

CQB day 2017

May 31 st

Faculdade de Ciências da Universidade de Lisboa



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Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

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Welcome to CQB day 2017

Since its foundation in 2001, Centro de Química e Bioquímica (CQB) has provided a research environment oriented toward fruitful collaborations between chemistry and biochemistry groups. Within this perspective, the Strategic Project for 2015-2020 (PEst 2015-2020), defined in 2014, and approved by FCT, should strengthen the links between groups around two thematic lines, reflecting the interest and expertise of CQB:

1. *Chemistry and biochemistry for a clean environment.*
2. *Human health: molecular interventions and regulation mechanisms.*

During the last CQB-Day, in June 2016, all the groups had the opportunity to present their contributions towards these topics, either orally or as a poster, and two oral presentations by the coordinators of the thematic lines showed the achievements. One year later, we propose to carry out an internal evaluation to prepare for the triennium evaluation planned by FCT at national level for the second half of 2017, and invited the three members of the International Advisory Board, Sir William Wakeham, Hans Peter Wessel and Roman Zubarev.

The program of CQB-Day 2017 will start with a brief opening session. Two invited lectures, two presentations dealing with the outcomes of the thematic lines and flash communications from the groups will follow. They will be combined with around 80 poster presentations from CQB members and young collaborators. There will be some prizes for the best selected posters. We hope to give a general idea of the wealth of ongoing projects and the increase of the degree of cross-fertilization between the twelve groups.

We count on all of you to make this CQB-Day 2017 even more successful than the previous ones and use this opportunity to discuss the progress of our Strategic Project, to strengthen collaborations between groups supported by novel scientific synergies, to find new common grounds for research, grasp the most advantageous funding opportunities, and start building the future.

Maria José Calhorda
CQB coordinator

Scientific Program

- 9.30h** **CQBday open session**, José Artur M. Simões, Ana Ponces Freire
and Maria José Calhorda
- 9.40h** **Invited Lectures**
- *Old challenges and new opportunities in chemical proteomics*, Roman A. Zubarev
 - *The role of activated carbon technologies for controlling emerging contaminants in water and wastewater treatment*, Maria João Rosa
- 10.40h** **Poster Communications & Coffee Break**
- 11.50h** **CQB Thematic Lines**
- *Chemistry and Biochemistry for a Clean Environment*, Maria José Calhorda
 - *Human Health: Molecular Interventions and Regulation Mechanisms*,
Rodrigo Almeida
- 12.30h** **Lunch & Poster Communications**
- 14.00h** **Science at CQB -Flash Communications**
- *Titanate nanotubes sensitized with silver nanoparticles: synthesis, characterization and in-situ pollutants photodegradation*, Beatriz Barrocas
 - *Biocompatible porous materials to be used as donors of therapeutic doses of nitric oxide*, Rosana V. Pinto
 - *Novel non-toxic antifouling strategies for biofouling control*, Elisabete R. Silva
- 14.30h** **Science at CQB - Flash Communications**
- *Synthesis and evaluation of antitumor activity of novel thiobenzanilides*,
Maria João Martins
 - *Synthesis and Anticancer Evaluation of Novel Azide-, Phosphoramidate- and Carboxamide-containing Nucleosides*, Rita Gonçalves-Pereira
- 14.50h** **Poster Communications & Coffee Break**
- 16.30h** **Science at CQB - Flash Communications**
- *Polymorphism in Molecular Organic Pharmaceuticals*, Carlos E.S. Bernardes
 - *Human fingerprints through the eyes of mass spectrometry*, Ana Assis
 - *Considerations on Sample Preparation in the Age of Green Analytical Chemistry*,
Nuno Neng
- 17.00h** **Science at CQB - Flash Communications**
- *Metabolic lighthouses in downy mildew resistance*, Marisa Maia
 - *Plasma membrane domains of filamentous fungi reorganize extensively during the lag phase*, Filipa C. Santos
- 17.20h** **Awards and Closing Session**, Maria José Calhorda

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Old challenges and new opportunities in chemical proteomics

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Novel potent anticancer agents need to be characterized in terms of their protein target, site of binding, mechanism of action, changes in the redox state the cancer cell death pathway. A set of proteomics tools are implemented to provide these characteristics.

The role of activated carbon technologies for controlling emerging contaminants in water and wastewater treatment

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Anthropogenic pressures and global climate change are putting increasing stress on Europe's freshwater resources, being responsible for sharp variations of raw water availability and quality, and for the degradation of water sources by emerging contaminants (ECs). Emerging contaminants include personal care products and pharmaceuticals, increasingly used by the population and not fully retained by the wastewater treatment plants, and cyanotoxins produced by toxic cyanobacterial (blue-green algal) blooms in surface waterbodies. In the last years, water regulators and authorities and the general public have expressed an increased concern regarding the presence of emerging contaminants in drinking water and treated wastewaters, as some may be implied in risk cancer increase, bacterial resistance to antibiotics and reproductive abnormalities in aquatic organisms. Besides the risk, these contaminants share a resistance, partial or total, to conventional treatments at the water treatment plants (WTPs) and urban wastewater treatment plants (WWTPs) since most of them are water soluble, polar to semipolar, organic compounds, of intermediate to low molar weight, and may be effective in the very low concentrations in which they often occur (pg/L to µg/L range).

The control of ECs in WTPs and WWTPs is therefore a priority that requires the assessment of the risks involved, the improvement of the current barriers and, if necessary, their rehabilitation with advanced treatment technologies. Activated carbon-based technologies are amongst the most promising solutions for they minimize the byproducts formation, but their sustainability and cost-efficiency still calls for activated carbon development and process optimization. An overview is presented on the projects that are being developed in LNEC Water Quality and Treatment Laboratory, some with CQB (A. P. Carvalho et al.), which use activated carbon based technologies for upgrading WTPs/WWTPs for controlling pharmaceuticals, personal care products and cyanotoxins. Emphasis is given to the chemical enhancement of conventional wastewater treatment using "green" powdered activated carbon options (www.life-impetus.eu), to biologically active carbon (BAC) filtration for drinking water treatment (CYANOBAC - PTDC/ECM/69610/2006) and to hybrid adsorption/low-pressure membrane processes for advanced drinking water production (www.life-hymemb.eu) and water reclamation aiming at water reuse (www.i-trust.eu, www.life-aware.eu).

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Titanate nanotubes sensitized with silver nanoparticles: synthesis, characterization and in-situ pollutants photodegradation

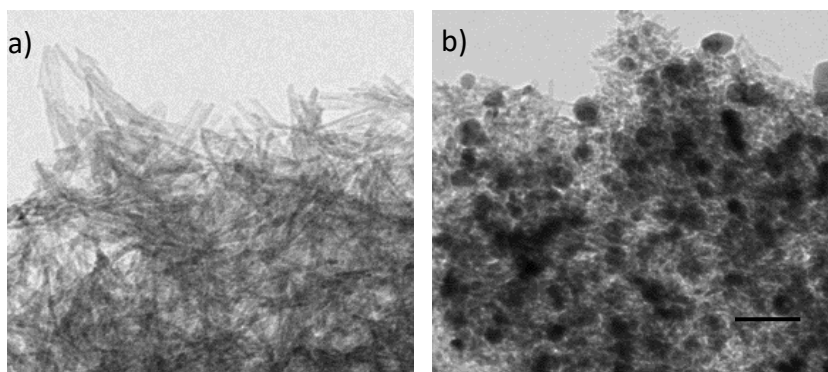
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Photocatalysis has attractive potential applications in many areas such as conversion of solar energy into chemical energy as well as an emergent advanced oxidation technique to remove pollutants from wastewater and/or air [1]. Many nanocrystalline semiconductors have been explored and examined in detail for their use possibilities in this area.

In this work, titanate nanotubes modified with Ag nanocrystalline particles (AgTNT), with improved photocatalytic performance for pollutants removal, were produced using a photo-reduction approach [2]. The prepared materials were structural, morphological and optical characterized using X-ray powder diffraction (XRD), transmission electron microscopy (TEM), diffused reflectance spectroscopy (DRS) and X-ray photoelectron spectroscopy (XPS).

The application of these new photoactive materials for terephthalic acid and phenol photocatalytic degradation was investigated. The reusability of the AgTNT was evaluated in four successive degradation assays. The sensitized sample demonstrated excellent catalytic reusability ability, without loss of photochemical stability and photocatalytic performance. Additionally, a continuous increase on the Ag nanoparticles, in number and size, during these experiments was observed. A mechanism for this continuous growth of the Ag nanoparticles, after being activated by the light, was proposed and will be discussed.



TEM images of the TNT (a) and AgTNT (b) prepared during 60 min of irradiation.

Acknowledgements

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References

- [1] M. Kaneko and I. Okura (Eds.), Photocatalysis: Science and Technology, Biological and Medical Physics Series, Springer, Berlin 2010.
- [2] B. Barrocas, C.D. Nunes, M.L. Carvalho, O.C. Monteiro, Appl. Surf. Sci. 385 (2016) 18-27.

Biocompatible porous materials to be used as donors of therapeutic doses of nitric oxide

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Nitric oxide (NO) is one of the few gaseous signalling molecules known to act as a transcellular messenger in many key physiological and pathological processes, being an attractive alternative for therapy of several diseases [1]. Conventional homogeneous NO donors are limited due to its systemic action, which compromises selectivity and may cause undesirable side effects [2]. This problem has boosted the development of new NO donors with the ability to release controlled doses of NO in a local biological target for a specific application.

In this context, porous materials with proven potential for gas adsorption have gathered particular interest for the delivery of exogenous NO. In this work, we present some of our recent advancements in this topic. The research was concentrated in three different types of materials: titanosilicates, clays and metal organic frameworks (MOFs). These materials have been synthesized and characterized to evaluate the appropriate porosity to store NO and, at the same time, to their biocompatibility.

Kinetic studies of NO adsorption and release were performed in both gas and liquid phases, using a microbalance associated with a high-vacuum system and using the oxyhemoglobin assay, respectively. Materials biocompatibility was evaluated through toxicity assays with and without NO-loaded using HeLa cells and primary human epidermal keratinocytes (HEKn). Moreover, the control of the biological processes in the presence of the different NO donors was evaluated through the inhibition of mitochondrial respiration and the acceleration of the cell migration that simulate a wound healing process.

According to the kinetic adsorption profiles, the materials feature good gas storage properties, loading between 3.5 to 7 % (w/w) of NO. Gas release studies showed that at least 60 % of the NO previously adsorbed was after released from titanosilicates and clays, indicating a partial irreversible adsorption, whereas in MOFs total release was observed. Liquid phase studies revealed a controlled release over time.

Toxicology results are very encouraging for titanosilicates and MOFs, even when using a high concentration (toxicity \approx 20 % at 24 h, 450 $\mu\text{g}/\text{mL}$). Some materials also show the ability to inhibit mitochondrial respiration at high concentrations (450 $\mu\text{g}/\text{mL}$), demonstrating the controlled release. Cell migration studies showed a migration acceleration up to 10 % for ETS-4 with NO loaded, comparing to the control (material without NO).

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References

- [1] Hirst, D.G., Robson, T., in:; McCarthy HO, Coulter JA (Eds.), Nitric Oxide Methods Protoc., Humana Press, Totowa, NJ 2011, pp. 1–13.
- [2] Keefer, L.K., Biomaterials: Thwarting thrombus. Nat Mater 2003, 2, 357–358.

