundles of [(PTA)Au(4-pyridylethynyl)] in water (PTA = 1,3,5-triaza-7-phosphaadamantane).

Analysis of the thermodynamic and photophysical parameters that modulate and are modulated, respectively, by Au(I) and Au(I)...Au(I) interactions has been performed and the results are supported by theoretical data.

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# A Brief History of Quantum Chemistry and Computers

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When did quantum chemistry begin? When did computer science begin? The answers to these two questions are complicated and intermingled. We propose to consider the period from 1927 to the present, from the differential analyzer to the latest graphics processors, along with parallel developments in the ability to make reliable chemical predictions of importance.



# Catalysis: the successful marriage between Carbon and other Elements in the Periodic Table

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The global energy crisis, reflected in the depletion of fossil fuels and growing of environmental pollution, has stimulated a great effort in the development of eco-sustainable chemical methods for biofuels and bio-products production as alternatives to petro-based derivatives, as well as new renewable energy conversion and storage chemical/electrochemical technologies. All these new methods and technologies needs new materials and carbon nanomaterials (carbon nanotubes and graphene) appear as a key choice, due to their intrinsic catalytic properties, as well as their excellent properties to act as nanosupports for several other materials with catalytic properties, specifically metal and metal oxides with nanometric sizes.

In this talk several examples of carbon-based materials will be presented as catalysts and electrocatalysts in several chemical reactions and electrochemical energy-related reactions.

Supported-metal (Co, Cu and Ni) and organosulfonic acid functionalized [1] carbon nanomaterials (including biochar) were prepared and the catalytic activity of these materials evaluated in biomass conversion: esterification of free fatty acids and levulinic acid; and hydrogenation of furfural and 5-(hydroxymethyl)furfural. Heteroatom-doped carbon nanomaterials were also studied in the selective reduction of nitro- into amine-arenes, with high catalytic activity and stability/reusability. Furthermore, several carbon materials (pristine and doped-carbon nanotubes, graphene flakes derivatives) nanocomposites with metals oxides: mixed valence cobalt oxide, phosphomolybdates and phosphotungstates have been successfully applied in energy-related electrochemical reactions involving hydrogen and oxygen evolution reactions (HER and OER, respectively), as well as oxygen reduction. [2]

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#### PL8

## Photoactive systems for solar energy conversion, luminescence and catalysis

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The research of our group is focussed on luminescence and photoinduced energy and electron transfer processes in organic molecules, metal complexes, supramolecular arrays and nanomaterials. In particular we investigate light harvesting and charge separation in model solar energy conversion systems, luminescent metal complexes, photoredox catalysts for organic synthesis. A survey of our work in these areas will be made, with focus on multichromophoric systems for solar energy conversion, photoactive Ir(III) and Cu(I) complexes as luminescent and photoredox materials, hybrids made of inorganic luminophores and carbon nonostructures. Emphasis will be put on strategies to tune and optimize excited state properties for enhanced photochemical, photoluminescence and photoredox performance.<sup>1-10</sup>

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# **KEYNOTES**



# REWATER- Sustainable and safe water management in agriculture: increasing the efficiency of water reuse for crop growth while protecting ecosystems, services and citizens' welfare

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Water is a vital resource for the agriculture economy. Yet, during the past decades, geographic and climatic features, as well as active release of man-made chemicals, have been driving to its depletion and loss of quality. Although reuse of wastewater (WW) from wastewater treatment plants (WWTP) may provide a way to fight water scarcity, it has certain associated risks. For example, the evaluation of water quality for irrigation is focused on conventional pollution parameters and doesn't include emerging contaminants (ECs) such as pharmaceuticals and specific pesticides that should also be monitored because of their reduced removal by conventional treatments. The potential presence of ECs in the effluent waters of WWTP may lead to contamination of receiving surface waters, which could be extended to soils, crops and, in a last instance, to human beings, thus limiting the application of treated WW in agriculture.

In the REWATER project<sup>1</sup> technologies able to produce a final integrated solution for reuse of WW for agricultural purposes are developed. Many scientific and technical advances have been achieved and some results will be presented: 1) monitoring of ECs (83 pharmaceuticals and 19 pesticides) in the Norte-Leiria WWTP (effluents and influents) and in the Lis river in 2 campaigns<sup>2</sup>; 2) fast screening of ECs using different electrochemical sensing platforms based on paper<sup>3</sup> and molecularly imprinted polymers (MIP)<sup>4</sup>; 3) removal of ECs through electrochemical (electrofenton<sup>5</sup>) and biological (biopellets<sup>6</sup> composed of microalgae (*Chlorella vulgaris*) and a fungus (*Aspergillus niger*)) treatment processes; 4) use of ecotoxicological tools to evaluate treated water for reuse and to create expeditious surveillance.<sup>7</sup>

The technologies developed in the REWATER project are expected to be extended to WWTPs worldwide.

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# NANOSTRUCTURATION EFFECT ON THE PHYSICAL CHEMICAL PROPERTIES OF IONIC LIQUIDS

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The level of nanostructuration in the ILs affects the trend of physical chemistry properties along the series and is dependent of the alkyl chain size, cation and anion nature. In some recent publication [1-5] we were able to give additional support to the nanostructuration effect on the thermodynamic properties of the [C<sub>N</sub>C<sub>1</sub>im][NTf<sub>2</sub>] IL family. Ionic liquids form nanoaggregates constituted by anions and cations giving rise to a network of highly polar areas ruled by coulombic forces and nonpolar ones corresponding to regions of alkyl chains dominated by van der Waals interactions.[3]



TREND SHIFT : thermodynamic properties ..... CAS ... Critical alkyl Size

Scheme 1: Nanostructuration effect on the physical-chemistry properties of ionic liquids

A significant differentiation of the trend of the thermodynamic properties before and after CAS (critical alkyl size of n=6) was observed due to the change of the cohesive electrostatic potential that rules the network packing both in solid and liquid phases. Further studies allowed us to unravel the role of IL nanostructuration and acidity on the preferential interactions established between the alcohol and the IL, the speciation and cohesive energy of protic ionic liquids [6] as well as their nucleation and growth of micro droplets of ILs deposited by physical vapor method onto different surfaces.[7]

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# Poções e Paixões na Sala de Aula

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O livro *Poções e Paixões – Ópera e Química* (Gradiva, 2018) será apresentado e discutido quanto ao seu potencial pedagógico e às possibilidades da sua utilização na sala de aula.





# Antibiotics' coordination frameworks: a new perspective towards improved properties and activity

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The pharmacological applications of metal-organic frameworks has been increasing in the last years, being especially focused on achieving controlled drug delivery and release.<sup>1</sup> Nevertheless, the direct coordination of drugs to "safe" metals<sup>2</sup> has been proving to be a viable pathway to trigger changes in important properties such as solubility and bioavailability, as well as in drug's activity. One further advantage is that synergistic effects of the metal can be explored. This approach can be particularly relevant in the quest against the global threat of multidrug-resistant bacteria.

Bactericidal agents, including antibiotics, drastically reduced the number of deaths caused by infections over the last 70 years, but due to their misuse and abuse, many microorganisms developed resistance mechanisms, causing thousands of deaths/year, and leading to an increased economic burden and productivity losses.

Bearing these concerns in mind, the goal of this work is to develop new coordination frameworks enclosing drugs (mainly antibiotics) and safe metals to increase their solubility and consequently bioavailability, trying simultaneously to explore synergistic effects with the metal for enhanced antimicrobial activity (**Figure 1**).<sup>3</sup>

Regarding the synthetic point of view, it is worth mentioning that this project is mainly focused on mechanochemistry, an environment-friendly technique that drastically reduces the amount of solvents and that has proven to be very efficient in different areas.



Figure 1: Preparation of coordination frameworks built from safe metal salts and active pharmaceutical ingredients

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# Nanocellulose fibers: biobased masterpieces for the development of sustainable functional materials

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In recent years there has been a growing trend towards the development of biobased functional nanocomposite materials. In this context cellulose nanofibers (have been playing a central role, due to the outstanding properties they impart to composites with both natural and synthetic polymeric matrices. Nanofibrillated cellulose, obtained from plant fibers processing, and bacterial cellulose, biosynthesized by several benign bacterial strains are produced in the form of highly swollen hydrogels (Figure 1) with completely with completely different properties mainly due to the physical entanglement of nanofibers in bacterial cellulose.



Nanofibrilated cellulose Bacterial cellulose

Figure 1: Visual and microscopic aspect of nanofibrillated and bacterial cellulose

In addition to notorious improvements in mechanical and thermal properties, often combined with transparency, cellulose nanofibers have been exploited in the preparation of functional materials with applications that span from the biomedical field (e.g. biocompatible and antimicrobial materials and pH sensitive materials for drug delivery), nanocomposite materials for transparent electronics; protonic and anionic conducive membranes for fuel cells, luminescent materials for optical applications among others have been reported.

The preparation of such functional materials requires the judicious functionalization of cellulose nanofibers and/or their compatibilization with the adequate molecular or macromolecular components.

An overview of the advances in these domains in our group, illustrated by the most sound examples, will be presented and discussed in this communication.

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# Alkanes or CO<sub>2</sub> to added value commodities - the role of C-scorpionate catalysts

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The development of sustainable efficient catalytic processes for the activation of abundant and inexpensive rawmaterials into high-added-value products remains a great challenge.

Alkanes, although being the richest potential source of carbon, are mainly used as non-renewable fossil fuels, leading to environmental issues, namely due to CO<sub>2</sub> formation. Carbon dioxide, in turn, is also a promising nontoxic low-cost carbon source for the development of sustainable chemical industry since CO<sub>2</sub>-based C1-chemicals can reduce the impacts of global warming and fossil depletion.

This work reports catalytic strategies for using inert alkanes or  $CO_2$  as carbon feedstock for the syntheses of functionalized added-value organic compounds, under sustainable conditions, such as the one-pot oxidation of cyclohexane to adipic acid<sup>1</sup> or the direct conversion of  $CO_2$  to methanol.<sup>2</sup> The catalysts are based on metal complexes bearing C-scorpionate poly(pyrazol-1-yl)methane ligands (**Figure 1**), where the interchange between bidentate and tridentate coordination modes of such ligands is at the core of the structural and chemical versatility of their metal complexes and is essential for their catalytic effectiveness and versatility.<sup>3</sup>



Figure 1: Schematic structure of C-scorpionate tris(pyrazol-1-yl)methanes  $RC(R'pz)_3$  (pz = pyrazolyl; R = H or substituent at the methine carbon; R' = H or substituent at the pz ring) and comparison with a scorpion.

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# Understanding the mechanism of CO<sub>2</sub> chemisorption on amine-modified porous adsorbent solid surfaces for gas capture applications

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Reaching a historic high of 32.5 gigatonnes in 2017, global carbon dioxide emissions from fossil fuels combustion continue to increase.  $CO_2$  removal technologies are part of the solution to tackle this crucial environmental challenge. Because of their lower regeneration cost, amine-modified porous silicas (AMPS) are among the most promising  $CO_2$ —adsorbents for replacing the decades-old liquid amine scrubbing technology. AMPS are "moisture-tolerant" and selectively chemisorb  $CO_2$  from low-concentration mixtures, important features for operating under large-point  $CO_2$  emission source conditions.

The nature of CO<sub>2</sub> species formed on AMPS surfaces determines the gas adsorption capacity/kinetics, selectivity, stability, and regenerability. However, a molecular-scale understanding of the CO2-AMPS adsorption process remains elusive, hindering our ability to design improved sorbents. Herein, we present the last research advancements recently obtained from our group towards a better understanding of these CO2-sorbent materials. New insights into the structure of chemisorbed CO<sub>2</sub> species formed on the surface of AMPS solid adsorbents functionalized with primary, secondary, tertiary and mixed primary-secondary amines are revealed by solid-state NMR (ssNMR) spectroscopy combined with computer modeling approaches, using materials loaded with <sup>13</sup>C-labeled CO<sub>2</sub>, under controlled CO<sub>2</sub> and H<sub>2</sub>O partial pressures. 1-4 This presentation shows a combination of 1D and 2D ssNMR experiments applied to as-prepared and H/D exchanged AMPS materials aiming at unraveling the nature of interactions of CO2-adducts formed in their surfaces,<sup>1</sup> employing either pure CO<sub>2</sub> gas or CO<sub>2</sub>/H<sub>2</sub>O binary mixtures. CO<sub>2</sub> species are engaged in complex hydrogen bonding networks involving amine amine and amine silanol interactions, where different populations of CO<sub>2</sub> species such as carbamate ion pairs, carbamic acid as well as very dilute species and moisture-induced CO<sub>2</sub> species can be distinguished. A first experimental ssNMR proof towards the identification of different CO<sub>2</sub> aggregation states will also be shown, which has been a longstanding problem.<sup>2</sup> This presentation illustrate the benefit of integrating spectroscopy and theoretical approaches to correlate the structure of surface CO<sub>2</sub> species with the enhanced CO<sub>2</sub>/CH<sub>4</sub> selectivies and CO<sub>2</sub> adsorption capacities observed in some of these solid CO<sub>2</sub>-sorbents.

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### Metal-free photocatalysis: a great step toward sustainability

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During the past few decades, photocatalysis has emerged as a green and sustainable technology due to its potential to solve energy and environmental problems. Heterogeneous photocatalytic reactions, driven by semiconductor nanomaterials, are becoming important for process intensification and safety in many environmental, chemical, pharmaceutical, and medical applications. The key for the implementation of such processes lays in the successful combination of energy-efficient irradiation, effective and sustainable catalysts, and appropriate reactor engineering. Graphite-like carbon nitride (g-C<sub>3</sub>N<sub>4</sub>) is a polymeric semiconductor which may be regarded as "doped" graphite in which carbon atoms are regularly substituted by nitrogen atoms.<sup>1</sup> The main bottlenecks for the application of this metal-free photocatalyst are the low surface area and the fast recombination of electrons and holes upon photo-excitation. This talk will present several approaches for boosting the activity of  $g-C_3N_4$  in distinct photocatalytic applications ranging from hydrogen production, chemical synthesis, water treatment, and in surfaces' cleaning and disinfection (Figure 1).<sup>2</sup> The use of such materials in structured photoreactors will also be discussed.



Figure 1: Modifications and photocatalytic applications of g-C<sub>3</sub>N<sub>4</sub>.

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## Exploring the colour and bioactivity of anthocyanin derivatives

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There is a growing market demand for the incorporation of plant-derived ingredients in new products in different industrial fields including the food and cosmetic industries. Anthocyanins are polyphenols arising from plant secondary metabolism. Besides their appealing colours, these compounds have been shown to display many antioxidant and bioactive properties such as free radical scavenging, metal-chelating, antimicrobial, wound healing and chemopreventive activities. From a nutritional standpoint, the ingestion of anthocyanin-rich foods has been positively correlated with health-promoting features. On the other hand, the ability to prevent oxidative damages has led to the incorporation of natural bioactives in lotions and facial creams to prevent skin diseases and premature ageing, therefore the biological activities of anthocyanins make them novel potential compounds for cosmetic formulations. However, native anthocyanins present a low solubility in lipophilic media, which compromises their effective application. Therefore, strategies have been conducted to overcome or partially solve this issue. Similar approaches are targeted for anthocyanin-derived pigments displaying unusual and appealing colours from orange to bluish hues. Other approaches may involve the use of lignin nanoparticles for the encapsulation of some derivatives such as pyranoanthocyanin dimers.

In this project, anthocyanins from industrial wastes are recycled and used in their genuine forms. Biological features of anthocyanin metabolites likely to occur in vivo are tested and compared with genuine anthocyanins. Enzymatic lipophilization is performed by addition of selected chain fatty acids to improve their solubility in lipophilic systems. Their biological activities are then assessed by developing a new skin barrier model using keratocytes living cells. Assays on the absorption of these bioactives at the skin level are performed and compared to native anthocyanins absorption. The behavior of the cells incubated with the lipophilized anthocyanins is also monitored continuously with a microeletrode-based biosensor device (Electric Cell-Substrate Impedance Sensing – ECIS). This new system allows a simple, fast and reliable screening of the capacity of the new lipophilized anthocyanins in comparison with the native ones to cross the skin barrier and at the same time to monitor cell morphology and perform cell-based assays including wound healing assays, all from a skin care standpoint.



### Life with Molybdenum

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2019 was declared by UNESCO as the "International Year of the Periodic Table of Chemical Elements" to celebrate the 150<sup>th</sup> anniversary of its creation by Dmitry Mendeleev. This communication aims to highlight one chemical element whose biological relevance is poorly recognised and largely disregarded: MOLYBDENUM.

An overview of the molybdenum-containing enzymes will be presented, showcasing the chemical versatility of this element that catalyses oxygen, hydrogen and sulfur atom transfer reactions.<sup>1</sup> The wide range of molybdenum biological roles will be discussed, with emphasis on its involvement in human health<sup>2</sup> and environmental issues<sup>3</sup>.



Figure 1: In biological systems, molybdenum is mainly found associated with one or two pyranopterin molecules that coordinate the metal by a cis-dithiolene group. The metal coordination sphere is completed by a diverse array of groups that allowed the evolution of enzymes with different physiological functions, such as <u>xanthine oxidase</u> and <u>sulfite oxidase</u> (involved in human health problems), <u>formate dehydrogenase</u> (responsible for the biological carbon dioxide and formate handling and an interesting biotechnological target for the development of devices for atmospheric carbon dioxide utilization) or <u>nitrate reductase</u> (responsible for the biological target to mitigate the soils and aquifers contamination). Molybdenum can also be found in a complex molybdenum/iron centre, present only in <u>nitrogenase</u>, the key enzyme responsible for the fixation (reduction) of atmospheric dinitrogen into the "organic" ammonium.

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### Greener analytical methods through miniaturization and automation

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The twelve principles of green chemistry have been proposed about 20 years ago in order to change the design, development and implementation of chemical products and processes through innovative ways to reduce waste, conserve energy, and discover replacements for hazardous substances.<sup>1</sup> More recently, the Member States of the United Nations adopted the 2030 Agenda for Sustainable Development<sup>2</sup> comprising 17 sustainable development goals that constitute a framework for ending poverty, for building economic growth, also addressing climate change and environmental protection. In this context, all branches of Chemistry, including Analytical Chemistry, should be revised and research endeavours should be directed to develop sustainable processes.

The present communication addresses how miniaturization and automation can introduce sustainability in analytical methods. Miniaturization fosters greener analytical methods through reduction of the amount of sample and reagents required for each analysis, with further decrease on effluent and waste generation. Automation also contributes to sustainable analytical methods. Besides also requiring low volumes (microliters to few millilitres), precise control of events (such as interaction with surfaces, mixing of reagents/sample, reading of analytical signal), regarding both time and space, allows the implementation of reaction/interaction strategies not feasible in batch-wise methods.

The impact of both miniaturization and automation will be demonstrated by examples concerning automation of solidphase extraction for sample treatment with online coupling to chromatographic methods,<sup>3</sup> for which the required amount of organic solvent is reduced up to ten times, along with utilization of < 20 mg of solid sorbent. The miniaturization and automation of ELISA protocols will also be discussed, as a significant reduction on time-to-result is attained (2 h to 5 min),<sup>4</sup> with an important decrease on sample and reagents consumption. Finally, the smartphone-based detection of analytes retained in solid supports will be addressed, comprising an in-situ method for screening of pollutants that requires minimal reagent volumes.

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## The biochemical principles and applications of carbohydrate microarrays

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Cell surfaces are decorated with complex carbohydrate structures, termed glycans, that are involved in many biological events through interactions with the corresponding carbohydrate-binding proteins (CBPs) that recognise them as ligands. However, understanding the mechanisms by which these interactions occur remains a challenging task. Furthermore, a detailed study of carbohydrate-protein interactions is often difficult due to: (a) the low availability of carbohydrate starting material; (b) the heterogeneity and complexity of the carbohydrate samples; (c) the less straightforward biosynthesis of carbohydrates when compared with nucleic acids and proteins and their no template-driven chemical synthesis; and (d) the low affinity of most carbohydrate-protein interactions, which require a multivalent presentation of carbohydrate ligands for detection of binding in microscale screening analyses.<sup>1</sup>

Carbohydrate microarray technologies have emerged in 2002 as a sensitive and powerful tool to study carbohydrateprotein interactions in a high throughput manner, and to elucidate oligosaccharide ligands that are involved both in endogenous biological processes and pathogen-host interactions.<sup>2,3</sup>

The Glycosciences Laboratory (<u>http://www.imperial.ac.uk/glycosciences/</u>) at Imperial College London, directed by Professor Ten Feizi, pioneered a neoglycolipid (NGL)-based microarray system, whereby hundreds of lipid-linked sequence defined glycans are immobilised on a solid surface and interrogated with several CBPs of biological and biomedical interest.<sup>2,3</sup>

This communication aims to provide an overview of the biochemical principles of the carbohydrate microarrays, including the design and construction of the arrays, preparation, and printing of glycan probes, followed by the analyses using different detection systems. Examples of carbohydrate microarrays applications, such as the analysis of viral proteins to elucidate pathogen interactions with host carbohydrates, investigation of the specificity of carbohydrate-binding proteins and identification of disease-related anti-glycan antibodies for diagnosis will be shown.

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### Manganese: The Black Swan

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Manganese has recently emerged as an excellent metal for catalysis. The vast natural abundance of manganese-it is the third most abundant transition metal in Earth's crust-together with its low price and non-toxicity render it a particularly attractive metal for catalysis. Recent advances have shown the impressive reactivity of this metal in various important organic transformations, including (de)hydrogenation, hydrosilylation, and transfer hydrogenation reactions.<sup>1</sup> Our research group has been fortunate to contribute to this surge. In this seminar, our recent work on the synthesis of new manganese complexes bearing N-heterocyclic carbenes, both imidazolylidenes and 1,2,3-triazolylidenes (**Scheme 1**) and their application in catalysis will be presented. Interestingly, the manganese complex [Mn(CO)<sub>3</sub>(bis-NHC)Br] (1) displayed an unprecedented activity for the selective electrocatalytic reduction of CO<sub>2</sub> to CO, reaching a maximum turnover frequency TOF<sub>max</sub> of 320000 s<sup>-1</sup>, which represents the highest TOF value ever reported for a manganese-based catalyst.<sup>2</sup> In addition, complex 1 displayed remarkable activity in the reduction of carbonyl groups through hydrosilylation reactions.<sup>3</sup> A wide variety of ketones were selectively reduced to the corresponding alcohols using phenylsilane and the cheap and readily abundant polymethylhydrosilane (PMHS) in the presence of catalytic amounts of 1. We have also prepared the first examples of manganese carbonyl triazolylidene complexes, including the unprecedent bimetallic Mn complex 2, and disclosed its excellent activity in the oxidation of alcohols to ketones and aldehydes.



Scheme 1: Manganese-NHC complexes applied in catalysis.

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## Solutions for improving energy efficiency in buildings

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The building sector will play a key role in the race for energy efficiency. Windows will have an important share in this respect. It has been estimated that smart window technology<sup>1</sup> will reduce up to 40% of the building's energy demand. The development of window systems enabling the control of sunlight transmittance (visible radiation) and solar heat gain (near-infrared (NIR) radiation), having UV harvesting ability, and exhibiting appealing colours, is sought to reduce energy use, increase the occupant's indoors thermal and visual comfort, improve outdoors view, and make buildings aesthetically more attractive.

The combination of amorphous indium zinc oxide<sup>2-4</sup> and indium molybdenum oxide<sup>5</sup>, which are conducting oxides transparent in the visible and NIR regions, with a hybrid electrolyte prepared by the sol-gel method,<sup>2,5</sup> a NIR-emitting seaweeds-derived k-carrageenan-based electrolyte<sup>3</sup>, or a nanofluid based on glucose-derived carbon dots functionalized with a thermotropic ionic liquid<sup>4</sup>, are valuable approaches to produce sustainable electrochromic<sup>2,3,5</sup>, thermotropic<sup>4</sup> and integrated thermotropic/electrochromic<sup>4</sup> devices with remarkable electro-optical performance.

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# **KN15**

# Polyelectrolyte interaction, confinement and adsorption

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An in-depth knowledge of polyelectrolyte behavior is of paramount importance in applications that range from gene therapy to deposition of layer by layer assemblies. In this communication, several aspects pertaining to polylectrolyte behavior in aqueous solution will be firstly discussed, including confinement, translocation and compaction.

Subsequently, focus will be given to the adsorption of polyions onto charged surfaces, containing either fixed or moving charges, which has long been recognized as a crucial phenomenon in biological and technological applications. An intuitive model relating polyelectrolyte adsorption with the imposed features of polarizable surfaces of different compositions and charges is discussed from results obtained using a coarse-grained approach.<sup>1</sup> Polyplex adsorption will also be addressed.

Finally, in a more specific point, it is know that both theoretical and experimental approaches consistently evidence the existence of a direct connection between the PAZ/3'-overhang binding affinity and siRNA's potency and specificity. An overall description of the systems is provided by atomistic simulations and free energy calculations that allow building a proposal for a robust and self-contained procedure for studying the factors implied in PAZ/3'-overhang siRNA interactions.<sup>2</sup> Results are important for the design of powerful and safe synthetic nucleotide analogues.

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# **KN16**

# Sustainable Synthesis of Tetrapyrrolic Macrocycles

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Sustainability is one of the major issues of our time. It has defined policies, economy and education in society as well as in companies and universities. Chemistry, as a central science for the development of society, has also been committed with sustainability. The settlement of the Green Chemistry philosophy and principles among the chemists dedicated to the development of synthetic processes is a reality. In the last decades synthetic chemists have developed new tools, searched for new reaction media and new reactivity pathways that could be used for the accomplishment of the Green Chemistry principles, looking for processes with increased sustainability.<sup>1</sup>

Porphyrins and their derivatives are profligate compounds in the sense that they are useful in a large variety of applications, from material science or several catalytic systems to cancer treatment. The synthesis of these compounds, which has been one of the focuses of our research group, was established keeping in mind the reaction yield, according to the philosophies at that time.<sup>2</sup>

During the last years we focused our efforts on the development of new sustainable synthetic processes for the synthesis of porphyrins and their derivatives, metalloporphyrins and hydroporphyrins. The introduction in these processes of the use of new synthetic techniques such as microwave and mechanochemistry, in water and solvent-free conditions, allow us to develop new processes, with the highest sustainability scores in the area. These results will be presented and discussed in this presentation (**Scheme 1**).<sup>3</sup>



Scheme 1: Sustainable synthesis of Porphyrins and their derivatives.

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# COMUNICAÇÕES ORAIS CONVIDADAS



# Selective photochemistry of 5-aminotetrazole derivatives; effect of the saccharyl moiety on the photostability

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The properties and applications of 2-methyl-(2*H*)-tetrazole-5-amino-saccharinate (**4**; Scheme 1) in catalysis and chelant-based chemotherapy stimulated investigations on its photostability.<sup>1a</sup> The photochemistry of monomeric **4** in solid argon (15 K) was compared with those of 2-methyl-(2*H*)-tetrazole-5-amine (**2**) and 1-methyl-(2*H*)-tetrazole-5-amine.<sup>1b</sup> Compounds were subjected to *in situ* narrowband UV-irradiation at different wavelengths. Reactions were followed by infrared spectroscopy, supported by B3LYP/6-311++G(d,p) calculations. Photochemical pathways for **2** and **4** proved similar but photodegradation of **4** was 20x slower, unraveling the photostabilizing effect of the saccharyl moiety that extends into the nitrilimine **6**, formed from **4**, and its antiaromatic 1*H*-diazirene isomer **7**, which proved photostable at 290 nm, unlike the 1*H*-diazirene **14**, formed from **2**. Analysis of the photochemistries of **2/4** (250 nm), including energy trends calculated for the isomeric C<sub>2</sub>H<sub>5</sub>N<sub>3</sub> species postulated/observed from photolysis and EPR results, enabled a deeper insight into the photodegradation mechanisms of 2,5-substituted tetrazoles. We postulate a pivotal singlet state imidoylnitrene species as common intermediate, which undergoes a Wolff-type isomerization to a stable carbodiimide (**8**, **15**; Scheme 1).<sup>2</sup>



Scheme 1: Proposed pathways from irradiation of a matrix containing monomeric 2 or 4, in solid argon (15 K).

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# Health

# Modulation of macrophage metabolism by phytochemicals and biomaterials: insights from metabolomics

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Macrophages are innate immune cells with an immense phenotypic plasticity, exhibiting a continuum of polarization states, from pro- to anti-inflammatory, which greatly depend on microenvironmental cues. Accordingly, the manipulation of macrophage activation through immunomodulatory compounds and biomaterials has emerged as an attractive strategy in the context of chronic inflammatory diseases, cancer, auto-immune diseases or tissue regeneration.<sup>1</sup> The development of such macrophage-targeted approaches requires elucidation of the mechanisms regulating their phenotypic and functional behaviour.

This work addresses the metabolic responses of macrophages to different stimuli, from bioflavonoids to nano and microparticles, with a view to shed light into their modes of action and potentiate their future development as immunomodulatory agents.<sup>2</sup> Metabolic profiling approaches such as NMR-based metabolomics and LC-MS-based lipidomics have been used for that purpose, aiming at achieving a holistic picture of macrophage metabolic reprogramming and its dependence on the stimuli employed.

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# Communication

# Building Artificial Enzymes Using the Metals of the Periodic Table

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UNESCO celebrates 2019 as the "International Year of the Periodic Table of Chemical Elements" and the 150th anniversary of its creation by Dmitry Mendeleev. Metalloproteins and metal-containing enzymes are well known to be essential to life. Synthetic Biochemistry and Inorganic Chemistry come together in a synergistic manner, in order to elucidate structure and functional aspects of metal sites in enzymes. In particular, small proteins and synthetic peptides involving rich sulfur coordination sites, such as Rubredoxins (Rds) and analogues, have been extensively used. The tetra-cysteinyl metal coordination site available in Rd has the surprisingly capacity of chelating a wide variety of metal ions (beyond Fe) such as Zn, Co, Cd, Ga, In, Hg Ni, Cu, as well as Mo (and W), with particular interest in modelling [Ni,Fe]-Hydrogenases and mononuclear molybdenum/tungsten-bis pyranopterin-containing enzymes (Mo/W-bis PDG) and other systems. The small peptide a3DIVL21C, that possesses a four cysteine residues environment (rubredoxin-like), can bind Mo, being another useful model for the sulfur rich environment of Mo/W-bis PDG. Other protein templates, such the Orange Protein (ORP), a small bacterial protein, that contains a unique molybdenum/copper (Mo/Cu) hetero-metallic cluster, [S<sub>2</sub>Mo<sup>VI</sup>S<sub>2</sub>Cu<sup>I</sup>S<sub>2</sub>Mo<sup>VI</sup>S<sub>2</sub>]<sup>3-</sup>, non-covalently bound, promotes metal protein derivatives by protein-assisted synthesis, harbouring novel and unique molybdenum heterometallic clusters, such as Mo/Fe-ORP, Mo/Co-ORP, Mo/Ni-ORP, or Mo/Cd-ORP, with distinct magnetic properties. Finally, iron-sulfur proteins are also considered as interesting templates for the synthesis of hetero-metallic cores of biological mimetic interest.

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# Health

# AN ODE TO NITROGEN: nitrogen-based functional groups in the core of new approaches to fight infectious diseases

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In celebration of the International Year of the Periodic Table of Chemical Elements (IYPT 2019), this communication will pay a little homage to the element with atomic number 7, Nitrogen, by making a very brief overview of the work developed in our group over the past 7 years, towards discovery of new strategies against infectious diseases. These strategies stand on organic and peptide synthesis approaches aiming at new anti-parasitic compounds<sup>1</sup> or antimicrobial peptides and derived materials<sup>2</sup>, where the reactivity of nitrogen-based functional groups always adopts a central role.



potent antimicrobial peptides inspired by Nature

antimicrobial peptide-grafted biomaterials and surfaces with antibacterial properties

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# Nanotechnology

# Structured proton wires – a design principle for biochemical regulation

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Regulation of protein function plays a key role in governing cellular homeostasis, development, adaption, health and survival. Regulation by substrate binding typically causes a structural transition of the protein that is propagated through signaling pathways to remote sites involving marked changes on the tertiary and sometimes even quaternary. However, the origin of these signals and the molecular mechanism of long-range signaling at an atomic level are a field of great dispute. The different spatial and time scales involved in signaling pathways make the experimental observation challenging, in particular positive allosteric effects are difficult to investigate given the short life-span of reaction intermediates and the difficulty of following structural changes with and without effector. Molecular simulations provide a unique way to tap into such mechanisms, not only by identifying the intermediates, but also the underlying dynamic events.<sup>1</sup>

In this communication, we will discuss how proton wires, constituted by highly structured titratable amino acid residues, can effectively coordinate the activity of two distant active sites in distances over 20 Å (**Figure 1**). The regulation process is modelled through classical molecular dynamics in combination with low-dimensional quantum treatments of protons. The main working example will be the human transketolase, a thiamine diphosphate-dependent enzyme. Given the ubiquity of acid/base catalysis, the use of proton wires arises a rather general design principle for future biotechnological applications.



Figure 1: Detail of the proton wire in human transketolase connecting both thiamine-diphosphate active sites (the latter are highlighted in yellow).

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### Environment

# Chemistry or free volume? Porous liquids for gas absorption

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The addition of small quantities of water to ionic liquids containing carboxylate anions has shown a considerable success in decreasing the viscosity of these promising gas absorbent phases, without changing their selectivity for carbon dioxide separation [1]. The drawback of this solution is that the absorbent mixtures often have a measurable vapour pressure that renders recycling difficult. Recent alternatives to tune selective, easy to recycle, liquid absorbents involve mixing ionic liquids to create multi-ionic fluids with appropriate properties [2,3].

We have recently shown that mixtures of 1-butyl-3-methylimidazolium acetate with 1-butyl-3-methylimidazolium tricyanomethanide ( $[C_4C_1Im][OAc]_{(1-x)}[C(CN)_3]_x$ ) maintain the capacity of chemically absorbing carbon dioxide [5] while exhibiting significantly lower viscosities than those of carboxylate-based pure ionic liquids. Designing mixtures of ionic liquids suitable for a given separation is hard as the enormous number of possible combinations renders structureproperty relationships difficult to establish and imposes the need for a molecular understanding of the interactions and structure of the ionic liquids. We have used the  $[C_4C_1Im][OAc]_{(1-x)}[C(CN)_3]_x$  mixture as a case study, its properties being explained at the molecular level using vibrational spectroscopy, NMR and molecular simulation data [5]. The relative importance of the chemical and physical absorption of CO<sub>2</sub> is assessed through a detailed thermodynamic study [4].

Improving the gas absorption and selectivity can also be accomplished by increasing the free volume available in the liquid phase. This is possible by combining porous solids with ionic liquids to form fluid phases with permanent porosity and able to reversibly absorb large quantities of gas [6].



Figure 1: Porous liquid based on ZIF-8 in the [P<sub>66614</sub>][Ntf<sub>2</sub>] ionic liquid.

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# Materials

# Alkaline Oxidation of Carbon Materials for Elemental Analysis

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Carbon Materials are present in our everyday lives. They are critical to the manufacturing of airplanes such as the Airbus A350 XWB (where more than half of the aircraft's structure is composite materials) or automobiles such as the Tesla Model S where ~54 kg of graphite are used as battery anodes. In addition to this, Nanocarbons (which include nanotubes and graphene) are drawing much attention for applications that span from single-molecule sensors to ultraselective desalination membranes.

Given the profusion of methods to produce Carbons, which may involve the use of transition metals as growth catalysts, it is key to understand the chemical profiling of the final products. In particular, when larger production volumes are handled and streamlined quality control protocols are needed, fast, accurate characterization techniques become paramount. Hyphenated inductively coupled plasma (ICP) methods are a staple of analytical laboratories. Coupled to optical or mass spectrometers, it is possible to measure the content of trace metals in solid samples. However, its application to Carbons is not without challenges, often due to the refractory nature of these materials. In an attempt to divert from the use of wet oxidizers or combustion approaches, we have been exploring alkaline oxidation (a.k.a. *fusion*) to disintegrate the carbon matrix. Recently, we validated the use of an alkali metal borate salt against a certified Nanocarbon (**Fig. 1**). <sup>1</sup> However, the scarcity of standards for Carbons is an issue to expand on this work. For this reason, neutron activation analysis and ion beam methods were employed as they provide independent concentration readings with a high level of confidence.<sup>2</sup>

In this communication, we will show how fusion can be applied to Carbons that range from certified reference materials to commercial blacks and lab-processed expandable graphite. In addition, we will also look into how the alkali metal salt interacts with the different powder materials probed.



Figure 1: A glass-like bead of a fused Nanocarbon standing on a platinum plate, a) top-side of the bead, b) bottom side-of the bead.

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### Environment

# Synthesis and emerging applications of β-functionalized porphyrin derivatives bearing *N*-heterocycles

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The physicochemical features displayed by tetrapyrrolic macrocycles like *meso*-tetraarylporphyrins render them particularly attractive to be used in a wide range of fields like supramolecular chemistry, catalysis, electronic materials, sensors and medicine.<sup>1</sup> The usefulness of this type of templates can be improved through the adequate functionalization of derivatives containing substituents like the formyl one at  $\beta$ -pyrrolic positions.<sup>1,2</sup> In this communication it will be discussed simple synthetic strategies developed by our group, giving access to porphyrins  $\beta$ -functionalized with *N*-heterocycles, such as imidazole or oligopyridines.<sup>3,4</sup> The ability of some of these systems substituted at  $\beta$ -pyrrolic position to be used as fluorescent and colorimetric chemosensors to recognize and to bind different metal ions will be also discussed.<sup>3c,d</sup> Additionally, the  $\beta$ -functionalization of the porphyrinic macrocycle with heterocyclic moieties containing nitrogens, allows their quaternization affording positively charged derivatives, able to be used as photosensitizers on the photoinactivation of bioluminescent *E. coli*, a Gram-negative bacterium model.<sup>4</sup>



Figure 1: Functionalization and applications of β-functionalized porphyrin derivatives bearing *N*-heterocycles.

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# Materials

# Single-Molecule Fluorescence from Porphyrins Enabled by Gold Nanodimer Antennas

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Fluorescence labeling is widely used for imaging or sensing applications and, for this purpose, strongly fluorescent dyes are available. Nevertheless, the performance of dye molecules can be limited by low excitation rates, because excitation cross sections are typically smaller than the molecule's physical dimensions. This limitation can be overcome by using metal nanoparticles as optical antennas. This approach has been explored to increase the sensitivity in fluorescence-based detection schemes [1], or to enable the detection of single-molecule fluorescence from weakly emitting molecules [2]. In this contribution, we will present our results on fluorescence enhancement by gold nanodimer antennas. Gold nanodimers were assembled from spherical gold particles using doubly-thiolated ds-DNA linkers to achieve narrow interparticle gaps. These assemblies are powerful antennas because of the large plasmon fields that can be reached in the gap hot-spots. In a previous study, it was indeed possible to measure top emission enhancements of three orders of magnitude for ATTO-655 dye [3]. The gold nanodimers were now employed for emission enhancement of porphyrin molecules. Porphyrins and related compounds are often used as building blocks for light harvesting systems. However, these molecules are typically weak emitters, which makes it difficult to detect their emission at single-molecule level. As expected, the antenna effect is more pronounced for a weak emitter and top enhancements of 10<sup>5</sup>-fold emission increase were observed in this case (Fig. 1). This extreme enhancement results from the combination of an antenna effect on the molecule's excitation rate of about 10<sup>4</sup>-fold with an increase of 2 to 10 times in the emission quantum-yield, as estimated from model simulations [4].



Figure 1. A) Scheme of a porphyrin molecule diffusing across the plasmon hot-spot of a gold nanodimer. B) Emission time trace showing intense bursts of enhanced fluorescence of a porphyrin interacting with a gold nanodimer.

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# Health

# Fighting metastatic cancers with ruthenium cyclopentadienyl compounds

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According to the World Health Organization, 9.6 million people died worldwide from cancer in 2018, nearly one sixth of all deaths.<sup>1</sup> This prohibitive numbers show the urgency to find new and alternative strategies to fight cancer. Even though there have been impressive advances in cancer therapies in the last years, there are still several major problems associated to cancer treatments, being the most striking: i) the lack of selectivity for the cancerous cells, responsible for the noxious side effects observed for the drugs in clinical use; ii) the intrinsic or acquired resistance to chemotherapeutics; and iii) the development of metastases, that are indeed the main cause of death by cancer. In this frame, we have been engaged in the discovery of a more selective and wide-range anticancer agents that might target the primary tumor, as well as their metastases. For that, new [Ru(η<sup>5</sup>-C<sub>5</sub>H<sub>5</sub>)(2,2'-bipyridine-R)(PPh<sub>3</sub>)]<sup>+</sup> based compounds endowed with specific targeting components to take advantage of the particular characteristics of tumor cells and tissues, such as their permeability to macromolecules and overexpression of several receptors, are being developed and their mechanisms of action studied.<sup>2-4</sup> When R is a biodegradable and biocompatible polymer and/or a biomolecule recognized by cancer cells in the structure of our compounds, one can benefit from a passive and/or active targeting, respectively (Figure 1). These compounds show remarkable cytotoxicity against several cancer cell lines with different degrees of aggressiveness and strong inhibition of key proteins known for their role in mechanisms of cell resistance. Through a wide set of biological assays, we disclose the features that this family of ruthenium complexes possess as promising anticancer and anti-invasion drugs.



Figure 1: Targeting cancer mechanisms incorporated in the design of new  $[Ru(\eta^5-C_5H_5)(2,2'-bipyridine-R)(PPh_3)]^+$  compounds.

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# Environment

# Development and application of waste-derived carbon materials for improving wastewater treatments

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Wastewater treatment facilities are facing new challenges due to the high prevalence of emerging contaminants, such as pharmaceuticals, often resistant to conventional treatments. Coping with this problem is essential to guarantee the protection of aquatic resources and ecosystems and it is particularly relevant in a time when potable water scarcity is seriously affecting the planet. The improvement of wastewater treatment efficiencies for the removal of recalcitrant contaminants assumes a decisive role in the attenuation of this environmental issue. In this sense, carbon materials and, in particular, activated carbons (AC), have proven to be effective in the removal of pharmaceuticals from wastewaters. However, the main disadvantages of using these materials in wastewater treatment include high cost, use of non-renewable sources as AC precursors and difficult separation from treated water.

This work aims to use cellulosic industrial wastes (from Pulp and Paper and Brewery industries) as alternative resources to produce carbon materials to be applied in the removal of pharmaceuticals from wastewaters. For this purpose, residual biomass from the referred industries were subjected to pyrolysis (biochar)<sup>1</sup>, to pyrolysis combined with chemical activation (powdered AC)<sup>2</sup>, and to pyrolysis combined with both chemical activation and *grafting* functionalization (functionalized AC), agglomeration (granular AC)<sup>3</sup> or magnetization (magnetic AC) (**Figure 1**). The different production schemes allowed to obtain materials with very distinct physico-chemical properties and suited for a pplication in different operation modes. The performance of the developed carbon materials was evaluated for a group of pharmaceuticals under batch (for powdered AC) and continuous (for granular AC) systems using real wastewaters. The obtained results indicated that cellulose-derived industrial wastes are adequate precursors of highly efficient carbon materials, capable to attain similar or higher performances than commercial AC.



Figure 1: Scanning electron microscopy images of (a) powdered activated carbon, (b) granular activated carbon and (c) magnetic activated carbon produced from primary pulp and paper mill sludge (magnification 10 000 x)

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# Industrial

# Recuperação de antocianinas de biorresíduos de *Ficus carica* L. e *Prunus spinosa* L.: propriedades corantes e bioativas

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A recuperação de biorresíduos da indústria alimentar tem vindo a ganhar relevância pela crescente procura da sua valorização enquanto fontes de compostos de interesse para posterior aplicação em diversos ramos industriais, como é o caso da indústria alimentar, têxtil, e farmacêutica, entre outras [1,2]. Assim, o presente estudo visa a recuperação de antocianinas a partir de biorresíduos de frutos: a casca de figo, rica em cianidina 3-rutinósido (C3R), e o epicarpo de abrunho, rico em C3R e peonidina 3-rutinósido (P3R). Foram testadas duas técnicas de extração, maceração (EM) e assistida por ultrassons (EAU), às quais se aplicou uma metodologia de superfície de resposta usando o desenho composto central circunscrito com cinco níveis em cada uma das variáveis independentes estudadas (tempo, proporção de água-etanol como solvente e temperatura (EM) ou potência (EAU)). O perfil de antocianinas dos diferentes extração (R; mg C/g R) e na amostra desidratada (A; mg C/g A) e o rendimento de resíduo obtido (g R/g A) como respostas para o modelo. Foi ainda avaliada a bioatividade (citotoxicidade e atividade antioxidante e antimicrobiana) dos extratos obtidos em condições ótimas, bem como o poder corante dos mesmos avaliados pela incorporação do extrato ótimo em produtos de pastelaria.

Para ambas as amostras, a EAU revelou ser a técnica mais eficiente, com condições ótimas de recuperação de C3R aos 21,3±0,6 min, 310±26 W e 100±1% de etanol no caso da casca de figo, com um rendimento de 0,5±0,2 g R/g A e um total de antocianinas de 9,0±0,8 mg C/g R e 4,3±0,1 mg C/g A. Por sua vez, a partir do epicarpo de abrunho foi possível obter um total de C3R e P3R de 18±2 mg C/g R e 11,8±0,8 mg C/g A, e um rendimento de 0,69±0,02 g R/g A, nas condições ideais de extração de 5,0±0.2 min, 400±32 W e 48±3% de etanol. Relativamente às propriedades bioativas, o extrato de casca de figo revelou um valor de EC<sub>50</sub> de 2447±2 µg/mL no método TBARS e valores de EC<sub>80</sub> de 515±31 e 1624±56 µg/mL, para 60 e 120 min, respetivamente, no ensaio OxHLIA. O extrato de epicarpo de abrunho apresentou valores de EC<sub>50</sub> (TBARS; 204,22±0,02 µg/mL) e EC<sub>80</sub> (OxHLIA; 303±3 e 540±3 µg/mL, para 60 e 120 min, respetivamente) inferiores, o que indica uma maior atividade antioxidante em ambos os ensaios. Ambos os extratos revelaram propriedades antibacterianas, inibindo o crescimento de 9 estirpes bacterianas (5 Gram-negativo e 4 Grampositivo), em concentrações entre 2,5 e 20 mg/mL. Para além disso, não apresentaram toxicidade em células não tumorais de fígado de porco, o que torna viável a sua aplicação em produtos alimentares sem problemas de toxicidade. Assim, o poder corante dos extratos antociânicos foi testado em produtos de pastelaria: o extrato de casca de figo foi incorporado em cobertura de "donut" e o de epicarpo de abrunho em "beijinhos", um doce típico do Brasil. Esta aplicação não alterou significativamente o valor nutricional das matrizes em estudo e, para além de conferir ao alimento a cor desejada, proporciona também propriedades antioxidantes e antimicrobianas.

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# Health

# **Decoding Glycan-Lectin Interactions in Cancer**

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Abnormal tumour glycosylation is a well-established hallmark of cancer.[1] In this context, tumour glycosylation can induce immunosuppressive signalling through glycan-binding proteins (lectins).[2] Therefore, the structural knowledge of how tumour-related glycans interact with lectins, enrolled in tumour immune modulation, is of paramount importance to rationalize the development of improved immunotherapies. In this communication it will be reported the molecular recognition of distinct tumour-related glycans against distinct immune-related lectins disclosed by concerted application of NMR binding experiments and molecular modelling protocols.[3,4,5]

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# Environment

# Multidimensional GC: Reality, alternative or just a separative extravagancy

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In gas chromatography, the evolution has been driven to achieve more "chromatographic space" in order to obtain a suitable (or increased) separation of all sample components, or for a selection of analytes. However, any single GC column, used in 1D-GC, is physically and statistically limited by its maximum number of theoretical plates and peak capacity. Historically, to overcame this limitation, the progress in the quest for more chromatographic resolution evolved, first from packed to capillary GC, to multiple separation phases using sequential column coupling, later to multidimensional GC (MD-GC) with heart-cut interfaces and finally to modern comprehensive two-dimensional GC (GCxGC) using modulator devices.

In a MD-GC system a heart-cut device, allows the isolation of a particular retention time window, quantitatively transferring these compounds from the first column, to a second column, where only the transferred compounds are separated and analyzed. In spite the efficiency of the heart-cut MD separation approach, MD-GC may be a very time consuming method to implement, with long analysis times and with the potential handicap that several consecutive transfers may not be practical. In fact, as more compounds are delivered to the second column, there is an increased likelihood of co-elution, jeopardizing the analysis purpose.

In Comprehensive two-dimensional gas chromatography (GC×GC) a modulator allows the complete transfer of all the sample components from the first column, to a second column that is connected sequentially. When orthogonality principles are achieved between both column's stationary phases, the GCxGC system can be explored in all its intrinsic potential, with enhanced system peak capacity, and good-to-optimum peak resolution. This analytical technique, when used in tandem with spectrometric detection systems, also allows better peak identification assignments, because it provides optimal analyte separations in the 2D space, that produce mass spectra with minimal interferences, allowing to obtain true mass spectra for the individually isolated compounds. Additionally, the reproducibility for both qualitative and quantitative measurements obtained by GCxGC systems are quite reliable. This reliability offers an additional graphical advantage: the 2D plot can be used by comparing the 2D plots of different analysis to find sample recognition compositional patterns. Consequently GCxGC becomes an election tool to analyze and characterize very complex samples.

This communication aim to demonstrate the utility and benefit of using Multidimensional GC on the analysis of complex samples to derive useful information based on the last years experience of the Resolution Group from FCT NOVA. The group research has been focused in developing 1D and 2D-GC methods suitable for complex sample analysis (food, biological and environmental) taking advantage of multi-capacity of both chromatographic modes, hyphenated with classical GC detectors (FID and NPD), mass spectrometry (GC-qMS and GC-TOFMS), and recently with olfactometry (GC-O) and electroantennographic detection (GC-EAD).

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# Food

# Foodomics platforms - new avenues to investigate food quality, traceability and bioactivity

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Since antiquity prominent scientists, including Antoine Lavoisier, Gay-Lussac, and Jacob Berzelius, concerned about food and nutrition issues, studied foods intensively and made discoveries of such fundamental importance to food chemistry being the most significant from late 1700s. In recent decades, impressive scientific and technologic developments in different fields changed the food analysis paradigm, which has moved from classical methodologies to advanced technologies that have been well established.

Currently, research in food science and nutrition is boosted thanks to the great potential offered by FOODOMICS in unraveling the huge complexity of food metabolome at the genetic and molecular levels, through the employment of advanced OMICS tools, namely metabolomics, lipidomics, proteomics and genomics. The main demands are directed towards food origin, shelf life, adulterations and food composition related with potential health benefits. Unfortunately, food adulteration and contamination events seems to occur with some regularity, which requires continued efficient vigilance accomplished by the development of rapid analytical and detection techniques for identification and/or quantification of characteristic components, adulterants and/or contaminants of food.

The FOODOMICS platforms, assuming an increasing centrality on the systematic establishment of volatomes, proteomes, lipidomes, and genomes, are emerging as self-standing research fields relying on well-established and recognized analytical methods such as mass spectrometry techniques (GC-MS and LC-MS/MS), in addition to modern spectroscopic approaches based on NMR (1H; 13C), IR and sensor technologies, to better characterize food matrices, identifying their components and defining nutritional properties. This comprehensive approach based on the integration of Foodomics platforms combined with high resolution analytical methodologies and data processing, seems to be the most promising strategy on food fingerprinting, in a non-selective way, as a tool to establish its composition, certify its integrity and elucidate some critical issues related with food safety, food quality, food traceability and food authenticity, constituting a useful support on detection adulterations and contaminations. In turn, this will progress our understanding of the biochemical, molecular and cellular mechanisms related with the health benefits of bioactive food components.

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# Health

# Dodecyl-containing Azide and Glucuronamide-based Nucleosides as Promising Anticancer Lead Molecules for Circumventing Chemotherapy Resistance

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Synthetic nucleosides, nucleotides and analogs have occupied a major place in chemotherapy, with a number of compounds in clinical use to treat various types of cancer. Most of these molecules act as antimetabolites, interfering with DNA synthesis through inhibition of key enzymes or by incorporation into the nucleic acid chain, which causes apoptosis with some selectivity to rapidly dividing cells [1-3]. Major issues of the currently used nucleos(t)ide analogs include their low bioavailability and the resistance that cancer cells often exhibit against their action, by inactivating them or hindering their transport or activation [2,3]. Thus, the development of novel nucleos(t)ide-based structures that may exhibit alternative mechanisms of action and overcome these drawbacks is of significant interest.

In this context, in this communication the synthesis and biological evaluation of novel nucleosides based on 5/6-azido xylofuranose/glucopyranose and D-glucuronamide moieties, which are rather unusual glycosyl units in nucleoside chemistry, and containing an O- or an N-dodecyl chain is presented. The synthetic pathways employed diacetone-D-glucose and glucofuranurono-6,3-lactone as precursors and involved the access to acetylated 5/6-azidoglycosyl donors or 1,2-di-*O*-acetyl furanuronamide or pyranuronamide derivatives and their further N-glycosydation with uracil or 2-acetamido-6-chloropurine. Some molecules were shown to exhibit potent antiproliferative activities in cancer cells with Gl<sub>50</sub> values similar or lower than that of a standard drug and to act via pathways that may be valuable to circumvent chemotherapy resistance, thus qualifying them as promising lead compounds for cancer.

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# Health

# Versatile biocompatible vesicles based on cationic/anionic surfactants: from rational design to biomolecular delivery

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There has been a continuous challenge to develop nanostructured colloidal systems, such as vesicles, polymers, dendrimers, nanotubes and nanoparticles, that efficiently protect and deliver biomolecules to target cells.<sup>1</sup> Vesicles assembled from suitable blends of cationic and anionic surfactants (catanionic vesicles) offer several distinctive features compared to conventional liposomes, namely facile formation, long-term colloidal stability, chemical robustness and versatility of size, surface charge and gel-to-liquid crystal phase transition temperature ( $T_m$ ).<sup>2</sup> For nanomedical applications, biocompatibility, biodegradability and low toxicity are further crucial.

Herein, we present recent results on selected catanionic vesicle systems, from mixtures composed of commercially available surfactants to those formulated with novel surfactants derived from amino acids (namely serine and lysine) with assorted molecular structure.<sup>3</sup> Tunability in size, surface charge and pH can be controlled by surfactant molecular structure and mixing ratio (**Figure 1**). Phase behavior studies, vesicle structural characterization, cell viability and in vitro delivery studies of biomolecules are shown and critically discussed.<sup>3</sup>



Figure 1: Fully serine-surfactant based catanionic vesicles as efficient nanocarriers for the anti-cancer drug doxorubicin.

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# **Materials**

# Photoswitching Supramolecular Host-Guest Systems

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The development of systems able to exist in different states whose interconversion can be controlled by different stimuli (light, ions, electrons) may contribute to the appearance of molecular-level devices and materials with new functionalities. Diarylethenes (DAE) have attracted considerable interest owing to their outstanding photochromic properties and photoswitching ability.<sup>1</sup> On the other hand, cucurbit[n]urils (CBn) are macrocyclic receptors that display high affinity for complementary guest molecules in aqueous solution. In particular, CB8 has the ability to form ternary complexes with applications in catalysis and supramolecular polymers.<sup>2</sup> On our search for photorheological fluids,<sup>3,4</sup> we have engaged in the design of supramolecular polymers based on diarylethenes containing terminal donor-acceptor moieties to be polymerized through CB8-assisted ternary complexes. In previously reported CBn:DAE complexes, the macrocycle binds to peripheral groups rather than the photoactive unit, precluding significant differences in the stability of the complexes upon switching between the open and closed forms.<sup>5</sup>

In this communication, the development of DAE-CB8 host-guest pairs with 1:1 association constant close to 10<sup>10</sup> M<sup>-1</sup> (Figure 1) with photoregulated guest exchange will be reported.<sup>6</sup> A recent example of another photoswitching supramolecular host-guest system based on a 2-hydroxychalcone / CB7 will also be presented.<sup>7</sup>



Figure 1: Photocontrolled complexation and release of high-affinity guest molecules on a DAE-CB8 host-guest system.

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# Environment

# Design, production and evaluation of a task specific cellulose-based polymer for wine stabilization

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Bottled white wines can turn hazy and form sediments which are associated with the presence of residual grape proteins. This has a negative organoleptic impact for consumers and may have severe economic impact<sup>1</sup>. Until now, the most effective way to remove proteins from white wines consists in the use of bentonite, a negatively charged clay, which can remove positively charged proteins from wines. Although effective, this procedure has some disadvantages such as waste disposal cost, since it is non-renewable, and the difficult settling of bentonite increases the complexity of filtration leading to a considerable loss of wine. These disadvantages amount to an estimated annual cost of U.S. \$1 billion to the world wine industry and therefore the search for an efficient alternative stabilization technique is a relevant research topic all over the world.

Dicarboxymethylcellulose (DCMC), a cellulose ether derivative, (Figure 1) was developed<sup>2</sup> and in reason of the introduced low pKa ether group ,it can perform ion exchange at low pH (2.5 - 3.5). The produced polymer has an high ability to remove positively charged molecules from wines. This technology uses a biodegradable source material (cellulose based polymer) easy to dispose after usage (e.g. compost, combustion). (**Scheme 1**), and proved to be reusable after appropriate regeneration.



Scheme 1: Synthesis of DCMC, a task specific cellulose-based polymer.

The produced polymers were tested at buffered low pH conditions for the removal of several positively charged molecules and in a model wine solution (pH 3.2, 12% ethanol, 5 g/L tartaric acid) for the removal of protein isolated from wine with promissing results. Moreover, the produced cellulose derivative has also the ability to be regenerated and reused, decreasing the costs associated with this new technique.

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# Food

# As melanoidinas. O que são, como se formam e para que servem?

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As melanoidinas são macromoléculas de cor castanha formadas durante o processamento térmico dos alimentos derivadas das reações de Maillard. Apesar de estarem presentes diariamente na nossa dieta, serem determinantes para a escolha dos alimentos pelos consumidores devido à sua cor castanha, Apesar da sua abundância e importância na dieta, as melanoidinas são ainda hoje em dia as macromoléculas alimentares mais enigmáticas, pois a sua estrutura química é ainda largamente desconhecida e, como resultado, a sua definição não apresenta nenhuma característica química associada, exceto o facto de conter nitrogénio. Esta falta de definição clara do que são quimicamente as melanoidinas é uma das razões para que, no século XXI, 107 anos após a sua primeira descrição pelo químico Francês Loius Camille Maillard<sup>1</sup>, ainda não existam respostas claras para as seguintes questões: qual a estrutura química das melanoidinas dos alimentos e qual o mecanismo da sua formação? Nesta comunicação apresentar-se-á o estado atual do nosso conhecimento sobre estas importantes macromoléculas alimentares

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support....

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# Health

# Supramolecular engineering of modular ECM-like functional nanobiomaterials to instruct cell behavior

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Over the past two decades the emerging field of supramolecular chemistry together with advances in medicine and nanotechnology have paved the way for the creation of complex architectures similar to those found in living organisms to develop regenerative therapies. Inspired by fascinating supramolecular landscapes, including the native extracellular matrix (ECM),<sup>1</sup> scientists have been boosted towards the fabrication of ECM-like supramolecular biomaterials aimed at recreating the structural and functional features of the native cellular microenvironment and, ultimately, regenerate and/or substitute damaged tissues and/or organs.<sup>2</sup> The ECM is formed through dynamic supramolecular self-assembly and highly-directed reciprocal recognition displayed mainly by polysaccharides and proteins *via* non-covalent interactions. To date, most of the developed systems still lack control in thickness and composition at nanoscale, and the functional dynamic nature and structural complexity found in biological systems, which limits many biomedical applications. In this talk, the supramolecular design of soft self-assembling functional nanobiomaterials will be featured aiming to direct cell behavior (**Figure 1**).<sup>3</sup> Those matrices encompass natural and synthetic polymers and self-assembling peptide amphiphiles displaying bioactive domains and are molecularly designed by combining the self-assembly strategy with the Layer-by-Layer assembly technology. The potential of the developed supramolecular biomaterials to stimulate cell-signaling pathways that are critical in regenerative medicine, in particular in muscle and neural tissue regeneration will be discussed.



Figure 1: (a) Schematic illustration of native ECM. Representative (b) SEM, (c) fluorescence microscopy and (d) immunofluorescence micrographs of C2C12 cells at 3 and 5 days of culture, respectively, on (alginate/K3PA)<sub>5</sub> nanofilms.

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# Health

# Desenvolvimento de formulações cosmecêuticas a partir de extratos obtidos de cogumelos

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Os cosmecêuticos podem ser definidos como uma combinação de um cosmético com um produto farmacêutico. Consistem em produtos aplicados topicamente sob a forma de creme, pomada ou loção, fornecendo os nutrientes necessários para uma pele saudável e contendo compostos biologicamente ativos que aportam benefícios semelhantes aos medicamentos.<sup>1,2</sup> Hoje em dia há uma tendência para o consumo de produtos contendo ingredientes naturais e a área da cosmética não é exceção. Assim, a comunidade científica tem vindo a procurar novos ingredientes naturais que possam ser utilizados como matéria-prima para a elaboração de novas formulações e os cogumelos representam uma fonte inexplorada.

Tendo por base esta nova tendência / exigência de mercado, o potencial cosmecêutico de algumas espécies de cogumelos (*Ganoderma lucidum* (Curtis) P. Karst e *Pleurotus ostreatus* (Jacq. ex Fr.) P. Kumm.) foi avaliado em termos de propriedades anti-inflamatórias, anti-tirosinase, antioxidante e antimicrobiana. Seguiu-se a caracterização detalhada dos extratos bioativos em termos de ácidos fenólicos, triterpenos e composição em ergosterol. Os extratos obtidos foram incorporados em cosméticos básicos e a avaliação da sua segurança *in vitro*, bem como das formulações desenvolvidas, foi realizada através dos ensaios MTT e LDH em linhas celulares de queratinócitos (HaCaT) e fibroblastos (HFF-1). A biodisponibilidade tópica dos compostos no extrato foi avaliada utilizando um aparelho de difusão de Franz com pele de orelha de porco como membrana de permeabilidade.

Os extratos testados apresentaram forte atividade antioxidante, anti-inflamatória e inibidora da tirosinase, além de apresentarem inibição microbiana contra alguns dos contaminantes mais frequentes que causam deterioração microbiana em cosméticos. Relativamente aos compostos bioativos identificados nos extratos, estes incluem o ácido ganodérico C2, ácido ganodérico D, ácido protocatéquico, ácido *p*-hidroxibenzóico e ácido siríngico. A segurança dos extratos utilizados foi confirmada pela ausência de toxicidade nas linhas celulares da pele.

Os resultados obtidos no presente estudo demonstram o potencial dos cogumelos como fonte de compostos bioativos, destacando estes recursos naturais como promissores ingredientes cosmecêuticos.

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# Environment

# Anticancer Drugs: a Growing Environmental Threat

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Cancer has risen concern among population due to its increasing incidence rates and mortality-related numbers. The administration of anticancer drugs has been the most common treatment approach nowadays – chemotherapy. The increasing prescription of anticancer drugs and the new trend of home chemotherapy have contributed to the rise on the amount of these drugs ending up in urban wastewater treatment plants, which are not designed to deal with these hazardous. As a result, anticancer drugs have been reported in different environmental waters [1], posing the environment and potentially the human health at risk.

According to the *Instituto Nacional da Farmácia e do Medicamento, I.P* (INFARMED, I.P.), 171 different anticancer drugs were consumed in Portugal between 2007 and 2015, accounting for a total of about five tons per year [2]. Among the most consumed are: mycophenolate mofetil (MMF), mycophenolic acid (MPA), capecitabine (CAP) and 5-fluorouracil. Predicted environmental concentrations were determined based on (i) consumption amounts, (ii) excretion factors, (iii) estimated degradations at wastewater treatment plants and (iv) the dilution factor from wastewater to surface water. Comparing those predicted environmental concentrations with the toxicological levels for aquatic organisms, risk was estimated for four anticancer drugs: MMF, MPA, bicalutamide (Bica) and cyclophosphamide (CYC) [2].

Urgent demands for effective treatment approaches to mitigate the entrance of anticancer drugs of most concern in the environment have emerged.

Concerning the physical processes, the feasibility of removal of one of the most consumed anticancer drugs worldwide, 5-fluorouracil, from wastewaters was investigated through the study of the main parameters affecting its adsorption on carbon-based materials, envisaging the use of tailor-made adsorbents (high specificity and effectiveness) [3]. The adsorption capacity was found to be mainly driven by the surface area of the materials and, at less extent, by their surface chemistry [3]. Concerning the kinetic of 5-fluorouracil adsorption on carbonaceous materials, oxygen content and the mesopore volume (and indirectly the total pore volume) revealed to be the predominant influencing factors [3].

The degradation of anticancer drugs of most concern in water by Advanced Oxidation Processes was also investigated. 5-fluorouracil is completely degraded in 30 min by Fenton's process, being achieved 50% of mineralization after 8 h of reaction [4]. Photo-Fenton proved to be more effective in the degradation of this anticancer drug, even when an iron concentration in compliance with the legislation for direct water discharge is used; 67% of mineralization after only 2 h of reaction and decrease on the toxicity against *V. fischeri* [4]. The performance of ozonation was studied in the degradation of the four anticancer drugs for which risk was estimated. While the degradation of MMF and MPA is almost instantaneous, CYC and Bica revealed to be more recalcitrant, reaching low degradation percentages even for a mgO<sub>3</sub>/mg<sub>DOC</sub> ratio > 5.

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# COMUNICAÇÕES ORAIS



# Nanoimmunoassays – Metal nanoparticles for sensitivity and Antibodies for specificity

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Metal nanoparticles (NPs) with different morphologies exhibit interesting and innovative chemical, optical and electrical nanoscale properties. These can be explored in the context of sensitivity improvement for biosensing applications<sup>1</sup>. The motivation for our work is key bio-/non-bio interactions occurring at the surface of these NPs when they are conjugated with detecting biomolecules (e.g., oligonucleotides, enzymes and antibodies/antigens)<sup>1,2</sup>. Techniques used in these studies are a mixture of spectroscopic (UV/visible, fluorescence, light dispersion, Raman/SERS) and biochemical (agarose gel electrophoresis, column chromatography) techniques, that are especially suited to study changes in nanomaterial properties, namely optical/plasmonic properties. Nanoimmunoassays based on gold nanoparticles (AuNPs) associate high sensitivity imparted by nanoscale properties with the well-known specificity associated with antibody detection. For the construction of AuNP-antibody or AuNP-antigen conjugates we synthesize AuNPs by reduction of a gold salt, under appropriate conditions for the intended NP morphology (e.g., spherical or starshaped). These AuNPs are further functionalized with an alkanethiol bifunctional linker. This linker presents at one end a thiol group that is strongly chemisorbed to the AuNP surface; and at the opposite end, a negatively charged carboxylic group. The 10 carbons-long aliphatic chain allows the formation of a tightly packed monolayer. This monolayer provides a biofriendly and uniform negatively charged surface at physiological pH, that we have been using successfully for protein conjugation, either covalently (EDC/NHS) or by physisorption<sup>3</sup>. Both approaches were used for the conjugation with monoclonal antibodies against malaria antigens in a competitive and fluorescence-based assay. The type of conjugation of the antibody to the AuNPs determines the activity of the antibody, with conjugates formed by physisorption being more active<sup>4</sup>. Further studies of these conjugates by Agarose Gel Electrophoresis (AGE) and Differential Centrifugal Sedimentation (DCS) revealed two different models for antigen binding to AuNP-antibody conjugates. Furthermore, DCS was used to show inhibition of antigen binding in the presence of human plasma, a realistic testing condition, of high relevance to the implementation of immunoassays at the clinical level<sup>5</sup>. Recent characterization data will be presented for star-shaped AuNP-antibody conjugates, further functionalized with a Raman probe, with intended utilization in a SERS (Surface-Enhanced Raman Spectroscopy)-based microfluidics platform for food toxin antigen detection<sup>6</sup>. Taking an innovative approach to immunoassays, we are using AuNP-synthetic antigen conjugates to detect circulating antibodies against pneumocystis. The proof-of-concept for this serological assay was established by AGE using sera from infected mice. Studies in human plasma indicate successful application of this detection scheme in a lateral flow immunoassay format, as a non-invasive strategy for detection of pneumocystis in clinical samples.

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# Modulating protein aggregation in cell models using modified steroids

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Protein aggregation is a biological process in which misfolded proteins aggregate and accumulate in intra- or extracellular media. Protein aggregation is intimately linked to the pathogenesis of many neurodegenerative diseases (such as Alzheimer's, Huntington, Parkinson's and prion diseases) but also in cancer and cardiovascular pathologies (e.g. atherosclerosis, heart failure and ischemic heart disease).<sup>1</sup> However, it is not fully understood how aggregates are formed and how the complex network of chaperones, the proteasome, autophagy and other regulatory factors are involved in their clearance.<sup>1</sup> Nevertheless, it is well accepted that lowering protein aggregates back to "normal" levels in cells could be an important therapeutic strategy to control or modulate neurodegenerative diseases.<sup>2</sup> In 2015, lanosterol was reported to reverse protein aggregation of crystallin clumps in mouse cataracts, due to its amphiphilic nature, being able to intercalate into and coat hydrophobic areas of large protein aggregates, making these water soluble again.<sup>3</sup> Taking into consideration this discovery, we believe that other steroids, such cholesterol (with the appropriate chemical modification),<sup>4</sup> can be good lead candidates to lower several types of protein aggregates. In this project a series of new hybrid-steroidal compounds was designed and synthesized, to address protein aggregates in different models and using techniques such as a high-throughput screening (HTS) (Figure 1). The design and synthetic strategy of the compounds, as well as the preliminary disaggregation results in different types of *in vitro* and *ex vivo* aggregation models will be discussed and rationalized in terms of structure-activity relationship, whenever possible.



Figure 1: Structures of the modified steroids and schematization of the HTS strategy.

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# Understanding the mechanism of action of a new spiro-β-lactam with dual anti-HIV and anti-Plasmodium activity using *in silico* target fishing

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By exploring the reactivity of 6-diazopenicillanates and 6-alkylidenepenicillanates<sup>1</sup>, Pinho e Melo's lab has recently synthesized a new spiro- $\beta$ -lactam with potent anti-HIV activity and anti-Plasmodium properties. This molecule, BSS-730A, presented a median IC50 of 0.015  $\mu$ M against HIV-1, 0.008  $\mu$ M against HIV-2 and 0.55  $\mu$ M against Plasmodium liver stage.

Despite the highly promising anti-HIV and anti-Plasmodium activities of the BSS-730A molecule, its mechanism of action remains elusive. Thus, target-fishing using *in silico* approaches have been explored in order to gather insights concerning BSS-730A's HIV molecular target. To this end, molecules with known target and relevant anti-HIV activity from ChEMBL and PubChem databases were organized in eleven different sets according to their target and, as query molecule, BSS-730A was compared with these sets by means of 2D fingerprints and 3D shape similarity searches. Results from both methods showed a similar trend, with the maximum similarity value being observed within the HIV Protease Inhibitors (PI) subset. The HIV PI set was also the only one which presented molecules sharing an ECFP4 fingerprint Tanimoto similarity coefficient with BSS-730A above the activity-relevant similarity value Tc=0.3, value above which two compounds hold a high chance to share the same activity, as reported by Bajorath et al<sup>2</sup> (Fig. 1). Substructure searches, pharmacophore mapping and docking studies also support the hypothesis of HIV Protease being the BSS-730A target.

Not underestimating the need for a more detailed experimental validation, the hypothesis that the main target of BSS-730A in HIV is the protease agrees with previous *in vitro* results indicating that the molecule exerts its action at a late stage of the HIV replicative cycle, i.e. the release and/or maturation of the virus particles.



Figure 1 - Bar chart representing the observed maximum Tanimoto (Tc) ECFP4 fingerprint similarities between BSS-730A and the compounds present on each HIV target data set. The similarity threshold proposed by Bajorath et al<sup>2</sup> as an indicatior of high likelihood of similar bioactivity (Tc  $\ge$  0.3) is represented as a dotted red line.

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CO4

# **Materials**

# Metal based lonic Systems for Sustainability

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Nowadays, the discovery of functional materials and processes that contribute for sustainability is highly relevant. Ionic liquids (ILs) and more recently deep eutectic solvents (DES) are reported as sustainable classes of task-specific materials possessing tunable properties according to desired applications<sup>1,2</sup>. In last years, we have reported the suitable combination between some metals (alkaline, transition metals and lanthanides) from periodic table and ionic systems with significant impact in catalysis, material science, energy and water treatment<sup>3-6</sup>.

Herein, we described some recent approaches of ILs and DES based metals and its possible applications (Figure 1):

a) Iron, Manganese and Lanthanides based ILs for application as magnetic and luminescent materials;

b) Supported Silica Nanoparticles in combination with ILs for catalytic applications;

c) Sodium, lithium and transition metals-based hydrophilic DES for application in electrochemistry (electrolytes and electrochromic devices);

d) Hydrophobic ILs & DES based on metal salts for application in water purification processes.



Figure 1: Metal based Ionic Systems (ILs and DES) for sustainability

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# **Materials**

CO5

# **Delayed Fluorescence Materials for Imaging Applications**

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Thermally-activated delayed fluorescence (TADF) is an unusual type of luminescence that has emerged as a powerful tool in the development of heavy-metal free organic light emitting diodes (OLEDs), owing to its ability to harvest energy from non-emissive triplet states.<sup>1</sup> TADF emitters display interesting photophysical properties such as luminescence in two distinct time regimes (nano- and microseconds), as well as an intrinsic sensitivity to oxygen and temperature.<sup>2</sup> Apart for their applicability in OLEDs, these features grant TADF emitters great potential as optical probes. Their long emission lifetime enables time-resolved fluorescence imaging methods, with unparalleled signal-to-noise ratio and resolution, and their sensitivity to media conditions enables optical oxygen and temperature sensing at the nanoscale. However, TADF emitters perform poorly in polar media and exhibit low aqueous solubility, which restricts their applicability beyond lighting devices.<sup>3</sup> To explore the great potential of TADF emitters towards imaging and sensing applications, we have developed a strategy to combining these compounds with silica nanocarriers (**Scheme 1**). In this work, we demonstrate that the nanomaterials provide an adequate and rigid environment to enable efficient TADF emission in aqueous media and circumvent solubility and biocompatibility limitations, ultimately allowing its application in fluorescence microscopy of live cells and sensing scenarios.



Scheme 1: Synthetic strategy to prepare dye-doped TADF emitting nanoparticles.

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# CO6

# Materials

# The thermosalient effect in Fe(III) salEen spin labile complexes

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Spin crossover (SCO) complexes have long been considered as promising candidates for the next generation of data storage devices.<sup>[1,2]</sup> SCO candidate compounds can be found among a limited group of  $3d^4$ – $3d^7$  transition metal ions, the most common being Fe(II), Fe(III) and Co(II). Fe(III), with its advantageous redox stability, is a good candidate for fabrication of SCO materials, an area towards which research has been moving.<sup>[3]</sup> Much effort has been expended in recent years to develop the materials assembly of SCO complexes and impressive results have been achieved in stabilising and isolating monodisperse nanoparticles, nanocrystals, nanowires, thin films, micro- and nanopatterned media, Langmuir- Blodgett surface mono- and multilayers and hysteretic soft media assemblies.

We recently synthesised mononuclear Fe(III) compounds, all displaying spin crossover, that show to be highly sensitive to the substituent on the ligand. Spin crossover profiles range from stepped to abrupt, two of which display hysteresis centred at room temperature. We also found that while the bromo-substituted compound undergoes a phase transition coupled with the thermosalient effect (TSE) resulting in crystal fragmentation with no loss of both SCO and hysteresis,<sup>[4]</sup> the iodo-subsituted undergoes a irreversible TSE-SCO.<sup>[5]</sup> Here we present the synthesis and characterisation of [Fe(X-SalEen)<sub>2</sub>]<sup>+</sup> derivatives and their self-assembly into nanostructured materials (Figure) using different fabrication techniques. Attempts to rationalise how the substituent affects the thermosalient effect are also discussed.



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# Materials

# **Enzyme-responsive silica nanocapsules**

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Nature's supramolecular self-assemblies sense and respond to their environments through various chemical and physical mechanisms often derived from dynamic hierarchical architectures. To reproduce Nature's chemistry, stimuli-responsive nanoparticles have been designed.<sup>1</sup> They modify their macroscopic behavior in response to stimuli. These so-called "smart" materials can show responses to the microenvironment of a disease and its cells.<sup>1</sup>

Among several types of drug delivery systems that have been developed, silica nanoparticles are extremely promising due to their biocompatibility and degradability that arise from the ability of silica to decompose into relatively harmless by-products.<sup>2</sup> Furthermore, the use of porous or hollow silica has emerged as one of the most promising strategies in the field of nanomedicine. Stimuli-responsive silica nanoparticles possessing a "sense and act" module for on-demand drug release are highly advantageous for drug delivery. As for triggering motifs, enzymes provide the most promising ones as enzymatic reactions are highly selective and efficient under mild conditions, and they do not require an external trigger as all organisms create special enzymes to help them thrive in their microenvironments.<sup>3</sup> Researchers can take advantage of this particular characteristic since most infection sites will overexpress a certain enzyme.

In this work we combine an innovative system able to encapsulate drugs, a biocompatible shell and a stimulus responsive controlled release system in a single silica nanocapsule. The silica shell was synthesized by a reverse nanoemulsion via a modified base-catalysed Stöber process involving a mixture of two silanes: tetraethyl orthosilicate (TEOS) and a silane derivative containing enzyme-cleavable responsive side linkages (**Figure 1**).