Novel non-toxic antifouling strategies for biofouling control

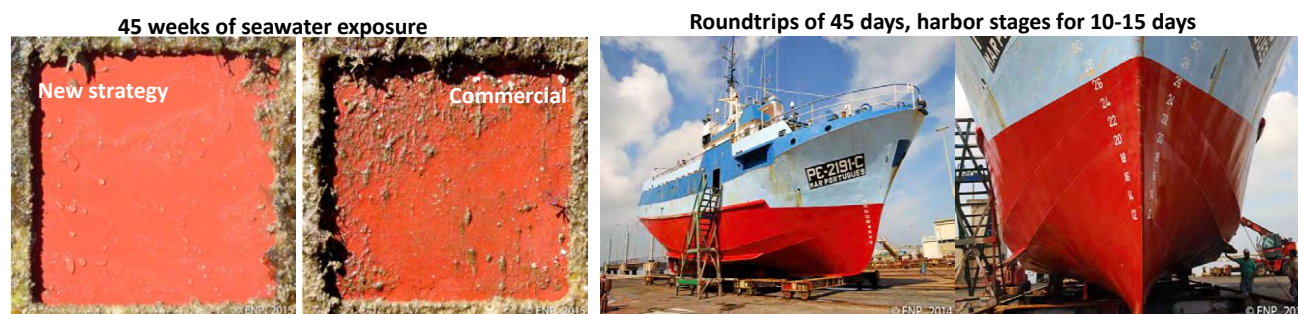
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Biofouling is one of the most serious problems in water-based systems (e.g. shipping, water purification units). It can promote substrate deterioration, systems clogging and fluids contamination, resulting in costly maintenance and retrofitting consequences. The most efficient methods to control biofouling is mainly based on a chemical strategy [1]. They comprise the direct and/or controlled releasing of toxic agents into the contaminated surface. However, the main drawback of those systems is the poor control on agents loss, and their continued release into the environment that has proven to cause serious side effects on ecosystems, mainly owing to their ecotoxicity and cumulative effect [2]. Rigid international regulations have been issued (BPD, EU Regulation N^o528/2012) which address the use of some current agents or antifouling products. More efficient and sustainable environmental-friendly antifouling solutions are sought.

In compliance with this global aiming, the present work shows the effective development of antifouling polymeric coatings (e.g. marine coatings), through an innovative non-releasing, long-lasting and environmentally friendly strategy, based on the chemical immobilization of biocides [3]. The antifouling efficacy of those materials at real static and dynamic conditions, and/or simulated conditions, has shown auspicious results, also suggesting an antifouling action mainly by contact. The immobilization ability has been confirmed through FTIR and RMN spectra analysis. Accordingly, even with the European Standards, an ecotoxicity study revealed that the environmental impact of the new antifouling materials is low. The proof-of-concept of this novel strategy on different applications, such as structured filters, aquaculture nets, microparticles, and on new nature-inspired biomimetic agents' based coatings, is on-going. This novel strategy is here presented as an attractive alternative to the actual conventional releasing strategies.



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References

- [1] A. G. Nurioglu, A. C. C. Esteves, W. Gijsbertus, J. Mat. Chem. B, 3 (2015) 6547-6570.
- [2] J. Chan, S. Wong, Biofouling, Types, Impact, and Anti-fouling. Pollution Science, Technology and Abatement Series, Nova Science Publishers, New York, 2010.
- [3] E. R. Silva, O. Ferreira, J.C. Bordado, Functionalization process for biocide immobilization in polymeric matrices, Patent Application, WO2016/093719 A1, 2016.

Synthesis and evaluation of antitumor activity of novel thiobenzanilides

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Cancer is a generic term for a large group of diseases where there is an uncontrolled growth of cells [1] and, according to the World Health Organization [2], caused 8.8 million of deaths in 2015. The number of cancer cases has been increasing worldwide due to the growth and/or aging of the population, as well as the prevalence of risk factors, including smoking and sedentary lifestyles, among others. Melanoma is not the most common type of skin cancer but it is the deadliest one [3], with a global incidence of almost 132000 cases each year [2]. Breast cancer is the most incident in women (almost 25% of the cases) both in developed and developing countries [2]. Due to the complexity and specificity of each cancer, it is necessary to develop new drugs and new and more effective therapies, in order to combat this problem.

In this context, we decided to synthesize a series of new thiobenzanilides and evaluate their activity against melanoma and breast cancer cell lines. Thiobenzanilides are compounds which are well known for their broad biological spectrum, showing antifungal, antimycotic, antibacterial, spasmolytic and also antitumoral activity [4]. In the present work, five new thiobenzanilide derivatives (Figure 1) were synthesized in a two steps pathway, and were characterized by 1D/2D NMR and IR. The structure of the compounds was chosen so that we could study the influence of R1 substituents on their anticancer activity. This activity was assessed against breast cancer human cells (MCF 7) and human melanoma cells (A375) using the MTT assay (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) colorimetric test, being determined for each compound the concentration which killed 50% of the cells, *i.e.*, the IC50 value.

So far, the majority of the compounds tested positive against both cell lines, in the micromolar range, and these are very promising results for this type of compounds.

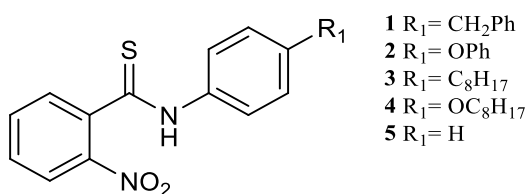


Figure 1- Structure of the new synthesized thiobenzanilides.

Acknowledgements

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References

- [1] H. A. Bhuvu, S. G. Kini, J. Mol. Graph. Model. 29 (2010) 32–37.
- [2] <http://www.who.int/cancer/en/>, accessed on May 8, 2015.
- [3] <http://www.skincancer.org>, accessed on May 8, 2015.
- [4] M. Kucinska, H. Piotrowska-Kempisty, N. Lisiak, M. Kaczmarek, H. Dams-Kozłowska, W. H. Granig, M. Höferl, W. Jäger, M. Zehl, M. Murias, T. Erker, Toxicol. Vit. 37 (2016) 148–161.

Synthesis and Anticancer Evaluation of Novel Azide-, Phosphoramidate- and Carboxamide-containing Nucleosides

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Nucleotides are key molecules in essential metabolic pathways for cell growth and division. The interference with such processes, which are frequently uncontrolled or over-activated in cancer cells, is a valuable therapeutic approach for cancer. Nucleoside and nucleotide analogs/mimetics have potential to compete with their physiological counterparts, which may result in the inhibition of nucleotide-mediated pathways and induce antiproliferative effects [1]. The feasibility of this rationale is well demonstrated by the various compounds of these types in clinical use. The access to new nucleoside/nucleotide-like structures and the study of their biological profile remains important in anticancer drug research.

Within the context of our interest in the development of new bioactive *N*-glycosyl compounds, we report herein on the synthesis of novel azido nucleosides, their phosphoramidates and glucuronamide-based analogs [2,3]. Some compounds exhibited potent antiproliferative activities in malignant cells, namely in chronic myeloid leukemia and in breast cancer cell lines, with GI₅₀ values in the micromolar concentration range. Further biological studies revealed that the most active nucleosides act by induction of cell cycle arrest or by caspase-mediated apoptosis.

In this communication, the chemical approaches towards the target compounds and the results of the biological evaluation will be disclosed.

Acknowledgements

Support for this work was provided by FCT through projects UID/MULTI/00612/2013 and IF/01488/2013/CP1159/CT0006.

References

- [1] L. P. Jordheim, D. Durantel, F. Zoulim, C. Dumontet, *Nat. Rev. Drug. Discov.* 12 (2013) 447–464.
- [2] N. M. Xavier, R. Gonçalves-Pereira, R. Jorda, E. Řezníčková, V. Kryštof, M. C. Oliveira, *Pure Appl. Chem.* (2017) DOI: 10.1515/pac-2016-1218.
- [3] N. M. Xavier, A. Porcheron, D. Batista, R. Jorda, E. Řezníčková, V. Kryštof, M. C. Oliveira, *Org. Biomol. Chem.* (2017) DOI: 10.1039/C7OB00472

Polymorphism in Molecular Organic Pharmaceuticals

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Since the middle of the last century, it has been widely recognized that many organic compounds can be obtained in more than one crystal structure, a phenomenon known as polymorphism. It also became apparent that the adopted crystal structure often exerts a significant effect in the solid-state properties of the compounds, so that, in fact, each polymorph should be regarded as a different material. The lack of control over polymorphism may, therefore, wreak havoc with the production, safe use, shelf life, and patenting of fine chemicals such as organic conductors, explosives, pigments, and pharmaceuticals. Polymorphism has, in fact, been of particular concern in the pharmaceutical industry since various examples have been reported where the unexpected appearance of new polymorphic forms at the production stage led to the recall of marketed medicines with enormous financial losses (e.g. the ritonavir and avalide cases).

Organic polymorphs can often coexist at the same temperature and pressure conditions, but they may evolve over time to the most thermodynamically stable one. Thus, once polymorphism has been identified and structurally characterized it is very important to define a stability hierarchy among different forms.

In this presentation, a small overview of ongoing polymorphism studies at the Molecular Energetics Group, involving model systems and active pharmaceutical ingredients, will be given. This will include the very recent determination of the relative stability of two known polymorphs of the anticancer drug erlotinib hydrochloride (Figure 1).

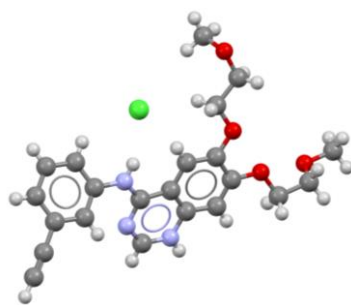


Figure 1. Molecular structure of erlotinib hydrochloride.

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Human fingerprints through the eyes of mass spectrometry

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Human fingerprints uniquely identify a subject and as such are of invaluable forensic value. Until now, human fingerprint analysis has been performed through a plethora of image recording and enhancing methodologies that produce an image that can be uniquely linked to a single subject. However, little is known of the biochemical composition of the physical trace that is translated into the fingerprint image. It contains endogenous substances (metabolites, proteins) as well as exogenous ones (grooming products, substance of food origin and eventually drugs and explosives). The detailed biochemical composition of a fingerprint adds a third dimension to its analysis and is of very high forensic potential. Chemical analysis of fingerprints has been recently initiated, but it has been performed in small scale and mainly through low resolution mass spectrometry instruments that are widespread in academic and forensic labs. However, the biochemical composition of a fingerprint may contain tens of thousands of chemical species, in vastly different relative concentrations and molecular weights, thus begging for the use of high-resolution mass spectrometry equipment. FTICR-MS (Fourier Transform Ion Cyclotron Mass Spectrometry) provides the ultimate resolving power and mass accuracy to unequivocally identify small molecules as well as proteins in the same sample. The main purpose of this project is to implement a forensic analysis workflow exploiting the biochemical composition of human fingerprints, using the highest resolution and mass accuracy that can only be provided by FTICR-MS. Preliminary results show that individual fingerprints are unique for each analysed subject, on a given moment, reflecting their daily habits. Also, it was possible to discriminate subject gender.

Acknowledgements

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Considerations on Sample Preparation in the Age of Green Analytical Chemistry

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Sample preparation plays an important role in several analytical or bioanalytical chemistry laboratories. This step is many times required particularly when trace analysis are involved (promoting a pre-concentration of the target analytes) or we are dealing with complex samples (eliminating interference compounds), prior the application of chromatographic or hyphenated techniques [1]. Meanwhile, the time usually necessary for sample preparation can be as high as more than 60 % of the overall time involved in the analytical procedure and the sources of error generated can be up to 30 %, particularly if the concentrations are below the parts-per-billion range [2]. For these reasons, over the past three decades, the passive or static microextraction sampling techniques have gained more acceptance in almost all scientific areas, due to the cost-effectiveness and much easier manipulation, simplification, miniaturization, strong reduction or absence of toxic organic solvents, as well as the low sample-volume requirements, in compliance with the principles of the green analytical chemistry (GAC) [3]. Recently, the *Separation, Science & Technology* group introduced a novel microextraction techniques, bar adsorptive microextraction (BA μ E), which have demonstrated remarkable performance in the analytical chemistry point of view and showed to be an effective alternative for many type of applications [4,5]. These devices have been successfully applied for trace analysis of several classes of priority compounds (*e.g.*, pesticides, drugs of abuse, steroid hormones, and disinfection by-products of water, pharmaceutical and personal care products, among many others) in several types of real matrices (*e.g.*, urine, saliva, environmental water, wastewater, tea and tobacco products, etc.).