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# **Materials**

**CO8** 

# Porous Metal-Organic Framework based materials for sustainable catalytic applications

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Metal–organic frameworks (MOFs), also known as porous coordination polymers, have been proven to be outstanding candidates for bridging the gap between zeolites and mesoporous silica. MOFs are constituted by metal ions/clusters interconnected by organic linkers and have captured widespread interest, achieving an explosive development over the past two decades. The crystalline nature, structural diversity, and tailorability, as well as ultrahigh surface area make MOFs find their potential applications in diverse areas, such as gas sorption and separation, chemical sensing, proton conductivity, biomedicine



Scheme: Illustration of the preparation of diverse porous materials from MOFs and MOF-based composites as templates/precursors.<sup>2</sup>

and catalysis. However, in numerous MOFs the structural stability and performance limits their practical applications, relatively to other porous materials. Consequently, distinct strategies have been used to prepare MOF based materials and overcome these disadvantages.<sup>1,2</sup>

The modification and derivation of MOFs, and their utilization as platform, template or subtract, opens up an avenue to the preparation of diversified porous materials with unique advantages in comparison to traditional pristine materials. Following our interest in the development and application of functional MOFs towards catalytic sustainable processes an overview of more interesting functional MOF-based materials prepared and investigated as catalysts in our research group is reported.

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#### **Culture and Education**

## Periodic Table and Theoretical and Computational Chemistry: a lesser-known link

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The history of the evolution and development of the Periodic Table (PT) is usually told following the line of contributions from Mendeleev (1834-1907) to Moseley (1887-1915) and Seaborg (1912-1999), sometimes with a few references to Bohr (1885-1962) and Pauling (1901-1994). This narrative neglects almost completely the contributions of the development of Theoretical and Computational Chemistry (T&CC) and Quantum Chemistry for the establishing of the actual Periodic Table and its causal explanation based in the ab initio theory. The purpose of the present communication is to emphasize the contributions of T&CC for the history of the Periodic Table, including references to Hartree, Mulliken, Coulson, and Pople, as well as to the relations of the PT with the modern basis sets methodologies used in electronic structure calculations, and force fields used in molecular mechanics (MM), molecular dynamics (MD), Monte Carlo (MC), and the myriad of classical, quantum, and hybrid methods available to the chemists.

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#### Culture

# Study of five iberian medieval iron-gall inks obtained through the use of historically accurate reconstructions

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Iron gall ink is one of the most important inks in the history of western civilization, and it was in widespread use from the middle ages until the beginning of the 20th century. The degradation of manuscripts catalyzed by iron-gall inks is a major conservation issue and a serious threat to the world written heritage<sup>1</sup>.

We have prepared five medieval inks using the same ingredients and similar methodologies. They are the result of research on Iberian written sources of medieval techniques and contained three basic ingredients (**Figure 1**): Fe<sup>2+</sup> obtained from an iron sulphate salt, a phenolic extract (tannins), and gum arabic<sup>1,2</sup>. Different additives, such as other metal ions and pigments, and different extraction conditions were applied. These variations of different additives were studied and its contribution to the specific ink recipe was revealed<sup>3</sup>.

All the extracts and inks were analyzed in threefold by HPLC-ESI-MS and HPLC-DAD. HPLC-ESI-MS allowed the identification of the phenolic compounds present both in extracts and inks. HPLC-DAD allowed the quantification of these compounds<sup>3</sup>.

The main goals of this work were: 1) to identify and quantify the major phenolic compounds present in the gall extracts and evaluate its variation by the addition of an iron sulphate salt and gum arabic when producing the iron-gall inks; 2) to identify and quantify the identify and quantify the effect of each additive on each tested recipe.



Figure 1: Basic recipe for an iron-gall ink. A: pentagalloylglucose; B: monogalloylglucose

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#### Health

# Design and synthesis of silver camphorimine compounds with high antimicrobial activity

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The high resistance of microorganisms to conventional antimicrobials represents a major concern to human life but it is simultaneously a challenge to the development of new antimicrobials. Alternative compounds to the existing drugs, in particular those that act through distinct mechanisms are of particular interest. Coordination compounds may perform as alternative antimicrobials if their toxicity meets the suitable values.

The synthesis of new complexes combining high antimicrobial and anticancer activity to be used alone or in synergy with commercially available drugs lead to the identification of several silver camphorimine complexes with high antimicrobial activity and reasonable cytotoxic properties.

The ongoing work<sup>1-3</sup> shows that the design of the camphor ligands ( $OC_{10}H_{14}NY$ , **Figure 1**) is of utmost relevance to drive the properties, reactivity and applications of the complexes. Silver was the obvious choice concerning the metal since it's antimicrobial properties are known since the antiquity. Nevertheless, other metals (*e.g.* Cu, Au) are also under survey to ascertain whether they help to overcome the toxicity drawback.



Figure 1: Types of complexes derived from camphor imine Igands: a) mono-hapto; b) di-hapto; c)- bridging; d)-camphor sulphonimine; e) bi-hapto (bicamphor); f) mono-hapto (bicamphor).

The assessment of the antibacterial activity of complexes of the type  $[Ag(NO_3)(OC_{10}H_{14}NY)_2]$  through the experimental determination of their MIC values showed that the characteristics of the camphor imine substituent (Y) may enable the activity against the *Gram*-positive: *S. aureus* Newman (Y=C<sub>6</sub>H<sub>5</sub>; 4-MeC<sub>6</sub>H<sub>4</sub>; 3,5-MeC<sub>6</sub>H<sub>3</sub>); the *Gram*-negative: *B. contaminans* IST408 (Y=NMe<sub>2</sub>; 3-CIC<sub>6</sub>H<sub>4</sub>; 4-CIC<sub>6</sub>H<sub>4</sub>; 4-CF<sub>3</sub>C<sub>6</sub>H<sub>4</sub>) and *E. coli* ATCC25922 (4-MeC<sub>6</sub>H<sub>4</sub>; 3,5-MeC<sub>6</sub>H<sub>3</sub>) or have no effect as for *P. aeruginosa* 477. Other parameters such as the bicamphor character also play a role in the biological activity (antimicrobial, cytotoxic).

The biological activity of the complexes will be discussed based on their structure, lipophilicity and redox properties.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia (FCT) for financial support through projects ID/QUI/00100/2013 and UID/BIO/04565/2013, and the NMR Network (IST-UTL Node) for facilities.

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#### **Culture and Education**

# "Química ao pé da letra": das raízes etimológicas às oportunidades de multidisciplinaridade e divulgação científica

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Dos alimentos aos transportes, dos medicamentos à tecnologia, a química tem um lugar central no nosso quotidiano. Não obstante tal centralidade, o carácter representacional e a linguagem hermética da química constituem frequentemente obstáculos ao seu ensino e divulgação. Torna-se, assim, desafiante mostrar a riqueza que espreita nos conceitos científicos para admirar a beleza da química e descobrir a simplicidade da sua linguagem [1-2]. No âmbito do Ano Internacional da Tabela Periódica dos Elementos, em Portugal, será publicado o livro "Química ao

pé da letra", que, através da definição e exploração etimológica de 118 conceitos centrais da química, procurará oferecer ao leitor, nomeadamente aos professores e estudantes de química, as ferramentas elementares para tirar partido da riqueza lexical, que se tece entre as dimensões macroscópica, submicroscópica e representacional desta ciência. Como a efeméride pede, observemos as palavras: tabela e periódica. A primeira deriva do latim tabela, ou seja, uma tábua (tabula) pequenina ou tabuinha. Já o adjetivo periódica leva-nos ao radical grego hodos (caminho). O prefixo peri- transmite a ideia de movimento à volta. Assim, periódico significa caminho em redor e usa-se para algo que ocorre regularmente. Outros termos do léxico guímico merecem o nosso olhar atento, como é o caso de símbolo químico. Este termo provém do grego symbolon, que resulta da junção do prefixo syn (conjuntamente) e o verbo balo (lançar, atirar). A palavra significa reunir, junção de duas metades correspondentes, confrontadas como sinal de reconhecimento ou contrassenha, por oposição a diabolo, donde provém diabo, que tem o sentido de separar. Também a etimologia de ácido é surpreendente. Ácido provém da palavra latina para agulha (acus) e tem raízes no indoeuropeu afiado (ak). Assim, ácido pode ser ligado a objetos afiados e não apenas ao paladar. O termo eletrão vem do grego elektron que, como o seu equivalente latino electrum, designavam uma liga composta por 4/5 de ouro e 1/5 de prata, mas também o âmbar amarelo, com propriedades elétricas. A palavra grega está associada a algo que emite brilho, pela sua relação etimológica com o adjetivo masculino elektror (brilhante). Na origem de catálise e catalisador temos o verbo grego katalyo, e o substantivo katalysis, formado pelo prefixo kata- (para baixo, contra) e o verbo lyo (desligar, soltar, libertar). O sentido inerente ao étimo grego é o de dissolver, deitar abaixo, destruir. A adoção da palavra grega (katalyo) mostra que o aumento de velocidade da reação química é comparado à destruição de uma cidade e à abolição de um estado de coisas, ou seja, de pôr um fim a algo.

Para além das raízes etimológicas de 118 conceitos do léxico químico, procurar-se-á, por fim, identificar e sistematizar estratégias que permitam tirar partido da riqueza e da variedade de conceitos centrais da ciência química que faz parte do nosso dia a dia para, por um lado, tornar o universo da química mais acessível e relevante e, por outro, promover o debate sempre imacabado sobre a natureza da ciência e a sua relação com a sociedade.

A aproximação ao léxico da química leva-nos ao fascínio de gostar de conceitos que ora estão tão presentes no dia a dia que quase nos passam despercebidos ou tão distantes do dia a dia que se tornam ameaçadores para quem deles pouco ou nada julga conhecer. O livro "Química ao pé da letra" poderá, portanto, constituir-se como um espaço propício ao diálogo multidisciplinar, visando a divulgação da química e desafiando as fronteiras tantas vezes rígidas da especialização académica [3].

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#### Materials

#### Bioactive chitosan-on-chitosan multilayered assemblies for biomedicine

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The marine environment is an extraordinary source of marine living resources from which a plethora of natural molecules and materials with specific and astonishing biological and chemical features can be readily extracted from. Among them, biopolymers, obtained from marine organisms, have widespread use in numerous biomedical applications, including in tissue engineering and regenerative medicine (TERM), as well as in sustained drug delivery.<sup>1</sup> In particular, chitosan (CHT) has been gathering considerable attention due to its proven biocompatibility and biodegradability, non-cytotoxicity, non-immunogenic, antibacterial and wound-healing properties.<sup>2</sup> However, CHT biopolymer shows limited stimuli-responsiveness, adhesiveness, bioactivity, bioinstructive behavior and unsuitable mechanical properties, thus do not triggering an enhanced biological response.<sup>2</sup> As such, the chemical functionalization of CHT provides a simple yet powerful way to assign such improved properties to the biopolymer and stimulate the development of innovative functional biomaterials/devices with tailor-made properties suitable to biomedical purposes.<sup>3</sup> Herein, emphasis will be given to selective chemical methodologies applied to CHT towards grafting desired bioactive and functional molecules. Moreover, the Layer-by-Layer (LbL) assembly technology will be employed to formulate innovative multifunctional biomaterials/devices, disclosing fine-tuned properties and functions at the nanoscale, by resorting to oppositely charged chitosan and chitosan-bioactive peptide molecules (Scheme 1). The build-up process will be monitored by guartz crystal microbalance, and the morphological properties studied by advanced microscopy techniques. The potential of such devices to be used in TERM, as well as in controlled drug delivery will be discussed.



Scheme 1: Schematic illustration of the multilayered biomaterials developed via LbL assembly technology.

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#### Health

### Synthesis and Biological Evaluation of Nature-Inspired Indole-Containing Alkaloids

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The emerging theme of drug resistances highlighted in cancer and infectious diseases has kept new challenges in drug discovery.<sup>1</sup> Secondary metabolites of natural products especially alkaloids containing an indole group have been crucial in drug discovery. Inspired by fiscalin B, reported as substance P antagonist, quinazolinone alkaloids derivatives containing an indole moiety were synthesized using two different methodologies – a highly efficient three-component one-pot microwave-assisted and a multi-step Mazurkiewicz-Ganesan approach (Scheme 1). Four series of 38 derivatives were obtained in low to moderate yields. Compounds were tested for their antitumor<sup>2</sup>, neuroprotection<sup>3</sup>, antibacterial, and antifungal activities. The stereochemistry of compounds was critical in all activities falling to (1*S*, 4*R*) configuration. Sixteen compounds exhibited weak to moderate tumor cell growth inhibitory activity. Four compounds showed potential for *in vitro* neuroprotection in Parkinson disease. Halogenated derivatives showed good antibacterial activity against clinical isolates resistant to methicillin (MRSA), and the isolation of enantiomers highlighted the active and inactive configurations.



Scheme 1: Synthetic approach toward the quinazolinone scaffold.

Throughout this work, structure-activity relationships were established and three hit compounds from quinazolinone scaffold emerged as potential drug candidates.

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#### Materials

# Morphological Modifications on Carbon Nitride for Enhanced Selectivity Towards the Synthesis of *p*-Anisaldehyde

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The aromatic aldehyde, *p*-anisaldehyde, is widely used in industry, and its production usually involves hazardous process conditions. Heterogeneous photocatalysis appears as a sustainable alternative to conventional organic synthesis processes, operating under environmentally friendly conditions, without compromising selectivity and yield<sup>1</sup>. Graphite-like carbon nitride (GCN) is a metal-free semiconductor extensively applied in photocatalytic processes once it absorbs light in the visible range ( $\lambda_{exc} > 400$  nm), constituting an advantage in solar-driven processes. By promoting physical and chemical modifications to gCN, its low surface area and high electron/hole recombination rate can be overcome<sup>2</sup>.

In the present work, GCN was morphologically modified through hard-templating routes using different silica templates. The materials, referred to GCN-UL, GCN-OM and GCN-MP, according their different morphology (UL: urchin-like; OM: ordered macroporous; MP: mesoporous), were tested in the photocatalytic conversion of anisyl alcohol (AA) to anisaldehyde (AAD) under UV-LED ( $\lambda_{max}$  = 370 nm) and visible-LED ( $\lambda_{max}$  = 417 nm) light irradiation.

a)



Figure 1. a) SEM micrographs of GCN and the modified catalysts. b) *Conversion (C), selectivity (S)* and yield (Y) determined for the photocatalytic synthesis of AAD over 4 h of reaction under UV-LED irradiation ( $\lambda_{max}$ =370 nm) in the absence of oxygen.

The developed catalysts revealed different morphologies when compared to GCN (Figure 1a). Their higher surface area may indicate more active sites for AA reactivity. Moreover, the quenching observed by photoluminescence intensity (not shown) may suggest a decrease in the electron/hole recombination by enhancing the reaction efficiency. Under UV-LED illumination, in the absence of oxygen, the GCN-based catalysts attained higher *C* and *Y* compared with GCN, yet the *S* to AAD (> 90%, Figure 1b) remained constant. The GCN-UL showed the best performance by achieving C = 64% and Y = 60% after 4 h reaction. In the presence of oxygen, GCN-UL continued to perform better with C = 92% and Y = 80%, only after 1.5 h of reaction. Using visible-LED illumination, the photocatalytic performance of all GCN-based catalysts was not significantly affected, which opens the possibility of using solar irradiation.

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#### Health

# Use of Phenanthroline Derivatives in Chemotherapy Treatments for Cancer and as Alternative Therapeutics in the Era of Antibiotic Resistance: Interaction with DNA and Modulation of the Efficiency

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Flat ligands, alone or within metal complexes, are active against tumor cells and may be used in chemotherapy. The activity of these drugs is related to their mode of interaction with DNA being the intercalation mode identified as the cytotoxic mode against tumor cells.<sup>1</sup> 1,10-phenanthroline (phen) was demonstrated to be effective towards several tumor cell lines.<sup>2</sup> and their derivatives also showed cytotoxicity. Moreover, it was observed that this cytotoxicity was deeply connected to the number and position of the functional groups incorporated in phen.<sup>1</sup> Different studies on the intercalation of small molecules in DNA have appeared in the bibliography during the last years<sup>3</sup> and some debate still remains about the intercalation/deintercalation process<sup>3</sup> and the mechanism that could explain the modulation of the cytotoxicity. In our work, we try to rationalize the role of weak interactions with the stability of the interaction and we extrapolate our results to the cytotoxic effects. The systems were mainly optimized by using semiempirical methods including dispersion effects. We also carried out DFT calculations including dispersion effects for the Energy Decomposition Analysis (EDA) and to perform the Quantum Theory of Atoms in Molecules (QTAIM) and the Non-Covalent Interaction (NCI) analyses to obtain topological pictures of the weak interactions that rules the intercalation process. Solvent effects were also taken into account by continuum approaches. Our results confirm the importance of weak interactions and we extrapolate the link with the cytotoxicity by means of a subtle balance between the stabilizing weak interactions and the destabilizing steric contribution (Figure 1). The role of desolvation energy is also crucial when looking at the stability of the studied systems.





Figure 1: Attractive (green) and repulsive (red) interactions for the 5,6-Me<sub>2</sub>phen and 3,4,7,8-Me<sub>4</sub>phen ligands intercalated between GC/CG base pairs via the Minor Groove.

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#### Health

### H<sub>2</sub>S-diclofenac vs diclofenac: effects on membrane lipids

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The efficacy of nonsteroidal anti-inflammatory drugs (NSAIDs) against inflammation, pain, and fever explains their worldwide use in the treatment of inflammatory conditions. However, the chronic therapy with NSAIDs is associated with a high incidence of adverse effects. This fact triggered the search for novel anti-inflammatory drugs with improved safety. One of the main strategies to improve NSAIDs tolerability comprises the modification of existing NSAIDs to release protective mediators *in vivo*, such as nitric oxide (NO) and hydrogen sulfide (H<sub>2</sub>S).<sup>1</sup>

Increasing evidence supports that the therapeutic and toxic effects of NSAIDs are related to their effects on membrane lipids.<sup>2</sup> Therefore, this project aims at characterizing the effects of H<sub>2</sub>S-diclofenac (a novel NSAID) and diclofenac (the parent NSAID) on membrane lipids to gain insights into the pharmacological mechanisms of the novel drugs.

Langmuir monolayers made of phosphatidylcholines and phosphatidylethanolamines were chosen as membrane model systems. The effects of drugs on membrane lipids were characterized using surface pressure-area isotherms and Brewster angle microscopy (BAM).

Differential effects of diclofenac and  $H_2S$ -diclofenac on the organization of membrane lipids were found, with the novel drug inducing more pronounced alterations in Langmuir isotherms and BAM images (**Figure 1**). This result is not auspicious for the gastric tolerability of  $H_2S$ -diclofenac, since alterations in the structure of membrane lipids are one of the key toxicity mechanisms of NSAIDs. In this sense, studies on drug-membrane interactions may be valuable to be implemented in the preclinical phase of the drug development to predict *in vivo* effects.



Figure 1: BAM images of 1,2-dipalmitoyl-*sn*-glycero-3-phosphocholine (DPPC) at 10 mN.m<sup>-1</sup> in the absence and presence of diclofenac and H<sub>2</sub>S-diclofenac (molar ratio: 9:1).

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#### Health

### 3HQs as Boronic Acid Hotspots for site-selective formation of iminoboronates

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In the field of modern bioconjugation, there is an increasing demand for reactions that are not only bioorthogonal, but also reversible under selected conditions.<sup>1</sup> Boronic acids (Bas) are excellent candidates for this kind of applications as they are stable under physiological conditions, have good biocompatibility and reversibly bind to diols in aqueous environment.<sup>2, 3</sup> 3-Hydroxy Quinolinones (3HQs) are isosters of Glycine that are also known to chelate various metals<sup>4</sup>, and also proved to allow reversible boronic acid conjugation in aqueous medium. The 3HQs derivatives that we synthesized showed remarkable binding capabilities with boronic acids in buffer solution (Ka= 698.7±17 M-1) and were further developed to be inserted in peptidic fragments as pseudopeptidic platforms. The attachment of our platform to peptides allowed for the formation of stabilized iminoboronates on N-terminal Cysteine residues. This technology was used to prepare reversible fluorescent conjugates with the Laminin peptide, which allowed to validate the 67LR as a potential target for the delivery of payload to HT29 cancer cells.



Figure 1: Delivery of borylated payload to HT29 cancer cells via reversible conjugates targeting the 67LR non-internalizing receptor

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#### Health

#### Triazene-based prodrugs for selective targeting of hypoxic solid tumors

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Displaying a broad-spectrum chemistry, triazenes are best known for their cytotoxic properties, as exemplified by dacarbazine and temozolomide, well-known anticancer agents. Triazenes exert their chemotherapeutic activity through a unique mechanism of action that involves formation of a reactive alkyl diazonium intermediate capable of alkylating DNA and promoting cell death.<sup>1</sup> Herein we report a triazene-based platform, **1**, that can be activated by nitroreductases<sup>2</sup> (NTRs) to undergo a self-immolative process that culminates with the release of the cytotoxic triazene. A series of nitroaromatic prodrugs **1** (**Figure 1**) of cytotoxic triazenes was synthesized and NTR-mediated hydrolytic activation was investigated by HPLC and LC-MS. Corroboration of the reduction reaction was attained through chemical reduction using zinc/acetic acid and by means of the synthetic des-nitro analogue. A549 cells (human epithelial lung carcinoma cells) were used as representative cell lines for bioreductive experiments. This strategy discloses a novel triazene release system, coupling targeting ability and a chemotherapeutic tool in a single entity.



Figure 1. Schematic representation of triazene prodrugs 1 activation by NTR selective targeting.

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#### Environment

# Chasing Boron: Optical Detection and Scavenging Materials for Wastewater Remediation

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Boron compounds are used in many industrial applications, including the manufacture of glass and ceramics, insecticides, fertilizers, semiconductors, soaps and detergents, flame retardants, high duress compounds, and pharmaceutical drugs. Boron is necessary both to human health and agriculture in trace amounts but becomes toxic above *ca.* 2 ppm.<sup>1</sup> High boron contents in water might result from industrial effluents or from soils containing borates and borosilicates.<sup>1</sup>

Boron is difficult to detect and to remove from water. Here we present two new boron optical detection methods based in hexahydroxytriphenylene <sup>2-4</sup> and two scavenging methods, one based on thermoresponsive core-shell polymer nanoparticles (PNP),<sup>5</sup> and the other on mesoporous silica nanoparticle (MSN) membranes (Figure 1).<sup>6</sup> The polymer particles have a core of poly(methyl methacrylate) (PMMA) and a thermosensitive shell with a brush composed of a copolymer of N-isopropylacrylamide (NIPAM), 2-aminoethyl methacrylate (AEMH) and D-gluconoamidoethyl methacrylate (GAEM) boron-chelating diol-containing monomers.<sup>5</sup> The MSN are surface modified with vicinal diol groups and crosslinked on cellulose acetate membranes.<sup>6</sup>

Our systems feature high efficiency for boron detection and removal from water, with the possibility for portable use in field applications.



Figure 1: Schematic representation of the strategies used for boron detection and scavenging.

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#### Energy

# Remarkable Solar-Driven H<sub>2</sub> Production from Polymeric Carbon Nitride Doped with Carbon and with Distorted Structure

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Solar-driven hydrogen (H<sub>2</sub>) generation from water splitting has received substantial attention during the last few decades as it has the potential to meet the growing global energy demand, providing a green and sustainable solution to the energy supplies. However, many challenges remain in solar-driven H<sub>2</sub> evolution such as improving the activity of the photocatalytic systems and to minimize the use of expensive electron donors and co-catalysts.<sup>1</sup> The low activity of most photocatalytic systems is often due to the low visible-light absorption, high recombination rate of electron-hole and low hydrolytic stability.

We report experimental evidence and computation (DFT) calculations to support an easy and alternative approach to enhance photocatalytic H<sub>2</sub> production. This objective is accomplished by engineering the structure of graphitic carbon nitride (g-C<sub>3</sub>N<sub>4</sub>) with carbon atoms and introducing defects, which substantially reduces g-C<sub>3</sub>N<sub>4</sub> band gap<sup>2</sup> from 2.7 to 2.0 eV. The synthesis procedure here reported plays a significant contribution to tailoring g-C<sub>3</sub>N<sub>4</sub> properties such as visible light absorption, charge-carrier recombination and surface area. The efficient charge transfer and separation, as well as the suppressed recombination of photogenerated electron-hole pairs, was demonstrated by photoluminescence (PL) emission spectroscopy, transient photocurrent measurements and electrochemical impedance spectroscopy (EIS). Based on the measured conduction band (CB) from Mott-Schottky plots and optical band gaps, the valence band (VB) was estimated for the modified semiconductor. Further characterization (diffuse reflectance (DRS), Fourier transform infrared and X-ray photoelectron (XPS) spectroscopies, X-ray diffraction (XRD), scanning and transmission electron microscopy (SEM/TEM)) allowed correlating structure with activity. As such, an impressive 20-fold improvement in visible-light H<sub>2</sub> generation was achieved when as compared to bulk g-C<sub>3</sub>N<sub>4</sub>, using EDTA and Pt as sacrificial electron donor and co-catalyst, respectively. Furthermore, significant amounts of H<sub>2</sub> were also produced in the absence of Pt avoiding, therefore, the need of (expensive) co-catalysts. This new metal-free photocatalyst brings photocatalysis a step closer to practical "solar-driven" applications, showing the enormous potential of g-C<sub>3</sub>N<sub>4</sub> modified materials in this field when properly engineered.

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#### Energy

### A computational study on the water splitting reaction by MXenes

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In 2011, a new family of 2D layered materials, the so-called MXenes, was obtained from selective etching the A element of the MAX phases from hexagonal layered ternary transition metal carbides, carbonitrides or nitrides, where M stands for an early transition metal, A stands for an element from a subset of groups 12-16, and X stands for carbon and/or nitrogen (**Figure 1**). The general formula of MXenes is  $M_{n+1}X_nT$ , where M and X are as in the MAX phases and T stands for the surface termination (bare or terminated with hydroxyl, oxygen or fluorine groups).

MXenes display high electrical and metallic conductivities, hydrophilicity, large surface area, tunable structure and superior oxidation resistance (in fact, they resist harsh synthetic conditions involving the etching with HF). All of these properties, which can suffer modification upon hybridization with other materials, underpin the huge application potential of MXenes in areas such as ecofriendly energy, water purification or catalysis.

In this communication, we report on first-principles calculations, based on density-functional theory, of the binding of water and its dissociation on M2C (carbides) and M2N (nitrides) bare surfaces of the M elements highlighted in **Figure 1** with the red dotted box The potential of the MXene heterogeneous catalysts for water splitting will be further compared with data reported in the literature for the water dissociation on the surfaces of pure metals and of metal alloys.<sup>1</sup>

1 H 100794			м	arly tra netal	nsition	A	etche elem	ent	x	carbon nitroge	or n						2 He 4 00 2002
3 Li 6941	4 Be 9.012102	5 6 7 8 9 B C N O F 10 11 12 12 11 14 14 17 11 12 14 14 17 11 12 14 14 14 15 14 14 14 15 14 14 14 15 14 14 14 15 14 14 14 15 14 14													9 F 10.9904032	10 Ne 20.1787	
11 Na 22.989709	12 Mg 24.3050	13 54 15 16 17 Al Si P S Cl 34 artinar 24 artisti 34 artista 2 2045 15 4543														18 Ar 39.940	
19 K	20 Ca 40.070	21 Sc 44.955912	22 Ti 47.887	23 V 50:04:15	24 Cr 51.0001	25 Mn 54.038045	26 Fe	27 Co 54.00198	28 Ni 58.6054	29 Cu 63.541	30 Zn 95.38	31 Ga 09.725	32 Ge 7244	33 As 74.92100	34 Se 78.00	35 Br 79.904	26 Kr 03.790
37 Rb 85.4070	38 Sr 87.82	39 <b>Y</b> 88.50585	40 Zr 91.224	41 Nb 92.90635	42 Mo 95.98	43 Tc	44 Ru 101.07	45 Rh	46 Pd 108.42	47 Ag 107.0002	48 Cd 112.411	49 In	50 Sn 116.710	51 Sb 121.760	52 Te 127.60	53 - 133 50447	54 Xe
55 Cs	56 Ba 137.327	57-71	72 Hf 17149	73 Ta 100.94788	74 W 103.64	75 Re 105.207	76 Os 190.23	77 Ir 192.217	78 Pt	79 Au 136 566560	80 Hg 200.59	81 <b>TI</b> 204.5833	82 Pb 2012	83 Bi 205.98040	84 Po	85 At [210]	86 Rn [222]
87 Fr [223]	88 Ra (224)	89-103 Adrides	104 Rf	105 Db [2010]	106 Sg (271)	107 Bh (272)	105 Hs (271)	109 Mt [274]	110 Ds [201]	111 Rg (200)	112 Cn (201)	113 Uut (214)	114 FI [209]	115 Uup	116 LV [29.5]	117 Uus (224)	118 Uuo (294)
			57 La	58 Ce	59 Pr 540.90705	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb 151.02505	66 Dy 162,500	67 Ho	68 Er 317.259	69 Tm	70 Yb 173.054	71 Lu 174,9000
			89 Ac (227)	90 Th 232 05808	91 Pa 231.03588	92 U 238.02891	93 Np (257)	94 Pu (244)	95 Am [243]	96 Cm (247)	97 Bk (247)	98 Cf (251)	99 Es (252)	100 Fm [257]	101 Md (254)	102 No (259)	103 Lr (282)

Figure 1: The periodic table of MAX phase elements (adapted from http://max.materials.drexel.edu).

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#### Nanotechnology

# Insight into the Interaction between Fluorescent Carbon Dots and Molecular By-Products of their Synthesis

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Carbon dots (CDs) are carbon-based nanoparticles with several advantageous optical and electronic properties, such as high photoluminescence, broadband optical absorption, biocompatibility, low toxicity, high photostability, and good water solubility.<sup>1</sup> Despite the development of various applications for CDs, the origin and mechanism of their photoluminescence remains to be clarified, with different authors proposing the role of quantum confinement effects, self-trapped excitons, edge states, delocalized surface states and exciton-hole recombination.<sup>2</sup> More recently, a few reports have demonstrated that part of the photoluminescence previously attributed to CDs results in fact from fluorescent molecular by-products, produced during the synthesis of the nanoparticles.<sup>2</sup>

Herein, we have aimed to the study of the effects exerted by these fluorescent by-products on the photochemical properties of CDs. To this end, we have proceeded to the synthesis of a CD via a microwave-assisted synthesis using citric acid and urea as precursors, followed by dialysis-based purification, which resulted in obtention of two fluorescent fractions: the CD and molecular by-products. XPS, mass spectrometry and FT-IR analysis identified by-products as derivatives of 4-hydroxy-1*H*-pyrrolo[3,4-*c*]pyridine-1,3,6(2*H*,5*H*)-trione (HPPT) (Figure 1).<sup>2</sup> Further luminescent studies focused on the photochemical response of both the CD and the HPPT derivatives to neutral and ionic species revealed a very interesting phenomenon: while the HPPT derivatives do not have any response to those species, they increase the photochemical response of the CDs toward them (Figure 1). This reveals a synergistic effect between the CD and the molecular by-products that can be useful for the development of new application for CDs.



Figure 1: chemical structure of HPPT (a). Fluorescence response of CDs to neutral and ionic species, in the presence of different amounts of fluorescent molecular by-products (b).

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#### Materials

# On Chondroitin Sulfate/Citric Acid Electrolytes as a New Electrolyte Material

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Chondroitin sulfate A (CSA) is a linear, negatively charged polysaccharide extensively investigated targeting biomedical applications. However, very few work has been done on its applicability as electrolyte material, in spite of the considerable amount of sulfonic groups attached to its backbone.

Herein we report the preparation and ionic conductivity properties of new electrolytes obtained from the combination of CSA with citric acid (CA). It has been found that CA plays a vital dual role in the formation in these electrolytes, acting as cross-linker and proton source, influencing in parallel the morphology of these electrolytes. Ionic conductivity values were found to be dependent on the CA mass ratio. For a mass ratio of 60.8%, for which a quasi-homogenous film was obtained, as indicated by both SEM and AFM, an ionic conductivity of about  $10^{-7}$  S cm<sup>-1</sup> was measured near room temperature. However, at 50 °C, the same electrolyte exhibited an ionic conductivity of  $10^{-5}$  S cm<sup>-1</sup>, two orders of magnitude higher than the value observed for both the CSA precursor at room temperature. Ionic conductivities were also found to increase with increasing relative humidity (RH). The same electrolyte achieved an ionic conductivity of  $3.7 \times 10^{-2}$  S cm<sup>-1</sup>, at 98% RH.



Figure 1: (A) Ionic conductivity isotherms of the CA concentration (B) relative humidity dependece of the ionic conductivity under different RH at 25 °C (B) for CSA and CA:CSA(X), with X = 0, 43.6, 60.8 and 82.3.

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# COMUNICAÇÕES EM PAINEL

A TABELA PERIÓDICA E OS ELEMENTOS DA VIDA

SAÚDE, ALIMENTAÇÃO E AMBIENTE

#### Health

# Thermochemistry of indane derivatives: analysis of energetic effect of the amino, methoxy and hydroxyl substituents

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The indane structure confers aromatic and aliphatic properties together in one rigid arrangement. This bicyclic structure provides a wide range of possibilities to incorporate specific substituents in different positions, thus being an attractive scaffold for medicinal chemists.<sup>1</sup> For instance, many indane derivatives are being used clinically to treat various diseases, such as indinavir, an HIV-1 protease inhibitor and indantadol, a potent Monoamine Oxidase (MAO)-inhibitor. The knowledge of the thermochemical properties of the indanes, as well as corresponding relationship with their structures, and the evaluation of their reactivity are particularly important for the applicability of these compounds in different areas. Thermochemical data for this type of polycyclic compounds are restricted to the indane itself, some of its alkylated derivatives and carbonyl-containing indene compounds,<sup>2</sup> therefore the present study is a contribution to extend the energetic characterization of this group of polycyclic compounds. The experimental and computational thermochemical results of six indanes are presented: 4-aminoindane, 5-aminoindane, 5-methoxyindane, 1-indanol, 2indanol and 5-indanol (Figure 1). The standard molar enthalpies of formation of the compounds in the condensed phase at T = 298.15 K were derived from their standard molar energies of combustion measured by static bomb combustion calorimetry. The standard molar enthalpies of sublimation/vaporization of those compounds at T = 298.15K were measured directly by high temperature Calvet-drop microcalorimetry. Additionally, using high level ab initio calculations, the gas-phase standard molar enthalpies of formation of these six compounds were obtained. The gasphase experimental results are analysed in terms of correlations between their structures (different substituents in the indane core) and energetic properties.



Figure 1: Structural formula of the compounds studied (from the center, in clockwise order): indane, 1-indanol, 2-indanol, 5-indanol, 4-aminoindane, 5-aminoindane and 5-methoxyindane.

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#### Health

# The health-promoting potential of *Salix* spp. bark: from the phenolic composition to the *in vitro* bioactivity

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*Salix* spp. (Salicaceae) cultivation has attracted attention, not only as source of biomass for energy generation, but also as source of extracts with health benefits.<sup>1</sup> Although salicin usually represents the marker bioactive of *Salix* spp. bark extracts, their flavanones and proanthocyanidins also exhibit interesting biological properties.<sup>1</sup> However, the phenolic composition and related bioactivity of *Salix* spp. bark extracts is still underexploited, particularly regarding to *S. atrocinerea* Brot., *S. viminalis* L. and *S. fragilis* L.,<sup>2</sup> whose knowledge may prompt innovative nutraceutical applications. Therefore, the present work aims at adding value to *S. atrocinerea* Brot., *S. viminalis* L. and *S. fragilis* L.,<sup>2</sup> whose knowledge may prompt innovative nutraceutical applications. Therefore, the present work aims at adding value to *S. atrocinerea* Brot., *S. viminalis* L. and *S. fragilis* L.,<sup>2</sup> whose knowledge may prompt innovative nutraceutical applications. Therefore, the present work aims at adding value to *S. atrocinerea* Brot., *S. viminalis* L. and *S. fragilis* L., bark, through the detailed characterization of phenolic compounds, by UHPLC-DAD-MS<sup>n</sup> analysis, and the evaluation of the *in vitro* antioxidant, anti-hypertensive and antibacterial effects of their extracts (**Scheme 1**).

Thirteen phenolic compounds, including 2 acetophenones and 2 proanthocyanidins were detected. *S. atrocinerea* Brot. extracts revealed the highest DPPH<sup>•</sup> and ABTS<sup>+•</sup> scavenging effects, as well as inhibitory activity on angiotensin I-converting enzyme. Considering the 24 h-inhibitory effect against *Staphylococcus aureus* growth, extracts of *S. fragilis* L., *S. viminalis* L. and *S. atrocinerea* Brot. bark were bactericidal at 1250 µg mL<sup>-1</sup>. Phenolic compounds may be associated to the bioactivity of *Salix* spp. bark extracts. In sum, these promising insights can contribute for envisaging the sustainable and integrative use of the studied *Salix* spp. bark extracts, in the spite of the biorefinery concept.



Scheme 1: Salix spp. bark valorization, via phenolic characterization and the in vitro bioactivity evaluation.

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#### Health

### Simple approach to the synthesis of a natural alkaloid – Cernumidine A

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Cernumidine A is a natural alkaloid, present in the leaves of *Solanum cernuum Vell*. (Solanaceae) a plant originated from southern and southeastern of Brazil. This compound display inhibition of interleukine-8 production by HT-29 colon carcinoma cells, and presents a singular aminoguanidine core.<sup>1</sup> The fact that several natural guanidine derivatives present diverse biological activities led this functionality to be an important building block in various pharmaceuticals. Cernumidine A presents a singular and not previously reported proline-based guanidine core ((2-aminopyrrolidin-1-yl)carboxamidine) condensed with an isoferulic (3-hydroxy-4-methoxycinnamic) acid unit (**Scheme 1**). This interesting structure with five consecutive C-N bonds was never reported in literature and although it seems a simple unit with only a labile stereogenic center, it presents a synthetic major challenge to a synthetic chemist. Biosynthetically it's supposed that this compound arose from oxidative decarboxylation of arginine previously to, or after derivatization with the isoferulic unit. Here we present our approach to the synthesis of cernumidine A and analogues involving the oxidative decarboxylation of L-proline followed by an intermolecular trapping of an iminium intermediate with nucleophiles (**Scheme 1**). Studies on the several oxidative reagents<sup>2,3</sup> as also reaction conditions used will be presented.



Scheme 1: Synthetic route for the synthesis of cernumidine A and analogues.

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#### Health

# Inhibiting metabolism and mitochondria-induced apoptosis in cancer cells: A structure-based virtual screening validation toward HK2 inhibitors

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Glucose is regarded as the main fuel of cancer cells and the glycolytic pathway has been demonstrated as a potential target to be explored for cancer treatment. Several enzymes involved in glycolysis, namely hexokinase 2 (HK2), are overexpressed in different types of cancer cells<sup>1</sup>. This enzyme is not only involved in the first and most determinant step of glycolysis and subsequently in the different branched pathways<sup>2,3</sup>, but also in the immortalization of cancer cells. When catalytically active, HK2 is able to bind to the voltage-dependent anion channel (VDAC) in the mitochondrial outer membrane, preventing the normal pro-apoptotic signalling. HK2-VDAC disruption should promote the binding of pro-apoptotic proteins to VDAC, therefore enhancing apoptosis in cancer cells<sup>4</sup>.

For this reason, the inhibition of the HK2 catalytic centre is proposed as a strategy to reduce the main source of energy to cancer cells, thus significantly decreasing cancer cell proliferation, avoiding HK2 binding to VDAC, and enhancing the apoptosis process. As an effort to find hit compounds able to interfere with the HK2 catalytic activity, a structure-based drug design strategy was implemented, leading to the virtual screening of several general databases such as DrugBank (~2000 molecules), NCI (~265 000 molecules), Chemoteca (~800 molecules) and some specific databases of natural product derivatives such as Ambinter (~10 000 000 molecules) and InterBioScreen Natural Products (~84 000 molecules). The virtual screening was carried out using molecular docking calculations through Gold 5.20 software. Molecules were prepared using Molecular Operating Environment (MOE2016 0802) and then docked into the HK2 catalytic site. Our results have suggested 2981 molecules with the potential to act as new HK2 inhibitors. Biochemical validation of the above-mentioned protocol is being conducted with 64 selected molecules.

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#### Health

## Synthesis and Analytical Applications of Glycerophospholipid Fluorescent Molecular Probes

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Lipids play critical biological roles in regulating many vital biological pathways and pathophysiological events. A considerable amount of lipid research relies on the use of tagged lipid analogues. However, given the size of an average lipid molecule, special care is needed for the selection of probes. If the size and intramolecular localization of the probe is not specifically taken into account, it may dramatically affect the properties of the lipids.<sup>1</sup> Fluorescent labelling is used as the preferred tool for the investigation of biological functions involving lipids, namely for clarifying metabolic pathways and molecular mechanisms of diseases where these molecules are of crucial importance.<sup>2</sup> In this work the state-of-the-art in the field of the synthesis and applications of organic fluorescent molecular probes for labelling glycerophospholipids is critically addressed, highlighting novel strategies for the synthesis of these molecules. The common approach to obtain a fluorescent lipid probe is to label it with a fluorescent moiety.1 Depending on the labelling position of the fluorescent moiety, there are two main classes of fluorescent lipids: headgroup labelled and acyl chain labelled (Figure 1, A).<sup>3</sup> The main drawback to this approach is that the relatively large and chemically distinct fluorophore may alter the interactions between the labelled glycerophospholipid and other membrane components, which can change the lipid distribution in natural environment. To overcome these limitations, the bioorthogonal chemical reporter strategy is becoming increasingly popular for the labelling of all kinds of biomolecules in their native environment. This solution is provided by using functional groups that are not aromatic. such as C-C triple bonds, which may be used for attaching fluorophores in the intact cell via click chemistry (Figure 1, B).4



Figure 1: A) Fluorescent lipid probes: (i) head-group labelled, (ii) acyl chain labelled. B) Lipid labelling by reaction of alkyne tagged lipid with an azido-fluorophore *via* click chemistry.

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#### Health

### **Design of Silicon-Based Vitamin D Analogs**

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Calcitriol, the hormonal form of Vitamin D3, has a broad spectrum of activities, being crucial in regulating mineral homeostasis, antiproliferative, pro-differentiative and immunomodulatory processes. The presence of the calcitriol receptor (VDR) in several types of tissues (including brain, skin, colon, breast, among others) makes it a therapeutic target for the treatment of associated diseases [1]. However, the hypercalcaemic effects associated with the use of pharmacological doses of natural calcitriol initiated the challenge to synthesize calcitriol analogues that display reduced calcaemic activity whilst retaining antiproliferative activity.

The knowledge of the key interactions in the co-crystallographic structure of 1,25D with VDR allows the design of new vitamin D analogues [2]. The introduction of silicon into bioactive compounds, improves drug activity [3], by increasing lipophilicity, solubility and cell tissue penetration, while improving the pharmacokinetic behavior and binding properties.

In this communication is presented the docking studies of some sila-analogues proposed for future synthesis, which have shown high binding affinity for the VDR, presumably due to the effect of Van der Walls interactions.



Figure 1: Structure of 1,25D (calcitriol) and schematic representation of new potentially active Silicon-derivative VDR ligands.

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#### Health

# Biomimetic approach to the synthesis of a singular and challenger pyrrolidine-guanidine core

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Guanidine derivatives can be found in several natural products from diverse origin<sup>1</sup> and this structural unit is present as building block in various pharmaceuticals. Guanidine compounds can also have diverse application as agrochemicals, sweeteners or as explosives among others. Because guanidines are super bases and oxoanion hosts, they are good supporting ligands in organometallic and coordination chemistry, as also good catalysts. A rare prolineguanidine-based compound was previously identified by the group from the leaves of *Solanum cernuum Vell*. (Solanaceae) a plant originated from southern and southeastern of Brazil.<sup>2</sup> This compound display inhibition of interleukine-8 production by HT-29 colon carcinoma cells. The pyrrolidine-based guanidine core ((2-aminopyrrolidin-1yl)carboxamidine) presented by Cernumidine A is condensed with an isoferulic (3-hydroxy-4-methoxycinnamic) acid unit (**Scheme 1**). This interesting structure with only a stereogenic center presents a synthetic major challenge to a synthetic chemist. Here we present our biomimetic approach to the synthesis of cernumidine A and analogues involving the derivatization of L-arginine followed by oxidative decarboxylation and intramolecular cyclization (**Scheme 1**). Studies on the several oxidative reagents<sup>2,3</sup> as also reaction conditions used will be presented.



Scheme 1: Biomimetic route to the synthesis of cernumidine A and analogues.

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#### Health

# Development of Torin2 Photo-Affinity Probes for Target Identification in *P. falciparum*

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Malaria, the mosquito-borne infectious disease caused by protozoan parasites of the Plasmodium genus, is an endemic disease in most tropical regions of the globe that despite the steady investment of the last decade, still represents a major public health concern with nearly half a million deaths a year reported for 2010-2017, and with last five years showing no reduction in the number of diagnosed cases. <sup>1</sup>

To overcome the need for drugs that act by different mechanisms than the ones currently in use, we've already shown that Torin2, a known ATP-competitive mTOR kinase inhibitor, is potent antimalarial with in vivo activity against both liver and blood stages, that is independent of the hosts mTOR pathway. Although no Plasmodium orthologs of mTOR exist, some high similarity sequences to the human mTOR exist in the parasite proteome, mainly at the kinase catalytic domain, corroborating the hypothesis that Torin2 acts by a different mechanism of action compared to the drugs currently in clinic. <sup>2,3</sup>

Here we report the development of photo-affinity labelling probes, achieved through the incorporation on the Torin2 scaffold of minimalist photocrosslinker and 'click chemistry' handles. We further disclose the preliminary results of their application in a mass spectrometry-based proteome profiling assays in parasite lysates and live cultures (**Scheme 1**). These are the pivotal results to elucidate the molecular targets of this class of compounds in P. falciparum and enable further pharmaceutical development of Torin2 based compounds as new alternative antimalarials.



Scheme 1: A. Structure of the Torin2 parent molecule. B. Structure of the Photo-affinity labelling probe I, derived from Torin2 by the introduction of a diazirine photoreactive moiety (in red) and a terminal alkyne handle for CuAAC chemistry (in green). C. Schematic overview of the protocol applied for P. falciparum cell-based proteome profiling. In red: Diazrine before (star) and after (circle) irradiation. In pink: TAMRA and/or Biotin azide capture reagents. CuAAC: Cooper(I)-catalysed alkyne-azide cycloaddition.

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#### Health

# Lithium determination in human serum with improved accuracy using potentiometric detection

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Lithium salts have been widely and effectively used as psychotherapeutic drugs in the treatment of bipolar disorders for more than 50 years. However, lithium requires careful determination of the correct dose for every patient because its levels are affected by each individual's metabolism and must be maintained within a relative narrow therapeutic range  $(0.5 - 1.2 \text{ mmol L}^{-1})^1$ . An overdose of lithium causes irreversible damage in the nervous system and kidneys and, in the other hand, a lithium level below the curable dose make the treatment ineffective. Therefore, lithium monitoring in blood serum has a critical and vital importance. Concerning this purpose, different analytical methods have been reported, namely atomic absorption spectrometry, flame emission photometry and potentiometry<sup>1</sup>.

Potentiometry based in ion-selective electrodes (ISEs) is widely used to perform billions of assays, mainly in clinical diagnosis through determination of electrolytes in biological fluids. ISEs allows simple measurements with inexpensive instrumentation and provide rapid results. However, for determination of lithium ions in blood serum, potentiometric sensors suffer from lack of selectivity towards sodium ions, since it is found naturally in human serum at quite high level (135 – 150 mmol L<sup>-1</sup>)<sup>2</sup>. Therefore, researchers have been still focusing on the developments of highly sensitive and selective lithium electrodes.

In this work, a lithium ISE based on a liquid polymeric membrane that contains lithium ionophore VIII and bis(butylpentyl)adipate (BBPA) as solvent mediator was successfully tested in flow injection analysis, presenting a linear slope of 53mV decade<sup>-1</sup> down to 0.1 mmol L<sup>-1</sup>. To overcome the low selectivity in the presence of sodium ions at physiological levels, a new approach based on the chemometric relationship between these two ions was tested. A quadratic 5-level D-optimal design was used with two variables (concentration of lithium and sodium ions) and one response (lithium signal, in mV) in a total of 15 experiments. Multiple linear regression (MLR) was used to correlate the potentiometric response with the independent variables. The model goodness-of-fit was evaluated using analysis of variance (ANOVA) at a 95% of confidence level, which include Q2 that is a measure of how the model will predict the responses for new experimental conditions, and R2 that is the percent variation of the response explained by the model. To validate the model, 13 independent experiments were used.

The model demonstrated a good prediction ability and a good correlation between the lithium concentration and the potentiometric signal, even in the presence of physiological sodium levels. The model has been tested through the analysis of spiked human serum in three levels of lithium concentration (below, within and above of therapeutic range) after a simple protein precipitation protocol. The results were quite promising because the method allowed determination of lithium in the post-spiked samples with great accuracy. However, the protein precipitation protocol should be improved in order to determine the lithium levels in the pre-spiked samples with great accuracy.

Future approaches include the determination of lithium levels in real samples from patients under treatment with lithium salts as well as the development of a simple electrochemical device for easily monitoring the lithium levels in order to minimise any risk of harm to the body.

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#### Health

# Activation of Natural Killer cells – targeting NKp30 with small organic ligands

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Natural killer (NK) cells provide rapid responses to viral-infected cells, and play a critical role in tumor immunosurveillance by directly inducing the death of tumor cells. Instead of acting via antigen-specific receptors, lysis of tumor cells by NK cells is mediated by alternative receptors, including NKG2D, NKp44, NKp46 and NKp30.

B7H6, a surface protein present on a broad panel of tumor cells, including lymphoma, melanoma and neuroblastoma, was identified as a ligand for the NKp30 receptor, namely through the structural elucidation of the NKp30-B7H6 complex. The comparison between the 3D structures of unbound and B7H6-bound NKp30 demonstrated marked conformational changes that may be a key-factor for the NK-response activation role of B7H6. Due to the difficulties in promoting the over-expression of the B7H6 marker in tumor cells, and the limited access to recombinant proteins and synthetic peptides, we set to design a family of small organic molecules (SOMs) capable of mimicking the effect of B7H6 on the NKp30 receptor.

Using computational tools (namely AutoDoc Vina) we designed a family of SOMs based on the structure of the NKp30 receptor. Synthetic, stability and overall binding score considerations were used to select a subfamily of ca. 15 compounds for synthesis. From these, 10 completely characterized entities were tested in an MS-based binding assay using the recombinant extracellular portion of the receptor, which led to the identification of one lead compound. Further refining of the lead structure, based on computational and synthetic approaches, was performed to improve the overall properties in terms of solubility, serum protein binding and stability.

Primary cultures of peripheral blood mononuclear cells (PBMCs) were used to probe the stimulation of NK cells by the lead compound.  $IC_{50}$  values below 1  $\mu$ M were found in TNF- $\alpha$ - and IFN-Y release assays with PBMCs and isolated human NK cells. Co-cultures of PBMCs and the human tumor cell line HepG2 were used to determine the effect of the lead compound in the cytotoxicity of NK cells. An increase of ca. 30% in NK cell cytotoxicity was found in cultures treated with 10  $\mu$ M of the lead compound.

Our lead compound was proven effective in activating the cytotoxic activity of NK cells, as demonstrated by the cytokine release and the tumor cell death assays. Further work aims to derivatize our ligands with tumor-targeting molecules to increase the specificity of the NK cell cytotoxic response.

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#### Health

# High-throughput screening of hydrochlorothiazide cocrystals by vibrational spectroscopy

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Low solubility active pharmaceutical ingredients (API's) are one of the biggest problems that the pharmaceutical industry must face nowadays. Cocrystals have been used as a viable solution to improve API solubility. Cocrystals are crystalline materials comprising at least two components (an API and a coformer) solid at room temperature and held together by non-covalent bonds. The screening of new cocrystals is one of the most important stages in cocrystal development. This stage is crucial for an efficient and rational cocrystal development however, is highly unpredictable and time consuming.<sup>[1]</sup> There is a lack of cocrystals screening methods capable of testing a wide range of coformers in a simple and fast way. Therefore, the aim of this work is to test a high-throughput cocrystal screening procedure based on vibrational spectroscopy: mid infrared, near infrared and Raman spectroscopy.<sup>[2, 3]</sup>

Hydrochlorothiazide (HTZ) is a poor soluble drug belonging to class IV of the Biopharmaceutical Classification System and was the API chosen for this study. Several coformers in two API:coformer ratios (1:1 and 1:2) were tested with different solvents, distributed in a 96-well plate (Figure 1). Cocrystallization was performed through a slurry ultrasoundassisted method. The study proved that vibrational spectroscopy techniques are feasible for cocrystal screening being able to determine cocrystal formation and purity.

Six coformers (adenine, citric acid, D(-)-mannitol, nicotinamide, *p*-aminobenzoic acid and tromethamine) produced cocrystals with HTZ These systems were afterwards subject to scale increase experiments to be further characterized by differential scanning calorimetry and X-ray powder diffraction and to determine cocrystals solubility.



Figure 1: 96-well plate used in ultrasound assisted cocrystallization for cocrystals screening.

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#### Health

# Development of a colorimetric immunosensor for *Toxoplasma gondii* serotyping

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Nanotechnology in medicine is becoming a major field, with promising applications in point-of-care diagnosis. Assays of colorimetric biosensing using gold nanoparticles (AuNPs) showed to be highly sensitive. There is an increasing need to develop or improve diagnosis/typing methods of infectious diseases in view of greater sensitivity and efficiency for both lab and field use. The aim of this work was to develop a simple, inexpensive, but highly efficient method for *Toxoplasma gondii* serotyping based on a bionanoconjugate biosensor. Toxoplasmosis is the most reported parasitic zoonosis in Europe, with implications in human health and in the veterinary field.<sup>1</sup> The expected biosensor is based on the optical properties of AuNPs, namely in the change in color from red to blue upon aggregation.<sup>2</sup> Gold nanoparticles were conjugated with a synthetic polymorphic peptide derived from GRA6 antigen specific for type II *T. gondii*. Different bioconjugation conditions were studied: AuNPs size, ratio [peptide] : [AuNPs] and pH. Sequential serum dilutions and two concentrations of salt were also tested. GRA6II-AuNPs aggregates in the presence of antibodies anti-GRA6II and with the correct concentration of salt.

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#### Health

# Carbon-Based Electrodes for Human Health Diagnosis: Detection of Stress Biomarkers in Sweat

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Stress related problems are being increasingly recognised as a global health issue. Monitoring of stress related biomarkers molecules in real time is of major importance to achieve a better understanding of stress physiology and pathophysiology. For biochemical evaluations, sweat represents a potential diagnostic fluid suitable for non-invasive sampling in the context of early and continuous biomarkers identification of stress diagnostics and its consequences in human health [1]. In this context, carbon-based materials are currently some of the most interesting tools to obtain analytical signals, in particular using electroanalytical techniques, due to its relative low cost versus its particular properties [2].

Analysis of biomarker levels in sweat is a potential tool for retrieving important data on human performance, health and well-being. In the present study, five biomarkers have been selected, L-Tyrosine, L-Phenylalanine, Dopamine, Serotonin and Hydrocortisone (Figure 1) for testing on different carbon-based electrodes. The goal is to determine the best representative sweat samples biomarkers and the best carbon-based materials to be used for its detection. The present results are the outcome of biomarkers patterns identification in simulated and real sweat samples by voltammetric techniques in the different electrode materials. The performance of the different carbon-based materials was compared.



Figure 1: Preliminary selected biomarkers for sweat samples analysis study.

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#### Health

### A first storage study of yoghurt produced under pressure

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Yoghurt is a semisolid dairy derivative fermented by two species of lactic acid bacteria (LAB), *Streptococcus thermophilus* and *Lactobacillus delbrueckii* ssp. *Bulgaricus*. These bacteria, when in favourable conditions for their growth and activity, use the nutrients naturally present in milk for their development, one of the metabolic pathways being lactic fermentation, producing lactic acid, leading to a decrease in pH that makes this product more stable, and with the aggregation of milk caseins [1]. Yoghurt is a world food product consumed and appreciated because of its structural characteristics, flavour and beneficial effects for health [2]. On the other hand, the composition of the yoghurt tends to change during its storage under refrigeration, due to the continuous activity of the remaining lactic acid bacteria and to the enzymatic activity. Most volatile compounds tend to decrease as well as the pH and firmness of the yoghurt [4]. As for syneresis, it increases until the first 10 days of storage, but then tends to stabilize. However, these changes depend essentially on the final pH of the yogurt after fermentation, the incubation temperature and the bacterial strains used [5]. Although fermentation occurs industrially under conditions favourable to the growth of lactic bacteria at atmospheric pressure, it is possible to create conditions for the fermentation to occur under unconventional conditions,

for example under high hydrostatic pressure [3] with potential to develop yoghurt with new characteristics, namely sensorial, due to possible metabolic changes induced by sub-lethal pressure. This work aimed to study refrigeration storage (4°C for 23 days) of yoghurt produced at 43°C under sub-lethal high pressure, at 10, 20, 30 and 40 MPa, in comparison with the fermentation process at atmospheric pressure (0.1 MPa). LAB (S. thermophilus and L. bulgaricus) and quality parameters like pH, titratable acidity, syneresis and colour were evaluated, along with textural analyses to infer how pressure would impact the obtained yoghurt along storage. In addition, a preliminary sensory analysis was conducted to ascertain the preference of the consumers for the yoghurts produced under pressure. Higher fermentation pressures resulted in slightly lower LAB loads (a maximum of 1.01 Log (CFU/mL)) and increased the fermentation time (a maximum of 3h 25 min) (Figure 1),





**Figure 1** -Variation of fermentation time according to pressure. Near to each point is represented the final pH obtained for each yoghurt produced.

syneresis (a maximum of 44 %), all for 40 MPa and firmness (a maximum of 2.5-fold) for 30 MPa. Under refrigeration, LAB were more active during the first 15 days of storage in yoghurts fermented under pressure (increasing loads up to 0.54 Log (CFU/mL)). Colour, pH and titratable acidity were not affected by pressure or storage [6]. Further research is of interest to ascertain the biotechnological potential of fermentation processes under sub-lethal high pressure in general and for yoghurt production.

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#### Health

# A naphthoquinones screening shows the ability of 5-hydroxy-1,4naphtoquinone to modulate cytochrome *b*<sub>5</sub> reductase activity

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Cytochrome  $b_5$  reductase ( $Cb_5R$ ) is a pleiotropic enzyme that participates in multiple cellular pathways.  $Cb_5R$  is able to produce superoxide anion, in the absence of electron acceptors and becomes stimulated in the presence of some redox partners like cyt *c*, leading to an increase of NADH oxidation rate and oxygen consumption (*1*, *2*). By other side, naphthoquinones are natural pigments widely distributed in nature, some of them with important biological activities for humans and others used in traditional medicine. In this work, we found that 5-hydroxy-1,4-naphthoquinone is able to uncouple the activity of recombinant human erythrocytes  $Cb_5R$  by inhibiting the electron pathway from NADH to its natural and artificial acceptors (**Scheme 1**). Moreover, upon complex formation with cytochrome  $b_5$  reductase, 5-hydroxy-1,4-naphthoquinone is able to act as an electron acceptor leading to a NADH consumption stimulation and increase of superoxide anion production. Our results suggest that  $Cb_5R$  is a potential target for 5-hydroxy-1,4-naphthoquinone toxicity upon erythrocytes exposure.



**Scheme 1**: Scheme of cytochrome  $b_5$  reductase mode of action in relationship to its electronic acceptors, in the absence (a), and presence of 5-hydroxy-1,4-naphthoquinone (b).

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#### Health

## **Stress Biomarkers Detection Through Non-Invasive Methods**

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Stress Human emotions study through biomarkers is a recent field with high importance to all modern society. Imbalanced parameters to external stimuli induce stress both physical as psychological<sup>1</sup> that has been related to several diseases and discordant social behaviour. In the STRESSENSE project, civilian, military and business' association researchers (from FCT-NOVA, CINAMIL/Academia Militar and CITEVE) are united with the common goal to study and early detect stress biomarkers, through non-invasive methodologies (using sweat as target biological fluid), and able to operate in field with real-time monitoring and integrated in wearables (Figure 1)<sup>2</sup>. The project has a multidisciplinary team for the biomarker's patterns identification and in-situ measurement devices development with extensive expertise in electrochemistry, biochemistry, biomolecules detection, materials and data-processing, together with knowledge associated to individuals' emotional and physical behaviour. The volunteers from Portuguese Army (Academia Militar) will take part of a case-of-study that will allow making the proof-of-concept of the new proposed medical methodology. After validation, the novel sensors will be integrated in fabrics aiming to attain a wearable device. The new biotechnology sensing devices to be developed have high interest to medicine, sports and health care services, allowing continuous monitoring of stress related parameters and its correlation to the global individual health conditions.



Figure 1: Project outline.

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#### Health

# Unforeseen tandem Ullmann type C – N coupling and dehydrative cyclization of a thioxanthone and guanidine

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Thioxanthones are heterocyclic compounds, capable of exerting multiple biological properties and prone to chemical modifications, making them privileged structures. Antitumor and efflux pump inhibition (EPI) are some of the most relevant activities displayed by these compounds. <sup>1</sup> The aim of this work is to find thioxantone derivatives capable of modulating bacterial efflux pumps and, therefore, fighting this antimicrobial resistance mechanism. Phenyl-arginine- $\beta$ -naphthylamide, an important resistance-nodulation-division efflux system inhibitor, comprises in its structure a guanidine moiety. As such, adducts with this scaffold were chosen for synthesis of novel bacterial EPIs following a structure-based design approach. <sup>2</sup>

The referred synthetic approach concerned a copper catalyzed Ullmann type C - N coupling, using potassium carbonate as base and methanol as solvent, at 100° C for approximately 48 hours. Unexpectedly, a further dehydrative cyclization occurred, yielding novel thiochromene quinazolines (**Figure 1**).

The structures of these compounds have been determined by <sup>1</sup>H and <sup>13</sup>C nuclear magnetic resonance, high-resolution mass spectrometry and X-ray crystallography. Although the formation of the quinazoline structure has been previously described through this reaction <sup>3</sup>, the thiochromene quinazoline scaffold herein described is novel, to the best of our knowledge, and the pursuit of its biological investigations should yield promising results.



Figure 1: General structure of a thiochromene quinazoline.

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#### Health

# Volatilomics skinprinting as an untargeted approach to identify putative biomarkers of neurodegenerative diseases

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Neurodegenerative diseases (NDDs) are a great public health concern. They constitute a heterogeneous group of disorders characterized by the progressive degeneration of the structure and function of the central or peripheral nervous system. Among NDDs, Alzheimer's and Parkinson's diseases are the most prevalent and their incidence is increasing concomitantly with the average life expectancy.<sup>1</sup> While there aren't yet robust biomarkers for most NDDs, their diagnosis relies essentially on the clinical symptoms. However, neurodegeneration begins long before the patient experiences any symptoms. Therefore, there is an obvious interest in the early diagnosis of NDDs. This would allow the anticipation of the treatment and mitigation of the negative effects of neurodegeneration.

The characterization of the volatile organic compounds (VOCs) composition of different human biofluids is being explored as a promising and non-invasive tool to unveil new biomarkers for the diagnosis of human diseases and infections. The VOCs profiles can provide important metabolic information, particularly about the metabolic changes caused by different clinical conditions, including NDDs. In this project we are developing new sampling procedures to explore the potential of skin VOCs as putative biomarkers for the non-invasive diagnostic of NDDs. In this context we are optimizing a solid phase micro extraction (SPME) methodology using polydimethylsiloxane (PDMS) membranes followed by gas chromatography coupled with mass spectrometry (GC-MS) to characterize the volatile profile of the skin of NDDs patients. Accordingly, several PDMS membranes of different suppliers and thicknesses were assayed and an effective and non-invasive method for the extraction and analysis of skin VOCs was developed. Ultimately, this will be a seamless tool for the identification of putative volatile biomarkers of different NDDs with a great potential to integrate in POCT devices for the clinical environment.

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#### Health

# Computational study of polyoxometalates in catalysis of phosphodiester bond hydrolysis for medical applications as artificial phosphoesterases

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The use of polyoxometalates (POMs) is arising as a promising alternative to cisplatin in treatments of cancer (1) due to its interactions with the phosphodiester present in DNA and RNA. In this study we analyse the interactions of POMs with model structures for the phosphodiester as 4-nitrophenilphosfate, the geometry, stability and reactivity for the hydrolitical cleavage of phosphoester bond will be studied in order to provide insight for a further design of nanobioinorganic artificial phosphoesterases.

For a complete understanding of the influence of the POM complex in the reaction mechanism, different structures of polyoxometalates will be considered to interact with the phophoester model compound,  $[X_2O_7]^2$ ,  $[X_5O_{15}]$ , and  $[X_7O_{24}]^6$ -(X=Mo, W). To achieve this aims, Density Functional Methods (DFT) have been employed to characterize the transition states for the phophoester hydrolysis in order to determine the reaction mechanisms and energy barriers.



Figure 1: hydrolysis of phosphoester cleavage catalysed by [Mo<sub>5</sub>O<sub>15</sub>]

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## Health

# Determination of nitrate and nitrite in human saliva with a specially designed microfluidic paper-based analytical device (µPAD)

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The concentration of nitrite and nitrate anions in human saliva has been primarily believed to be correlated with oral cancer and other disfunctions and infections in the mouth. However, newly found benefits to the presence of these ions in the oral cavity have been reported in a few recent studies. In any case, there is a connection between the NOx salivary concentration and the human health and therefore it has become more and more relevant to understand this connection. In this context, the objective of this work was to develop microfluidic paper-based analytical devices ( $\mu$ PADs) for nitrite and nitrate determination (**Figure 1**) in human saliva samples.

The choice of this type of approach is justified by the advantages provided by these devices, which make them ideally suited to conduct on-hand analyte determinations. While many of the current monitoring techniques require specialized skills, laborious laboratory processes, or/and expensive equipment, µPADs provide a very quick and cheap analytical measurement. Also, the minimal use of reagent and sample, coupled to its portability, makes the developed devices ideally suited for unskilled operators and regular monitoring. In this work, the determination of the nitrite and nitrate anions was based upon the modified colorimetric Griess reaction, in which the conversion of nitrate to nitrite was achieved using zinc powder.



Figure 1: Calibration curves for nitrite and nitrate determination obtained with the displayed µPADs devices.

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## Health

## Montelukast metabolic studies: a Mass Spectrometry approach

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Montelukast (MTK), a drug used in asthma management in children and adults, is a cysteine leukotriene receptor antagonist. Recently, MTK has been repurposed for other therapeutic applications, namely as an anti-inflammatory agent in the central nervous system. This opens the possibility of using MTK in some neurodegenerative disorders (e.g. Alzheimer's disease). MTK is also being studied as chemopreventive and adjuvant in cancer therapy and as preventive agent in cardiovascular risk settings. (1–3)

Despite its benefits, MTK metabolism is poorly understood and the U.S. Food and Drug Administration (FDA) recommends continuing ongoing surveillance due to the reported (particularly neuropsychiatric) adverse effects. To date, only five phase 1 and two phase 2 MTK metabolites have been identified and no association between metabolites and the adverse effects has been established. (4)

Taking into account the potential new applications of MTK, our initial goal was to evaluate the *in vitro* metabolism of MTK. To address this question, we performed MTK incubations with human liver S9 and microsomal fractions, and with recombinant human cytochrome P450 systems, as well as with different model peroxidases. The incubation products were analyzed by high performance liquid chromatography coupled to high-resolution electrospray ionization tandem mass spectrometry (HPLC-ESI-HRMS/MS).

In addition to the known MTK metabolites, we identified multiple new phase I metabolites that resulted from hydroxylation at different sites, S-oxidation, N-oxidation and oxidative dealkylation. Differences in the MS fragmentation patterns allowed us to identify the positions where oxidations took place, affording an unequivocal identification of the metabolites. In the presence of the adequate co-factors, we also identified new MTK-derived phase II metabolites, including glucuronides and glutathione and cysteine conjugates. Since MTK binds glutathione and cysteine, both under metabolic and non-metabolic conditions, these reactions could be biologically relevant. The involvement of a free radical-mediated pathway, with no need for bioactivation, could be related to the toxic effects attributed to MTK.

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## Health

# New anti-inflammatory drugs: less, equal or more topical actions on membrane lipids?

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Nonsteroidal anti-inflammatory drugs (NSAIDs) are used to treat inflammatory conditions (inflammation, pain and fever). Toxic adverse effects, associated with the long-term therapy with NSAIDs, are the main reason leading the discovery of new drugs with improved tolerability. One of the main strategies to achieve safer drugs is the association of existing NSAIDs with protective mediators, such nitric oxide (NO), phosphatidylcholines and hydrogen sulfide (H2S), that will be released *in vivo*.<sup>1</sup>

NSAIDs gastrointestinal toxicity is related to their effects on membrane lipids of the gastric mucosa.<sup>2</sup> Thus, this work aims to evaluate the effects of new NSAIDs, namely  $H_2S$ - and NO-indomethacin, and the corresponding traditional NSAID (indomethacin) on membrane lipids.

Langmuir monolayers, made of phosphatidylcholines and phosphatidylethanolamines (the main phospholipids of the gastric mucosa), were the chosen membrane mimetic systems. The evaluation of the interactions between the drugs and the membrane lipids were performed using biophysical techniques: surface pressure-area isotherms and Brewster angle microscopy.

Indomethacin, H<sub>2</sub>S-indomethacin and NO-indomethacin altered the organization of membrane lipids. Notably, the compounds associated with protective mediators exerted more pronounced effects (**Figure 1**), suggesting that they may be associated with a higher incidence of topical actions in the gastric mucosa. The balance between the deleterious topical actions and the protective effects of gasotransmitters will dictate the overall toxicity of these drugs *in vivo*. Even though, these studies are of utmost importance to predict the topical effects of novel drugs on membrane lipids and to choose the best candidates for clinical evaluation.



Figure 1: Surface pressure-area isotherms of 1,2-dipalmitoyl-*sn*-glycero-3-phosphocholine (DPPC) in the absence and presence of indomethacin and H<sub>2</sub>S-indomethacin (molar ratio: 9:1).

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## Health

# Amino Acids Profile for Assessing Serra da Estrela Cheese Producers

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This work has the purpose to evaluate if the Serra da Estrela cheeses collected from 6 producers have typical chemical characteristics, with controlled variability, considering that cheeses were produced during different time periods, the raw milk comes from different animals, and that the cheese processing may slightly differ between cheesemaking producers. For this, the cheeses' amino acids profile was used, since it gives evidence at chemical level about cheese's nutritional characteristics.

In this study, 6 cheese certified producers located in different municipalities of the region of Serra da Estrela were selected, being collected 24 cheeses, which were stored in plastic tubes at -20°C until analyzed. For each cheese, two samples were evaluated by UPLC–MS/MS (Dionex Ultimate 3000 UPLC instrument from Thermo Scientific, USA) equipped with a diode-array detector and coupled to a mass detector Linear Ion Trap LTQ XL mass spectrometer (ThermoFinnigan, San Jose, CA, USA) equipped with an ESI source. The chromatographic separation was carried out on a U-VDSpher PUR C18-E 100mm×2.0 mm id, 1.8 µm column (VDS optilab, Germany) and its temperature was maintained at 40 °C. The mobile phase was composed of (A) 0.1% (v/v) formic acid in water and (B) 0.1% (v/v) formic acid in acetonitrile/water (50:50, v/v), using a multistep gradient program at a flow rate of 0.40 mL/min and an injection volume of 5 µL. Data acquisition was carried out with Xcalibur®data system (ThermoFinnigan, San Jose, CA, USA).

The overall quantitative amino acid profile, found in the studied cheese samples included the following compounds: arginine, histidine, lysine, cysteine, asparagine, glutamine, glutamic acid, serine, threonine, aspartic acid, valine, methionine, proline, isoleucine, tyrosine, phenylalanine and tryptophan. In general, for each amino acid, a linear regression coefficient of determination (R<sup>2</sup>) greater than 0.98 was obtained. The experimental data were treated using a linear discriminant analysis (LDA), as the supervised pattern recognition method, aiming verifying if the amino acids profile (17 amino acids) could be used to correctly classify cheese samples according to their producer. An internal evaluation was considered using k-folds in order to minimize model over-fitting (reducing the risk of over-optimistic results) and the search included the evaluation of the optimal number of variables in the LDA model, between 2 to 17 independent variables, using a meta-heuristic simulated annealing variable selection algorithm.<sup>1,2</sup> Data was standardized (centered and scaled) and the obtained models in the cross-validation allowed an average classification accuracy superior to 90%, while the best model allowed correct classifications with a predictive sensitivity (proportion of positive correct classifications) greater than 95%.

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## Health

# Ternary complexes of fluoroquinolones as promising metalloantibiotics

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Fluoroquinolones (FQs) are antibiotics that have a large spectrum of action against Gram-negative and some Gram-positive bacteria. Nevertheless, the misuse and overuse of antibiotics has triggered the development of bacterial resistance mechanisms against these drugs. <sup>1-2</sup> One of the strategies to circumvent this problem is the complexation of FQs with copper (II) and phenanthroline (**Figure 1**). These complexes, known as metalloantibiotics, are very stable under physiological conditions and might adopt an alternative translocation pathway through the bacterial membranes. <sup>3</sup> In order to clarify the translocation pathways in Gram-negative bacteria, the location of FQs and metalloantibiotics was assessed through the changes in the thermotropic properties of the *E. coli* total lipid extract liposomes in the presence of the compounds, by steady-state fluorescence anisotropy. Microbiological studies using susceptible *E. coli* strains and their derived porin-deficient mutants were also performed to evaluate the role of OmpF and OmpC in the translocation of FQs and metalloantibiotics was determined against several MDR clinical isolates. The biophysical and biological results obtained show a much more hydrophobic location of the metalloantibiotics than of the pure FQs and suggest that metalloantibiotics have a promising ability to bypass, at least, one of the metanisms of the bacterial resistance to fluoroquinolones (based on alterations on the permeability of the bacterial membrane). All studies were performed under physiological conditions of pH and temperature and comprised five FQs and the respective metalloantibiotics.



Figure 1: Representation of the cationic complex [Cu(cpx)(phen)] +, from <sup>3</sup>.

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## Health

# Anti-Candida Performance of gold and silver camphor imine complexes

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The synthesis of new silver and gold complexes using camphor imines as ligands (**Figure 1**) aims at identify molecules with high antimicrobial properties that may act as alternative drugs to fight resistance of fungi and bacteria to the antimicrobials actually in use. According to the European Centre for Disease Prevention and Control, infections by bacteria are responsible for ca. 33 000<sup>1</sup> deaths *per* year while fungal infections caused by Candida reach yearly 700,000 people with an estimated mortality rate of ca 45%, according with information obtained by the Global Fund for Fungal Infections.

Within the ongoing work, several silver (e.g.  $[Ag(NO_3)L]$ , [Ag(OH)L], [AgCIL], $[AgL_2(\mu-O)]$ ) and gold complexes  $[Au(CN)L] \cdot CH_3CN$ ,  $K[Au(CN)_2L]$  (**Figure 1**) with camphor ligands (L) were synthesized and characterized by spectroscopic (NMR, FTIR) and analytical techniques. The use of camphor imines as ligands has the peculiar attractive that through the choice of the mono- or bi-camphor character and the imine substituent (Y or Z) the electronic and steric properties of the complexes can be tuned.



Figure 1: Representative examples of the complexes under study.

The antibacterial activity (S. aureus Newman, B. contaminans IST408, E. coli ATCC25922, P. aeruginosa 477) and the antifungal properties against the more relevant infectious Candida species (albicans, glabrata, parapsilosis, tropicalis) of selected Ag(I) complexes were experimentally assessed through their MIC values.<sup>2,3</sup> In some cases the cytotoxic properties (IC<sub>50</sub>) towards A2780 and A2780cisR cell lines were also evaluated as well as their toxicity towards HEK 293 cell line.<sup>4</sup>

To try to reduce the toxicity of the complexes that was evaluated towards V79 lung fibroblasts, the Ag(I) was replaced by the Au(I) core and  $NO_3$  by OH<sup>-</sup> or Cl<sup>-</sup> and the antifungal activities of the new complexes were evaluated. The results show that the anti-Candida (albicans, glabrata) activities of Ag and Au complexes with the same ligands are very different. The gold complexes display rather lower activity than the related silver complexes in agreement with a silver based antimicrobial activity.

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## Health

# Quality by design development of fusogenic magnetoliposomes

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Liposomes were the first delivery systems to make the transition from concept to clinical application, and they are now an established technologic platform with considerable clinical acceptance. Currently, there are about 15 therapeutic products available on the market, and there are several other liposome preparations in various stages of clinical trials.<sup>1</sup> Yet, there is still potential to improve them, and the combination of liposomes with magnetic nanoparticles enables the formation of multifunctional vesicles with a magnetic targeting for drug or gene delivery, magnetic fluid hyperthermia controlled drug release and contrast in imaging, which allows theranostic. In particular, the combination of liposomes with superparamagnetic iron oxide nanoparticles (SPIONs) are promising because of their magnetic behavior and their biocompatibility.

In this context, this work aimed to optimize SPIONs-loaded liposome formulations using a Box-Behnken design. Liposomes were prepared by the thin film hydration method followed by sonication, and the synthesis of SPIONs was performed through a microwave assisted method. In a quality by design concept to assist formulation and process design, the first step is to pre-define the desired final product quality profiles. This study focused on two critical formulation qualities, namely the SPIONs encapsulation efficiency and formulation particle size. These two product qualities are very important for both manufacturers and clinical application. A higher percentage of SPIONs encapsulation can reduce the manufacturing cost and increase the triggering of the heat rise while allowing greater flexibility in dosing. Another goal was to achieve a particle size lower than 300 nm, to enable administration and permeation through body tissues.