The present contribution is an overview on the main advantages of BA μ E in the age of GAC, including the novel improvements introduced, making this technique a more eco-user-friendly analytical approach.

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References

- [1] J. van der Geer, J.A.J. Hanraads, R.A. Lupton, *J. Sci. Commun.* 163 (2010) 51–59.
- [2] S. Mitra, *Sample Preparation Techniques in Analytical Chemistry*, first ed., John Wiley & Sons, New Jersey, 2003.
- [3] J.M.F. Nogueira, *TrAC*, 2015, 71, 214-223.
- [4] N.R. Neng, A.R. Silva, J.M.F. Nogueira, *J. Chromatogr. A* 1217 (2010) 7303–7310.
- [5] J.M.F. Nogueira, *Anal. Chim. Acta*, 757 (2012) 1–10.

Metabolic lighthouses in downy mildew resistance

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Metabolomics studies have been gaining attention through the years since they allow a comprehensive qualitative and/or quantitative analysis of the slightest changes in the cell, tissue or organism, in response to intrinsic or extrinsic factors. These metabolomics changes are closely related to the observed phenotype making it an ideal tool for a wide range of industries.

In the wine industry, a complete understanding of the metabolic composition of *V. vinifera* cultivars is extremely important, not only for productivity and quality improvement, metabolic pathway engineering and food safety assessment, but also to understand their physiology and response under stress conditions [1]. *V. vinifera* cultivars, frequently used for wine production, are highly susceptible to fungal diseases. One of the most destructive vineyard diseases is downy mildew, caused by the biotrophic oomycete *Plasmopara viticola* (Berk. et Curt.) Berl. et de Toni [2], resulting in serious negative effects in several countries' economy. Thus, a metabolic characterization of grapevine leaves towards the identification of biomarkers is a promising new approach for a better understanding of the innate resistance/susceptibility of some cultivars to *P. viticola*. We developed a metabolite extraction method for grapevine leaves [3], performed a large scale metabolic characterization using Fourier Transform Ion Cyclotron Resonance MS (FTICR-MS) and identified several metabolic entities that enable a constitutively discrimination between resistant and susceptible plants. These biomarkers will lighten the path for precision agriculture and sustainability in the wine industry.

Acknowledgements

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References

- [1] U. Roessner, L. Willmitzer, and A. Fernie, *Plant Cell Rep.*, vol. 21, no. 3, pp. 189–196, 2002.
- [2] C. Gessler, I. Pertot, and M. Perazzolli, *Phytopathol. Mediterr.*, vol. 50, no. 1, pp. 3–44, 2011.
- [3] M. Maia *et al.*, *EuPA Open Proteomics*, vol. 12, pp. 4–9, 2016.

Plasma membrane domains of filamentous fungi reorganize extensively during the lag phase

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Sphingolipids (SLs) are, in addition to glycerophospholipids and sterols, the main structural lipids of biological membranes of eukaryotes and SL-enriched membrane domains have been implicated in many fundamental cellular processes ranging from antifungal resistance to apoptosis [1-4]. The crucial role of complex SLs in fungal membrane structure and dynamics has been a neglected theme in the context of the fungal resistance health threat recognized by the World Health Organization (WHO).

The first model organism used in this work was *Neurospora crassa*, a filamentous fungus, in the conidial stage, which presents ideal features to study SL-enriched domains, namely very low ergosterol content. Several changes in lipid metabolism and in the membrane composition of *N. crassa* occur during spore germination. However, the biophysical impact of those changes was unknown. Thus, a biophysical study of *N. crassa* plasma membrane, particularly SL-enriched domains, and their dynamics along conidial germination was prompted.

Two *N. crassa* strains, wild-type (WT) and slime, which is devoid of cell wall, were studied. Conidial growth of *N. crassa* WT from a dormancy state to an exponential phase was accompanied by membrane reorganization, namely an increase of membrane fluidity, occurring faster in a supplemented medium than in Vogel's minimal medium. Regarding biophysical properties strongly affected by ergosterol, the plasma membrane of slime conidia lays in between those of *N. crassa* WT and *Saccharomyces cerevisiae* cells [5]. Finally, SL-enriched domains in a gel-like phase were found in both *N. crassa* strains, but were particularly compact, rigid and abundant in the case of slime cells, even more than in budding yeast *S. cerevisiae*. This novel type of domains found in our group, starts to emerge as a general feature of fungal membranes.

This work was the starting point for the study of the plasma membrane biophysical properties of filamentous fungi in the presence of antifungal agents, namely Staurosporine, which are currently under investigation.

Acknowledgements

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F.C.S. acknowledges PhD. Scholarship SFRH/BD/108031/2015.

References

- [1] Cowart, L. A. et al., *Biochim. Biophys. Acta*, 1771 (2007) 421-431.
- [2] Fernandes, A. S. et al., *Apoptosis*, 18 (2013) 940-948.
- [3] Fernandes, A. S. et al., *Fungal Genetics and Biology*, 48 (2011) 1130-1138.
- [4] Castro, A. et al., *Eukaryotic Cell*, 9 (2010) 906-914.
- [5] Santos, F.C. et al., *Biochim. Biophys. Acta – Mol. Cell Biol. Lipids*, 1862 (2017) 156-166.

Electroless Precipitation, an Electrochemical and Microgravimetric study

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The fully oxidized state of polyaniline (pernigraniline form) spontaneously reduces, in acidic medium, to produce protonated emeraldine. So, it is expected that in the presence of metallic ions that can act as oxidizing species, spontaneous deprotonation occurs with simultaneous reduction of the metal ion - eventually to zero oxidation state – continuing the process while the polymer is exposed to the solution [1]. Since the state transitions of PANi (Protonated Emeraldine - Pernigraniline) occur between 300mV and 800mV vs. SCE, metal ions undergoing electroless precipitation should have a reduction potential in this potential window, limiting this reduction process to noble metals [2]. This spontaneous, selective and sustained reduction of metal ions is of particular importance in the field of extractive metallurgy [3].

In this work, the process of electroless precipitation of silver from acidic dilute solutions of silver ions is investigated. Thin PANi films were electrochemically synthesized in platinum and vitreous carbon electrodes and exposed to 1 mM silver solutions for different periods at ambient temperature. The effect of film thickness and immersion time in the silver extraction efficiency was evaluated by optical microscopy and electrochemical characterization of the pristine films and those that were exposed to the silver containing solutions. It was observed that the amount of reduced silver increases with polymer thickening.

The synthesis process and the redox conversion of the modified electrodes were evaluated by Electrochemical Quartz Cristal Microbalance (EQCM). Furthermore, it was unequivocally determined that the amount of silver hold in the PANi film is correctly obtained by the integration of the silver oxidation peaks resulting from the voltammetric response of the modified electrodes. This methodology was applied to quantify and understand the viability of reusing the polymer for multiple extraction runs. It was determined that the modified electrode can extract silver for 18 consecutive runs.

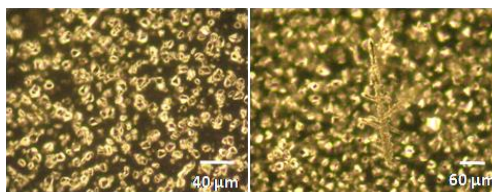


Figure 2: Micrographs of dispersed silver in polyaniline films

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References

- [1] L. M. Abrantes, J. P. Correia, *Mat. Sci. Forum.* 191 (1995) 235-240.
- [2] V. Lyutov, V. J. Tsakova, *Solid State Electrochem.* 15 (2011) 2553-2561.
- [3] P. Ting, K.H. Neoh, E.T. Kang, K.L. Tan, *J. Chem. Tech. Biotechnol.* 59 (1994) 31-36.

Study of enthalpies of sublimation of organometallic compounds

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The ability to study the behaviour of a system at the molecular level to predict macroscopic properties is a long-term goal in chemistry and engineering, since it has the potential to reduce the need for expensive and time-consuming experimentation. Molecular dynamics (MD) is perhaps the most promising cost-effective computational technique to perform these studies. It is a general approach that, based on simple atom-atom pair's potential calculations, currently allows the investigation of many physical processes. The key aspect of this methodology is the definition of an intermolecular potential function capable of accurately describing the interactions. However, although a large set of parameters exist for, e.g. hydrocarbon compounds, no reliable parametrization exists for materials containing transition metals, which are extremely important to model, for example, proteins. Thus, the work here described, is part of an ongoing project at the Molecular Energetics Group (CQB-FCUL), to produce a parametrization suitable for the study of compounds containing transition metals, by MD simulations.

One way to accurately establish interaction potentials, involves the determination of a set of parameters that reproduce the cohesive energy of materials – which can be obtained from the enthalpy of sublimation of the compounds – and the spatial arrangement of the molecules (e.g. crystal structures). Although values of enthalpies of sublimation can be found in the literature, these are frequently not assigned to a well characterized crystal structure, leading to large discrepancies between published data. Thus, in this work, enthalpies of sublimation of organometallic compounds were determined for well characterized materials, both in terms of chemical and phase purity. A focus was employed to compounds containing rhenium (e.g. methyltrioxorhenium and decacarbonyl-dirhenium) due to the importance of this metal in the development of new non-radioactive materials for imaging in nuclear medicine and radiotherapy, for the diagnostic and treatment of cancer.

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Hysteresis in solution for an alkyl functionalized iron(III) complex

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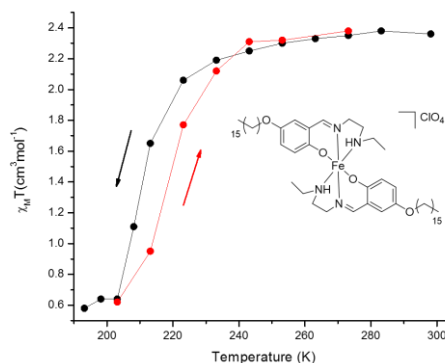
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The ability of certain first row transition metal ions to switch electronic state with thermal or optical stimulus has long been cited as having excellent potential for data storage, and in recent years the emphasis has moved from synthesis of new examples towards suitable engineering of existing complexes into polymeric or amphiphilic environments.[1] Amphiphilic compounds have proved to promote self-assembly in solution with some few examples displaying hysteresis. This opens new opportunities for solution processing magnetic materials.[2]

Here we present the preparation of an alkyl functionalised iron(III) compound [Fe(LOC16)2]ClO₄, Figure 1. The magnetic profile of the compound was analysed both in solid state and solution with the latter showing the formation of a cooperative system proved by the spin crossover with a hysteresis window of 15 K around 220 K. The nature of both the spin crossover and hysteresis was further investigated using different techniques such as NMR, SQUID, EPR, UV-visible spectroscopy and Mössbauer spectroscopy.



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References

- [1] M.A. Halcrow (Ed.), Spin-Crossover Materials: Properties and Applications, John Wiley & Sons Ltd., Chichester, 2013
- [2] P.N. Martinho, Y. rtin, B. Gildea, C. Gandolfi, G. McKerr, B. O'Hagan, M. Albrecht, G.G. Morgan, Dalton Trans. 41 (2012) 746

Oxidation of Sulfides with Mo (nanostructured) materials

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Since the first report on the synthesis of sulfoxides by Marcker in 1865 [1], many processes for the conversion of sulfides to sulfoxides using nitric acid, hydrogen peroxide, dinitrogen tetroxide, ozone, peracids, hydroperoxides and many other reagents have been developed. Sulfoxides and sulfones have found many applications in pharmacy and other fields such as engineering plastics and polymers. Oxidation of sulfides is the most direct approach for the synthesis of sulfoxides and sulfones. Many different catalysts have been applied for oxidation of organic substrates but in order to make this process rapid, selective and consist of higher yields of products, the use of catalysts is mandatory. As a result of the apparent interest in the perfection of oxidation product synthesis, many explorations have been commenced to develop catalysts for oxidation, e.g. supported metal oxides as well as homogeneous transition metal complexes [2].

In this work new nanostructured materials were synthesized and characterized. Their application as catalysts in the oxidation of sulfides to sulfoxides has been studied afterwards.

The catalyst was prepared from molybdenum chloride (V) (MoCl_5) using a hydrothermal method. Molybdenum trioxide (MoO_3) nanoparticles were obtained, which were characterized by infrared spectroscopy (DRIFT) and powder X-ray diffraction (XRD).

The use of the MoO_3 nanoparticles as catalysts was then aimed at the oxidation of sulphides to sulphoxides. The reactions were studied by varying some key parameters, namely the oxidizing agent (*tert*-butyl hydroperoxide and hydrogen peroxide), the oxidizing agent ratio, temperature (room temperature, 55, 80 and 110 °C), solvent (dichloromethane, toluene and acetonitrile) and the substrate (diphenyl sulfide, dimethyl sulfide and methylphenyl sulfide).

In most reactions, oxidation to sulfoxide occurs selectively when using *tert*-butyl hydroperoxide. When using hydrogen peroxide as oxidizing agent only in a single reaction the transformation of sulfoxide to sulfone is observed. From the set of substrates tested, dimethyl sulphide seems to be the one for which the catalytic system is not ideal, as no conversion was observed even after tests at 110 °C.

It was possible to verify that most of the catalytic studies were finished after 6h30, at most. However, some of them were very fast reactions, being completed in just 10 or 15 minutes.

In summary, the best reaction conditions obtained were at lower temperatures, at 55 °C, where the conversion of sulfoxide was 100% in dichloromethane and using 200% *tert*-butyl hydroperoxide obtained after just only 5 minutes reaction time.

Acknowledgements

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References

- [1] C. Marcker, Ann. 136 (1865) 75.
- [2] M.M. Javadi, M. Moghadam, I. Mohammadpoor-Baltork, S. Tangestaninejada, V. Mirkhani, H. Kargar, M. N. Tahir, Polyhedron 72 (2014) 19–26.

TBCCD1 and OFD1, a novel centrosomal protein partnership with a role in human ciliopathies?

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Cilia are hair-like appendages, consisting of a microtubule (MT)-based ciliary axoneme, that fulfill critical motility and sensory functions required for normal embryonic development and also for homeostasis of adult tissues. At their base, cilia have a centriole/basal body, which can be derived from the centrosome, and that nucleates the ciliary axoneme (primary cilia). Centrosomes consist of a pair of centrioles surrounded by the pericentriolar matrix that nucleate/organize the cytoskeleton and are implicated in cell migration, adhesion and polarity, while in mitosis they assist spindle pole formation [1]. Importantly, centrosomal and cilia malfunctions are implicated in human diseases. Abnormal centrosome numbers are associated with aberrant cell divisions and are thought to contribute to aneuploidy and tumor formation. Moreover, mutations in genes coding for centrosomal proteins cause microcephaly, dwarfism and ciliopathies [2]. The number of identified ciliopathies is growing and they are typified by often overlapping clinical manifestations e.g. infertility, obesity, brain and skeletal developmental problems, blindness and kidney cysts.

We have identified a centrosomal TBCC domain-containing human protein (TBCCD1) whose depletion in human retina cells (RPE1) severely affects the position of the centrosome relative to nucleus with impact in Golgi apparatus (GA) and primary cilia assembly [3]. Recent observations by our group showed that: a) TBCCD1-depletion phenotype of centrosome mispositioning was partially rescued by taxol, a MT stabilizing agent; b) displaced centrosomes had less MTs organized in an asymmetric aster. This was accompanied by altered distribution patterns of both acetylated MTs and Cep170, a protein present in centrosome subdistal appendages and associated to MT; c) Upon MT depolymerization followed by recovery, misplaced centrosomes slowly polymerize the MT aster that ultimately becomes disorganized. We have also screened for TBCCD1 interactors and found a rich interaction space composed of several well-known proteins encoded by genes involved in ciliopathies, such as OFD1. The *Ofd1* gene is mutated in the Oral-facial-digital syndrome, an X-linked dominant ciliopathy characterized by oral anomalies, facial dysmorphism, polydactyly and defects of the CNS like microcephaly. Our preliminary results show that TBCCD1 depletion, besides affecting cilia assembly, disturbs OFD1. Experiments are being carried out to establish a functional relationship between TBCCD1 and OFD1.

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References

- [1] Bettencourt-Dias, M., & Glover, D. M. *Nature Reviews. Molecular Cell Biology*, 8 (2007) 451–463.
- [2] Waters, A. M., & Beales, P. L. *Pediatric Nephrology*, 26 (2011) 1039–1056.
- [3] Gonçalves, J., Nolasco, S., Nascimento, R., Lopez Fanarraga, M., Zabala, J. C., & Soares, H. *EMBO Reports*, 11 (2010) 194–200.

Nanostructured platforms for sensitive immunosensors

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Clinical samples are composed by several biological molecules within a wide range of concentrations, therefore, the detection of target analytes, usually present in trace amounts, requires a method with high detection limit [1]. Using the natural antibody-antigen affinity, immunosensor platforms are a useful approach that combines stability, biocompatibility, versatility with high sensitivity [2]. One of the most popular approaches to improve the detection limit of optical immunosensors, such as those using the surface plasmon resonance (SPR), is the incorporation of nanoparticles (e.g. Au, Fe₃O₄) [3].

Considering the sandwich assays, where small target molecules can be detected using a couple of antibodies, the nanoparticles can be used i) to increase the amount of the primary antibody, if used on the biorecognition layer or, ii) to label the secondary antibody (e.g. change of the refractive index), when employed on the detection layer of the sandwich type immunosensor. We are developing innovative strategies to tackle both challenges, by combining adequate nanoparticle biofunctionalization methodologies with *in situ* dithiocarbamate chemistry [4], to properly immobilize antibody molecules [5] on gold surfaces. Apart from the optical detection techniques (SPR, conventional and imaging ellipsometry) to follow the antibody-antigen reaction, we are also using electroactive molecules (e.g. epinephrine, porphyrin, ferrocene) to label gold and semi-conducting nanoparticles in order to amplify the detection limits by using electrochemical techniques.

Overall, we aim to develop a useful approach that can be tailored for the sensitive detection of cancer biomarkers, in clinical trials, or small pollutants (e.g. toxins) in environmental samples.

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References

- [1] X. Liu, Q. Dai, L. Austin, J. Coutts, G. Knowles, J. Zou, H. Chen, Q. Huo, *J. Am. Chem. Soc.* 130 (2008) 2780-2782.
- [2] I. Almeida, J.T. Marquês, W. Liu, Y. Niu, R.F.M. de Almeida, G. Jin, A.S. Viana, *Colloids Surf., B* 136 (2015) 997-1003.
- [3] Y. Uludag, I.E. Tothill, *Anal. Chem.* 84 (2012) 5898-5904.
- [4] I. Almeida, F. Henriques, M.D. Carvalho, A.S. Viana, *J. Colloid Interface Sci.* 485 (2017) 242-250.
- [5] Y. Niu, A.I. Matos, L.M. Abrantes, A.S. Viana, G. Jin, *Langmuir* 28 (2012) 17718-177

Electrochemical oxidation of paraquat in neutral medium

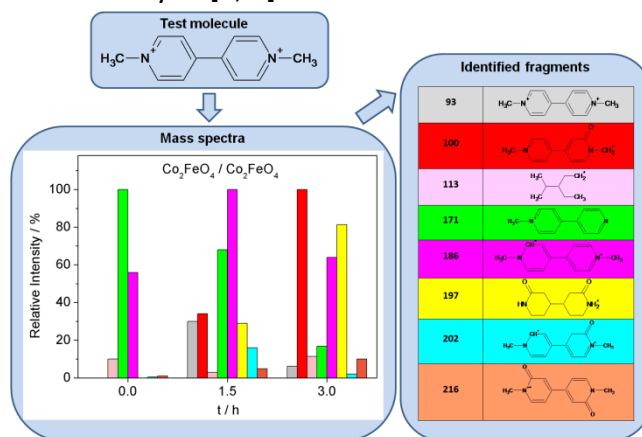
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Contamination of water due to the presence of pesticides is one of the serious environmental problems with a major public health impact closely related to agricultural development. Paraquat is one of the most toxic and widely used herbicides in the world. Although it is prohibited by European Union, it is still used in developing countries in other continents. As a nonselective contact herbicide, it is present as an environmental pollutant both in soil and in surface waters. It represents a threat to human health because even at very low doses, this herbicide can pass treatment steps in a water treatment plant and reach the water distribution systems. Studies of the degradation of this compound by biological and photochemical processes are cited in the literature, but complete degradation is not achieved. References to electrochemical methods are scarce [1, 2].

This communication presents the electrochemical oxidation of paraquat in aqueous solutions using steel, Pt and pelleted Co_2FeO_4 electrodes. The oxide electrodes were structural and morphological characterized by XRD and SEM and electrochemical by cyclic voltammetry. Paraquat electrochemical oxidation was carried out by electrolysis at constant current and monitored by UV-vis spectroscopy and mass spectrometry. Different anode/cathode pairs were used. Mass spectrometry analysis indicates that the main intermediate oxidation products were monopyridone and dipyrindone derivatives. A quite high removal was obtained with the electrode $\text{Co}_2\text{FeO}_4 / \text{Co}_2\text{FeO}_4$ after 3h of electrolysis [2, 3].



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References

- [1] N. Klammerth, S. Malato, M.I. Maldonado, A. Agüera, A.R. Fernández-Alba, *Environ. Sci. Technol.* 441 (2010) 792–1798.
- [2] M.A.M. Cartaxo, C.M. Borges, M.I.S. Pereira, M.H. Mendonça, *Electrochim. Acta* 176 (2015) 1010–1018.
- [3] M.H. Florêncio, E. Pires, A.L. Castro, M.R. Nunes, C. Borges, F.M. Costa, *Chemosphere* 55 (2004) 345–355.

Photo-degradation of citalopram in surface water: Identification of transformation products

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Citalopram, a selective serotonin reuptake antidepressant inhibitor (SSRI), has a high consumption in the world for the treatment of depression.¹ There are numerous studies that have detected this drug in effluents and surface waters but there are few studies of the fate and transformation products (TPs) in the environment or in the wastewater treatment plant (WWTP).^{2,3} The processes of formation of TPs are important pathways for emerging compounds in environment, their identification is fundamental to understand the risks that may cause in the environment.

The objective in this study is to identify the formation of TPs of citalopram that might be found in the environment, by means of simulations of photo-degradation under controlled conditions that may occur in the aquatic environment and in the wastewater treatment plant.

TPs were identified and elucidated by ultra-high-performance liquid chromatography (UHPLC) coupled to a hybrid quadrupole time of flight mass spectrometer (QTOF MS) operating in both positive-ion and negative-ion mode.

The experiments resulted in 6 possible identified TPs. There was an increase in TPs formation, named TP-PH1 (C₁₉H₁₇N₂O₂F), TP-PH2 (C₁₉H₁₉N₂O₂F), and TP-PH3 (C₂₀H₁₉N₂O₂F), over time. Another TP, named TP-PH4 (C₂₀H₁₉N₂O₂F), showed stability over time. Desmethylcitalopram (TP-PH2, C₁₉H₁₉N₂O₂F) and citalopram N-oxide (TP-PH5, C₂₀H₂₁N₂O₂F) human metabolites, were detected in these experiments and showed that the compounds can be formed under UV-light.

The probable structures of TPs were established based on two prediction tools softwares: EAWAG-BBD: Pathway Prediction and Bruker MetabolitePredict. Analyses were based on accurate mass and on the fragmentation observed in the MS spectra and the mass errors were less than 5 ppm. A possible degradation pathway was proposed for the formations of TPs and the stability and formation of TPs was monitored in the experiments.

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References

1. OECD. Health at a Glance: Europe 2012. OECD Publishing
2. Evgenidou, E. N. et al., Science of the Total Environment. 2015, 505, p.905–926.
3. Subedi, B.; Kannan, K. Science of the Total Environment. 2015, 514, p.273–280.