Thus, the effects of lipid concentration, SPIONs concentration and sonication time on encapsulation efficiency, size and polidispersity of the formulations were assessed (Figure 1). The optimized formulation was selected based on the model predictions and was experimentally prepared. The characteristics of the final formulation were in accordance with the predictions of the model.



Figure 1. Surface plot of fitted responses for (A) mean size (nm) and (B) encapsulation efficiency (%), depending on lipid concentration and sonication time variations, considering the same concentration of SPIONs.

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### Health

# Lewis Base Promoted Hydrosilylation of C=X Bonds with Pinacol-derived Chlorohydrosilane

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Catalytic hydrosilylations have been extensively explored in both academia and industry for the reduction of carbonheteroatom unsaturated organic compounds. A significant progress in metal-free hydrosilylation methods which is mostly achieved with Lewis bases/acids, has led to mild and selective reactions devoid of costly and toxic metal catalysts<sup>1,2</sup>.

To this end, we have developed a novel 5-membered cyclic pinacol-derived chlorosilane (**Scheme 1**) and explored its reactivity in a mild and selective Lewis bases promoted hydrosilylation protocol for the reduction of salicylaldehydes<sup>3</sup> and 2'-hydroxyphenone-derived iminiums<sup>4</sup> (**Scheme 2**). Our reduction systems have demonstrated good to excelent chemo and regioselectivity. Different Lewis bases were identified as the best promoters for the hydrosilylation with this novel pinacol-derived chlorosilane, depending on the electronic nature of the C=X bond. Nevertheless wide substrate scope and high functional group tolerance was observed for both systems studied, and the experimental observations reasoned based on density functional theory studies.



Scheme 1: Preparation of pinacol-derived chlorosilane (PCS).



Scheme 2: Lewis base promoted hydrosilylation of salicylaldehydes and 2'-hydroxyphenone-derived iminiums

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## Health

# Cationic photosensitizers and protein inhibitors: finding new ways to target antimicrobial resistance

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Over the last few decades, no major discoveries have been made regarding new, ground-breaking, antibiotics, which could resolve or, at least, delay the worrying onset of infections by multi-resistant gram-negative bacteria infections.<sup>1</sup> This has trigged an increasing interest in the search for different antimicrobial action mechanisms for which low to no resistance has yet been observed.

To this effect, photodynamic inactivation (PDI)<sup>2</sup> is a promising alternative, light-dependent, therapy for the treatment of localized infections.(Scheme 1) Herein we present our developments on the synthesis of a family of cationic phthalocyanines with varying structural features such as size of the cationizing alkylic chain, degree of cationization and central coordinating metal, which were obtained in good yield (42-71%). The antimicrobial activity of these new entities in combination with white light was tested against gram-positive, gram-negative bacteria and fungi. Remarkable differences were found between all cationic phthalocyanines as some were highly active in killing gramnegative species (*E. coli, P. aeruginosa*) and *C. albicans* in concentrations as low as 100 nM while leaving mammalian cells relatively unharmed, which makes them promising leads for treatment of localized infections.<sup>3</sup> We found a unique structure-activity relationship for this family of cationic tetra-imidazolyl phthalocyanines in the sense that it does not follow what was previously established by other authors, which may give new insights on the rational design of photosensitizers for use in PDI.

In parallel to this approach, new therapeutic solutions are needed for a systemic treatment of infections, which may encompass the design of novel inhibitors of underexplored bacterial targets. One of such targets is the subunit b of DNA gyrase,<sup>4</sup> for which there are no clinically available antibiotics with widespread use. Here we report our approach towards the development of new Gyrase b inhibitors based on computer-aided drug design, namely pharmacophore screening, de novo design and molecular docking.



Figure 1 - Schematic representation of PDI using the aforementioned family of cationic phthalocyanines.

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## Health

# Synthesis of new chemical entities based on Tetrapyrrolic Macrocycles for Medical Imaging

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Molecular imaging is a tool that allows the creation of visual representations of various parts of the human body, through the use of a single functional molecule, in order to detect early stage tumors and pharmacokinetic processes, drug action mechanisms and tumor growth processes, taking advantage of the strengths of each modality. Closely related, the emergence of "noninvasive" *in vivo* imaging revealed several "high-end" contrast agent based technologies, e.g. Positron Emission Tomography, Magnetic Resonance Imaging and Optical Fluorescence Imaging.<sup>1,3,4,5</sup>

Herein we report the synthesis of modulated tetrapyrrolic macrocyles to be used as potential redox Mn(III)/II) MRIcontrast agent, 64-Cu radiolabed to be used as potential PET contrast agents for early tumor detection and also some NIR dyes for FI imaging. We will also present some in vivo experiments to discuss the influence of structural modulation on the final tumor selectivity.



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## Health

## In vitro cholinesterase inhibition of five medicinal plants

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The number of people living with Alzheimer's disease is increasing worldwide. Current treatments include cholinesterase inhibitors such as donepezil, galantamine and rivastigmine and the N-methyl-D-aspartate receptor antagonist memantine. However, these drugs only relieve the symptoms, forcing scientific community to seek for alternatives. Nature remains the best source of drugs and drug leads and the therapeutic role of medicinal plants has been recognized as a result of the scientific scrutiny performed in the last decades to prove if treatment claims are confirmed or not. Thus, this study aimed at evaluating the potential of the aqueous extracts obtained from five medicinal plants – *Lavandula angustifolia* Mill., *Rosmarinus officinalis* L., *Curcuma longa* L., *Trigonella foenum-graecum* L. and *Hypericum perforatum* L. – to inhibit the activity of acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE).

From all the tested extracts, those of *R. officinalis*, *H. perforatum* and *L. angustifolia* were the most active ones against AChE ( $IC_{50} = 1068 \mu g/mI$  and  $IC_{25} = 368 \mu g/mI$ ;  $IC_{50} > 1549 \mu g/mI$  and  $IC_{25} = 1166 \mu g/mI$ ; and  $IC_{50} > 2800 \mu g/mI$  and  $IC_{25} = 1524 \mu g/mI$ , respectively). For BuChE, the same order of potency was observed for these extracts, with *R. officinalis* being the most active one ( $IC_{50} = 859 \mu g/mI$ ). A weak inhibition was observed for the extracts produced with *C. longa* and *T. foenum-graecum*. In order to establish a relationship between the observed bioactivities and extracts composition, HPLC-DAD analyses were carried out revealing the presence of several classes of phenolic compounds, including hydroxycinnamic acids, *C*-glucosyl-flavones, flavan-3-ols, *O*-glucosyl-flavones, flavan-ones and curcuminoids.

The results provided evidence of the value of medicinal plants as a source of health-promoting phenolic compounds.



Figure 1: AChE and BuChE inhibition of *R. officinalis* (O), *H. perforatum* ( $\blacksquare$ ) and *L. angustifolia* ( $\Delta$ ).

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## Health

# Unraveling Selectivity Issues in Palladium-catalyzed Quinoline N-Oxide C-H Activation

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Transition-metal catalysis is key for the organic synthesis behind many natural products, agrochemicals and, most importantly, active pharmaceutical ingredients.<sup>1</sup> In this scope, Pd-catalyzed C-H activation is extremely important, allowing for instance the coupling between carbon atoms of different molecules. Wu *et al.* have attempted the synthesis of modified quinoline N-oxides in different experimental conditions<sup>2</sup> and have found that these determine whether the C-C coupling occurs on C-8 or C-2 positions of the substrate and if it is accompanied by side-reactions that lead to functionalized products. In general, in the presence of PdCl<sub>2</sub>, when the oxidant is TBHP, BQ or DTBP, the reaction occurs at C8 (Scheme 1) and **A** is obtained. Addition of water leads to the formation of **B**. Pd(OAc)<sub>2</sub> is a poor catalyst for this C8 activation, but it activates the C2 position,<sup>3</sup> in analogous conditions, to yield **C**. Three possible products have, thus, been obtained (Scheme 1). Here, we explore the mechanisms of these competing reactions using a DFT methodology (Gaussian09, PBE0/Def2-TZVP (Pd)//6-311G<sup>\*\*</sup> (others)). The pathways for the C-C coupling in positions C-2 and C-8 of the substrate were calculated with both PdCl<sub>2</sub> and Pd(OAc)<sub>2</sub> as catalysts. The role of radicals on C8 activation and the occurrence of a nucleophilic attack by a water molecule on C-2 along with C-H activation of C-8 was also studied. A mechanism for these reactions will be proposed.



Scheme 1: Experimentally observed reaction paths for Pd(II)-catalyzed quinoline N-oxide C-H activation.

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## Health

# Effect of Hyperbaric Storage on Blood Preservation

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Blood is a high value product, whose storage and preservation are of major importance. Currently, the storage of blood and its components is made under refrigeration conditions (1-6 °C) or freezing, having a self-life of 35-42 days for red blood cells and whole blood, 5 days for platelets under refrigeration and up to an year for frozen plasma<sup>12</sup>. However, the self-life of these products is limited due to the haemolysis rate, microbial growth and protein denaturation, depending on the blood component.

In this work, a new preservation methodology (hyperbaric storage, HS) was used to study and evaluate the possibility to preserve blood. HS is being widely studied for the storage of products under mild hydrostatic pressure (up to about 200 MPa) for different periods of time, and has been mainly applied in food matrices as a possible replacement/improvement method to conventional refrigeration processes<sup>3</sup>.

The application of hydrostatic pressure treatments for pasteurization in blood was reported before<sup>45</sup> with a pressure range bigger than the pressures used in HS, aiming non-thermal pasteurization, promoting destruction of red blood cells.

In this study, porcine blood (with and without a preserving additive solution) was stored between 0.1 and 50 MPa with temperatures of 10°C and uncontrolled room temperatures (~20°C) to evaluate the effect of pressure (HS) on microbial growth, haemolysis rate and pH. Refrigerated samples (RF) were also used as control for further comparation.

Results showed that microbial growth was inhibited when used pressures of 50 MPa with or without the combination with low temperatures. However, for this pressure, haemolysis rate was higher, reaching 0.8% of haemolysis (the limit clinically used to discard blood) before the 35 days of shelf-life when kept under RF conditions. For lower pressures (25 MPa) and 10°C, the haemolysis is slower, however microbial growth was verified at rates similar to refrigeration, but for both pressures, the haemolysis rate was superior than the haemolysis rate for the samples storage under RF conditions (control).

The use of HS in combination with lower temperatures might show better results, since metabolic rates are lower minimizing the haemolysis rate and will be studied further.

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## Health

## Síntese de Potenciais Agentes Bimodais para Imagiologia Médica

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A Imagiologia Médica (IM) envolve a utilização de várias tecnologias não invasivas para criar imagens distintas do interior do corpo humano, com o intuito de permitir o diagnóstico precoce de diferentes patologias.<sup>1,2</sup> Algumas das modalidades mais importantes em IM são a tomografia por emissão de positrões (do inglês PET)<sup>3</sup>, e a imagem por ressonância magnética (do inglês MRI)<sup>2</sup>,existindo também outras em grande desenvolvimento, como por exemplo a imagem por ressonância de fluor-19 (do inglês <sup>19</sup>F-MRI)<sup>3</sup>.

Individualmente, cada técnica pode não ser capaz de fornecer toda a informação necessária; contudo a combinação de mais que uma técnica poderá possibilitar o aumento da eficiência do diagnóstico pelo fornecimento de imagens com melhor precisão e resolução, e assim obter, informações moleculares e fisiológicas anatómicas dos tecidos com elevada sensibilidade e resolução espacial facilitando, posteriormente, o tratamento das doenças. Uma vez que estas técnicas necessitam da utilização de agentes de contraste, nos últimos anos tem-se verificado um crescente interesse no desenvolvimento de agentes de contraste bimodais, de forma a ultrapassar as deficiências inerentes de cada técnica.

Nesta comunicação apresentamos a síntese e caracterização de três classes de N-ligandos, nomeadamente porfirinas, salens e ciclenos, para potencial obtenção de compostos bimodais para aplicação em técnicas combinadas de imagiologia médica (PET, MRI ou <sup>19</sup>F-MRI) (Figura 1).



Figura 1: Estrutura do composto bimodal sintetizado.

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## Health

# Spectrofluorimetric determination of iodine in urine samples with on-line UV photooxidation using a miniaturized analyzer chip in a multi-syringe flow system

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lodine is a nutrient and a component of the thyroid hormones essential for human growth and development <sup>1</sup>. The determination of the iodine status is based on the concentration of iodine excreted in urine <sup>2</sup>. Several detection systems are used to quantify iodine in urine, namely spectrophotometric, potentiometric, and ICP-MS. Most of the spectrophotometric methods for the determination of urinary iodine are based on the Sandell-Kolthoff reaction <sup>3</sup>. The method proposed in this study consists in a fluorometric detection of the catalytic effect of iodide on the redox reaction between Ce(IV) and As(III), using the Sandell-Kolthoff reaction, in a miniaturized chip-based flow manifold. This method was based on a previous work using an advanced three-dimensional chip device and direct spectrofluorimetric quantification of iodide in sea water <sup>4</sup>. The proposed method was adjusted for the determination of iodine in urine samples; this implied to eliminate interferences (namely from thiocyanate) and release iodine from organo-iodine compounds. To accomplish this objective, an on-line oxidation process aided by UV radiation was implemented in the developed system. The developed method is simpler, faster and more sensitive than the classic approach of the Sandell-Kolthoff reaction <sup>3</sup>.

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### Health

## New fluorescing tools for detection of protein aggregation

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Luminogenic materials have attracted much interested recently, in particular fluorophores with aggregation-induced emission enhancement (AIEE).<sup>1</sup>

Protein aggregation is well documented and is related with aging and age-related diseases, such as neurodegenerative (Alzheimer, Huntington, Parkinson or prion disease), cancer and cardiovascular (atherosclerosis, heart failure and ischemic heart disease).<sup>2</sup> Fluorescence-based techniques have been a reliable tool for the study of such protein aggregates, especially fluorophores with AIE properties.<sup>3</sup>

The synthesis of new fluorophores will be presented, such as boron complexes with pyridine/phenol ligands (**Scheme 1**). Boron complexes are known to be highly fluorescent in solution, and have been used in biological imaging as fluorescent probes. Their sensitivity to the surrounding environment allowed their use as sensor, for example to monitor the presence of toxic substances. The peripheral aromatic rings are responsible for the AIEE properties of the dyes. Herein we report our recent work on the synthesis and characterization of new fluorophores, as well as the study of their AIEE properties. The application of the best performing candidates as protein aggregates fluorosensors in *in vitro* and *ex vivo* models will also be addressed.



Scheme 1: Synthesis of new Boron complexes.

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## Health

# Dealing with copper stress - multicopper oxidases in pathogenic Grampositive bacteria

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Copper is an essential trace element required by all organisms, as a structural and/or catalytic cofactor in several enzymes. However, free copper ions are highly toxic due to their ability to generate reactive oxygen species, via Fentontype reactions, which damage lipids, DNA and proteins<sup>1</sup>. Thus, it is crucial for any organism to tightly control the intracellular concentrations of copper ions, a role played by dedicated homeostasis systems, including coppertransporting P-type ATPases, copper chaperone and, more recently identified, the multicopper oxidases (MCO) that are present in several microorganisms, mainly Gram-negative<sup>2,3,4</sup>. Copper derivatives are commonly used as feed supplements for livestock and as bactericidal agents. Furthermore, copper is also used by the host immune system to prevent infection, present at higher levels in the brain and lungs, organs that are infection sites of *Staphylococcus aureus* (meningitis and pneumonia). The emergence and transfer of multidrug resistance genetic elements that also carry heavy metal resistance genes is increasing and is particularly relevant for multi-resistance development in *S. aureus*.

The aim of this study is to clarify the role of multicopper oxidases in copper resistance of different strains of *S. aureus*. The multicopper oxidase gene were cloned for heterologous expression in *Escherichia coli* and purified to homogeneity. The biochemical and kinetic properties are currently being performed. In parallel, the minimal inhibitory concentration (MIC) to copper and other heavy metals are being estimated for different *S. aureus* strains, for aerobic, microaerobic and anaerobic growth conditions, as well as the impact of copper on the biofilm formation.

The results obtained until now showed that the *S. aureus* MCO heterologously produced presents copper oxidase activity. We observed that the copper MIC is strain-dependent, and is associated with the presence and localization (chromosome/plasmid) of the operon that contains the MCO. Furthermore, the impact of copper in bacterial growth was shown to be higher under anaerobic conditions.

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## Health

# Hemoglobin-Acrylamide Adduct - a Spectroscopic Study

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Acrylamide is a neurotoxic and carcinogenic organic compound<sup>1</sup> that is able to bind to several biomolecules and form adducts, through the glycation process and the *in vivo* Maillard Reaction, interfering with the biological functions of these molecules. In this work the acrylamide ability to bind to hemoglobin was examined using different spectroscopic techniques. Hemoglobin is one of the most abundant intracellular blood proteins, and the binding of acrylamide could alter some of its properties, such as its stability and function to transport oxygen<sup>2,3</sup>.

The interaction of the acrylamide with hemoglobin was accessed in a 20:1 ratio, and after a 72h-incubation period, a decrease of ca. 50% in the absorbance of the hemoglobin's Soret band was observed, suggesting that acrylamide could be binding in close proximity to the heme or heme pocket. This observation was confirmed by perturbation of the Circular Dichroism spectrum in the visible region, which also showed changes consistent with perturbation of the heme pocked. These perturbations do not correspond to the loss of the heme group and were partially reverted after passing the protein through a size-exclusion chromatographic matrix.

Further studies are being carried out, namely analysis of the interaction by mass spectroscopy to determine whether the interaction between hemoglobin and acrylamide has a covalent in nature, and if so, determine its binding site. The identification and characterization of the hemoglobin-acrylamide adduct is of extreme importance and it can be used as a biomarker for the exposure to this organic compound.

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## Health

# Spiropyrazoline oxindoles: Promising p53 pathway activators for the development of new anti-tumor drugs

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One of the most appealing targets for developing anticancer treatments is the p53 transcription factor. This protein is involved in tumor suppression by triggering cell death, cell cycle arrest and senescence, and it is inactivated in all types of cancers either by mutation or inhibition by endogenous negative regulators (e.g. MDM2 and MDMX). Several p53-MDM2 interaction inhibitors have been developed and some are currently in clinical trials. However, recent studies indicate that to take full advantage of p53 activation, both MDM2 and MDMX need to be targeted. As most MDM2 inhibitors lack significant potency against MDMX there is a huge interest to develop dual inhibitors of MDM2 and MDMX.<sup>1</sup> We have developed novel chemotypes that activate the tumor suppressor p53 by inhibition of the p53-MDMs interactions. Structure-activity relationship studies led to the discovery of promising inhibitors which are being optimized towards clinical candidates.<sup>2</sup> More recently, we have reported spiropyrazoline oxindoles (**Figure 1**) that are able to induce apoptosis and cell cycle arrest, and upregulate p53 steady-state levels, while decreasing its main inhibitor MDM2 in human colorectal carcinoma cell line.<sup>3</sup> These compounds were also able to reduced stemness, while promoting chemotherapy sensitization in glioma cancer cells (GL-261).<sup>4</sup>

In this communication, recent developments in the optimization of this scaffold will be discussed, with a focus on the development of dual inhibitors of MDMX and MDM2.



Figure 1: Optimization of spiropyrazoline oxindoles as MDM2/X inhibitors.

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## Health

# Automated solid-phase extraction using a bead-injection lab-on-valve approach coupled to liquid chromatography and mass spectrometry for determination of tranexamic acid in urine

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Tranexamic acid (TXA) is an important antifibrinolytic agent used in adult trauma patients with on-going significant haemorrhage, or at risk of significant haemorrhage within 8 h of injury.<sup>1,2</sup> Results from clinical trials suggest a wide variability in response to TXA and, thus, the optimum dose and administration schedules of TXA are subject of intense research. In fact, the elucidation of the pharmacokinetics and pharmacodynamics of this drug is still under scrutiny. TXA has been determined in different types of biological matrices, such as plasma, serum and urine.<sup>2</sup> In this determination, the success of sample preparation step is crucial for the elimination of interfering compounds from the matrix and also for analyte pre-concentration.<sup>2,3</sup> Solid-phase extraction (SPE) is one of the most versatile methods of sample preparation and the automation of this approach increases precision by reducing human intervention.<sup>3</sup> Therefore, the main purpose of this work was the development of an automatic micro-solid phase extraction (µSPE) method coupled to liquid chromatography and mass spectrometry for the determination of TXA in urine samples. The SPE procedure was implemented using bead injection (BI) in a mesofluidic lab-on-valve (LOV) flow system to perform this procedure automatically. The different SPE steps, from sample loading to analyte elution, were controlled by computer programming. For the implementation of the µSPE-BI-LOV method, three commercially available sorbents were tested, namely OASIS-HLB, -MCX and -MAX. Furthermore, different SPE parameters were evaluated, including eluent and carrier composition, matrix removal solution and sample loading volume. Separation and detection were based on ultra-high-performance liquid chromatography coupled to triple quadrupole-tandem mass spectrometry.<sup>4</sup> Chromatographic separation was achieved using a BEH Amide column (50 x 2.1 mm; 1.7 µm particle size), maintained at 40 °C. The mobile phase consisted of a mixture of acetonitrile-aqueous ammonium bicarbonate (pH 7.4; 10 mM), at a flow rate of 0.1 mL min<sup>-1</sup>. The MS was operated in positive ionization mode (ESI<sup>+</sup>) and data was acquired in selected reaction monitoring (SRM) mode (m/z 158.25 > 95.15 for quantification, and m/z 158.25 > 123.20 for identification). Preliminary experiments using TXA standards revealed that OASIS-HLB and -MCX sorbents permitted to achieve higher recovery percentages (ca. 80%). However, as higher repeatability was obtained using OASIS-HLB, this sorbent was selected for further experiments. Concerning matrix removal, the use of 0.1% (v/v) of formic acid as washing solution permitted to increase analyte recovery. The eluent composition and the sample loading volume were also studied, with a mixture of acetonitrile-aqueous ammonium bicarbonate (pH 7.4; 10 mM) (75:25, v/v) and 1000 µL of sample providing, respectively, the best results. On the other hand, the use of aqueous ammonium bicarbonate (pH 7.4; 10 mM) or water as carrier did not affect the analyte recoveries. The method is currently under development targeting the application to urine samples recovered during scoliosis surgery.

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## Health

# Synthesis of New Hetero-Arylidene-9(10*H*)-Anthrone Derivatives and Biological Evaluation as Antiproliferative Agents

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Anthraquinones are privileged structures from natural sources, such as pigments, vitamins, and enzymes. Besides their utilization as dyes, anthraquinone derivatives have long been used in medical applications.<sup>1</sup> The anthrone analogs are compounds similar to anthraquinone where a carbonyl group is replaced by a substituted alkene. Some anthrone derivatives have shown potent *in vitro* antitumor activity.<sup>2</sup> Recently, we disclosed for the first time, an hetero arylidene-9(10*H*)-anthrone (1, R=Et, X=I) formed by reaction of 9-anthracenecarboxaldehyde with 1,2-dimethyl-3-ethylimidazolium iodide (2, R=Et, X=I) under basic conditions (Scheme 1).<sup>3</sup> In continuation of this work, two main approaches were followed towards the preparation of new hetero arylidene-9(10H)-anthrone derivatives (1), using the imidazolium ring substituents and the counter anion as targets for structural diversity. The cytotoxicity of the compounds was analyzed in human ovarian (A2780) and colorectal (HCT116) carcinoma cell lines and in normal human fibroblasts showing different activities mainly as a function of the R group.



Scheme 1: Synthesis of hetero arylidene-9(10H)-anthrone (1) derivatives.

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## Health

# Synthesis of porphyrin-peptide conjugates by copper(I)-catalysed azide-alkyne cycloaddition

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Porphyrin macrocycles are a class of naturally occurring molecules involved in several important biological processes ranging from oxygen transport to photosynthesis. These macrocycles present a number of potential applications, including as optical sensors and as photosensitizers (PSs) for photodynamic therapy (PDT) of cancer.<sup>1</sup> In the last 20 years, various porphyrin-peptide conjugates have been synthesized as promising PSs showing improved pharmacokinetic, solubility and specificity to the cancer tissues.<sup>2</sup>

Here, we describe the synthesis of new porphyrinic bioconjugates *via* the copper(I)-catalysed azide-alkyne cycloaddition (Huisgen [3+2] cycloaddition) of the azide functionalized metalloporphyrin **1** and an alkyne, aiming to achieve new PSs for application in PDT. The cycloaddition was optimized using metalloporphyrin **1** and phenylacetylene, in the presence of L-ascorbic acid sodium salt and copper(II) sulfate, in DMSO, and then applied to the anionic peptide **2**, which is known to cross efficiently the blood-brain barrier (BBB) (Scheme 1).<sup>3</sup> Experimental procedures and spectroscopic data of the new macrocycles, including conjugate **3**, will be presented and discussed.



Scheme 1: Copper(I)-catalysed azide-alkyne cycloaddition of metalloporphyrin 1 and anionic peptide 2.

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## Health

# Ohmic heating approach to pyridyl and *N*-methylpyridinium analogues of rosamines: photophysical properties and behavior towards ethanol

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From the photophysics point of view, rosamine compounds are excellent backbones to engineer fluorescent molecules featuring robustness and chemical versatility suited for a wide range of fluorescence measurements and imaging.<sup>1</sup> Here we prepared a new series of pyridyl analogues of rosamines (**2a-c**) by employing two methodologies (Scheme 1): (i) the conventional approach involving the *p*-toluenesulfonic acid catalyzed condensation of a pyridinecarboxaldehyde with 3-(diethylamino)phenol in propionic acid, under oil-bath heating, and (ii) the novel ohmic heating assisted condensation under 'on water' conditions, followed by oxidation. The 4-pyridyl rosamine (**2a**) was further converted into *N*-methylpyridinium analogue (**2a\_Me**) via *N*-alkylation using methyl iodide in *N*,*N*-dimethylformamide.

The compounds were characterized by NMR, UV-Vis and fluorescence spectroscopies, single-crystal X-ray diffraction and thermogravimetric analysis in order to infer the influence of the position of the nitrogen atom, and also of the cationization of the pyridyl ring, in the physicochemical properties of these xanthene rings.

The behavior of compounds **2a** and **2a\_Me** in ethanol solution was studied by spectroscopic methods. The results revealed that although no change was detected with **2a**, an extinction of color and fluorescence was observed for **2a\_Me**, which resulted from the addition of one ethanol unit to the electrophilic position 9 of the xanthene-pyridinium derivative with the formation of compound **4a**. This process is reversible, meaning that compound **2a\_Me** can be rapidly recovered by decreasing the pH (eg with trifluoroacetic acid), pointing to a potential application of **2a\_Me** as a chemosensor of alcohols.



Scheme 1: Synthesis of pyridyl and N-methylpyridinium analogues of rosamines and sensing behavior of 2a\_Me towards ethanol

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## Health

# In silico studies towards new BACE-1 inhibitors

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Beta-site APP-cleaving enzyme (BACE-)1 is a type-1 membrane-anchored aspartyl protease playing an essential role in the release of A $\beta$  peptides and Alzheimer's Disease (AD) progression. Hence, the development of potent BACE-1 inhibitors represents a logical approach for AD therapy development and it have been widely explored by the pharmaceutical industry worldwide.<sup>1</sup>

Herein, we report the design of a virtual library of 300 compounds for *in silico* BACE-1 inhibition assessment. These compounds arise from the conjugation of several fragments with aliphatic and aromatic amines, motifs identified in the literature by their ability to establish essential interactions with the amino acids present in the catalytic pocket of BACE1.

Affinity for BACE-1 was measure through the binding energy estimation of the ligand-protein complex. Additionally, the compounds designed were assessed through the Lipinsky's rule of 5 and additional attributes crucial for central nervous system (CNS) drugs were also considered.<sup>2</sup>

The most promising compounds will be synthesized through suitable and green N-alkylation techniques and their biological activity will be assessed in *in vitro* studies. Preliminary synthetic procedures to obtain the first derivatives will be presented.

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## Health

# Exploratory assessement of carbonylative Suzuki coupling for the synthesis of benzophenones

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Xanthones are secondary metabolites that are found in terrestrial or in marine environments.<sup>1,2</sup> This class of compounds shows several interesting biological activities, namely, antimicrobial, antitumor, anti-inflammatory, among others.<sup>3</sup> The development of routes for the synthesis of xanthone derivatives has stirred great interest.<sup>3</sup>

Benzophenones are important key intermediates in the synthesis of xanthones. The most common methodologies to obtain these important precursors are the Friedel-Crafts acylation of arenes or the 1,2-nucleophilic addition.<sup>3-5</sup> Alternatively, new strategies based on palladium-catalyzed carbonylative Suzuki coupling reactions have been developed.<sup>4,5</sup>

In this work, we performed an exploratory assessment of carbonylative Suzuki coupling for the synthesis of benzophenones (**Scheme 1**). The effect of the substituents in aryl bromide *ortho* or/and *para* positions was evaluated making to react a range of aryl bromides with the same aryl boronic acid. The best reaction selectivity and yields were accomplished by testing different palladium catalysts, ligands, bases, and solvents. These results allow the fine optimization of this synthetic pathway.



Scheme 1: A carbonylative Suzuki coupling reaction to obtain a benzophenone in one step, using an aryl bromide and an aryl boronic acid.

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## Health

# Fluorescent Boronic Acid Salicylidenehydrazone (BASHY) complex for studying lipid droplets influence on drug effectiveness

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Lipid droplets (LDs) are intracellular lipid-rich organelles that regulate the storage of neutral lipids and recently they were found to be involved in many physiological processes, as well as diseases including obesity, diabetes and cancers.<sup>1</sup> Interrupting cancer progression involves a variety of biological process to be considered and multifunctional constructs with stability and reversible proprieties are necessary to internalize and release cargo into cells.

On the basis of our experience<sup>2</sup> we envisioned that a promising strategy to create such compounds could take advantage of iminoboronates, prepared by using Schiff-base ligands and BAs.

Here is presented the development of the synthetically and functionally flexible BASHY (boronic acid derivated salicylidenhydrazone) complexes. This platform builds on straightforward multicomponent condensation reactions, implying salicylidenehydrazones, phenylglycoxylic acid and boronic acid. We demonstrated that BASHY complexes exhibit a fluorescence nature along with selectivity towards cytoplasmic lipid droplets substructure without any appreciable cytotoxicity.<sup>2</sup> Bearing this in mind along with its reversibility nature, we envisioned that BASHY complex could be used to investigate the distribution of a drug between the LDs and the cytosol. Therefore, several boronic acid salicylenhydranone complexes were synthesized and once the BASHY complex was optimized we installed a cytotoxic drug (Figure 1). Confocal microscopy images (Figure 1) shown accumulation of BASHY-drug complex into LDs and cell viability highlighted a substantially difference of IC50 values between the drug alone and the BASHY-drug, indicating that LDs might influence of LD on drug effectiveness.



Figure 1: a) Modal boronic acid salicylidenehydrazone complex featuring a cytotoxic drug; b) Confocal images of HT-29 cells incubated with a BASHY complex.

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## Health

# Metal Catalysed Regioselective Esterification of Sucrose: A Library of Phenylpropanoic Esters Against Cancer

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Phenylpropanoic sugar esters are a class of naturally occurring active substances, mainly found in oriental medicinal plants, with a scope of activity ranging from antioxidant to antibacterial as well as recognised for their anti-tumoral properties<sup>1</sup>. Though relatively simple in structure, few have been the successful attempts to obtain them in the laboratory, hampered mainly by the fact that the poor regioselectivity between similar functional groups in sugars restrains the feasibility of current methods and their reproducibility in industrial scales<sup>2</sup>.

Our study aims for the development of reliable and effective methods for the synthesis of a library of phenylpropanoic esters derived from sucrose. The different compounds obtained are meant to be tested and screened for their biological activities, with particular emphasis on their applications on cancer treatment.

One of our most appealing discoveries is the possibility of directly enhancing the regioselectivity of certain hydroxyl groups in the sugar moiety if a complex between the latter and a transition-metal salt is induced in a strong basic medium<sup>3</sup> (**Scheme 1**) and we are currently developing this pioneer protocol.

Our observations led to conclude that cobalt and copper chloride salts give the best results in terms of regioselectivity, yield and decreased reaction time. To further extend our knowledge about the metal-chelate directed acylation method, we are also experimenting with other halide salts, namely zinc, calcium, nickel and iron, as well as with derivatized molecules of sucrose. Thus, our work can lead the development of novel drugs and resourceful cancer therapies.



Scheme 1: General scheme for the metal-chelate direct esterification of sucrose molecule.

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## Health

# Fighting HIV-1 infection: a novel poly(alkylidenamine)-based dendrimer as a potential microbicide

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Human Immunodeficiency Virus (HIV) due to the high number of new infections occurring each year remains a problematic disease. About 80% of all infections are from sexual transmission and women are more vulnerable with further than half of the infected cases.<sup>1</sup> The pursuit for finding new nanomaterials, such as dendrimers, to support in the diagnosis, treatment, and prevention of this kind of diseases is highly significant.<sup>1,2</sup>

Here, we describe the preparation and characterization of a low generation of anionic poly(alkylidenamine) dendrimers with carboxylate (G1-G3) and sulfonate (G1-G3) terminal groups (**Figure 1**), with the goal to be used as microbicides. The cytotoxicity and antiviral activity were evaluated using the TZM.bl cell line and R5-HIV-1<sub>NLAD8</sub> and X4-HIV-1<sub>NL4.3</sub> isolates. The results showed that G1C and G1S dendrimers present high inhibition against R5-HIV-1<sub>NLAD8</sub> (more than 85%) and X4-HIV-1<sub>NL4.3</sub> isolates by blocking the HIV-1. Indeed, the mechanism of action of the dendrimers revealed that they could directly interact with the virus interfering with their entry in cells (**Figure 2**). Moreover, their antiviral activity was preserved at different pH values. The *in vivo* studies with the G1C and G1S dendrimers presented that both are biocompatible, with no visible irritation or inflammation detected in the vaginal epithelium. Therefore, these dendrimers present to be effective, safe and are strong candidates to be used as a topical microbicide.





Figure 1: a) Prepared anionic poly(alkylidenamine) dendrimers with carboxylate (G1-G3) and sulfonate (G1-G3) terminal groups; b) generation 1 of the anionic dendrimers.

Figure 2: Representation of the interaction of the dendrimers and the HIV-1.

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## Health

# A metabolomics-inspired workflow for MS drug metabolism studies

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Drug research is a challenging field aimed at developing molecules to improve health, quality of life and life span. However, a high number of promising compounds never reach the market due to toxic and pharmacokinetic properties. Industry R&D departments' and academic research groups are increasingly using Mass Spectrometry approaches to identify and assess the potential toxicity, not only of early stage candidates but also of approved drugs. This affords a more risk-wise R&D process that also contributes to the post-market drug safety monitoring studies.

Common metabolism studies often involve several experiments where the target compounds are incubated with enzymes/cells/tissues of interest in order to understand their metabolic profile. An exhaustive study of possible metabolites must thereafter be performed, and a metabolite database maintained, using proprietary software such as Bruker's Data Analysis and TASQ (Target Analysis for Screening and Quantitation), a task that can be prone to errors.

With the advancement of IT, new software has been developed to help in data. Software as MZmine 2<sup>1</sup> and TASQ are two examples of how automation can help users to expedite data processing. Based on the database created with results from a small set of samples, these new tools are able to process high amounts of data according to user-defined methods. This means that the user is able to create different data sets aiming at the identification of specific metabolites based on chemical formula, m/z value, retention time, peak area and isotopic pattern, for example, leaving the harsh work of repeated data processing to be taken by the software, saving time in data processing.

To evaluate the applicability of this methodology in the context of a metabolomics analysis, we profiled the metabolism of model drugs montelukast (MTK), nevirapine (NVP) and tamoxifen (TAM). MTK, a cysteine leukotriene receptor 1 inhibitor, which is associated with some adverse effects, mainly neuropsychiatric effects in children, of still unkown etiology. In this approach, a database was created comprising all the known and identified metabolites. This dataset was then analyzed by MZmine software comparing samples of microsomal and S9 fraction incubations of MTK with the appropriate controls. In all cases, all the known metabolites were found and correctly identified automatically by the software, with no false positives. Correct identification of MS ions was accomplished by automated comparison of MS2 ions and isotopic pattern profiling, proving the applicability of MZmine in high-throughput studies of drug metabolism. The same methodology was applied to characterize the metabolic fate of both NVP and TAM, giving rise to a set of results that mimic those described in the literature both qualitatively and quantitatively.

In the future, this methodology will be applied in more complex studies, including patient-derived samples and animal studies, further completing the metabolite database beyond phase I and II metabolites, including conjugation and detoxification products and even adducts with small peptides and other relevant biomolecules. The implementation of such high-throughput methods will contribute to a faster and more accurate identification of possible reactive metabolites, implicated on the adverse reactions of the tested compounds, in large datasets generated in multi-point and multi-condition experiments.

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## Health

## Xanthene-based optical sensor for metal ions type M(II)

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The development of optical sensors based on the use of fluorescent molecules (fluorophores) is a science field with a high impact in health and environmental issues.<sup>1</sup> Typically, the fluorescent-based sensors are designed using fluorescent organic molecules such as xanthene derivatives (rhodamines and fluoresceins), which are known to possess excellent photophysical properties in solution, such as high quantum yield and intense fluorescence spectrum in the visible region.<sup>2</sup> These excellent properties can be complemented with the introduction of receptors, such as 3-hydroxy-4-pyridinones, allowing the optical detection of several species, like metal ions type M(II) and M(III), small molecules or gases.

In this work we explore the synthesis of high-performance sensing xanthene molecules characterized by enhanced fluorescence properties, high selectivity and ease implementation in optical sensors devices. As an example of the work being developed, we started by preparing a rosamine-based compound (Ros-2NH<sub>2</sub>, Fig. 1A), with two amino substituents in the positions 3, 6 of the xanthene core, that was further functionalized with a 3-hydroxy-4-pyridinone derivative (Fig. 1B). The photophysical properties, including UV-Vis, fluorescence and quantum yield, of the new compounds were studied. Furthermore, the ability of the conjugate to selectively detect metal ions type M(II) was evaluated.



Figure 1: Schematic representation of the rosamine-based compound Ros-2NH<sub>2</sub> (A) and the xanthene-receptor conjugate (B).

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## Health

## The quest for new antibiotics: synthesis of potential DNA gyrase inhibitors

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One of the most alarming health concerns of the modern world is the increasing number of multi-resistant bacteria in hospitals, for which current antibiotic treatments are becoming ineffective.<sup>1</sup> This outlook has directed our attention towards the synthesis of new chemical entities that can function as inhibitors of a given bacterial target. DNA gyrase is an ATP-dependent enzyme responsible for the negative supercoiling of bacterial DNA, which in turn facilitates its uncoiling for transcription or replication purposes.<sup>2</sup> Current inhibitors of DNA gyrase (quinolones, fluoroquinolones) have enjoyed great clinical success in the treatment of infections by both Gram-positive and Gram-negative bacteria, however several resistance mechanisms have already been reported comprising changes in the drugs' accessibility to the target and mutations in the binding site.<sup>3</sup> This warrants the search for alternative, underexplored, binding sites for which no mutations have yet been developed and thus offer a new therapeutic solution for infections by multi-resistant bacteria.

With the help of computer-aided drug design techniques, namely pharmacophore screening and ligand docking, we identified key structural features that molecules should have for the inhibition of the ATP binding site of *Escherichia coli*'s DNA gyrase. Herein, we present the results regarding the synthesis of computational designed benzoimidazoyl heteroaromatic substituted chemical entities, aiming the development of a new active antibiotic for *E. coli*.

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## Health

# Quantification of salivary magnesium using a microfluidic paper based analytical device (µPAD)

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Magnesium is a mineral present in the human body involved in several physiological processes, namely acting as a cofactor in more than 300 enzymatic reactions. It allows the proper functioning of the enzymes enabling several reactions in the body. In this context, due to the importance of this mineral for human health, its concentration for each tissue/fluid must be monitored; otherwise, there could be a case of magnesium deficit (hypomagnesemia), or excess of magnesium (hypermagnesemia). <sup>1</sup>

The magnesium cation is present in the saliva at about 0.2 mM. However, some studies show that certain pathologies/disturbances, namely cystic fibrosis and burning mouth syndrome,<sup>2</sup> may be associated with alterations in the concentration of the salivary magnesium. Thus, its quantification in saliva can be an indicator of those pathologies.

Microfluidic paper-based analytical devices (μPADs) have several benefits that make them ideally suited to conduct in-situ, on-hand determinations. While many of the current monitoring techniques require specialised skills, laborious laboratory processes, or/and expensive equipment, μPADs provide a quick and cheap analytical result. Additionally, the low-cost, easy-disposable and intrinsic portability of the μPADs, make them ideal devices for regular monitoring i.e. routine consultation.

In this context, the objective of described work was to design a  $\mu$ PAD for a fast, in-the moment, reliable magnesium quantification in human saliva (**Figure 1**). The method was based on the reaction between magnesium and eriochrome cyanine dye, generating a coloured complex, quantified through pixel readings. The overall consumption of both reagents and sample is rather low. The developed  $\mu$ PAD enables to determine the salivary magnesium concentration as an economical and in-situ alternative to be used by unskilled operators.



Figure 1: Schematic representation of developed µPAD: a) exploded view of the assembly; b) colour scheme of the calibration curve.

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## Health

## New inhibitors for Matrix Metalloproteinases for dentin bonding agents

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Adhesive resins are the most common human-synthetic material interface. Their applications enable the reproduction of esthetics and mechanical strength of tooth and the repair of caries lesions, being dental caries a disease that affects 90% of the world's population<sup>1</sup>. However, the clinical application of these materials has encountered durability limitations<sup>2</sup>. In the long term this interface allows free acid residues to dissolve hydroxyapatite<sup>3</sup> and activates matrix metalloproteinases (MMPs) that degrade collagen fibers<sup>4</sup>, thus inducing restoration failure. Furthermore, inhibitors for different types of human MMPs are important against a number of diseases and are particularly relevant for cancer therapy<sup>5</sup>. The search for new types of selective inhibitors towards different MMP is crucial for medical applications. Previously, we have designed and synthetized several new compounds to inhibit degradation of collagen fibers by MMPs<sup>6,7</sup>. Herein, we are presenting the calculations of the computational docking affinity of these molecules towards the active site of several MMPs, the tests of biochemical inhibition and evaluation of mechanical resistance after aging. These molecules can be directly included to commercial dental adhesive systems. Some MMP have a tunnel at active site, where inhibitors can dock and be cyclized with light, for irreversible inhibition (Figure 1).



Figure 1: Light cyclized irreversible inhibition of MMPs.

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## Health

# Development of Bionanosensors for the Diagnosis of Infectious Diseases using the Phage Display Technology

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Zika is an infectious viral disease which had a recent worldwide outbreak. This flavivirus is transmitted by the *Aedes aegypti* mosquito. At this time, there is still no vaccine to prevent Zika infection and no pharmacological agents to treat it. The present diagnostic tools for this disease are based on serological/molecular studies and on antigen and/or genome detection. These diagnostic methods are time-consuming, require specialized and expensive laboratory equipment and present low specificity, since cross-reactivity with other similar viruses is common and will originate false positive results.<sup>1</sup> Unfortunately, no routine and accurate assay for the diagnosis of Zika infection is currently available. Therefore, the main purpose of this project is to develop an approach, based on the phage display technology, that will allow for an early, rapid and differential routine diagnosis of Zika.

The phage display technique is based on the presentation of randomized peptide sequences on the surface of bacteriophages. In this technique, a gene encoding a protein of interest is inserted into a phage coat protein gene, causing the phage to "display" the protein on its outside while containing the gene for the protein in its inside, resulting in a physical link between genotype and phenotype. Using this technology, large peptide libraries can be displayed in the phage surface and used for affinity screening of specific target molecules.<sup>2</sup> Phages bound to a specific target go through several repeated cycles, in order to produce a phage mixture enriched with the relevant phage-displaying peptides that specifically recognize disease target molecules with high sensitivity and selectivity. The target-bound bacteriophages are amplified, and the correspondent peptides identified and characterized. The corresponding DNA is also sequenced and analyzed in order to identify and characterize the Zika-specific peptides.

In this work, a commercially available phage library is being screened against an antibody specific for Zika, in order to identify the peptides that will be used further in the development of bionanosensors as diagnostic tools for Zika infection. This will provide new insights into the development of robust bionanosensors for sensitive viral detection and serotyping. The main goal is to identify and generate phage-displayed peptides that specifically recognize the disease target molecules, with high sensitivity and selectivity. The desired outcome is the development of an innovative biosensing method for non-invasive, rapid, and in real time diagnosis of the disease.

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## Health

# Synthesis, characterization and antifungal activity of a new caffeine-based Nickel NHC

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The development of metal complexes containing N-heterocyclic carbenes (NHC) for medicinal applications has been grown considerably in the last decade, taking advantage of fine-tuned electronics and sterics and a strong metal-carbon bond. This is proved by the increasing number of publications on NHC transition-metal complexes as metallopharmaceuticals with silver(I) and gold(I) as antibacterial and anticancer agents.<sup>1,2</sup> At present, the challenge is focused on conferring these complexes a higher selectivity, and in line with this, the development of NHCs based on bioactive ligands is central. In this regard, purine derivatives have been employed as ligand precursors for NHC synthesis, mostly with silver(I), gold(I) and palladium, being active as anticancer agents.

Herein we present two new Nickel NHC complexes synthetized by direct metalation of the corresponding methylated caffeine with Nickelocene, NiCp<sub>2</sub><sup>3</sup>. The compounds were characterized by NMR, Elemental Analysis and X-Ray crystallography. Kinetic studies demonstrate that the formation of compound **3** is followed by the formation of compound **2**. The toxicity of the two compounds against *Candida Glabrata* and *Candida Albicans* has been tested. Compound **2** shows better activity compared to compound **3** and notably shows higher toxicity against *C. Glabrata* than against *C. Albicans*. These results indicate the potential of compound **2** as an antifungal agent.



Scheme 1: Methylated caffeine reaction with Nickelocene, in DMF at 100°C.

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### Health

## New BODIPYs for photodynamic therapy on human lung cancer cells

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Cancer is a worldwide disease, causing numerous deaths every year, being the lung cancer the most incident and the deadliest for both men and women. The need for new and more effective therapies with fewer side effects is a concern [1-3]. Photodynamic Therapy (PDT) relies on the administration of a photosensitizer that is subsequently activated by irradiation with visible light of appropriate wavelength. As a result, reactive oxygen species (ROS) are produced leading to cell death. PDT use in the treatment of cancer is still limited, due to the low number of new approved drugs. In light with this, this work aims to develop new photosensitizers for PDT. As an alternative class of the porphyrin-based photosensitizers, eight compounds of the family of the boron–dipyrromethenes have been synthesized and evaluated on the human lung cancer cell line A549. In this study, we used the MTT and SRB assays to assess the cytotoxicity of the compounds with concentrations ranging from 0,1 to 50  $\mu$ M. Several compounds were photocytotoxic at the higher concentration studied. The most effective compound in the photocytotoxicity studies was the **BODIPY 5** when used in a concentration of 10 and 50  $\mu$ M. Our preliminary results suggest that **BODIPY 5** has very good antitumor properties, which encourages further studies with this new molecule.



Figure 1: Structure of BODIPY 5 (A) and MTT assay results for 48 hours after treatment (B).

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## Health

## New ε-Caprolactam and γ-Lactam-Derived Amines as acetylcholinesterase inhibitors

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Alzheimer's disease (AD) is a progressive and degenerative brain disorder characterized by loss of neurons and synapses in the cerebral cortex and certain subcortical regions. Clinically, the symptoms can include problems such as loss of memory, language deterioration, mood swings, and loss of body functions, ultimately leading to death. At this time, acetylcholinesterase inhibitors (tacrine, donepezil, rivastigmine, and galantamine) and *N*-methyl-*D*-aspartate receptor antagonists are the only approved drugs that can provide a palliative, therapeutic strategy in mild forms of AD. Unfortunately, there is no means to cure, or even slow, the progression of the disease. This alarming situation needs further effort to develop more effective drugs for treatment of AD.<sup>1</sup>

Recently we reported an unexpected and unusual reactivity of 2-methyl imidazolium salts (1) towards aryl aldehydes, where 1 can act as an oxidant to the conversion to the respective carboxylic acid<sup>2a</sup> or ultimately, catalyse the ring opening of DBU or DBN to  $\varepsilon$ -caprolactam- and  $\gamma$ -lactam-derived imines (2) further reduced to lactam-based 1,3-diamine (3).<sup>2b</sup> Reaction was extended to anthracene-aldehyde compounds (Scheme 1) and the results towards acetylcholinesterase inhibition of the compounds 2 and 3 will be presented.



Scheme 1: General procedure for the synthesis of -Caprolactam and y-Lactam-Derived Amines.

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## Health

## Synthetic approaches to 3-substituted 1H-pyrazole-5-carbaldehydes as precursors for antinecroptotic inhibitors

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Necrosis has been traditionally regarded as passive and unregulated, therefore very little efforts had been made to investigate its mechanism, despite of its prevalence in human pathology. However, the identification of necroptosis' (a regulated form of necrosis) pathway mediators, such as receptor interacting protein kinase-1 (RIPK1) and 3 (RIPK3), and mixed lineage kinase domain-like (MLKL), and its impact in critical human illnesses, led to an intensive, but unaccomplished, search for high quality necroptosis inhibitors.<sup>1,2</sup>

In order to find new necroptosis inhibitors, a high throughput cell-based phenotypic screening of AstraZeneca's compounds was performed in the iMed.ULisboa. New RIPK1 inhibitors hits, with  $IC_{50}$  values in the sub micromolar range and different scaffolds from the known necroptosis inhibitors<sup>3</sup>, were identified.

In this project, several 3-substituted 1H-pyrazole-5-carbaldehydes, precursors of the new antinecroptotic inhibitors' scaffold, were synthesised through two different methodologies (**Scheme 1**). The diversified groups introduced in the pyrazole C-3 position are crucial to synthesise dissimilar final structures, with the same new RIPK1 inhibitors' scaffold. These new molecules will be useful to develop relevant structure activity relationships, that will guide future derivations to create compounds with higher activity.



Scheme 1: Synthesis of the 3-substituted 1H-pyrazole-5-carbaldehydes.

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## Health

## N-Heterocyclic Carbenes Based on mRNA-Caps: Synthesis and Antiproliferative Activity

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The formation of 7-methylguanosine (7-MeG) at 5'-end of mRNA in eukaryotes is fundamental step in transcription.<sup>1</sup> This apparently simple modification protects mRNA from nucleases, increasing its stability towards degradation. The presence of 7-MeG in mRNA is required to initiate translation, regulates eukaryotic protein synthesis, pre-mRNA splicing and nucleocytoplasmic transport. Once methylated, 7-methylguanosine acquires a positive charge due to the quarterisation of N7, and the corresponding C8-H becomes exchangeable.<sup>2</sup> This reactivity has been attributed to the transient formation of an ylide and the corresponding N-heterocyclic carbene (NHC) and mirrors the typical reactivity found for imidazolium salts. Recently, McNaughton and co-workers showed that single stranded DNA labelled with 5'cap-2'fluoro-N7-Methyl guanine reacts with acetone, and suggest that the reaction likely proceeds through a reactive ylide or N-heterocyclic carbene.<sup>3</sup> We have examined methodologies for the formation of NHC complexes from 7-MeG and related purines with platinum(0) compounds (**Figure 1**). Additionally, and based on our previous results with guanine derivatives, we examined anti-proliferative properties of these compounds. These results will be discussed in this communication.



 $R_1$  = Ribose  $R_2$  = H, Me [M] = Pt(PPh\_3)\_2Br, Pt(PPh\_3)\_2H

Figure 1: Platinum NHCs derived from guanosine.

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## Health

## Small molecule pharmaceutical salts or co-crystals: insights from NMR Crystallography

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Solid active pharmaceutical ingredients (APIs) are easily engaged in hydrogen bond networks and other intermolecular interactions in their supramolecular structure, largely due to the presence of several functional groups. Their crystal packing arrangements thus play an important role defining physicochemical properties of solid dosage forms. The structural characterization of solids is usually obtained using X-ray diffraction (XRD) techniques, and a full detailed description of the intra- and intermolecular distances and angles is usually obtained. However, XRD may present limitations in probing local interactions involving light atoms such as hydrogens. Solid-state (ss) NMR spectroscopy is a well-established technique in pharmaceutical sciences, highly sensitive to the local environment of a given nucleus often used in tandem with XRD. ssNMR is particularly useful to study the strength and nature of hydrogen bonds as well as other packing interactions having the potential to discriminate between salts and co-crystals mostly by means of <sup>1</sup>H, <sup>13</sup>C and <sup>15</sup>N ssNMR in nitrogen-containing compounds. NMR crystallography provides complementary structural information by combining the high sensitivity of ssNMR towards short-range local structure with the accuracy of powder x-ray diffraction (PXRD) to probe long-range order.<sup>1</sup> DFT calculations are employed in geometry optimization of hydrogen atoms and to obtain theoretical ssNMR chemical shifts that are compared with experimental data for structural validation, increasing the success rate and confidence level of the final structure.<sup>1a</sup> This approach has been applied to several multicomponent pharmaceutical co-crystal/salt systems, involving theophylline (TP),<sup>2</sup> salicylic acid, azelaic acid,<sup>3</sup> gabapentin<sup>4</sup> and adamantylamine<sup>5</sup> drugs. All systems were prepared using the liquid-assisted grinding method. Herein we present a series of case studies where solid-state NMR was particularly decisive in providing further structural insight. For instance, (i) the unexpected absence of intermolecular interactions engaging the amino groups in TP:4-aminobenzoic acid,<sup>2</sup> (ii) determining the co-crystal/salt nature in APIs,<sup>5</sup> (iii) providing insight on the packing interactions in lamellar structure of gabapentin salts<sup>4</sup> originated from sulfonate-based ionic liquids and (iv) solving <sup>1</sup>H disorder in the crystal structure of drugs.<sup>2</sup> The results show the advantageous use of XRD and ssNMR techniques in tandem with computer simulations for structural elucidation.

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## Health

## Driving ferulic acid to the small bowel by desorption from resin

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Ferulic acid is a secondary metabolite, a phenolic acid widely present in plants, known for its antioxidant and antiinflammatory activities. The absorption of this organic molecule from food sources is very low because of its conjugation with other biomolecules, while the free form is highly absorbed by the stomach and the small intestine. This means that the ingested bounded form will not be released until it reaches the colonic bacteria and the free form will be absorbed in the stomach before it has the chance to reach the small bowel. Its administration might help prevent conditions where antioxidant protection may be implicated, such as degenerative diseases or conditions affecting the gastrointestinal tract. The possible administration of ferulic acid during the digestion process after its immobilization on a solid matrix was explored.<sup>1</sup>

This approach relies on the immobilization of ferulic acid by adsorption on a neutral FDA approved polystyrene resin which is not absorbed or anyway altered by the gastrointestinal tract. The main interactions between ferulic acid and the resin are hydrophobic and depend highly on the pH of the surrounding media. These findings suggest that the acid pH of stomach prevents the release of ferulic acid whereas the alkalinity of the intestinal media causes its ionization, lowering its interaction with the resin, and consequently, its release. This novel methodology could be a possible alternative to the administration of this potent antioxidant to this segment of the gastrointestinal tract.

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## Health

## Development of a coffee substitute beverage with benefits for elderly population

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Coffee is one of the most popular drinks in the world, but due to its high caffeine content its consumption should be moderate. Despite the many benefits provided by coffee, such as reduction of insulin levels and risk of some cancers, there are also disadvantages associated with consumption of this beverage, e.g.: increased blood pressure and the risk of developing hypercholesterolemia, osteoporosis and different cancers.

A new beverage was produced using roasted seaweed with carob and oats. This alternative drink intends to simulate the sensory properties (body, aroma and taste) of coffee. According to the knowledge acquired to date, kelp has never been used for this purpose. It also intends to take advantage of the neuroprotective and bioactive characteristics of algae in the coffee substitute, being our target consumers the older population, in addition, to solve a serious and common problem: iodine deficiency, thanks to the presence of this element in algae.

Three seaweed abundant in the Portuguese coast were used in order to choose the seaweed with the sensory properties most like coffee. After washing and roasting the algae was ground in a coffee mill. The oat flakes and carob flour were also toasted and ground.

Mixtures with different ratios of roasted seaweed, carob and oats were prepared and their contents in sodium, potassium, calcium and magnesium were determined. To assess its bioactivity, the total phenolic content, total flavonoids and total phlorotannin's were quantified and the antiradical activity using DPPH<sup>•</sup> and ability to inhibit AChE were evaluated for the obtained beverage. Iodine, total proteins, total lipids and total sugars were also analysed. A sensorial analysis was also performed. The functional beverage was compared with other substitutes on the market and with the coffee itself.

The substitute produced had similarities to coffee in terms of colour, taste, body and texture, being even more like coffee than other substitutes already available on the market, such as barley and chicory. In general, the mixtures presented higher content of calcium, sodium and iodine, phenolic compounds and phlorotannin's when compared with other beverages. In these mixtures the high iodine content, moderate neuroprotective activity and high antiradical activity stands out regarding other beverages.

The elderly population avoids coffee because of the potential health problems it may cause. Thus, the drink intends to simulate all sensory properties of coffee, taking advantage of its neuroprotective and antioxidant properties, allying it with other important properties of algae (e.g. iodine), carob and oats. In the near future more chemical and sensory testing will be done to improve these substitutes.

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## Health

## Novel Biosensor Based on Acetylcholinesterase/Poly(Neutral red) – Deep Eutectic Solvent / Fe<sub>2</sub>O<sub>3</sub> Nanoparticles Modified Electrode for Acetylcholine Determination, a Neurotransmitter in Alzheimer's disease

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The choice of suitable platforms for enzyme immobilization is mandatory since this may influence enzyme biocompatibility, catalytic properties, stability and sensitivity, as well as retention of enzyme activity. Therefore, to fabricate a biosensor with high performance, efforts need to be made in the development of new and advanced electrode materials as electrode support. In recent decades, much progress has been made in applying nanomaterials such as metal nanoparticles, carbon materials and conducting polymers to design novel enzyme biosensors. They offer biosensing platforms an increase of the surface transducing area, which in turn increases the sensitivity and often electrocatalytic effects, besides preserving the enzymatic activity for a longer time period, due to their biocompatibility [1]. Deep eutectic solvents (DES) are systems formed from a eutectic mixture of Lewis or Bronsted acids and bases which can contain a variety of anionic and/or cationic species. They incorporate a hydrogen bond acceptor (HBA) and a hydrogen bond donor (HBD), which are able to give a eutectic mixture with a melting point much lower than either of the individual component. DES have properties in common with ionic liquids, such as good conductivity and chemical stability, and wide electrochemical window that is important for polymer electrosynthesis, which often requires a high potential for radical generation. Other advantages are low cost, low toxicity and no need for time-consuming steps of synthesis, which make them ideal for biosensor applications [2,3]. This work concerns the development of a novel amperometric enzyme biosensor based on acetylcholinesterase (AChE) immobilized on poly(neutral red) (PNR) films electropolymerized on Fe<sub>2</sub>O<sub>3</sub> magnetic nanoparticle modified electrodes for the detection of acetylcholine, a neurotransmitter essential for processing memory and learning. Its decrease in both concentration and function is associated with Alzheimer's disease. PNR films were formed by potential cycling in ethaline (choline chloride + ethylene glycol) DES with the addition of different ionic species as acid dopants i.e. NO<sub>3</sub>, SO<sub>4</sub><sup>2</sup>, Cl, ClO<sub>4</sub>. The novel nanocomposite films were characterized by scanning electron microscopy, cyclic voltammetry and electrochemical impedance spectroscopy. The use of ethaline-DES contributed significantly to good polymer film growth with superior conductivity in relation to films of PNR obtained in aqueous solution, and thence to improvement of the biosensor response. The electrode support with the best electrochemical properties was used for AChE immobilization using glutaraldehyde cross-linking. The analytical performance of the novel biosensor was evaluated in terms of limit of detection, linear concentration range, as well as operational stability and reproducibility in phosphate buffer aqueous solution. It was successfully tested by application to the measurement of acetvlcholine in artificial body fluids.

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## Health

## Synthesis and Evaluation of Benzoic Acid Derivatives as Prodrugs for the Treatment of Tuberculosis

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Tuberculosis (TB), a disease caused by a *Mycobacterium tuberculosis* is one of the top 10 causes of death in the world.<sup>1</sup> The emergence of resistance against to the first line TB drugs, such as pyrazinamide<sup>2</sup>, has led to the need for new approaches. One interesting approach is the use of prodrugs that often have showed improved biological activities over active drugs with poor absorption or difficulty to pass over membranes.<sup>3</sup>

Previous studies demonstrate that weak acids have a significant antimycobacterial activity, which increases at acidic pH. Moreover, esters of those acids revealed to be a viable alternative since they diffuse more easily through the cell membranes, and inside the mycobacterial cell they will be converted into the weak acid.<sup>2,3</sup> Nonetheless, to be effective, they must be resistant to hydrolysis in human plasma and be activated once inside the mycobacteria.<sup>3</sup>

In this work, esters of benzoic acid (BA) containing electron withdrawing groups on the aromatic ring, in order to decrease the pKa of the liberated acid, were synthetized. In addition, alkyl chains with variable lengths, ranging from propyl to tetradecyl, were used for alkoxy group of the esters. The purpose of using different alkyl chains was to evaluate the effect of the Long Chain Alcohol (LCA) on the plasma stability and activity of the esters. The chemical and enzymatic stability of these derivatives has been studied in phosphate buffer and in human plasma, respectively, **(Scheme 1)** by HPLC. The activity of the compounds was studied against *M. tuberculosis*.



X = 4-NO2, 3,5-NO2 e 4-CF3 R = Propyl to Tetradecyl

Scheme 1: Synthesis and Hydrolysis of Esters of Benzoic Acid Derivatives. (A 1. SO<sub>2</sub>Cl<sub>2</sub>, THF or CH<sub>2</sub>Cl<sub>2</sub>, 88 °C 2. ROH B. CDI, 1. CDI, THF, rt 2. ROH)

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## Health

## Prospective epigenetic inhibitors in cancer: Design and biological evaluation

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Cancer figures among the leading causes of morbidity and mortality worldwide. Recently, the role of epigenetic pathways in cancer disease development and progression have been studied and new anticancer targets have been proposed. Polycomb repressive complex 2 (PRC2) is an epigenetic regulator that catalyzes the trimethylation of lysine 27 in Histone 3 (H3K27me3), a process that facilitates chromatin compaction and gene silencing.<sup>1</sup> The overexpression of EZH2, the catalytic subunit of PRC2, is implicated in the development and progression of a variety of cancers with the worst prognosis.<sup>2</sup> Thus, the therapeutic targeting of EZH2 has attracted significant attention for the development of selective small molecule inhibitors.

To contribute to the discovery of new EZH2 inhibitors, we carried out a computer-aided drug design (CADD) campaign to find hit molecules for testing in biological assays and/or for synthesis. First, a panel of unique 3D-pharmacophore models were generated, validated and optimized using LigandScout Advanced 4.2.1 software [3] and information relating to the key interactions and the 3D-geometries associated with inhibition of EZH2 activity were obtained. The prioritized models were used in two computational hit finding campaigns: Virtual Screening and De Novo Design. During the Virtual Screening, a unique 3D-pharmacophore-based method (iscreen) from LigandScout was used and several databases (e.g., DrugBank, NCI, MuTaLig Chemotheca, and our in-house libraries) were computed and screened. The interesting virtual hit molecules with high inhibition potential totalled more than 60 compounds. Preliminary biochemical and cell-based assays results reveal inhibitors. Notably, many of the putative EZH2 hits from the *in-silico* studies showed clean and safe off-target and ADME-Tox profiles. In parallel to the above, we started a *de novo* design campaign based on selected pharmacophore models and new scaffold cores for EZH2 inhibition have been identified. The structures obtained from *de novo* design are now being synthesized for *in-vitro* evaluation by EZH2 and ADME-Tox assays.

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## Health

## Design and synthesis of new triazene anticancer hybrid compounds

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Metastatic melanoma is one of the most deadly skin cancers that develops in melanocytes, showing a poor prognosis in advanced stages. Unfortunately, all available therapeutic regimens present low response rates and several side effects (survival rate less than 10% in 10 years). For advanced melanoma, standard chemotherapy showed lack of selectivity and high toxicity and is mostly ineffective. Therefore, new therapies to deal with this lethal disease are urgently necessary, not only to improve the cure rate but also the patients life quality<sup>1,2</sup>.

In this communication, we present the design and synthesis of new triazene hybrid compounds potentially useful for the treatment of metastatic melanoma. These new triazene hybrid compounds **3** incorporate two drug pharmacophores (a triazene moiety and a sulfur substituted phenol) in a single chemical entity. The advantage to join covalently these two different moieties is the expectable ability of the new molecules to act through different mechanisms of action. On one hand the triazenes are DNA alkylators, and on the other hand the sulfur substituted phenol can induce a specific apoptosis mechanism in melanoma cells<sup>3</sup>. Besides this advantage, compounds **3** are also expected to be excellent tyrosinase substrates. Tyrosinase is an enzyme overexpressed in melanotic tumor cells and a molecular target for antimelanoma development drugs<sup>4</sup>. We expect that when these hybrid compounds interact with tyrosinase in tumor cells they are oxidized and allowed the simultaneous release of both pharmacophores, promoting the targeting properties of the compounds.

The stability of these compounds as well as the activation by tyrosinase will also be presented.



Scheme 1- General synthesis of triazene hybrid compounds 3.

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## Health

## Synthesis of cyanovinylquercetin derivatives with potential biological activity

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The relevance of natural poly-hydroxylated phenolic substances, such as flavonoids, is well established. These compounds display a range of important biological and pharmacologic activities.<sup>1</sup> The potential of this type of compounds is strongly dependent on their structural features, namely the degree of hydroxylation and/or the presence of other substituents or conjugations.

Quercetin is a natural occurring flavonol found in various fruits, nuts, herbs, and vegetables, presenting a prominent antioxidant capacity and a wide range of beneficial biological activities such as anti-inflammatory, anticancer or antiviral.<sup>2</sup> Active methylene compounds present an important role in organic synthesis allowing the modification of functional groups, such as the formyl group, giving access to new compounds with different or improved biological properties.<sup>3</sup> The resulting vinyl-substituted compounds can be further transformed, namely into heterocyclic compounds.

Herein we present a synthetic route to the quercetin derivatives **2**. The experimental details of the syntheses and the structural characterization of the obtained products will be presented and discussed.



Figure 1: Synthesis of new quercetin based derivatives.

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## Health

## Synthesis of new *N*-glycosylated flavonoid derivatives with potential antiinflammatory action

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Flavonoids are polyphenolic compounds widely occurring in Nature, being present in fruits, vegetables, seeds, roots, stems and leaves.<sup>1</sup> They present several pharmacological properties, such as antioxidant, anticancer, antiviral, antiallergic and anti-inflammatory activities.<sup>1,2</sup> A large number of flavonoids occur in nature conjugated with sugars (*O*glycosides and *C*-glycosides) and they also present a varied biological activity. Some flavonoids regulate the activity of enzymes and the synthesis of mediators responsible for the inflammatory process. The anti-inflammatory activity of these compounds is also a result of their ability to interact with various enzymes.<sup>3</sup> Triazole derivatives also have a particular relevance due to their application in the medicine field. 1,2,3-triazole have been used as drugs because they possess numerous biological properties, such as antiviral (anti-HIV), anti-allergic, antimicrobial and antiinflammatory activities.<sup>4</sup> Considering the biological properties exhibited by these heterocyclic compounds, we wanted to develop new glycosylated flavonoids-1,2,3-triazole dyads with purpose of advancing potentially improved therapeutic agents.

Herein we will present the results on the synthesis of novel *N*-glycosylated flavonoid derivatives (**Figure 1**) using a well-known transformation. The structure of all synthesized compounds was established by NMR techniques.



Figure 1: Novel *N*-glycosylated flavonoid derivatives.

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## Health

## New anticancer metallodrugs

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During the last years the development of structurally novel coordination compounds with diverse biological properties, such as antimicrobial, anti-inflammatory, antifungal, antioxidant and anticancer activities, is an increasing field of Medicinal Inorganic Chemistry. Among the most promising coordination compounds, are metal-drug complexes, *ie*, metallodrugs. This fact is based in a potential synergistic effect when metal ions are combined with molecules that are biologically active <sup>1,2</sup>. Non-steroidal anti-inflammatory drugs (NSAIDs) are an important class of therapeutic molecules that are used as analgesic, anti-inflammatory and antipyretic agents. In comparison with single NSAIDs, the metal centre in metal-NSAIDs complexes has the possibility of different coordination moieties, geometries and redox states that can be used to create new structures which are able to interact with targets in unique ways. Moreover, these metallodrugs may have lower toxicity and higher pharmaceutical effects as compared to free drugs.<sup>3,4</sup> Herein, the synthesis of novel cobalt, nickel and copper complexes with several N-donor ligands and different NSAID's (diclofenac and ibuprofen) is reported. The metallodrugs were characterized using Fourier-transform infrared spectroscopy (FTIR), elemental analysis (EA), X-ray diffraction (XRD), and thermogravimetric analysis (TG). Interaction of the metal-NSAIDs complexes with BSA and DNA were evaluated as well as their anticancer and antioxidant activities.



Figure 1: Structure of one of the metallodrugs.

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## Health

## Development of a synthetic route towards $N^4$ , $N^9$ -disubstituted 4,9-diaminoacridines: On the way to multi-stage antimalarials

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Malaria is one of the deadliest infectious diseases in the world and was responsible for 435 000 deaths in 2017, namely by Plasmodium falciparum species.<sup>1</sup> Antimalarial drugs are the unique weapon to fight this disease once there is no vaccine yet. Generally antimalarial chemotherapy targets mainly the pathogenic blood stage in humans. However, there is an urgent need of new, economic and safe drugs in order to: (i) block parasite transmission to the vectors, (ii) target parasite forms that, for some species, remain transiently dormant in the liver, and (iii) overcome the resistance against artemisinin-based treatments emerging in some vulnerable population in Africa. Consequently, malaria eradication is only possible with the discovery of new multi-targets drugs.<sup>2</sup> Mepacrine (MP, Scheme 1), the first synthetic antimalarial drug, was widely employed but it was rapidly superseded by chloroquine (CQ, Scheme 1), whose efficiency, bioavailability, and safety were far superior. By "dissecting" the chemical structure of QN, the acridine moiety of MP can be seen as the fusion between CQ and the heterocycle core of primaguine (PQ, Scheme 1), another emblematic antimalarial, active against all liver forms of the parasite, and gametocytes. In this context, and based on the fact that one fast and low-cost strategy to accelerate antimalarials development is to recycle classical pharmacophores, the aim of this work is the development a yet unexplored multi-step synthetic route towards 4,9-diaminoacridines (Scheme 1).<sup>2</sup> These can be regarded as respectively corresponding to the fusion between CQ and PQ derivatives. As expected, the preliminary in vitro results showed that the new compounds preserved the activity of the parent drugs, with activity against blood-stage, as in CQ, as well as against all liver forms and gametocytes, similarly to PQ.



Scheme 1: Schematic representation of the synthesis of the target compound.

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## Health

## A new approach to obtaining active drugs against Tuberculosis. Mycobacterial esterase-activated co-drugs

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It has long been expected that the problem of tuberculosis would be solved at the beginning of this century. However, not only this didn't happen, but also new strains resistant to the antibiotics have emerged. Our research group has found that some long chain alcohols (LCAs) had antimicrobial activity "per se" ant tested the concept of mutual prodrugs containing LCA in pirazinoic acid derivatives and found that the activity of the compounds was significant even on strains resistant to pyrazinamide (PZA)<sup>1</sup>. We believe that this finding opens a window of opportunity in the development of new drugs, because it allows the creation of mutual prodrugs containing active molecules and LCAs which may have a synergistic action and an improved penetration into the mycobacteria due to their more appropriate lipophilia.

We consider that the ideal candidates will be esters obtained by reaction between a drug containing a carboxylic acid function (CA) and an LCA (Figure 1). Since mycobacteria are rich in esterase activity, it is possible to use a mycobacterial esterase to activate the drugs at the site of action, nonetheless, the esters need to be stable in human plasma.

Various acids with tuberculosis activity are suitable for conjugation with long chain alcohols, as benzoic acid itself, but the list is extensive, including the classic p-aminosalicylic acid, pyrazinoic acid or the quinolones group<sup>2,3</sup>. In order to achieve the proposed objectives, we synthesized a series of weak acid esters of quinolones with different long chain alcohols and will present the synthesis of the compounds together with stability and activity data.



Figure 1: Synthesis of a levofloxacin ester, which is one of the several quinolones to be investigated, using the synthetic method Bergstro, 2013<sup>4</sup>.

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## Health

## Synthesis of polyhydroxychalcones and flavones

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Chalcones are compounds containing a 1,3-diarylprop-2-en-1-one framework, also known as benzalacetophenones or benzylidene acetophenones. These compounds occur in nature as secondary metabolites of terrestrial plants and are precursors of flavonoids biosynthesis.<sup>1</sup> Natural and synthetic chalcones are recognized by their remarkable biological properties, such as antioxidant, anti-inflammatory, anti-tumoral and anti-hyperglycemic (inhibitors of  $\alpha$ -amylase and  $\alpha$ -glucosidase activities) activities.<sup>2</sup> Above all, polyhydroxychalcones are well known to have significant antioxidant activity.<sup>3</sup> Moreover, chalcones are excellent scaffolds for synthetic manipulations to get other relevant compounds.<sup>2</sup> In this communication, we present our recent results on the synthesis and structural characterization of two families of polyhydroxychalcones **3** and **4** with different substitution patterns. These compounds were obtained following two different synthetic strategies: i) classic Aldol condensation of the appropriate acetophenones **1** with methoxy-substituted benzaldehydes (**2**, R<sup>2</sup> = OCH<sub>3</sub>), using NaOH in MeOH at room temperature, followed by BBr<sub>3</sub>-promoted cleavage of the methyl groups; and ii) direct condensation of the appropriate acetophenones **1** with hydroxy-substituted benzaldehydes **2**, using La(OTf)<sub>3</sub> as a catalyst in dry toluene at reflux (**Scheme 1**). The advantages and limitations of both strategies will be discussed. The synthetized chalcones (**4**, R<sup>2</sup> = OCH<sub>3</sub>) were also used as precursors for the synthesis of hydroxyflavones (**5**).



Scheme 1: Two different strategies for the synthesis of polyhydroxychalcones 3 and 4 and their transformation into flavones 5.

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## Health

## Meropenem-based Ionic Liquids and Salts as anti-microbial agents

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Nowadays, antimicrobial resistance is a significant health problem and efficient alternatives are very important and urgent.  $\beta$ -lactams are a class of semi-synthetic antimicrobial agents which arose from penicillin and possess a wide spectrum of application. Meropenem is a broad-spectrum antibacterial agent from the more recent carbapenem family of  $\beta$ -lactam antibiotics, which is administered intravenously to treat intra-abdominal infections, bacterial meningitis, and also rifampicin-resistant and multidrug-resistant tuberculosis.<sup>1</sup> Tuberculosis (TB) is one of the top 10 causes of death worldwide and the world's leading cause of death from an infectious disease. Despite treatable, the indiscriminate use of anti-TB drugs has led to the development of multidrug-resistant tuberculosis.<sup>2</sup>

Over the last years, our research has focused on tackling drug resistance and other associated drug limitations, such as low solubility, limited bioavailability or tendency to polymorphism, by the combination of Active Pharmaceutical Ingredients (APIs) with biocompatible counter-ions in order to form API-based Organic Salts and Ionic Liquids (API-OSILs)<sup>3,4</sup>. In the past, we observed *in vitro* antibiotic resistance reversal by ampicillin-based OSILs on Gram-negative and Gram-positive bacteria (RDIC >100 and 1000) which agrees with the theoretical prediction of drug improvement.<sup>5</sup> Herein, we report our latest developments in the field of API-OSILs using antibiotics as anions, namely Meropenem as anionic  $\beta$ -lactam antibiotic in combination with appropriate biocompatible organic cations (Figure 1). The prepared API-OSILs were characterized by standard spectroscopic techniques (NMR and FTIR) and thermal analyses (DSC). Additionally, the solubility in water and biological fluids as well as the toxicological profile of new API-OSILs are presented.



Figure 1 - Meropenem based API-OSILs

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## Health

## Fluoride: recent perspectives on the health effects caused by excessive exposure to this periodic table element

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The aim of this communication intends to underline some recent perspectives on the potential health effects cause by excessive exposure to fluoride. From our point of view this issue definitely needs to be addressed with proper attention. Fluoride occurs naturally in the environment from the weathering of fluoride containing rocks and soils, leaching into groundwaters. According to the WHO, areas with naturally occurring fluoride in water above 1.5 mg/L are known as fluoride endemic areas. Fluoride is also released into the environment via coal combustion and other industrial sources. The major sources of human exposure are, tea, dental products, pesticides and drinking water. In some countries fluoride is added to drinking water to provide public dental health protection. Fluoride is a trace element that is necessary for the human body. A proper amount of fluoride not only prevents dental caries, but also promotes calcium and phosphorus sediment in the bone. However, an excessive exposure to fluoride is associated with greater chance of developing health effects such as dental fluorosis (a mineralization disorder of the dental enamel) [1]. On the other hand, several studies have shown that the developing human brain may be exposed prenatally to fluoride as it readily crosses the placenta. In fact, there is a direct relationship between the serum fluoride concentrations of maternal venous blood and cord blood indicating that the placenta is not an effective barrier to the passage of fluoride to the fetus [2]. In this regard, the central nervous system may be vulnerable to fluoride as it may accumulate in brain tissues and affect the hippocampus, the central processor of memory, which can be reflected in learning and memory functions. Many relevant studies support the hypothesis that fluoride has in fact potential effects on the neurodevelopment in children. affecting mostly their cognitive capacities, starting in early prenatal stages of life, reflecting later at school age and likely continuing into adulthood. Thus, fluoride must be considered a significant developmental neurotoxicant. For example, children in fluoride endemic areas, exposed to drinking water with fluoride concentrations ranging from 0.57 mg/L to 11.5 mg/L showed an average IQ decrement of about seven points [3]. High levels of fluoride exposure during pregnancy are in fact associated with global measures of ADHD (attention-deficit/hyperactivity disorder) [4]. Other studies conducted in fluoride endemic areas have demonstrated adverse effects from excessive drinking water fluoride exposure on the cardiovascular system. Two case control studies in Turkey examined 63 endemic fluorosis patients and 45 exhibited carotid artery atherosclerosis which contributed to cardiac dysfunction [5]. Another relevant study in aborted fetuses of mothers living in endemic fluoride areas reported changes in neurotransmitters compared with levels of aborted fetuse of mothers living in non-endemic areas [2]. Additionally, it has been demonstrated that fluoride exposure has the potential to disrupt thyroid functioning. In fact, adults living in Canada who have moderate-to-severe iodine deficiencies and higher levels of urinary fluoride may be at an increased risk for underactive thyroid gland activity [6]. Within this context, our group conducted a survey study where 15 commercial samples of mineral waters and 15 commercial samples of tea and infusions consumed by the portuguese population were analysed. In the case of mineral waters samples were chosen in order to cover different regions of Portugal. As teas and infusions it concerns, the most common ones were analysed including, black tea, white tea, green tea, chamomile, lemon balm, peppermint or lemon verbena, among others. The concentrations of fluoride in the studied samples were carried out by direct potentiometry using a fluoride ion selective electrode and an Ag/AgCl reference system. The obtained results revealed the presence of fluoride in almost all the analysed samples. In fact, in some water samples as well as in some tea samples, the fluoride concentration overcomes the average value recommended by the World Health Organization, which is 1,0 miligrams of fluoride per liter of water.

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## Health

## Synthesis, Pharmacological and Biological Evaluation of PLG Picolinoyl Peptidomimetics as Positive Allosteric Modulators of D<sub>2</sub> Receptors

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L-prolyl-L-leucylglycinamide (PLG, Figure 1) is a neuropeptide cleaved from the hormone oxytocin that acts as a positive modulator of dopamine receptor  $D_2$ .<sup>1.2</sup> In this work it is described the synthesis and pharmacological evaluation of picolinoyl-based peptidomimetics of PLG (Figure 1) as dopamine modulating agents. These peptidomimetics were tested for their ability to enhance the maximal effect of *N*-propylapomorphine (NPA) at dopamine  $D_2$  receptors. Compound **6b** produced a statistically significant increase in the maximal NPA response at 10 pM (11.9 ± 3.7%), which is similar to the effect of PLG in this assay at same concentration (18.3 ± 9.1%). Functional assays corroborate the activity of peptidomimetic **6b** as positive modulator of  $D_2$  receptor. Cytotoxic and neurotoxic assays were performed for peptidomimetic **6b** using HEK 293T cells and cortex neurons from 19-day-old Wistar-Kyoto rat embryos, respectively, suggesting this analogue display no toxicity effect in these assays up to 100 µM. Conformational energy minimization for **6b** shows that this peptidomimetic cannot adopt the postulated type-II  $\beta$ -turn bioactive conformation, endorsing the possibility of an extended bioactive conformation as claimed by other researchers as a second bioactive conformation of PLG. Additionally, it was found that compound **5b** displays a marginal neuroprotective effect under oxidative stress promoted by H<sub>2</sub>O<sub>2</sub>. Overall, the pharmacological and toxicological profile of **6b** and its structural simplicity makes it a potential lead compound for further development and optimization.



Figure 1: PLG and active picolinoyl-based peptidomimetic 6b chemical structures.

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## Health

## Synthesis and Reactivity of Steroidal 1-Azadienes towards Carbonyl Compounds under Enamine Catalysis

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Steroids are a class of natural and synthetic compounds that are widely distributed in nature and exhibit a wide spectrum of biological activities.<sup>1</sup> The structural modification of the steroidal basic core is a strategy used successfully to modulate their biological properties.<sup>2</sup> In this context, we developed a diastereosselective synthetic route to chiral penta- and hexacyclic steroids through annulation reaction of steroidal *N*-sulfonyl-1-azadiene **1** with ketones under enamine catalysis.<sup>3</sup>

In order to extend this novel approach to new penta- and hexacyclic steroids we set out to explore the reactivity of the steroidal 1-azadiene 1, derived from 16-DPA, towards a range of ketones and aldehydes in the presence of pyrrolidine. Azadiene 1 reacted with ketones, namely 1,4-cyclohexanedione monoethylene acetal and phenylacetone to give the corresponding chiral steroids 2 through annulation reaction. Interestingly, steroidal 1-azadiene 1 reacted with aldehydes to give the hetero-Diels-Alder cycloadducts 3 (Scheme 1a). This chemistry was extended to other steroidal scaffold, namely 1-azadiene 5, a carbonyl protected 16-dehydroprogesterone oxime 4 derivative (Scheme 1b). Details of this study will be presented and discussed.



Scheme 1: a) Reactivity of steroidal 1-Azadiene 1. b) Synthesis of new steroidal 1-azadiene 5.

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## Health

## Building an enzymatic reactor towards a finer *in vitro* drug metabolism model

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One of the critical steps in drug design and development is the evaluation of drug safety. A non-neglectable number of current and under development drugs present toxic side effects of light to severe impact that in most cases come from drug bioactivation to a reactive electrophile during the normal cellular detoxification process. This is of particular importance in therapies used to manage life-lasting chronical heath problems.

One of the key steps in toxicity evaluation is the pre-clinical study of the potential metabolic pathways of drugs, that can be accomplished with purified enzymes, cell fractions, tissue samples or test animals. Within this paradigm, we have successfully sub-cloned His-tagged human sulfotransferases 1A1 and 1B1 and cytochromes P450 2C9 and 2D6 into toxicity-resistant expression-competent *E. coli* hosts.

Upon expression and purification, enzymatic activity tests were performed to characterize their activity, and it has been observed that these recombinant enzymes maintain not only their catalytic efficiency but also their substrate specificity and give rise to the expected products. These tests were performed with model substrates like phenol, and with substrates with well-characterized metabolic pathways, in particular the anti-retroviral nevirapine, the selective estrogen recetor modulator tamoxifen and the leukotriene receptor antagonist montelukast, three drugs that are used chronically world-wide and are associated to serious side-effects. Nevirapine was shown to be metabolized in this system to the corresponding hydroxy-derivatives, with the various products found in ratios matching those of the *in vivo* studies. Tamoxifen was found to be dealkylated and hydroxylated to various oxidation products, in agreement with the literature data.

To further develop this *in vitro* model for drug metabolism, we have immobilized the recombinant proteins on Ni-based supports, and the global enzymatic properties of the proteins were maintained unaltered.

Immobilization conditions are currently being fine-tuned in order to increase the yield of formation of different drug metabolites in conditions of co-immobilization, where different proteins can be used simultaneously to generate not only a set of drug metabolites coming from multiple catalysis but also where isoform preference can be studied *in vitro*.

Taken together, these results support the use of simple yet accurate *in vitro* enzyme reactors as predictors of drug metabolism, and can be used during all phases of drug development in order to rule out molecules with an higher toxicity risk and contribute to safer therapeutic approaches.

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## Health

## New Pyrazolylquinolones: Synthesis and Antioxidant Activity

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The oxidation state of cells is regulated by the non-enzymatic (eg. glutathione, ubiquinone, vitamin E, β-carotene, phenolic compounds) and by the enzymatic (eg. superoxide dismutase, catalase and glutathione peroxidase) antioxidant systems whose production/expression decreases with aging, being necessary to strengthen the antioxidant defenses of the body to prevent it from oxidative stress unwanted effects. The search of new drugs with antioxidant properties is an active field of medicinal chemistry because oxidative stress is well-known to be involved in the pathogenesis of lifestyle-related diseases, including atherosclerosis, hypertension, diabetes mellitus, neurodegenerative diseases and cancer.

Quinolones and pyrazolines are nitrogen heterocycles of recognized importance in medicinal chemistry because of their remarkable biological properties. Quinolones are known to possess neuroprotective and antioxidant activity.<sup>1,2</sup> On the other hand, pyrazolines have anti-inflammatory and also antioxidant activity.<sup>3</sup> The objective of this work was to combine these two key scaffolds in one single molecule, the pyrazolylquinolones **2** [3-(3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)quinolin-4(1*H*)-one], to obtain new compounds with enhanced antioxidant activity. A series of pyrazolylquinolones **2** was synthetized, in good yields (37-82%), starting from (*E*)-3-(3-aryl-3-oxoprop-1-en-1-yl)quinolin-4(1*H*)-ones **1** by reaction with hydrazine derivatives in refluxing methanol (**Figure 1**). The *in vitro* free radical scavenging activity (FRSA) of these compounds against DPPH<sup>+</sup>, ABTS<sup>++</sup> and NO<sup>+</sup> radicals was evaluated. It was found that pyrazolylquinolones **2** are much more active than their precursors, the (*E*)-3-(3-aryl-3-oxoprop-1-en-1-yl)quinolin-4(1*H*)-ones **1**, showing FRSA better than ascorbic acid, except for the non-substituted derivative (**2b**,  $R^2 = H$ ) (**Figure 1**). Important structure-activity relationship (SAR) studies were established that guided the design of new derivatives for further biological evaluation. More details concerning the synthesis of compounds **1** and **2**, their structural characterization, antioxidant activity and SAR studies will be presented and discussed in this communication.



Figure 1: Synthesis of pyrazolylquinolones 2 and their ABTS++ radical scavenging activity in comparison with ascorbic acid.

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## Health

## Study of the effect of chronic kidney disease on urea and ammonia levels in saliva using a sequential injection system with potentiometric detection

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Chronic Kidney Disease (CKD) is a growing health issue worldwide, causing the death of 60,000 people annually. End-stage patients require renal replacement therapies, such as peritoneal dialysis (PD), in order to eliminate part of the uremic toxins built up in the body that, in health, would be eliminated into the urine. The accumulation of these toxins leads to biochemical alterations in different body sites, including the oral milieu. Both salivary urea and ammonia, the latter resulting from the hydrolysis of urea by urease-producing commensal oral bacteria, are increased in CKD patients. For this reason, it has been suggested that assessing these parameters could be of potential use to monitor kidney function and even diagnose renal disease. Taking all this into consideration, this work aimed to develop a sequential injection (SI) system to assess and compare salivary urea and ammonia levels between CKD patients and healthy individuals.

A SI system for the potentiometric detection of urea and ammonia in saliva samples was developed and validated. The enzymatic conversion of urea was carried out in-line prior to the detection with a combined ammonia electrode. The developed SI system was applied to samples collected from 38 healthy individuals, constituting the control group, as well as to samples collected from 38 CKD patients undergoing peritoneal dialysis, followed at the outpatient clinic of the Nephrology Department of São João Hospital Centre. The average values obtained for salivary ammonia were 16.8±12.3 mg/dL and 64.9±38.1 mg/dL, and the average values for salivary urea were 19.4±13.9 mg/dL and 87.4±46.2 mg/dL for the control and study groups, respectively (**Figure 1**). Both parameters proved to be statistically different (p-value<0.05) between healthy and diseased individuals, which proves that the developed methodology successfully assessed theses parameters in a wide quantification range.



Figure 1: Average salivary ammonia and urea values for healthy individuals (control group) and for CKD patients.

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## Health

## Royleanone derivatives from *Plectranthus* spp. as new P-glycoprotein inhibitors

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P-glycoprotein (P-gp) is an efflux pump that reduces the intracellular drug accumulation, preventing drug-target interactions. P-pg is often overexpressed on the surface of tumor cells. P-gp inhibition is applied in cancer therapy to overcome multidrug resistance.<sup>1</sup>

Royleanones are bioactive compounds frequently found on *Plectranthus* genus. The compound  $7\alpha$ -acetoxy-6 $\beta$ -hydroxyroyleanone (Roy, Figure 1) exhibits promising *in vitro* antiproliferative activity. Other cytotoxic diterpene 6,7-dehydroroyleanone (DeRoy, Figure 1), has the ability to evade the activity of P-gp. These royleanones are the major compounds of the acetonic extract *P. grandidentatus* and the essential oil of *P. madagascariensis*, respectively. Additionally, both diterpenes have hydroxyl groups suitable for derivatization, which have drawn our attention for the possibility of exploring their reactivity.<sup>2</sup>

In this work, several hemi-synthetic reactions were performed in the lead compounds (Roy and DeRoy) to prepare a library of new compounds. The general toxicity of the new royleanone derivatives was evaluated. Results showed that the correspondent benzoylated derivatives improved toxicity when compared to Roy and DeRoy. Furthermore, the most promising compounds were tested in multidrug resistant NCI-H460/R cells overexpressed of P-gp. Molecular docking studies were also performed in a murine P-gP structure. The benzoylated and dibenzoylated products showed promising results in both molecular docking and biological studies. Further derivatives are currently been prepared for structure-activity relationships and new drug development based on the royleanone scaffold.



Figure 1: Natural royleanones from *Plectranthus* spp.

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## Health

## iLIQUID4Malaria – synthesis, physico-chemical properties and antimalarial activity of new organic salts derived from antimalarial drugs and fatty acids

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New organic salts with antimalarial activity have been prepared through a simple and inexpensive method, namely, neutralization of antimalarial amines such as chloroquine and primaquine with natural fatty acids. The respective covalent analogues (amides) were also prepared by addition-elimination reactions *via* standard *in situ* peptide coupling methods, in order to compare the effect of ionic *vs.* covalent bond on the properties of the compounds **(Scheme 1)**.<sup>[1]</sup>

The thermal stability of both the organic salts and amides was evaluated by simultaneous thermal analysis (STA), which combines thermogravimetry and differential scanning calorimetry (DSC). Also, considering the amphiphilic nature of fatty acid salts, the new organic salts produced have been further characterized regarding their interfacial and aggregation properties.

Finally, the antimalarial properties of all compounds was assessed *in vitro* both on liver- and blood-stage parasites, which showed that (i) all compounds are active; (ii) amides are better than the salts against liver-stage parasites; (iii) the salts stand out against blood-stage (disease-causing) parasites; (iv) there is an optimal size for the fatty acid chain.

Altogether, this work demonstrates that organic salts derived from classical antimalarial drugs may open a new doorway towards sustainable low-cost approaches to fight malaria, a disease that mostly affects low to middle income countries.



Scheme 1: preparation of the target organic salts (left), and of their covalent amide analogues (right).

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## Health

## A green synthesis of a spirooxadiazoline oxindole chemical library

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The spirooxindole skeleton is found in numerous natural products and biologically active compounds, and is a very attractive scaffold for organic and medicinal chemists.<sup>1</sup> As a consequence, there is a huge interest in industry and academia to develop novel spirooxindoles that have good potency against therapeutic targets. Currently, three spirooxindoles, NITD609, CFI-40095 and SAR405838, have achieved clinical trials for the treatment of diseases such as, malaria and human cancers. Previously, we have shown that spiro-1,2,4-oxadiazoline oxindoles have antitumoral activity in breast and colon cancer cell lines, by inducing apoptosis and cell cycle arrest, by upregulating p53 steady-state levels, while decreasing its main inhibitor MDM2.<sup>2</sup> In this communication, we will report our most recent results on the development of the regioisomer spiro-1,3,4-oxadiazoline oxindole scaffold to obtain novel activators of the p53 pathway (Scheme 1). Normally, these compounds are obtained by a 1,3-dipolar cycloaddition of isatin derivatives with nitrile imines formed *in situ* from hydrazonoyl chloride derivatives using dichloromethane and triethylamine, as solvent and base respectively.<sup>3</sup> Herein, we will disclose our results on the development of a greener method of synthesis with higher reaction yields.



Figure 1: Spiro-1,2,4-oxadiazoline oxindole (1) scaffold and its regioisomer spiro-1,3,4-oxadiazoline oxindole (2). Spiro-1,2,4oxadiazoline oxindoles (1) have antitumoral activity, by inhibiting the interaction p53-MDM2.

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## Health

## Synthesis of tetraoxane-pyrimidine hybrids with potential inhibitory activity in liver stage malaria parasites

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Malaria is a disease caused by parasites from *Plasmodium* genus. Development of antimalarial drugs has been predominantly focused on the blood stage of the malaria parasite, which is responsible for the symptoms associated to the disease. The liver stage of Plasmodium infection is an obligatory step in the maturation and replication of mosquito-delivered parasites toward generating the erythrocyte-infective forms<sup>1</sup>. It is highly desirable to target the live stage in order to eradicate malaria for efficacious and safe tools for malaria prophylaxis <sup>2</sup>, furthermore, there is a limited number of available compounds actives against non-erythrocytic parasites <sup>3</sup>.

Currently, only a few drug targets are fully validated for the hepatic stage of malaria. Building on our previous results on liver stage (active endoperoxides)<sup>4</sup>, we now report the synthesis of tetraoxane-pyrimidine hybrid compounds containing a reactive warhead that may lead to reversible inhibition of parasitic cysteine hydrolases (Figure 1). These compounds can undergo a reaction with a catalytic cysteine residue to form a reversible abduct, and have the potential to be used as probes to gain a better understanding of the mechanism of action as well as identify the potential active cysteine containing target(s) for this class of liver stage inhibitors. In this communication we will present the synthetic strategy to prepare the hybrid inhibitors and their potential as antimalarial agents.



Figure 1: General structure of Tetraoxane-Pyrimidine derivative

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## Health

## (Photo)switchable azaaurones: antimycobacterial activity and metabolic reactivity

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Tuberculosis stands as one of the most lethal diseases worldwide, with 1.6 million deaths reported in 2017.<sup>1</sup> Regarding current therapies, the emerging resistance alongside low therapy compliance are key factors in increasing disease burden and mycobacteria proliferation.<sup>2</sup> It is urgent to find new potent drugs against *Mycobacterium tuberculosis*, that may overcome the resistance problem and simplify the treatment.

Azaaurones are potent antimycobacterial agents, with MIC<sub>99</sub> values as low as 0.37  $\mu$ M against *M. tuberculosis H37rv* strain.<sup>3</sup> SAR analysis revealed that *N*-acetyl azaaurones display improved activity when compared to their NH counterparts, while being rapidly metabolized. *N*-Acetyl azaaurones are typically synthesized as inseparable mixtures of the *E* and *Z* isomers. We now report, for the first time, the synthesis, photoisomerization, biological evaluation, and metabolism study of the *E* and *Z* isomers of diversely *N*-substituted azaaurones. (Scheme 1) Metabolic- and photoisomerization studies reveal that the stereoelectronic properties of *N*-substituent play a determinant role in the isomerization rates. Here, we also disclose the structure-activity and structure-metabolism relationships for these novel antimycobaterial agents.



Scheme 1: Photoisomerization, biological evaluation, and metabolism study of the E and Z isomers of N-substituted azaaurones.

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## Health

## The influence of metal core in the formation and stability of G-quadruplex/porphyrin adducts

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G-quadruplexes (GQ) are DNA secondary structures that are reported to be found in several genome regions of biological significance, especially in the telomeres,<sup>1</sup> which are non-coding regions at the ends of the chromosomes. Telomeres act as chromosome "sealants" stabilizing the linear strands and preventing their damage. In normal somatic cells, telomeres are shortened in the process of DNA replication and eventually become too short to protect the chromosome, leading to cell senescence and death. Many cancer cells can counteract this shortening by increasing the level of activity of telomerase, a reverse transcriptase enzyme, which allows continual cell division without telomere shortening. Telomerase is expressed in a range of cancer cells<sup>2</sup> and stabilization of GQ structures in the terminal region of the telomeres has been reported to inhibit telomerase activity. Consequently, GQ have emerged as a new class of novel molecular targets for the design of anticancer drugs.<sup>3</sup>

Several studies have shown that porphyrins and analogues, in special, 5,10,15,20-*tetrakis*(1-methylpyridinium-4yl)porphyrin (**TMPyP**) exhibits high affinity to GQ and thus it is a potential telomerase inhibitor. However, it is also recognized that this cationic ligand has poor selectivity for GQ over duplex DNA structures. Selectivity for quadruplex over duplex DNA is a fundamental attribute, as the drug must be able to recognize quadruplex DNA in the presence of a large amount of duplex DNA, in the cellular nucleus.<sup>4</sup>

In this study different metals, such as Ag, Cu, Co, Ni, Pd and Zn were introduced in the **TMPyP** core. By using UV-Vis titrations, the influence of the metal on the formation and stability of porphyrin-DNA adducts (quadruplex or duplex) was studied. From the obtained results it was possible to evaluate the stoichiometry of the adducts, the binding constants and the selectivity of the selected metalloporphyrins to GQ structures. Formation of stable porphyrin-DNA adducts for all the ligands with both DNA structures was observed and the metalloporphyrins coordinated with Ag and Pd seemed to be the most selective ones to GQ structures.



Figure 1: G-quadruplex-ligand adduct formation and telomerase inhibition

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## Health

## Development of serine-derived surfactant liposomes for the sustained delivery of doxorubicin into cancer

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Liposomes are among the most suitable nanocarriers for drug delivery, but improvements are still needed in terms of efficacy. We have recently developed catanionic vesicles based on cationic (16Ser) and anionic (8-8Ser) serine-based surfactants. Both net negatively charged— x(16Ser)=0.20, where x(16Ser) is the cationic surfactant molar fraction— and positively charged—x(16Ser)=0.58—vesicles are available, hence providing a surface charge-tunable system.<sup>1</sup> The *in vitro* performance of these vesicles was evaluated for the delivery of the anticancer drug doxorubicin (DOX) using a cancer cell model (A549).<sup>2</sup> The neat surfactants and both vesicle formulations present low toxicity, with high cell viability for concentrations below 32  $\mu$ M. DOX is successfully encapsulated in the vesicles, resulting in a surface charge switch to negative for the 0.58 system, making both the 0.20 and 0.58 DOX-loaded vesicles relevant for systemic administration. Cell uptake studies using flow cytometry and confocal microscopy show drug accumulation near nuclear regions (**Figure 1**) and an increase of cell uptake up to 250% and 200% for the 0.20 and 0.58 vesicles, respectively, compared to the free DOX. The *in vitro* cytotoxicity studies further show that DOX-loaded vesicles induce cell death, confirming the therapeutic potential of the formulations.<sup>2</sup>



Figure 1: Confocal microscopy images of the DOX-loaded catanionic vesicles showing DOX (red) accumulation around nuclear regions (blue).

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## Health

## Ionic Liquids and Organic Salts from Active Pharmaceutical Ingredients

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Major weaknesses of active pharmaceutical ingredients (APIs) are related with their low bioavailability and permeability, as well as polymorphic behavior, which negatively impact on their pharmaceutical efficiency and activity. Over the last years, the combination of APIs as anions or cations with biocompatible organic counter ions as Organic Salts and Ionic Liquids (API-OSILs) has risen in academia as an immediate tool to overcome such shortcomings<sup>1</sup>.

In this communication, we present our latest developments in the combination of APIs from different therapeutic families as anions, such as cephalosporins (cefuroxime), NSAIDs (ibuprofen)<sup>2</sup> and bisphosphonates (zoledronic, alendronic and etidronic acids)<sup>3</sup>. These APIs were combined with appropriate biocompatible organic cations, such as choline, alkylpyridiniums and alkylimidazoliums (see Figure 1).

The prepared API-OSILs were characterized by standard spectroscopic techniques (NMR, FTIR) as well as thermal analysis (DSC) to evaluate the mitigation or elimination of the polymorphic behaviour presented by the parent APIs. Furthermore, the solubility in water and biological fluids as well as the toxicological profile and biological activity of such new API-OSILs will be presented and discussed.



Figure 1: Chemical structure of selected APIs for preparation of API-OSILs.

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## Health

## Microwave-assisted synthesis of 2-benzylchromones and further structural functionalization

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The search for novel drugs, as well as, for simpler and greener alternatives for its synthesis remains as one of the main focus of several medicinal chemistry projects. Chromones (4*H*-chromen-4-ones) contemplate a naturally occurring class of compounds widely distributed in Nature, particularly in plants.<sup>1</sup> This singular ring system has emerged has as a privileged scaffold in medicinal chemistry, mainly due to its unique structural features and diverse biological activities<sup>2</sup>, from its anti-inflammatory activity<sup>3</sup> to its potential action against Alzheimer's disease.<sup>4</sup>

Throughout the past few years, 2-benzylchromones (3) have been synthesized through a Baker-Venkataraman rearrangement, using 2'-hydroxyacetophenones (1) and ethyl 2-phenylacetates (2) as starting materials, with conventional heating. This procedure allowed the group to understand the influence of different substitution patterns in the efficiency of this particular procedure. However, the extended periods of reaction necessary to accomplish the synthesis of 2-benzylchromones (3) led to the search for a synthetic alternative. Thus, microwave irradiation emerged as a suitable approach to the obtention of this type of compounds in shorter periods of reaction, with similar results.

In addition to this novel synthetic procedure, and following the obtention of some interesting secondary products, a few structural functionalizations have been performed in these compounds in order to improve any potential biological activity of these compounds. Thus, considering its reactivity, these modifications are mostly focused in the methylene group of the 2-benzylchromones, consisting in oxidations and Wittig reactions, obtaining 2-benzoylchromone and 2-styrylchromone derivatives, respectively.



Figure 1. Alternative synthetic routes for 2-benzylchromones

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## Health

## *N*-Acetylgalactosamine Mimetics Towards Protein-Protein Interaction in Alzheimer's Disease

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Alzheimer's disease (AD) is a protein misfolding pathology, causing dementia in over 40 million people worldwide. Cellular prion protein (PrP) is a high-affinity binding partner of amyloid  $\beta$  (A $\beta$ ) oligomers, the most toxic species in Alzheimer's pathology<sup>1</sup>. It has been demonstrated that *N*-acetylgalactosamine (GalNAc) and other monosaccharides, such as *N*-acetylglucosamine and mannose *O*-glycosylated, when attached to Ser/Thr side chain of a PrP, via an  $\alpha$ -glycosidic linkage, promote the inhibition of amyloidogenesis in AD<sup>2</sup>. In this context, we have synthetized new GalNAc mimetics, including phenyl selenogalactosides with additional contacts in the GalNAc core structure, to improve the interactions with PrP and to investigate the binding affinity with A $\beta_{1-42}$ . The study, at the highest possible resolution, of the intermolecular interactions of the new chemical structures with A $\beta_{1-42}$  oligomers was investigated by NMR methods, namely saturation transfer difference NMR (STD-NMR) and <sup>19</sup>Fluorine NMR (F-NMR) protocols, in tandem with molecular modelling techniques. Different methods, such as rapid equilibrium diffusion (RED) were attempted for the evaluation of the interaction. These experiments have shown different interaction results regarding C2 substitution and anomeric heteroatoms, such as O, S and Se with A $\beta_{1-42}$  oligomers.

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## Health

## Effect of high pressure processing on a functional acorn beverage

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In recent years, consumers have become increasingly aware of the impact of nutrition on their health, increasing the demand for healthy and nutritious products. 1 The current lifestyle has led consumers to look for more convenient and ready-to-eat products. In this sense, consumption of plant-based beverages is an interesting healthier alternative once it can be an excellent way to increase the intake of bioactive compounds.2 Although unprocessed plant-based beverages have a short shelf life, the high pressure processing (HPP) opens the door to obtaining nutritional and sensorial improved fresh products in relation to traditional thermal processed products.3 The acorn is very abundant in Portugal but still is sub-valorised to the point of staying in the field without any use, despite their high nutritional value, phytochemical compounds, antioxidant, anticarcinogenic and cardioprotective properties.4,5 This fruit has potential use in the treatment of specific diseases such as cardiovascular or neurodegenerative diseases, which triggered the interest in integrating the acorns into the human diet.5

This work aimed to develop a functional acorn beverage, free of gluten and lactose, only with acorn and water as ingredients. Thereafter, the impact of pasteurization by HPP (450 and 600 MPa during 5, 12.5 and 20 minutes) and conventional thermal processing (85°C for 30 minutes) on physical-chemical characteristics of the final product was assessed.

In terms of colour, the parameter b\*, was different, mainly between the thermal processed and the rest of the samples. The pH of the untreated samples was lower than that of the pasteurized ones. The degree brix is very low in all samples, which indicates that the presence of simple sugars is almost null, with slight differences in the thermally processed samples. Total phenolics (Folin Ciocalteu method) as well as antioxidant activity (ABTS and DPPH methods) did not show great differences between treatments, and the phenolic profile was evaluated, giving gallic acid as the main phenolic compound of this beverage. In addition, the effect of the initial acorn leaching and of the processing on the content of hydrolysable tannins was studied, since these compounds are responsible for the undesirable astringency of the acorn. With this study, some basic physical-chemical aspects of an acorn beverage were determined, in order to proceed with the development of a functional beverage with this fruit that is a surplus in Portugal.

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# COMUNICAÇÕES EM Painel

A TABELA PERIÓDICA E OS ELEMENTOS DA VIDA Saúde, Alimentação e ambiente

## CPF1

## Food

## High pressure processing, a non-thermal technology affecting potato tuber quality

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Potatoes are important tubers for human consumption, providing an essential source of energy and great nutritional characteristics for human health. However, before consumption, potato tubers need to be cooked mainly due to the indigestibility of starch<sup>1</sup>.

High pressure processing (HPP) is a non-thermal technology that has been widely used not only for food preservation but also for the modification of biopolymers, such as starch and proteins, and to accelerate infusion processes. HPP and other emerging non-thermal technologies (namely pulsed electric fields, irradiation, cold plasma, and ultrasounds) have been applied in the treatment of potatoes, and have shown to improve various aspects associated with either the quality of potato tubers or subsequent processing, such as time and energy for potato slicing<sup>2</sup>. Specifically in relation to the effect of HPP on the quality of potato tubers, several studies in the literature have shown that HPP affects potato starch, enzymes, texture and physiological processes. Regarding potato starch, a pressure treatment of 600 MPa for 5 and 30 min induces modifications in the starch granule and starch gelatinization, respectively<sup>3</sup>. Furthermore, the activity of oxidative enzymes (polyphenol oxidase and peroxidase) is incremented by pressure<sup>4</sup>, and HPP can be used as a nonthermal and chemical-free alternative to control the sprouting of potato tubers<sup>5</sup>. Moreover, cell permeability and infusion of molecules into potatoes increase with application of pressure, and processing times are reduced<sup>6</sup>.

In this work, by applying a range of pressure between 100 and 500 MPa, for 2.5 min, it was possible to observe a decrease of up to 42% in the firmness of whole potato tubers, with or without peel, and packaged in water or under vacuum. In addition, by applying 200-600 MPa for 2.5 min, the energy for potato cutting reduced up to 45% (**Figure 1**), the surface roughness decreased, and the release of sugars from potatoes increased with the applied pressure. Besides, the increase of salt concentration in the exterior water of potato sticks induces the expulsion of water, reducing their moisture content.

In conclusion, HPP is a non-thermal technology that affects the quality of potato tubers at several levels, namely at the textural, physical and chemical level and for this reason, it may be used as a pre-processing treatment for the production of potato products with different/better sensorial, textural and nutritional properties.



Figure 1 - Image of a potato stick before and after pressurization treatment, and results of texture analysis by a cutting test with a knife.

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# Food

# Physical and Chemical characterization of anthocyanins from Purple-Fleshed Sweet Potato

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Anthocyanins represent one of the most amazing classes of compounds among polyphenols.

These molecules have unique characteristics such as their structural dependence on pH [1]. The kinetic and equilibrium network of anthocyanins has been widely assessed in order to understand their behavior and stability under different pH conditions.

Among the different types of anthocyanins, Purple-Fleshed Sweet Potato (PFSP) anthocyanins primarily exist as polyacylated and poly-glycosylated structures derived from Peonidin and Cyanidin [2]. Acylation with various phenolic acids makes PFSP anthocyanins unique and also provides some advantages towards pH and heat resistance, light sensitivity, and overall stability [3], as anthocyanins are known to be reactive compounds that have their stability affected by oxygen, heat, light, pH and enzymes [4]. The study of their equilibrium network is therefore essential. Also, anthocyanins are reported to have poor light-emitting properties, however the scarce information on this matter was performed with monoglucosides and non acylated anthocyanins [5].

Thus, the aim of this study was to characterize the physical and chemical properties of anthocyanins from red wine. For that, a structural characterization of two main Purple-Fleshed Sweet Potato anthocyanins was performed using LC-MS and NMR techniques. The study of the equilibrium network was performed with the use of *pH jump* techniques and the fluorescence properties of the two isolated anthocyanins were also assessed.

The results suggested a higher stability at a broader range of pH values (with lower hydration and higher acidity constants) of the isolated anthocyanins when compared to the already published kinetic and equilibrium parameters of the parent non acylated anthocyanin. Also, unique fluorescence properties were reported for the anthocyanins of PFSP for the first time with an ex/em pair of  $\lambda_{ex}$  610 nm/  $\lambda_{em}$  640 nm. A biological experiment was performed using gastric and intestinal cell lines, and PFSP anthocyanins intracellular localization with the use of fluorescence microscopy techniques.

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#### Food

# Effect of high pressure processing on raw dairy cream

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Thermal processing remains the dominant method for food preservation, due to its low cost, high productivities and effectiveness on increasing products shelf-life (1). However, despite the fact that this treatment is necessary to destroy vegetative microorganisms that may be pathogenic or cause spoilage, and to inactivate enzymes, depending on the food matrix, it may not be the most adequate process, since it relies on extensive heat transfer that may cause considerable changes on the product's quality, including the development off-flavours and destruction of important thermolabile nutrients (2).

Food products' safety and quality are the two major factors that influence the choices made by today's increasingly demanding consumers. This seek for more natural products that are fresher, tastier, nutritious and free from chemical preservatives, has been driving the emergence of non-thermal technologies, such as high pressure processing (HPP). This emerging food processing technology may extend shelf life, mainly due to its microbial inactivation, without any thermal treatment or use of preservatives (clean label foods), ensuring food quality/safety, thus reducing food waste/losses.

Dairy cream can be considered a perishable product, since it has a pH close to neutral values (around 6.7) and high water activity (around 0.97), thus requiring a pasteurization treatment in order to increase its shelf-life (3,4). Traditionally, most of the cream produced for retail consumption and industrial use is thermally pasteurized (5). In this

study, raw cream was subjected to thermal pasteurization and to HPP (450 MPa for 5 min and 600 MPa for 5 and 15 min) and then stored under refrigeration (4 °C), in order to compare the effect of both pasteurization treatments on cream's microbiological and physicochemical parameters. Concerning cream's microbial load, by the 51<sup>st</sup> day of storage, total aerobic psychrophiles (Figure 1) and lactic acid bacteria counts of thermally pasteurized samples had already surpassed 6.00 log CFU/mL, while HPP samples at 600/5 were still microbiologically acceptable. The effects of HPP on inoculated Escherichia coli and Listeria innocua were also analysed, being HPP able to significantly reduce their counts. In general, pH, colour, viscosity and fatty acids were not significantly altered (p>0.05) by the different processing conditions and storage. On the other hand, volatile compounds of all treated samples presented a tendency to increase throughout the storage period particularly acids and aliphatic hydrocarbons.



Figure 1: Microbial growth of total aerobic psychrophiles on initial raw cream, after heat treatment and after pressure treatment under 450 MPa (450/5) and 600 MPa (600/5) during 5 min. Microbial counts  $\geq$ 6.0 log CFU/mL were considered not consumable and those < 1.00 log CFU/mL are below the detection limit.

In conclusion, these results highlight the potential of HPP for a safe extension of dairy cream's microbiological shelflife, representing a better alternative to conventional thermal pasteurization.

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# Food

# Perfil fenólico e atividade citotóxica dos diferentes constituintes da Cynara cardunculus L. var. altilis

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*Cynara cardunculus* L., mais vulgarmente conhecida por cardo, é uma planta herbácea nativa do Mediterrâneo e pertencente à família *Asteraceae*. Esta espécie é maioritariamente cultivada em países como Portugal, Espanha, Itália e França e consumida em diversos pratos, devido à sua composição nutricional e à presença de vários compostos com propriedades medicinais (antimicrobianas, diuréticas, coleréticas, antioxidantes). Apresenta elevado potencial industrial e comercial devido às suas múltiplas aplicações, nomeadamente na produção de queijo, papel, de biodiesel, biomassa e bioenergia.<sup>1,2</sup> A expansão das suas aplicações industriais e o consequente interesse comercial associado, foi o principal contributo para o aumento do seu valor económico e do seu cultivo.<sup>2</sup> A valorização de todos os seus constituintes é de extrema importância, no sentido de reduzir desperdícios e, simultaneamente, contribuir para a sua valorização.

Neste trabalho, foi avaliada a composição fenólica e a atividade citotóxica de diferentes constituintes do cardo (pedúnculo, folhas, brácteas e sementes). As amostras de cardo cultivado (var. *altilis*) foram obtidas na Grécia em maio de 2018. A composição fenólica dos extratos hidrometanólicos foi analisada por HPLC-DAD-ESI/MS. Foi também avaliado o potencial citotóxico usando o método colorimétrico da sulforrodamina B, utilizando quatro linhas celulares tumorais humanas: HeLa (carcinoma cervical), HepG2 (carcinoma hepatocelular), MCF-7 (adenocarcinoma de mama), NCI-H460 (carcinoma de pulmão) e uma linha não tumoral PLP2 (cultura primária de células hepáticas de porco).

As quatro partes do cardo apresentam diferenças na composição e no conteúdo de compostos fenólicos. As folhas demonstraram uma maior variedade de compostos fenólicos, tendo sido identificados treze compostos. No pedúnculo e brácteas foram identificados um total de onze compostos. Por sua vez, as sementes são o constituinte com menor variedade destas moléculas, tendo sido identificados apenas quatro compostos. Relativamente à quantidade de compostos fenólicos, as folhas foram o tecido vegetal que demonstrou uma maior abundância, seguidas das brácteas, sementes e pedúnculo. Em todas as partes estudadas os compostos maioritários foram os ácidos cafeoilquínico e dicafeoliquínico. Em relação ao potencial citotóxico, todas as partes inibiram a proliferação das linhas celulares testadas. Contudo foram as folhas que demonstraram maior potencial citotóxico. Relativamente às PLP2, as concentrações de inibição são significativamente superiores às demonstradas para as linhas celulares tumorais. Este estudo demonstrou que a composição e abundância de compostos fenólicos, bem como a atividade citotóxico, varia de acordo com o tecido vegetal. As folhas foram a parte com maior quantidade e variedade de compostos fenólicos e, consequentemente, maior potencial citotóxico. Este estudo sugere eventuais aplicações do cardo na

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### Food

# Avaliação das propriedades bioativas dos frutos de Solanum melongena L.

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Ao longo do tempo, tem sido cada vez mais clara a preocupação do consumidor em seguir uma dieta saudável e equilibrada. Deste modo, a preferência por fruta e vegetais tem sido cada vez mais evidente, sendo estes uma fonte de moléculas capazes de beneficiar a saúde do consumidor na prevenção de algumas doenças<sup>1</sup>. A beringela (fruto da planta *Solanum melongena* L.), pertence à família Solanaceae e surge como uma excelente alternativa para incorporar numa dieta saudável, visto ser uma importante fonte de nutrientes e compostos com potencial bioativo, que intervêm beneficamente na saúde do comsumidor<sup>2</sup>.

No presente estudo, foi realizada uma avaliação nutricional e química dos frutos de *S. melongena* analisando, separadamente, a polpa e o fruto completo (polpa e epicarpo).

O perfil nutricional (teor em proteínas, cinzas, gorduras, hidratos de carbono e energia) foi avaliado aplicando metodologias oficiais de análise de produtos alimentares (AOAC), os açúcares livres foram identificados/quantificados utilizando um sistema de cromatografia de alta eficiência acoplada a um detetor de índice de refração (HPLC-RI), os ácidos orgânicos foram determinados por cromatografia líquida ultra-rápida com um detetor de fotodíodos (UFLC-PDA) e os ácidos gordos por cromatografia gasosa acoplada a deteção por ionização de chama (GC-FID).

Os resultados evidenciaram um teor de humidade superior a 90%, em ambas as amostras avaliadas, tal como era expectável. Relativamente ao valor nutricional, salienta-se o baixo teor em gordura, hidratos de carbono e valor energético. A composição em açúcares revelou a presença de várias moléculas, como frutose, glucose, sacarose e trealose, obtendo-se uma concentração de açúcares totais de 3,0 ± 0,1 e 2,89 ± 0,01 g/100 g de massa fresca de fruto completo e polpa, respetivamente. Os resultados também revelaram a presença de outras moléculas, particularmente ácidos orgânicos. Na determinação de ácidos gordos, foram identificados 17 compostos, destacando-se o ácido palmítico (C16:0), seguidamente do ácido esteárico (C18:0), como maioritários em ambas as amostras estudadas.

De acordo com os resultados obtidos foi evidente que os frutos de *S. melongena* mostraram ser uma boa opção para enriquecer a dieta dos consumidores, podendo incorporar uma dieta baixa em gordura e hidratos de carbono.

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# Food

# Plant-based FOS and GOS: So easy, yet so difficult

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Oligosaccharides are a heterogenous group of short-chain carbohydrates that can comprise between 2 and 10 simple sugars units. Sugars of this length have many functions in the lives of animals being found on the plasma membrane of animal cells, where they can play a role in cell recognition. Oligosaccharides such as Galacto-oligosacharides (GOS) and Fructooligosaccharides (FOS) are functional foods known for their capability to act as prebiotics.<sup>1</sup>

They are able to escape the enzymatic digestion in the upper digestive tract, reaching the colon intact where they can be selectively fermented by the probiotic bacteria. Therefore, they promote several healthy effects to the consumers such as inhibition of undesirable bacteria, reduce of intestinal disturbances, stimulation of absorption and retention of minerals and reduce the risk of colon cancer.<sup>2</sup>

These non-digestible oligosaccharides have different sources of production. Industrially, the most used processes are the enzymatic hydrolysis of polysaccharides or enzymatic transglycosylation reactions using disaccharides as starting materials: sucrose for FOS and lactose GOS. Due to new trends in the market, plant-based OS get a renovated interest.<sup>3</sup> In this study, we focused in the obtention of FOS and GOS using plant matrixes (Yacon roots and chickpea seeds respectively) through simple and easy extraction methods using water, studying the effects of time, temperature and ratio matrix to water (w/v).

However, the obtained extracts contained proteins, lipids, pectines, saponins, mono- and disaccharides along the pretended prebiotic sugars. Purification steps are needed to increase the obtained oligosaccharides concentration and value. The real challenge to work with natural extracts is the purification process, especially in terms of separation the low molecular sugars that do not contribute to the desired properties of oligosaccharides. The present paper discusses the effectiveness of purification methods possible to scale up and compatible with food industry, such as adsorption in activated charcoal and charcoal-celite systems, precipitation with anti-solvents and liquid-liquid extraction.

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# Food

# Antimicrobial peptides as potential alternatives to prevent food spoilage

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In 2015 it was estimated that on average the world consumption of antibiotics was 45 mg·kg<sup>-1</sup> for cattle, 148 mg·kg<sup>-1</sup> for chicken and 172 mg·kg<sup>-1</sup> for pigs. Various studies suggested that low dosage exposure of antibiotics to livestock creates ideal conditions for the development of resistances and their spread between animals.<sup>1</sup> Consequently, there is an increasingly robust global campaign to ban the use of synthetic antibiotics from agriculture, livestock management and the agro-food industry (AFI). Therefore, increasing the shelf life (commercial validity) of food products, and the use of sustainable production and consumption processes are some of the current challenges faced by the AFI. Furthermore, the current increase in consumer demand for natural 'organic' foods has forced companies and researchers to explore different ways to improve their market penetration by offering products with improvements in freshness, quality and food safety.<sup>2</sup> This has made the AFI to suffer rapid changes in the last few years, including the use of antimicrobial peptides (AMP) as a mean of prevention of food spoilage.

AMP are well-known components of the innate immune system that are rapidly gaining relevance, as opposed to conventional antibiotics which effectiveness is declining. This is explained by a group of special features, including wide activity spectrum, high efficacy at low concentrations, and low propensity for eliciting resistant microbial strains. In the particular case of this study, peptides derived from milk proteins will be the major focus since many sequences reveal bioactive properties when released during enzymatic hydrolysis.<sup>3</sup> For this purpose, we have synthesised various sequences using manual and automated solid phase peptide synthesis to test on a panel of selected bacterial species susceptible to contaminate smoked sausage.

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### Food

# Development of an improved analytical approach, US-QuEChERS<sub>dSPE</sub>/UHPLC-PDA, to quantify pesticide residues in potatoes

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Pesticides have been associated to human health hazards, ranging from headaches to cancer, reproductive and endocrine system disruption. Inappropriate use of pesticides may also cause damage to the environment, increase resistance in the target pest organisms and deleterious effects of non-target organisms.<sup>1</sup> The European Union (EU) set directives for pesticides usage, establishing maximum residue limits (MRLs) in fruits and vegetables.<sup>2</sup> It is very important to monitor if the pesticide residues are below the MRLs in food matrices and evaluate if they pose a risk to the health of consumer and environment.

The purpose of this work was to develop a fast and improved analytical approach to identify and quantify pesticide residues in potatoes (Solanum tuberosum L.) cultivated at Madeira Island based on QuEChERS assisted by ultrasound procedure (US-QuEChERS) combined with ultra high-pressure liquid chromatography equipped with a photodiode array detection system (UHPLC-PDA). The selected pesticides were the most commonly used in Madeira Island. They include insecticides (e.g. chlorpyrifos, acrinathrin, deltamethrin,  $\lambda$ -cyalothrin) and fungicides (e.g. thiabendazole, cymoxanil).

The parameters that influence the US-QuEChERS extraction efficiency and UHPLC-PDA resolution, such as extraction solvent, buffered salts, stationary phases, gradient conditions, and eluents, were assayed and optimized using a central composite design (CCD). The best performance was obtained using 30 min of ultrasound (US) agitation, 50% of acetonitrile (ACN) acidified with 0.1% phosphoric acid (PhA) as extraction solvent and a combination of magnesium sulphate: sodium chloride: disodium hydrogencitrate sesquihydrate: trisodium citrate dihydrate as partition salts in a ratio of 1:1:0.5:1. For extract clean-up a combination of magnesium sulphate and primary secondary were found the most efficient. A binary mobile phase with a gradient program was used, combining acidified H<sub>2</sub>O (0.1% PhA) and ACN with a flow rate of 150  $\mu$ L/min. A high strength silica Acquity CORTECS analytical column (2.1 mm x 100 mm, 1.8 m particle size) packed with a trifunctional C<sub>18</sub> alkyl phase, kept at 30 °C, was the better choice for the separation of the selected pesticides.

After optimization, the method was validated according with IUPAC guidelines. The validated method showed to be selective for the studied pesticides, and good linearity, with correlation coefficient ( $r^2$ ) higher than 0.997. The limits of detection (LOD) ranging from 0.005 (chlorpyrifos) to 2.581 (thiabendazole) mg/L, whereas the limit of quantification (LOQ) limit from 0.015 (chlorpyrifos) to 7.821 (thiabendazole) mg/L. In relation to accuracy, the obtained values were higher than 87.7, while to the repeatability and the reproducibility values were lower than 20 %. The matrix influence the extraction efficiency of  $\lambda$ -cyalothrin and acrinathrin by presenting higher values than the expected 125 % from literature.

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# Food

# Hyperbaric Storage of Raw Fresh Meat from a Microbiological Point of View

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The development of new food preservation methodologies is of great interest since refrigeration (RF), the most commonly used preservation methodology, is responsible for high energy consumptions leading to a high carbon footprint.

In 1968, the unfortunate accident of the research submarine Alvin was the starting point for the development of a new food preservation methodology. This submarine remained sunk over 10 months at a depth of 1540 m ( $\approx$ 4 °C), and surprisingly, when it was recovered some foods were found in consumable conditions.

Although at that time some studies were carried out regarding the possibility to preserve food under pressure, only after 2012 further studies with different food products (e.g., fruit juices, ready-to-eat meals, fish) allowed to conclude that not only the microbial growth inhibition can be obtained but also microorganisms' inactivation could be achieved when food is preserved under pressure, while overall physicochemical parameters are maintained. Hyperbaric Storage (HS) relies on food storage under pressure (50–150 MPa) at low temperatures (5-15 °C), as a complement to RF, or at variable room temperature (RT), as an alternative to RF, during days to months.

This work aimed to demonstrate the HS feasibility on the control of the endogenous microflora of raw fresh meat, pork and bovine, at different HS conditions: 50 - 100 MPa and  $10 \,^{\circ}\text{C}$  – variable RT, being these compared to the traditional RF (4  $^{\circ}\text{C}$  and atmospheric pressure).

From all tested HS conditions, 50 MPa at variable RT was the only one that did not allow to guarantee the microbial quality of both

meat samples over 15 days, since the initial microbial loads increased more than 1 and 2 log units for total aerobic mesophiles (TAM) and lactic acid bacteria (LAB), respectively, in several samples, although *Enterobacteriaceae* (ENT) and yeasts and moulds (YM) presented microbial loads reductions higher than 1 and 2 log units, respectively. Notwithstanding, as expected, RF presented even worst results on the microbial control over 15 days since all microorganisms revealed an increase of its loads reaching values above the safety limits for this kind of food product. On the other hand, when fresh raw meat was preserved at 60 MPa/10 °C and 75 MPa/25 °C/or variable RT it was observed not only a microbial inhibition along storage (up to 60 days), but also a microbial inactivation in most of the cases, for instance, reductions higher than 2, 1, 1 and 2 log units, for TAM, ENT, LAB, and YM, respectively. Meat preservation at 100 MPa at variable RT allowed a faster microbial inactivation in many samples being reached values below 1.00 log CFU/g just after 3 or 7 storage days.

HS was also tested when *E. coli* and *L. innocua* were present in raw fresh meat. Inoculated samples with these microorganisms allowed to observe the HS feasibly in its control up to 60 days, being verified that 60 MPa/10 °C and 75 MPa/25 °C were capable to inactivate them, reaching values below 1.00 log CFU/g for *E. coli* and reductions higher than 1 log unit for *L. innocua*.

At the end, it was possible to conclude that HS is capable to control the microbial load of raw fresh meat over storage, as well when inoculated with pathogens, up to 60 days, being these results much better than the ones obtained in the traditional RF.

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# Food

# On-line HPLC-DPPH screening method for evaluation of radical scavenging phenols extracted from *Moringa oleifera* leaves

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*Moringa oleifera* Lam, is the most widely cultivated species of a monogeneric family, the Moringaceae, which is native to the sub-Himalayan tracts of India, Pakistan, Bangladesh and Afghanistan. It is grown in West, East and South Africa, Tropical Asia, Latin America, The Caribbean, Florida and The Pacific Islands.<sup>1</sup> Extracts of *M. oleifera* have shown to exhibit potent antioxidant activity against free radicals, prevent oxidative damage to major biomolecules, afford significant protection against oxidative damage and exhibit antibacterial and antifungal activities, mainly attributed to its content in phenolic compounds.<sup>2,3</sup>

The phenolic profile of Moringa oleifera leaves from trees located in Oued Souf and Tamanrasset, desert region south Algeria, was characterized by a real-time HPLC coupled to the DPPH assay, together with high-resolution mass spectrometry (HPLC-DAD-ESI-MS<sup>n</sup>) studies. The contribution of each component to the overall radical scavenging capacity was evaluated for water, hydroalcoholic and hydroacetonic extracts of *M. oleifera* leaves. Hydroacetonic extracts (70% acetone) exhibit the highest amount of phenolic compounds (57 ± 3 mg GAE/g), as well as the highest flavonoid content (9.12 ± 0.01 mg QE/g). Twelve compounds, mainly phenolics, were identified by high-resolution orbitrap mass spectrometry. Among these, chlorogenic acids (3-caffeoylquinic acid and 4-caffeoylquinic acid) as well as quercetin glycosides (quercetin-3-O-glucoside, quercetin-3-O-galactoside and quercetin 3-O-(6"-malonyl) glucoside) are the most potent quenchers of DPPH radical both for hydroethanolic and hydroacetonic extracts. Aqueous extracts exhibit a quite different behaviour, with citric acid and quinic acid, arising from the oxidation of the chlorogenic acids, acting as the unique antioxidants.

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# Food

# Determination of antioxidants and total polyphenols in cabbages (*Brassica oleracea*) irrigated with wastewater contaminated with toxic metals.

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The use of treated water from Wastewater Treatment Plants (WWTP) for irrigation presents challenges that need to be clarified and then overcome. One of the challenges is the use of treated water from WWTP for the irrigation of vegetables. The use of treated water for gardening raises the question of the contamination of vegetables by toxic metals and other compounds harmful to humans [1].

In this study our concern is to determine to what extend the antioxidant activity and total polyphenols can be affected by the contamination of the vegetables when irrigated by water contaminated with toxic metals, namely cadmium, chromium, nickel and lead. Regarding this concern, our group implemented a research project in which synthetic treated water was used for controlled irrigation of cabbage (*Brassica oleracea*). This specie is the most common vegetable in Portuguese vegetable gardens and is usually consumed cooked. Synthetic waters were prepared with the concentration of each metal equal to the Limit Emission Value (LEV), 1/3 of the LEV and 2/3 of the LEV. The Limit Emission Value considered in this study corresponds to the maximum discharge concentration of the studied metals established by the Portuguese legislation (DL 236/98). The effect of irrigation with solutions of individual Cd, Cr, Ni and Pb was studied, as well as the effect of solutions prepared with all the metals together in the same concentrations. The use of synthetic waters allowed the effective control of metal content in the water and minimized the risk of microorganism's proliferation.

This horticultural specie was analysed to determine the antioxidant activity using the DPPH method and the total content of polyphenols present in the extracts was determined using Folin Ciocalteu method, in order to determine to what extent, the metal content used in irrigation water affects the levels of antioxidants and polyphenols. [2] [3]

Within a short-term period, we expect to have more results concerning this aspect of our research project and thus allowing us to gather some more information about the effect of toxic metals in antioxidants and polyphenols levels on vegetables irrigated with contaminated water.

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# Food

# Effect of contaminated water with toxic metals in cabbage (Brassica oleracea) growth rate

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The need of water for agriculture has increased in recent years in Portugal, particularly in the south of the country (Alentejo and Algarve) where new cultivation areas consume water from irrigation systems (Algueva and Mira) that may be needed to supply the local populations. It is also in the most southern areas of Portugal where the risk of global warming will be felt more seriously and sooner. It will then be urgent to evaluate the reuse of water produced in Wastewater Treatment Plants (WWTP) for farm irrigation. The water produced in the WWTPs has to meet the quality requirements defined in the law (DL 236/98) and has the advantage of providing nutrients and micronutrients to the species without the intensive use of fertilizers. The major concerns about the use of processed water from WWTPs are linked to the presence of pathogenic microorganisms and their content in toxic metals. Even a small quantity of heavy metals has harmful effects on man and other animals, due to the lack of mechanisms for their removal from the organism. Nowadays heavy metals are omnipresent in the environment because of industry, automotive traffic (combustion engines) and electricity coal-fired plants. The continuous use of metal contaminated wastewater in irrigation may also result in soil contamination.

A study was carried out, in which synthetic waste water was used for cabbage (Brassica oleracea) irrigation. Synthetic waters were prepared with the concentration of each metal (Cr, Cd, Ni, Pb) equal to the maximum discharge concentration of the studied metal (VLE), 1/3 of the VLE and 2/3 of the VLE established by the Portuguese legislation. The effect of the metals on cabbage growth was monitored by measuring the size of twelve leaves in six different cabbages for each irrigation situation. A total of 108 leaves were followed and their area measurements were statistically analyzed. Leaf growth rate averages are shown in Figure 1. It should be noted that all plants were grown in the same greenhouse to ensure the same environmental conditions. The plants were watered every two days with one litre of water containing the metals under study.



Figure 1 – Effect of toxic metals in the growth rate of Cabbage in a month.

As can be seen in figure 1, cabbage irrigated with tap water has the highest growth rate. For the remaining metals, and also for water containing all metals, the behaviour is diverse. However, maximum metal concentration is not always the most inhibitory situation of plant growth. For Cd and Pb the higher concentrations correspond to higher growth rates. These conclusions will be supported by the analysis of the metal content in each studied plants.



# Food

# Analysis and discrimination of magic mushrooms by ATR-IR and chemometrics

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Hallucinogenic mushrooms, or "magic mushrooms", as they are commonly named, are natural occurring fungi, belonging to the category of hallucinogens, as lysergic acid diethylamide (LSD). Some of the effects consumers can feel are alterations in mood and state of consciousness, alteration on visual, auditory and sensory perception, synesthesia, euphoria, and also anxiety, depression, fear and panic attacks.<sup>1</sup>

The consume of magic mushrooms was associated to some accidents, mostly among young people, occurred in the past, and which had resulted in deaths. With the alteration of the state of mind, people are more likely to risk behaviours, like trying to fly, or criminal offences, as public nuisance or traffic offences. More dramatic cases were also reported with magic mushrooms associated to murders.<sup>2,3</sup>

The psychoactive substances present on magic mushrooms are psilocybin and psilocin, two molecules from the family of serotonin, which are controlled substances since 1971 with the United Nation Convention on Psychoactive Drugs, which makes mushrooms, in general, a possible object of study in forensic cases, to discover if they are hallucinogens or not. In Portugal, these substances are also controlled.<sup>2</sup> As magic mushrooms can occur naturally, and there is a huge number of species of mushrooms, some of them visually similar to the hallucinogenic species, there is a need of develop fast, simply and non-destructive techniques for a right identification of mushrooms, even for people who are not expert on the mycological field, in forensic cases. The non-destructive techniques are the most preferred in forensic analysis.

Vibrational spectroscopy, including Attenuated Total Reflectance Infrared Spectroscopy (ATR-IR), combined with chemometric tools has been gained importance, not only in forensic field, but in chemical in general, because of the fast and reliable analysis of untreated samples by ATR-IR, which spectra are hardly interpreted by naked eye, but easily when chemometric analysis is performed.<sup>4</sup>

In this work, ATR-IR spectroscopy was combined with chemometric analysis in order to analyse a spectral dataset of mushrooms. The regression method modelled by OPLS-DA with the analysed spectra, was able to discriminate the mushrooms species and hallucinogenic mushrooms were well separated by other species, enable the method to be used as a first analysis technique to find if seized mushrooms have forensic interest or not.

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# Food

# Matrizes vegetais de interesse cosmético e alimentar: casos de estudo com Aloe vera (Aloe barbadensis Mill.) e haskap (Lonicera caerulea L.)

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A procura do mercado por compostos bioativos e corantes de base natural é dinamizada por um consumidor cada vez mais consciente e alertado para as consequências negativas que o consumo excessivo de alguns compostos artificiais provoca a longo prazo.<sup>1</sup> As indústrias cosmética e alimentar são as mais suscetíveis a esta pressão e, por isso, em colaboração com a academia, procuram substitutos de base natural (na sua grande majoria provenientes de plantas). Neste sentido, este trabalho procura valorizar novas matrizes vegetais (filete de Aloe vera - Aloe barbadensis Mill. - e bagas de haskap - Lonicera caerulea L.) e respetivos resíduos (casca de Aloe vera) como fonte de compostos de interesse cosmético e alimentar. As amostras de Aloe vera e haskap foram liofilizadas e reduzidas a pó. O valor nutricional foi avaliado seguindo métodos oficiais de análise de alimentos.<sup>2</sup> Os perfis em açúcares, ácidos gordos, tocoferóis e ácidos orgânicos foram determinados por técnicas cromatográficas. Os compostos fenólicos foram caracterizados por HPLC-DAD/ESI-MS e a atividade antioxidante foi avaliada pelos ensaios de base celular TBARS (inibição da formação de substâncias reativas do ácido tiobarbitúrico) e OxHLIA (inibição da hemólise oxidativa).<sup>3</sup> O filete de Aloe vera mostrou ser particularmente rico em água, revelando também altos teores de fibra e hidratos de carbono disponíveis, nomeadamente glucose e frutose. Verificou-se uma particular abundância de ácidos gordos saturados, com contribuição maioritária dos ácidos palmítico e esteárico. Relativamente aos perfis em tocoferóis e ácidos orgânicos, o α-tocoferol e o ácido málico, respetivamente, foram os compostos mais abundantes. Relativamente ao haskap, os hidratos de carbono foram os macronutrientes maioritários, apresentando frutose e glucose como principais acúcares livres. Foram detetadas quantidades consideráveis de ácidos orgânicos, dos quais se destaca o ácido ascórbico e uma prevalência de ácidos gordos polinsaturados, com predominância do ácido linoleico. As cromonas (aloesina ou aloeresina B) e as antronas (aloína A ou barbaloína e aloína B ou isobarbaloína) foram os grupos de compostos mais abundantes nos extratos de Aloe, tendo sindo detetados em maior quantidade nos extratos de casca. A aloesina e aloína são reconhecidos pelos seus efeitos cicatrizantes e laxativos, respetivamente, encontrando-se entre os metabolitos secundários mais importantes desta espécie. O extrato de casca foi particularmente eficaz em proteger os eritrócitos do dano oxidativo induzido por radicais livres, o com um valor de IC<sub>50</sub> próximo ao do Trolox (padrão). Nas bagas de haskap, os compostos fenólicos não-antociânicos maioritários foram os ácidos 3-O-cafeoilquínico cis e trans e a quercetina-3-O-glucósido; tendo-se destacado também uma antocianina, a cianidina-3-O-glucósido. A amostra apresentou uma relevante atividade antioxidante, com capacidade de inibição da peroxidação lipídica e da hemólise oxidativa. Assim, este trabalho evidenciou que a casca de Aloe vera e as bagas de haskap são uma fonte interessante de compostos de elevado valor acrescentado com aplicação nas indústrias cosmética e alimentar.

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# Food

# Otimização do processo de extração utilizando folhas de *Ocimum basilicum* var. *purpurascens* para a obtenção de um ingrediente corante

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Ocimum basilicum var. purpurascens (vulgarmente conhecido como manjericão vermelho rubi) é uma planta anual, pertencente à família das Lamiaceae, apresentando uma cor púrpura devido à presença de compostos antociânicos. Estas moléculas apresentam um elevado interesse industrial, devido às suas propriedades corantes e bioativas (atividade antioxidante e antimicrobiana). Com a finalidade de maximizar a extração destes compostos a partir de matrizes naturais, aplicam-se modelos matemáticos, nomeadamente a metodologia de superfície de resposta (RSM), onde se avaliam as respostas do método de extração a diferentes variáveis<sup>1</sup>. O objetivo deste trabalho consistiu em otimizar o processo de extração de compostos antociânicos, particularmente derivados de cianidina e pelargonidina, recorrendo ao RSM, de forma a promover a utilização destes pigmentos a nível industrial.

As folhas do manjericão vermelho rubi foram submetidas a extrações assistidas por calor, a fim de obter um extrato rico em compostos antociânicos. Para se otimizar o processo de extração foi aplicado um desenho composto central circunscrito (*DCCC*) com 5 níveis para cada uma das variáveis avaliadas. Assim, as variáveis estudadas foram: tempo de extração (t, 20-120 min), temperatura (T, 25-85 °C) e solvente (S, 0-100 % de etanol, v/v). A determinação do perfil antociânico foi realizada através de um sistema de HPLC-DAD-ESI/MS e a quantificação destes compostos nos extratos foi utilizada como variável de resposta. A avaliação das propriedades bioativas do extrato obtido, foi efetuada através de ensaios de citotoxicidade, utilizando linhas celulares tumorais (HepG2, NCI-H460, MCF-7 e HeLa) e uma cultura de células primárias não tumorais (PLP2), e de avaliação da atividade antimicrobiana (utilizando um painel de bactérias Gram-positivo e Gram-negativo, e fungos).

As condições ótimas de extração dos compostos antociânicos foram:  $t=65,37 \pm 3,62$  min,  $T=85,00 \pm 1,17$  °C e  $S=62,50 \pm 4,24$  %, originando um extrato rico nestas moléculas com 114,74  $\pm 0,58$  mg de antocianinas por g de extrato. Relativamente às propriedades bioativas do extrato otimizado, este revelou inibição do crescimento celular nas linhas HeLa (GI<sub>50</sub>= 213  $\pm 9 \mu$ g/mL) e HepG2 (GI<sub>50</sub>= 198  $\pm 9 \mu$ g/mL) e ausência de citoxicidade na linha PLP2 (GI<sub>50</sub> >400  $\mu$ g/mL). Na atividade antimicrobiana, os resultados obtidos foram satisfatórios para a maioria das bactérias e fungos testados, apresentando valores de CMI (concentração mínima inibitória) entre 0,75 - 0,075 mg/mL, para Salmonella typhimirium e Listeria monocytogenes/Escherichia coli, respetivamente.

Os resultados obtidos neste estudo permitem concluir que as folhas do manjericão vermelho rubi são uma matriz promissora para a extração de compostos corantes e bioativos, utilizando solventes verdes e tempos de extração reduzidos, suscitando elevado interesse ao nível de vários setores industriais, tais como o sector farmacêutico e alimentar.

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# COMUNICAÇÕES EM Painel

A TABELA PERIÓDICA E OS ELEMENTOS DA VIDA

SAÚDE, ALIMENTAÇÃO E AMBIENTE

# Environment

# Low-temperature Thermodynamic Study of the Empty Clathrate Hydrates

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Clathrate hydrates (CHs) are naturally occurring guest-inclusion compounds, that can be found in the Earth permafrost regions and in deep-sea oil and gas pipelines where they act as clogging agents inhibiting the flow of industrially relevant fluids (oil, natural gas); commercial interest in CHs sparks from their ability to act as natural reservoirs for large volumes of CO<sub>2</sub>, via injection into deep sea at depths of 3200 m, where hydrostatic pressure can reach 325 bar. Furthermore, the amount of CH<sub>4</sub> eventually trapped in natural methane CHs deposits, essentially in seafloor sediments, is expected to be quite significant  $(1-5\times10^{15} \text{ m}^3)$ .<sup>1</sup> Such inclusion compounds have also been observed in comets and outer planets, and their occurrence has been suggested in particular on Mars, Saturn, Uranus, and Neptune.<sup>2</sup> The empty structure of CHs is made up of approximately tetrahedrally arranged H<sub>2</sub>O molecules, linked amongst themselves via strong hydrogen bonds, and giving rise to an ice-like crystalline solid exhibiting two or three distinct roughly symmetrical cages where guest molecules can be encapsulated. Here we focus on sl structures (**Figure 1**) because it is the most commonly occurring polymorph under natural environments where CH<sub>4</sub> is the principal species for hydrate formation.<sup>3</sup>



**Figure 1:** Pictorial representation of small (5<sup>12</sup>) and large (5<sup>12</sup>6<sup>2</sup>) cavities of a sl clathrate hydrate, containing 20 and 24 H<sub>2</sub>O molecules, respectively, and complete p–V–T surface obtained from the calculations. Only the oxygen atoms in the polyhedral vertices are included. Note that the cavities obey Euler's convex polyhedra theorem: Face + Vertices = Edges + 2.

The thermodynamics of the metastable empty sI CHs are probed<sup>4</sup> over broad temperature and pressure ranges ( $100 \le T/K \le 220, 1 \le p/bar \le 5000$ ), using large-scale molecular dynamics simulations and compared with available experimental data at 1 bar. The whole p-V-T surface is interpreted using the universal form of the Parsafar and Mason equation of state, with an accuracy of 99.7–99.9 %. Framework deformation brought about by applied temperature follows a parabolic law, and there is a critical temperature above which the isobaric thermal expansion becomes negative, 94.7 K (1 bar) and 166.2 K (5000 bar). Response to the applied (p, T) field is analysed in terms of an angular and length descriptors of a canonical tetrahedral structure, and observed to occur mainly by means of angular deformation for (p, T) > (2000 bar, 200 K). The length of the hydrogen bonds responsible for framework integrity is insensitive to the thermodynamic conditions and its average value is  $\overline{r}_{(0-H)} = 0.25$  nm.

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# Environment

# **Urban Mines – Sustainable Resources of Rare and Precious Metals**

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Rare and precious metals (RPMs) can be defined as those metals with a scarce natural abundance, widely scattered in the earth's crust, but simultaneously being at the front of the cutting-edge technologies we know today due to their unique and irreplaceable physicochemical properties. The main result of this state of affairs is that the natural (primary) resources are not enough to sustain the increasing demand for RPMs; accordingly, at the end of the useful life of the devices containing RPMs, those waste (secondary) materials should be recycled to definitively contribute to the sustainability of our planet and to the inherent circular economy. Those secondary materials are commonly known as urban mines (UM), and the RPMs concentrations in UMs typically exhibit higher grades than the ones appearing at the natural origins.<sup>1,2</sup> Examples of precious metals in UMs are gold, silver and the platinum-group metals (platinum, palladium, rhodium, iridium, ruthenium) and lithium, indium, gallium, germanium, molybdenum, tungsten and vanadium are the most relevant rare metals.<sup>1,2</sup>

The subject of this communication is a tribute to the International Year of the Periodic Table, since it describes the crucial roles played by several chemical elements in our day-to-day life. Following the identification of the end-of-life devices containing the above-referred RPMs (**Figure 1**) this communication intends to provide additional information about their typical distributions in UMs, to highlight the main processes currently in use for their recycling, and to outline some prospective alternatives under investigation. A special emphasis will be given to the PGMs recycling from automobile and chemical industry catalysts, the main subject of the group research for some years.<sup>3,4</sup>



Figure 1: Some examples of end-of-life devices containing RPMs.

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# Environment

# Searching for sustainable exploitation of Lupinus albus L. in Portugal

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*Lupinus albus* L. is a Portuguese endemic species that grows spontaneously under severe climate conditions. This Lupinus has high protein content, comparable to soybean, and is used as human food, and animal feed. (36-52% protein, 5-20% oil, 30-40% fiber).[1] *L. albus* L. is bitter due to its content in quinolizidine alkaloids, whereas the sweet species are imported from Australia and Chile.

Several extraction methods of quinolizidine alkaloids from *L. albus* L. were assayed in order to find a water saving debittering process. Extractions were performed in acidic and basic media, with organic solvents and alternative solvents. Supercritical CO<sub>2</sub> extraction was assayed at different temperatures and pressures and with co-solvent modifiers. All methods were compared as to their efficiency by quantitative profiling of lupanine (the more abundant alkaloid) by GC-FID, using caffeine as internal standard [2]. The amount of alkaloids extracted were compared with those obtained for a commercial Portuguese lupin snack.

The life cycle assessment study showed that lupin grown in Portugal is a competitive option when used for domestic meal production. It showed a better performance than importing Australian lupin seeds and producing soybean in Portugal. Only very rapid growth soybean cultivars can be sown in Portugal and even those have shown a high sensitivity to cold-induced stress, reflected on lower yields and even crop deaths. Imported soybeans from Canada had the best environmental performance, mainly because this crop did not require irrigation when modelling AquaCrop results. Irrigation is one of the main process contributors for all the impact categories studied.

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# Environment

# Synthesis and Anion Complexation by Fluorescent Hexahomotrioxacalix[3]arene Receptors

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Over the last fifteen years, anion recognition by macrocyclic compounds, as calixarenes, has become a very important field within supramolecular chemistry. Applications involving anion recognition with important roles in biology, medicine and environmental areas, such as sensing, extraction and separation, transport across membranes, organocatalysis and formation of supramolecular assemblies, have been particularly developed.<sup>1</sup>

Urea receptors based on calixarenes that only use hydrogen bond donor units to bind the anions have been developed. By other side, calixarenes with fluorophoric groups have been studied, due to their optical sensing ability for a large scale of analytes.<sup>2</sup>

Following our previous research on anion binding by dihomooxacalix[4]arene ureido receptors,<sup>3-5</sup> we extended now our research into the study of hexahomotrioxacalix[3]arene with fluorophoric groups.

The present work reports the synthesis and the NMR conformational analysis of two hexahomotrioxacalix[3]arene trisubstituted receptors (1 and 2) bearing naphthyl urea groups on the lower rim via a propyl and butyl spacer, respectively, in the partial cone conformation. Their complexation properties were assessed by proton NMR, UV-Vis absorption and steady-state fluorescence studies in different solvents.



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# Environment

# Photodegradation as a sustainable process for the removal of antibiotics from aquaculture effluents

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Antibiotics constitute a large class of pharmaceuticals widely used in the treatment of both human and animal diseases. Aquaculture systems are considered as one of the major sources of the aquatic pollution by antibiotics. Such type of pollution is particularly concerning due to bacterial resistance which, according to the World Health Organization, is presently one of the most important health threats. Therefore, it is essential to draw possible strategies to remove antibiotics from aquaculture effluents before release into the environment. In order to do so, naturally occurring processes must be considered, being the photochemical degradation one of the most significant removal mechanisms. Photodegradation may occur either directly - the pollutant absorbs photons able to induce chemical transformations - or indirectly, through photosensitizers, among which humic substances (HS) may be included - photosensitizers absorb the light generating reactive oxygen or halogen species, which are then responsible for the degradation of the target compound.

The main objective of this work was to investigate the photodegradation of the antibiotics sulfadiazine (SDZ) and oxolinic acid (OXA), using a solar radiation simulator, aiming to assess the potential of photodegradation as a remediation process in aquacultures. With the mentioned objective in mind, both direct (in ultrapure water (UPW)) and indirect (in presence of HS fractions (humic acids (HA), fulvic acids (FA) or XAD-4)) photodegradation studies were performed. Also, studies at different pH values were conducted in order to assess the influence of this parameter in the antibiotics photodegradation rate. In the particular case of SDZ, results indicated that the presence of HS markedly influenced its photodegradation. For instance, in presence of FA, SDZ photodegradation was much faster than in phosphate buffer (PB), with a SDZ half-life time ( $t_{1/2}$ ) of 1.76 h (in comparison with a SDZ  $t_{1/2}$  in PB of 6.8 h). This study provided a more-detailed understanding on the possibility of using photodegradation as a sustainable process in the treatment of aquaculture effluents.

Keywords: Antibiotics, photochemical degradation, natural photosensitizers, aquaculture, remediation strategies.

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# Environment

# Chromium (VI) removal from wastewater of the tannery industry by PABA-MCM-41 functionalized mesoporous material

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The leather industries are one of the main responsible for the contamination of the environment with chromium species.<sup>1</sup> Various methods have been used in the Cr ions removal from aqueous media. The adsorption process has attracted considerable attention due to its operational facilities. Therefore, it is of extreme importance the development of innovative and efficient adsorbent materials to be used in the removal of toxic elements from wastewater. The mesoporous materials were synthesized for the first time in the 1990s by researchers at Mobil Oil Corporation.<sup>2</sup> The M41S family is widely known among mesoporous materials, which is composed of MCM-41, MCM-48, and MCM-50. Nevertheless, among these the MCM-41 is the family member that is most studied in the literature, mainly due to its structural and textural properties, such as controllable pore diameter, mechanical and thermal stability, high surface area and pore volume. Thus, in this work, the functionalized mesoporous material (PABA-MCM-41) was used for the Cr (VI) removal in leather samples (Scheme 1). The synthesis of PABA-MCM-41 was performed according to the method described previously by our research group.<sup>2</sup> Batch experiments were performed using univariate methodology for the following variables: pH, concentration of Cr (VI) standard, time, dose, and reuse of the PABA-MCM-41 adsorbent material. The optimum pH of the adsorption process was equal to 3, the adsorbed amount increased with the increase in initial Cr (VI) concentration, as well as with increase of the PABA-MCM-41 amount. The adsorption efficiency increased with the time and the equilibrium was reached in approximately 80 min, with maximum adsorption efficiency of 98.3%. The adsorption kinetic and equilibrium data were satisfactory fitted with the non-linear pseudo-first order and Freundlich models, respectively. Leather samples presented Cr (VI) concentration values above of the maximum values regulated by European Union. The PABA-MCM-41 presented Cr (VI) removal percentages values for the real samples between 97.5-99.2%. The PABA-MCM-41 has not presented matrix effect in the adsorption process, and thus allowing its application in wastewater contaminated with heavy metals.



Scheme 1: Extraction of the Cr solution and adsorption process of the Cr (VI) by PABA-MCM-41 mesoporous material.

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# Environment

# Development of Electrochemical Genosensors for the Detection of Toxic Dinoflagellate *Alexandrium spp.*

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Microalgae represent a photosynthetic microorganisms' group that inhabit both salt and fresh waters. These microorganisms, namely several species of dinoflagellates (e.g. *Alexandrium spp.*)<sup>1</sup>, are mostly harmless; however, some species produce toxins classified as unsafe to human health. The uncontrolled proliferation of such species results in a hazardous occurring event designated harmful algal blooms (HAB). The effects of these episodes can lead to severe ecological and socio-economic impacts (e.g. decrease of the local tourism, fishing and port activities, the contamination or death of the nearby wildlife, discoloration of the beach coasts). Therefore, the need for a rapid, selective and in real time detection device that can monitor the presence of these microalgae in aquaculture waters is critical to prevent human, ecological and economical losses.

In this work, an analytical approach based on electrochemical genosensor techniques was developed to create a lowcost platform able to detect the dinoflagellates: *Alexandrium minutum* and *Alexandrium ostenfledii*.

The design of this genosensor consisted of several steps including: i) Sensing phase: Creation of a mixed selfassembled monolayer (SAM) composed by a linear DNA capture probe (DNA-CP) and mercaptohexanol (MCH) onto screen-printed gold electrodes (SPGE) surface; ii) Heterogenous hybridization of complementary DNA sequence (DNA target) by using a sandwich format assay with enzymatic labels and iii) Electrochemical detection by chronoamperometry using an enzymatic scheme to amplify the electrochemical signal (**Figure 1**).