Halogen Effect on Spin Crossover Molecules

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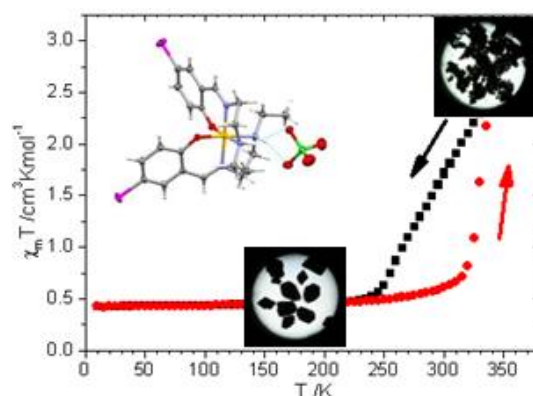
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Technological advances have been pushing the limits of chemistry for the last few years towards creating more efficient and multifunctional molecules and materials. A phenomenon that shows great promise in molecular electronics is spin crossover (SCO).[1] This switching can be harnessed to develop materials with a wide range of possible applications such as memory or sensing nano-devices.[2] Halogen derivatized SCO molecules are of great interest as they can interact with neighboring molecules through either halogen or hydrogen bonds and additionally they can be modified through substitution or coupling reactions conferring additional properties and high versatility to the SCO molecules.[3,4]

Here we report the synthesis and characterization of halogen derivatized SCO compounds with an Fe(III) metallic center coordinated to tridentate (N₂O) Schiff-base ligands. We have found that all compounds exhibit SCO with profiles ranging from gradual to abrupt with hysteresis. Detailed studies on the halogen influence on these are complemented with DFT calculations using recently developed spin state specific functionals.



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References

- [1] Gamez, P.; Costa, J. S.; Quesada, M.; Aromí, G., Dalton Trans. **2009**, 38, 7845.
- [2] Létard, J.; J. Mater. Chem. **2006**, 16, 2550.
- [3] Devid, E. J.; Martinho, P. N.; Kamalakar, M. V.; Šalitroš, I.; Prendergast, Ú.; Dayen, J. F.; Meded, V.; Lemma, T.; González-Prieto, R.; Evers, F.; Keyes, T. E.; Ruben, M.; Doudin, B.; van der Molen, S. J., ACS nano **2015**, 9, 4496.
- [4] Gaspar, A. B.; Ksenofontov, V.; Seredyuk, M.; Gülich, P., Coord. Chem. Rev. **2005**, 249, 2661.

Capture of Small Molecules by Metal-Organic Structures

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Host-guest structures have proved to be useful for the recognition and activation of small molecules [1]. Cascade complexes with polyaza ligands have demonstrated ability to bind different small molecules by adapting their binding sites towards these molecules. Nelson's cryptands [2] are an example of a dynamic structure with useful applications, which demonstrated the ability to capture and convert CO₂ to carbonate and methyl carbonate following its coordination to encapsulated metal ions. Here we explore the fixation chemistry of small molecules by derivatised dinuclear Cu(II), Ni(II) cryptands (Figure 1) where the phenyl ring was modified towards engineering these metal-organic structures into supramolecular assemblies. Attaching electron withdrawing or electron donating groups to the phenyl ring proved to affect their ability to capture CO₂. Synthesis of the cryptates were performed under N₂ and CO₂ atmosphere, to understand the substituent effect, DFT studies were performed, and their behaviour was studied by cyclic voltammetry.

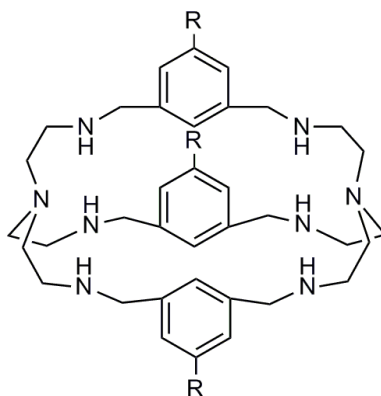


Figure 1 Derivatised cryptands.

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References

[1] D-C Zhongab, T-B Lu, Chem. Comm., 2016, 52, 10322-10337.

[2] Y. Dussart, C. Harding, P. Dalgaard, C. McKenzie, R. Kadirvelraj, V. McKee, J. Nelson, J. Chem. Soc., Dalton Trans., 2002, 1704.

A Comparative Study on the Energetics and Structure of Hydroxybenzoyl Compounds

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Polymorphism, the ability of a compound to crystallize in more than one solid form, is a phenomenon that can considerably affect the properties of materials (e.g. melting point, solubility, colour). As such, different polymorphic forms should be regarded as different materials, although formed by the same molecular unit.

Studies of polymorphism involving families of structurally related molecules are particularly interesting to understand how the interplay of molecular size, shape and intermolecular interactions may affect the packing architectures and relative stability of different crystal forms. One such family is that of 4-hydroxybenzoyl compounds, $\text{HOC}_6\text{H}_4\text{C}(\text{O})\text{R}$ ($\text{R} = \text{H}$, alkyl; Figure 1), differing only in the length of the alkyl chain bonded to the carbonyl group. Based on these materials it is, for example, possible to investigate how the hydrogen bond pattern sustaining the packing is affected by changes in the alkyl chain length and how these changes are eventually reflected by thermal events detected by calorimetric methods.

In this work, a comparative structural and energetic study of the 4-hydroxybenzoyl family of compounds will be presented. Polymorphism was identified for $\text{R} = n\text{-C}_4\text{H}_9$, $n\text{-C}_6\text{H}_{13}$, and the single crystal X-ray diffraction structures for $\text{R} = \text{C}_2\text{H}_5$, $n\text{-C}_4\text{H}_9$, $n\text{-C}_5\text{H}_{11}$, and $n\text{-C}_6\text{H}_{13}$ were determined for the first time. Although significant differences between the crystal structures are noted along the $\text{HOC}_6\text{H}_4\text{C}(\text{O})\text{R}$, calorimetric measurements showed that the cohesive energies are approximately additive.

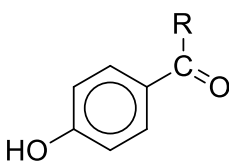


Figure 3. Molecular structure of 4- hydroxybenzoyl compounds ($\text{R} = \text{H}$, CH_3 , C_2H_5 , $n\text{-C}_4\text{H}_9$, $n\text{-C}_5\text{H}_{11}$ and $n\text{-C}_6\text{H}_{13}$).

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Polymorphism Studies in Niflumic Acid, Phenylbutazone, and Erlotinib Hydrochloride

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Polymorphism, the ability of a substance to crystallize in more than one lattice arrangement, is currently a major concern for the pharmaceutical industry, because it can strongly affect the design, clinical timelines, manufacturing, shelf-life, bioavailability, and patenting of solid dosage forms. Albeit the molecule does not change, different packing architectures can originate significant differences in physicochemical properties, such as fusion temperature, compressibility, and solubility/ dissolution rate, which play a key role in the production and performance of active pharmaceutical ingredients (API). The lack of control over polymorphism, therefore, creates serious problems for the production and safe use of medicines. There is also interest in controlling the morphology of crystals for processing reasons: cubic crystals will, for example, filter and wash easier than plate-like crystals.

The control of polymorphism and morphology of crystals is intimately related with crystallization since this is by far the most widely used method to obtain crystalline forms.

Here we describe studies of crystallization and polymorphism (structural and energetics) for three APIs namely, niflumic acid, phenylbutazone, and erlotinib hydrochloride (Figure 1). The first two are currently used for the treatment of rheumatoid arthritis and the third one is applied in cancer therapy. Despite being marketed, all these compounds have problems of ill defined polymorphism. The investigation relied on a variety of techniques, such as X-ray diffraction (XRD), microscopy, diffuse reflectance infrared Fourier transform spectroscopy (DRIFT), differential scanning calorimetry (DSC), and solution calorimetry.

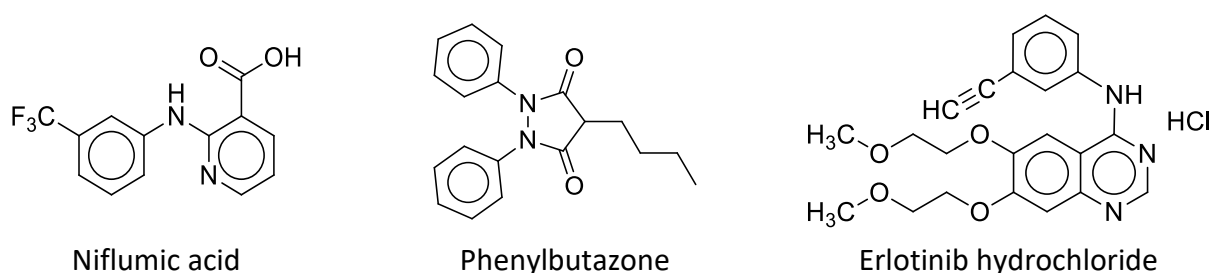


Figure 1. Molecular structures of niflumic acid, phenylbutazone, and erlotinib hydrochloride

Acknowledgements

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Iron(III) complexes for Electropolymerized Magnetic Films

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The construction of complex hybrid materials which combine different properties, i.e. multifunctional materials, has been at the heart of research in recent years. Among these, our interest is focused upon polymeric complexes that have the potential of featuring switching magnetic properties combined with electrical conductivity properties, with the goal of using conductivity by applying an external electric field to control the bistability in magnetic molecules and materials. For that, we wish to approach the fabrication of multifunctional materials using a common electrochemical strategy to prepare a conducting polymer thus preparing films with conducting polymers and spin crossover cations. Spin crossover (SCO) can occur in transition metal complexes when a suitable ligand field is present. In the case of iron(III), the transition occurs from a high spin $S=5/2$ state to a low spin $S=1/2$ state.¹

As a polymerisable unit, 3'-bromo-2,2':5',2''-terthiophene is particularly attractive because of its electrochemical stability and its high conductivity, both properties indispensable for preparing conducting polymers.² As a magnetic switching unit, the $[\text{Fe}(\text{salEen})_2]^+$ has been selected due to its known SCO behavior.³ Here we report the synthesis of both ligand and Fe(III) complexes that are used to materials development through electropolymerization of the thiophene unit. The magnetic properties of both complexes and polymer are also investigated.

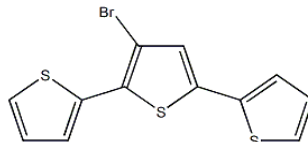


Figure 1. Electropolymerizable unit.

Acknowledgements

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Ingrid Suzana acknowledges financial support from Erasmus+ and from l'État managed by the Agence Nationale de la Recherche in accordance with l'Idex Sorbonne Universités in the context of the program « Investissement d'avenir / Bourse de mobilité internationale » of Sorbonne Universités.

References

- [1] David J. Hardinga, Phimpaka Hardinga, Wasinee Phonsrib, Elsevier B.V., *Coord. Chem. Rev.*, 2016, 313, 38–61
- [2] Brandon Djukic and Martin T. Lemaire, *Inorg. Chem.*, 2009, 48 (22), 10489–10491
- [3] Ana I. Vicente, Abhinav Joseph, Liliana P. Ferreira, Maria de Deus Carvalho, Vítor H. N. Rodrigues, Mathieu Duttine, Hermínio P. Diogo, Manuel E. Minas da Piedade, Maria José Calhorda, Paulo N. Martinho, *Chemical Science*, 2016, 7, 4251-4258

Mo nanomaterials to sulfoxides reduction

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The development of sustainable catalytic protocols for the deoxygenation of organic compounds, frequently involved in the synthesis of bioactive targets, is very important. Particularly, the deoxygenation of sulfoxides is of extraordinary relevance in biological processes, as well as in organic synthesis as a key step in several reaction sequences. Accordingly, numerous catalytic methods have been developed in the past decades to perform this transformation[1]. In this sense, considerable efforts have been done in the catalyst development for sulfoxide reduction and, therefore, significant achievements have been accomplished including the use of non-metal or abundant, inexpensive and non-toxic Mo, Zn, Cu or Fe based catalysts. Dioxomolybdenum(VI) complexes have been extensively studied, much of the interest in these compounds is derived from their oxygen atom transfer chemistry. Recyclable, inexpensive, and stable catalysts are desirable for industrial and synthetic applications. With this in mind, in this work MoO₃ nanoparticles have been synthesized and characterized, they were prepared by a hydrothermal method using molybdenum chloride (V) (MoCl₅). Molybdenum trioxide (MoO₃) nanoparticles were obtained and characterized by infrared spectroscopy (DRIFT) and X-ray diffraction (XRD)[2]. Resulting material was tested as catalyst in the reduction of sulfoxides to its corresponding sulfide. Studies were made by varying several parameters such as the solvent (which, in turn, made it necessary to also vary the reactional temperature), the presence or absence of a reducing agent, an acid promoter, and the substrate effect. Throughout the studies, the same catalyst was used in the same percentage. In most of the reactions, the conversion of sulfoxide in sulfide had a low percentage. However, there were some tests which presented highly satisfactory results.