The best analytical conditions were used to study the relationship between electrochemical signal and DNA target concentration.



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# Environment

# Theoretical study of the $O(^{1}D) + H_{2}O(X^{1}A_{1})$ reaction

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The reactivity of the oxygen atom in the first excited electronic state,  $O(^1D)$ , is important in various fields of chemistry, and its reaction with water plays na important role in the  $HO_x$  chemistry, which in turn participates in the stratospheric ozone depletion cycle.<sup>1</sup>

A full dimensional potential energy surface (PES) for the ground state hydrogen peroxide molecule,  $H_2O_2$ , was aecently reported.<sup>2</sup> This PES accurately reproduces all the reaction channels and the minimum energy pathways for the different chemical reactions involved in the  $O(^1D) + H_2O(X^1A_1)$  reaction system (see Figure 1). The aim of this work is to study theoretically the gas phase reactions involved in the  $O(^1D) + H_2O(X^1A_1)$  system, considering this new full dimensional ground state PES.



Figure 1: Contour plot for the  $O(^1D) + H_2O(X^1A_1)$  planar interaction potential where an oxygen atom is moving around a  $H_2O$  molecule kept fixed at its equilibrium geometry. Contours start at -0.425 Eh and are equally spaced by 0.02 Eh. The dashed line represents the dissociation energy for the reaction (-0.29845 Eh).

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# Environment

# **Electrochemical Biosensor for Bisphenol A Determination**

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Environmental contamination is a major issue nowadays. Besides well-known polluting agents, so-called contaminants of emerging concern (CECs) are compounds, which were not previously found in the several ecosystems or only at negligible levels. They include pharmaceuticals and personal care products, endocrine-disrupting compounds (EDC), flame retardants, pesticides, artificial sweeteners, etc. and they can affect aquatic ecosystems and even human health<sup>1</sup>. Among them, bisphenol A (BPA) is an EDC with estrogenic activity, used as monomer for the industrial production of polycarbonate. It has been detected in several matrices, such as sediment, edible oils, foodstuff, water, liver, muscle, sewage, atmospheric particulate matter, milk, urine or human serum<sup>3</sup>. The traditional techniques used for its detection are usually based on chromatography. However, these methodologies have some drawbacks such as the lack of portability, the complex preparation and clean-up steps, the expensive required equipment, which can be overcome by the use of biosensors, also reducing analysis times and reagents volume. Biosensors are by definition devices that use specific biochemical reactions mediated by isolated enzymes, immunosystems, tissues, organelles or whole cells to detect chemical compounds usually by electrical, piezoelectric or optical signals<sup>4</sup>.

Thus, in this work, we have developed an electrochemical BPA biosensor based on the copper-containing polyphenol oxidase enzyme, Laccase. The selected enzyme was mixed with chitosan and an ionic liquid, 1-butyl-3-methylimidazolium tetrafluoroborate in order to form a homogeneous composite and to increase the laccase stability. This bioconjugate was then deposited onto multiwalled-carbon nanotubes (MWCNTs) modified screen printed carbon electrodes (CSPEs). The experimental parameters such as the amount of enzyme, ionic liquid, chitosan and MWCNTs were optimized in order to maximize the biosensor sensitivity. Electroanalytical data will be presented, discussed and compared with previously developed BPA biosensors<sup>5</sup>.

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# Environment

# The termolecular reaction $H + O_2 + M \rightarrow HO_2 + M$

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Potential Energy Surfaces (PES) are used to study the rate of elementary reactions and their dynamics, being useful to compute state-to-state rate constants. Unfortunately, in a complex reactive system, many elementary reactions are normally involved and the overall study becomes difficult. The usual approach to study such system is to make use of all the system's available rate constants and build a system of master equations. This procedure is based in the assumption that reactants are in thermal equilibrium. But studies seem to indicate that the number of non-reactive collisions can be small and the energy distribution of the intermediate species may be far from the Boltzmann distribution. MreaDy program (Multi-process Reactions Dynamics), aims to reproduce complex mechanisms, such as the hydrogen combustion, using accurate PES. This is accomplished by defining a global Potential Energy Surface (gPES) for the process in question, integrating various PESs, each one of them representing an elementary reaction that is expected to play a role in the chemical process, and performing reactive classical dynamic calculations on it.1 MReaDy was modified in order to study the pressure dependence of the reaction  $H + O_2 + M \rightarrow HO_2 + M$ . This reaction is one of the main sources of uncertainty when modelling hydrogen combustion chemistry, and being a termolecular reaction, it cannot be studied using normal classical trajectory programs. We start with hydrogen atoms and oxygen molecules, forming by collision excited HO<sub>2</sub>\* radicals. We can count how many of the excited HO<sub>2</sub>\* radicals are stabilized by collisions at 1500, 2000, and 2500 K and pressures of 10, 20, 30 and 50 atm., and we calculate the formation rate of stable HO<sub>2</sub> radicals. We present preliminary results for this process showing a clear increase of the rate constant with pressure. We are also able to study the rate constants of the different reactions present in the system.



Figure 1: Obtained reaction rate constants for the reactions present the system.

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# Environment

# Preparation of highly porous nanofibers of cobalt-cerium bimetallic oxides and use as catalysts for CO<sub>2</sub> valorization

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Electrospinning is an efficient, flexible and versatile technique that allows the production of nanofibers with diameters ranging usually from (50 to 500 nm). In this work, the synthesis of nanoporous bimetallic compounds with high porosity was studied aiming the production of polymeric nanofibers that were posteriorly submitted to a calcination process leading to the formation of highly porous nanofibers of Co-Ce bimetallic oxides. Such materials were tested as catalysts for the selective hydrogenation of  $CO_2$  into value-added products, e.g. hydrocarbons.

To produce the bimetallic nanofibers a precursor solution containing the polymer and metal salts as reagents, e.g.  $Co(NO_3)_2.6H_2O$  and  $Ce(NO_3)_3.6H_2O$  were used and three different polymers tested: i) polyvinylpyrrolidone (PVP) in absolute ethanol, ii) poly(methyl methacrylate) (PMMA) in tetrahydrofuran (THF) or N, N-Dimethylformamide (DMF) and iii) polystyrene (PS) in THF or DMF.<sup>1,2</sup> The type of polymer, metal nitrates concentration, solvent and calcination treatment on the morphology and surface area of the fibers were investigated. Preliminary results show that the surface area of the electrospun fibers was very homogeneous, between 30 to 50 m<sup>2</sup>/g, with the PS fibers showing the largest surface area for a PS concentration on the solution of 20 % wt. After calcination, the surface area of the fibers increases greatly, between 140-160 m<sup>2</sup>/g for the bimetallic oxide nanofibers, showing also the desired high porosity.

The results obtained for the hydrogenation of CO<sub>2</sub> show also that the catalysts are stable and very active for the production of methane.<sup>3</sup>

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# Environment

# Metoprolol photodegradation products in the presence of natural fulvic acids (FA) or porphyrins: identification by HPLC-UV-MS<sup>n</sup>

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Metoprolol is a highly prescribed  $\beta$ -blocker drug for the treatment of heart diseases. It is known that metoprolol is inefficiently removed in the wastewater treatment plants and it has been detected not only in the treated effluents, but also in natural waters.<sup>1</sup> Therefore, the awareness of its fate in the environment is a vital question, photodegradation being a key degradation pathway.

Although the direct photodegradation of metoprolol by solar light seems to be irrelevant, there are evidences in the literature that metoprolol suffers indirect photodegradation, and that dissolved humic matter has an important role as photosensitizer. Nevertheless, the identification of the photoproducts formed in the presence of humic matter is scarce, since only two photoproducts had been identified. If, on one hand, photodegradation in the environment is important, on the other hand, photosensitized degradation can be an alternative treatment to remove this pharmaceutical from contaminated water.

Porphyrins are recognized as effective photosensitizers and can be an interesting key in phototreatment of water contaminated with micropollutants such as pharmaceuticals. Porphyrins already showed to be efficient photocatalysts for the degradation of dyes, chlorophenols and other pollutants. The present work intends to compare the degradation of metoprolol under simulated solar radiation in the presence of a) fulvic acids (FA) extracted from a river, and b) 5,10,15,20-tetrakis(pentafluorophenyl)porphyrin (homogeneous and heterogeneous) as photosensitizers. During the photodegradation experiments the formation of several new products was detected, which were separated and identified by HPLC-UV-ESI-MS<sup>n</sup>. Experiments using the heterogeneous porphyrin photocatalyst under real solar irradiation were also performed, and similar results were obtained. Kinetic comparison of metoprolol photodegradation in buffer solution and in real wastewater treatment plant effluent showed that the efficiency of the immobilized porphyrin was not decreased by the complex matrix of the effluent.<sup>2,3</sup>

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# Environment

# Removal of pirimicarb pesticide from aqueous solutions by adsorption onto chestnut shells

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In the last years, the presence of pesticides in aquatic environments has increased mainly as a result of the intensification of agricultural activities.<sup>1</sup> Pesticides represent an important class of pollutants due to their reported toxicity even at trace levels. Therefore, their removal is an increasing concern. Among the different techniques that can be used to remove these contaminants, the adsorption is proposed as the best one due to its inexpensiveness, universal nature and ease of operation. In recent times, the scientific community is focusing its attention in the search of new low-cost adsorbent materials, such as wastes from forestry, agricultural or industrial activities.<sup>2</sup>

An abundant waste from the food industry, chestnut shells, was selected for this work. This waste has been extensively studied to recover bioactive compounds such as antioxidants<sup>3</sup>, but there is not so much bibliography about its adsorption capacity.<sup>1</sup> In the present work, the possibility of using chestnut shells for the removal of the pirimicarb pesticide from aqueous solutions was evaluated. For that, chestnut shells were dried at 40 °C for 24 hours, and milled to size 1 mm. The moisture and ash content, as well as the volatile matter were determined in chestnut shells. Kinetic and equilibrium adsorption studies were also performed. The results of the kinetic studies performed with the biosorbent showed that the pseudo-second-order model fitted well to the experimental data and the equilibrium was reached within 180 min. Freundlich and Langmuir isotherms were used to analyze the equilibrium data obtained at different adsorption conditions, and it was observed that Langmuir's model provided better fit to the equilibrium data. The maximum adsorption capacity reached a level of 0.71 mg of pirimicarb per g adsorbent. Column assays are being carried out to validate the effectiveness of the chestnut shells for pirimicarb adsorption. These first results suggest that the use of chestnut shells could represent a low-cost and eco-friendly alternative to other adsorbents for the pirimicarb removal from aqueous solution.

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### Environment

# A new rote to product hydrocarbon from free fatty acids

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The transesterification reaction to produce biodiesel has been extensively investigated and it is well established that alkaline catalysed transesterification is strongly affected by the presence of free fatty acids. These can significantly affect the transesterification progress. The presence of these acids in concentrations higher than 2% can hinder the reaction and form surface active molecules with significant complications in the purification step due to the formation of stable emulsions<sup>1</sup>, and furthermore, the fatty acids leads to the deactivation of the alkaline catalysts<sup>2</sup>.

The main purpose of transesterification is primarily to reduce viscosity to values closer to the conventional petro-diesel because high viscosity leads to operational problems in diesel engines, such as deposit formation on engine parts and eventual engine failure<sup>3</sup>.

In this work, it is proposed a new route to convert free fatty acids contaminants into fuels. In this process, the fatty acid is reacted with NaOH to form a carboxylate. This sodium complex is then thermally treated to decompose and to produce fuels based on H2 and hydrocarbons. Besides, the NaOH used in the carboxylate production is recovered at the end of the process (Figure 1).

The carboxylates were prepared reacting oleic acid with NaOH in molar ratios of 1:0.7, 1:1, 1:1.5 and 1:2 (oleic acid:NaOH). Under thermal decomposition (Figure 2), at 550 °C for 20 min, 10 °C min<sup>-1</sup>, the decomposition of the carboxylates produced three fractions: solid, liquid and gas (Figure 3). These fractions were characterized by TG (Thermal Analysis), TG/MS (Thermal Analysis/Mass Spectrometry), Raman Spectroscopy, DRX (X-ray diffraction), SEM (Scanning Electron Microscopy) and NMR (Nuclear Magnetic Resonance).

The products are basically carbonates and carbon. Liquid products are a complex mixture of hydrocarbons and the gaseous products are hydrocarbons having up to 4 carbons, oxides of carbon and hydrogen.

In this work it was proposed a way to purify oils contaminated with fatty acids. We believe that this method is environmentally friendly considering that important mixture of gases ( $H_2$ , CO and CO<sub>2</sub>) are produced and separated during the process and also the NaOH may be recovered at the end of the cycle.



Fig. 1. General diagram of thermal decomposition of sodium oleates



Fig. 2. Thermal Analysis (TG) under argon, for pure oleic acid, 0.7 Na, 1.0 Na, 1.5 Na and 2.0 Na.



Fig. 3. The distribution of the three obtained fractions (solid, liquid and gas).

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# Environment

# Optimization of ultrasound-assisted extraction parameters of antioxidant compounds from Portuguese vine canes

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Grapes are one of the major fruit crops produced throughout the world, and for many countries, such as Portugal, these fruits represent a crucial part of the economy<sup>1</sup>. Nevertheless, grape production is not a fully optimized process, and is very far from being considered an agro-industrial sector based on a circular economy. Despite the richness of grapes wastes in polyphenols, usually they end up discarded; in the case of vine-canes they are typically incorporated in the soil or incinerated<sup>2</sup>. Depending on the vine varieties, it is estimated that for each hectare of vineyard 1,75 tons of vine-canes wastes are produced<sup>3</sup>. Considering that polyphenols possess a powerful antioxidant capacity with a wide range of health benefits, vine-canes could be used to obtain bioactive extracts which could be further used in the nutraceutical, cosmetic, pharmacological, enological, and food additive industries.

The present work aims to evaluate the extraction efficiency of phenolic compounds from Portuguese vine-canes by ultrasound-assisted extraction (UAE). For that, two Portuguese grape varieties, namely *Touriga Nacional* (TN) and *Tinta Roriz* (TR) from Dão region were used and the influence of time and type of solvent on the extraction yield was evaluated. From the tested solvents (ethanol, butanol and isopropanol), 50% aqueous ethanol proved to be the most efficient. Considering the influence of the extraction time, the obtained results demonstrated that performing UAE for longer than 15 min does not had advantageous since the amount of phenolic compounds extracted does not increase substantially (15.5 ± 0.5 and 20.1 ± 0.6 mg<sub>GAE</sub>/g dry sample, for 15 and 60 min extraction for TN variety with the lab scale sonicator, respectively). A possible scale-up of the extraction method was also considered, through the comparison of UAE performed with a lab ultrasonic probe (200 mL) to a pilot scale one with 1500 mL volume. Considering there was no major losses, and in some cases there was even an increase in the phenolic content and antioxidant activity from the pilot scale extracts (18.7 ± 1.2 and 20.6 ± 1.1 mg<sub>GAE</sub>/g dry sample for TN variety with lab and pilot scale sonicated reactor, respectively), a scale-up of the UAE process can be considered profitable. Work is in progress in order to identify by high performance liquid chromatography which are the phenolic compounds contributing to the antioxidant properties of vine cane extracts. Those results may be useful, to choose the best industrial area for the application of antioxidant-rich vine cane extracts.

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# Environment

# Catalytic wet peroxide oxidation of caffeine over functionalized biochar materials developed from compost obtained from municipal solid waste

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Waste management through mechanical biological treatment consists on using separated organic fraction of municipal solid waste to feed anaerobic digestion processes, resulting in a solid stream, further processed to compost, which can be used as fertilizer. Nowadays, compost production is higher than the existing demand, and the expected developments on up-coming directives ruling "End-of-waste" criteria are leading to barriers on waste-derived fertilizers use.<sup>1</sup> In this context, this work deals with the valorisation of compost, through the production of low-cost materials to be applied in catalytic wet peroxide oxidation (CWPO) of synthetic wastewater contaminated with caffeine, used as a model persistent pollutant of emerging concern. Materials from compost treated with H<sub>2</sub>SO<sub>4</sub> (CSA), calcined at 800 °C (CSA-800) and functionalized with ethylene diamine tetraacetic acid (CSA-800@EDTA), and functionalized with tetraethyl orthosilicate followed by ethylene diamine tetraacetic acid (CSA-800@TEOSEDTA), were prepared and characterized. All catalysts developed from compost have revealed much higher removals of caffeine by CWPO when compared to the non-catalytic run (**Figure 1**). The catalyst prepared by treatment with sulfuric acid, calcination at 800 °C and functionalization with EDTA (CSA-800@EDTA) shows the highest catalytic activity and allows to reach conversions of caffeine higher than 99.9% after 4 h.



Figure 1: Caffeine evolution upon reaction time with catalysts developed from compost.

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# Environment

# Synthesis of value-added compounds from carbohydrates

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The sustainable conversion of biomass into biofuels, chemicals, drugs, and various materials is currently one of the most challenging tasks for the academics and industry. Among biomass resources, carbohydrates form by far the largest natural source of carbon and are considered the ideal feedstock for the production of platform of value-added compounds.

In this communication, we report the one-pot synthesis of a variety of value-added compounds from different carbohydrates (**Scheme 1**).<sup>1-3</sup> For example, we describe the highly efficient and selective conversion of carbohydrates into 5-ethoxymethylfurfural (5-EMF) and ethyl levulinate (EL), potential alternative biofuels, and into 5-hydroxymethylfurfural (5-HMF), furfural and levulinic acid (LA), versatile precursors for petrochemical, chemistry and pharmaceutical industries, catalyzed by HReO<sub>4</sub>.<sup>1</sup> The synthesis of furfurylamines<sup>2</sup> and  $\alpha$ -aminophosphonates,<sup>3</sup> important building blocks in drug synthesis, will be also discussed.



Scheme 1: Conversion of carbohydrates into value-added compounds.

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# Environment

# Structure-Property Study on the Degradation of Recalcitrant Trimethoprim Antibiotic by Tetrapyrrole-based Catalysts

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The presence of antibiotics in the environment, even at very low concentrations, is a major problem in our days, since their continuous input constitute, a potential risk for aquatic and terrestrial organisms, namely by the development of multi-resistant bacteria.<sup>1</sup> Some antibiotics, e.g. trimethoprim, show extreme resistance to biological degradation processes and usually are discharged intact from conventional treatment plants. Therefore, research has been directed towards the application of non-biological processes for the destruction of these recalcitrant pollutants in waters, with emphasis on advanced oxidation processes (AOPs),<sup>2</sup> through generation of hydroxyl and other radicals to oxidize the recalcitrant, toxic and non-biodegradable pollutants to several by-products and eventually to inert end-products.<sup>3</sup> Metal complexes of tetrapyrrolic macrocycles are known to be excellent biomimetic oxidation catalysts in a variety of reactions,<sup>4</sup> of which the degradation of organic pollutants is a leading topic.<sup>5</sup> Particularly, emphasis is given to promote sustainable processes through the use of non-toxic oxidants (e.g.  $O_2$  or  $H_2O_2$ ) and the heterogeneization of the

In this communication, we present our recent accomplishments on the synthesis of metal complexes of tetrapyrrolebased catalysts and their structure-property relationship study on the degradation of antibiotics, namely trimethoprim.



Figure 1: (Photo)degradation of pesticides and antibiotics in water matrix by using tetrapyrrolic based catalysts.

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# Environment

# Terpene-based metallophthalocyanines: Synthesis, characterization and catalytic applications in CO<sub>2</sub> activation

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Increasing concerns about global warming and a potential energy crisis has prompted the search for new technologies for converting CO<sub>2</sub>, a notorious greenhouse gas from fossil fuel burning. Due to the high chemical inertness of CO<sub>2</sub> molecule, chemical reactions involving CO<sub>2</sub> activation usually face large energy barriers and require the development of highly effective catalysts.<sup>1,2</sup> In this context, phthalocyanine macrocycles can be considered promising catalysts, due to the facile modulation of their aromatic backbone. Moreover their easy complexation with different metals allows fine-tuning their Lewis acidity, thereby increasing their catalytic activity and selectivity.<sup>3,4</sup> Among them, phthalocyanine catalysts based on terpene derivatives are particularly attractive since terpene molecules are a highly abundant natural source of chirality.

In the present work, we report the synthesis and characterization of a new family of chiral metallophthalocyanines (Zn(II), Cu(II), Cr(III)), from cheap and widely available terpenes (menthol, myrtenol, etc) as raw materials (yields between 60-70%). Spectroscopic and photophysical characterization, such as electronic absorption (singlet and triplet) and fluorescence emission spectra in solution and in the solid state, together with quantum yields and lifetimes will be presented and discussed. Furthermore, their potentialities as catalysts in CO<sub>2</sub> addition to small heterocycles (epoxides, aziridines) will be evaluated in order to appraise the effects of the metal and terpene scaffold on the catalytic activity and selectivity.



Figure 1: CO<sub>2</sub> addition reactions catalyzed by terpene-based metallophthalocyanines.

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# Environment

# Visible light induced photocatalytic degradation of venlafaxine: Kinetics and transformation products

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Venlafaxine (VEN) is an antidepressant drug widely consumed and frequently found in the environment, which shows that conventional treatment plants do not completely remove the pollutant.<sup>1</sup> Degradation methods such as photocatalysis were highlighted in recent decades for having a few advantages which include low cost, chemical stability and environmentally friendly. The most studied and applied photocatalyst is TiO<sub>2</sub>, but it has limitations due to its low radiation absorptive capacity under visible light spectrum. This work aimed to evaluate the photocatalytic degradation of VEN using titanium nanowire synthesized from TiO<sub>2</sub> and doped by cobalt (Co-TNW) under visible light radiation.<sup>2</sup> In addition, the degradation pathway was elucidated using an UHPLC UltiMate 3000 LC system (Thermo Fischer Scientific, Germany) coupled to a mass spectrometer QTOF Impact II (Bruker Daltonics, Germany) in full scan mode and product ion scan for the analysis of fragmentation patterns. The photodegradation experiment consisted of spiking 10 mg L<sup>-1</sup> VEN in tap water with 20 mg of Co-TNW for photocatalysis. 500 W mercury-xenon arc lamp was used as radiation source and borosilicate glass was employed to cut-off the UV radiation to simulate solar radiation. Aliquots were withdrawn at certain times, centrifuged and frozen for analysis.

The results showed that there was no adsorption of VEN on the catalyst for one hour in the darkness. Degradation kinetics followed the pseudo-first order reaction with the correlation coefficients above 0.99 for photolysis and for photocatalysis. The degradation rate constant resulted in 0.0374 h<sup>-1</sup> and 0.0728 h<sup>-1</sup> for photolysis and photocatalysis, respectively, and the use of Co-TNW as catalyst, showed a degradation rate twice as high when compared to undoped TNW with the half-life of 9.5 h<sup>-1</sup> (**Figure 1a**). Furthermore, it was observed that during the photocatalysis six transformation products (TPs) could be elucidated (**Figure 1b**), whereas in photolysis only three TPs were identified (**Figure 1c**). However, there was no degradation of these TPs during photolysis, as observed in the time profile. Overall, TPs were formed by hydroxylation, demethylation and oxidation processes.



Figure 1: (a) Pseudo-first order kinetics of VEN, (b) time profile of TPs during photocatalysis and (c) time profile of TPs during photolysis

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## Environment

# Solar Photodegradation of Florfenicol in Aquaculture Effluents: an alternative to prevent environmental contamination

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Florfenicol (FLO) is a bacteriostatic antibiotic of broad spectrum used in marine and fresh aquaculture. Its major problem is the time that it takes to degrade in the environment. It is resistant to hydrolysis and direct photolysis under solar light, and a half-life of more than 90 h has been reported in the literature for its indirect photodegradation in freshwater.<sup>1</sup> Indirect photodegradation can be promoted by photosensitizers existing in natural waters, such as nitrate or dissolved organic matter (DOM). Under solar irradiation, DOM gives rise to reactive species such as DOM excited triplet states, singlet oxygen or OH radicals, which can induce the degradation of contaminants. However, the photosensitizing effect of DOM depends on its origin and composition<sup>2</sup>.

In this work we studied the degradation of FLO in brackish aquaculture water, under simulated sunlight. The solar light simulator emits radiation in the 290 - 800 nm range, with an irradiance of 550 W/m<sup>2</sup>. FLO quantification was made by HPLC-UV, at 223 nm, using a C18 reversed-phase column. It was observed that the matrix of the brackish aquaculture water promotes the photodegradation of the compound, since it degrades faster than in ultrapure water. In brackish aquaculture water, the photodegradation of FLO follows a pseudo 1st order kinetics and the half-life time is 70h. In order to evaluate the influence of the main constituents of the aquaculture water, namely sea salts and DOM, on the FLO photodegradation, experiments were performed using synthetic solutions of FLO in ultrapure water containing sea salts (21‰) or estuarine fulvic acids (FA) which are representative of DOM. Those experiments were made at pH 7.3 (pH of aquaculture water). While sea salts do not promote the FLO photodegradation, FA (20 mg/L) showed to be important photosensitizers. However, considering the possibility of using sunlight for water treatment prior to discharge into the environment, the half-life time obtained in the aquaculture water (70h) is still too high. Thus, the use of the 5,10,15,20-tetrakis(pentafluorophenyl) porphyrin (H<sub>2</sub>TF<sub>5</sub>PP) as an artificial photosensitizer was considered as an alternative for enhancing the FLO photodegradation under solar light. This porphyrin proved to be an efficient photosensitizer for the photodegradation of other organic contaminants<sup>3</sup>, but the same was not observed in the case of FLO. The addition of H<sub>2</sub>TF<sub>5</sub>PP to FLO solutions in ultrapure water did not promote FLO photodegradation. Since the porphyrin is very efficient in producing singlet oxygen, these results suggest that this is not the reactive species involved in the photosensitizing effect of FA. The involvement of the excited triplet state of FA (3FA\*) as main reactive species was also excluded, since the bubbling of the solution with N<sub>2</sub> to remove dissolved oxygen, which is a quencher of <sup>3</sup>FA\*, did not increase the photodegradation rate. Another reactive species which can be involved in the photosensitizing effect of FA is the OH radical. Then, TiO<sub>2</sub> nanoparticles, known to produce OH radicals in solution, were tested as photocatalyst for the degradation of FLO. With the addition of TiO<sub>2</sub> to aqueous solutions of FLO in ultrapure water, almost 100% photodegradation of FLO was achieved in only 10 min of irradiation. These promising results open new perspectives for aquaculture effluents treatment, being a good alternative to solve the spreading of this antibiotic in the environment.

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### Environment

## Purification of antibiotics from water streams using task specific ionic liquids

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Water resources are the main vehicle for the environmental dispersion of chemical pollutants. Consequently, the development of new methods to promote the purification of the contaminants from water is highly required. It is very relevant the possibility to combine an efficient extraction methodology with high-precision analytical methods for a correct identification and quantification of water samples containing pollutants, particularly pharmaceutical drugs, such as antibiotics, which are permanently released into the environment. The presence of these contaminants in the environment may cause risks to ecosystems and to human since they are designed to have a specific action on the human body and to act in very low concentrations.<sup>1</sup>

lonic liquids (ILs) are organic salts with low-melting points possessing peculiar physical and chemical properties and significant interest for extraction and separation applications.<sup>2, 3</sup>

In this work, several task-specific hydrophobic ionic liquids based on methylimidazolium and alkylpyridinium cations have been synthetized and characterized. These classes of organic cations were combined with hydrophobic fluoridebased anions such as bis(trifluoromethane)sulfonylimide (NTf<sub>2</sub>). Also, some polymeric hydrophobic ionic liquids<sup>4</sup> have been developed in order to improve the capacity to remove some contaminants using solid-liquid extraction processes. The most promissory ionic liquids and polymeric ILs have been tested for liquid-liquid extraction and adsorption studies. The extractive capacity for selected antibiotics (amoxicillin, ampicillin, oxytetracycline, ciprofloxacine, enrofloxacine and chloramphenicol) using the best ionic systems have been evaluated. The remaining quantitity of antibiotic still present in the water phase, after each extraction/adsorption was quantified by UPLC-DAD and UPLC-MS/MS and the results are present in this communication (**Scheme 1**).





The best ionic systems (ILs and polymer ILs) for extraction/purification processes will be applied in real contaminated water samples in order to understand the potential of our application.

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## Environment

# Smartphone-based analytical methodology for the determination of sulfonamides in surface waters

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Antibiotics are widely used worldwide, both in human and veterinary medicine. The incomplete metabolization of antibiotics and the incorrect use and discharge represents a major environment issue because their residues can accumulate in different compartments, including water. Monitoring the antibiotics levels in water is essential to assess the risk to aquatic ecosystems and to prevent the development of antimicrobial resistance.<sup>1</sup>

This work aims to study the chemical and detection aspects to be incorporated in a new methodology to evaluate *insitu* sulfonamides in surface waters. Sulfonamides are preconcentrated in solid-phase extraction membranes, followed by the addition of a colour reagent that allows the development of a red-violet colour proportional to the amount of retained sulfonamides. The quantification is performed using an automatic image processing algorithm, running on a customized smartphone app.

A poly-(styrene divinylbenzene) - reversed phase sulfonate (SDB-RPS) membrane was selected to perform solid-phase extraction and to work as a solid platform for colour development, due to its high efficiency for sulfonamides retention. For the colour development, the reagent 4-dimethylaminocinnamaldehyde (1.25 mM) showed the best sensitivity for most of the tested sulfonamides.

A protocol for sulfonamides retention, colour development and image acquisition was implemented. To test the performance of the developed methodology, standards prepared from three different sulfonamides (sulfadiazine, sulfamethazine and sulfadimethoxine) were analysed. Calibration curves using sulfamethoxazole (SMZ) standards (0 up to 20  $\mu$ g L<sup>-1</sup>) were constructed, using three colour spaces: CIELAB, RGB and HSV. Regarding the CIELAB colour space, the *a\_star* component provided the highest sensitivity (slope of 0.5734 L<sup>-1</sup>  $\mu$ g). The calibration curves obtained for the *b\_star* and *L* components presented lower slope values (0.3023 and 0.3228 L<sup>-1</sup>  $\mu$ g, respectively). The colour stability on the solid support was studied, demonstrating that there was no important change in the developed colour after five minutes of reagent addition. The influence of different sample volumes in the retention of sulfamethoxazole in the solid support discs was also tested in order to attain lower detection limits, compatible to environmental analysis. Currently, the developed method is being tested and validated with real samples.

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## Environment

# Vineyard pruning waste valorization: exploitation of supercritical extraction to obtain interesting compounds for industrial applications

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Especially in Mediterranean countries, where the wine industry is well developed, large amounts of vine pruning wastes are produced every year. Currently, these wastes have no commercial value and presents a management cost, but they have been proved to be a powerful source of phenolic compounds with antioxidant properties, cellulosic sugars and derivatives.<sup>1,2,3</sup>

Usually, conventionally extracting techniques using organic solvents are still widely used to recover polyphenols. However, these methods have several drawbacks such as long processing times, low selectivity and low extraction yields, which could be over-come with the application of non-traditional technologies.<sup>4</sup> Among these technologies, supercritical fluid extraction (SFE) is an environment-friendly technology, which offers several advantages over conventional extraction techniques.

According to our knowledge, there has been no work carried out to study on the optimal variables for the SFE of total polyphenols and sugars from Portuguese vine canes. For that, the supercritical CO<sub>2</sub> assisted extractions were performed under the temperature of 40 °C, 5 mL/min of CO<sub>2</sub> flow rate and 0.125 mL/min of co-solvent flow rate. The effect of pressure, ranging from 100 to 200 bar, and co-solvent (ethanol, isopropanol and 1-butanol) were investigated. Preliminary results showed that increasing the SFE pressure resulted in higher amount of phenolic compounds (46.5 ± 3.9 mg<sub>GAE</sub>/L), as well as higher antioxidant activity (0.80 ± 0.07 mg<sub>TE</sub>/L). Furthermore, HPLC analysis is in progress to sugar content determination. These first results highlighted the potential of using Portuguese vine canes as a source of phenolic compounds for food and cosmetic applications and sugars to high value platform molecules for bioproducts and biopolymers.

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## Environment

## **Gas-Phase Ion Chemistry Studies with Noble Gases**

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For some years, we have been using Fourier transform ion cyclotron resonance (FTICR) and quadrupole ion trap (QIT) mass spectrometry (MS) to examine the gas-phase ion chemistry of the lanthanides from La to Lu (except Pm), the actinides from Th to Cm, and several *d* transition elements.<sup>1</sup> We revealed new species and determined thermodynamic properties of neutral and ionic molecules. Recently, we have also focused our attention on the chemistry of the noble gases,<sup>2</sup> particularly of Kr and Xe as a prelude to future experiments with highly radioactive and scarcely studied Rn. FTICR and QIT possess unique capabilities to perform complex sequences of ion manipulation, investigate

ion/molecule reactions, including kinetics measurements and mechanism evaluation, and examine structural features via ion-activation methods, such as collision-induced dissociation (CID). These capabilities can afford energetics data on the examined species and reactions.

We will present examples of the coordination of very soft ligands to Cu(I) (e.g. Figure 1, coordination of N<sub>2</sub>) and Au(I) ions and of the potential coordination of noble gases to these transition metals. We will also show examples of the reactivity of Kr and Xe ions with oxidizing and fluorinating agents.



Figure 1: Mass spectrum showing coordination of dinitrogen to [Cu(CH<sub>3</sub>CN)]<sup>+</sup> during CID of [Cu(CH<sub>3</sub>COO)(CH<sub>3</sub>CN)]<sup>+</sup>.

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## Environment

## CO<sub>2</sub> conversion to phenyl isocyanates by uranium(VI) bis(imido) complexes

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The imide functionality is an important ligand class in coordination chemistry, particularly in high-oxidation-state earlytransition-metal complexes. The electron-rich and reactive M=NR bonds make the compounds attractive precursors for stoichiometric or even catalytic transformations with a range of unsaturated substrates, including CO<sub>2.1</sub>

In the last years, the number of characterized uranium imido complexes was also increased, driven by the challenge of understanding the role of f-orbitals in chemical bonding and reactivity,<sup>2</sup> in particular, the U(VI) trans-bis(imido) species, which are isoelectronic with the thermodynamically stable uranyl ion, [O=U=O]<sup>2+</sup>.

We have demonstrated that the electron-rich uranium(III) complex [UI{(<sup>tBu2</sup>OAr)<sub>2</sub>Me<sub>2</sub>-cyclam}] is able to cleave the N=N azobenzene bond and form the trans-bis(imido) complex [U(=NPh)2(<sup>tBu2</sup>OAr)2Me2-cyclam}].<sup>3</sup>

Herein, we will show that uranium(VI) trans-bis(imido) complexes supported by a cyclam derivative react with CO<sub>2</sub> to selectively form uranium oxo-imido complexes with extrusion of aromatic isocyanates. DFT investigations were also performed in order to elucidate the mechanistic aspects of the observed reactivity.



Scheme 1. Synthesis of the trans-[O=U=NPh]<sup>2+</sup> complex [U(O)(NPh){κ<sup>4</sup>-{(<sup>tBu2</sup>ArO)<sup>2</sup>Me<sub>2</sub>-cyclam})]

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## Environment

# Interactions of pharmaceutical compounds in their photocatalytic degradation: effects of water matrices and ionic content

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The development of efficient technologies for the removal of recalcitrant and toxic pharmaceuticals from wastewaters has been a subject of intensive research in the field of environmental protection. It is established that the application of advanced oxidation processes (AOPs) leads to high mineralization rates of organic pollutants from urban wastewater treatment plants.<sup>1</sup> Among the AOPs, heterogeneous photocatalysis has been appointed as a promising technology for degradation of a wide range of micropollutants (MPs) found in wastewaters.<sup>2</sup> Thus, the main goal of this work targets the application of an efficient photocatalytic process based on polymeric carbon nitride towards degradation of diclofenac (DCF) and metoprolol (MET). The influence of water matrix, initial pollutant concentration, radiation source and the presence of ionic species is evaluated to understand the MPs photocatalytic degradation mechanism, DCF and MET spiked in river water matrix following apparent first-order kinetics (Figure 1).



Figure 1: Normalized concentration (C/C<sub>0</sub>) of DCF and MET using river water as matrix. Experimental conditions: 33.6  $\mu$ M of each MP; 1.0 g L<sup>-1</sup> of catalyst; light emitting diodes with a  $\lambda_{max}$  = 417 nm.

In the absence of photocatalyst, DCF is already slightly converted under visible light ( $\lambda_{max} = 417$  nm) illumination. Under photocatalytic conditions, the rate of DCF degradation increases, leading to total degradation in 20 min reaction, either when individually spiked or in mixture with MET. On the contrary, the rate of removal of MET by photocatalysis reduces in the presence of DCF. These preliminary results reveal that the removal of MET is negatively affected by the presence of DCF in the solution, using visible light driven photocatalysis.

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## Environment

## Extraction and quantification of pharmaceutical drugs in aqueous matrices

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The increasing demand of modern societies for the production and use of chemical compounds coupled with inefficient sewage collection and treatment systems, results in an inadequate release of all types of pollutants in the environment.<sup>1</sup> Emerging pollutants are potentially toxic substances that although typically found in very small concentrations can produce hazard effects on the environment. Due to their very small concentrations they are not yet included in the water quality monitoring programs neither in the environmental control legislation standards. Pharmaceutical and Personal Care Products (PPPs) represents an important group of emerging pollutants due to their continued increase in worldwide consumption and to their inherent capacity to induce physiological effects in very low doses, which raises concerns about the potential adverse effects on humans, animals and environmental systems.<sup>2</sup>

In this work, it will be presented the development and validation of an analytical methodology based in solid phase extraction (SPE) and high performance liquid chromatography with diode array detection (HPLC-DAD). The method is validated through its application using real samples of aqueous matrices obtained from different hydric media (swimming pools, rivers and wastewater treatment plants). To extend the scope of the analytical method and thereby a more comprehensive study, the study includes five pharmaceutical drugs that belong to four different pharmacological classes, namely, an analgesic (paracetamol), two antibiotics (azithromycin and sulfamethoxazole), an anticonvulsant (carbamazepine) and a stimulator of the central nervous system (caffeine). These compounds were selected due to their high use and medical prescription levels and consequently leading to a high probability of environmental contamination. In **Figure 1**, the molecular structures of the compounds under study are presented.



Figure 1: Chemical structures of the studied compounds.

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## Environment

# Monitoring of non-steroidal anti-inflammatory drugs in hydric media from the Bragança region

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Emerging micropollutants are substances found in the environment in very low concentrations, at scales ranging from nanograms to micrograms per liter. Usually, wastewater treatment plants are not designed with the purpose of removing these pollutants.<sup>1</sup> Non-steroidal anti-inflammatory drugs (NSAIDs) are some of the most prescribed drugs worldwide in order to relief pain and inflammatory conditions. Several studies report the presence of these pharmaceuticals in different aqueous matrices.<sup>2</sup> Therefore, in this work will be presented an extensive set of experimental results obtained for the development and validation of a complete methodology used to identify and quantify five selected NSAIDs (acetylsalicylic acid, diclofenac, ibuprofen, ketoprofen and naproxen) in samples collected from different hydric media of the Bragança region, northern Portugal. The molecular structures of the studied compounds are presented in **Figure 1**.

Experimental results includes the optimization of solid phase extraction (SPE) and high performance liquid chromatography with diode array detector (HPLC-DAD) operating conditions, namely, SPE recoveries, HPLC mobile phase composition and pH based on different acetonitrile/water/trifluoroacetic acid contents under isocratic or gradient modes, and optimum wavelengths to improve limits of detection and quantification, among others. The SPE extraction is performed using Chromabond<sup>®</sup> HLB cartridges, and the optimized extraction process resulted in mass recovery values between 86.5% and 99.3%. After SPE extraction the samples were analyzed by HPLC-DAD using a C18 column, a 60%acetonitrile:40%water:0.01%trifluoroacetic acid solvent composition and a flow-rate of 1.2 mL/min. The selected wavelengths were 219 nm for ibuprofen, 224 nm for acetylsalicylic acid and naproxen, 254 nm for ketoprofen and 275 nm for diclofenac. The experimental methodology was validated using real samples from different aqueous matrices collected in the Bragança region.



Figure 1: Chemical structures of the analyzed compounds.

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## Environment

# Improving oxidation of aromatic contaminants with simultaneous production of H<sub>2</sub>O<sub>2</sub> by photoactivated carbon nitride materials

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Water management is a fundamental condition for sustainable development. Therefore, the present research focused on the improvement of environmental protection technologies for water and wastewater treatment. In particular, environmentally-friendly carbon-based advanced oxidation processes, such as heterogeneous photocatalysis using carbon nitride as optical semiconductor, can represent a viable solution to achieve water sustainability.<sup>1</sup> To this end, we have synthesised visible-light photoactive carbon nitride materials, seeking the generation of oxidising agents and the conversion of several organic compounds typically found in wastewaters.<sup>2</sup> A thermal exfoliation post-treatment step was implemented to improve the pristine material efficiency.<sup>3</sup> The performance of the exfoliated photocatalyst was assessed under different experiments to find the optimal conditions for oxidation. Ten compounds were chosen according to their chemical structure, and the degradation mechanism was studied. We tested synthetic mixtures of these selected aromatics, and oxidation rates were obtained (**Figure 1**). The simultaneous *in situ* evolution of hydrogen peroxide was also evaluated. The results suggest the formation of highly reactive hydroxyl radicals under certain conditions. Moreover, photo-Fenton like reactions were studied by adding iron, boosting radical formation and improving mineralisation rates.



Figure 1: Evolution of the normalized concentration ( $C/C_0$ ) of the selected aromatic compounds (PH: phenol; CT: catechol; RC: resorcinol; HQ: hydroquinone; BA: benzoic acid; HBA: hydroxybenzoic acid; PCA: protocatechuic acid; GA: gallic acid; MOP: methoxyphenol; TYR – tyrosol) in an aqueous mixture ( $C_0 = 0.640 \text{ mmol L}^{-1}$ ; 0.50 g L<sup>-1</sup> catalyst load; air saturation) under visible light emitting diodes irradiation (maximum wavelength of 417 nm).

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## Environment

# Biparametric sequential injection system with on-line solid phase extraction for the determination of copper and zinc in waters

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Solid phase extraction (SPE) is a technique widely used for sample pre-treatment in analytical chemistry. SPE allows for selective analyte separation from complex matrix interferences. Under certain conditions, SPE can also be a strategy for pre-concentration of a specific analyte present in low concentrations. In this scenario, a biparametric sequential injection system using SPE for the separation of copper and zinc followed by their individual spectrophotometric determination was developed (**Figure 1**).

To conduct all determinations using a single manifold, a non-selective reagent, 4-(2-pyridylazo) resorcinol (PAR), was chosen as the colour reagent. SPE using two different sorbent materials was the chosen strategy to selectively separate and allow the determination of the individual metal ions. Materials used for the copper and zinc ion retention were Chelex 100 and a PVC-based polymer inclusion membrane (PIM), respectively.

Chelex 100 resin is a styrene divinylbenzene copolymer, which acts as a chelating resin. It is usually used to bind metal ions, and the metal affinity depends on the solution pH. PIMs are thin, flexible and stable polymeric films that can selectively retain chemical species and, when functionalized with di-(2-ethylhexyl)phosphoric acid (D2EHPA), presents high affinity for zinc.<sup>1</sup> The use of the mentioned sorbents was explored to separate the two metal ions.



Figure 1: Biparametric sequential injection manifold for Cu and Zn determination. C1 – PIM column; C2 – Chelex 100 column; P – Syringe pump; HC – Holding coil; SV – Selection valve; RC – Reaction coil; L – Light source; FC – Flow cell; D – Spectrophotometer.

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## Environment

# Improvement of a sequential injection method for the determination of chromium (VI) in waters using a GlobalFIA platform

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Recreational waters, both coastal and inland, are stressed by anthropological activities, with consequent contamination by inorganic persistent pollutants. In this scenario, we propose to develop automatic flow based methods for real-time monitoring of persistent pollutants. These methods are expected to present advantages over existing ones in terms of cost, reagent consumption, portability and speciation of analytes.

Chromium is a heavy metal element and exists commonly in the oxidation states of Cr(VI) and Cr(III) in water samples. Chromium (VI) is one of the persistent inorganic pollutants with particular importance. This transition metal is added to marine paints and primers, acting as anticorrosive agent. <sup>1</sup>The reference methods for Cr(VI) determination use toxic reagents or display low sensitivity.<sup>2</sup> One of the active areas of green chemistry research is to devise analytical methods that reduce or eliminate the use and generation of hazardous substances.

In this work, we intended to explore a compact and miniaturized GlobalFIA platform to improve of a sequential injection method for the determination of Cr(VI), shown in **Figure 1**. This method was based on the detection of a blue unstable intermediate compound resulting from the reaction of Cr(VI) with hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) in acidic medium. <sup>3</sup> The idea is to explore the use of low toxicity reagents/products associated with the portability of the GlobalFIA equipment.



Figure 1: Sequential injection manifold for chromium(VI) determination: S, sample or standard; T, transporter (H<sub>2</sub>O); R, hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and sulfuric acid (H<sub>2</sub>SO<sub>4</sub>); P, milliGAT pump; SV, 10 port selection valve; HC, holding coil; OF, optical fibers; FC, flow cell; LS, Light source, tungsten lamp; D, Detector, spectrophotometer USB-4000; W, waste.

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### Environment

## Synthesis and Characterisation of Manganese Complexes Bearing Triazolylidene and Triazole Ligands

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Mesoionic carbenes (MIC), in particular 1,2,3-triazolylidenes, have emerged as an interesting subclass of Nheterocyclic carbene (NHC) ligands, due to their strong  $\sigma$ -donor capability and easy synthetic access through click chemistry. In addition, these MIC ligands can act as electron reservoirs in redox transformations, displaying a noninnocent behaviour when coordinated to metal centers.<sup>1</sup> In comparison to noble metals (Ir, Ru, Rh), the synthesis of 1,2,3-triazolylidene complexes of first-row transition metals and their application in catalysis has been scarcely studied. In particularly, the chemistry of Mn with triazolylidenes remains unexplored with only one example reported in the literature. In a recent publication, we described the first examples of carbonyl manganese complexes with chelating or bridging di(1,2,3-triazolylidene) ligands and their application in catalysis.<sup>2</sup> Here, we present the synthesis and characterisation of a new family of Mn(I) carbonyl complexes with bidentate ligands containing pyridine/triazolylidene fragments (Fig. 1). A combination of cyclic voltammetry and IR data allows to estimate the donor/acceptor properties of these chelating ligands. In addition, photochemical studies with complexes I-V will be discussed.



Figure 1: Mn complexes bearing chelating MIC and triazole ligands.

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## Environment

# A Manganese N-Heterocyclic Carbene Catalyst for Reduction of Sulfoxides with Silanes

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Manganese is a non-toxic, inexpensive and earth abundant metal, and therefore is a perfect candidate for catalysis whether as a replacement for precious metals or in the search for novel reactivity. In fact, the development of manganese catalysis has experienced a spectacular growth in the last few years.<sup>1</sup> To date, manganese complexes have been widely used in C-H activation, (de)hydrogenation, and in the reduction of carbonyl groups, including aldehydes, ketones, esters, amides, and C=C/C=C unsaturated bonds through hydrosilylation reactions.<sup>2</sup>

In this communication, the first reduction of sulfoxides catalysed by a well-defined manganese complex is presented. A variety of sulfoxides are reduced to the corresponding sulfides in high yields using phenylsilane, diphenylsilane, and the economically feasible 1,1,3,3-tetramethyldisiloxane (TMDS) as reducing agents in the presence of a Mn-NHC complex (NHC = N-heterocyclic carbene). The reactions are performed under air and without the need of any additive (**Figure 1**).



Figure 1: Manganese N-heterocyclic carbene catalyst for reduction of sulfoxides with silanes.

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## Environment

# GC-MS Analysis and Total Phenolic, Ascorbic Acid and Tannin Contents in Methanolic Extracts of *Lactarius sanguifluus* (Paulet) Fr. Collected from North-western Morocco

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*Lactarius sanguifluus* (Paulet) Fr. is a wild edible mushroom belonging to Russulaceae family and commonly known as bloody milk cap. *L. sanguifluus* were collected from northe-western Morocco under the reforested *Pinus halepensis* and identified during the year 2018<sup>1,2</sup>.

The first phase of this study consisted in the chemical analysis using Gas chromatography–mass spectrometry (GC-MS) and in the bioactive compounds (Total Phenolic, Ascorbic Acid and Tannin Contents) estimation by spectrophetometric methods, using UV-Vis.

The fuiting body of *L. Sanguifluus* was dried, crushed (20 mesh), and extracted with methanol. The extract were derivatized and analyzed by GC-MS which allowing the identification more than 65 compounds (**figure 1**). The achieved data revealed a high diversity of chemical families in which are included carboxylic acids, sugars, saturated and unsaturated fatty acids, sugar alcohols, amino acids...etc<sup>3</sup>.

Regarding bioactive compounds in methanolic extract, the total phenolic content was determined with Folin-Ciocalteu reagent and Gallic acid was used as standard compound<sup>4</sup>, while the ascobic acid content determined with Metaphosphoric acid reagent and I-ascorbic acid was used as standard compound<sup>5</sup>, and tannin content was estimated with Vanillin-HCI reagent and catechin was used as standard coumpound<sup>6</sup>. The results obtained will be presented in this communication.



Figure 1: GC-MS analysis of methanolic extract of L. sanguifluus

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## Environment

# Comparative study of photocatalytic degradation of carbamazepine using Co, Ni -doped titanium oxide and (P, W) co-doped titanium oxide under UV-A light and visible-light irradiations

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Carbamazepine (CBZ), is antiepileptic drug which widely consumed and one of the persistent and most commonly detected drugs in the aqueous environment, cannot be effectively removed by conventional waste water treatment plants.<sup>1</sup>

In this work the photocatalytic degradation of carbamazepine (CBZ) and its metabolites in aqueous solutions was investigated by using UV-A light and visible-light irradiations. The photocatalytic experiments were carried out using pure synthesized titanium oxide and Co, Ni-doped and (P, W) Co-Doped TiO<sub>2</sub> nanoparticles, with high concentration carbamazepine 9 mg/l. The Degradation of the CBZ was monitored by high-performance liquid chromatography (HPLC), and mass spectrometry (MS).

The results indicate that 67.40% of the initial concentration of CBZ was degraded in presence of pure  $TiO_2$  under UV light, 35.08% for P, W Co-doped  $TiO_2$ . The Co-doped  $TiO_2$  showed an efficiency of 34.74% toward the degradation of CBZ, while the Ni-doped  $TiO_2$  nanoparticles showed the lowest efficiency toward Carbamazepine photocatalytic degradation. The obtained results of the photocatalytic degradation of carbamazepine under visible-light in presence of the synthesized nanoparticles are lower than the obtained results under UV-A light irradiations.

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## Environment

## Characterization of the Essential Oil of Thymus capitatus

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Medicinal plants play an important role in the life of humanity. Man has used various plants found in his environment, to cure all types of diseases [1].Despite the progress of pharmacology, the therapeutic use of medicinal plants is very present in developing countries such as Morocco.

The present work aims at the valorisation of an Aromatic and Medicinal Plant very widespread in Morocco, likely to be endangered called Thyme, known in Morocco under the name of "Zaâtar". The scientific name of this plant is "*Thymus capitatus*", it belongs to the Lamiaceae Family, Order Lamiales, s / E Angiosperms.

Thyme is a plant that grows spontaneously in northern Africa (Morocco, Tunisia, Algeria, and Libya), Egypt, Spain as well as in Siberia and Northern Europe. However, most species are concentrated around the Mediterranean basin [2]. Chemical analysis of the essential oils extracted by hydrodistillation from the leaves of *Thymus capitatus* reveals the presence of a major compound such as Carvacrol, accompanied by other constituents at relatively low levels: Thymol (28,20%), $\gamma$ -Terpinene (4.92%) and Linalol (3,86%) - summing approximately 98,7%.



Chromatogram of essential oil of Thymus capitatus

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### Environment

## Selective Reduction of Esters to Alcohols with Manganese(I) N-Heterocyclic Carbene Complexes

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Manganese carbonyl complexes have been used for several applications such as catalysis, biological activity and magnetic materials. The increase interest on these types of complexes is related to the metal ion biocompatibility, abundancy and low price when compared to other metal ions of the same group in the periodic table (e.g. rhenium).<sup>1</sup> N-Heterocyclic carbenes (NHCs) have been extensively used as ligands yielding metal complexes with enhanced catalytic activities and stability due to their strong  $\sigma$ -donor and weak  $\pi$ -acceptor properties. However, there are very few examples of Mn(I)-NHC complexes in catalysis. Recently, our group has developed a new family of carbonyl manganese complexes bearing bis-NHCs that displayed remarkable catalytic activity in a variety of reactions including, reduction of carbonyls and oxidation of alcohols to aldehydes and ketones.<sup>2-4</sup> Motivated by these findings, we became interested in exploring further the potential of [Mn(bis-NHC)(CO)<sub>3</sub>Br] (1) complexes in catalysis. Here, we described the reduction of esters to alcohols with silanes mediated by Mn complexes 1 and 2 (Figure 1). Interestingly, complex 1 displayed excellent catalytic performances, affording high yields of the corresponding alcohols in neat conditions at 100 °C with PhSiH<sub>3</sub>. Under these conditions, a wide variety of esters were selectively reduced to the corresponding alcohols in high yields. The replacement of an NHC unit with a pyridine ring was found to significantly affect the catalytic performances, decreasing the catalytic activity for ester reduction.



Figure 1. Reduction of esters employing Mn(I)-NHC catalysts 1 and 2.

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## Environment

## Development of a Sensing Method and Water Treatment Process for Diphenylamine

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One of the biggest scientific and technological challenges of the near future is to solve the scarcity of good quality water suitable for human and animal consumption. Water quality can only be achieved by a series of physicalchemical processes and the more contaminated the water is, more treatment is required. Although the task of water treatment is relatively simple to control from the microbiological point of view, the presence of organic pollutants and their disinfection by-products (DBP) makes it a difficult task from a chemical and human health risks point of view.<sup>1</sup> One of these organic pollutants is diphenylamine (Figure 1), which is a common soil and water contaminant, due to its uses as a precursor of azo-dyes and non-steroidal drugs, stabilizer for propellants and as a preservative.<sup>2a</sup> Given its high toxicity, the widespread presence of diphenylamine in water resources constitute a serious environmental problem.<sup>2b</sup>

Herein, we focused on the development both of an analytical method for the detection and quantification of diphenylamine, and of a water treatment towards its degradation. Diphenylamine sensing was achieved by using a chromatographic approach, based on a HPLC coupled to a diode array detector (DAD). This approach exhibits good selectivity, a LOD and LOQ of 1 and 3  $\mu$ M (respectively), and a wide linearity range of 0-80  $\mu$ M. The degradation of diphenylamine was achieved and studied by comparing different disinfection approaches: reverse osmosis, UV irradiation, and use of chemical disinfectants (as chlorine and H<sub>2</sub>O<sub>2</sub>).



Figure 1: 3D structure of diphenylamine.

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## Environment

# Unravelling the mechanism of high-temperature CO<sub>2</sub> capture on lithium silicates using solid-state NMR

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High CO<sub>2</sub> concentration in the atmosphere is the main cause of climate change and its reduction is crucial for the environment. Solid sorbents for CO<sub>2</sub> capture generally exhibit better efficiency and stability than liquid counterparts showing excellent performance for post-combustion applications.<sup>1</sup> Pre-combustion CO<sub>2</sub> capture is an alternative<sup>2</sup> involving the reaction of a fuel with O<sub>2</sub> or air and/or steam to vield CO and H<sub>2</sub>. CO is then converted to CO<sub>2</sub> which is separated resulting in a hydrogen-rich fuel. In this respect, there is a need for solid sorbents capable of capturing CO<sub>2</sub> at high temperatures (650-750 °C). Lithium orthosilicate is one of the best-reported sorbents for this purpose. Improved kinetics of CO<sub>2</sub> capture with nanowires of lithium silicates and lithium tungstate, has been reported recently.<sup>2</sup> However, these nanowires were not stable against agglomeration/sintering during high-temperature CO2 capture and lost capture performance after few sorption-desorption cycles. In this respect, there is a need for sorbents with i) high CO<sub>2</sub> capture capacity at high temperatures, ii) faster rate of CO2 adsorption/desorption, iii) stability for a large number of cycles. In this work, we have designed and synthesized Lithium Silicate Nanoflowers (LSN), using Dendritic Fibrous Nanosilica (DFNS). DFNS has high surface area and excellent physical and textural properties,<sup>1</sup> making it highly accessible as opposed to porous silicas (SBA-15). LSN showed exceptionally high CO<sub>2</sub> capture capacity (close to theoretical value) and ultra-fast kinetics (33 wt. % CO<sub>2</sub> capture in 3 minutes). Here we will also present details on the characterization of these LSN using high-resolution <sup>1</sup>H, <sup>29</sup>Si, <sup>13</sup>C, <sup>6/7</sup>Li solid-state MAS NMR experiments to identify the structure of the different phase interconversions upon CO<sub>2</sub> adsorption. This has led to fundamental insights into the CO<sub>2</sub> capture mechanism of lithium silicates.

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## Environment

# Metal substitutions of rubredoxin metal cluster, stability studies and structural implications

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The metal binding motif (Scys)<sub>4</sub> is present in many proteins, assuming structural, regulatory or catalytic roles. Rubredoxin (Rd) isolated from *Desulfovibrio gigas* (**Figure 1**) is one of the simplest iron–sulphur proteins known (5.6 kDa). The four cysteine motif binds one iron atom in a tetrahedral coordination mode. The iron site may be easily replaced by other metals, making it perfect to mimetize the catalytic centre of other more complex metalloproteins. Fe-Rd and Zn-Rd were heterologously expressed in *Escherichia coli* adding either FeCl<sub>3</sub> or ZnCl<sub>2</sub> to the growth minimal M9 media and both proteins were purified. Co and Ni-Rds were obtained performing metal substitutions using apo-Rd as template. Growth conditions were optimized using Ni<sup>2+</sup> and Co<sup>2+</sup> salts instead of Fe<sup>2+</sup> attempting to obtain Ni-Rd and Co-Rd through biological metal insertion.

Purified Fe, Ni and Co-Rds were characterized by different spectroscopic techniques. Circular Dichroism (CD) of different Rds were performed, being the protein stability studied by CD using the far and visible regions of the spectra. Protein stability was complementary evaluated by Differential Scanning Calorimetry.

Zn-Rd was isotopically labelled with <sup>15</sup>N and the labelled apo-protein was obtained by removing the metal ion as previously described in literature<sup>1</sup>. NMR studies using <sup>1</sup>H-<sup>15</sup>N HSQC spectra of both Zn-Rd derivative and apo-Rd were obtained to elucidate the structural differences between the two forms.

Keywords: rubredoxin (Rd), circular dichroism, calorimetry, nuclear magnetic resonance.





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### Environment

## Incorporation of a Molybdenum atom in a Rubredoxin-Type Center of a de Novo-Designed α<sub>3</sub>DIV-L21C Three-Helix Bundle Peptide

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Approximately one-third of all proteins and enzymes require one or more metal atom(s) to perform their function(s). This remarkable interaction between a specific protein scaffold and a metal atom represents a landmark on the evolution of life on earth. Presently, the rational design and engineering of small, simple and stable peptides scaffolds to mimic catalytic metal-centres of complex proteins is an important goal in the area of protein design and search for centres with environmental, biotechnological and academic impact. [1]

In this work, a de novo  $\alpha_3$ DIV-L21C peptide [2] that possesses a rubredoxin-type centre (tetra-cysteinyl sulphur environment) as metal binding site [**Fig.1**], was used to incorporate a Mo atom to mimic, specifically, the tetra-thiolate environment in the active site of molybdenum-*bis* pyranopterin-containing enzymes (Mo-*bis* PDG), like the enzymes of the dimethylsulfoxide reductase (DMSOR) family [**Fig.2**]. The DMSOR family is the most diverse of the four Mocontaining families and include enzymes with environmental significance like the formate dehydrogenase (HCOO<sup>-</sup>  $\rightarrow$  CO<sub>2</sub> + 2e<sup>-</sup> + 2H<sup>+</sup>), the nitrate reductase (ONO<sub>2</sub><sup>-</sup> + 2e<sup>-</sup> + 2H<sup>+</sup>  $\rightarrow$  NO<sub>2</sub><sup>-</sup> + H<sub>2</sub>O) and the arsenite oxidase (AsO<sub>3</sub><sup>3-</sup> + H<sub>2</sub>O  $\rightarrow$  OAsO<sub>3</sub><sup>3-</sup> + 2e<sup>-</sup> + 2H<sup>+</sup>). [3]

The Mo– $\alpha_3$ DIV-L21C peptide was characterized by ICP to confirm the 1:1 protein/metal ratio under the reconstitution conditions tested. Using UV/Vis spectroscopy, a broad band with a maximum absorption at 320 nm was observed (with an extinction coefficient of 12000 M-1.cm<sup>-1</sup>). Circular dichroism (CD) studies in the visible spectral region confirm the metal incorporation and enable to study the Mo– $\alpha_3$ DIV-L21C peptide thermal stability. A positive band with a maximum at 394 nm was observed. Differential Scanning Calorimetry (DSC) was also used to perform a thermal denaturation analysis and define the thermal denaturation profiles of both apo– $\alpha_3$ DIVL21C and holo– $\alpha_3$ DIVL21C forms. Thermograms of the holo form fitted well to a two-peak model and thermodynamic parameters have been defined for each state (first peak with a primary melting temperature (Tm) = 56.3 °C,  $\Delta$ HCal = 203.4 kcal.mol<sup>-1</sup>; a second peak with a Tm = 58.8 °C,  $\Delta$ HCal = 436.9 kcal.mol<sup>-1</sup>). The electrochemical behaviour of the novel Mo– $\alpha_3$ DIV-L21C peptide was also evaluated. Further spectroscopic and activity studies are in progress, to consider this peptide scaffold a structural and functional analogue to some Mo-*bis* PGD enzymes.



**Figure 1**: Synthetic apo- $\alpha_3$  DIV-L21C peptide in blue (modelled with ExPASy SWISS MODEL Workspace) and native apo-rubredoxin\* in cyan. Sulphur atoms in yellow. \*built in Chimera (PDB entry: 2DSX)



Mo-bis PGD enzymes

**Figure 2**: Structure of the molybdenum centre of the DMSOR family (removed from [3]). Only the *cis* dithiolene group of the pyranopterin cofactor is represented. X, Y = S, Se, O, Asp, Ser, Cys, SeCys.

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## Environment

## Phase transitions properties of five dichlorinated substituted benzenes

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The effects of exposure to pesticides on humans and on the environment are a continuing concern and therefore the knowledge of properties with important applications in predicting the environmental mobility of these compounds and of their degradation products (metabolites) is of major importance. Thus, a thermodynamic study of phase transitions of five dichlorinated substituted benzenes was performed. The vapor pressures of the crystalline phase of 2,4-, 2,5- and 2,6- dichlorobenzoic acids and also of 2,6-dichlorobenzonitrile were measured using the Knudsen effusion technique<sup>1</sup> over the temperature ranges, T = (335.2-357.2) K, T = (332.1-354.3) K, T = (321.1-343.3) K and T = (295.3-319.2) K, respectively. Using the diaphragm manometer static method,<sup>2</sup> the vapor pressures of both crystalline and liquid phases of 2,4-dichlorobenzonitrile were measured in the temperature range T = (303.0-380.0) K. This technique was also used for complementing the range of the vapor pressure measurements of 2,6-dichlorobenzonitrile between T = (328.7 and 391.8) K. The standard molar enthalpies, entropies and Gibbs energies of sublimation for the compounds studied and also of vaporization for 2,4-dichlorobenzonitrile, at reference temperatures, were derived from the experimental results. The temperatures and molar enthalpies of fusion of the five benzene derivatives were determined using differential scanning calorimetry. The contributions of the carboxylic and cyano groups and also of the chlorine atom to the sublimation properties of the compounds studied were confirmed.



Figure 1: a) Plots of Inp against 1/T for 2,4-, 2,5- and 2,6- dichlorobenzoic acids.  $\circ$ , small effusion orifices;  $\Delta$ , medium effusion orifices and  $\Box$ , large effusion orifices. b) Phase diagram of 2,4-dichlorobenzonitrile:  $\bullet$ , vaporization (static);  $\Delta$ , sublimation (static); plot of the vapor pressures against reciprocal temperature for 2,6-dichlorobenzonitrile:  $\Delta$ , sublimation (static);  $\blacktriangle$ , sublimation (Knudsen effusion).

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## Environment

# A Novel Nanocomposite Film Electrode Based on Poly (Methylene Green) – Deep Eutectic Solvent / Fe<sub>2</sub>O<sub>3</sub> Nanoparticles for Electroanalytical Determination of Dapsone

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Antibiotics are often employed to treat diseases and promote animal growth. However, antibiotic gradually accumulates in food products, drinking water and the environment. They can have negative effects on human health, such as hearing loss, toxicity to kidneys, poor effectiveness in disease treatment and even lead to antibiotic-resistant bacteria. Therefore, reducing and monitoring the use of antibiotics is extremely important to protect human health and safety.<sup>1</sup>

Dapsone is an anti-leprotic and antibacterial drug widely used as an antibiotic in animals to prevent and treat a diversity of diseases including, sarcoma, malaria, leprosy and tuberculosis. Over the past decades, new indications for dapsone were successively identified, and it gained widespread use. Currently, a variety of methods has been reported in the literature for monitoring dapsone residues in the environment such as flow injection chemiluminescence, liquid chromatography (HPLC), spectrophotometry, etc. However, these methods require expensive equipment, have high testing costs and require complex sample processing. Thus, it is highly desirable to develop a simple, inexpensive and accurate analytical method for monitoring dapsone residues in the environment.<sup>2</sup> Electrochemical detection is fast-response, low-cost instrumentation as well as affordable cost per sample analysis, simple and timesaving operation, high sensitivity and selectivity. In electrochemical analysis, the key component is electrode modification, which requires the selection of suitable materials to improve the analytical performance.<sup>3</sup>

This work concerns the development of a novel electrode configuration based on poly(methylene) (PMG) films electrodeposited on Fe<sub>2</sub>O<sub>3</sub> nanoparticle modified glassy carbon electrode (GCE) for the detection of dapsone. Poly(methylene) (PMG) was electrodeposited by potential cycling in ethaline (1choline chloride: 2 Ethylene glycol) deep eutectic solvent and H<sub>2</sub>SO<sub>4</sub> as doping acid. The polymer films electrosynthesized in ethaline had superior electrochemical properties than their analogues produced in aqueous solution and were used as the sensing platform. The novel modified electrode was characterized by scanning electron microscopy, cyclic voltammetry and electrochemical impedance spectroscopy. The analytical determination of dapsone was carried out using differential pulse voltammetry. Parameters that influence dapsone determination were optimized, such as Fe<sub>2</sub>O<sub>3</sub> nanoparticle loading and chitosan loading, used to attach the nanoparticles on GCE, buffer pH, scan rate and accumulation time and potential. The results achieved were compared with those from the literature with similar electrode architectures. Selectivity, stability and applications in waters and artifial body fluids will also be discussed.

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## Environment

# Bioaccessibility and kinetic leaching profile of zinc in solid pet food samples assessed through a flow-based dynamic approach

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Bioaccessibility assessment is of uttermost importance when developing compound feed for animals since it is an essential step to study the absorption of nutrients. Dynamic leaching methods, where extraction fluids are continuously propelled through the solid sample, have several advantages when compared to batch-wise extraction methods, such as less time required for the extraction procedure, the possibility of automation, and the study of the leaching kinetics.<sup>1</sup> In the present work, the bioaccessibility and leaching kinetics of zinc, a trace element that possesses several biological functions, as a component of numerous metalloenzymes and influencing the metabolism of several biomolecules,<sup>2</sup> were studied using a flow-based dynamic approach. An extraction chamber composed by a combination of a reusable polypropylene disk holder containing a membrane filter inside with a commercially available syringe filter was used to retain the solid, with the extraction fluid being propelled continuously by two syringe pumps working in tandem. Assay parameters like the flow rate, the extraction chamber configuration, the amount of solid sample, and the composition of the extraction fluids were evaluated. To obtain leaching profiles, zinc was determined by flame atomic absorption spectroscopy. Fourteen commercially available complete dry dog food samples from three different market segments (*economic, medium* and *premium*) were evaluated.

The percentage values of bioaccessible zinc ranged from 49.0 to 70.0%, which is in good agreement with the values obtained for the batch extraction protocol under equilibrium conditions (n = 3). Regarding kinetic parameters, obtained after fitting the results into an exponential decreasing function, the fast leachable zinc ranged from 83 ± 1 to 313 ± 5 mg per kg of sample, with associated rate constants varying from 0.162 ± 0.004 to 0.290 ± 0.014 min<sup>-1</sup>.

These results show the applicability of the developed flow system to the evaluation of zinc bioaccessibility from different sources (inorganic *vs.* organic) aiming to develop new compound feed for dogs. Furthermore, the proposed system can be used to perform extractions in other products, like pharmaceutical and environmental solid samples and, since it uses a reusable disk holder, it constitutes a more environmentally sustainable proposal.

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## Environment

## Development of a new support platform for glyphosate biosensor

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Glyphosate (N- (phosphonomethyl) glycine) is a non-selective broad-spectrum herbicide for weed control. It is used in more than 750 products for agricultural, forestry, urban and domestic use. It is estimated that 6.1 billion kilograms of this product were used worldwide in the last decade. Glyphosate when applied to plants acts by specifically inhibiting the 5-enolpyruvyl shikimate 3-phosphate synthase (EPSPS), an enzyme involved in the production of aromatic amino acids such as tryptophan, phenylalanine and thyroxine. Studies have shown the presence of glyphosate in human blood and urine. However, the World Health Organization considered it a toxicologically harmless compound for humans. This controversy triggered research where they found that this compound has carcinogenic, mutagenic, reprotoxic and disruptive effects of endocrine function<sup>1</sup>. Therefore, the importance of the detection of glyphosate in various environmental matrices arises. Thus, it becomes a challenge for the scientific community to determine it, because it is a molecule with low solubility in organic solvents, it does not have chromophores or fluorophores and needs to use derivatization agents, if the detection is by optical processes<sup>2</sup>. Therefore, traditional photometric and fluorometric detection methods have limitations that can be overcome by electrochemical processes, in particular by the use of biosensors. The objective of this work is to develop an enzymatic biosensor for the detection of glyphosate with high sensitivity, reduced response time, easy construction and operation to determine this contaminant in environmental samples.

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## Environment

# Iron porphyrin-catalysed Si-H and B-H insertion with aryldiazoacetate esters *via* carbene intermediates

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Carbene chemistry is widely established as an important toolbox for the organic chemist. The last decades saw the implementation of a diverse set of metal complexes for carbene-mediated insertion reactions, either with noble metals (Rh, Ir, Ru, Au, Ag, etc...), Copper or Cobalt. While a vast number of catalysts are reported for these reactions, most have limited reactivity, are expensive and/or not selective. Nevertheless, they allow the insertion of N, S, O, Si and B nucleophiles, as well as the synthesis of cyclopropanes and a number of multicomponent reactions.<sup>1,2</sup>

The earth-abundant element Iron has been somewhat neglected in carbene chemistry; only a limited set of Fe(II) complexes are described due to the instability of Fe(II) species and its prompt oxidation in the presence of oxygen.<sup>3</sup> An exception is made to the application of Fe(III) porphyrins to either amination, hydroxylation, cyclopropanation or C-H insertion reactions.<sup>4,5</sup> Still, the use of Fe(III) porphyrins as stable and earth-abundant catalysts for the insertion of weak nucleophiles, such as silanes and boranes, has not yet been reported.

In this work we thus explored the reactivity of several metal porphyrins, namely iron porphyrins, in the insertion of a set of silanes and boranes. It stands as an attractive alternative to the aforementioned reactivity, using cheap and abundant metal precursors to create stable Fe(III) catalysts that open the possibility of immobilization and reuse. The reaction conditions were here optimized and the substrate scope determined accordingly. An additional DFT analysis revealed some mechanistic details of these reactions.



Scheme 1: Insertion of silanes or borane complexes catalyzed by metal porphyrins.

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## Environment

## Remoção de Hg(II) de águas salinas utilizando macroalgas vivas

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Este trabalho teve como objectivo estudar a remoção de mercúrio de águas utilizando seis diferentes tipos de macroalgas marinhas vivas, nomeadamente Ulva lactuca (verde), Ulva intestinalis (verde), Fucus vesiculosos (castanha), Fucus spiralis (castanha), Gracilaria sp. (vermelha) e Osmundea pinnatifida (vermelha), O mercúrio é um metal tóxico de carácter persistente que pode ser acumulado nos organismos aquáticos e amplificado ao longo da cadeia trófica causando diversos impactos ao meio ambiente e à saúde humana. Diferentes cenários realistas de contaminação foram estudados com concentrações de Hg(II) de 50, 200 e 500 µg L<sup>-1</sup> em águas com elevada salinidade (composição semelhante à água do mar). Massas fixas de 3 g L-1 (em peso fresco) de cada alga foram adicionadas em sistemas batch de 1 L e as experiências foram realizadas durante 72 horas. O processo de bioacumulação foi avaliado através da análise das concentrações de Hg(II) na solução ao longo do tempo. De um modo geral as algas verdes mostraram-se mais eficientes, a Ulva intestinalis apresentou percentagens de remoção de 98, 99 e 97 % enquanto que a Ulva lactuca apresentou percentagens de remoção de 99, 91 e 98 % para as concentrações de 50, 200 e 500 µg L-1, respectivamente, ao fim de 72 horas. A Gracilaria sp também apresentou uma excelente performance removendo completamente todo o Hg(II) da solução de concentração mais baixa após 48 horas. Das macroalgas estudadas a Osmundea pinnatifida apresentou o pior desempenho, com reduções nas concentrações de Hg(II) em solução de 80, 70 e 67 %. Relativamente à cinética do processo de remoção de Hg(II), podemos concluir que este é relativamente lento e que ao fim das 72 horas as algas parecem apresentar tendência para poderem reduzir ainda mais a concentração de Hg(II). Este fato é explicado pelo processo de bioacumulação envolver não só ligações do elemento à superfície das macroalgas através da biosorção, mas também envolver processos metabólicos de absorção. Análises das concentrações de metal nas algas após a exposição mostraram que todo o mercúrio retirado ficou de fato concentrado nas algas. Com este estudo pretende-se contribuir com uma alternativa sustentável e amiga do ambiente para processos de remediação de águas, onde massas muito pequenas de macroalgas (entre 300 e 450 mg L<sup>1</sup> em peso seco) sejam capazes de atingir concentração finais de contaminante nas águas que sejam vestigiais, transformando-as em águas próprias para o consumo humano.

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## Environment

# An optical-based approach towards Nitrogen, Phosphorus and Potassium assessment for smart nutrient deployment

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The development of the fertigation industry has been a challenge, in the last few decades, especially in what concerns the sensing and/or quantification of Nitrogen, Phosphorus and Potassium (NPK). Without a technology capable to accurately quantify the plants' nutrients demand, growers will continuously misuse fertilizers and most importantly, water. Innovations in distinct areas like micro-flowing [1] signal deconvolution [2] or optimization of the efficiency of fertirrigation systems [3] are reported.

Despite the existing technology, there is still not a durable nor robust solution for on-line and real-time measurement of NPK. The majority of the commercial offers for NPK sensing rely on Ion-Selective Electrodes (ISE) or wet chemistry for colorimetric assessment, which are either costly or time-consuming.

In this work we investigated the feasibility of a sensing mechanism that is able to quantify the presence of NPK in water, employing optical based sensors combined with optical fibers, with their inherently advantageous properties. Using this spectroscopic technique with advanced chemometrics and Artificial Intelligence (AI), to retrieve information on nutrients and/or contaminants content from the complex spectral data of the samples, we were able to quantify the presence of NPK in effluent water from real crops from local producers, with errors of 0.28%, 4.61% and 5.07%, respectively.



Figure 1: a) Knowledge map with analyte-specific spectral features and b) software isolated spectral features enabling a basis for calibration and quantification.

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## Environment

## Chromium removal from contaminated waters using ferrite nanoparticles

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Industrial activities lead to the release of hazard elements present in effluents of these industries to the environment. Chromium is among the most toxic trace elements present in industrial liquid effluents<sup>1</sup> whose levels in waters should be reduced to promote the water reuse. Magnetic nanoparticles (NPs) have been used efficiently as sorbents for the sorption of contaminants from waters by using magnetic separation technologies <sup>2,3</sup>. Previous works on the application of sorption technologies for the removal of chromium have focus on mono-elemental spiked ultra-pure water and using unrealistic concentrations of chromium <sup>4</sup>.

This work intended to evaluate Cr(III) sorption from waters with distinct chemical composition, using variable amounts of nanosorbent and subsequent magnetic separation. Spinel type ferrite nanoparticles (NPs: Fe<sub>3</sub>O<sub>4</sub>, MnFe<sub>2</sub>O<sub>4</sub> and CoFe<sub>2</sub>O<sub>4</sub>) have been synthesised and characterized by a plethora of techniques (XRD, FTIR, STEM, Chemical Analysis, BET Method, Magnetic Studies and Isoelectric Point). The ferrite NPs were evaluated for their sorption characteristics for chromium present in water samples (**Figure 1**). The experiments were performed by varying the amount of sorbent, pH, ionic strength and organic matter content. The results showed that both manganese and cobalt ferrite NPs are efficient nanosorbents for the removal of aqueous Cr(III). In particular, CoFe<sub>2</sub>O<sub>4</sub> NPs have proved to be a promising material for the treatment of wastewaters and industrial effluents due to the ease and reproducibility of synthesis, rapid removal of waters by magnetic separation, combined with the fact that this material causes low amounts of solid waste, and the possibility of being reused reducing its cost.



Figure 1: Schematic representation of sorption of Cr(III) using magnetic nanoparticles.

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## Environment

## Micro/nano heterogeneous catalysts for bioenergy sustainable processes

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Considering heterogeneous catalysts for transesterification reaction, calcium oxide (CaO) is a widely used catalyst due to being cheap, non-corrosive, economically benign, easy to handle and having a high basicity compared to homogeneous base catalysts<sup>1</sup>.

Using CaO nanocatalysts, it is possible to overcome some of these drawbacks, as they present higher surface area and catalytic activity, thus allowing to achieve a significant improvement on transesterification efficiency<sup>2</sup>.

In the present work, CaO from natural sources was micronized using the SAS (Supercritical Anti-Solvent) technique with Supercritical CO<sub>2</sub>. The obtained nanocatalysts were then analysed by SEM and DLS.

The transesterification of soybean oil into biodiesel using these catalysts (**Scheme 1**) was tested at 60° C with methanol reflux. Reaction conditions such as reaction time, methanol/oil molar ratio and catalyst loading amount were studied as well as its effect on the yield of the triglyceride conversion into FAME.

Another very promisor sustainable processes for 2<sup>nd</sup> generation biofuel production, with significant less energetic inputs than the conventional thermochemical processes were, the production of syngas through the water electrolysis with carbon source (e.g., liquified biomass), at lower pressure and temperature<sup>3</sup>. The environmental sustainability can be supported by the RENEFUEL project, aiming to produce synthetic fuels, such as methane, methanol and di-methyl ether (DME), which can be a renewable alternative to fossil fuels as solutions for mobility. The work, currently under development, is directed to the production of biomethane from the electrolytic syngas produced in a 1 kW pilot plant.

The tests carried out, until now, have shown the high potential of this electrochemical process to produce renewable synthetic fuels, an alternative to fossil fuels, with several possible applications, such as rural electrification, in remote locations (for example, islands and mountain villages) and, as an alternative for energy storage or as fuel for mobility.

CH <sub>2</sub> –OOC–R <sub>1</sub>			R <sub>1</sub> –COO–R		СН <sub>2</sub> –ОН
CH–OOC–R <sub>2</sub> +	- 3ROH	Catalyst ◀───	R <sub>2</sub> -COO-R	+	сн_он
CH <sub>2</sub> –OOC–R <sub>3</sub>			R <sub>3</sub> -COO-R		CH <sub>2</sub> –OH
Triglyceride	Alcohol		Esters		Glycerol

Scheme 1: Transesterification reaction to produce biodiesel, under micro/nano heterogeneous catalysts.

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## Environment

# Carbon-based nanomaterials as alternative sorbents for the recovery of rare earth elements

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As the world moves towards a cleaner, greener and more technological future, the use and demand for REEs will increase at the same speed. The society has never been so much dependent on electronic and electric devices as it is today, and that means REEs dependency. As a result, e-waste has become a worldwide problem to governments not only due to the environmental problems that have emerge from the incorrect treatment and storage of e-waste but also because the amount of e-waste which is increasing each year (50 million tonnes in 2018) (Critical Raw Materials -European Commission Report, 2018). Another concern to the tech industries and governments is the future of REEs supply. Currently, they are considered as the "vitamins" of modern industry. However, the high demand and the limited resources of REEs, combined with the environmental problems associated with their exploration, enforce the development of new ways to recover these elements from e-waste and wastewaters. In this way, the development of low-cost techniques and materials with high efficiency for REEs recovery is extremely important to face potential environmental problems and REEs supply issues. Carbon nanostructure materials applied in solid phase extraction to recover metals have increased considerably in the last decade (Yu et al., 2015). In this way, the main objective of this work was to develop an efficient carbon-based composite towards the recovery of REEs. Most of the sorption studies reported in the literature were performed with ultrapure waters spiked with tens to hundreds mg/L of single REE, the objective is to study the recovery from waters of different matrices and under environmental realistic concentrations. Two different carbon-based nanomaterials were synthetized and evaluated for the REEs (La, Ce, Nd, Eu, Gd, Tb, Dy and Y) recovery capacity. It was used different amount of sorbent and different waters, like mineral and saline waters. Average recovery percentages around 100% were obtained in mineral water and, in saline water, the recoveries decrease to ca. 50 to 60% using 100 mg/L of sorbents. Results were adjusts using kinetic models and the sorption mechanism that better described the results was chemisorption. The application of the nanocomposites tested for the recovery of REEs from aqueous solutions confirms that the carbon-based composites have a great potential to be used in this field.

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## Environment

## A Review of CFD Radiation Simulation in Photoreactors

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In recent years, the use of photo-assisted technologies has received increasing attention mostly due to the possibility of using solar light, a renewable and economical source of energy, for the activation of several processes namely water and wastewater treatment, chemical synthesis, energy production, etc. Radiation distribution is an indispensable parameter in the simulation of photochemical and photocatalytic systems. We simulated the light intensity distribution inside the reactors by solving RTE (Radiative Transport Equation) and it is dependent on parameters as type and position of the lamp, reactor geometry, radiation wavelength, the optical properties of the medium, specifications of reactor walls and operating conditions (inflow and outflow rate, the catalyst type and chemicals concentrations)<sup>1</sup>.

Numerical simulation has gradually become a powerful technique to study the radiative heat transfer in absorbing, emitting and scattering media<sup>2</sup>. Thus, CFD (Computational Fluid Dynamics) became a useful tool for simulation, enabling an integrated analysis of reactors through simultaneous modelling hydrodynamics, species mass transport, reaction kinetics and photon flux distribution (RTE)<sup>3</sup>.

In this work, we present a review of radiation modelling in photoreactors. The P-1, DO (Discrete Ordinates), and MC (Monte Carlo) models were used to solve the RTE in a three-dimensional annular geometry (Figure 1) with a laminar regime flow.



Figure 1: 3D Annular Photoreactor geometry.

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## Environment

# Laboratory evaluation of the physical and chemical degradation of a polypropylene geotextile in marine environments

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Geotextiles are polymeric materials used in the construction of many civil and environmental engineering structures, such as waste landfills, roads, railways, embankments or coastal protection structures. The advantages of using these materials include the ease of installation, high versatility and efficiency, low cost and low environmental impact. In marine environments, the geotextiles can be in contact with many agents capable of inducing unwanted changes in their properties, affecting their performance and reducing their lifetime.<sup>1</sup> The most common degradation agents in these environments include seawater, oxygen, solar radiation and other weathering agents, biological agents and the action of waves, currents and tides.<sup>2</sup> Polypropylene (PP) (polymer most used for manufacturing geotextiles) has a relatively good resistance against many chemical species and biological degradation. However, it has a poor resistance against oxidation induced by heat (thermo-oxidation) or by ultraviolet radiation (photo-oxidation).

In many applications, the geotextiles have to perform correctly their functions for a relatively long period of time (often, many years). Being impossible to determine their long-term behaviour before construction, it is necessary to predict their degradation over time. These predictions are normally based on data obtained from durability tests, where the geotextiles are exposed (often under accelerated conditions) to the degradation agents.

This work evaluates the resistance of a PP geotextile (stabilised with 0.2% of the additive Chimassorb 944, *w/w*) against some physical and chemical degradation agents present in marine environments. The geotextile was exposed to some laboratory durability tests: immersion in liquids (deionised water, seawater and an aqueous solution of sodium chloride 35 g/L), thermo-oxidation (oven-ageing method: exposure at 110 °C in a normal oxygen atmosphere) and artificial weathering (exposure in a weatherometer to ultraviolet radiation, water spray and condensation). The geotextile was (1) exposed in isolation to each durability test (single exposure) and (2) exposed successively to combinations of two or more durability tests (multiple exposures). The damage induced by the durability tests was evaluated by monitoring the changes occurred in the tensile properties of the geotextile.

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## Environment

# Validation and uncertainty evaluation of total phosphorus variation in a large Tagus river area

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The management of environmental resources is based on defining limits and controlling pollution sources, and the regular monitoring of environment quality trends. The detection of environment quality trends requires the ability to perform representative characterisations of a large environmental area where studied parameter is reported with uncertainty.<sup>1</sup>

This work describes the validation and uncertainty evaluation of total phosphorus measurement in a river water sample by ion chromatography after sample digestion with Caro's reagent<sup>2</sup>, and the determination of the uncertainty of sampling a large river area at a specific depth.

The bottom-up evaluation of total phosphorus measurement in a river water sample involved the determination of phosphate measurement uncertainty by the Linear Least Squares regression model, after checking regression model assumptions, and the assessment of sample digestion uncertainty by difference between the dispersion of recovery test of ## and ## solutions and the instrumental quantification uncertainty.<sup>3,4</sup>

The sampling uncertainty was estimated by the Monte Carlo Simulation of mean river water composition by taking the estimated total phosphorus of various water samples, GPS coordinates uncertainty and measurement repeatability. The collected information estimated system heterogeneity and the uncertainty from single or composite sampling.<sup>5</sup> This work allowed to define how sampling should be performed to estimate a total phosphorus variation in river water larger than a minimum total phosphorus value.

(Figure 1).



Figure 1: Uncertainty components for estimating the variation of total phosphorus in a river area.

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## Environment

## Synthesis and biological evaluation of porphyrin-pyrrolidine conjugates

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Porphyrins are a family of intensely coloured aromatic tetrapyrrolic compounds, which have been proven useful as photosensitizers in Photodynamic Therapy, a technique which has been used to combat a wide array of diseases, from psoriasis to cancer.<sup>1,2</sup> Due to the proliferation of antibiotic-resistant bacterial strains, PDT has also been proposed as a potential alternative to conventional antibiotic use in combating infections.<sup>3</sup> In PDT, the photosensitizer is able to interact with molecular oxygen when exposed to light, producing reactive oxygen species, such as singlet oxygen, which are able to disrupt cellular structures, triggering cell death.<sup>2,3</sup> It has been previously shown that  $\beta$ -formylation of the porphyrin macrocycle can be used as the first step in introducing brand new functional groups into porphyrins.<sup>4</sup> In the present communication, this pathway was used to introduce pyrrolidine derivatives into the  $\beta$  position of the macrocycle, with the purpose to synthetize new porphyrin-pyrrolidine conjugates with potential antibacterial activity. The synthesis, characterization and biological evaluation of the newly obtained compounds will be discussed.



Figure 1: Synthesis of porphyrin-pyrrolidine conjugates using 5,10,15,20-tetraphenylporphyrin as a starting material.

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### CPEV58

### Environment

# QM/MM study of the reaction mechanism of the extremozyme Glucuronoyl Esterase as a sustainable approach for Biofuel production

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Enzymes catalyze a myriad of chemical reactions essential to life maintenance. Their best performance is typically achieved under physiological conditions and they are tremendously sensitive to any environmental fluctuations. A group of enzymes called extremozymes possesses the ability of performing the same biological tasks under severe settings.

The Glucuronoyl Esterase (GE) is an enzyme found in the thermophilic *Myceliophthora thermophile*, and displays great industrial potential for biofuel production<sup>1</sup>. Cellulosic ethanol is obtained from degradation and further fermentation of lignocellulose (wood, grasses, or the inedible parts of plants). The primary steps involve the breakdown of this raw material, including the dissociation of lignin, cellulose and hemicellulose, the three polymers that constitutes lignocellulose. GE, first discovered in a wood-rotting fungus, cleaves the ester bonds between hemicellulose, cellulose and lignin<sup>2</sup>, thus, becoming of great interest to the biofuel industry.

Using QM/MM methods, we are currently studying the catalytic mechanism of GE based on a proposed mechanism<sup>3</sup> consisting of a catalytic triad (Ser-His-Glu), which orchestrates a concerted reaction: a Ser nucleophilic attack to the ester group of the substrate is concomitant, although asynchronous, with the deprotonation of Ser by His (**Fig. 1**). Upon the nucleophilic attack, the leaving group is promptly protonated by the positively charged His. From our research, we were able to identify the Transition State 1 (TS1) of this athermal reaction, with an estimated activation barrier of *ca.* 18 kcal/mol, as well as the formation of the oxyanion hole upon the TS1, and a potential water molecule involved in the stabilization of the leaving group. In future studies, we aim to characterize the deacylation reaction that regenerates the enzyme for a new cycle, and to conduct mutagenesis studies to enhance its catalytic rate for industrial standards.



Figure 1: Proposed Mechanism of Glucuronoyl Esterase.

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# COMUNICAÇÕES EM Painel

A TABELA PERIÓDICA LUMINESCENTE MATERIAIS, ENERGIA E NANOTECNOLOGIA

### Materials

# Temperature-responsive logic gate nanoparticles for cellular hyperthermia

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The quest of temperature monitoring at micro and nanoscales has been a path of interest in many research contexts, such as cellular hyperthermia. In this case the answer to the question "did the system locally exceed a certain threshold temperature?" can be more accurate and useful than a continuous temperature monitoring. Following this question, we developed a system based on iron selenide (Fe3Se4) magnetic nanoplatelets that are capable of behaving both as an actuator and as a sensor, simultaneously, while recording temperature fluctuations above a defined threshold. Such nanoplatelets are considered hard magnets, which means that they retain a magnetic moment even in the absence of an applied magnetic field. Additionally, they present a magnetic phase transition that occurs at a defined temperature (Tc), which is slightly above room temperature and can be easily modulated by tuning their size. Therefore, below Tc, we can set a well-defined magnetization that will remain unchanged until Tc is crossed.

Adapting methods from literature, new iron selenide nanoplatelets were developed with great control over size and, consequently,  $T_c$  – between 0 and 60 °C. Nanoplatelets with  $T_c$  tuned to 42 °C were applied in a cellular hyperthermia assay using prostate cancer cells and different thermal doses (induced by a Near-Infrared LED). It was observed that for low thermal doses, the threshold of 42 °C was not crossed and most cells appeared to be viable, whilst in the case of high thermal doses, the results show the opposite. <sup>1</sup> This shows the potential of such materials to behave as logic gates having temperature and magnetic field as inputs and as the output a Yes/No answer to the question "was the 42 °C barrier crossed?". This proof of concept was a pioneer assay using hard nanomagnets in a biological application, opening the pathway to other note-worthy applications.



Figure 1: Experimental scheme of the use of iron selenide nanoplatelets as logic gates for a cellular hyperthermia assay.

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### Materials

# Towards enhanced selective gas adsorption in post-synthetic modified metal–organic frameworks

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Metal-Organic Frameworks (MOFs) are made by linking inorganic and organic units leading to a wide array of geometries, sizes, and functionalities.<sup>1</sup> More than 20,000 different MOFs have been reported and studied within the past decade. The surface area values of such MOFs typically range from 1000 to 10,000 m<sup>2</sup>/g, thus exceeding those of traditional porous materials such as zeolites and carbons.<sup>2</sup>

Most of the necessary functionalities cannot be introduced into MOFs directly via de novo syntheses. However, these can be accessed through post-synthesis modifications on the reactive moieties of the linkers and/or nodes without disrupting the metal–linker bonds.<sup>3</sup> Specific modifications with organic groups within the MOFs network have already proved a successful methodology to enhance their adsorption capabilities concerning certain gases such as N<sub>2</sub>, CO<sub>2</sub> and methane. Conversely, the majority of air contaminants (anthropogenic hazardous pollutants) including NO<sub>x</sub>, SO<sub>x</sub>, CO, H<sub>2</sub>S, NH<sub>3</sub>, volatile organic compounds (VOCs), and polycyclic aromatic compounds (PAHs) released from both static and mobile sources, are still by comparison less studied.<sup>4</sup> Herein, Mg-MOF-74 is post-synthetically modified with different amines (Figure 1) in order to improve and fine-tune its characteristics in the adsorption of anthropogenic hazardous air pollutants.<sup>2</sup>



Figure 1: Post-synthetic modification with Mg-MOF-74 for air purification aaplication.

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### Materials

# Reactive modelling of sol-gel polycondensation in the presence of templates

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The polycondensation of silicic acid, methylsilicic acid, or their mixture was studied by reactive force field simulation. These were found to be feasible systems for the simulation of the two-step acidic hydrolysis - alkaline condensation of their alkoxysilane counterparts, usually taken experimentally as sol-gel precursors. The approach avoided the alkoxysilane hydrolysis step and allowed high degrees of polycondensation at relatively low temperature (700-1000 K), from the computational efficiency perspective. Being the ultimate interest of the present study the sol-gel polycondensation of templated gels whose microstructural pattern is affected by the presence of a template, the role of the intermolecular forces was decisive, and prompted for the reach of high polycondensation with the lowest possible temperature. Polycondensation with added damascenone did not result in any perceived templating effect, i.e damascenone was not able to interact significantly with the growing clusters, in a way that would allow its occlusion or a surface molding effect on the clusters. A possible reason for that is the intermolecular interaction strength being too weakened at the temperatures set for the simulations. However, when using luteolin as the template, a molecule with several hydrogen bond interaction points, it was possible to observe different microscopic events involving the template molecules, some of them corresponding to actual templating effects, such as partial enveloping by network around the template (Figure 1). These restricted events did not allow the inference of any macroscopic property of the final gel. However, it was shown that polycondensates shaped by the template or a template dimer may be obtained.



Figure 1: Snapshot showing a partially enveloped LUT molecule at a late stage of polycondensation

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### **Materials**

# Stabilization of bluish pyranoanthocyanin pigments in aqueous systems using lignin nanoparticles

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Lignin nanoparticles (LNP) loaded with pyranoanthocyanin dimers (PD) and portisins (P) were produced using nanoprecipitation and dialysis techniques. The results obtained for LNP and P-LNP showed particles presenting sizes around 200 nm with a very narrow size distribution (PDI  $\leq$  0.2) using both methods. For PD-LNP, the nanoprecipitation method yielded particles with high particle sizes (Z-average  $\approx$  800 nm) and PDI  $\approx$  0.45 when compared to the dialysis method that produced particles with an average size around 200 nm and a PDI below 0.2. Concerning the average zeta potential ( $\zeta$ ), values around – 40 mV were obtained for both methods. TEM, SEM and STEM images showed that the particles present a spherical and compact shape and that these characteristics were maintained for 28 days at room temperature. High encapsulation efficiencies of 86±2 and 85±4 were observed for PD and P, respectively. LNP stability was followed at pH  $\geq$  5 for at least 7 days and the LNP encapsulated systems (PD-LNP and P-LNP) showed a good colour stability towards pH change after 8 days of incubation, when compared with the pure bluish pigments.



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### Materials

### CB8-bis(pyridinium)dithienylethene host-guest pairs: structural diversity

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Cucurbit[n]urils (CBn) are pumpkin-shaped macrocyclic receptors that display very high affinity and selectivity for complementary guest molecules in aqueous solution. Diarylethenes, that display a light responsive equilibrium between open and closed forms, have proved to work as suitable guest in such systems. In fact, previous work<sup>1</sup> has identified a high-affinity 1:1 complex formed between cucurbit[8]uril and the water-soluble photochromic bis(pyridinium)dithienylethene derivative **1** that displays nanomolar affinity in the closed form (**1c**) and 100-fold lower affinity in the open form (**1o**). This differential binding affinity confers light-responsive properties to the host–guest system, allowing remote control over the association/dissociation process in the nanomolar concentration range and photoregulation of the complexation of classic high-affinity pairs through competitive binding.

As a follow up of this work, dithienylthene derivatives **2**, **3** and **4** were synthesized<sup>2-5</sup> and their association constants with CB8 were measured in order to investigate how specific structural variations affect the stability of the host-guest complexes. The results of this study are expected to pave the way towards a rational design of high-affinity stimuli-responsive host-guest complexes.



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### **Materials**

### **Control of Molecular Conformation with Near-Infrared Laser Light**

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Our current research is focused on studies of molecular structure, conformational dynamics, tautomerism, vibrational properties, photochemistry of biological and photochromic molecules, molecular switches, reactive intermediates and systems with open electronic shells, vibrationally-induced chemistry, and quantum-mechanical tunneling.

In our work, we use the low-temperature matrix isolation: an experimental method where guest molecules are immobilized in rigid and inert materials under cryogenic conditions. Bands in infrared and near-infrared spectra of matrix-isolated species have typical widths of a few wavenumbers. This affords much valuable spectroscopic information, with a possibility to reliably distinguish individual spectroscopic signatures of different conformers.

Under these conditions, and using monochromatic laser light, we can selectively excite a chosen conformational state and achieve vibrationally induced conformational control.<sup>1-3</sup> Particularly interesting, we have demonstrated that selective excitation of vibrational overtones allows conformational changes in a molecule. Typically, we use first overtones of stretching modes of the OH, NH, or NH<sub>2</sub> groups, located in the near-infrared (in the 7100-6600 cm<sup>-1</sup> range). In this report, our specific attention is focused on the possibility of conformational control involving remote fragments with heavy atoms (such as methoxy or aldehyde groups).<sup>3-6</sup> These bi-directional isomerizations constitute examples of vibrationally activated molecular switches.

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### **Materials**

# Hexahomotrioxacalix[3]ureido-Based Anion Receptors: High Selectivity for Carboxylate lons

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The development of synthetic receptors for the complexation of anions is still a strong research area in supramolecular chemistry, due to the recognized importance of anions in biological and environmental areas.<sup>1</sup> The versatile macrocyclic compound calixarenes have been widely used as anion receptors. The introduction of (thio) urea units in the macrocycle scaffolds provides receptors that use mainly NH groups as hydrogen-bond donors to interact with the anions.

Following our previous studies on anion binding by dihomooxacalix[4]arenes,<sup>2-4</sup> we have recently extended our research into the study of hexahomotrioxacalix[3]ureido receptors.

In this work, three *p-tert*-butylhexahomotrioxacalix[3]arene tri-substituted derivatives (**1a**, **1b**, and **2**) in the cone and partial cone conformations and containing phenyl(thio)urea groups on the lower rim via a butyl spacer were obtained. Their binding properties towards several relevant anions were assessed by proton NMR titrations. The results are discussed in terms of the receptor conformation.



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### Materials

# Dye-Sensitized Solar Cells based on Pyranoanthocyanin derivatives

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Dye-sensitized solar cells (DSSCs) have drawn a lot of attention from the scientific community due to their ease of fabrication, low cost and competitiveness with different photovoltaic systems.<sup>1</sup> Following the work of Grätzel, several types of pigments such as the original ruthenium(II) complex,<sup>2</sup> and organic dyes,<sup>1</sup> have been used as light absorbers, showing the importance of exploring systematically other types of dyes. Anthocyanins are the main polyphenolic dyes found in young red wines, which are transformed into more stable structures such as pyranoanthocyanins, during wine ageing and maturation.<sup>3</sup> The first reported DSSC using a natural anthocyanin displayed a conversion yield of 0.56% and paved the way for sustainable DSSCs based on renewable resources.<sup>4</sup> Pyranoanthocyanins have been shown to be more resistant to hydration than anthocyanins and constitute a photosensitizer family with great potential for bio-inspired DSSCs.<sup>3</sup> Still, the best known efficiency reported for pyranoanthocyanins, prior to the present work, was 0.006%.<sup>3</sup>

In this work, a series of bio-inspired pyranoanthocyanin derivatives were designed, synthesized and applied for the first time as dye sensitizers in DSSCs. A relation was established between dye structure and cell efficiency. Specifically, the presence of the catechol unit was shown to increase electron injection to the TiO<sub>2</sub> semiconductor. An overall efficiency of 1.57% was obtained for the best performing compound (Figure 1).



Figure 1. J-V curve of the best performing pyranoanthocyanin derivative, methylpyranocyanidin-3-glucoside.

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### **Materials**

# Nanostructured MoS<sub>2</sub>/Titanate nanotubes for Catalytic Reduction of Nitroarenes

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Nitroarenes reduction is a relevant process to amino compounds formation. These amino compounds are extremely important in a variety of chemical industries such as dyes, pigments, agrochemicals, herbicides, pharmaceuticals, rubber manufacturing, chelating agents and textile.<sup>1</sup> However, the presence of a catalyst is mandatory for the success of these nitroarenes reduction reactions.

Here, it is reported the synthesis, characterization and application of hybrid titanate nanotubes (TNT) modified with molydenum disulfide (MoS<sub>2</sub>/TNT) in catalytic reduction reactions of several nitroarenes.

Titanate nanotubular sample was prepared by a hydrothermal approach, using an amorphous precursor.<sup>2</sup> Afterwards, the molydenum disulphide nanoparticles were produced in the presence of the TNT particles, using the same method.<sup>3</sup> The prepared materials were characterized by several techniques, including Powder X-Ray Diffraction (XRD), Diffuse Reflectance Infrared Fourier Transform Spectroscopy (DRIFT) and Diffuse Reflectance UV-vis Spectroscopy (DRS).

In order to assess the MoS<sub>2</sub>/TNT catalytic performance, different reduction reactions of nitroarenes were studied. Reactions were conducted by mixing solutions of each substrate (*p*-nitrophenol, *p*-nitroanisole, *m*-nitrophenol, *p*-nitrotoluene, 1-chloro-*p*-nitrobenzene and methyl-*p*-nitrobenzoate) with the reducing agent – sodium borohydride (NaBH<sub>4</sub>) in the presence of the catalyst (**Scheme 1**). For each substrate, the performance of the catalyst was evaluated by UV-vis spectroscopy during 120 min. The final solutions were analysed by Gas Chromatography-Mass Spectrometry (GC-MS) to assess reactions selectivity.

The results show that the obtained reaction products were the expected amino compounds. However, this process it is only successful in the presence of the MoS<sub>2</sub>/TNT as catalyst. Under these conditions, the faster reaction was observed for the *p*-nitrotoluene reduction. The substrate that requires more time to be catalytic reduced was the *p*-nitrophenol, reaching 50 min of reaction time.



Scheme 1: Proposed mechanism for *p*-nitrophenol catalytic reduction (adapted from [4]).

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### Materials

# Photophysical characterization of two phosphorescent dinuclear cupper iodide complexes: impact of crystalline network

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Centrosymmetric { $Cu_2(\mu-I)_2$ } based complexes 1 [ $CuI(PMe_2Ar^{XyI})_2$  and 2 [ $CuI(PEt_2Ar^{Mes})_2$ , despite of their quite similar structures show very different emission behaviour upon excitation of the powder samples at room temperature. A faint orange emission of 1 and a much brighter greenish emission of 2 with respectively 5.76% and 19.43% photoluminescence quantum yield were observed. The photophysical behaviour of these compounds in liquid solution, solid-solid Zeonex solution and powder samples at room temperature and 77 K was investigated. According to TD-DFT calculations in both 1 and 2 transition to S<sub>1</sub> the first singlet excited state is symmetry forbidden, and S<sub>2</sub> is the initial symmetry allowed singlet excited state. That is any IC from S<sub>2</sub> would lead to the dark state S<sub>1</sub>, thus emission can be observed only as phosphorescence if the initially S<sub>2</sub> excited state can undergo ISC to the triplet manifold (**Figure 1**). DFT calculations indicate that a doubly degenerate state is populated upon photo-excitation hence a geometrical distortion of the excited molecule is expected through a First Order Jahn-Teller distortion (JT) which by itself conducts a S<sub>2</sub>→S<sub>1</sub> transition, done by group theory calculations and the technique of projection operators, shows that the manifestation of Jahn-Teller Effect is conditioned by crystal packing so that among these similar structures just 2 whose crystal lattice blocks the JT active modes exhibits phosphorescence also at room temperature.



Figure 1: Structures of 1 and 2; Suggested Phosphorescence Mechanism(Dashed line : non-radiative transitions)

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### Materials

### Novel water-soluble fluorescent chemosensors for anion detection

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The word "chemosensor" is commonly used to described a molecule capable of recognizing the presence of a specific analyte based on chemical interaction, providing a measurable response which is quantitatively proportional to the analyte.

Coordination chemistry has allowed for a rapid boost on cation sensors over the 1990s, while the development of anion sensors did not experience the same growth. Nevertheless, the chemistry around chemosensor systems for anions as evolved tremendously in the past decade.<sup>1</sup> In particular, a strong effort by the scientific community was directed once more towards coordination chemistry, as a means to interact with anions via non-classical/non-covalent interactions.<sup>2</sup> Organic and inorganic phosphates are amongst the most important class of anions, due not only to their essential roles in intracellular metabolic regulation, but also to their widespread presence in our environment (e.g. fertilizers for agriculture).<sup>3</sup> However, detection of phosphates in aqueous media is difficult because of the high stability of the solvation sphere by water molecules, which strongly hinder the interaction of a low concentration sensor with the anion. In this sense, Hamachi and collaborators have developed a series of fluorescent sensors based on di-2-picolyl-amine (DPA) receptors units, which complexed preferentially with Zn<sup>2+</sup> or Cd<sup>2+</sup> and, subsequently were used to detect phosphate derivatives.<sup>4</sup>

In this work, two new fluorescent sensors are presented, each bearing two DPA units. A thorough study on the optical properties of both sensors was performed, in terms of cation binding and subsequent anion response. Apart from strong fluorescent responses, both sensors are capable of working in aqueous environment, which highlights their potential for intracellular imaging/sensing applications.



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### Materials

# Copper-based nanoparticles - synthesis and characterization

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Copper nanoparticles (CuNPs) are particularly appealing materials for the replacement of more expensive and less earth-abundant metals such as silver and gold, which are used in several commercial processes. Copper also displays good electronic, antimicrobial, optical, and chemical properties. In spite of this, the use of copper is limited due to its intrinsic instability under atmospheric conditions, *i.e.* copper is prone to oxidation. Various efforts have been made to increase the stability of CuNPs, including the association of CuNPs with organic structures such as polymers.<sup>1,2</sup>

The main goal of this project was focused on the preparation and characterization of long-term stable Cu-based NPs using different strategies. The particles were synthesized using the environmentally friendly ascorbic acid (AA) as a reducing agent. The fourth generation hydroxyl-terminated polyamidoamine (G4-OH PAMAM) dendrimer and polyvinylpyrrolidone (PVP) polymers were used to control the growth of the particles. Several reaction parameters were tested including pH, temperature, and concentrations.

The samples were characterized using various techniques in order to assess the physicochemical properties and stability. These include Ultraviolet-Visible (UV-Vis) Spectroscopy, Nuclear Magnetic Resonance (NMR) Spectroscopy, and Scanning Electron Microscopy (SEM) coupled with Energy-Dispersive X-ray Analysis (EDX).

The results for the particles obtained by the PVP route indicated the presence of Cu-based particles with diverse shapes (e.g. polyhedral, spherical, and disk-like) and at different oxidation states depending on the pH and temperature. The effect of the addition of more AA and PVP contributed to the decreasing size and increasing homogeneity of the final product, respectively.

The UV-Vis spectra of the samples prepared using the PAMAM route suggested the successful synthesis of the Cubased dendrimer entrapped nanoparticles (Cu-DENPs). The <sup>1</sup>H NMR data showed that the samples remained stable for at least one month.

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### Materials

# Functionalization of generation four PAMAM dendrimers – the fluorination effect

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The use of dendrimers has been broadly reported due to their attractive physical and chemical properties, such as low viscosity, void space<sup>1</sup>, well defined 3D globular structure, and monodispersity<sup>2</sup>. Although the fluorination of these synthetic hyperbranched polymers was shown to exhibit significant DNA condensation, enhanced binding affinity towards proteins, and improved intracellular release and transfection efficiency<sup>3,4</sup>, much remains to be done regarding their application in the biomedical field.

Based on our expertise on the development of dendrimers for biomedical applications<sup>5</sup>, generation four poly(amidoamine) (PAMAM) dendrimers were functionalized with 2,3,5,6-tetrafluoro-4-hydroxybenzoic acid<sup>6</sup>, a fluorinated compound, or 4-hydroxybenzoic acid, the non-fluorinated parent compound that presents anti-fungal and anti-bacterial properties, as well as high sigma receptor affinity, thus being employed as a preservative in drugs and pharmaceutics<sup>7,8</sup>. The objective of the use of both compounds, fluorinated and non-fluorinated, for the conjugation with dendrimers is to evaluate the fluorinated dendrimer vis. the non-fluorinated dendrimer biological properties.

The synthesis (**Scheme 1**) was made adding the reagents, using increasing molar equivalents, to a concentrated PAMAM dendrimer solution, under magnetic stirring for two days. After dialysis and lyophilization, the resulting compounds were characterized by NMR (<sup>1</sup>H, <sup>13</sup>C, <sup>19</sup>F, COSY, and HSQC), FTIR, MALDI-ToF, UV/Visible, and Fluorescence spectroscopy. The characterization confirmed the successful functionalization of the dendrimer with the compounds at different functionalization degree, enabling us to proceed for the biological studies.



Scheme 1: Reaction of PAMAM G4-NH<sub>2</sub> with 4-hydroxybenzoic acid or 2,3,5,6-tetrafluoro-4-hydroxybenzoic acid.

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### **Materials**

# Hyaluronic Acid-Modified Dendrimer Entrapped Gold Nanoparticles

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For a long period, advances in cancer treatment have only been translated into improvements in patient care but not into the improvement of early-stage diagnosis<sup>1</sup>. Therefore, nanomedicine has become a rapidly emerging field, allowing for the use of nanoparticles (NPs) in several biomedical applications in order to overcome conventional challenges.

Being the most widely studied dendrimers, poly(amidoamine) (PAMAM) dendrimers are a class of highly branched, monodisperse molecules with a well-defined structure and composition. Due to this, they are considered perfect templates for the synthesis of inorganic nanoparticles (NPs)<sup>2</sup> such as gold (Au) NPs, which are widely used as imaging agents for X-ray computed tomography (CT) due to their strong X-ray attenuation properties<sup>3</sup>.

Due to the abundance of amine groups on the periphery of the dendrimer, toxicity and safety are always a concern. Thus, the use of plain PAMAM dendrimers for targeted delivery is limited by their intense positively charged surface, leading to a need in the modification of their surface groups with targeting molecules, imaging agents and/or drugs<sup>4</sup>. Hyaluronic acid (HA) is a naturally occurring glycosaminoglycan composed of alternating sugar residues of dglucuronic acid (GlcUA) and N-acetyl-d-glucosamine (NAG) units, which is involved in several cellular responses, including proliferation, differentiation, mobility and adhesion. HA can recognize different cellular receptors including CD44, the major cell surface receptor for HA, over-expressed on several tumor cell surfaces but expressed at low levels in normal cells<sup>5–8</sup>.

Regarding the development of a new imaging agent for targeted CT imaging of CD44 overexpressing cancer cells, HA-modified dendrimer-entrapped gold nanoparticles (Au DENPs) were prepared. For this, HA, was conjugated to anime-terminated generation 5 PAMAM dendrimers (G5.NH<sub>2</sub>). This conjugate served as a template for the synthesis of Au DENPs. Characterization results of the formed HA-modified Au DENPs were obtained by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy, dynamic light scattering, zeta potential measurements, UV-Vis spectroscopy and SDS-PAGE. Preliminary cytotoxicity studies on three different cell lines for the obtained compounds will also be presented.

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### **Materials**

# **Coumarin-based chromophores for DSSCs**

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The development of organic sensitizers for Dye-Sensitized Solar Cells (DSSCs) involves the design of molecules having a donor (D),  $\pi$ -bridge and acceptor (A) moieties (D– $\pi$ –A). This push–pull structure can induce the intramolecular charge transfer (ICT) from subunit D to A through the  $\pi$ -bridge upon light absorption (Figure 1). Coumarins are one of the largest classes of fluorescence sensors<sup>1</sup>, which accounts for their increased application as fluorescent probes<sup>2</sup>. They are also promising candidates as donor moieties in D– $\pi$ –A dyes for DSSCs, especially when electron-donating substituents are introduced at the 7-position and the extension of the  $\pi$  system occurs though the 3-position. By well-established and previously described methodologies on palladium coupling reactions for the synthesis of coumarin-based chromophores for DSSC<sup>3</sup>, the extension of the  $\pi$ -electron system was endeavored with thiophene and benzotriazole bridges. Photochemical and photophysical characterization will be presented as well.



Figure 1: Schematic representation of the D- $\pi$ -A structure of an organic dye.

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### **Materials**

# Metal-Organic Frameworks for Cultural Heritage preservation: the case of acetic acid removal

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Low concentrations of acetic acid found in indoor air at museums poses serious preservation problems. Recently, we have proposed the application of Metal Organic-Frameworks (MOFs), with a combination of hydrophobicity and optimized interactions (Figure 1), to capture acetic acid more efficiently than current adsorbents. We demonstrated how a subtle combination of sufficient hydrophobicity and optimized hostguest interactions allows to overcome the challenge of capturing traces of this very polar volatile organic compound in the presence of humidity.<sup>1</sup> The optimal MOFs do not show polar groups in the inorganic node or have lipophilic but polar (e.g. perfluoro) groups functionalized to the organic linkers. We established that MOFs can be a viable solution to this highly challenging problem in the Cultural Heritage protection, which is a new field of application for this type of hybrid materials.



Figure 1: Four MOF architectures, MIL-101 type, UiO-66 type, MIL-140 type and ZIF type, were explored with several modifications to enhance the selective capture of acetic acid in the presence of water.

Based on these novel results, a European project is currently developing packages that apply the MOFs on the preservation of films and photographs.<sup>2</sup>

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### Synthesis and characterization of Magnetic nanoparticles

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Ferrites are some of the most important magnetic nanoparticles and have potential applications in wastewater treatment, magnetic sensors, and possible use in medicine in drug delivery systems or in cancer treatment.<sup>1-4</sup> From the literature search two magnetic nanoparticles were found to be of possible interest for applications in the shoe industry, the magnetite  $(Fe_3O_4)^5$  and the cobalt ferrite  $(CoFe_2O_4)^4$ .

The syntheses of the magnetite (Scheme 1-a) and the syntheses of cobalt ferrite (Scheme 1-b) are drafted bellow.



Scheme 1: a) magnetite synthesis where green dots are  $Fe^{2+}$ , the blue dots are  $Fe^{3+}$  and the yellow dots are  $O^{2-}$ ; b) cobalt ferrite synthesis where the blue dots are  $Co^{2+}$ , the yellow dots are  $Fe^{3+}$  and the red dots are  $O^{2-}$ .

The optimization of the synthesis and purification procedures will be presented and discussed, in particular those parameters that allow to increase the production, keeping size and shape of the nanoparticles under control. The characterization will also be presented.

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### Materials

# Computational study of the selective separation of air constituents through graphene nanowindows

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Since its isolation in 2004<sup>1</sup>, graphene has been one of the most popular topics of research in the materials field. Graphene is a single atomic plane of graphite with peculiar characteristics, such as one-atom-thickness, robustness and chemical stability, which have already been explored for a wide range of applications<sup>2</sup>.

The usage of graphene sheets as a membrane for separation of gases or ions in solution was one of the first applications to be described in the literature, as their single-atom-thick wall can provide almost negligible resistance to permeation. Although pristine graphene and defective graphene are impermeable even to the smallest gas Helium<sup>3</sup>, it is possible to create holes in graphene sheets that allow the selective passage of water, ions and gases.

This project aims at studying molecular sieving properties of porous graphene, using density functional theory (DFT) calculations. The rim-chemistry of different functionalization of the nanowindows can alter the permeation rate of molecules through the graphene membrane. Another important aspect to study is the opening and closing of nanowindows due to different functionalization<sup>4</sup> and interactions with transient chemical species<sup>5</sup>.

Current work has been focused on building a suitable quantum computational methodology based on recent and accurate DFT functionals. Preliminary results with the atmosphere constituent Argon (**Figure 1**) have shown a good comparison to previous studies based on classical molecular dynamics (MD), in which a 2,73 Å wide nanowindow, functionalized with a hydroxyl and an ether group (*nwind\_modelb*), is able to permeate selectively N<sub>2</sub>/O<sub>2</sub>/Ar. Two stationary states, open- and closed-nanowindow, are observed with a difference in energy of  $\Delta E = 1,3 \text{ kJ mol}^{-1.4}$ .



Figure 1: Preliminary study of the permeation of Argon through nanowindow nwind\_modelb with 3 different optimization approaches.

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### Materials

# **Chiral Mesoporous Materials in Oxidation Catalysis**

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Catalysis is a core concept in chemistry, playing an important role in biological and industrial processes. Mesoporous materials are among the inorganic materials that have experienced a high development in recent years, owing to their applications in many fields, namely heterogeneous catalysis.<sup>1,2</sup> Nanoparticles represent an important alternative in the design of new materials and compounds for research in catalysis, as they can act either as (semi)heterogeneous catalysts or catalyst supports since they quickly disperse in common solvents.<sup>3</sup> Chiral porous materials have attracted much attention on account of their potential applications in many areas, such as enantio-separation, chiral catalysis, chemical sensors and drug delivery.<sup>4</sup> However chiral matrix mesoporous materials have been reported<sup>5</sup> but applications in catalysis are scarce. In this work synthesis of chiral matrix mesoporous materials was accomplished using ammonia as co-surfactant.<sup>2</sup> The prepared material retains the basic structure of the silicon-based matrices, but with a confined helical environment of the channels. Modification of the inner surface by reaction with catalytic metal nanoparticles was accomplished.



Scheme 1: Schematic representation of the synthetic pathway

On this work we have synthesized and characterized two new materials suitably modified as chiral materials for hosting metal nanoparticles. Catalytic applications of this composite material in oxidation catalytic processes of styrene, *trans*  $\beta$ -methylstyrene, 4-chlorostyrene and 4-methylstyrene have being fostered. They were tested three different solvents, dichloromethane, acetonitrile and toluene, two different temperatures (328 and 353K) and different amounts of added oxidant (150 and 200%). Mo is known for these relevant catalytic properties, as it is active in important catalytic reactions. The synthesized material has been characterized by means of suitable spectroscopic techniques (XRD, TGA, SEM, TEM, and FTIR). The performance of the obtained composite materials on oxidation catalysis was evaluated and the products (conversion and yield) were analyzed by gas chromatography-mass spectrometry (GC-MS). From the achieved results it is possible to say that the obtained conversion were from moderate to higher for the desired products, and in terms of selectivity it is possible to observe that were obtained better results for the desired products at lower temperature.

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### **Materials**

# Cobalt Oxide-based Nanomaterials as Heterogeneous Catalysts for the Reduction of Nitroarenes

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The reduction of nitroarenes is a key process as the products, aromatic amines are important intermediates in the synthesis of chemicals such as antioxidants, dyes, pigments, photographic, pharmaceutical and agricultural materials.<sup>1</sup> The reduction of nitroarenes using reducing metals such as zinc, tin and iron has been reported in presence of an acid or salts, but without sub-products in the end of the reaction.<sup>2,3</sup> A crucial issue for the general application of catalysts for nitro reduction is selectivity.

Heterogeneous catalysts to hitto reduction is selectivity. Heterogeneous catalysts demonstrate several advantages over homogeneous systems, such as easy recovery and recycling of the catalysts. Naturally, due to their high surface area, easy separation and reusability a variety of materials ranging from metal nanoparticles to bulk materials<sup>1</sup> are being researched as heterogeneous catalysts.

Co-oxide nanomaterials have been known as promising catalysts for use in the reduction of nitroaromatic compounds.<sup>4</sup> Oxide-based catalysts are generally synthesized through calcination at a high temperature of raw materials that are preliminarily prepared through various methods: solid state reaction, precipitation, solgel or hydrothermal. These treatments allow tuning the surface properties to attain promising catalysts, obtaining after the final step, new calcined metal oxides. To this end, three different temperatures of calcination and



Figure 1. TEM image of Co oxide-based nanomaterial

under two different atmospheres (N2 and air) have been used to prepare Co oxide-based catalysts.

The structure and surface of the prepared Co oxide-based materials were characterized by Powder X-Ray Diffraction (*p*XRD), Scanning Electronic Microscopy (SEM) and Transmission Electronic Microscopy (TEM). To study the catalytic reductions of different nitroarenes, the performance of these new Co oxide-based nanomaterials with different substrates has being conducted for *p*-nitrophenol, *p*-nitroanisole, *m*-nitrophenol, *p*-nitrotoluene, 1-chloro-*p*-nitrobenzene, *p*-nitroaniline and methyl-*p*-nitrobenzene.

All reactions were carried out with the substrate and the reducing agent – sodium borohydride (NaBH<sub>4</sub>) in the presence of the catalyst. As will be discussed the methodology followed proved to be a good strategy since the use of the Co-Oxide nanomaterials leads to 100% conversion and selectivity after 5 min in several tested substrates. Results show that only the catalysts or the reducer were used any catalytic activity towards the amine compounds was obtained.

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### **Materials**

# **Enhanced Proton Conductivity in Layered Coordination Polymers**

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Research on Metal-Organic Frameworks (MOFs) and Coordination Polymers (CPs) is currently driven towards the need to employ such materials in technological areas. Our research group has focused on the design of novel networks based on polyphosphonic acid ligands and rare-earth cations. With these building units we obtained highly robust dense networks exhibiting, in many cases, multifunctionality (e.g., photoluminescence combined with catalytic activity). In this work we describe our most recent efforts to design and prepare novel crystalline layered CP materials based on gadolinium metal centres and the flexible triphosphonic acid nitrilotri(methylphosphonic acid) (H6nmp). Two new obtained by employing small changes in the experimental conditions, namely materials were  $[Gd(H_4nmp)(H_2O)_2]Cl 2H_2O$  (1)<sup>1</sup> and  $[Gd_2(H_3nmp)_2] \cdot xH_2O$  (x = 1 to 4) (2). Interestingly, 1 converts into 2 with a notable increase in protonic conductivity (Figure 1). 1 is a charged layered material counter balanced by chloride ions, with the protonic conductivity values of 1.23×10<sup>-5</sup> S cm<sup>-1</sup> at 98% RH at 40 °C. At 98% RH and 94 °C 1 exhibits a conductivity of 0.51 S cm<sup>-1</sup>, being to date the highest one ever reported for a proton-conducting MOF. This increase is observed during a structural transformation into 2, that occurs at high temperature and RH. While this remarkable conductivity is observed only after transformation and by maintaining the high humidity conditions, as-synthesized 2 also shows conductivity values of 3.79×10<sup>-2</sup> Scm<sup>-1</sup> at 94 °C and 98% RH, ranked as one of the highest reported for MOFs.<sup>2</sup>



Figure 1 - Schematic representation of the structural transformation of  $[Gd(H_4nmp)(H_2O)_2]Cl\cdot 2H_2O$  (1, *left*) into  $[Gd_2(H_3nmp)_2]\cdot xH_2O$ (2, *right*) (x = 1 to 4) at high temperature and humidity.

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### **Materials**

# Chalcone/Sulfocalix[4]arene-Based Supramolecular Amphiphiles for Light-Controlled Drug Delivery

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Encapsulation of pharmaceutical compounds in drug delivery vehicles provides a viable strategy to enhance bioavailability by improving factors such as solubility, stability, toxicity, ability to cross membranes, etc. In addition, the controlled release of cargo drugs in their active form is of crucial importance to increase efficiency and reduce toxicity.<sup>1</sup>

Supramolecular amphiphiles, i.e., amphiphilic species that upon interaction with a host molecule forms a supramolecular complex which promotes self-assembly into aggregates of nanometric dimensions such as micelles and vesicles, show great promise as drug delivery vehicles.<sup>2</sup> The dynamic and reversible nature of the noncovalent interactions endows the resultant aggregates with excellent stimuli-responsive features.

In this work we have synthetized an amphiphilic trans-chalcone that was shown to form complexes with psulfonatocalix[4]arene. The host-guest complexation promotes self-assembly into nanoaggregates which dissociate upon light exposure as a result of flavylium formation.



Scheme 1: Supramolecular amphiphile assembly and disassembly.

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### Materials

# **Multifunctional Breathing Metal-Organic Frameworks**

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Studies on solid-state matter are intimately associated with the innate rigidity of compounds. These "traditional" concepts have recently been challenged with the rise of porous coordination polymers (PCPs) or Metal-Organic Frameworks (MOFs) and their intrinsic properties. Dynamic structural transformations of MOFs triggered by external stimuli, are some of the examples that have recently received particular interest, mainly because they retain the same topology than those of more rigid structures and, at the same time, show important flexibility.

This communication reports our recent findings in phosphonate yttrium-based Metal-Organic Frameworks (MOFs), [Y(H₅btp)]·2.5H<sub>2</sub>O (**2**), formulated as [Y(H₅btp)]·5.5H<sub>2</sub>O (1),  $(H_3O)[Y_2(H_5btp)(H_4btp)] \cdot H_2O$ (3) and [Y(H<sub>5</sub>btp)]·H<sub>2</sub>O·0.5(MeOH) (4), which were prepared using a "green" microwave-assisted synthesis methodology to promote the self-assembly of the tetraphosphonic organic linker [1,1'-biphenyl]-3,3',5,5'-tetrayltetrakis(phosphonic acid) (H<sub>8</sub>btp) with Y<sup>3+</sup> cations. This new family of functional materials, isolated in bulk quantities, exhibits a remarkable breathing effect. Structural flexibility was studied by means of X-ray crystallography, thermogravimetry, variabletemperature X-ray diffraction and dehydration and rehydration processes, ultimately evidencing a remarkable reversible Single-Crystal to Single-Crystal (SC-SC) transformation solely through the loss and gain of crystallization solvent molecules. Porous materials 2 and 3 were further studied to ascertain their performance as heterogeneous catalysts and proton conductors, respectively, with outstanding results being registered for both materials. Compound 2 showed a 94% conversion of benzaldehyde into (dimethoxymethyl)benzene after just 1h of reaction. The protonic conductivity of 3 at 98% of relative humidity (2.58×10<sup>-2</sup> Scm<sup>-1</sup>) was among the highest registered among MOFs, with the great advantage of the material to be prepared using a simpler and sustainable synthesis methodology.



I wish to give a personal and heartfelt "thank you" to all the collaborators and students involved in the research in my group over the past years. All contributed immensely with work and discussions to the great body of results. This body of work was developed within the scope of the project CICECO-Aveiro Institute of Materials, FCT Ref. UID/CTM/50011/2019, financed by national funds through the FCT/MCTES and when appropriate co-financed by FEDER under the PT2020 Partnership Agreement. Fundação para a Ciência e a Tecnologia (FCT, Portugal) is also gratefully acknowledged for funding this research and dissemination of the results.

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The presentation will be mainly based on the following publications from our research group:

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### Materials

# Development and characterization of low-cost adsorbent materials from wastes of biodiesel production

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Biodiesel industry generates huge amounts of residues/byproducts (dry and wet) for which there is not yet sustainable and fully valorization. Considering the large volumes of glycerol coming from biodiesel production, it is imperious to find new applications for this chemical.<sup>1</sup> In the present work, glycerol-based carbons were prepared by a two-step procedure: carbonization with sulfuric acid, adapting the procedure described in literature,<sup>2</sup> followed by chemical or thermal activation. The study is part of a larger project aiming the valorization of residues from biodiesel production in a previous study.<sup>3</sup> Both activation methods resulted to a considerable generation of porosity in the obtained materials. What can be undertaken from the analysis of the textural parameters is that chemical and thermal activation of glycerol-based *Chars* produced the material with the most developed microporous network.

Highly microporous materials with apparent surface area around 2000 m<sup>2</sup> g<sup>-1</sup> were obtained. Regardless the temperature used, thermal activation promoted a smaller porosity development, composed practically only by micropores. Different temperatures do not have significant effect on the *apparent area*. SEM micrographs show that the materials are constituted by interconnected spheres with diameters of  $\approx$  1-2 µm. The FTIR and pH<sub>PZC</sub> data reveal the acidic nature of the surface functional groups, which is in line with the high amounts of sulfur and oxygen detected in the elemental analysis.



Figure 1: Adsorption-desorption isotherms and SEM of the glycerol-based-carbons.

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### Materials

# Storage and delivery of biologically active H<sub>2</sub>S by microporous zeolites and titanosilicates

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In the present work, microporous zeolites (4A and Y) and titanosilicates (ETS-4 and ETS-10) have been studied for the adsorption and therapeutical release of hydrogen sulfide ( $H_2S$ ). Results of  $H_2S$  adsorption isotherms in the materials are presented in the Figure 1.

H<sub>2</sub>S used to be considered as a toxic molecule<sup>1</sup> but, in 2005, a paper in Science drew attention to its beneficial physiological effects, showing that H<sub>2</sub>S can induce a state of hibernation in rats<sup>2</sup>. Recently, the anti-inflammatory properties of H<sub>2</sub>S have also been highlighted<sup>3</sup>. H<sub>2</sub>S exogenous donor systems are still at the experimental stage and mainly involve NaHS. Given its high toxicity, H<sub>2</sub>S concentration has to be maintained in a very narrow concentration range<sup>4</sup>. To date, there are only a few studies addressed the subject of H<sub>2</sub>S storage in porous materials for therapeutic purposes<sup>5</sup>, so, much work remains to be done.

To be used in drug delivery, a material must be biocompatible. Because biocompatibility is an essential feature of any drug-delivery material, the cytotoxicity of these materials was also evaluated.



Figure 1: H<sub>2</sub>S adsorption isotherms at 25 °C on microporous materials.

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### **Materials**

# A DFT study on SWCNT End-Functionalization: Intramolecular Hydrogen Bonds as a Molecular Gate

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Since their discovery, carbon nanotubes and other related nanomaterials are on the spotlight due to their unique molecular structures and properties<sup>1</sup>. The cage like structure of carbon nanotubes is especially appealing as a route to isolate drug molecules until they reach a specific cellular target where they can be delivered<sup>2</sup>. In this sense, many studies have been published concerning the topic of carbon nanotube cellular toxicity, indicating that in certain conditions the nanomaterials present very little risks, and thus suitable to the drug delivery scope<sup>3</sup>.

Accordingly, this project aims to explore a novel covalent end-functionalization of single-walled carbon nanotubes (SWCNTs) through density functional theory (DFT) calculations. It is proposed that the end-functionalization with a carboxylic acid derivative establishes a pH sensible molecular gate, considering intramolecular hydrogen bonds between the introduced functions which prevent diffusion of molecules from inside the SWCNT to the surrounding medium. The pH sensibility of the molecular gate arises from repulsion between deprotonated functions, leading to a conformational change upon deprotonation. Furthermore, the protonated functions are also predicted to oscillate between closed and open conformations, however, is it reasonable to assume that the closed state is preferred (**Scheme 1**). Preliminary results for the conformational transition in the gas phase show energetic differences of -12.10, -17.36 and -18.10 kcal-mol<sup>-1</sup> for the (8,0), (9,0) and (10,0) systems, respectively.



Scheme or Figure 1: Representation of a) a functionalized fragment; b) (8,0) system in closed conformation; c) (9,0) system in closed conformation;

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### **Materials**

# **New Optical Sensors for Boron Detection**

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Boron can be beneficial to human health and agriculture in trace quantities, but becomes toxic to both humans and crops in excessive quantities.<sup>1</sup> Boron compounds are used in many industrial applications, including the fabrication of soaps and detergents, glass and ceramics, insecticides, fertilizers, semiconductors, flame retardants, high duress compounds, and pharmaceutical drugs. High boron contents in water might be the result of residual waters discharges or leaching from rocks and soils containing borates and borosilicates.<sup>1</sup>

Following our previous results using polyaromatic vicinal diols (based on 2,3,6,7,10,11-Hexahydroxytriphenylene) as boron sensor,<sup>2,3,4</sup> in this work we have tested some fluorescent natural compounds bearing aromatic vicinal diols for their suitability as optical sensors for the detection of boron, in the forms of boric acid and phenylboronic acid, in aqueous media (Figure 1).

We have checked the fluorescence and UV-vis absorption of the compounds in the absence and presence of boron (phenylboronic acid or boric acid) at several pH values in order to find the optimal pH range for boron sensing for each sensor, and then we determined other characteristics such as the limits of detection or the interference of other species.



Figure 1: Natural compounds studied here as possible boron sensors.

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### Materials

# Synthesis and characterization of rGO/M 2wt%-N co-doped (M=Co, Fe, Mn, Ni, Cu and Rh) as abiotic electrocatalyst for oxygen reduction reaction

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The development of new and non-precious metal electrocatalyst based on transition metals for the oxygen reduction reaction (ORR) is the key to promoting the improvement of the energy conversion technologies such as fuel cells. The design of such catalysts requires active catalytic sites and a homogeneous and extensive dispersion of these centers over an accessible surface area [1]. Single-atom catalysts have become a new research hotspot in the field of heterogeneous catalysis due to the maximization of exposure of the atom [2]. However, the stabilization of the active structure of metal centers cannot be achieved during the catalytic reaction due to aggregation and migration of the metal atoms. Therefore, the immobilization of single-atom on a carbon matrix is essential to get a sustainable electroactivity of the material.

Hereby, we report a novel, low-cost and simple strategy for the synthesis of a 2 wt% metal catalyst supported in nitrogen-reduced graphene oxide (M 2%/rGO, M = Co, Fe, Mn, Ni, Cu and Rh) for the ORR, showing new insights on the co-doping of carbon materials. The synthesis of the catalyst was achieved by the extra exfoliation of commercial graphene, followed by the oxidation and insertion of the metal in the porous network. A serial of physical characterization of the catalysts strongly suggest the presence of the metal on the structure and its electroactivity towards ORR is evaluated by linear sweep voltammetry with a rotating disc electrode in neutral solution. Among the synthesized catalysts, iron and cobalt doped rGO catalysts exhibits the highest electrocatalytic activity with the highest onset potential, showing comparable activity to the commercial Pt nanoparticles catalysts in neutral media. The present work provides new strategies to synthesize non-precious metal catalysts for ORR that can be employed to design cathodes used in fuel cells as power supplies for implantable medical devices.



Figure 1: Oxygen reduction reaction in the presence of Fe 2% / rGO and Co 2% / rGO; Comparative LSV with rGO and Pt nanoparticles (PBS pH 7.4).

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### Materials

# **Bio-MOFs for Osteoporosis: how to prepare them?**

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Bio-Metal-Organic Frameworks (bio-MOFs) are highly ordered systems constructed from metallic centres in coordination with organic linkers, being that at least one but preferably both building blocks present intrinsic therapeutic properties. In this way, these infinite networks can combine the pharmaceutical efficiency of distinct components used as part of the network itself, allowing the delivery of large quantities of drugs.<sup>1</sup> The present work focuses on the development of new bio-MOFs for the treatment of osteoporosis, a disease with a significant impact on today's society. The networks are designed to combine both (i) the anti-osteoporotic properties of a well-known bisphosphonate drug (alendronate, used as organic linker); with (ii) the beneficial effects of calcium ions (used as metallic centres).

Hydrothermal synthesis conditions were used to prepare two distinct bio-MOFs: (i)  $[Ca(H_3alen)]$ ·H<sub>2</sub>O and (ii)  $[Ca(H_4alen)_2]$ . Upon an extensive characterization – by X-ray diffraction (SCXRD and PXRD), NMR, FT-IR, electron microscopy (SEM and EDS), thermogravimetric and elemental analyses – it was noticeable that, despite having practically the same composition, the bio-MOFs have distinct crystalline structures (Figure 1). When envisioning future applications, these structural differences may be of great importance because they can induce distinct biological outcomes regardless the almost equal composition.<sup>2</sup>



Figure 1: Structural representation of (i) [Ca(H<sub>3</sub>alen)]·H<sub>2</sub>O and (ii) [Ca(H<sub>4</sub>alen)<sub>2</sub>] bio-MOFs.

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### Materials

# Sustainable inorganic materials for Luminescent Solar Concentrator applications

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Luminescent solar concentrators (LSC) appear as a new technology that promises to achieve the goal of transforming conventional energy-passive glazing systems into semi-transparent photovoltaic (PV) Windows.<sup>1</sup> LSC consist in a material doped with a fluorophore that down-converts solar light through luminescence which is waveguide-propagated to the window edges where it may be converted into electricity by PV devices.<sup>2</sup>

Towards this goal, environmental-friendly transparent glasses with high photoluminescence yield and high Stokes shifts have received special attention due to their stability and luminescent optical properties.<sup>3</sup> In this work aluminoborosilicate and borosilicate glasses are used as matrix for luminescent centers such as copper, tin and manganese (Fig.1). The glasses were tested with organic PV solar cells under a simulated sunlight irradiation. In all cases it was verified an increase of the open-circuit voltage (Voc) and short-circuit current density (Jsc) coupled with an increase of efficiency compared with the blank (without glass).



Figure 1: Samples under a UV light (364 nm). Glasses doped with different emissive centers: tin, copper, europium and manganese (from left to right).

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### **Materials**

# Carbon Nanomaterials from Coffee Grounds of Vending Machines: Synthesis and Characterization

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Carbon nanomaterials have a unique place in nanoscience owing to their exceptional electronic, mechanical, thermal, optical and chemical properties, and have found application in several areas as composite materials, materials for energy storage and conversion, sensors, biological labelling, drug delivery and nanoscale electronic components.<sup>1-5</sup> Coffee is one of the most valuable products in the world trade, and is also part of our culture. However, coffee production and later use generates huge amounts of coffee wastes and by-products, such as coffee grounds,<sup>6</sup> which prompts for their possible valorisation.

In this context, we herein report the synthesis of luminescent coffee-carbon nanomaterials (Coffee-CNMs) derived from the coffee grounds of vending machines by a one-step hydrothermal process, where the effects of temperature and additives on the luminescence properties of Coffee-CNMs were determined. In addition, the proximate analysis (total phenols, flavonoids, tannins, carbohydrates, proteins, lipids and ashes) of coffee grounds was conducted.

The structural features of Coffee-CNMs were studied by FTIR and <sup>1</sup>H/<sup>1</sup>3C NMR and their photophysical properties investigated by means of steady- and time-resolved fluorescence and ground-state absorption.

The Coffee-CNMs exhibit blue-green fluorescence ( $\lambda_{em max} = 462$  nm upon excitation at 380 nm), a remarkable photostability and a broad pH useful working range, prospectively pointing to their use in several applications.



Figure 1: (a) Coffee tree; (b) Coffee beans; (c) Coffee; (d) Coffee Grounds; (e) Aqueous dispersions of Coffee-CNMs (0.1 mgmL<sup>-1</sup>) under daylight (e1) and UV light (366 nm; e2) illumination.

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### **Materials**

# Reversibly bonded nanoparticles for self-healing coating materials

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Water-borne polymer nanoparticles have proven their value as nanomaterials for coating applications with reduced environmental impact and mechanical high-performance. [1,2] On the other hand, synthetic self-healing materials are a class of new emerging smart materials with the ability to self-repair physical damage. [3,4]. Here, we combine both approaches by developing water dispersions of polymer nanoparticles that form films by polymer diffusion and dynamic covalent chemistry. The low glass transition temperature of poly(butyl methacrylate) (PBMA) provides high mobility of the macromolecules and allow simultaneous actuation of reversible imine crosslinking. [4] The mobility of the polymer chains during film formation depends on the temperature, chain length and degree of cross-linking, and can be assessed by fluorescence methods. [5]

We developed aqueous dispersions of monodisperse polymer nanoparticles, either functionalized with aldehyde or with amine groups (Figure 1). In films cast from a mixture of both dispersions, interdiffusion of the polymer chains promotes the contact between the two functional groups (aldehyde/amine), originating the crosslinking reaction. The imine bond is reversible in the presence of water, allowing the healing of damage to the films.



Figure 1: Reversible crosslinking: imine bond formation.

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### **Materials**

# Green Technology on Development of Smart Materials for Biosensing

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The demand and production of biological products are increasing,<sup>1</sup> with a consequent intensification of the separation and purification processes involved.<sup>2</sup> Typical technologies for purification of biomolecules are based on chromatography using resins or silica. Nevertheless, these technologies are very expensive, and in some cases, cannot achieve high efficiency and have no specificity.<sup>3</sup>

Affinity materials have been developed taking advantage of the combination of Molecular Imprinting technique with supercritical fluid technology. CO<sub>2</sub> is abundant, easily available in high purity, non-toxic, non-flammable and very accessible critical temperature and pressure.<sup>4</sup>

Supercritical carbon dioxide (scCO<sub>2</sub>) has been used as solvent and porogenic agent in the development of high affinity materials for several applications, such as purification of Active Pharmaceutical Ingredients (API), removal of contaminants from water, and on-off sensors,<sup>5</sup> typically small contaminants and drugs.

Herein, synthetic smart affinity polymers were developed for the first time towards a biomolecule using this green technology. Polymers were obtained as dry, free flowing powders (**Fig. 1**). The preliminary binding results are quite promising, revealing a very attractive, fast and cheap way to obtain quite sensitive biosensor for a wide range of applications.



Figure 1: High-pressure reactor with the developed polymer inside.

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## Materials

# Synthesis, structural and physical-chemical characterization of blue pyranoflavyliums-4-(dimethylamino)-cinnamyl dyes

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The aim of this work was to synthetize blue pyranoflavyliums dyes (Figure 1) from the reaction of 2-(4´-dimethylamino)-5,7-dihydroxybenzopyrylium and 2-(4´-dimethylaminostyryl)-5,7-dihydroxybenzopyrylium with 4-(dimethylamino)cinnamic acid.

These dyes are very interesting from the technological point of view since they present stable chromatic features comparing with their precursors and display a blue colour ( $\Box$ max>600 nm). The structure of the pyranoflavylium dyes was confirmed by ESI-MS analysis and NMR (1H, 13C, HMBC, HSQC, gCOSY and NOESY). Their respective kinetic and thermodynamic constants were studied by UV-Vis.



Figure 1: Structure of the blue pyranoflavyliums-4-(dimethylamino)-cinnamyl synthesized.

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## **Materials**

# Development of collagen nanoparticles for cartilage regeneration

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Human articular cartilage is an avascular structure, which, when injured, presents significant hurdles to repair. Many cartilage repair methods have been developed so far, however, many of them are very invasive and do not bring a long-term solution. The use of nanotechnology and tissue engineering in cartilage regeneration has been shown to be very promising for the treatment of cartilage diseases.<sup>1</sup> Compounds from marine resources have been studied as raw materials for the construction of drug delivery systems for biomedical applications and tissue engineering due to several properties, such as biocompatibility, biodegradability and specific capacity to target and mimic human natural tissues.<sup>2</sup>

In this work, collagen from marine resources (jellyfish and blue shark) was used to produce nanodelivery systems for the incorporation of growth factors (GFs) for cartilage regeneration. Type II collagen forms the cartilage structure and its destructions is a primary factor in promoting cartilage regeneration, whereas GFs, such as insulin-1 growth factor (IGF-1), transforming growth factor- $\beta$  (TGF- $\beta$ ) and basic fibroblast growth factor (bFGF) are known to promote chondrogenesis, but have short half-lives *in vivo* and are rapidly degraded.<sup>3</sup> Therefore, the encapsulation of GFs in collagen nanoparticles is proposed in order to prevent degradation and allow a controlled release for cartilage regeneration.

Collagen nanoparticles were produced by two methods in order to optimize their size range. The optimized results have shown that nanoparticles obtained using jellyfish collagen had a size around 300 nm, while the nanoparticles using blue shark collagen reached almost 600 nm. The same occurs with the polydispersity index, were the jellyfish collagen nanoparticles had lower values, between 0.2 and 0.3, and blue shark collagen nanoparticles presented higher values, between 0.5 and 0.6. Jellyfish collagen nanoparticles also had slightly more negative charge than blue shark collagen nanoparticles (around -40 mV), which enables a repulsive effect between nanoparticles, avoiding their aggregation and granting a higher stability in aqueous dispersions. Through transmission electron microscopy one could confirm that the jellyfish collagen nanoparticles maintained the triple helix conformation of collagen and revealed images of nanoparticles with a similar size range as the above reported values obtained by dynamic light scattering.

In the future, the nanosystems will be tested for their ability to incorporate GFs and their therapeutic efficacy for proliferation and differentiation of cells, prior to the use in 3D matrices.

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## **Materials**

# Application of evolutionary algorithms to aid in the design of materials

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Evolutionary algorithms (EAs) are state-of-the-art methods, especially devoted to perform global geometry optimization in chemistry, that can be employed to obtain fundamental insight about the structure of matter either at the molecular level or at the mesoscale. EAs fall in the class of bio-inspired algorithms, in the sense they are based in principles usually associated to the evolution of living beings. Thus, each structure that belongs to the possible set of solutions of the global optimization problem (i.e., the population) may be subjected to crossover and mutation (i.e., the genetic operators). In particular, the EAs developed by our group<sup>1</sup> follow a steady-state strategy, where the number of structures is kept constant during the optimization process and, in each generation, new solutions resulting from the application of genetic operators have to compete with their "parents" to enter in the population. The whole process is repeated for several generations, which leads, in principle, to an effective exploration of the searching space. In this communication, we overview the main applications of EAs carried out in our group for more than ten years and perpective their use in acquiring information about self-assembly processes, which is relevant for designing novel materials. Specifically, we present the most stable structures of 2D and 3D colloidal clusters<sup>2</sup> as well as of aggregates involving coronene molecules;<sup>3</sup> examples of such systems are shown in Figure 1. From these results, it is particularly interesting to identify the relationship between the structure and the corresponding interaction potential, which may be useful to best tune the conditions to obtain a specific material.



Figure 1: Low-energy clusters of 2D oppositely-charged (a) and 3D positively-charged colloidal particles, and coronene (c).

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## Materials

# Laponite<sup>®</sup>-based nanogels for the treatment of osteoporosis

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Osteoporosis is a skeletal disease that affects millions of people worldwide, defined by lower bone density and, consequently, higher vulnerability to fractures, often associated with high treatment costs that are expected to rise in the next decades, as the prevalence of elders in the population increases.

Bisphosphonates, such as alendronate, are the most prescribed drugs to treat this illness, for their effectiveness in the various types of osteoporosis, and inexpensiveness, though they present low gastrointestinal absorption and bioavailability, complex dosage regimens and adverse side effects that often discourage patients from properly following the treatment.<sup>1</sup>

Laponite<sup>®</sup> is a synthetic clay used to protect drugs against degradation in the physiological environment, having been shown to induce osteogenic differentiation, thus being a promising compound for bone-targeted drug delivery systems.<sup>2</sup>

To overcome the disadvantages exhibited by alendronate, Laponite<sup>®</sup>-based nanogels loaded with alendronate are proposed as a new drug delivery system for the treatment of osteoporosis by reducing osteoclast activity, through alendronate, while also promoting osteoblastic activity, through Laponite<sup>®</sup>.

The formed nanogels were round, negatively-charged and had roughly 180 nm in diameter as revealed by Dynamic Light Scattering (DLS) analysis. Transmission electron microscopy images of the systems were consistent with DLS studies. Both the effects of freezing/thawing and lyophilization on nanogel size were evaluated. Alendronate incorporation efficiency was high as determined by both <sup>31</sup>P NMR and UV-Vis spectroscopy after a derivatization reaction. Furthermore, nanogels' swelling properties and biodegradability behavior was also studied.

The developed Laponite<sup>®</sup>-based nanogels protected the cells when comparing with the use of alendronate alone, leading to low cytotoxicity and no hemotoxicity. They were also effective on the differentiation of human mesenchymal stem cells into osteoblasts. Cell culture experiments showed that the nanogels were able of inducing *in vitro* bone formation, as assessed by alkaline phosphatase activity, osteocalcin and histochemical staining of mineral deposits.

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## **Materials**

# **MoO<sub>3</sub> Nanomaterials as Versatile Oxidation Catalysts**

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Metal- and metal-oxide-containing nanostructures with different morphologies (nanowires, nanobelts, nanofibers, etc) are known to exhibit better tunable properties in fields such as gas sensors, electrodes or optoelectronics than their conventional macro-sized counterparts.<sup>1</sup> In this context,  $MoO_3$  nanoparticles have attracted a great deal of attention due to their unique physical and chemical properties, which differ from those in the bulk, especially in what concerns their high surface-to-volume ratio.<sup>2</sup>



Figure 1. TEM (a) and SEM (b) images of  $MoO_3$  synthesized nanoparticles.

MoO<sub>3</sub> nanoparticles can be synthesized by different methods, being the hydrothermal synthesis the most popular one. This is a low temperature process which yields various nanostructures with controlled size, stoichiometry and shape.<sup>3</sup> In this work we report the preparation of  $\alpha$ -MoO<sub>3</sub> nanoparticles with an average size below 100 nm by solvothermal synthesis of MoO<sub>2</sub> nano-crystalline particles and subsequent thermal oxidative annealing.<sup>4</sup> The MoO<sub>3</sub> nanoparticles were used as catalysts and revealed to be very active in olefin epoxidation and sulphide oxidation<sup>5</sup> using *tert*-butylhydroperoxide (tbhp) or hydrogen peroxide as oxygen source. Catalytic tests show that the catalyst leads to the desired products with high selectivity. The catalyst performance was quite good under a wide temperature range, different solvents and oxidants. It is also possible to conclude that the H<sub>2</sub>O<sub>2</sub> was used as oxidant and yielded promising results, which will be further explored. In addition, this catalyst has the advantage of being prepared via a simple synthetic procedure.

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## Materials

# Preparation and characterization of optical sensors based on biopolymers

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The purpose of the present work is the use of components extracted from waste or by-products of the fishing industry, namely biopolymers, in order to exploit its potential for the application in the synthesis of membranes for use as optical sensors of heavy metals.

The synthesis of these membranes began with some previously published procedures and its subsequent adaptation to the intended purpose at hand<sup>1,2</sup>. Some innovative syntheses have been developed, that successfully combine different biopolymers, namely chitosan, fucoidan and chondroitin sulfate, which possess varying degrees of metal retention ability and siloxane. The structural fragilities of the resulting membranes were studied, and by using glycerol as a plasticizer and glutaraldehyde as a crosslinking agent, it was possible to improve the malleability and swelling degree. Since the aim of this study is to obtain an optical sensor primarily for the determination of the Pb<sup>2+</sup>, the incorporation of a chromophore sensitive to this cation was performed, namely dithizone (Figure 1). Due to the flexible chemical structures of these biopolymers, it was possible to use the molecular imprinting of Pb<sup>2+</sup> with the intuit to improve membrane selectivity and capacity for this species, something that is still scarcely explored in the literature, having only been published to date an article about molecular imprinting of metal cations in biopolymer membranes<sup>3</sup>. The synthesized membranes were later characterized using different techniques such as FTIR, TGA, BET and UV-Vis. For a deeper insight into the sorption properties of the membranes for lead cation, as well as their starting materials, batch biosorption studies were performed for an array of concentrations. Initially, the different constituting biopolymers were separately studied in aqueous form through dialysis membranes. The resulting solutions of these studies were analyzed by atomic absorption spectroscopy.

In the future, it is intended to determine the detection limit of the various membranes to lead in aqueous solution, as well as whether the effect of imprinting reduces membrane interaction with interfering species. If possible, the affinity of the synthetized membranes could also be tested for the cadmium cation in solution.



Figure 1: Study of the incorporation of dithizone and effect of Pb2 + on the membrane through UV-Vis spectrometry

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## Materials

# pBMP-2 delivery using chitosan/hydroxyapatite nanoparticles for osteoporosis treatment

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Nanotechnology is a promising area of research that allows gene delivery without compromising cell integrity and viability.<sup>1</sup> Having in their composition a wide variety of compounds, like those derived from marine resources, nanomaterials may be a very interesting biomedical tool. Indeed, marine compounds can be easily used and may have valuable properties like biocompatibility, biodegradability, malleability, anti-inflammatory and antimicrobial actions, which can be useful for several diseases, such as osteoporosis.<sup>2</sup> As an approach for osteoporosis treatment, nanoparticles made of chitosan (CHI) combined with hydroxyapatite (HA) were developed for the delivery of the BMP-2 (Bone Morphogenetic Protein-2) gene into human mesenchymal stem cells (hMSCs) aiming at their osteogenic differentiation and induction of bone formation.

The prepared hybrid nanomaterials (CHI/HA) were combined with a plasmid DNA encoding BMP-2 (pBMP2) to obtain nanoplexes. As assessed by Dynamic Light Scattering, agarose gel electrophoresis, zeta potential measurements and Picogreen<sup>®</sup> intercalation assay, these nanomaterials had a good capacity to neutralize and condense pDNA, giving rise to nanoplexes with a hydrodynamic diameter around 200 nm. The cytocompatibility of the nanoplexes was very good when evaluated *in vitro* using hMSC cells and a metabolic activity assay (resazurin reduction assay). Transfection efficiency was studied by measuring BMP-2 expression. Osteogenic differentiation studies on the transfected cells were performed by measuring early (alkaline phosphatase activity) and late (osteocalcin expression) markers of osteogenesis, as well as by the formation of calcium and phosphate deposits in culture.

Overall, the results have shown that the developed nanomaterial considerable enhances the level of transfection achieved by the pBMP-2, enhancing stem cells differentiation into osteoblasts and bone formation *in vitro*. These preliminary results demonstrate effective outcomes from the CHI/HA nanohybrid as a gene delivery vehicle for the treatment of osteoporosis.

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## **Materials**

# **Diastereomeric Resolution of Inherently Chiral Calix**[4]arenes

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Calix[4]arenes are among the most well-known cyclic oligomers<sup>1</sup> which, owing to their well-preorganized bowl-shaped intramolecular cavities and easiness of functionalization at their upper and lower rims, are particularly suited for hostguest chemistry namely as artificial receptors toward neutral and ionic molecular species, including optically active amines.<sup>2</sup>

Several different approaches have been developed in the past toward the synthesis of inherently chiral calixarenes (ICCs).<sup>3</sup> Recently we have disclosed a synthetic route for a new type of luminescent ICCs whose chirality stems from the existence of a chirality plane in the quinol moiety of the oxacyclophane ring.<sup>4,5</sup> Albeit the optical resolution of the racemic ICCs by chiral HPLC has been achieved, some practical limitations were found in this method since only tiny amounts of the enantiopure ICCs were obtained, severely limiting their use as enantioselective sensors or chiral selectors. In order to overcome such an issue, we turned our efforts to an indirect resolution method *viz*. separation of diastereomers formed upon reaction with a chiral auxiliary followed by conventional chromatography (flash column, PTLC, or HPLC with non-chiral phases) and removal of chiral auxiliary. Hence, following our previous route to this class of ICCs (*e.g.* **CALIX-OCP-CBZ-CSs**) were carried out. One of such involve the covalent attachment of (1*S*)-10camphorsulphonyl chloride (**CSC**) to the calixarene skeleton (**Scheme 1**). The reaction proved difficult to accomplish probably due to the high steric hindrance around the phenolic group. The same reaction was also attempted with less bulky compounds (distal dipropyl and dibenzyl derivatives of calix[4]arene tetraol) with better results. In this contribution, synthetic details as well as the NMR and electronic circular dichroism (ECD) of isolated diastereomers and chiral mono/disubstituted calixarenes obtained from achiral calixarenes will be presented and discussed.