Acknowledgements

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References

- [1] F. J. Arnáiz, R. Agudo, M. R. Pedrosa, A. De Cian, *Inorg. Chim. Acta* 347 (2003) 33-40.
- [2] C. I. Fernandes, S. C. Capelli, P. D. Vaz, C. D. Nunes, *Appl. Catal. A: Gen.* 504 (2015) 344–350.

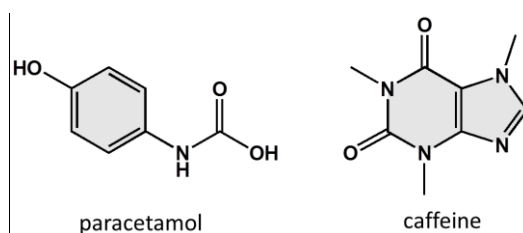
Efficient degradation of paracetamol and caffeine catalysed by iron oxide nanoparticles

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Pharmaceuticals have extended our life expectancy and have allowed us to live virtually pain free and healthier lives. However not all the changes have been good: Pharmaceutical and Personal Care Products (PPCPs), including antibiotics, analgesics, antipyretics, disinfectants, hormone cytostatic agents, and immunosuppressive drugs, are being detected in aquatic environments. This enormous ecological footprint from our daily routines consists of molecules that did not previously exist. Paracetamol is an anti-inflammatory and analgoantipyretic drug, available in numerous pharmaceutical formulations often in combination with caffeine and some other drug substances. Among the variety of PPCPs identified in drinking water, paracetamol and caffeine are referenced due their widely use.

In this work, we investigate the possibility of using iron oxide nanoparticles consisting essentially of hematite ($\alpha\text{-Fe}_2\text{O}_3$) for the photocatalytic degradation of paracetamol and caffeine in aqueous medium. This study was also prompted by the environmental safety provided by the nontoxic properties of iron oxide derivatives. Besides pure hematite, samples containing a magnetite core, enabling their easy removal and reuse, and covered by hematite, were investigated. Under UV light and in the presence of these nanoparticles, a fast and total degradation of both acetaminophen and caffeine occurred after approximately 45 min. The analytical techniques of HPLC and Liquid chromatography in combination with electrospray ionization mass spectrometry were used to follow pollutants concentration evolution during irradiation. Based on experimental data, it was possible to analyse the degradation of both acetaminophen and caffeine. The catalytic performance of these iron oxide nanoparticles was also found to be better than other systems frequently used in photodegradation, both in terms of sustainability and environmental concerns.[1] The use of these magnetic hematite-based nanoparticles should benefit future applications in water and wastewater treatment.



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References

- [1] Edgar Moctezuma, Elisa Leyva, Claudia A. Aguilar, Raúl A. Luna, Carlos Montalvo, *Journal of Hazardous Materials* 243 (2012) 130–138

Molar and excess molar surface areas of water + ethanol mixtures

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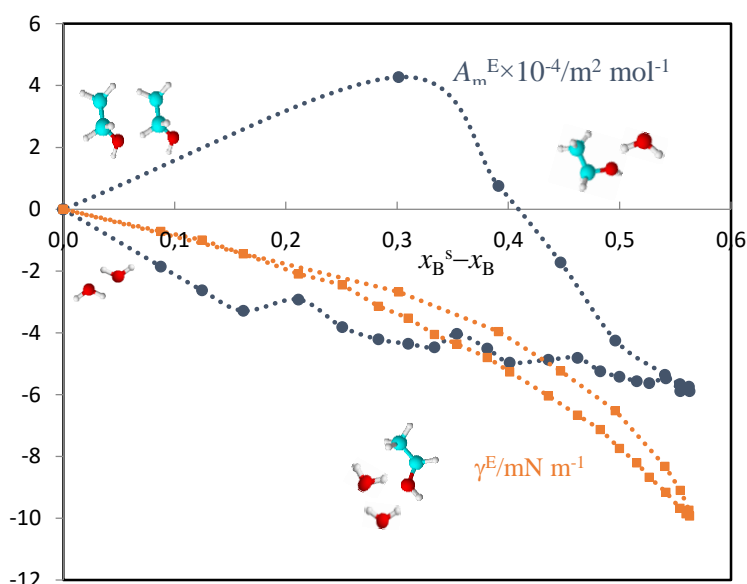
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The molar surface area, A_m , has been a neglected property of liquid mixtures, which may be used as a surface probe over different liquid mixtures regions. A thermodynamic approach to calculate molar surface areas for planar binary liquid mixtures, from the relative adsorption of the surface-active component, $\Gamma_B^{(A)}$, and the surface phase compositions, x_B^s , derived from pure constituent properties, was developed. This approach was applied to aqueous ethanol mixtures at 298 K, using surface tension and bulk activity coefficients from literature [1-4].

In the real mixture, a sharp drop in A_m is observed upon adding ethanol to water, resulting in large negative excess molar surface areas, A_m^E . These negative excess values persist up to an ethanol-rich domain in the surface at equilibrium with an approximately equimolar bulk mixture, then pass to positive excess values, reach a maximum and finally drop to the limiting zero value. Excess molar surface areas are related to the differential enrichment of ethanol in the surface phase, which is defined as the difference between its surface and bulk phases equilibrium mole fractions. For maximum surface enrichment, the excess molar area is a minimum and the Gibbs relative adsorption of ethanol is a maximum, findings which are interpreted at a molecular level in terms of an uneven surface phase with changing thickness accompanying ethanol molecules orientation [5-7].



Acknowledgements

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References

- [1] M.S.C.S. Santos, J.C.R. Reis, *ChemPhysChem* 15 (2014) 2834–2843.
- [2] M. Aratono, T. Toyomasu, M. Villeneuve, Y. Uchizono, T. Takiue, K. Motomura, N. Ikeda, *J. Colloid Interface Sci.* 191 (1997) 146–153.
- [3] R. Strey, Y. Viisanen, M. Aratono, J.P. Kratochvil, Q. Yin, S.E. Friberg, *J. Phys. Chem. B* 103 (1999) 9112–9116.
- [4] M.S.C.S. Santos, J.C.R. Reis, *ChemPhysChem* 16 (2015) 470–475.
- [5] R.S. Taylor, R.L. Shields, *J. Chem. Phys.* 119 (2003) 12569–12576.
- [6] C.M. Phan, C.V. Nguyen, T.T.T. Pham, *J. Phys. Chem. B* 120 (2016) 3914–3919.
- [7] Y. Gong, Y. Xu, Y. Zhou, C. Li, X. Liu, L. Niu, Y. Huang, X. Zhang, C.Q. Sun, *J. Raman Spectrosc.* 48 (2017) 393–398.

Surface tension of 1-Ethyl-3-methylimidazolium dicyanamide aqueous mixtures between 290 and 330 K

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Room temperature ionic liquids (RTILs) are a class of organic salts with melting point temperatures below 100 °C, which have been extensively studied over the last two decades, in view of their potential industrial applications, ranging from industrial solvents for chemical reactions and extraction processes to their use in absorption refrigeration systems. Their low volatility, low flammability, and high thermal stability render RTILs ideal candidates for use as heat transfer fluids [1-2]. Furthermore, ILs are readily recyclable, and often considered “green solvents”, a label, nowadays known not to be general, but explaining the large number of publications on the evaluation of ILs thermophysical properties. Heat transfer efficiency, in any type of heat exchanger, is significantly influenced by fluid mass transfer and surface heat exchange, rendering thermal conductivity, density, viscosity, and surface tensions relevant properties. Generally, IL viscosity poses the major constraint, a drawback that may be overcome using IL mixtures, with a low viscosity “green” solvent like water, driving the evaluation of composition dependence of these properties essential.

In this work, 1-Ethyl-3-methylimidazolium dicyanamide, ([C₂MIM][DCA]) + water (W) mixtures were studied in view of the IL low ecotoxicity and thermal conductivity [3, 4]. The mixtures were prepared by weight, and the water content checked by Karl Fisher titration with a Mettler Toledo Easy KFV. The surface tension of aqueous mixtures, between 290 and 330 K were determined with an automatic Kruss K100MK2 tensiometer, using the Du Noüy ring method and monitoring the sample temperature with an external Pt 100 sensor.

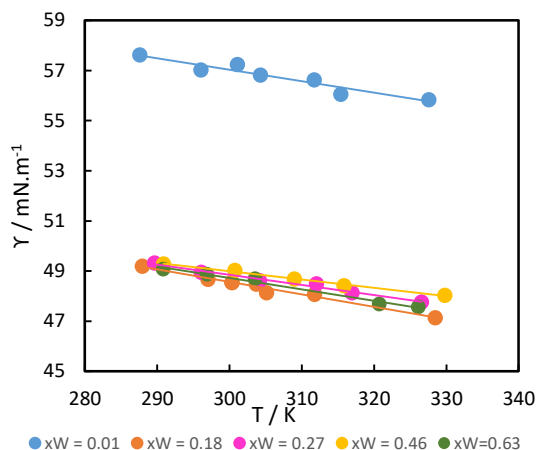
Significant deviations are found in the literature data for the temperature dependence of the pure IL [5,6], and the results obtained here are in-between published data.

Acknowledgements

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References

- [1] V. V. Wadekar, *App. Therm. Eng.* 111 (2017) 1581–1587.
- [2] H. Chen, Y. He, J. Zhu, H. Alias, Y. Ding, P. Nancarrow, C. Hardacre, D. Rooney, C. Tan, *Int. J. Heat Fluid Flow* 29 (2008) 149–155.
- [3] M. C. Cumicheo, L. Nobre, A. F. Santos, I. M. S. Lampreia, M.S.C.S. Santos, F.J.V. Santos, H. Segura, C.A.N. Castro, *J. Chem. Eng. Data*, 60 (2015) 3766–3775.
- [4] F.J.V. Santos, M. Matos Lopes, M.J. Lourenço, A. F. Santos, M.S.C.S. Santos, C.A.N. Castro, *Asian Thermophysical Properties. Conference 2016, Japan.*
- [5] J. Klomfar, M. Soucková, J. Pátek, *J. Chem. Eng. Data*, 56 (2011) 3454–3462.
- [6] P. Navarro, M. Larriba, J. García, F. Rodríguez, *J. Chem. Thermodynamics* 76 (2014) 152–160.