Scheme 1: Synthesis and Optical Resolution of ICCs.

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## Materials

# Silica Polymer Nanoparticles for pH-activated controlled release

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Implementation of Controlled-Release Systems (CRSs) requires the use of materials that are susceptible to specific physical/chemical stimuli and a vehicle to prevent premature interactions between the environment and the loaded cargo<sup>1,2</sup>. Among a variety of inorganic-based nanomaterials, mesoporous silica particles (MSNs) have several attractive features for application as a delivery system, due to their high specific surface areas, large pore volumes, high mechanical stability, and a great diversity of surface functionalization options<sup>3,4</sup>. We developed novel hybrid MSNs composed of a mesoporous silica nanostructure core and a pH-responsive polymer shell<sup>5</sup>. The polymer shell was prepared by RAFT polymerization of 2-(diisopropylamino)ethyl methacrylate (DPAEM) (pKa ~6.5), using a hybrid grafting approach. The nanoparticles have diameters of ca. 100 nm at pH < 6.5 and ca. 60 nm at pH > 6.5. An excellent control of cargo release is achieved by the combined effect of electrostatic interaction of the cargo with the charged silica and the extended cationic polymer chains at low pH, and the reduction of electrostatic attraction with a simultaneous collapse of the polymer chains to a globular conformation at higher pH (Figure 1). The system presents a very low (almost null) release rate at acidic pH values and a large release rate at basic pH, resulting from the squeezing-out effect of the coil-to-globule transition in the polymer shell.



Figure 1: Representative scheme of the behaviour of SRB-loaded MSN-pDPA.

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## Materials

# Synthesis of Chol-Dox conjugates and self-assembly with TPGS into Prodrug-based Nanomaterials for Combinatorial Tumor Chemotherapy

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Covalent conjugation of drug molecules to natural-based lipids through functional chemical linkages are referred as lipid-drug conjugates (LDCs). These conjugates have demonstrated diverse advantages such as improved stability, reduced toxicity, tumor targeting and enhanced drug loading capacities.<sup>1</sup> In this work, a novel LDC was firstly prepared by covalently conjugating cholesterol with Doxorubicin (Chol-Dox), which was self-assembled with tocopherol polyethylene glycol 1000 succinate (TPGS) using thin-film hydration method to prepare a prodrug-based drug delivery nanosystem (Figure 1, left) <sup>2</sup>. The Chol-Dox/TPGS assemblies (molar ratio 2:1, 1:1 and 1:2) were able to form nanoscale particles with average hydrodynamic particle diameter from 100 to 200 nm, surface zeta potential of -20.6 to -0.4 mV, and remarkable solution stability (30 days). Notably, the uptake and cytotoxicity of the nanoassemblies in cancer cells could be adjusted by changing the molar ratio of Chol-Dox and TPGS. Moreover, the optimized Chol-Dox/TPGS assemblies (1:2) showed remarkable proliferation inhibition properties in two breast tumor cell lines: MCF-7 and MDA-MB-231 (Figure 1, right). The results demonstrated that the Chol-Dox/TPGS assemblies can be employed as promising candidates for prodrug-based nanomaterials for combinatorial<sup>3</sup> tumor chemotherapy.



Figure 1: left: self-assembly of Chol-Dox and TPGS to form Chol-Dox/TPGS prodrug-based nanoassemblies in aqueous solution; right: their enhanced tumor proliferation inhibition properties in MCF-7 and MDA-MB-231 cells.

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## **Materials**

# Design of effective carbon nitride supports for selective photocatalytic synthesis of aromatic aldehydes

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In the last decades, we have assisted to a raising concern in dealing with the ecological impact of the conventional industrial processes for organics production. The result is the appearance of several studies aiming at the development of new energy-efficient and greener methods for organic synthesis. Traditional chemical industry requires the use of hazardous oxidants/reductants and harsh operation conditions, such as high temperature and pressure. Photocatalytic synthesis processes can operate under mild conditions, reducing the volume and the toxicity of the generated residues. Moreover, the possibility of being activated by natural energy sources, such as sunlight, or by low energy consumption radiation sources like Light Emitting Diodes (LEDs), contribute to reduce energy costs. For these reasons, heterogeneous photocatalytic reactions have gained high relevance on process intensification and safety in many environmental, chemical and medical applications.

Selective conversion of aromatic alcohols to the corresponding aldehydes is considered an important chemical transformation from the industrial point of view. The major challenges dealing with the photocatalytic synthesis of aromatic aldehydes are related to the development of efficient catalysts and appropriate reaction systems, seeking for maximized yield and selectivity<sup>1</sup>.

In the present work, we used carbon nitride  $(C_3N_4)$  based materials in the photocatalytic oxidation of several aromatic aldehydes namely, benzaldehyde, anisaldehyde, vanillin, piperonal, tolualdehyde. A comparison on the performance between conventional batch photocatalytic reactors using the photocatalysts catalysts in a slurry, with continuous flow reactors using immobilized catalysts is described. The nanosheets of  $C_3N_4$  were successfully immobilized in glass Raschig rings and polyester fabrics, avoiding the catalysts separation procedure, which allows work under continuous operation mode. We tested several immobilization conditions for optimize the performance of the photocatalytic process, namely the number of  $C_3N_4$  depositions on the glass rings, and the pre-treatment of the polyester support with nitric acid, aiming an increase on the interactions between the support and the photocatalyst.

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## **Materials**

# Matrix-isolated 5-Methoxy-Benzlmidazole: Control over multiple conformational equilibria

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Matrix isolation coupled with infrared spectroscopy is a unique technique that has grant several developments in the field of conformational analysis of molecular systems. The bands in the infrared spectra of matrix-isolated molecules are very narrow (on the order of 1 cm<sup>-1</sup>), which allows to monitor conformational isomerization reactions in great detail.<sup>1</sup> Annealing of the sample<sup>2</sup> or narrowband infrared irradiation<sup>3</sup> are some of the tools used to manipulate the conformational population of a matrix-isolated compound. Ensuring that only the desired conformer, of a specific molecular system, is present in the matrix it is possible to do all sorts of studies on individual conformers.

In this work, the conformational space of 5-Methoxy-BenzImidazole (5MBI) was studied both theoretically and experimentally. Theory predicts that 5MBI may exist in two distinct tautomeric forms (1*H* or 3*H*), and each tautomeric may adopt two conformational isomers (*A* or *B*). According to the calculated relative energies, each of these forms should be populated in the gas phase in an amount (between 5 and 50%) enough for its experimental detection. Indeed, upon deposition of 5MBI monomers into inert gas matrixes, signatures of the four structures have been identified in the experimental infrared spectra. Surprisingly, we established that the conformational populations within each tautomeric form changed with time, just by exposure of the sample to the source of the spectrometer (see Figure 1). The kinetics of this isomerization will be presented as a function of different matrix gas host (Ar, Xe) and sample temperature during the exposure. The effects of annealing or selective vibrational excitation of the 2v(NH) over the conformational populations will be discussed. As expected, the relative amounts of each tautomer remained the same over the entire experiment, due to the inaccessible high energy barrier for the hydrogen atom transfer.



Figure 1: Conformational populations of 5-Methoxy-BenzImidazole monomers (1*H-A*, 1*H-B*; 3*H-A*, 3*H-B*) isolated in a Xe matrix at 30K, as a function of exposure of the sample to the source of FTIR spectrometer Nicolet 6700 (in minutes).

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## **Materials**

# Light, Ruthenium, Dendrimers... Action!

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New types of hybrid photodiodes (HPD) have been developed in the past few years, especially due their potential in the field of image sensing and biomedicine.<sup>1</sup> The chase for low cost, low temperature response, long lifetime, high response and sensitivity to light, high gain photodiode and low noise lead to development of new organic, inorganic or hybrid semiconductors.<sup>2</sup>

The unique properties of the dendrimers scaffold allowed the construction of donor-acceptor semiconductors having both electron donor and electron acceptor units connected with  $\pi$ -bridges.<sup>3</sup> In this work, based on previous work<sup>4</sup> promising low cost, low current, stable photodiode devices were produced under room temperature, using one single layer of a biocompatible matrix (agarose) incorporating poly(imidazolone amine) (PIMAM) dendrimers and ruthenium dyes using a stainless steel electrode (**Figure 1**). These devices achieved nA dark currents along with good detectivities.



Figure 1: Chemical structures of a donor-acceptor PIMAM dendrimer and ruthenium dye.

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## Materials

# Imprinted hollow TiO<sub>2</sub> microspheres - Optimization of the synthesis and recognition performance evaluation

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Molecular imprinting technology, often described for the creation of molecularly imprinted materials with tailor-made binding sites complementary to the template molecules (in shape, size and functional groups), it has been indicated as promising in different areas namely in photocatalysis<sup>1</sup>. The molecular imprinting founded on microstructures based on TiO<sub>2</sub>, especially in the hollow spherical shape, has been attracting attention for selective photocatalysis, since hollow TiO<sub>2</sub> microspheres present unique properties of multiple reflection and diffraction of light, surface permeability, light capturing capacity, surface area, low density, among others<sup>1</sup>. A few preparation methods and template molecules have already been employed to produce imprinted TiO<sub>2</sub>. As far as we know, only 4 reports refer to the preparation of TiO<sub>2</sub> structures with molecular imprinting in the particulate form<sup>2-5</sup>, none of them as hollow microspheres. This work aims at the optimization of synthesis procedures leading to new hollow TiO<sub>2</sub> microspheres imprinted with bilirubin, with higher photonic efficiency and high photocatalytic selectivity. The materials optimized for hollowness and bilirubin recognition were subjected to studies of adsorption of bilirubin. The recognition performance was evaluated through the determination of host-guest affinity constants, selectivity and capacity, heterogeneity and mass transfer kinetics. Taking into account the promising results obtained in the recognition studies (**Figure 1**) the materials optimized for hollowness and bilirubin recognition will be subjected to UV radiation exposure tests in a photoreactor so as to ascertain the photocatalytic properties of the imprinted hollow TiO<sub>2</sub> microspheres and the corresponding non-imprinted ones.



Figure 1: Characterization of bilirubin-imprinted TiO<sub>2</sub> hollow microspheres: a) SEM image, b) Pore size distribution, c) nitrogen adsorption isotherms and d) bilirubin adsorption isotherms of (■) imprinting and (●) non-imprinting.

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## Materials

## Nanocatalysis: A Powerful Instrument for Wastewater Valorization

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The environmental concern about water pollution with harmful compounds has been increasing.<sup>1</sup> The design of efficient catalysts for the transformation of toxic organic pollutants into compounds with high added-value and lower toxicity has raised.<sup>2</sup> Nitroarene compounds, such as 4-nitrophenol (4-NP) and 4-nitroaniline (4-NA), are environmentally hazardous, highly toxic and identified as priority pollutants to eliminate by Environmental Protection Agency.<sup>3</sup> Nevertheless, the products, 4-aminophenol (4-AP) and 4-aminoaniline (4-AA), are valuable compounds for many industries, namely, to produce rubber, antioxidants, pharmaceuticals and dyes.<sup>4</sup> Thence, the development of efficient and eco-friendly metal catalysts to be applied in the conversion of nitroarenes into the corresponding amine derivatives is crucial. Metallic nanoparticles (NPs) are difficult to remove from the reaction medium and tend to aggregate due to their high surface energy, leading to a decrease of their catalytic activity.<sup>5</sup> The strategy to overcome this problem is to anchor the nanoparticles onto solid supports. TiO2 is an excellent solid support for metal NPs due to its thermal and chemical stability, non-toxicity, relative low cost and semiconducting properties.<sup>6</sup> In this work Au and Ag NPs were immobilized onto TiO<sub>2</sub> solid support through the adsorption of the metal salt precursors onto TiO<sub>2</sub> surface and posterior reduction of Au<sup>3+</sup> and Ag<sup>+</sup> to metal Au<sup>0</sup> and Ag<sup>0</sup>, respectively, using various reducing agents: citric acid, sodium borohydride or light source ( $\lambda$  = 340 nm). The influence of the type of reducing agent and its concentration on the Au and Ag NPs formation, loading, oxidation state and type of bond stablished with the TiO<sub>2</sub> solid support was investigated. Moreover, the effect of the type of immobilized NPs (Au versus Ag) on the catalytic performance of the corresponding nanocomposites was assessed. The efficiency of the prepared materials was evaluated in the heterogeneous catalytic reduction of 4-NP and 4-NA substrates in aqueous solution at room temperature and using sodium borohydride as reducing agent.

Both Au- and Ag-based catalysts led to a total conversion of 4-NP within 260 and 40 s, respectively and the reaction followed a pseudo-first-order kinetic with rate constants (*k*) of  $19.1 \times 10^{-3}$  and  $94.2 \times 10^{-3}$  s<sup>-1</sup>, respectively, demonstrating the higher catalytic performance of the Ag-based material. For the 4-NA reduction, the highest catalytic performance was observed with the Au-based material, achieving total conversion within 90 s with *k* =  $29.4 \times 10^{-3}$  s<sup>-1</sup>, while the Ag-based material reached total conversion within 120 s ( $k_a = 16.6 \times 10^{-3}$  and  $k_b = 27.5 \times 10^{-3}$  s<sup>-1</sup>). After catalysis, the grafted Au NPs retained their metallic state, whereas the Ag NPs were partially oxidized, which was detrimental for their subsequent catalytic activity. The Au and Ag-based TiO<sub>2</sub> catalysts could be reused for 10 consecutive cycles without any treatment, with the Au-based catalyst showing the highest stability and robustness for both substrates.

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## Materials

# Development of Double Emulsions from *Sambucus nigra* L. Berry Extract as pH Stable Colorant Formulations

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Anthocyanins are flavonoids, one of the largest groups of water-soluble vegetable pigments, having also sweetening and antioxidant properties. They are characterized by different colors, such as red, purple, blue and violet. However, their color stability is compromised by variations in pH, temperature, moisture, and luminosity conditions.<sup>1</sup> The berries of Sambucus nigra L. have high contents of anthocyanins (cyanidin-3-O-sambubioside and cyanidin-3-Osambubioside-5-O-glucoside), being a promising option as food coloring agents.<sup>2</sup> Therefore, this work aims to stabilize the natural hydrophilic colorant obtained from S. nigra through the preparation of double emulsions (water/oil/water, W/O/W). The S. nigra berries were extracted by crushing the fruits to obtain the juice, followed by spray drying to obtain the dry extract. For the preparation of the double emulsions, the procedure was the one described by Paula D. A. et al. with some modifications.<sup>3</sup> Briefly, for the first emulsion, the water phase comprised 55 mg/L of the extract and 5% Polyglycerol polyricinoleate (PGPR), homogenized under stirring (20000 rpm, 5 min). This phase was dispersed into corn oil at a W/O ratio of 0.4. (Figure 1 – (A)). Thereafter, the second emulsion was prepared by dispersing the previous emulsion in a water phase comprising Tween 80 and gum Arabic, tested at different concentrations. The final W/O/W emulsion was prepared at different primary emulsion/water ratios and stirred at 6000 rpm during 2 min using an Ultra-Turrax system. The produced emulsions were analyzed by optical microscopy (OM) using a Nikon eclipse 50i microscope to assess size and morphology. This analysis showed the presence of spherical and individualized droplets with an estimated particle size between 13 and 16 µm. (Figure 1 - (B)). The role of these emulsions as pH stable colorants were tested using different buffers (pH 4-7), as shown in (Figure 1-(C)), which also presented the comparison with solutions prepared from the original S. nigra extract. The obtained results pointed out for an improved stability and color homogeneity among samples in the tested pH range.



Figure 1: (A) Simple Emulsion, and (B) Double emulsion, and (C) Testing at different pHs (4-7).

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## Materials

# Melt dispersion *versus* spray congealing to produce wax solid particles added with β-carotene as natural colorant based systems

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The trend towards the use of natural colorants as substitutes of the artificial ones has been increasing due to their health-related benefits. However, it is a major challenge for the industry to maintain the stability of systems based on natural colorants under processing conditions (e.g. temperature). In this work, colorant systems for application in food matrices based on β-carotene, a lipophilic compound, were developed by two different productive processes: i) melt dispersion, and ii) spray congealing technique. Melt dispersion was tested at a wax/water ratio of 12.5% (w/w) using a chemical system comprising beeswax (melting temperature of 64 °C), distilled water, and Tween 80 as surfactant (HLB of 15). Briefly, beeswax was melted, β-carotene added (1.2%, w/w) and homogenized by stirring. Thereafter, this mixture was transferred to water previously heated at 80 °C and added with the Tween 80 (0, 0.5, 1, and 3%, w/w), and vigorously stirred at 2,000 rpm. The size evolution during the productive process was checked by optical microscopy by taking aliquots at 5, 10, 15 and 20 minutes in order to establish the best productive conditions. Finally, the mixture was cooled using an ice bath and the produced particles recovered by decantation, thereafter dried and stored for further analysis. For the spray congealing method, particles were produced from the mixture of beeswax and β-carotene without the use of surfactant (1.2% of β-carotene). Briefly, beeswax was melted with gentle stirring following by the adding of the colorant to achieve homogenization. The used equipment was a Mini Spray Dryer B-290 Buchi adapted to work in the spray-congealing mode. After production the particles were recovered and stored for further analysis. The final particles were characterized by FTIR, DSC/TG, SEM and particle size determined by laser diffraction. The colorant power, determined by colorimetry, was thereafter correlated with the obtained particle size. Dispersibility of the particles in water was also tested from the obtained powders. Comparing the two systems (Figure 1), the one based on melt dispersion gave rise to particles with lower size and with better dispersibility in water due to the use of a surfactant agent. These two features are important characteristics aiming at their use as food colorant systems. The work in progress will proceed with the testing of the produced colorant systems in model food matrices.





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## **Materials**

# Dipeptide Nanopores. A Non-Equilibrium Molecular Dynamics Study

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In recent years great attention has been paid to the capture and release of gases with the aid of nanoporous solids. The design of new-generation porous materials has enabled the creation of innovative technologies for the removal of green-house gases from exhaust fumes, and their recycling and transformation.<sup>1</sup> Such porous molecular crystals of natural origin seem most attractive for their applications as gas absorptive materials. Porous dipeptide crystals are one of these materials and has long been an area of interest in structural, biological, and materials sciences.

Within the family of dipeptides capable of forming porous crystalline structures, herein, we present a theoretical study of two representative dipeptide nanopores: L,L-diphenylalanine (FF) and L-Valyl–L-Alanine (VA). Their crystal structures are hexagonal (space group P6<sub>1</sub>) and show open nano-channels, which are accessible from the gas phase (**Figure 1**). The interior part of the channels is lined with: hydrogen-bond donors and acceptors in charged groups (-NH3<sup>+</sup> and – COO<sup>-</sup>) in case of FF crystalline, and aliphatic groups in the case of VA nanopore. The channel cross-sections is 9.2 Å and 4.7 Å respectively for FF and VA. Therefore, they represent a good platform for probing gas absorption and diffusion in microporous crystals with a diversity of channel sizes and shapes. The ordered organization of building blocks into defined nanostructures relies on specific molecular recognition which is facilitated by a combination of non-covalent interactions, including hydrogen bonds, electrostatic interactions,  $\pi$ –  $\pi$  stacking, hydrophobic forces, non-specific van der Waals forces, and chiral dipole–dipole interactions. Although these forces are relatively weak, when they are present in large number, they can govern the self-assembly of molecular building blocks into superior and ordered structures.

The studies employed Molecular dynamics (MD) simulations, which is a valuable computational tool to investigate phenomena in a nanometric scale, in studies of the thermodynamics, mechanical and transport properties of porous materials, providing complementary insight into experimental data.<sup>2</sup> Based on the structures obtained from X-ray crystallography, molecular models of several different dipeptide structures were built which are used in Molecular Dynamics simulation studies using AMBER and GROMACS software. Results have shown so far the stability of LL and VA model structures, which is important to ensure their suitability for the next stages of gas adsorption and transport simulations.



Figure 1: The channels viewed along the axis: a) L,L-diphenylalanine (FF) and b) L-Valyl-L-Alanine (VA).

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## **Materials**

## Water-in-oil nanoemulsions as vehicles of natural antimicrobial agents

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Nanoemulsions are emulsified systems characterized by droplets in the nanometer size range, which confer to these systems several advantages like superior stability to storage and improved bioavailability and bioefficacy of added functionalities. They can be formulated in different physical forms (creams, liquids or sprays) and require a low surfactant amount to form stable systems<sup>1</sup>. In this way, the production of water-in-oil (W/O) nanoemulsions based on natural ingredients, like natural base-oils, is an interesting alternative to replace the traditional synthetic products. Thus, the present work aims to develop nanoemulsion systems based on sweet almond oil, able to show long stability to comply with industrial applications. For this purpose, a systematic study was performed, by testing the influence of different W/O ratios (10/90, 20/80, 30/70, and 40/60) using an emulsifier system composed by Span 80/Tween 80 mixture (54/46 ratio, v/v). The nanoemulsions were prepared using a two-step procedure, where the first one corresponded to the primary W/O emulsion preparation, by using a mechanical homogenizer (11000 rpm, 5 min). Then, in the second step, droplet size was reduced using a high-pressure homogenizer (HPH), till a total number of passages (cycles) of 24. The effect of the used number of cycles on the droplet size was studied by optical microscopic (MO) analysis using samples recovered after 12, 21 and 24 cycles. In order to study the nanoemulsion stability along the storage time, the MO analysis was done periodically till a final time-frame of 6 months at room temperature. For that, the nanoemulsion physical appearance was inspected periodically by visual analysis, and a photographic registry made to document the detected evolution. Among the tested ratios, 40/60 give rise to nanoemulsions of higher stability, fulfilling 6 months of storage without any modification (Figure 1). This study allowed the development of stable nanoemulsions, suitable for the controlled delivery of active compounds, which are being currently tested with natural antimicrobial extracts (work in course).



Figure 1: Stability of nanoemulsions at different preparation stages and W/O ratios (a). Microscopic analysis of the 40/60 W/O ratio: primary emulsion (b), 12 cycles homogenization, preparation day (c) 12 cycles homogenization, 6 months under storage (d).

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## **Materials**

# Synthesis and photoluminescence studies of colloidal NaGdF<sub>4</sub>:Tm<sup>3+</sup>/Yb<sup>3+</sup> phosphor for optical thermometry application

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Trivalent lanthanide doped upconversion phosphors materials convert low energy to high energy under infrared radiation. Such materials have supremacy application, like security, temperature sensing, bioimaging, etc. Usually, fluorides exhibit high chemical stability and low phonon energies compared to oxides and sulfides. Thulium is a good dopant with ytterbium, resulting in a phosphor with an intense blue emission after an excitation at 976 nm.<sup>1</sup>

In this project,  $Tm^{3+}/Yb^{3+}$  co-doped NaGdF<sub>4</sub> has been synthesized by thermal decomposition method using oleic acid and 1-octadecane as precursors. The as synthesized phosphor has monodisperse in cyclohexane. The particle morphology and size is measured by scanning electron microscopy. The phase formation has been confirmed by Xray characteristic. Upconversion emission spectra have been recorded by CCD spectrometer using 976 nm excitation wavelength. Downconversion emission spectra have also measured by using xenon arc lamp. In both cases emission bands were found at 452, 477, 647, 697 and 802 nm corresponding to the  ${}^{1}D_{2}\rightarrow {}^{3}F_{4}$ ,  ${}^{1}G_{4}\rightarrow {}^{3}H_{6}$ ,  ${}^{1}G_{4}\rightarrow {}^{3}F_{4}$ ,  ${}^{3}F_{3}\rightarrow {}^{3}H_{6}$ and  ${}^{3}H_{4}\rightarrow {}^{3}H_{6}$  transitions, respectively. The effect of the magnetic field was studied on the emission intensity. The CIE color coordinate invariation of colloidal phosphor is also demonstrated. The present phosphor may be applicable for making optical temperature sensing probe and optical heater. <sup>2</sup>



Figure 1: Upconversion emission spectra of colloidal Tm<sup>3+</sup>/Yb<sup>3+</sup> co-doped NaGdF<sub>4</sub> phosphor and their CIE color coordinate diagram at different laser pump power.

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## **Materials**

# Synthesis and characterization of cobalt doped titania nanomaterials: application in photocatalytic degradation of methyl orange under UV-A and visible light irradiation

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The TiO<sub>2</sub> and Co-TiO<sub>2</sub> nanoparticles (NPs) as photo catalysts have been successfully prepared by sol-gel and precipitation methods. The prepared photocatalysts were characterized by XRD, FT-Raman, UV–vis DRS, SEM, EDX, XPS, N<sub>2</sub> adsorption/desorption at -196°C. The obtained XRD results showed the presence of the anatase phase for both nanomaterials. The XPS analysis confirmed the presence of cobalt with TiO<sub>2</sub>.

The band gap energies of the materials was estimated from the UV–Vis DRS results, pure  $TiO_2$  had a band gap energy of 3.11eV, Co– $TiO_2$  nanomaterials with 1wt% and 10 wt% of cobalt content showed a red-shift, giving a band gap of 3.08 ev and 2.98 ev, respectively.

The photocatalytic response of Co-TiO<sub>2</sub> nanomaterials was analyzed for the degradation of the organic dye methyl orange (MO), under both UV-A and visible light irradiations. The results showed that an optimum level of cobalt (1% of weight) in the Co-TiO<sub>2</sub> NPs, enhanced the photocatalytic activity toward methyl orange photodegradation under visible light. The exploration of the MO degradation mechanism showed that  $O_2^{\circ}$  radicals were the main reactive species.

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# Bioinspired Copper(II) Complexes and Coordination Polymers: Structural Features and Applications

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As an extension of our research on the synthesis and catalytic application of bioinspired multicopper(II) cores,<sup>[1-3]</sup> the current presentation will focus on the self-assembly generation of new copper(II) compounds bearing aminoalcohols as principal *N*,*O*-ligands. Herein, we will discuss the influence of pyromellitic acid (H<sub>4</sub>pma) as a recognized linker to produce 0D complexes or 2D coordination polymers, as well as the catalytic application of the obtained compounds toward the mild homogeneous oxidation or hydrocarboxylation of cycloalkanes.

*N*-methyldiethanolamine (H<sub>2</sub>mdea), *N*-benzylethanolamine (Hbea), triisopropanolamine (H<sub>3</sub>tipa), *N*,*N*-dimethylethanolamine (Hdmea) or *N*-ethyldiethanolamine (H<sub>2</sub>edea) were applied as *N*,*O*-building blocks to generate five novel copper(II) compounds, namely [Cu(H<sub>1.5</sub>mdea)<sub>2</sub>]<sub>2</sub>(H<sub>2</sub>pma) (**1**), and [{Cu<sub>2</sub>( $\mu$ -Hmdea)<sub>2</sub>}<sub>2</sub>( $\mu$ 4-pma)]<sub>n</sub>·2nH<sub>2</sub>O (**2**), [Cu<sub>2</sub>( $\mu$ -bea)<sub>2</sub>(Hbea)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub> (**3**), [Cu<sub>2</sub>(H<sub>3</sub>tipa)<sub>2</sub>( $\mu$ -pma)]·7H<sub>2</sub>O (**4**), [{Cu<sub>2</sub>( $\mu$ -dmea)<sub>2</sub>(H<sub>2</sub>O)}<sub>2</sub>( $\mu$ 4-pma)]<sub>n</sub>·4nH<sub>2</sub>O (**5**), [{Cu<sub>2</sub>( $\mu$ -Hedea)<sub>2</sub>}<sub>2</sub>( $\mu$ 4-pma)]<sub>n</sub>·4nH<sub>2</sub>O (**6**), [{Cu(bea)(Hbea)}<sub>4</sub>( $\mu$ 4-pma)]<sub>n</sub>·2nH<sub>2</sub>O (**7**). Self-assembly synthesis and structural features of these copper(II) compounds will be discussed.

Moreover, the obtained copper(II) compounds act as highly efficient pre-catalysts for the mild homogeneous oxidation and hydrocarboxylation of cycloalkanes (**Figure 1**). Based on cycloalkane, overall product yields up to 45% were achieved and the effects of various reaction parameters were investigated: loading and type of pre-catalyst, amount and kind of acid promoter, influence of water, and the substrate scope (**Figure 1**).<sup>[4,5]</sup> The unusual water promoting effect will be highlighted.



Figure 1: Mild oxidation and hydrocarboxylation of cyclohexane catalyzed by bioinspired copper(II) aminoalcohol derivatives.

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## **Materials**

# Synthesis of doped and non-doped inorganic Halide Perovskite Quantum Dots

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Metal halide perovskite crystal structures have emerged as an attractive class of optoelectronic materials due to their excellent optical absorption and emission properties. Restricting the physical dimension of the crystallite to the nanometer scale revealed quantum-confinement effects similar to those presented by traditional chalcogenide quantum dots. The synthetized inorganic perovskite quantum dots (IPQD) were characterized mainly by spectroscopic measurements (absorption and photoluminescence emission spectra). The employed synthesis process was the Hotinjection method  $(HI)^1$  – most common method for synthetizing quantum dots. The initial synthetized quantum dots had the chemical structure of CsPbX<sub>3</sub> (X = Cl, Br, I or a mixed halide system). Posteriorly, this already known synthesis was modified in order to dope the previous quantum dots with different metals, focusing in Cu<sup>+1</sup> and Cd<sup>+2</sup> for systems containing Bromide as the halide. The obtained samples showed smaller full width at height maximum (FWHM), when compared with the blank (non-doped) samples, and improved stability (samples doped with Cd<sup>2+</sup>). This synthesis method was compared with the doping mechanism already existing for these materials - post-synthesis cation exchange reactions - and an increase of the dopant present in the final sample was observed for the employed method in this work<sup>2</sup>. Samples with lodide has the halide were also tested and the emission profile was significantly improved when compared with the non-doped samples. The observed optical properties and empirically improved stability make these nanocrystals promising materials in several optoelectronic applications, namely LEDs, solar cells, lasers, among others.

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## **Materials**

# Emissive sulfur species confined in artificial hackmanite

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Hackmanite is a natural sodalite mineral with sulfur in its composition and a chemical formula of Na<sub>8</sub>[SiAlO<sub>4</sub>]<sub>6</sub>(Cl,S)<sub>2</sub>. This mineral has yellow-orange emission, due to the presence of S<sub>2</sub><sup>-</sup> clusters<sup>[1]</sup>. In artificial hackmanite these photoluminescent have high Stokes shifts, ca. 250 nm, high external quantum efficiency (EQE) and stability at high temperatures<sup>[2]</sup>. These compounds are rare-earth-free (compounds in the list of critical raw materials, according to the European Commission<sup>[3]</sup>) and can be used as an alternative to the commercial phosphors in LED technology. Artificial hackmanite can be synthesized in laboratory through a solid-state synthesis, starting from the LTA zeolite<sup>[2]</sup>. Since high sulfur concentrations can induce self-quenching in luminescence<sup>[2,4]</sup>, samples with different concentrations of sulfur were made, based on the following stoichiometry: Na<sub>8</sub>[SiAlO<sub>4</sub>]<sub>6</sub>S<sub>x</sub>Cl<sub>2-2x</sub>, in an electric furnace at 900° C during 1h, under reducing atmosphere of 5% H<sub>2</sub>, 95% Ar (v/v). Photoluminescent species S<sub>2</sub><sup>-</sup> were found in sodalites with low sulfur concentrations, a different type of clusters was found (tentatively S<sub>4</sub><sup>2-</sup> species) with emission in NIR region. Sodalite was deposited on a glass surface, at a temperature of 750° C, and it remained luminescent.

The presence of silver clusters in zeolite structures can induce several emission colors, e.g. white, high EQE (up to 97%) and large Stokes shift<sup>[5]</sup>. All these optical properties make them suitable candidates in lightning applications. Therefore, in order to extend the applicability of the developed sulfur sodalite zeolites, a new method of encapsulating metals that typically are not part of the structure, as silver, was studied. With the introduction of silver into the sulfur sodalite structure, white luminescence compounds were obtained.

Due to their remarkable optical properties, the obtained sodalite zeolites are quite promising to be used as phosphors in commercial LEDs

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## Materials

# Breaking the mould: Exploring higher oxidation states in early lanthanide anions generated in the gas phase.

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Oxides along with halides are the key compounds that Dmitri Mendeleev used to classify metals within the periodic system as they are the quintessential indicators of valency or formal oxidation state. The recent identification<sup>1</sup> of Praseodymium (V) in the form of gas phase oxides has opened up the fascinating possibility that early lanthanides may not be as chemically dull as previously thought. While cerium has been known for a long time to be able to lose all the electrons in its valence shell and attain the +4 oxidation state its heavier neighbours, praseodymium and neodymium did not have any examples showing a similar chemistry<sup>2</sup>. The reason why lanthanides have such a short span of oxidation states is principally due to poor electron screening of the 4f shell which causes it to have core like features after a third ionisation.

In this presentation I will give some in silico insights of the structural features of anions of the type  $[LnO_2(NO_3)_2]^-$ (Ln=Ce,Pr,Nd) detected by mass spectrometry and address the trend in their detected hydration pathways.



Figure 1: a) Molecular structure of Pr(V) dioxido-nitrate [trans- $PrO_2(NO_3)_2$ ]; b) the corresponding NBO  $\sigma$  and c)  $\pi$  bond bonds.

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## **Materials**

# Synthesis, characterization, and adsorptive properties of Chitosan

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In this work, natural Chitosan (CS) has been successfully prepared from chitin (figure 1) witch was extracted from shrimp shells collected in Meknes city (Morocco) The structural, optical and morphological properties of the purified biomaterial have been investigated using various techniques such as XRD, FT-IR, UV-Vis DRS, and SEM. The adsorption properties of the as-prepared biomaterial were then evaluated in aqueous solution in presence of methyl orange (MO) in dark. The obtained results showed that, the chitosan is efficient for the adsorption of MO A series of experiments was also conducted to optimize various parameters such as the amount adsorbed, pH, and initial dye concentrationin dark.



Figure 1: transformation from chitin to chitosan

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## **Materials**

# Natural-dyeing solutions for leather applications

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At present, consumers' concerns with health and well-being, along with environmental problems, pose new challenges to the leather industry. In this context, the toxicity of the commonly used synthetic dyes represent an environmental problem and a risk to human health. These issues motivated the development of new solutions based on non-toxic natural ingredients. Nevertheless, one of the main disadvantages of natural dves use is related with the lack of chemical bond between the dye and the collagen fibers. Thus, auxiliary agents like mordant agents are required to ensure an effective bonding, and the efficacy of the dyeing process is dependent on the used conditions (mordant stage and concentration, dyeing time, etc.). In this context, carminic acid, a water-soluble natural dye extracted from the female cochineal insects, which presents high stability to heat and light, was tested in the dying process of leather by the mordant process with three mordant agents. The mordant treatment was done prior to the dyeing process (pre-mordant stage) for 60 min at 40 °C, and the dye uptake was thereafter studied as function of the used concentration (1.0 and 6.0%, based on leather weight (OLW)) during the dyeing stage (40 °C, for 180 min) (the performed assays were named CA and numbered sequentially). For that, leather and dyeing solution samples were recovered at 30, 60, 90, 120 and 180 minutes. The efficiency of the dyeing process was evaluated by measuring the dye exhaustion, dye uptake and color variation ( $\Delta E$ , relative to the original sample) of the dyed samples. The establishment of molecular mordant/dye interactions was inspected by Fourier Transform Infrared (FTIR) analysis, showing evidences of the typical vibrations assigned to dye and leather's collagen interactions mediated by the mordant agents. The highest values of dye exhaustion and dye uptake were 26.12% and 0.023 gdve/gleather, obtained with potassium aluminum sulfate at 6.0% OLW and 180 minutes of dving process (CA3). Appositively, the lowest values were 6.58% and 0.007 gdve/gleather, obtained with aluminum sulfate at a concentration of 1.0% OLW (CA5). Based on  $\Delta E$  values, the more intense color was observed for the CA2 sample (Figure 1), when aluminum sulfate was used as mordant agent at a concentration of 6.0% OLW. In a general way, the overall results pointed out for the viability of the use of carminic acid as a natural dyed solution for leather components.



Figure 1: (a) Examples of dyed leather samples and (b) ΔE results along the dyeing process.

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## **Materials**

## Fluorescent Supercapacitors: Energy Storage on Smart Fashion Textiles

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In a year marked by the celebration of the 150 years of the Periodic Table, it is noteworthy that the Periodic Table continues to be an essential tool to understand the properties of elements/materials, such as oxidation states, thermal and electrical conductivity and **luminescence**. These properties allow the development of several technologies including biochemical sensors, light-responsive textiles, electronic devices, energy storage systems, among others [1]. The development of smart materials/sensors combined with the advances in computer science lead to a new Era: the *Internet of Things*. Nowadays, the society is increasingly connected with new intelligent technologies, which enable the connection with everything all over the world through a simple electronic device. However, the **energy demand** of these devices became a current concern. To address this issue, energy storage devices, such as supercapacitors (SC) and batteries, are available in the market. One of the main challenges is to develop new SC with higher energy storage capacity and shorter charging time. In particular, in the field of wearable technologies, the design of textile SCs based on **nanotechnology/nanomaterials** emerged as a promising strategy [2], since they allow improving the performance of SCs, while maintaining the flexibility, lightness and comfort of the fabrics. These features are highly important in the **fashion** world, for the development of multifunctional electronic textiles combining energy storage with light responsive properties, and fancy colors.

In this work, nanomaterials with luminescent and electrical properties were used to develop a dual-function textile photo-SC that, simultaneously, presents fluorescent properties by the action of UV light and stores energy (Figure 1). To achieve that goal, textile substrates were coated with a conductive carbon nanomaterial (CN) and a fluorescent pigment and used as electrodes to produce the smart textile photo-SC (SC\_CN\_FP). For comparison, a non-fluorescent SC was also produced (SC\_CN). Various characterization techniques such as XRD, FTIR-ATR and SEM-EDS confirmed the successful preparation of the functional textiles. Textile devices revealed a double layer capacitive behavior. The SC\_CN\_FP presented lower internal resistance of 556.0  $\Omega$  than SC\_CN (743.3  $\Omega$ ) and higher specific capacitance of 8.98 F g<sup>-1</sup> (**vs**. 8.10 F g<sup>-1</sup> for SC\_CN). The energy and power densities were 3.24 W h kg<sup>-1</sup> and 383.0 W kg<sup>-1</sup> (**vs** 3.06 W h kg<sup>-1</sup> and 328.7 W kg<sup>-1</sup>), respectively. The exposure of the textile SC to UV light ( $\lambda$  = 254 and 365 nm) lead to a change of its color, conforming its versality to the fashion area. This type of devices is a revolutionary technology for the world of fashion and electronic smart textiles.



Figure 1 – Response of the dual-function textile photo-supercapacitor device to visible and UV light ( $\lambda$  = 365 nm and 254 nm).

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## **Materials**

# Hierarchical Fe(II)@HMOR zeolite for catalytic oxidation under microwave radiation

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The aim of this work is to optimize the experimental conditions to prepare heterogeneous catalysts based on supported iron species incorporated onto hierarchical MOR zeolite by mechanochemical grinding. The catalytic behavior of the prepared catalysts is studied in 1-phenilethanol oxidation into acetophenone using microwave radiation as a heating source (scheme 1).



Scheme 1: Oxidation of 1-phenilethanol into acetophenone under microwave heating.

Commercial HMOR from Zeolyst, with a Si/AI =10 was used as a starting material. Hierarchical HMOR samples were prepared according to the procedure described in [1] using 0.4 or 0.8 M NaOH solutions as alkaline agents at 65 °C for 30 min, followed by acid treatment (AT) with 0.1 M HCl at 70 °C for 6 h. The zeolite materials were characterized by XRD powder diffraction and low temperature N<sub>2</sub> adsorption. A preliminary study was performed using commercial HMOR zeolite. The iron species, from FeCl<sub>2.4</sub>H<sub>2</sub>O or FeCl<sub>3.6</sub>H<sub>2</sub>O precursors were introduced using a ball mill (Retsch PM 100) where the grinding parameters: speed and time, as well as the type and amount of iron precursor were optimized. The catalytic reaction was carried out in a microwave reactor (Anton Paar) using H<sub>2</sub>O<sub>2</sub> as oxidant agent, where the influence of the reaction parameters was studied: agitation speed and time. The reaction products and unconverted reactants were analysed by gas chromatography (Fisons) with FID detector. Lixiviation tests were also performed, and no significant loss of Fe particles were detected during the catalytic essays. Upon optimization the best achieved experimental parameters were: grinding conditions: 500 rpm and 5 min for zeolite samples loaded with 0.2% Fe (from FeCl<sub>2.4</sub>H<sub>2</sub>O). The optimized microwave reaction conditions were: 100 °C, 600 rpm and 50 min. The optimized experimental parameters were applied to the Fe loaded hierarchical MOR samples where it was found that NaOH concentration (0.4 or 0.8 M) has no significant impact on the product selectivity. However, upon acid washing the treated samples show distinct behaviors: HMOR 0.4 AT showed a decrease of product selectivity of about 5 % whereas HMOR\_0.8AT presented more than 10% increase.

As a brief conclusion, the preliminary results of this study point out to the influence of desilication conditions of HMOR zeolite that most probably influences the location and distribution of Fe species on HMOR porous matrix, that impact on the catalytic behavior of Fe loaded catalysts.

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## **Materials**

# (Aminophenyl)porphyrins as precursors for the synthesis of porphyrin-modified siloxanes

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Polysiloxanes are polymers composed of a Si-O-Si backbone and organic radicals linked to silicon atoms, being polydimethylsiloxane the most representative material of this family. One important application of siloxane materials is as a flexible spacer in the preparation of semi-conducting materials since due to their low dielectric constants, siloxane moieties have a small impact on the electronic properties of a semi-conductor but can provide different physical attributes to the final material.<sup>1</sup> Porphyrins are also important compounds for incorporating in functional materials due to their photophysical properties such as high absorption coefficients in the visible region and tunable fluorescence emission.<sup>2</sup> Usually, porphyrins retain their photochemical properties after the incorporation in polymerbased devices, generally by electropolymerization or mixing into polymers. We hereby present our results regarding the microwave-assisted synthesis of aminoporphyrins and subsequent reaction with an epoxide siloxane, providing two new porphyrin-modified siloxanes, which were found to preserve the optical properties of the porphyrin chromophore as revealed by their absorption and emission spectra.



Figure 1: Porphyrin-siloxane dimer and corresponding UV-Vis and Fluorescence spectra in CHCI<sub>3</sub>.

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## Materials

# Boosting carbon nitride photocatalytic efficiency by a simple NaCl templating method

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Graphite-like carbon nitride (GCN) appeared recently as a multifaceted catalyst applied in a wide range of photocatalytic processes.<sup>1</sup> A simple and effective way to improve the photocatalytic activity of bulk GCN is thermal exfoliation of the parent carbon nitride (GCN-T).<sup>2</sup>

In this work, we report one green and scalable procedure for the synthesis of GCN based on a NaCl templating method. Different amounts of NaCl were mixed with dicyandiamide and submitted to a thermal treatment according to an optimized procedure.

We evaluated the photocatalytic activity in the synthesis of benzaldehyde (BAL) from benzyl alcohol (BA) in an aqueous medium, under visible LED irradiation ( $\lambda_{max}$  = 415 nm) and air flow. At 30 min reaction, the BAL yield in the presence of GCN-NaCl is three times higher than in the presence of GCN-T (Fig.1a). The results are in agreement with the observed quenching of the photoluminescence intensity. This can be explained in terms of the decrease in the recombination of the photogenerated electron-hole pairs. We will present the results based on the reutilization capacity of the materials and their characterization. Additional experiments will be attempted on the photocatalytic synthesis of several value-added molecules.



Figure 1: Photocatalytic production of BAL (a) and photoluminescence spectra (b) using bulk GCN, GCN-T and GCN-NaCl catalysts.

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## Materials

# Ohmic heating assisted synthesis of metallochlorins

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Current synthetic chemistry is on a quest to fulfil most green chemistry requirements through the development of efficient reactions with easily isolated products, while saving time and energy consumption. Various techniques such as microwave irradiation, sonochemistry and photochemistry<sup>1</sup> were already stablished on meeting these requirements. A less explored, but highly potential method for chemical synthesis is ohmic heating ( $\Omega$ H), in which an AC electrical current is passed through an aqueous media which generates heat *in situ*. Additionally,  $\Omega$ H has other advantages such as being environmentally friendly and the possibility of an efficient reaction scale-up.<sup>2</sup> Metallochlorins have been widely explored due to their biomimetic characteristics of chlorophylls, with promising applications as photosensitizers for photodynamic therapy of cancer and as dyes in solar cells. Having previously established an efficient method for the synthesis of several metallochlorins using microwave irradiation,<sup>3</sup> we will now present our results regarding the synthesis of pyrrolidine or isoxazolidine-fused metallochlorins using  $\Omega$ H. Our studies involved the use of different zinc(II) and copper(II) salts (**Figure 1**), in order to evaluate the effect of the different anions (e.g., acetate, chloride or sulfate) in the reaction outcome.



Figure 1: Synthesis of pyrrolidine (X = C) or isoxazolidine (X = O)-fused metallochlorins.

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## **Materials**

## Structural and energetic insights on the o-hydroxyacetonaphthone isomers

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The formation of intramolecular hydrogen bonds (IMHB) in organic compounds can provide them photophysical properties with a multiplicity of applications in various scientific and technological domains. The o-hydroxyacetonaphthone isomers (structural formulae presented in **Figure 1**) present a close proximity and orientation of the carbonyl oxygen towards the hydrogen of the hydroxyl group, enabling the formation of an IMHB.<sup>1</sup> Generally, upon photo-excitation of these compounds a fast acid-base reaction can occur via the IMHB resulting in a tautomeric transformation from the ground state enol form to an excited keto form (excited state intramolecular proton transfer, ESIPT). Compounds displaying ESIPT phenomena are drawing considerable attention due to their unique properties which facilitate novel optoelectronic applications, particularly focusing on chemical sensors, fluorescence imaging, proton transfer lasers, and organic light-emitting diodes (OLEDs); furthermore, they are also used as fluorescence probes on microenvironments of biological systems.

Energetic and structural studies regarding the isomers 1'-hydroxy-2'-acetonaphthone and 2'-hydroxy-1'acetonaphthone were performed based on both experimental and computational research. The massic energy of combustion and the phase transition enthalpies were measured by static bomb combustion calorimetry and Calvet microcalorimetry techniques, respectively. For the computational studies, the G3(MP2)//B3LYP method was used, since it is an appropriate theoretical procedure for this class of compounds. The combination of experimental and computational data enabled the determination of the enthalpies of sublimation and formation of these compounds, both in the crystal and gas phase. The IMHB energetics *o*-hydroxyacetonaphthone isomers and their corresponding tautomeric structures will be also analysed.



Figure 1: Structural formulae for 1'-hydroxy-2'-acetonaphthone (a) and 2'-hydroxy-1'-acetonaphthone (b).

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## **Materials**

## Inversion symmetry breaking polyoxometalates hybrids colloids for heat control

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While colloidal particles usually have spheroid, tubular or lamellar shapes, colloids based on hybrids made of polyoxometalates (POMs) and organic moieties have exotic non-reciprocal shapes, being morphologically different in opposite directions, i. e., breaking inversion symmetry. This peculiar property is key in tools and applications aiming at flow rectification; i. e. applications as diodes and valves where the flow is different in forward and backward direction. In the context of electronics, the development of solid-state diodes controlling the flow of electric charge is a mature field. However, in the context of heat, the development of solid-state diodes is still at their infancy. Solid-state materials behaving as heat diodes are expected to be valuable since chemical, physical and biological processes are intrinsically determined and controlled by temperature. To this aim, we developed arrow-shaped POM-hybrids breaking inversion symmetry (Figure 1) and we show the impact of this symmetry breaking in the conduction of heat across the arrows, based on experimental thermal images and finite element modeling. We found that arrow growth occurs at the surface of precipitates, resembling the growth of chemical gardens. We also found the heat is better conducted in the forward direction of the arrows being side-flushed when conduction occurs in the backward direction, in an agreement between experiment and simulations



Figure 1: Scanning electron microscope images of the colloidal particles obtained. (a and b) cones with different sizes; (c) harpoons; (d, e, f) flowers with distinct features. Temperature maps obtained with finite element analysis on an harpoon (g).

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## Materials

# Extending the functionality of nucleobases through regioselective *N*-derivatization

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DNA is one of the most powerful biomolecules in nature being responsible for storing, encoding and transmitting the genetic information in all living organisms through its basic molecular building blocks - the natural nucleobases (adenine (A), guanine (G), thymine (T) and cytosine (C)). Besides, the high complementary and unique programmability endowed to canonical Watson-Crick base-pairing (A-T and C-G), via highly-selective hydrogen-bonding interactions. has turned nucleobases into remarkable self-assembling units for the bottom-up assembly of intricate yet versatile and functional 2D and 3D supramolecular nanoarchitectures.<sup>1</sup> In fact, the high-fidelity molecular recognition capability assigned to complementary nucleobases is crucial to tailor material's properties in a controlled manner. For example, complementary base-pairing has been used as a reliable method for cross-linking pendent polymers, as well as for patterning functional nanostructures in a very programmable fashion.<sup>2</sup> Having in mind the ability of nucleobases to act as highly versatile organic building blocks, several synthetic methodologies have been developed towards functionalizing such small molecular recognition units with different functional groups for modulating their physicochemical properties and reactivity.<sup>3</sup> Herein, we will present the new synthetic approaches developed towards the more efficient and regioselective N-alkylation and N-allylation of the nucleobases (Scheme 1) as well as the structural characterization of the resulting compounds. Such nucleobase derivatives pave the way for the development of complex and innovative materials and devices with nanoscale features for addressing a wide range of applications, including in biosensing, drug/therapeutic/gene delivery, nanomedicine, tissue engineering and regenerative medicine, as well as in optics, optoelectronics, and energy.



Scheme 1: Nucleobases' chemical structures and representative schematic illustration of cytosine's functionalization.

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## **Materials**

# Gold Nanocluster in a Polymeric Matrix as Hybrid Nanoparticles

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Gold Nanoclusters (AuNCs) are nanostructures with a few gold atoms and dimensions below 2 nm. They have been increasingly studied due to their unique properties, such as size-dependent luminescence, very high photostability, catalytic activity, low toxicity and biocompatibility. [1] Applications across different fields, from medicine and biology to physics and chemistry, include catalysis, sensing, imaging and theranostics.[2]

We are mainly interested in the application of AuNCs as labels for advanced optical imaging and sensing. Our aim is to explore the AuNCs optical properties when these are incorporated in nanomaterials to increase their stability. One of our strategies is to prepare polymer nanoparticles containing a very large number of AuNCs, using miniemulsion polymerization. [3] This allow us to maintain the AuNCs optical properties (NIR fluorescence emission) for imaging and optical targeting.

Polymer-AuNCs hybrid nanoparticles were prepared trough photo-miniemulsion polymerization of methacrylate monomers, resulting in monodisperse nanoparticles with diameters around 50 nm (Figure 1A), high colloidal stability and optimized optical properties. The materials further show emission enhancement in the NIR region upon formation of plasmonic gold nanoparticles (AuNPs) that interact with the AuNCs, [4,5] resulting in an increase brightness of the nanoparticles (Figure 1B).



Figure 1: A) SEM image of polymer nanoparticles containing AuNCs. B) Fluorescence emission spectrum of polymer-AuNCs nanoparticles containing AuNPs (λexc=550 nm)

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#### Materials

## Deepshifts: Towards DFT quality chemical shifts using deep learning

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The emergence of modern artificial-intelligence (AI), led by impressive developments in Deep Learning (DL), is disrupting the role of computational material science by enabling automated characterization and inverse-design of materials. AI-based methods lend themselves to faster execution rates by abstracting the fundamental nature laws into simpler nonlinear models that retain the ability to describe the underlying phenomena being studied.

An area that can highly benefit from this new field of research is NMR chemical shift calculations. The available *ab initio* approaches that take into consideration the full quantum environment of the sample under study are computationally expensive, despite providing accurate results, whereas existing prediction methods, despite executing almost instantaneously, only look at the connectivity map of the sample and, therefore, neglect any neighbour effects that are frequently important (such as explicit solvation, h-bonds, conformation variability, etc). A hybrid model that simultaneously combines *ab initio* like quality and execution speed can enable interesting applications for material characterization.

This communication reports the development of Deepshifts, a state-of-the-art deep learning framework that yields DFT quality <sup>1</sup>H chemical shifts of organic molecules containing H,C,N,O. The model was trained using 2.7 million conformations from 61 thousand molecules, totalizing 50 million <sup>1</sup>H chemical shifts calculated at the B3LYP/6-31G(d,p) level, yielding an average test loss of 0.104 ppm. Preliminary results show that the model simultaneously captures the intrinsic topology of the system and intra/intermolecular arrangements (Figure 1).



Figure 1: DFT vs inferred (Deepshifts) chemical shifts for a cluster of 10 water molecules.

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#### Materials

# ProtoSyn: a prototyping software package for protein modeling and structure prediction

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Protein design is the field of synthetic biology that aims at developing *de-novo* custom made proteins and peptides. One of the challenges of protein design is the correct prediction of 3D conformations of molecules from the amino acid sequence alone. This and other challenging tasks in modern science boil down to the exploration of molecular structures in smart and efficient ways. With this aim in mind, over the last year, we've developed ProtoSyn at CICECO, University of Aveiro: a Julia-based software package for molecular modeling that allows a fast reconnaissance of the conformational 3D space, energy evaluation according to state of the art force fields and smart, customizable algorithms for Monte Carlo and Molecular Dynamics applications.

Using the ProtoSyn API, the correct 3D structures of small proteins (up to 80 amino acids) were predicted to resolutions bellow 3Å in just over 15 minutes (Figure 1) showing promising results and encouraging further development and testing cycles. The main goal of ProtoSyn is to allow scientists to explore and prototype medium to high resolution protein structures in *de-novo* design efforts in a fast, easy and reliable approach.



Figure 1: ProtoSyn: an application programming interface for molecular modeling. The structure of the human hyperplastic discs protein (PDB: 1I2T) was predicted (green) to resolution < 2.5Å in just under 30 min.

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#### Materials

# Tuning the photophysical properties of trans-A2B corroles

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Corroles are aromatic tetrapyrrolic ring-contracted macrocycles and have been attracting considerable attention due to their unique photophysical and chemical properties. The inner core of these macrocycles provides a trianionic coordination sphere able to stabilize metal ions in high valent oxidation state, providing a challenging template for the filling of the so called "periodic table of corroles". In fact, metallocorroles possess key photophysical properties as high excitation coefficients, fluorescent quantum yields, phosphorescence and photostability to be used in different therapeutic applications namely as photosensitizers in photodynamic therapy<sup>1</sup> of oncological and non-oncological diseases, as contrast agents for biomedical imaging, but also as catalysts<sup>2</sup> and sensors.<sup>3</sup> In fact, the development of new strategies for corrole synthesis and adequate functionalization<sup>4</sup> at the  $\beta$ -pyrrolic positions or at the *meso* positions allow the tuning of these photophysical properties for a specific application.

In this communication and under the context of therapeutic applications, we report the synthesis, structural and photophysical characterization of  $A_2B$ -type *meso*-arylcorroles (Figure 1) and of metal complexes adequately functionalized to be used in nanoscale thermometry.



Figure 1: *trans*-A<sub>2</sub>B-Type *meso*-aryl substituted corrole.

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#### **Materials**

### **Development of new Glucose-based Surfactants for Industrial Application**

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Surfactants are currently indispensable molecules because of their cleaning, dispersing, foaming and emulsifying properties. They are extremely used in cleaning products, cosmetics, pharmaceuticals, among ither applications. However, the increased production of surfactants has been associated with some environmental problems.[1, 2] Therefore is imperative to develop new sustainable and viable alternative routes for the substitution of these surfactants, and this can be achieve by the development of new classes of surfactants from renewable sources, such as sugarbased surfactants.

Sugar-based surfactants are amphiphilic molecules containing sugar headgroups and aliphatic tail. They show interesting interfacial properties[3] and excellent ecological behavior due to their biodegradability and virtual lack of toxicity. Sugar based surfactants possess key advantages compared to conventional surfactants and therefore they can potentially replace the latter in the market [4]

In this work, non-ionic and cationic sugar-based surfactants were chemically synthesized and characterized. Glucose was used as the headgroup and two amine derivatives, with different lengths, were used as nonpolar part. Surface tension of the novel surfactants was studied, and the results compared with some of the most commonly used industrial surfactants: diethanolamine cocoamide and dodecyltrimethylammonium chloride, a nonionic surfactant and a cationic surfactant, respectively.

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#### Materials

# Evaluation of Rhodamine B Photocatalytic Degradation Over Ternary Graphene/CuS/Fe<sub>3</sub>O<sub>4</sub> Nanocomposites

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With the discovery of new chemical routes for the synthesis of monolayer graphene, multi-layer graphene and graphene flakes, researchers are actively involved in the incorporation of inorganic nanoparticles on graphene and its derivatives. These materials could be applied as superadsorbents, ultrasensitive sensors, advanced environmental and water splitting photocatalysts, chemical solar cells, fuel cells, and supercapacitor and rapid charging/discharging batteries and many others. In particular, an enormous interest in using graphene oxide (GO) or reduced GO (rGO) as supporting matrix to anchor metal oxide/sulphide nanoparticles, with the aim of preparing novel photocatalysts has been observed<sup>1</sup>. However, the direct grafting of these types of nanoparticles onto graphene without previous modification with oxygen-containing moieties is more attractive, since the presence of oxygen-containing functional groups modifies the electrical conductivity of graphene, which in turn can reduce the nanocomposites efficiency in some applications, e.g., photocatalysis. Keeping these factors in view, we envisage the direct intercalation of graphene nanoflakes (GFs) with metal oxide/sulphide. The high surface area given by the graphene material and the tuned bandgap energy characteristic of metal oxide/sulphide nanoparticles grant the nanocomposites high adsorption of dye molecules and fast photo-excitation of charge carriers respectively.<sup>2</sup>

Herein, graphene-based nanocomposites were fabricated through the combination of GF with CuS (semiconductor with a narrow band gap suitable for visible light photocatalysis) and/or Fe<sub>3</sub>O<sub>4</sub> (semiconductor that can prevent potential CuS photocorrosion with additional benefit of easy magnetic separation of the catalyst). The selection of

Fe<sub>3</sub>O<sub>4</sub> makes it possible to utilize Fenton-type catalysis and constitutes a cost-effective and environmentally-friendly way to depollute textile dyeing industry wastewater.

The adsorptive and photo-Fenton catalytic properties of the GFbased nanocomposites were evaluated using Rhodamine B (RhB) as model dye in a photocatalytic chamber equipped with halogen lamp (150 W) in the absence/presence of  $H_2O_2$ .

The adsorption efficiency for GF@CuS-Fe<sub>3</sub>O<sub>4</sub> was 6.5% after 180 min of contact period, whereas for the other materials was significantly higher: GF 97.6%, GF@CuS 60.9% and GF@Fe<sub>3</sub>O<sub>4</sub> 31.4%.

The photo-Fenton catalytic behavior of all nanocomposites followed the first-order kinetic model (Figure 1). The rate constants of photocatalytic RhB removal for GF@CuS-Fe<sub>3</sub>O<sub>4</sub> was 2.1, 5.1 and 15.0 times higher than those of GF@CuS, GF@Fe<sub>3</sub>O<sub>4</sub> and pristine Fe<sub>3</sub>O<sub>4</sub>, respectively. The GF@CuS-Fe<sub>3</sub>O<sub>4</sub> nanocomposite could completely remove RhB after 60 min irradiation, whereas the GF@CuS, GF@Fe<sub>3</sub>O<sub>4</sub> and pristine Fe<sub>3</sub>O<sub>4</sub> only removed 75.6, 80.9 and 30.8%, respectively.



Fig. 1 First-order kinetic fitting curves of RhB over different photocatalysts: 1 - none, 2 -  $H_2O_2$ , 3 -  $H_2O_2$ /Fe<sub>3</sub>O<sub>4</sub>, 4 -  $H_2O_2$ /GF@CuS, 5 -  $H_2O_2$ /GF@Fe<sub>3</sub>O<sub>4</sub>, 6 -  $H_2O_2$ /GF@CuS-Fe<sub>3</sub>O<sub>4</sub>.

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#### **Materials**

# Inhibition of human neutrophil elastase by mean of enriched polysulfone membrane by synthetic elastase inhibitor

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Chronic kidney disease patients undergoing haemodialysis (HD) treatment suffer from chronic inflammation caused by the disease associated conditions and by the long-term contact of blood with artificial material of HD membrane. As consequence of inflammation, the patients have elevated risk of cardiovascular diseases, and therefore markedly higher mortality rate, compared to healthy population.<sup>1</sup>

One of the promising approach to diminish inflammation is to inhibit human neutrophil elastase (HNE), which is excessively released from overstimulated neutrophils during the HD treatment. Synthetic inhibitors with structure derived from 4-oxo- $\beta$ -lactams showed to be highly potent and selective in inhibition of free circulating HNE. The inhibitors react with an active site of HNE and cause irreversible enzyme inhibition.<sup>2</sup>

The enrichment of HD membrane with inhibitor could provide direct HNE inhibition during the treatment procedure. For this purpose, in-house prepared polysulfone membrane was enriched with newly synthetized inhibitor containing 4-oxo- $\beta$ -lactam structure. The ability of modified membrane to diminish elastase activity was evaluated *in vitro*, using kinetic fluorometric assay. Membrane with identical composition, without inhibitor, was used as a blank membrane.

Two enrichment approaches were evaluated: direct incorporation of the inhibitor into membrane structure during the preparation process; and adsorption on membrane surface after immersion in inhibitor solution.

Using the adsorption technique, we reached the inhibition of HNE activity up to 30 %, while the direct incorporation didn't show such as satisfactory result. Different inhibitor concentrations (100; 50; 20; 10 nM) were used for superficial adsorption to reach the maximal inhibition, however the adsorption capacity of the membrane has to be further studied, in order to obtain the best initial inhibitor concentration. The inhibitor in all tested concentrations was evaluated for haemolytic activity in order to screen the hemocompatibility of the tested compound. None of the evaluated concentration did cause lysis of erythrocytes.

These preliminary results show, that adsorption of the newly synthetized HNE inhibitor on the polysulfone membrane used directly for HD procedure could represent new promising therapeutic strategy to diminish negative impact of elevated HNE levels, presented by the chronic kidney disease patients.

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#### **Materials**

# Non-covalent functionalization of carbon nanotubes: synergistic effects using polymer/surfactant systems as dispersants

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Carbon nanotubes (CNTs) have become important and exciting nanomaterials for a wide range of applications.<sup>1</sup> Because of CNT insolubility in aqueous media, surfactants or surface-active polymers are often used to functionalize and stabilize the exfoliated material, owing to the electrostatic or steric repulsions provided by the adsorbed amphiphile.<sup>2-4</sup> Although surfactant/polymer systems have been extensively investigated<sup>5</sup>, studies regarding their use for non-covalent functionalization of CNTs are scarce. Yet, surfactant/polymer association could greatly enhance the dispersibility and applicability of the CNTs.<sup>1</sup>

Herein, we have explored a methodology to exfoliate highly entangled powders of multi-walled carbon nanotubes (MWNTs), under stringently controlled conditions, in aqueous surfactant/polymer mixtures combining (i) non-ionic surfactant with ionic polymers and (ii) ionic surfactants with non-ionic polymer. From the profile of the dispersibility curves, several quantitative parameters were extracted, which altogether permit reliable comparisons between the different systems investigated. Strong surfactant/polymer synergistic effects were found, with the maximum MWNT dispersibility being attained at much lower dispersant concentration when compared to the individual components. SEM imaging further shows a significant degree of MWNT debundling in the as-obtained dispersions (Fig. 1). These studies are of great interest for the choice of optimal conditions and dispersants to obtain non-covalently funcionalized MWNTs, which can then be applied as building blocks for novel composite materials and nanostructured coatings.



Figure 1: SEM micrograph of MWNTs individually dispersed by a CTAB/PVP mixture.

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#### **Materials**

# New photoactive MOFs assembled by mechanochemical procedures for energy applications

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This communication will present a new approach in the preparation of metal-organic frameworks (MOFs), as active hybrid materials for energy applications. Until today, there is still a limited number of MOFs studied for PVs (photovoltaics), however there are infinite possibilities of porous networks yet to be discovered, with semiconducting behavior and stability over time. The reported structures prepared by solvothermal procedures are mainly assembled with low molecular weight ligands, such as terephthalic acid. The novelty is to introduce ligands and co-ligands with improved light harvesting properties in MOFs, such as diphenyl anthracene (DPA), naphthalene diimides (NDIs) and perylene diimides derivatives (PDIs).

Mechanochemistry stands out as a promising synthetic technique when using high molecular weight ligands, usually extremely insoluble. Additionally, offers an enclosed solvent-free reaction medium with well-defined parameters that enable the optimization of reactivity, with lower reaction times and improved yields [1]. In this communication we will present a successful two step synthesis of a 2-D MOF (CPO-5), where two ditopic ligands, coordinate to zinc units (Scheme 1). Starting from a pure MOF template (FALGEG), the synthesis is straightforward when a second organic entity is added (4,4'-bipyridine). Both functional materials (FALGEG and CPO-5), isolated in bulk quantities, were studied by several solid-state characterization techniques including: powder X-ray diffraction (PXRD), Fourier transform infrared (FT-IR), scanning electron microscopy (SEM); energy dispersive X-ray spectroscopy (EDS), as well as thermogravimetric analysis (TGA). A new, simple and sustainable synthetic route to obtain CPO-5 was developed, and using the same approach, DPyA (9,10-bis(4-pyridyl) anthracene) reactivity was already studied with promising results. A new platform was successfully designed to isolate new MOFs with a wider range of framework complexity (and photoactive response).



Scheme 1 - Schematic representation of the mechanosynthesis assisted methodology to obtain CPO-5. Crystal packing of CPO-5 highlighting the 2-fold catenated structure.

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### **Materials**

# Monomers units for PDLC Smart Windows with PME: the bigger the better?

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I wanted more Cause bigger is better And biggest is best! If you take my advice You'll outshine all the rest!

Cast - Sofia the first

Conventional PDLCs need continuity of energy supply for keeping ON state, which can be a very limiting aspect for many applications. However, PDLCs with PME besides are lower power consumption can be used in digital memory devices based on write-read-erase cycles. For this, a prototype has been assembled as proof of the concept to be used in the digital process of recording information with 1 and 0 language.



Figure 1: PDLC with permanent memory effect unit.



Figure 2: Multiplexing drive scheme of optical data storage in an 8x8 passive matrix using PDLC with permanent memory effect units.

But, will the pre-polymers used to prepare PDLC films with the best PME be the biggest? It seems so, but only to a certain extent. Or with the most branched chains? Or with more crosslinked chains? It seems so, but only to a certain extent.<sup>1-2</sup> Or will the crystallinity of polymers be affected by the size of the pre-polymer chain? It seems not, but only to a certain extent

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#### **Materials**

# Sensing of metal ions in biological media using Europium Carbon Dots

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In the last years, carbon dots (C-dots) have drawn tremendous attention from the scientific community because of their unique photoluminescence properties, high photostability, low toxicity and good biocompatibility.<sup>1-3</sup> In particular, the excellent fluorescent properties of nitrogen doped C-dots have been explored in bioimaging and biosensing. C-dots are described as discrete, quasispherical particles with sizes below 10 nm mainly composed of a carbon core with varying proportions of sp<sup>2</sup> and sp<sup>3</sup> carbons. Several strategies have been proposed to synthesize C-dots that either follow a bottom-up approach, starting from natural organic precursors (citric acid), or a top down approach, starting from bulk carbon materials (e.g. graphite, carbon fibers, graphene oxide). In this work, we proposed a facile one-step hydrothermal synthesis method to prepare C-Dots using citric acid, urea and europium nitrate as the only precursors. The potential application of this europium doped C-dots (C-dots–Eu<sup>3+</sup>) for radiometric sensing of metal ions in biological media was evaluated. A noticeable effect of photoluminescence quenching of Cdots–Eu<sup>3+</sup> was observed only in the presence of silver and mercury (**Figure 1**).



Figure 1: Effect of the metal ion (50 µM) on the photoluminescence emission of the Europium doped C-dots.

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#### **Materials**

### SERS substrates made from centrifugation-deposited silver nanostars

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Surface Enhanced Raman Spectroscopy (SERS) is a highly sensitive analytical technique, allowing detection of trace amounts of analytes. Raman signals are enhanced by several orders of magnitude for analytes adsorbed on silver or gold nanostructured surfaces. The most successful examples of the applications of this technique to the analysis of biomedical samples have been with disposable substrates. These can easily be coupled with portable sensors to be used at the point-of-need.<sup>1</sup> In this work, plasmonic SERS substrates based on silver nanostars (AgNSs)<sup>2</sup>, were produced by an easy and inexpensive method. This method consists on the deposition, by centrifugation<sup>3</sup>, of a colloid of chemically-synthesized AgNSs on an 8x8 mm glass slide. This simple procedure ensure a minimum interference of the AgNSs capping agent on SERS spectra. A high density of AgNSs on the glass surface was confirmed by scanning electron microscopy (Figure 1A). Using standard Raman probes, such as crystal violet and rhodamine 6G as model analytes. Crystal violet was used as a probe when using the 532 nm laser line as excitation, while rhodamine 6G was used for measurements with the 633 nm and the 785 nm laser lines as excitations. Representative Raman and SERS spectra of rhodamine 6G at 10<sup>-2</sup> M and 10<sup>-4</sup> M are shown in Figure 1B. Enhancement factors were calculated by the normalized area of a chosen peak, present both in Raman and SERS spectra. Enhancement factors of 10<sup>4</sup> (crystal violet) and 10<sup>3</sup> (rhodamine 6G) were obtained. These SERS-active substrates obtained by a straightforward method, showed an equal or better analyte detection performance than commercially available substrates, which are much more expensive than the ones described in this work.



Figure 1: A – Scanning electron microscopy micrograph of the substrate (tilted). B – Rhodamine 6G Raman Raman (bottom) and SERS (top) spectra, acquired using the 633 nm line as excitation. Analyte concentrations of  $10^{-2}$  M for Raman and  $10^{-4}$  M for SERS.

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### Nature's inspiration in the design of a multi-responsive molecular machine

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This work presents some results of new bio-inspired molecular devices. Since 2016, with the Nobel prize for Chemistry attributed to molecular machines, the field has gained notoriety across society. One of the most well-known class of devices are rotaxanes, host-guest complexes that resemble a wheel going around an axle. Herein, we present pseudo-rotaxane type devices in which the axle is constituted by a synthetic analog of a natural class of compounds: Anthocyanins, a family of dyes responsible for many colors found in nature. Since lilac's blue to the red of wine, anthocyanins constitute a versatile class of compounds since they can be pH, light and thermal-responsive initiating a complex cascade of reactions (fig.1) that in some cases can be resumed to two major species, one stable at low pH, the flavylium cation (AH<sup>+</sup>), and another at higher (moderately acidic/neutral pH, the trans-chalcone (Ct)<sup>[1]</sup>.

Using the flavylium cation as a part of our axle, we get control over the system and an interchangeable axle, since we can go from the flavylium cation to the trans-chalcone and vice-versa using external stimuli. Besides pH, many chalcones respond to light by isomerizing to the cis form. At an adequate pH, although the trans-chalcone is the thermodynamic product, the flavylium cation can be metastable and remain in that form for a few hours, until thermal re-conversion to Ct.

This work will then present some results on the formation of supramolecular complexes between a flavylium type derivative that contains a bipyiridium moiety and a macrocycle like the pumpkin shaped cucurbiturils (Scheme 1). The stoichiometries of complex formation will be analyzed and the complex studied, essentially, by NMR and other spectroscopic techniques such as UV-Vis absorption and fluorescence emission. Due to the presence of the electrosensitive moiety, cyclic voltammetry was also used to characterize the complex.



Scheme 1: Pseudo-rotaxane formed between flavylium derivative and cucurbit[7]uril. The macrocycle moves around the axle when flavylium chages to *trans*-chalcone and vice-versa.

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# Comparing Hydrogen- with their Fluorine-moieties Counterparts in Ionic Liquids: Heat Capacities and Vaporization Properties

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Fluorinated ionic liquids (FILs), defined as ILs composed of cations or anions (or both) containing perfluoroalkyl chains with a number of carbon atoms  $C \ge 4$ , have unique properties, e.g., a powerful tensioactive character, which can be profitably used in the handling of biomaterials and in separation processes.<sup>1</sup> At a molecular level, if the anions or the cations also contain sufficiently long hydrogenated alkyl chains, they constitute the first example of liquids presenting three well-defined nanostructured domains (polar, apolar hydrogenated, and apolar fluorinated).<sup>2</sup>

Basically, to date, no accurate vaporization studies have been performed for FILs. Herein, the vapor pressure of neat, highly pure, ILs with perfluoro-sulfonate anions, namely,  $[C_2C_1Im][CF_3SO_3]$ ,  $[C_2C_1Im][C_4F_9SO_3]$  and  $[C_2C_1Im][C_8F_{17}SO_3]$ , (**Scheme 1**), has been measured and the standard ( $p^0 = 10^5$  Pa) molar enthalpies and molar entropies of vaporization have been calculated. A high-accuracy Knudsen effusion apparatus, combined with a quartz crystal microbalance, was used.<sup>3</sup> Moreover, the heat capacities at T = 298.15 K of the studied ionic liquids were measured, for the first time, using a high-precision heat capacities, have also been measured for ILs with hydrogenated-sulfonate anions,  $[C_2C_1Im][CH_3SO_3]$ ,  $[C_2C_1Im][C_4H_9SO_3]$  and  $[C_2C_1Im][C_8H_{17}SO_3]$ .

MD Simulations have been performed to gain insights into their structure and interactions, and the simulated vaporization properties have been compared to the experimental ones.



Scheme 1: Fluorinated Ionic Liquids: 3-methyl-2-ethylimidazolium cation and perfluoroalkyl-sulfonate anions.

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#### Materials

# Preparation and characterization of nanostructured substrates for application in SERS spectroscopy

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The RamSERS project proposes the development of a highly innovative solution that combines a portable Raman instrument with the use of innovative SERS substrates with innovative functionalization strategies with a high sensitivity for breast cancer biomarkers. One of the steps of this project is the preparation and characterization of nanostructured substrates for application in surface-enhanced Raman scattering (SERS) spectroscopy, namely polyethylene terephthalate (PET) substrates with silver and copper nanoparticles. In the case of silver nanoparticles (AqNPs) synthesis, the research was done based on the possible simplification of the Turkevich's method. As described in the literature<sup>1</sup>, the formulation of this method implies a reduction reaction of the silver cation by a reducing agent, so the AgNPs were synthesized by chemical reduction of the silver nitrate using trisodium citrate dihydrate as the reducing agent (Scheme 1). Regarding copper nanoparticles (CuNPs), after a literature study, the synthesis was based on the methodology of Tang et al.<sup>2</sup>, consisting of the use of ethylene glycol (C<sub>2</sub>H<sub>6</sub>O<sub>2</sub>) as solvent, sodium hypophosphite monohydrate as reducing agent and hexadecyltrimethylammonium bromide (CTAB) and polyvinylpyrrolidone (PVP) as stabilizers (Scheme 1). In order to prepare the substrates is necessary to subject the PET to an activation with 40% (v/v) ethylenediamine before nanoparticles deposition take place. Several methods of proceeding to the deposition of the nanoparticles on the PET were also studied, being the centrifugation the chosen method. Throughout the process of preparation of the substrates several characterization analyses were performed, such as UV-Vis spectroscopy and dynamic light scattering (DLS) of the nanoparticle synthesized solutions, FTIR-ATR, atomic force microscopy (AFM), scanning electron microscopy (SEM) and, of course, Raman spectroscopy of the nanostructured substrates. Nanostructured substrates with AgNPs showed enhancement factors of 10<sup>6</sup>, however, as regards CuNPs, a good stabilization on PET deposition has not yet been achieved.



Scheme 1: Silver and copper nanoparticles synthesis, PET deposition and characterization.

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# Removal of emerging contaminants (PhACs) in water by polymer membranes

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Human activity and population growth have led to the increase of pollutants in surface waters. Among the main pollutants are the active pharmaceutical compounds (PhACs). These have been detected in effluents from wastewater treatment plants (WWTP), demonstrating resistance to elimination by conventional treatments. In this way concentrations of these compounds that could be toxic and cause harmful effects on human health and aquatic species can reach the freshwater bodies and domestic networks (1). The membrane filtration processes stand out as promising alternatives for the final quality of the water, easy operation, low costs and less space required. The polysulfone membranes (PSU) have been used in microfiltration and ultrafiltration processes due to their physical-chemical resistance and thermal stability. However, its main disadvantage is fouling of the membrane due to its hydrophobic nature, which decreases the permeate flow over time. To counteract this problem additives are incorporated in the membrane to improve its hydrophilic character (2). The objective of this work is to study the effect of the presence and concentration levels of PSU, polyvinylpyrrolidone (PVP) and polyethylene glycol (PEG) on the hydrophilic characteristics of the membranes. The influence of the molecular weight of the PVP and PEG additives separately on the performance of the membranes will also be evaluated. In the future, the incorporation into the membrane of chelating chemical compounds will be evaluated for the removal of different compounds, in particular non-steroidal anti-inflammatory drugs (NSAIDs), in waters for domestic consumption.

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#### **Materials**

# A molecular dynamics study of 2-mercaptobenzothiazole in (Zn<sub>2</sub>Al) layered double hydroxides

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The 2-mercaptobenzothiazole (MBT) molecules intercalated in Mg-Al or Zn-Al LDHs provide an active protection effect.<sup>1</sup> The difficulty to characterize the interlayer of LDH with experimental techniques demands theoretical methods. In the interest of computational tractability, the choice for investigating these systems relies on the classical molecular dynamics (MD) simulation approach.<sup>2</sup>

It this communication, we will present the results of a MD study of a realistic  $Zn_2AI$  layered double hydroxide (LDH) model with intercalated MBT species. Neutral and anionic forms of MBT were used to span a significant pH range, with the aim of unveiling the structure and composition properties of the systems prepared in the experimental laboratory. With that goal in mind, the proportion of MBT and water molecules in the LDH interlayer was correlated with experimental x-ray diffraction (XRD) data.<sup>3</sup>

The analyses of the trajectories with several different analytic tools explained the MBT/water and MBT/MBT<sup>-</sup> equilibrium inside the LDH and the interactions responsible for the experimental observations (XRD and thermal gravimetic analysis, TGA). The distribution of molecules in the LDH interlayer shows a layer of water near the hydroxides, a second layer grown over the first layer, the sulfur of the thioamide group of MBT facing the surface of LDH, and the 6-member rings directing to the interlayer for avoiding the water molecules.

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# C2 Methylation effect on the 1-Alkyl-2,3-dimethylimidazolium Trifluoromethanesulfonate Ionic Liquids

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This work presents the study of the methylation effect at the C2 position of the imidazolium ring on the physicochemical properties of ionic liquids (1-alkyl-2,3-dimethylimidazolium trifluoromethanesulfonate ionic liquids,  $[C_nC_1C_1im][OTf]$  (n = 2,4, see **Figure 1**). The thermal behavior and thermal stability of both ionic liquids was evaluated by differential scanning calorimetry and thermal gravimetry respectively. High precision, isobaric heat capacities, of these two ionic liquids were measured using a drop calorimeter.<sup>1</sup> The temperature dependence of the vapor pressure was measured by a Knudsen effusion method combined with a quartz crystal microbalance.<sup>2</sup>



Figure 1: Molecular structure of  $[C_nC_1C_1im][OTf]$  (n=2,4).

The experimental vapor pressure data was fitted to the integrated form of the Clausius-Clayperon equation and the enthalpies and entropies of vaporization were derived. The effect of C2 methylation will be evaluated and analyzed by comparison with the physicochemical properties of the non-methylated analogues.

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# Synthesis and Characterization of Doped 2D Materials for the Photocatalytic Reduction of CO<sub>2</sub>

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Worldwide energy demand is increasing with the increase in human population and the global improvement of life conditions, leading to higher consumption of fossil fuels and to the increase of CO<sub>2</sub> emissions.<sup>1</sup> Therefore, the development of new sources of energy is of great interest to the scientific community in the XXI century. Nowadays, several technologies that can transform renewable energy into fuels have been studied and applied, such as solar energy. Among these technologies, the photocatalytic reduction of CO<sub>2</sub> in water is of great interest because it utilizes CO<sub>2</sub> as a carbon feedstock for the production of fuels, with solar light as a source of energy.<sup>2</sup> The photocatalysts currently in use for the CO<sub>2</sub> reduction suffers from low visible light absorption and high electronhole recombination.<sup>3</sup> Therefore, the development of efficient and selective photocatalysts for this process is a major goal.4

In the present work, several two-dimensional (2D) photocatalysts were developed and characterized by different techniques. Graphitic carbon nitride, g-C<sub>3</sub>N<sub>4</sub> (g-CN) was synthesized by thermal decomposition of dicyandiamide yielding bulk g-CN, followed by a thermal treatment to obtain g-CN nanosheets.<sup>5</sup>

Reduced graphene oxide (rGO) was synthesized from commercial graphite by a modified Hummers' method followed by reduction with ascorbic acid.<sup>3</sup> Molybdenum disulphide (MoS<sub>2</sub>) was prepared by a one-step reaction of potassium thiocyanate and molybdenum trioxide, in a teflon-lined autoclave at 180 °C and autogenous pressure. Several composites of MoS<sub>2</sub>/rGO and MoS<sub>2</sub>/g-CN, with different percentages of rGO and g-CN, were also prepared by impregnation.

The morphology of the materials was studied by scanning electron microscopy (SEM). The texture and surface chemistry of the materials were studied by N<sub>2</sub> adsorption-desorption, infra-red spectroscopy (FTIR-ATR), X-ray photoelectron spectroscopy (XPS) and by thermogravimetric analysis (TGA). The photocatalysts were also characterized by diffuse reflectance spectroscopy (DRS), steady-state photoluminescence (PL) and X-ray diffraction (XRD).

The photocatalytic activity of the materials was assessed towards CO<sub>2</sub> reduction using a medium pressure mercury lamp as light source (UV-visible).

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# A trinuclear oxidodiperoxido-molybdenum(VI) complex with single triazole bridges

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Triazoles (1,2,3-triazole and 1,2,4-triazole) are especially interesting since they combine the coordinative abilities of both pyrazoles and imidazoles.<sup>1</sup> They are effective ligands for bridging Mo<sup>VI</sup> centers that are also linked by  $\mu$ - $\dot{O}^{2-}$  groups.<sup>2</sup> We have been studying triazolylmolybdenum(VI) oxide hybrids as (pre)catalysts for the oxidation of olefins (epoxidation), sulfides, alcohols, and aldehydes.<sup>3-5</sup> The use of 1,2,4-triazole leads to [MoO<sub>3</sub>(trz)<sub>0.5</sub>] consisting of layers of corner-sharing {MoO<sub>5</sub>N} octahedra with the organic subunits projecting into the interlamellar regions.<sup>2, 3</sup> The compound displayed a truly unique reaction-induced self-separating (RISS) catalytic behavior when used with aqueous H<sub>2</sub>O<sub>2</sub> as oxidant.<sup>3</sup> It reacts with the oxidant to form a soluble active species and exhaustion of the oxidant leads to spontaneous reassembly of the 2D structure of [MoO<sub>3</sub>(trz)<sub>0.5</sub>]. Finally the compound precipitates, allowing straightforward recovery and reuse. This was, to our knowledge, the first report of a self-precipitating catalyst with an extended 1D, 2D or 3D crystalline structure. To better understand the behavior of [MoO<sub>3</sub>(trz)<sub>0.5</sub>] as a RISS catalyst, it was necessary to ascertain the nature of the active species formed in solution. To this end we have studied the reaction of MoO<sub>3</sub> with H<sub>2</sub>O<sub>2</sub> in the presence of 1,2,4-triazole, and after isolation obtained the trinuclear oxidoperoxido complex (Htrz)<sub>2</sub>[Mo<sub>3</sub>O<sub>6</sub>(O<sub>2</sub>)<sub>4</sub>(trz)<sub>2</sub>]·H<sub>2</sub>O. The trinuclear species is the first example of a discrete Mo<sup>VI</sup> complex bearing 1,2,4-triazole ligands, and a rare case of a discrete metal-triazole complex that contains only single [M-(N-N)-M] bridges. The compound was explored in olefin epoxidation with hydroperoxides, epoxide alcoholysis, and aldehyde acetalization.

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#### Materials

# Proteoglycan mimic copolymers by glycosaminoglycan end-on ligation

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Glycosaminoglycans (GAGs) are negatively charged polysaccharides present in the extracellular matrix (ECM) and basement membrane of multicellular organisms. In their native environment, GAGs are usually presented as brush-like molecules – proteoglycans (PG) – in which the polysaccharide moiety is attached by its reducing end to a core protein chain. PGs can serve as protein reservoirs (growth factors, chemokines and cytokines), protecting them from enzymatic degradation, or triggering cell signaling pathways.<sup>1</sup> Because of these multiple roles, GAGs have been proposed as therapeutics for a variety of diseases such as thrombosis, amyloid diseases and therefore efforts have been made by preparing glycopolymers that mimic their properties.<sup>2</sup> However, most of the currently available approaches for synthesis of PG mimics have two main disadvantages: they either include modification of the GAG's main chain blocking the functional groups responsible for their bioactivity or (Fig.1a) use oligosaccharides which are, in our opinion, too short to mimic the multivalent interactions governing the GAG bioactivity (Fig 1b).<sup>3</sup>

Herein, we show that GAGs (hyaluronic acid, chondroitin sulfate and heparin) with high molecular weight can be conjugated via their reducing end to different branched synthetic cores by oxime reaction and thus to generate multivalent star (Fig.1c)- and brush-like (Fig. 1d) copolymers.<sup>4</sup> We further demonstrate that the bioactivity of the conjugated GAGs is preserved: they bind specifically growth factors (e.g. FGF-2, determined by isothermal titration calorimetry) and the bioactivity of the copolymers is proportional to the number of the grafted GAG chains. The obtained PG mimics self-assemble with proteins into microfibers that can be valuable as ECM mimics.



Figure 1

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#### **Materials**

### Characterization of thyme essential oil by NMR spectroscopy

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Essential oils are plants secondary metabolites, which are widely used in the perfumery, food and pharmaceutical industries. In general, volatile oils or essential oils are predominantly constituted by two or three components, mostly terpenic hydrocarbons and terpenoids. *Thymus vulgaris* L. (Lamiaceae) is native from the southern Europe and the Mediterranean, where it has been used since ancient times as a flavor ingredient in culinary. In addition to its use in foods, *T. vulgaris* is a well-known herbal medicine that has been used for thousands of years to treat alopecia, dental plaque, dermatophyte infections, bronchitis, cough, inflammatory skin disorders and gastrointestinal distress. The major constituents of commercial *T. vulgaris* essential oil are thymol (23%–60%),  $\gamma$ -terpinene (18%–50%), *p*-cymene (8%–44%), carvacrol (2%–8%), and linalool (3%–4%). *T. vulgaris* oil, as well as thymol, have shown antibacterial, antifungal, and anti-inflammatory effects, accounting for its the medicinal uses. Several chemotypes of thyme, based on essential oil compositions, have been established, including thymol, carvacrol, linalool, borneol, geraniol, sabinene hydrate, as well as a number of multiple-component chemotypes.<sup>1</sup>

The quality of essential oils has been widely evaluated by gas chromatography coupled to mass spectrometry (GC-MS) and gas chromatography equipped with a flame ionization detector (GC-FID). Typically, analysis by these techniques take around 90 min and this is a limiting factor in situations where time is determinant. The quantification of the major constituents of commercial essential oils is vital, because they are extracted from different sources and their price varies with their content. Unlike chromatography, nuclear magnetic resonance (NMR) spectroscopy is a quick and non-destructive method, and it does not require calibration curves. The NMR method allows simultaneous quantitation of many components using one internal standard and a single spectrum. Moreover, it is not necessary to employ a high purity internal standard similar to the analyte of interest for accurate quantification. In addition, NMR can be used for quantification of compounds that degrade at elevated temperatures, which cannot be determined by GC.<sup>2</sup> The aim of this work was to characterize and quantify the major constituents of thyme essential oil using different NMR techniques. In a first approach, using <sup>1</sup>H, <sup>13</sup>C and 2D NMR, it was possible to identify the main compounds thymol, pcymene and  $\gamma$ -terpinene, thought the observation of the aromatic ( $\delta_H$  9-6 ppm) region. However, due to the extensive overlap of peaks in the other zones of the spectra, it was not possible to identify the multiple signals observed in these regions. Fractionation of the oil was then carried out by column chromatography and the characterization of the resulting fractions by the same techniques enabled the identification of a considerable number of other components such as linalool, myrcene, thymol methyl ether and carvacrol methyl ether. A quantitative method using <sup>1</sup>H NMR, could be also implemented enabling to quantify almost all the constituents identified in the oil. This quantification method could be a powerful tool to perform a rapid assessment of the essential oils composition and to evaluate their stability.

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#### **Materials**

# Novel Imidazole Based Azo Dyes as New Chemosensors

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Azo dyes account for 60–70% of all dyes produced in the world. They are the most dominant artificially synthesized dyes that are widely used in various types of industries such as ink, paper, leather, plastic, textiles, food additives, therapeutic agents etc. Azobenzenes have been targeted for potential applications in areas of electronics, drug delivery, nonlinear optics, optical storage media, chemosensors, liquid crystals, photochemical molecular switches, molecular shuttles, nanotubes and in the manufacture of protective eye glasses and filters. A major challenge of their interest in this area is the development of chromophores with characteristics like high chemical stability, thermal stability over a wide temperature range and having two forms easily detectable by a method that does not cause irreversible molecular alterations.<sup>1,2</sup>

In contrast to azobenzenes, heterocyclic azo compounds are less well investigated, although they have shown brilliant color and chromophoric strength.<sup>2</sup>

Here we report novel heterocyclic azo compounds with interesting photochemical properties. In a recent work, novel imidazole azo dyes were prepared in mild reaction conditions through an efficient method. All the products were isolated as dark red solids and their structures were assigned on the basis of <sup>1</sup>H, <sup>13</sup>C and 2D NMR and IR spectroscopy. These solids exhibited visual color changes in acid and basic solutions ranging from deep blue, to brilliant red colors. Solvatochromic effects were also observed in a series of polar and non-polar solvents. These visual changes were further studied by UV-Visible and NMR spectroscopy to investigate the photochemical behavior of these new molecules. Photochemical properties observed could be rationalized on the basis of the *cis-trans* isomerism and tautomeric equilibrium. These properties may found wide applications in various fields of science and technology, such as chemosensors and optical switches.

Characterization data and photochemical properties of these novel imidazole based azo dyes will be presented and discussed.

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#### Materials

## Valorization of sugars obtained by liquefaction of lignocellulosic materials

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Wood residues are raw materials for the extraction of sugars resulting from depolymerization of the lignocellulosic biomass.<sup>1</sup>This accessible and abundant materialhas also been used for bio-oil production,<sup>2</sup> and has a unique potential as a sustainable source of energy,<sup>3</sup>and of sustainable materials.

The components present in the wood biomass are cellulose, hemicellulose and lignin. Among these components, hemicellulose and cellulose can lead to the formation of simple sugars by the liquefaction process, while lignin leads to the formation of phenols, which composition is still thoroughly investigated.<sup>4</sup>The study of lignocellulosic biomass liquefaction process remains a challenge as the chemical reactions and mechanisms occurring during the liquefaction process are not yet clear.<sup>5</sup>

Residues of eucalyptus wood are composed of 45% cellulose, 17% pentoses and 22% insoluble lignin. However, fractions composed of sugars, originated by the process of liquefaction, have not yet undergone thorough studies and characterization, and their valorization toward a sustainable process is also not yet accomplished.

The objective of this work is to investigate the recovery of sugars from the eucalyptus liquefaction process. The relevance of this research stems from the lack of in - depth investigations that elucidate the resulting mixtures and lead to the characterization of the sugars generated during the process. The aqueous fraction originated by the process of liquefying the biomass of the eucalyptus will be determined and evaluated, as well as its components which may be used for industrial or agro-industrial applications, and as raw material for the production of compounds with potential as antioxidants or for the pharmaceutical industry.

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#### Materials

### Handling fine chemicals thermokinetics in risk management

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In case of exothermic decomposition reactions, the heat flow observed is proportional to the reaction rate. If the sensitivity of the equipment that measures this heat flow is known, and the assumption is made that the decomposition proceeds via an n<sup>th</sup> order reaction, one can use a conservative activation energy to extrapolate a reaction power output at a given temperature of interest.

Due to the high amount of heat generally released during decomposition reactions, their triggering probability needs to be calculated and a process safe working temperature established. The time to maximum rate under adiabatic conditions (TMR<sub>ad</sub>) characterizes the amount of time for decomposition to take place at a given temperature and represents the probability of occurrence of a thermal runaway – under an unexpected scenario, a larger TMR<sub>ad</sub> leads to more time for the plant operators to apply the corresponding safety measures thus avoiding a thermal runaway. This type of methodology is routinely employed at Hovione where the R&D Technologies and Process Safety group makes use of the Differential Scanning Calcrimeter's low cost and high throughout as a powerful ally in thermal

makes use of the Differential Scanning Calorimeter's low cost and high throughput as a powerful ally in thermal degradation screening studies. In fact, this allow us to use only a few milligrams of highly valuable material in detriment of more complex and time-consuming methods. In this context, a few case studies are disclosed where this approach was used to effectively manage manufacturing processes hazards risk.



Figure 1: Schematic representation of a runaway scenario and the practical meaning of time-to-maximum-rate under adiabatic conditions (TMR<sub>ad</sub>). Tp – Manufacturing process temperature;  $\Delta T_{ad}^{dec}$  – Adiabatic temperature rise for the decomposition reaction.

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#### Materials

# New Tetracopper(II) Homogeneous Catalysts for Mild C–H Functionalization of Alkanes

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Three new tetracopper(II) coordination compounds were easily generated from  $Cu(NO_3)_2$ , a trifunctional aminoalcohol sulfonic acid (H<sub>3</sub>bes, *N*,*N*-bis(2-hydroxyethyl)-2-aminoethanesulfonic acid) as a principal building block, and a benzene carboxylic acid as a supporting ligand (i.e., benzoic (Hba), 4-hydroxybenzoic (Hfba), or 3hydroxybenzoic (Hthba) acid). The obtained microcrystalline products,  $[Cu_4(\mu-Hbes)_3(\mu-H_2bes)(\mu-L)]\cdot 2H_2O$  (L = ba<sup>-</sup> (1), fhba<sup>-</sup> (2), and thba<sup>-</sup> (3)), were isolated and fully characterized by FTIR (Fourier-transform infrared spectroscopy), elemental analysis, ESI-MS (Electrospray Ionisation Mass Spectrometry), and single-crystal X-ray diffraction methods [1]. Compounds 1–3 were applied as efficient and versatile homogeneous catalysts in the oxidative C–H functionalization of alkanes (propane and cycloalkanes) showing a remarkable level of activity. Two different model reactions were explored: (1) mild oxidation of alkanes with hydrogen peroxide to give alcohols and ketones, and (2) mild carboxylation of alkanes in the presence of carbon monoxide, water, and potassium peroxodisulfate to give carboxylic acids [Scheme 1]. For these reactions, effects of different parameters (acid promoter effect, loading of substrate, oxidant and catalyst, substrate scope, and effect of water), as well as mechanistic and selectivity characteristics, were studied and discussed [2,3].



Scheme 1: Model hydrocarbon oxidation reactions catalyzed by bioinspired tetracopper(II) cores.

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#### CMP96

#### Materials

### Structural effects on the linear and nonlinear properties of nanographenes

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Due to their optical properties, water solubility and easy functionalization carbon dots (CDots) became especially attractive as a platform for biomedical (imaging, sensing, drug delivery). However, their uncontrolled synthetic procedures led to a quite heterogeneous material making it impossible to control its properties and engineering the material for specific applications.<sup>1</sup> To overcome this limitation, we initiated the study of the photophysical properties of well-defined nanographenes containing heptagonal carbocycles mimicking the structure of CDots. The step-by-step controlled synthetic procedure of these molecules leads to a homogenous material with well-defined molecular structure.<sup>2</sup> The presence of seven-membered rings induces a saddle-shape curvature in the planar network pushing the structure out of the plane affecting significantly their linear and nonlinear properties. For a set of nanographene molecules, the effect of the nature of the edge groups, the distortion from planarity and the conjugation length on the photophysical properties were studied, with emphasis on the two-photon absorption and emission.

Figure 1 illustrates the differences in the emission spectra and the two-photon absorption maxima with the changes on molecular structure of nanographenes and CDots.



**Figure 1.** Comparison between the Emission spectra (left) and the Two-photon brightness connected with the FWHM of the emission for new nanographene molecules (2hc, 2h, 2hbc, 1ho), ribbon-shape nanographene (2hlc) [2] and CDots [1].

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# COMUNICAÇÕES EM Painel

A TABELA PERIÓDICA LUMINESCENTE MATERIAIS, ENERGIA E NANOTECNOLOGIA

#### Energy

# Amine Functionalized Perylenediimides: Influence of the Number and Position of Substituents on the Optical and Electrochemical Properties

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The quest for a sustainable energy future is linked to the development of novel materials with enhanced structural, photochemical and electrochemical properties. Perylenediimides (PDIs) show interesting properties, such as near-unity fluorescence quantum yield, excitation in the visible/NIR region, strong and reversible electron-accepting character, and high electron mobility [1]. Recently they have been extensively studied as organic field-effect transistors, as fluorescent solar collectors, in organic photovoltaics, or as bioimaging agents.[2]

The properties of PDIs can be modulated by introducing appropriate substituents in the imide group (to change solubility or allow immobilization) or in the perylene core (bay or ortho positions, affecting the electronic and optical properties). Our group have shown how bay substituents induce different torsion angles to the perylene core for crystalline organic semiconductors [3] or tune the photophysical properties (visible to NIR fluorescent emission) for bioimaging [4].

In this communication, we evaluate the influence of the number and position of amine substituents in the bay region, namely pyrrolidine, on the optical and electrochemical properties of the final derivatives. A detailed comparative studiy based on these molecules shed light on the substitution effect and intermolecular interactions in their photophysical and electrochemical properties.





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#### Energy

### BODIPY (meso-phenyl-meso) dimer as photovoltaic material

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Derivatives of boron-dipyrromethene (BODIPY) constitute an important class of chromophores. The BODIPY dyes can be applied in an extensive variety of applications, such as cellular imaging, photodynamic therapy, drug-delivery or organic photovoltaics [1-4].

The strong absorption in the visible spectra region, the photochemical and chemical stability, good solubility, the general suitable HOMO/LUMO frontier orbital energy levels, made BODIPYs excellent compounds to be applied as electron-donor materials in organic photovoltaic cells.

Following our own work on the use of BODIPYs as photovoltaic materials [5], in this communication we present the synthesis and characterization of a *meso-meso* BODIPY dimer. This BODIPY dimer has all the main properties to work efficiently as electron-donor material since it exhibits strong absorbance in the visible spectrum, good solubility and suitable HOMO and LUMO energy orbitals to work as donor material in the bulky heterojunction BODIPY/PCBM layer, based solar cells.



Figure 1: BODIPY (meso-phenyl-meso) dimer and its frontier molecular orbitals

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#### Energy

# Thermochemical studies of *N*-phenylmorpholine and *N*-(4-piperidinyl)morpholine

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Morpholine derivatives have relevant applications in broad areas of the industry (namely as corrosion inhibitors, dye solvents, textile lubricants, ink eradicators, and optical brighteners), in the pharmaceutical area (synthesis of analgesics, local anaesthetic, antidepressants and antibiotic agents), as well as in the agriculture (as bactericides, fungicides, herbicides, and antioxidants.)

Experimental and computational studies of *N*-phenylmorpholine and *N*-(4-piperidinyl)morpholine were performed to evaluate and understand the energetic effects inherent to the substitution of the hydrogen of the amino group in the morpholine scaffold<sup>1</sup> by phenyl and 4-piperidinyl substituent groups (**Figure 1**). This communication reports the standard energies of combustion and the standard enthalpies of sublimation of those two morpholine derivatives obtained from combustion calorimetry and Calvet microcalorimetry measurements, respectively. These data were used to derive the standard enthalpies of formation of each compound, in the crystal and gaseous phases, at T = 298.15 K. Computational calculations were performed using the G3(MP2)//B3LYP composite method.

The structural changes and the inherent energetic effects associated with the presence of different substituents in the amino group will be analysed.



Figure 1: Structural formulae for morpholine (a), N-phenylmorpholine (b) and N-(4-piperidinyl)morpholine (c).

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#### Energy

# Thermochemical study of $\gamma$ -butyrolactone

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The access to thermochemical parameters of the compounds and their correlation with the corresponding chemical structures has been contributing for several decades, for the development of the knowledge on the reactivity of species. In fact, the knowledge of thermodynamic and structural properties of compounds are relevant tools on the design of new routes of synthesis leading to new materials with different characteristics and applications. The lactones constitute a family of compounds widely used as natural flavourings and as fragrances, among others.<sup>1-3</sup> In this work we describe the thermochemical study of  $\gamma$ -butyrolactone (**figure 1**), in order to clarify incoherent thermodynamic data available in the literature. To realize the experimental study, we used static-bomb combustion calorimetry and Calvet microcalorimetry techniques. The data obtained allowed to derive the enthalpies of formation in liquid and gaseous phases, and the enthalpy of vaporization. The results will be discussed in comparison with related ones available.



**Figure 1:** Molecular structure of  $\gamma$ -butyrolactone.

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#### Energy

# $\mu$ FlowCal: High resolution differential flow microcalorimeter for the measurement of heats of mixing/reaction

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In this work is presented the description, test and performance of a new differential microcalorimeter, " $\mu$ FlowCal". The  $\mu$ FlowCal is a twin microcalorimeter of the heat conduction type, designed to work in isothermal conditions. This calorimeter was designed to measure precisely and accurately the heat of mixing of two fluids (200  $\mu$ L of pure compounds or mixtures) in all ranges of composition in isothermal mode and in a range of temperatures close to room temperature.

The mixing of the two fluids takes place in a borosilicate glass micromixer/microreactor (model LTF-MX of the MR-Lab Series of the Little Things Factory) assembled horizontally. The reactor's design (see scheme 1) allow the liquids to be mixed in a series of two layer crossed channels promoting mixing by repeated level change and cross flow and then to flow through a unique channel for a certain path in the reactor. Heat flow sensors are localized above and below the reactor, in this two different areas, allowing the monitoring of the heat flow in the mixing area and after (scheme 1). Four aluminium blocks conduct the heat from/to the reactor to/from the four Peltier thermopile heat flow sensors (Peltier elements, model HT4-6-F2-2143 of the ThermaTEC<sup>TM</sup> Series of Laird<sup>TM</sup> Thermal Systems). The microcalorimetric signal consists in two independent heat flow signals. To guarantee isothermal conditions the calorimeter was constructed with a heat sink of high heat capacity, providing inertia to temperature fluctuations, and it is inserted in a thermostated air box that guarantees a short-time temperature fluctuation of the microcalorimeter heat sink block better than  $\pm 10^{-4}$  K.



Figure 1: Schematic presentation of the *µ*FlowCal principle of operation and view of the main constituents of the microcalorimeter core.

The calorimeter was calibrated electrically by Joule effect, testing different power levels. Enthalpies of dilution of aqueous sucrose solutions were measured testing the performance of the calorimeter and the influences of the flow rate, the injected volume and the viscosity in the calorimetric results. Calorimetric signal was also evaluated concerning its short and long-time noise, linearity and baseline drift.

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#### Energy

# Electrocatalytic behavior towards OER of POM@ZIF nanocomposites prepared via a room temperature 'in situ' approach

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The continuous and dramatic increase of global demand for energy resources makes it urgent to develop affordable nanostructured materials to act as efficient electrocatalysts (ECs) in the energy-related reactions. Specifically, the efficient electrocatalysis of the oxygen evolution reaction (OER), the half-reaction for the water splitting process, will be crucial for the real implementation of fuel cells, regenerative batteries, and electrolyzer systems. Some oxides containing platinum group metals (PGMs), e.g., ruthenium and iridium oxides (RuO<sub>2</sub> and IrO<sub>2</sub>), have been reported as the materials with the best electrocatalytic performances for the OER process. However, the extremely elevated costs of PGMs, along with the scarceness and lack of reliable suppliers, strongly encouraged the research on development of alternative and affordable OER electrocatalysts.<sup>1</sup> Regarding this challenge, the desirable features shown by Zeolitic Imidazole Frameworks - ZIFs - (RT synthesis, high and ordered porosity, N-containing ligands and different metal compositions) and PolyOxoMetalates - POMs - (anions consisting of three or more transition metal atoms linked together by oxygen atoms, exhibiting attractive electrocatalytic properties) makes that the efficient integration of POMs anions into the ZIF cavities in order to produce electrocatalytic nanocomposites became a hot topic during the last years.<sup>2</sup> For this reason we have successfully prepared several novel POM@ZIF nanocomposites via RT 'in situ' approach, synthesizing ZIF-8(Zn) and ZIF-67(Co) in the presence of two different Co-containing POMs -SiW<sub>11</sub>Co(H<sub>2</sub>O)O<sub>39</sub> and SiW<sub>9</sub>Co<sub>3</sub>(H<sub>2</sub>O)O<sub>39</sub> - at different concentrations. This has allowed us to assess the effect of the Co atoms interactions on the electrocatalytic activity exhibited by these new nanomaterials, as well as, the influence of



the POM loading on their structural and electrocatalytic features. Thus, the POM@ZIF structures have been characterized by ICP-OES, XRD, XPS, IR and SEM analysis and, finally, their electrocatalytic behaviour were tested by cyclic voltammetry (CV), and their activity towards the oxygen evolution reaction (OER) process in alkaline electrolyte were also studied through acquisition of the corresponding linear sweep voltammetry (LSV) curves. (Figure 1).

Figure 1: OER polarization curves obtained by LSV (KOH 0.1 M solution, scan rate = 5 mV s-1, rotation speed = 1600 rpm) for ZIF-67 and two SiW9Co3@ZIF-67 nanocomposites with different POM loadings.

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#### Energy

# Energetics of methyl esters of long chain fatty acids with importance to biodiesel production

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Biodiesel is composed of alkyl esters of fatty acids (FAMEs) and it is usually synthesized by chemical or enzymatic catalysis mainly from renewable resources. Thermodynamic data on those esters are indispensable for optimization of the synthesis conditions, heat management, as well as for separation processes. The purpose of this study is to obtain accurate experimental values for standard molar enthalpies of formation of methyl palmitate and methyl stearate in gaseous state, due to the lack of consistency of the thermodynamic values presented in literature for these and other components of biodiesel. From combustion calorimetry experiments we derived the standard molar enthalpies of formation of these esters in condensed phase, considering Washburn corrections and using in the calculations the mass of sample derived from the recovered mass of CO2 produced. Those values were combined with the standard molar enthalpies of sublimation obtained using Calvet microcalorimetry.

Additionally in this work, we focused on the relationships between energetics and FAMEs molecular structure, thus providing useful detailed information on some members of the FAMEs family, whose experimental study revealed very difficult or even impossible to accomplish, and also the necessary details. We conducted very accurate quantum chemical computational studies, including the effects of electronic correlation (G3MP2, DLPNO, DFT/B3LYP, etc) for the experimentally studied esters and for a number of other FAMEs. The preliminary results of such studies will be presented and rationalized in order to further understand the molecular and/or electronic details which determine the adequacy of any individual member of the family in the process of biodiesel production.

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#### Energy

# Polymeric Carbon Nitride Doped with Graphene for Light-Driven Hydrogen Generation

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One of the main challenges facing today's society is the impending energy crisis tightly linked to global warming and to constantly increasing greenhouse gas emissions. The photocatalytic production of solar fuels (hydrogen, H<sub>2</sub>) is regarded as a promising technology to overcome these issues.<sup>1</sup> However, the development of stable heterogeneous photocatalysts active in the visible region that can produce H<sub>2</sub> in high quantum yields is still a challenge. The metal-free semiconductor carbon nitride (g-C<sub>3</sub>N<sub>4</sub>) has a suitable electronic band structure for photocatalytic water splitting (band gap of 2.7 eV).<sup>2</sup> However, the limited absorption in the visible region and fast charge-carriers recombination limits its photocatalytic capability. Graphene, a two-dimensional sheet of carbon atoms with a honeycomb structure has attracted increasing interest as a catalyst, being combined with other materials for promoting the photocatalytic activity in many instances, including H<sub>2</sub> generation.<sup>2a</sup>

The present work is dedicated to the development of g-C<sub>3</sub>N<sub>4</sub>/few layer graphene (FLG) materials for photocatalytic H<sub>2</sub> production through water splitting. Bulk g-C<sub>3</sub>N<sub>4</sub> (CNb) was prepared by calcination of the precursor dicyandiamide (DCN),<sup>1</sup> while FLG was synthesized by catalytic chemical vapour deposition at 650 °C using a fluidized bed reactor during 10 min.<sup>2b</sup> CNb doped with FLG was prepared by adding different amounts of FLG to DCN, followed by calcination at 500 °C. The resulting powders were washed with water and dried in an oven, yielding xFLG/CNb materials (x = wt.% of FLG), and were comprehensively characterized with different physicochemical techniques. Photocatalytic H<sub>2</sub> generation tests were carried out in aqueous media by irradiating the catalysts during 3 h with LEDs (420 nm) in the presence of Pt (co-catalyst) and EDTA (sacrificial electron-donor). Experimental results reveal that all doped materials produce a higher amount of H<sub>2</sub> as compared to CNb. FLG content was found to affect the photocatalytic activity of g-C<sub>3</sub>N<sub>4</sub>, as follow: 2FLG/CNb (57 µmol) > 1FLG/CNb (44 µmol) > 3FLG/CNb (43 µmol) > 0.5FLG/CNb (39 µmol) > CNb (15 µmol). The best performing material, 2FLG/CNb, enhanced four times the production of H<sub>2</sub> compared to pure CNb. This finding was attributed to a synergistic effect between both materials, leading to lower electron-hole recombination (confirmed by photoluminescence) and increased specific surface area (26 m<sup>2</sup>/g for 2FLG/CNb composite *vs* 11 m<sup>2</sup>/g for CNb).

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#### Energy

# QM/MM study of DszB reaction mechanism for the biodesulphurization of crude oil

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The presence of sulphur in fossil leads to the release of suphur oxides into the atmosphere upon combustion, which are harmful for the environment and end up forming acid rain and contaminating wildlife. Therefore, legislative measures are being created to further reduce the concentration of sulphur allowed in fossil fuels [1].

The method that is currently used for the desulphurization of crude oil is ineffective in desulphurizing hindered hindered hydrocarbons such as dibenzothiophenes.

To overcome this technical difficulty, research is focusing more and more on alternative desuphurization methods such as biodesulphurization (BDS).

An enzymatic pathway, the 4S pathway, was found in a bacteria living in crude oil extracts, *Rhodococcus erythropolis*. This enzymatic pathway is able to perform the BDS of the most hindered compounds in crude oil extracts. It employs 4 different enzymes: DszC and DszA are flavin monooxygenases that oxidize the sulphur of DBT's; DszD provides the FMNH2 for the monooxygenases; DszB cleaves the carbon – sulphur bond, leaving the carbon skeleton intact [2].

In this study we use Quantum Mechanics/Molecular Mechanics and Molecular Dynamics methods to predict the reaction mechanism of DszB.

We have found that DszB first uses its catalytic Cys27 to protonate the substrate, releasing the SO2 in the active site. Then the Cys27 thiolate is reprotonated with a water molecule and the remaining hydroxide spontaneously reacts with the SO2, forming the secondary product, HSO3-. The first step is the rate-limiting one with deltaGact= 20.88 kcal.mol-1 (Scheme 1).

These findings can be used to better understand the mechanism of DszB and create mutants with improved desulphurization activity, turning BDS into a better alternative for the desulfurization of DBT's.



Scheme: Theoretical purpose of the reaction mechanism of DszB.

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# CPEN10

# Energy

# New compounds for environmentally friendly solution-processed organic photovoltaic devices

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The global increase of energy consumption, the depletion of fossil fuels and excessive pollution have led to the development of new clean energy technologies, such as solar photovoltaics based on organic semiconductors (OPVs – Organic photovoltaics). However, this technology still needs improvements to be considered competitive. Device lifetimes and efficiency levels of large area devices as well as the sustainability of its fabrication process needs further developments to comply with the technical requirements imposed by the market.<sup>1</sup> The development of new materials, with improved optoelectronic properties and beneficial processing, as solubility in environmentally friendly solvents, if succeeded, will very likely launch OPVs as a truly «green» renewable energy technology.

In this communication, the synthesis, characterization and application of new organic semiconducting materials with advantageous properties, namely solubility in solvents of low toxicity, such as ethanol, is presented. The new materials correspond to compounds (small molecules, SMs) and conjugated polymers (CPs) based on a quinoxaline (Q) or a [1,2,5]thiadiazolo [3,4-gquinoxaline (TQ) core functionalized with oligo(ethylene oxide) chains (EO), as solubilizing groups (**Figure 1**).<sup>2</sup> Additionally, a new polymer of the class of polythiophenes, but also functionalized with EO groups, synthesized for applications in the active layer of OPV devices in combination with the synthesized TQ derivatives, is also presented (**Figure 1**). OPV devices in which the active layers are composed of the new materials processed from various solvents, including low toxic mixtures of ethanol and anisole, are presented.



Figure 1: Chemical structures of the synthesized compounds for applications in organic photovoltaic devices.

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# CPEN11

### Energy

# Metallic Reduction Via Eletroless Using Electrosynthesised Films With Polyphenazine

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It is well known that conductive polymers containing nitrogen atoms in their structure have the capacity of reducing spontaneously noble metals ions in diluted solutions, being this process designated as eletroless.<sup>1-3</sup> Molecules derived from phenazine may contain several nitrogen atoms and be electropolymerizable, leading to films formation with some electroactivity on electrode surfaces.<sup>4</sup>

This work reports the optimization of the eletropolymerization of the Neutral Red (N<sup>8</sup>,N<sup>8</sup>,3-trimethilphenazine-2,8,diamine chloride), a dye of the same group of phenazine with four nitrogen atoms in its structure (**Figure 1**). It is also evaluated the capacity of this films to reduce metal ions in diluted solution by eletroless precipitation, with main focus on ions that can be considered harmful to environment (e.g. Hg<sup>2+</sup>, Pb<sup>2+</sup>, Cd<sup>2+</sup>) or with high economic value (e.g. Ag<sup>+</sup>, Au<sup>3</sup>). First it was studied the electrosynthesis of this polymer in order to obtain adherent and electrochemically stable films, through a careful selection of the technique (potenciodynamic, potenciostatic) and the conditions of the formation (concentration of the monomer, pH, support electrolyte, synthesis charge). It was taken particular attention to the efficiency of the procedure, using analytical techniques that allow accompanying the variation of the presence of metallic ions in the solution after each exposition of the polymeric film to the medium



Figure 1: Chemical structure of Neutral Red dye.

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# CPEN12

# Energy

# Modelling Collision Dynamics with Neural Networks and Statistical Methods

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When modelling chemical processes in interstellar space, the main problem is the large number of non-reactive collisions between the different species present in the interstellar media. Despite the very low temperatures and density of the interstellar clouds, these collisions give rise to observable waves of matter and energy transfer.

As the interstellar gases are mainly composed by hydrogen molecules in a ratio of one million to one of each other atomic species, the dynamics of the gas is dominated by the non-reactive collisions between the hydrogen molecules, which must be considered when modelling such a system. The computation of such collisions is a strong time-consuming step that contributes to model the reaction environment, but has low influence on the outcome of the reactive collisions that contribute to the formation of the interstellar molecules other than hydrogen.

Artificial Intelligent (AI) algorithms such as Neural Networks (NN)<sup>1</sup> are a strong candidate technique to predict the outcome of these  $H_2...H_2$  non-reactive collisions. Using quasi-classical trajectory calculations as implemented in the Venus<sup>2</sup> program and the  $H_4$  potential energy surface of Boothroyd *et al.*<sup>3</sup>, we have computed a Calibration Set of 45 000 collisions with initial energies reproducing the energy distribution of the interstellar gases, ranging from 10 K to planetary forming disks at 1 000 K. This set has been used to calibrate a NN algorithm, which has been tested with another computed Test Set of similar dimension.

As a complement, a statistical approach based on the similarities of a new collision with the collisions of the Calibration Set has been implemented. Defining a similarity distance between the initial condition of two collisions, we can predict the outcome of a test collision as the same of the closest trajectory, or of a weighted average of a small number of closest collisions (n=3, 5,10).

In this presentation we compare these two approaches and their application to model a cloud of interstellar hydrogen cloud.

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# COMUNICAÇÕES EM Painel

A TABELA PERIÓDICA LUMINESCENTE MATERIAIS, ENERGIA E NANOTECNOLOGIA

#### Nanotechnology

# Photocatalytic self-cleaning functional fabrics using graphene oxide/carbon nitride materials

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The development of functionalized textiles with self-cleaning and antimicrobial properties have been drastically increasing in the recent years. New concepts have been investigated based in the incorporation of biocidal agents, which are very useful for a wide variety of applications.<sup>1</sup> However, there is still some contradiction on the incorporation of these functional additives due to their side effects upon contact with the human skin, as well their spread into the environment.

Currently, the core research topic in textile industry is the development of eco-friendly, non-toxic, metal free and antimicrobial and biocompatible materials. Carbon-based nanomaterials have been applied as innovative antimicrobial agents due to physical and chemical properties, and therefore attracting wide attention in the heterogeneous photocatalysis field.<sup>2</sup> Polymeric carbon nitride (g-C<sub>3</sub>N<sub>4</sub>) has received widespread interest among researchers in a variety of (photo)catalytic applications due to its narrower bandgap (2.7 eV), low-cost synthesis and non-toxicity. In addition, reports have been showing that coupling graphene oxide (GO) with g-C<sub>3</sub>N<sub>4</sub> may improve the efficiency of the photocatalytic disinfection process.<sup>3</sup>

In the present work, a g-C<sub>3</sub>N<sub>4</sub> aqueous colloid (here labeled as colloidal CN) was obtained by ultrasonic exfoliation. GO was synthetized by oxidation of graphite through the modified Hummers' method.<sup>4</sup> For the preparation of the colloidal GO/CN composites a certain amount of GO suspension was added to the colloidal CN. The cotton fabrics were immersed in the colloidal CN or GO/CN and heated at 40 °C for 3 h. Then, the functional fabrics were passed through a two-roller foulard, followed by a thermal step using a thermofixation chamber. The colloids (CN and GO/CN), and the coated fabrics were characterized by several techniques.

Preliminary results showed high photocatalytic self-cleaning activity was achieved, using caffeine and Rodamine B as target contaminants under visible light radiation. In brief, the functional textiles proposed in the present work eliminate the need for frequent washing, as they are effective, the carbon phase allowing degradation of organic molecules that can stain the fabric. In addition, the CN-based colloids presented high performance in the inactivation of a common potentially pathogenic microorganism.

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# Nanotechnology

# Sol-Gel Immobilization of Green-Emitting Carbon Dots

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Carbon dots (CDs) are carbon-based nanoparticles with several interesting optical and analytical properties, such as photo and chemical stability, biocompatibility, low toxicity, high photoluminescence, large Stokes shift and water solubility.<sup>1</sup> They can also be obtained from simple and green approach, such as hydrothermal and microwave strategies.<sup>1</sup> Due to these features, CDs have been gaining importance in the different fields, such as imaging, sensing, fabrication of optical devices and photocatalysts.<sup>1</sup>

The development of novel practical applications for CDs would benefit from their immobilization. However, CDs present a tendency to suffer from aggregation-induced luminescence quenching in the solid state, which means that they are highly emissive in solution and but are significantly quenched in the solid-state.<sup>2</sup> This has been attributed to excessive resonance energy transfer (RET), direct  $\pi$ - $\pi$  interactions, and interparticle coupled surface states.<sup>2</sup>

Herein, we report the sol-gel immobilization of CDs via a gelation reaction with tetraethyl orthosilicate (TEOS). The CDs are produced via microwave-irradiation by using citric acid and urea as precursors. The fabrication of silica-CDs composites allowed the formation of highly fluorescent gels with green emission, upon gelation of TEOS (Figure 1).



Figure 1: silica-CDs composites with (right figure) and without (left figure) blacklight irradiation.

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## Nanotechnology

# Homo and bimetallic metalloporphyrin nanostructured materials with catalase-like activity

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Synthetic catalysts that mimic catalase activity are of great interest and have been studied for application in the treatment of numerous diseases originated by oxidative stress.<sup>1</sup>

Novel binary structures have been obtained in a straightforward and eco-sustainable way by ionic self-assembly (ISA) of oppositely charged metalloporphyrin tectons.<sup>2</sup> Currently, we are developing metalloporphyrin (MP) nanostructures using for the first time Fe<sup>III</sup> and Mn<sup>III</sup>porphyrins in order to obtain homometallic structures (Mn-Mn or Fe-Fe) and heterometallic structures (Fe-Mn). The materials have been characterized by SEM, UV-vis and XPS (**Figure 1**) and different-size nanostructured features have been obtained depending on the pH of the syntheses. The nanomaterials show improved catalase-like activity relatively to the individual MPs and furthermore, their activity is shown to be dependent on the structures size, the peripheral groups of the MP (R = H or CH<sub>3</sub>) and the role of Mn and Fe as central metals.



Figure 1: Binary materials prepared by ionic self-assembly of metalloporphyrin tectons

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# Nanotechnology

# Stimuli-sensitive self-assembled tubules based on lysine-derived surfactants as nanocarriers for proteins

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Drug delivery vectors based on amphiphilic molecules present considerable advantages, namely versatility in physicochemical properties and sensitivity to stimuli. Amino acid-based surfactants, in particular, are rather promising amphiphiles for this purpose<sup>1</sup> because of their enhanced biocompatibility compared to conventional surfactants. In addition to forming micelles and vesicles, they can self-organize into other complex supramolecular structures, such as fibers, twisted ribbons, helical tapes and nanotubes.<sup>2,3</sup>

Herein, we have studied a family of novel anionic double-chained lysine-based surfactants, with variable degree of chain length mismatch. Because of their peculiar structure, these compounds are able to form in water tubular structures with assorted morphologies, as evidenced by video-enhanced light microscopy (VELM), scanning electron microscopy (SEM and cryo-SEM), cryogenic transmission electron microscopy (cryo-TEM) and atomic force microscopy (AFM).<sup>3</sup> The loading ability of the tubules towards lysozyme, under varying experimental conditions, has been investigated *inter alia* by differential scanning microcalorimetry, gel electrophoresis and UV/VIS spectroscopy, with the goal of assessing the efficiency of these aggregates as pH- and temperature-sensitive nanocarriers for a model biomolecule. Results on the stability of the native and loaded tubules when in contact with different fluids (serum, artificial saliva, artificial sweat, blood), and on their toxicity in human cells, are also presented and discussed.



Figure 1: Tubular nanostructures of 8Lys16 in water (0.5% w/w) as observed by: a) VELM, b) cryo-SEM, c) cryo-TEM.

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## Nanotechnology

# Following Hydrogen Combustion Constrained by Nanotubes

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We present preliminary studies on the effect of carbon nanotubes in the combustion of molecular hydrogen. The confinement of reactants in nanoscale media has been the subject of recent experimental and theoretical studies. In particular, the confinement of molecules in carbon nanotubes has shown to have considerable effect on increasing their reactivity at low temperatures. This has been justified by orientation effects of the confined reactants and to the increase of the collision probability due to reflection on the nanotube walls. Over the last years, it has been reported that small systems do not necessarily have the same properties as the large ones.

According to the standard combustion theory,<sup>1-3</sup> gas mixtures in small volume containers are not able to react. This is due to the absence of an ignition mechanism to produce initial radicals in the reactor and to the reaction inability to sustain itself, since the heat escapes too quickly. Despite that, recent work in nano and micro nanobubbles,<sup>4,5</sup> produced in microsystems using electrochemical decomposition of water with a fast switching of voltage polarity, has demonstrated that nanobubbles containing the stoichiometric mixture of H<sub>2</sub> and O<sub>2</sub> disappear very quickly due to the spontaneous reaction and the short-lived microbubbles, formed by coalescence of H<sub>2</sub> and O<sub>2</sub> nanobubbles, ignite the reaction destroying the bubble in a short time provoking pressure jumps and temperature raise between 20 and 60 °C. The pressure jumps have been proposed to be used in a new type of microengine.<sup>6</sup> According to the authors, the reaction mechanism is not yet clear, but it is obvious that the process is surface dominated and happens without significant temperature increase.<sup>4</sup>

Recently, we have developed an innovative method to model complex systems. The MReaDy<sup>7</sup> program builds a global Potential Energy Surface (gPES), defined by integrating diverse PESs, each one of them representing an elementary reaction that is expected to play a role in the chemical process. The program MReaDy, which has shown to accurately model the gas phase combustion of a mixture of hydrogen and oxygen, has been adapted to study the same reaction confined in a carbon nanotube at different conditions of nanotube diameter, gas pressure and temperature. To accomplish this, we introduced a potential for the carbon nanotube, including the intermolecular forces between the carbon atoms and the reactant molecules.

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# Nanotechnology

# Star-shaped gold nanoparticle interfaces for improved protein direct electrochemistry

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One of the main challenges for protein bioelectrochemistry is achieving efficient electronic coupling between the biomolecule and the electrode. This is particularly significant for direct electron transfer (DET) based devices, in which the protein exchanges electrons directly with the electrode, such as in 3<sup>rd</sup> generation electrochemical biosensors. DET is often difficult to achieve because the protein's redox centers are shielded by the polypeptide chain, imposing a kinetic barrier that prevents fast interfacial electron transfer. Important progress has been made by using nanostructured materials for electrode modification, such as gold nanoparticles (AuNPs).<sup>1</sup> Their unique chemical, optical, and electrical properties have led to the successful use as electrode functionalization materials, including the development of enzyme based electrochemical sensors with enhanced performance. In fact, the excellent biocompatibility and large surface-to-volume ratios of AuNPs create suitable microenvironments for high loading of enzymes, while allowing the maintenance of their native structures and activities. Furthermore, thanks to their high electrical conductivity, the rates of electron transfer with the enzyme's redox centers can be significantly accelerated.<sup>2</sup>

Herein we have explored star-shaped gold nanoparticles (AuNS) as promoters of the DET of a well-known heme containing protein, the small cytochrome *c* from horse heart. The star-shaped morphologies display different curvatures and enhanced surfaces areas in comparison with the traditional spherical AuNPs. The AuNS were functionalized with bifunctional alkanethiol capping agents, namely anionic alkanethiols (mercaptoundecanoic acid, MUA, and 4-mercaptopropionic acid, 4-MBA) and small peptides. The nanomaterials were deposited on the surface of pyrolytic graphite electrodes and used to study the direct electrochemical response cytochrome *c*, either in solution or upon immobilization on AuNS electrodes. When the protein was in solution, the electron transfer rate constants were up to two orders of magnitude higher on electrodes modified with MUA and 4-MPA functionalized AuNS, in comparison to non-modified electrodes and AuNPs coated with the same capping agents. Conjugation of the protein with the AuNS and subsequent immobilization on the PG electrode enabled preserving its native structure, despite a slight negative shift in redox potential. In turn, layered films of AuNS and cytochrome *c* resulted in an altered conformational state of the protein, as indicated by a low reduction potential and the triggering of peroxidase activity. We showed that the later strategy could be used to develop a 3<sup>rd</sup> generation hydrogen peroxide biosensor based on immobilized cytochrome *c*.

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# Nanotechnology

# Highly Transparent, Conductive and Flexible Electrodes for Electrochromic Devices Using a "Green" Hybrid Copper-Nanowire-Reduced-Graphene-Oxide Coating

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This work reports the use of novel transparent electrodes employing copper-nanowires/reduced-graphene-oxide hybrid coatings using green synthetic methods for electrochromic displays. Those electrodes are robust and combine sheet resistances lower than  $30\Omega$ .sq<sup>-1</sup> and transmittances higher than 70%. These properties make these electrodes suitable for flexible electronic applications when coated on flexible substrates as polyethylene terephthalate (PET).

As proof-of-concept, this work evidences the successful use of these substrates to produce high-performance electrochromic devices. The produced substrates were coated with PEDOT (Poly(3,4-ethylenodioxythiphene)) by spray-coating, assembled with the know-how of *Ynvisible*®, giving rise to high color contrasts, high coloration efficiencies, fast switching times and a long durability.

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Figure 1: Electrochromic devices produced with PEDOT spray-coated on the CuNWs/GO electrodes.

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## Nanotechnology

# A theoretical-experimental study of the electronic and photophysical properties of Gd- complexes with different halogen-substituted DBM-Cα ligands

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In this work, the  $\alpha$ -halogenation of DBM (dibenzoylmethane) was achieved by following the scheme1 below and using the corresponding *N*-halogen-succinimide (NCS, NBS or NIS) as the source of halogens. The structure elucidation of DBM- $\alpha$ halogenated (DBM- $\alpha$ X and X = CI, Br, I) was obtained by NMR, X-ray crystallography, FTIR and FT-Raman and mass spectrometry. Additionally, UV-VIS and PL spectroscopies were used to study the electronic and photophysical properties.



Scheme 1:  $\alpha$ -halogenation of DBM

Density functional theory/time-dependent density functional theory (DFT/TD-DFT) calculations were performed on a series of gadolinium(III) complexes of DBM- $\alpha$ X ligands with the general formula Gd(DBM- $\alpha$ X)<sub>3</sub>(H<sub>2</sub>O)<sub>2</sub>. The effect of such substitution on the structural, electronic and photophysical properties is established. Absorption and phosphorescence spectra calculations show that different halogen substituents have different effects on absorption peak positions and triplet state.

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# COMUNICAÇÕES EM Painel

A TABELA PERIÓDICA NA SALA DE AULA COMUNICAÇÃO, CULTURA E ENSINO

# **Culture and Education**

# A Tabela Periódica e a Vida

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No Ano Internacional da Tabela Periódica vamos construir um exemplar tridimensional desta estrutura, com informação básica sobre cada elemento. Esta Tabela Periódica tridimensional será formada por cubos, feitos em k-line, com 10 cm de aresta, que encaixam em varões de madeira permitindo a sua rotação. Cada face lateral do cubo conterá informação diferente sobre o elemento: na face principal inserem-se nome, símbolo químico, número atómico, número de massa, pontos de fusão e de ebulição, densidade, raio atómico e espectro de emissão; as outras faces contemplam dados sobre a descoberta do elemento, questões de saúde relacionadas com o elemento e curiosidades. As dimensões permitem o transporte da Tabela para salas de aula, sendo assim um material didático para a aprendizagem de matérias programáticas do Ensino Básico e Secundário e também um artefacto que estimula os mais jovens para o estudo das ciências exatas e do conhecimento em geral.

Este projeto está enquadrado no objetivo da flexibilidade curricular do 10º ano, envolvendo as disciplinas de Física e Química A, Biologia e Geologia e Matemática A, as respetivas professoras e os alunos de uma turma de 10º ano de Ciências e Tecnologias, da Escola Secundária do Restelo, com a colaboração de alunos de 11º ano do curso de Ciências e Tecnologias e de alunos de 9º ano, da mesma escola.

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# **Culture and Education**

# **DesQ2019 – Chemistry Challenges for Young Chemistry Students**

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It has been recognized that in Portugal, as in many other countries, is difficult to motivate young students for advanced studies in chemistry. It is our responsibility, as teachers, to circumvent those difficulties, introducing innovative methods of lecturing, namely using the new technologies, and new methodologies turning chemistry out to be a more attractive study area. Within the scope of the International Year of the Periodic Table of Chemical Elements (IYPT2019) the Polytechnic Institute of Tomar has designed and implemented an online activity for secondary school students named "*Desafios da Química 2019*" (Chemistry Challenges 2019) - DESQ2019. Participants had to solve a total of ten different challenges placed online weekly along ten weeks. The solution to each challenge was a chemical symbol of a chemical element from the periodic table. Figure 1 shows an example of a placed challenge.

The presentation will focus on the activity structure and on a revision of the placed challenges, engendering an opportunity to make a digression trough the Periodic Table highlighting some curiosities related with a few chemical elements. With this activity it was possible to increase the attractiveness of chemistry to young students and thus the interest in pursuing higher level chemistry studies.



Figure 1: Online placed challenge for the DesQ2019 activity.



# **Culture and Education**

# Aquário Biológico

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O nitrogénio encontra-se presente em diferentes tipos de ecossistemas, sendo particularmente importante para ecossistemas aquáticos, podendo torná-lo, em determinadas condições, num ambiente tóxico para os organismos aquáticos<sup>1</sup>. De entre os compostos nitrogenados presentes na água, dá-se especial ênfase ao amoníaco (NH<sub>3</sub>) e ao ião amónio (NH4<sup>+</sup>) pelo grau de toxicidade que podem apresentar quando as suas concentrações se encontram elevadas.<sup>1</sup> A fitorremediação é um processo que permite a descontaminação e filtração da água através do uso de plantas que vão utilizar os compostos nitrogenados potencialmente tóxicos em meio aquático, transformando-os em nutrientes vitais para o desenvolvimento e produtividade desses mesmos meios. No presente trabalho, alunos do 12ºano nas disciplinas de Química e Biologia, realizaram uma experiência, com base no conceito de fitorremediação, de modo a testar a capacidade de um sistema fechado, constituído por um aguário de 13 L ligado a um recipiente plástico com 53 L de capacidade para estabilizar a concentração de amoníaco no aquário, filtrando a água e repondo as concentrações dos compostos nitrogenados, como nitratos. O recipiente de plástico contém diferentes camadas de materiais no seu interior. Inicialmente e em baixo, encontramos uma camada de rocha calcária de granulometria de 1,5 a 2,5 cm coberta por geotêxtil. Uma fina camada de cerâmicas porosas foi adicionada por cima do geotêxtil e coberta por uma camada de areia relativamente fina. De seguida, encontra-se outra porção de geotêxtil onde foi colocado substrato juntamente com as plantas escolhidas. A rocha calcária de maior tamanho serve para acumular água entre os interstícios, sendo possível drená-la através de um furo realizado no fundo de uma das laterais do recipiente plástico. A camada de cerâmicas porosas permite a proliferação, crescimento e fixação de bactérias desnitrificantes. O geotêxtil, material constituído essencialmente por polipropileno, é formado por tecidos permeáveis que, quando usado em associação com o solo, tem a capacidade de separar, filtrar e drenar. A areia permite filtrar e separar a água que por ela passa das substâncias sólidas. O substrato das plantas foi aquecido a 80°C para eliminar possíveis bactérias e fungos e tanto a areia como as rochas calcárias foram lavadas e esterilizadas a 100 °C. Zantedeschia aethiopica é uma planta que prolifera rapidamente e acumula os compostos nitrogenados presentes na água, sendo, por isso, usada nesta experiência para filtrar a água proveniente do aquário.<sup>2</sup> A ligação entre o recipiente e o aquário foi feita através de uma mangueira de 12 mm de diâmetro. A água do aquário é levada pela mangueira até ao recipiente, caindo gota a gota por cima das plantas e respetivo substrato. O recipiente plástico encontra-se ligeiramente mais alto que o aquário, permitindo que a água regresse, por ação da gravidade, ao interior do aquário. Esta ligação entre o aquário e o recipiente plástico permite que a água se mantenha em circulação, formando um ciclo. Como fonte de compostos nitrogenados, foram utilizados peixes da espécie Carasius auratus. Outro aquário, montado com uma bomba de ar e filtro, é utilizado como grupo de controlo, tendo o mesmo número de seres vivos. Durante a experiência, foram medidos e registados os valores de nitratos, nitritos, fosfatos, amónia e pH de dois em dois dias nos dois aquários até ao fim da experiência. Uma vez por semana realizou-se uma troca parcial de água (TPA), em que se retirou um terço da água dos aquários e substituíuse por água engarrafada. Nos dias de TPA, as medições foram realizadas antes e depois da troca de água. Este estudo permitiu demonstrar a capacidade fitorremediadora do sistema com planta Zantedeschia aethiopica e a sua possível utilização no combate à poluição.

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# **Culture and Education**

# Mobile Learning in Biodiesel's Synthesis by Homogeneous and Heterogeneous Catalysis

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The potential of multimedia applications, adapted to the contexts of teaching and learning, can be seen as important teaching tools in the different dynamics of the classroom<sup>1</sup>. In addition, there is a great popularity and familiarity with mobile devices present features which will enhance potential users<sup>1</sup>. The rise of these resources is a fact that can be explored in the educational process, using the pedagogical model called Mobile Learning<sup>1,2</sup>. Mobile devices are necessary tools that can be used to facilitate learning. We need them to supplement schools resources, to extend learning process outside the class walls, to prepare students for working life after their graduation<sup>3</sup>. In the last few years, the automobile industry has been trying to find alternatives, in order to decrease the dependency on fossil fuels. One of the solutions can be vehicles containing a regular combustion engine that can be used in the combustion of biodiesel. This research study was made by students of Chemistry of the12th grade. The main goal of this project was to synthetize biodiesel by transesterification of refined soybean oil, using in a comparative way, homogeneous (basic) or heterogeneous catalysis using laboratory materials. This work used two different kinds of catalysts: homogeneous catalyst, KOH, and heterogeneous catalysts (a catalyst developed by the Chemistry and Biochemistry Department of Science Faculty of University of Porto, REQUINTE). Transesterification of waste cooking soybean oil and metanol, in the presence of homogeneous catalyst was carried out at room temperature and in presence of heterogeneous acid catalyst was conducted at a 117 °C. Mobile devices were used during the project in order to take photos and record videos during every step of the procedure. Different types of apps (Gocongr, Animoto, Stupeflix etc) were used to report the results. With this project students concluded that, although, homogeneous base catalyst has fast reaction rates it has the loss of catalyst and soap formation. With the heterogeneous catalyst, catalyst can be recovered and reused and there is no soap formation. This experience was also helpful to conclude that the students involved in this project deepened and applied their previous and new learning, improved their critical thinking, creativity as well as their communication skills, increased their autonomy, organizational management of work, interpersonal relations and motivation towards new projects.

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#### **Culture and Education**

# Multistate system of 7-diethylamino-4-pyridinebenzopyrylium

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Pyridinechalcones are 2-hydroxychalcones where the phenyl is substituted by a pyridine ring.[1] 4-Pyridinechalcone shows no formation of flavylium cation due to protonation of the pyridine at pH~4.[1]. Introduction of an amino group in position 7 allows direct conjugation between the amine and the benzopyrylium ring allowing formation of flavylium cation. These new flavylium compounds show a pH-dependent equilibrium network similar to 7-(N,N-diethylamino)-4'-hydroxyflavylium[2] and those of 2-hydroxychalcones.[3] It was possible to identify ten species in the chemical reaction network of 7-diethylamino-4-pyridinebenzopyrylium (MeOH: H<sub>2</sub>O 1:1; 0.5 < pH < 12). Structural elucidation of the synthesized compound was done by <sup>1</sup>H- and <sup>13</sup>C-NMR, elemental analysis, ESI-MS and by X-ray crystallography. The several species present at the equilibrium were fully characterized by <sup>1</sup>H NMR and <sup>13</sup>C NMR. The thermodynamic of the multistate (**Scheme 1**) and its kinetics was studied by <sup>1</sup>H NMR and UV-vis absorption including stopped flow.



Scheme 1. The multistate of species observed in the compound 7NPy4.

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### **Culture and Education**

# Os Recursos Geológicos e a Tabela Periódica

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A sociedade atual explora recursos geológicos (minérios, hidrocarbonetos, salmouras ou rochas ornamentais) que possuem a maioria dos elementos químicos. Nove elementos, por terem uma semivida muito curta, não se extraem de recursos geológicos e alguns não têm sequer aplicação (fora do campo da investigação científica). Cinco elementos (oxigénio, nitrogénio, árgon, xénon e crípton) extraem-se da atmosfera, não sendo por isso considerados recursos geológicos. De facto, dos noventa e dois elementos químicos "naturais" (noventa e quatro, se considerarmos o plutónio e o neptúnio detetados em teores de 10<sup>-12</sup>/átomo de U, em raros jazigos de urânio), setenta e oito elementos exploram-se em rochas e minerais da crusta terrestre. O estudo dos recursos geológicos é cada vez mais pertinente pois a sociedade tem vindo a aumentar exponencialmente o consumo destas matériasprimas. Os futuros geólogos de prospeção e de mina devem possuir um bom conhecimento da totalidade ou da generalidade dos recursos, e isso só é possível conhecendo a mineralogia e a geoguímica que lhes estão associadas. Na atualidade muitos dos estudantes que cursam o ensino universitário revelam um grande défice em conhecimentos da tabela periódica, em mineralogia e em geoquímica. Uma forma de cativar o interesse dos estudantes nestas temáticas é apresentar-lhes uma Tabela Periódica dos Recursos, ilustrada com uma imagem de um mineral / recurso importante para cada elemento. A tabela permite, simultaneamente, salientar e relacionar o mineral com o recurso e com o elemento químico em termos de propriedades físico-químicas e interesse económico. Tendo como "pano de fundo" a Tabela Periódica dos Recursos torna-se mais fácil explicar a tipologia dos recursos geológicos de cada elemento químico, já que muitos elementos se relacionam entre si quer do ponto de vista químico quer em termos de recursos geológicos, (Li-Cs, Ta-Nb, Au-Ag, Al-Ga, Pb-Ag, As-Sb, platinóides, lantanóides-Y-Sc, etc). A vertente geoeconómica também pode ser explorada através de exemplos de aplicações no quotidiano dos recursos geológicos e dos elementos ou produtos deles derivados.



# **Culture and Education**

# Game "Perfil Químico": protagonism and knowledge about the periodic table

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Games and play activities in chemistry teaching have been widely used. Teachers with the intention of producing more dynamic classes make use of these resources, as they stimulate the student's curiosity, participation initiative and self-confidence; but also enhances the development of language, mental and concentration skills, and practice social interactions and teamwork<sup>1,2</sup>.

The game "Perfil Químico" is an adaptation of the traditional game Perfil®, a trademark of the toy company Grow®. The game was initially applied at the Instituto Federal de Mato Grosso, Campus Avançado Diamantino and later the proposal was expanded to Escola estadual Plena Plácido de Castro, where one of the elective courses offered only works with ludic games in chemistry and mathematics teaching, being the students themselves protagonists in the elaboration of the game to be executed by them later. The objective was to subsidize the teaching of the periodic table, improving students' understanding of the organization of the elements and their particular characteristics in the periodic table.<sup>3</sup>

All the components of the game were adapted, from the board, which became the periodic table, to the format and obviously the subject addressed in the letters. The students should search for characteristics of the chemical elements, using as a research source the textbook, internet or simply the periodic table and elaborate 4 (four) tips to form the letters that were printed on common sulphite paper then cut out and glued on colored cardboard paper as shown in Figure 1.

The division for the application of the game was the choice of the students, and could be played individually 1 (one) against 1 (one), in doubles 2 (two) against 2 (two) or in groups. The game was still applied in the common base classes, in the regular discipline of chemistry taught by the teachers who participated in the mediation for the confection and application of the game in the elective discipline.



Figure 1: Image of the cards and application of the game.

Two questionnaires were applied, one before and one after the game to verify the efficiency of the play methodology used. The game alone is not enough for understanding the content, how the teacher accomplishes the approach assists in the process and this should be put under evaluation. The game chemistry showed to be an excellent strategy of protagonism of the student in the research and preparation of the cards and how natural to the use of ludic activities in teaching, was shown like mechanism of disciplinary interaction.

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# **Culture and Education**

# A Tabela Periódica celebrada na sala de aula

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O vasto património (i)material da Escola Sá de Miranda (ESM), desde uma tabela de pesos atómicos de 1912, entre outros quadros parietais, a livros do séc. XIX à contemporaneidade, permitiu a realização de atividades como visitas orientadas ao Museu da Escola, construção de uma Tabela Periódica com material reciclado vencedora de um concurso da Universidade do Minho, realização de um vídeo com a teatralização de um trecho da vida de Dimitri Mendeleiev, uma Oficina de Formação para docentes, uma Tabela Periódica pintada em cacifos e outros recursos pedagógicos de natureza interdisciplinar no paradigma da Era Conceptual.

Numa perspetiva de educação inclusiva, em que é fundamental o princípio da flexibilidade curricular (Decreto-Lei n.º 54/2018, de 6 de julho), foram criados cenários de aprendizagem inovadores para o 3.º ciclo, para os cursos profissionais e científico-humanísticos, para a comunidade escolar em geral e de formação para os professores. Neste âmbito, serão dadas sugestões de materiais diversos e casos reais, a saber: aparatos parietais; sinopse para teatro; material elaborado para um concurso; utilização de livros, textos e poemas; jogos; Tabela Periódica para invisuais. A experiência tem mostrado que materiais deste tipo ajudam na implementação de práticas pedagógicas em sala de aula, à luz dos princípios base do desenho universal para a aprendizagem (DUA): proporcionar múltiplos meios de envolvimento; proporcionar múltiplos meios de representação e proporcionar múltiplos meios de expressão.

O recurso ao património (i)material sob este ponto de vista pode, ainda, favorecer a associação da dimensão fortemente cultural da Escola à sua dimensão inclusiva e promover o trabalho colaborativo entre docentes sempre que o objetivo do(s) projeto(s) seja celebrar o **Ano Internacional da Tabela Periódica dos Elementos Químicos**.

Palavras chave: flexibilidade curricular, inclusão, quadro parietal, Tabela Periódica, trabalho colaborativo.

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# **Culture and Education**

# The Periodic Table of the Elements: A cross millennia inspiring and inclusive tool

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The Periodic Table of the Elements in an iconic symbol of science. Envisioned 150 years ago by Dmitri Mendeleev, the chemistry elements have been arranged in a simple way, thus helping scientists to know and understand better their fundamental properties. Since the early days the Periodic Table has been growing with the discovery of new elements, and its representation has been also a creative exercise for many scientists. Imagination has no limits and today we can find hundreds of versions. Some quite exquisite! This versatility allows its use as a tool to communicate science to youngers, with a special focus in disabled students. This communication will show how blind/visually impaired or deaf students may also join us in the discovery of science using inclusive periodic tables,<sup>1,2</sup> and other teaching tools inspired in the Periodic Table (**Figure 1**).<sup>3,4</sup>



Figure 1: Examples of teaching tools using or inspired by the Periodic Table of the Elements.

Acknowledgements: We thank Carlos Martins for text translation to the Portuguese Sign Language and Casa Pia de Lisboa for the production of the Portuguese Sign Language Periodic Table of Videos.

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# **Culture and Education**

# A História das Ciências e a evolução da Tabela Periódica: Um estudo com manuais escolares de 10º ano

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A relevância da História das Ciências (HC) para a formação integral do aluno, nas dimensões pessoal, social e científica, é reconhecida pelos especialistas na área da educação em ciências, bem como pelos currículos portugueses. A evolução histórica da Tabela Periódica (TP) constitui um contexto privilegiado para possibilitar o reconhecimento de que o conhecimento científico está em permanente evolução, apresentando um carácter dinâmico, e que as descobertas científicas estão dependentes dos contextos sociais, políticos, económicos e religiosos das épocas em que ocorrem. Neste contexto, a presente investigação tem como finalidade compreender como é feita a abordagem histórica da TP pelos autores de manuais escolares (ME) nas duas últimas gerações de ME portugueses de 10º ano, a fim de indagar se tem havido evolução na forma como o conteúdo histórico da TP é apresentado.

Para isso, realizaram-se dois estudos centrados na análise de conteúdo de ME de 10º ano, averiguando-se como é que a história da TP é inserida nos ME e que referências são feitas à história da TP. Consideraram-se duas gerações de ME: a primeira, correspondente a todos os ME de 10º ano (8 ME) disponíveis para adoção no ano letivo de 2007/2008, elaborados no âmbito do Programa de Física e Química A (FQA) de 10º ano; a segunda, correspondente a todos os ME de 10º ano (7 ME) disponíveis para adoção ano letivo de 2015/2016, elaborados no âmbito das Metas Curriculares de FQA.

Os resultados revelaram que todos os ME apresentam conteúdo histórico sobre a TP. No que concerne à primeira geração de ME verifica-se que: o conteúdo histórico sobre a TP é pouco desenvolvido; grande parte dos ME veicula a ideia de que a evolução da TP se processou de forma linear, através de etapas independentes, e não explora a ideia de que o conhecimento científico resulta de uma construção coletiva. Relativamente à segunda geração de ME: o conteúdo histórico sobre a TP é mais desenvolvido; grande parte dos ME continua a veicular a ideia de que evolução da TP se processou de forma linear; no entanto, uma grande parte dos ME transmite a ideia de que a TP resultou de uma evolução ao longo do tempo, inclui o contributo de vários cientistas e está aberta à incorporação de novos elementos químicos.<sup>1</sup>

Os resultados do presente estudo parecem sugerir uma evolução na forma como o conteúdo histórico relacionado com a TP é incluído nos ME. Contudo, existem ainda limitações relacionadas com o valor educativo do conteúdo histórico para a contribuição do desenvolvimento da consciência dos estudantes sobre o entendimento de como se desenvolve o conhecimento científico.

Tendo em conta estes resultados, parece necessário fazer um investimento, cientificamente fundamentado, na elaboração de ME e intervir na formação de professores, de modo a permitir-lhes desenvolver competências para colmatarem as lacunas existentes nos ME, no que respeita à história da TP.

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# **Culture and Education**

# Separation of Flavonoids and Anthocyanins from Roses

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In Chemistry, the use of experimentation is the key to the success in the teaching / learning process, particularly in the younger classes. The approximation of chemistry to the real world is an important contribution to awakening and motivating students to this area of knowledge. On the other hand, since chemistry is a crucial science for the explanation of all phenomena in the physical and biological environment, it is necessary to reverse the current image of chemistry, usually associated with images of pollution and environmental disasters. Thus, the development of simple and high visual impact experiments that uses accessible and sustainable materials is a current theme.<sup>1</sup>

The colors of flowers and fruits are due to three classes of pigment molecules: chlorophylls, carotenoids, flavonoids (including anthocyanins). Carotenoids originate the yellows, oranges and reds (tomato lycopene). Anthocyanins are molecules whose colors can range from red, purple or blue. In yellow roses the major pigments are flavonols and carotenoids, while anthocyanins are the most important pigments in red roses. A qualitative relationship had been established between the intensity of petal coloration and the anthocyanin content. Anthocyanidin 3,5-O-diglucoside (cyanin) and anthocyanidin 3-O-glucoside (chrysanthemin) are the main components in roses. A series of flavonol glucosides, like quercitrin, are also important components that form loose associations with anthocyanins and have been reported as responsible for the stabilization of rose anthocyanin chromophore.<sup>2</sup>

Aiming to find simple experimental activities, performed with easily accessible materials and less hazardous solvents, several studies were carried out and led to the development of a very simple and high visual impact liquid-liquid extraction technique, that enables the separation of anthocyanins and flavonoids from red roses petals. This sustainable activity may be implemented in Universities, allowing the teaching/learning of key concepts in practical classes of Organic Chemistry. It can be also used in Secondary Schools to demonstrate several concepts of Chemistry Curricula listed for Secondary Education.

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# **Culture and Education**

# Phytochemical characterization and determination of biological activity of the hydroethanolic extract of barks of plants from Angola

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Medicinal plants are a source of medicines in several communities worldwide, for treatment of several pathogenic infections.<sup>1</sup> However, many of them are used without the characterization of their components.<sup>2</sup>

This work intends to characterize compounds extracted from plants such as *Aloe congolensis*, *Securidaca longipedunculata*, *Diospyro batocana*, *Sansevieria liberica Gerome* and *Labroy* and also *Ximenia americana c. Lineu*, all used in traditional medicine in Angola. Soxhlet extractions were performed with n-hexane and cold liquid-solid extractions with acetone and ethanol.<sup>3</sup> The barks, roots and leaves of the plants were used. The extractions were carried out from the solvent of lower polarity (n-hexane) to the one of greater polarity (ethanol). In this way several extracts were obtained that were analyzed.

The antioxidant activities of the plant extract samples in ethanol and acetone were analyzed by the DPPH method <sup>4,5</sup> and significant antioxidant activities were obtained for two plants (*Diospyros batocana* and *Ximenia americana* and *Lineu*). According to the Index of Antioxidant Activity (AAI), the ethanol extracts obtained from the leaves and roots of *Diospyros batocana* and the acetone extract from the *shells of Ximenia americana c. Lineu* have a very strong antioxidant activity. The remaining extracts exhibit poor or moderate antioxidant activity.

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# **Culture and Education**

# Quest for the first Periodic Table in Portugal: the influence of Ferreira da Silva on popularization of chemical nomenclature (1877-1910)

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When researching the early echoes of the Periodic Table of Elements in Portugal, one may find an interesting peculiarity: the first known mention to "Dmitri Mendeleev's periodic law" can be found in an essay by Agostinho de Sousa, a chemistry student of the Polytechnic Academy of Porto in 1880.<sup>1</sup> Mirroring the opinions of Portuguese scientists, the Polytechnic Academy in the early 1880's still viewed the atomistic theories as outcasts. The established element classification of renowned chemists, such as Berthelot, for the study of chemical phenomenon were still dominant. Considering the peripherical position of Portugal in the European scientific scenery, this communication aims to address the introduction of Mendeleev's Periodic Table on Portuguese higher educational system, particularly at the Porto Academy.

While he was at the Polytechnic Academy, Agostinho de Sousa attended the classes of prominent Portuguese chemist António Joaquim Ferreira da Silva (1853-1923) and learned "Mendeleev's law". Significantly, the debate on the "classification and nomenclature of chemical substances" rose to prominence with Ferreira da Silva.<sup>2</sup> The lack of harmony between chemists on a common ground for chemical nomenclature widened the gap between scientific recognition of Portuguese and European scientists. Ferreira da Silva saw beyond the narrow view of fundamentalists. He argued that there "must be a space for the emergence of new theories" that could explain and complement newfound chemical knowledge.<sup>2</sup>

In this communication, we discuss the first references on the Periodic Table of Elements in Portuguese academia. The efforts of Ferreira da Silva to popularize chemical nomenclature and periodization went beyond the recognition of the "periodic law". He set the stage for the academic debate of new chemical classification methods. By being the first Portuguese faculty member to recognize "the values and merits of the atomistic theory" he addressed this contrast of ideas in several educational publications.<sup>2</sup> With the changes on chemistry teaching that he introduced in the 1880's at the Polytechnic Academy, we can sustain an idea that allow us to postulate a Portuguese academia before and after Ferreira da Silva.<sup>3</sup> In a way, his internationally recognized expertise on analytical chemistry was a driving force on sustaining new leaps on harmonizing chemistry elements between scientists. But what lengths had is academic influence? By 1892, he was among the select few who shared the stage with Dmitri Mendeleev in international meetings to "harmonize chemical nomenclature". By looking at new printed and manuscript sources (namely the correspondence of the Laboratory of the Polytechnic Academy of Porto), we argue that Ferreira da Silva pushes the idea of empowering chemists and students with the necessary tools to disseminate the "science at the service of the people".

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