Non-toxic coatings for biofouling prevention on structured materials

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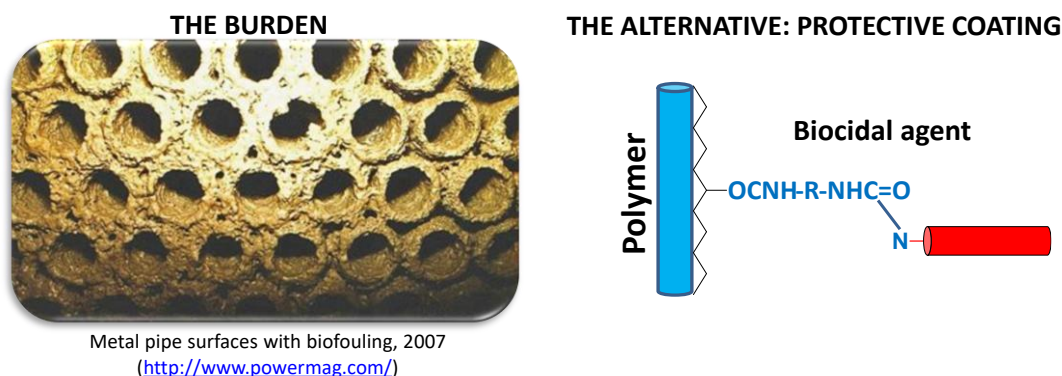
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Fluid contamination with microorganisms (biofouling) causes serious environmental/economic penalties and healthy risks on several applications (e.g. water circuits, air conditioning) ⁽¹⁾. This work aims to develop a new non-toxic solution able to control biofouling, through innovative approaches such as the immobilization of biocidal agents (ex. Econeas) in polymeric coatings for surfaces protection. For the immobilization of biocidal agents in polymeric matrices, a recent patented method was used, in which non-releasing biocidal systems were developed by providing new functional biocides (e.g. Econeas-NCO) capable of being tethered in polymeric coatings ⁽²⁾. No damage on biocides structures was identified from FTIR and RMN spectra analysis after their functionalization.

Bioactivity assessment of functional biocides and coatings containing tethered biocides evidenced antimicrobial activity, particularly against *S. aureus* microorganisms, suggesting that the biocide properties were not significantly affected by the immobilization in the polymeric matrix.

Preliminary coating tests of the obtained antifouling/antimicrobial polymeric systems were performed on different types of structured supports (e.g. monolith). Uniform polymeric films were obtained. Adhesion tests are on-going.

Accordingly, with the European Standards, these coating systems were classified as non-toxic for the environment. The next step of this work is to develop an experimental method to confirm the effectiveness of the coated supported structures against biofouling (Olga Ferreira, FCT- PhD Grant PD/BD/128370/2017) in order to simulate the real conditions for several applications (e.g. water circuits, air conditioning). This approach is presented as a promising non-toxic self-cleaning strategy.



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References

- [1] Lejars, M.; Margailan, A.; Bressy, C. *Chem. Reviews* 112, 4347-4390, 2012.
 [2] Silva, E.R.; Ferreira, O.; Bordado, J.C. Patent Application, WO2016/093719 A1, 2016.

Solution enthalpies of 1-hexyl-3-methylimidazolium tetrafluoroborate: a solvent effect study

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Ionic liquids are a class of chemical compounds that have been extensively studied over the past thirty years [1]. These studies include, among other applications, their use as solvents in extraction processes and in chemical reactions. Also their physiochemical and thermodynamic characterization has been given much attention in the past few years. Despite the great number of results available in the literature, the vast majority of studies consider ionic liquids only from the point of view of solvent and not as a possible solute.

In the sequence of other studies previously carried out by the Structure and Reactivity Group of CQB [2], the objective of this study was to evaluate how 1-hexyl-3-methylimidazolium tetrafluoroborate interacts with solvents of different polarities and acid-base properties, using a methodology based on quantitative structure-property relationships, QSPRs [3].

With this purpose in mind, we have measured the enthalpies of solution of 1-hexyl-3-methylimidazolium tetrafluoroborate ($c \approx 0.01 \text{ mol}\cdot\text{dm}^{-3}$) in 14 solvents with different chemical functionalities, at 298 K. The obtained QSPR model equations permitted the identification and quantification of the prevailing solute-solvent interactions. Results disclosed the relevant and positive role of solvents' Lewis acidity/dipolarity, measured by the Dimroth and Reichardt E_T^N parameter, and the less pronounced and negative effect of solvents' dipolarity/polarizability in the solution process of this IL.

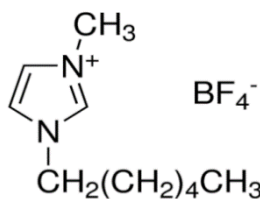


Fig.1. 1-Hexyl-3-methylimidazolium tetrafluoroborate

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References

- [1] Ionic Liquids: Theory, Properties, New Approaches. Alexander Kokorin (Eds.), InTech, 2011.
- [2] M. Reis, R. E. Leitão, F. Martins, J. Chem. Eng. Data, 55 (2010) 616-620.
- [3] M. Reis, N. Nunes, R. Elvas-Leitão, F. Martins, Thermochim. Acta, 604 (2015), 140-144.

Determination of Taurine in Energetic Drinks by HPLC and MS

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Nowadays, beverages with the addition of stimulant components also known as energy drinks have a great impact on the society routine. In Austria in 1989, the energy drinks were created and were used to stimulate metabolism by providing energy, activating alertness and reducing sleepiness. Energy drinks have a wide composition such as vitamin B, caffeine, creatine, guarana, glucoronolactone, taurine, among others. All this components are responsible for the energy in the human body.^{[1], [2]}

The main objectives of this work were to identify and quantify taurine in three different energy drinks such as Red Bull, Burn and + Power. The HPLC, MS and UV/Vis methods were used to perform the study due to its sensitivity, selectivity and high resolution.^[3]

Taurine, also known as 2-aminoethanesulfonic acid, is one of the most common free aminoacids and has not a chromophore group. Therefore, taurine does not absorb in UV/Vis region and needs to be derivatized.^[4]

Stock standard solution of taurine 0.5% with ninhydrine 0.2% was prepared and dissolved in 70% ethanol (v/v) during 30min at 70°C. After cooling, the stock standard solution was diluted in several solutions between 0.01 and 0.1mg/mL concentration to draw the calibration curve.

The equipments used were a HPLC from VWR Hitachi with an autosampler L-2200, a pump L-2130 and a diode array detector L-2455; a FTICR-MS Apex Qe 7 Tesla from Bruker Daltonics with an electrospray ionization source; and an UV/Vis 160 A from Shimadzu. All the results were processed by Excell (version office 2016) and DataAnalysis software (version 4.1).

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References

- [1] D. L. Orth, Journal of Chemical Education. 78 (2001) 791-792.
- [2] B. McConn, Concordia College Journal of Analytical Chemistry. 3 (2012) 47-52.
- [3] J. S. Salgueiro, "Nova estratégia bioanalítica baseada em cromatografia líquida e espectrometria de massas em *tandem* para a qualificação de aminoácidos em matrizes biológicas: uma ferramenta clínica e experimental", tese de Mestrado (2015).
- [4] K. A. Todorova, I. P. Pencheva, International Journal of Nutrition and Food Sciences. 4 (2015) 1-8.

Characterization and Identification of *Cedrus Atlantica*, *Cupressus Funnebris*, *Corymbia Citriodora* and *Eucalyptus Radiata* by GC-MS

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Essential oils are volatile oils taken from any part of a plant and are responsible for the particular odour and/or flavour of each plant. Each essential oil has a different chemical composition that is influenced by even small variations, such as where the plant was grown.[1] For this reason it is important to know the botanical name of the plant because a different Latin name can correspond to a different chemical compositions and each can have distinctive applications.[2]

MS is an analytical technique that allows to find which components are in a variety of samples by their different mass-to-charge ratio in an electromagnetic field.[3] One advantage of MS is that can be used with several techniques such as HPLC, GC, among others.[4] GC-MS is a good analytical technique to study and analyse complex mixtures as essential oils.

In this project, the main goals are to characterize and identify the different components of four essential oils such as *Cedrus Atlantica* (Atlas Cedar), *Cupressus Funnebris* (Funereal Cypress), *Corymbia Citriodora* (Citron-scent Gum), *Eucalyptus Radiata* (Narrow-leaved peppermint). Other goal is to compare different families at same species.

The samples (200 µL) were prepared and dissolved in hexane (400µL). *Corymbia Citriodora* was necessary to filter with a 0.45µm pore size filter before injection, which meant using double quantities.

The equipment used was a Trace GC Ultra coupled to an ITQ 900 mass spectrometer with an automatic injector Triplus Rsh from Thermo Scientific. The results were acquired and processed by Xcalibur (version 1.2). All the peaks were identified by comparison with literature and data from multiple libraries such as NIST, Mainlib and Wiley 6.

Acknowledgements

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References

- [1] National Center for Biotechnology Information from PubMed Health consulted in May 6, 2017.
- [2] C. R. Manion, R. M. Widder, *American Journal of Health-System Pharmacy*. 74 (2017) 153-162.
- [3] E. J. Dasch, *Salem Press Encyclopedia of Science* (online) consulted in March 16, 2017.
- [4] R. W. Smith, *Salem Press Encyclopedia of Science* (online) consulted in March 16, 2017.

Characterization and identification of *Rosmarinus Officinalis*, *Cymbopogon Flexuosus*, *Citrus Aurantium Flower Oil* and *Citrus Aurantium Amara* by GC-MS

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Essential oils are a natural, complex mixture of volatile compounds, mostly monoterpenes (10 atoms of carbon) and sesquiterpenes (15 atoms of carbon), that are extracted from roots, flowers, leaves, peel, seeds, wood or bark of aromatic plants by distillation or solvent extraction. Since Antiquity, essential oils are used in different areas such as food, cosmetics, perfumery, aromatherapy and lately in medicine, biotechnologies and pharmacy. The main reason is due to the characteristics of essential oils as odoriferous, taste, antiseptic, anti-viral, antioxidant, anti-bacterian, among others.^[1]

GC-MS is an instrumental technique that allows to separate (GC) and identify (MS) compounds of a complex mixture if the sample is sufficiently volatile and thermally stable. Those characteristics make GC-MS an ideal analytical technique for the analysis of low molecular weight compounds found in environmental materials such as essential oils.^[2]

In this work, we used GC-MS to characterize and identify the different compounds of four essential oils like *Rosmarinus Officinalis*, *Cymbopogon Flexuosus*, *Citrus Aurantium Flower Oil* and *Citrus Aurantium Amara*. All the samples (200 µL) were prepared and dissolved in hexane (400µL).

The apparatus used was a Trace GC Ultra coupled to an ITQ 900 mass spectrometer with an automatic injector Triplus Rsh from Thermo Scientific. The results were acquired and processed by Xcalibur (version 1.2). All peaks above 5% of relative abundance were identified using literature and databases like Mainlib, Wiley 6 and NIST.^[3-5]

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References

- [1] C. L. Prins, C. S. L. Lemos, S. P. Freitas, *Revista Brasileira de plantas Medicinai*s. 8 (2006) 92-95.
- [2] Bristol University (online) consulted in May 2017.
- [3] A. K. Genena, "Extração e caracterização do extrato de alecrim (*Rosmarinus officinalis* L.): estudo de sua ação antioxidante", tese de Mestrado (2005).
- [4] I. L. Azevedo, A. C. de Almeida, E. R. Martins, W. C. Lima Nogueira, D. E. de Faria Filho, S. P de Oliveira, J. P. Bicalho Prates, C. Neves de Souza, *Acta Veterinaria Brasilica*. 10 (2016) 25-31.
- [5] G. Dugo, I. Bonaccorsi, D. Sciarrone, R. Costa, P. Dugo, L. Mondello, *Journal of Essential Oil Research*. 23, (2011) 50-51.

Determination of Caffeine in different teas by HPLC and MS

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Tea is a healthy beverage enjoyed by most population in the world and is a mixture of phytochemicals, such as polyphenols, catechins and caffeine.^[1] The medicinal effects of tea include anticancer activity, anti-obesity, antidepressant, anti-inflammatory, antimicrobial, among others.^[2]

Caffeine, also known as 1,3,7-trimethylxanthine, is a naturally alkaloid present in several leaves, seeds or fruits in many plants. Some studies show that caffeine increases metabolism and physical performance, improves humour, reduces risk of heart diseases and promotes more mental concentration. However, an excessive ingestion of caffeine can cause negative effects like irritability, anxiety, headaches and insomnia^[3].

In this work, the main goals were to identify and quantify caffeine in green tea (*Camellia sinensis*), black tea (*Camellia sinensis*) and Tilia (*Tiliaceae*) from Tetley. Each tea has an unique character, taste and chemical profile.

Stock standard solution of caffeine 1mg/mL was prepared and dissolved in milliQ water. Several solutions between 0.01 and 0.1mg/mL were diluted through the stock standard solution to draw the calibration curve.

The analytical techniques used were a HPLC from VWR Hitachi with an autosampler L-2200, a pump L-2130 and a diode array detector L-2455; and a FTICR-MS Apex Qe 7 Tesla from Bruker Daltonics with an electrospray ionization source. In HPLC, the stationary phase was a reversed phase and the mobile phase was a binary system in gradient elution. All the results were processed by Xcalibur (version 1.2) and DataAnalysis software (version 4.1).

Acknowledgements

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References

- [1] D. del Rio, A. J. Stewart, W. Mullen, J. Burns, M. E. J. Lean, F. Brighenti, A. Crozier, Food Chemistry. 52 (2004) 2807-2815.
- [2] C. D. Fernando, P. Soysa, SpringerPlus. 5 (2016) 1-5.
- [3] A. Belay, K. Ture, M. Redi, A. Asfaw, Food Chemistry. 108 (2008) 310-315.

Fe(II) Spin Crossover Coordination Polymers

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There is a great interest in engineering electronic systems integrated with molecular switches, thus reducing considerably the size of such molecular devices. The spin crossover (SCO) compounds have emerged 20 years ago as promising materials for molecular electronics. This phenomenon is characterised by bistability at a molecular level, and a compound can switch between two distinct magnet states, the low spin (LS) and the high spin (HS). This switching can be triggered by external stimuli such as temperature, pressure and irradiation. The 1,2,4-triazole unit and derivatives have been quite successful in promoting highly cooperative SCO systems when coordinated to iron(II) metal centres.^[1-3]

We synthesized new 4-amino-1,2,4-triazole (fig.1) derivatives where this ligand was coordinated to iron(II) to obtain new SCO complexes. Their characterization was made by FTIR spectroscopy, elemental analysis, and ¹H NMR measurements, and their magnetic behaviour was investigated by SQUID magnetometry. The redox properties of the compounds were studied by cyclic voltammetry and films of the complexes were prepared by drop casting onto ITO electrodes. The performance of the modified electrodes with the Fe(II) magnetic films for energy storage was also investigated.

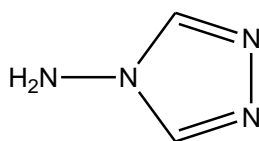


Figure 4. 4-amino-1,2,4-triazole.

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References

- [1] O. Roubeau, *Chem. Chem. Eur. J.* (2012), 18, 15230 – 15244.
- [2] W. Wang, B. Ji, C. Zhang, X. Cao, *Inorg. Chem. Commun.* (2016), 67, 55–59.
- [3] M. M. Dirtu, A. D. Naik, A. Rotaru, L. Spinu, D. Poelman, Y. Garcia, *Inorg. Chem.* (2016), 55, 4278–4295

Development of natural fiber-metal chalcogenides nanoparticles with photocatalytic properties for pollutants degradation

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Throughout the years the modification of fibers caught the scientists' special attention, in particular due to the possibility of using nanoparticles (NPs) to improved their characteristics and impart new properties.¹ Examples include antimicrobial/antibacterial, self-cleaning and photocatalytic properties being the later relevant for pollutants degradation processes.^{2,3}

In this work Bi_2S_3 ZnS NPs were used to modify cotton, the natural fiber. The synthesis and modification was performed *in situ* obtaining the modified cotton with Bi_2S_3 , ZnS and a mixture of both NPs. The prepared materials were characterized by different techniques, such as, XRD, EDS, DRS, FTIR, SEM, TEM and surface area measurements.

The successful modification of the fibers was confirmed by DRS and SEM analysis. The mixture of both NPs presents a higher superficial area than the pristine NPs, although the XRD analysis did not allowed the ZnS identification due to the very small size of crystallites, it was confirmed by EDS analysis. On the other hand, the increasing adsorption ability of NPs in the order $\text{Bi}_2\text{S}_3 > \text{Bi}_2\text{S}_3\text{-ZnS} > \text{ZnS}$. The complete degradation of a dye from the leather industry was attained using $\text{Bi}_2\text{S}_3\text{-ZnS}$ NPs under visible light irradiation for 6 hours. Encouraging results have also been obtained for NPs modified cotton fibers, with about 60 % degradation achieved with the Cotton-ZnS composite.

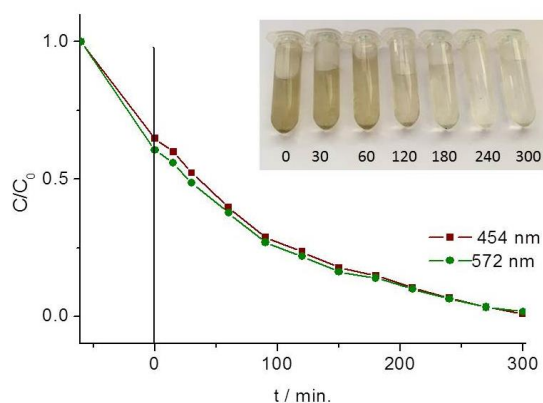


Figure - Photocatalytic performance of the $\text{Bi}_2\text{S}_3\text{-ZnS}$ mixture under visible light irradiation for the degradation of a dye used in the leather industry.

Acknowledgements

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References

- [1] A.K. Yetisen, H. Qu, A. Manbachi, H. Butt, M.R. Dokmeci, J.P. Hinstroza, M. Skorobogatiy, A. Khademhosseini, S.H. Yun, *ACS Nano* 10 (2016) 3042–3068.
- [2] S.T. Dubas, P. Kumlangdudsana, P. Potiyaraj, *Colloid Surface A* 289 (2006) 105-109.
- [3] M. Rastgoo, M. Montazer, R.M.A. Malek, T. Harifi, M.M. Rad, *Ultrason. Sonochem.* 31 (2016) 257-266.

Amine modified titanate nanotubes and nanowires: Synthesis and photocatalytic degradation of psychoactive substances

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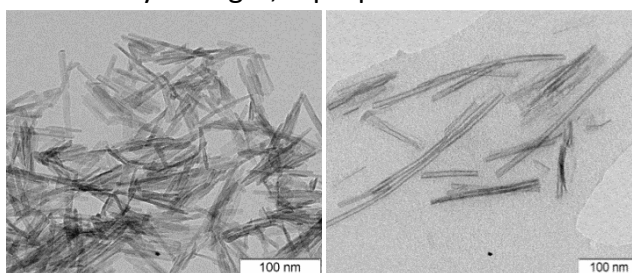
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In this work, new hybrid nanomaterials, with improved photocatalytic performance for emergent pollutants removal, were obtained through sensitization of titanate nanotubes (TNT) and nanowires (TNW) with ethylenediamine (EDAmine) to produce NTNT and NTNW materials, respectively. The prepared materials were structural, morphological and optical characterized by XRD, TEM, DRS and XPS. The results show that TNT and TNW with identical diameter/length ratio, but distinct surface area, were obtained using the same experimental conditions (solvents, time and temperature) but different precursors [1,2]. No modifications on the structure and morphology were detected after EDAmine incorporation but an increase on the visible light absorption and on the point of zero charge were observed.

The application of these new hybrid nanomaterials on photocatalytic degradation of emergent pollutants was investigated. First, the evaluation of hydroxyl radical ($\bullet\text{OH}$) production, using the terephthalic acid as probe was studied and the highest catalytic activity was achieved by the NTNT sample. The photocatalytic ability of the sensitized materials for the psychoactive substances, caffeine and theophylline, and for phenol degradation was afterwards evaluated. The results show that, within 60 min under UV-vis radiation, the NTNT sample was the best catalyst for all the degradation processes, achieving 60% of photodegradation efficiency for caffeine and 98% for phenol and theophylline 20 ppm solutions, respectively.

Based on the obtained results, a mechanism for the charge-transfer processes in the NTNT hybrid nanoparticles, after being activated by the light, is proposed and discussed.



TEM images of the TNW (a) and TNT (b) samples.

Acknowledgements

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References

- [1] M.R. Nunes, O.C. Monteiro, A.L. Castro, D.A. Vasconcelos, A.J. Silvestre, *Eur. J. Inorg. Chem.* 28 (2008) 961-965.
- [2] E.K. Ylhäinen, M.R. Nunes, A.J. Silvestre, O.C. Monteiro, *J. Mater. Sci.* 47 (2012) 4305-4312.

Bioevaluation of natural compounds

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We have been developing work in the bioactivity study of infusions and isolated compounds from several origins. Different molecules have been found with biological activity such as inhibitory intestinal absorption of cholesterol [1], antioxidant activity [2], inhibitory enzymes as acetylcholinesterase [3] and HMG CoA-reductase [1], and also compounds with anticancer activity [4]. The compounds have been identified by LC-MS / MS and the biochemical action studied using several cell lines. FTIR spectroscopy methodologies and electrophoresis are also in use to determine structural changes in proteins when in contact with bioactive molecules. Action studies are underway in therapeutic targets of the mechanism of inhibition of cholesterol absorption by the isolated compounds and also interaction between drugs and bioactive molecules.



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References

1. A. A. Arantes, P. L. Falé, L.C.B. Costa, R. Pacheco, L. Ascensão, M. L. Serralheiro. Inhibition of HMG-CoA reductase activity and cholesterol permeation through Caco-2 cells by caffeoylquinic acids from *Vernonia condensata* leaves, *Brazilian Journal of Pharmacognosy*, 26 (2016) 738-743.
2. J. Henriques, M.J Ribeiro, P.L. Falé, R. Pacheco, L. Ascensão M. H, Florencio, M.L.M. Serralheiro Valorization of kiwifruit production: leaves of the pruning branches of *Actinidia deliciosa* as a promising source of polyphenols. *Eur Food Res Technol.*, 243 (2017) 1-11. doi:10.1007/s00217-017-2845-y
3. A. Ressaissi, N. Attia, P. L.V Falé, R. Pacheco, V. H. Teixeira, M. Machuqueiro, C. Borges, M. L. M. Serralheiro. Aqueous Extracts from Nopal (*Opuntia Ficus-Indica*): Antiacetylcholinesterase and Antioxidant Activity from Phenolic Bioactive Compounds. *IJGHC* 5 (2016) 337-348.
4. M. J. Martins, F. Martins, R. Pacheco, S. Santos. Synthesis and evaluation of antitumor activity of novel thiobenzanilides. Poster, CQB day 2017

New insights on the immobilization mechanism of *Escherichia coli* onto activated carbons

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Adsorption on activated carbons is a well-established method used in water treatment to remove numerous pollutants. Microorganisms present in water can become immobilized in the adsorbent, possibly affecting the adsorption process. As new forms of adsorbents are developed, it is important to understand the impact of these materials' properties in the mechanism of bacteria immobilization, to conclude about the possible advantages of using these new materials for water treatment purposes [1,2].

In this work, the influence of the adsorbent morphology (granular, powder and cloth), texture and surface chemistry in the immobilization of *E. coli* cells in aqueous media was investigated.

The results indicate that favorable electrostatic interactions carbon surface-cells is a key factor in bacteria immobilization by activated carbons that must be complemented by its morphology and textural characteristics. For basic carbons, electron microscopy results revealed that powder morphology allows the formation of agglomerates carbon-cell-cell-carbon. In the case of granular and cloth samples the data already obtained suggest that, in an initial stage, individual cells adhere to the external surface of the carbon particles (more efficiently in cloth morphology). Further assays, considering different cellular densities and the simultaneous presence of pharmaceutical compounds in the aqueous medium are being performed.

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References

- [1] X. Bai, X. Ma, F. Xu, J. Li, H. Zhang, X. Xiao, The drinking water process as a potential source of affecting the bacterial antibiotic resistance, *Sci. Total Environ.* 533 (2015) 24-31.
- [2] J. Rivera-Utrilla, M.I. Bautista-Toledo, M.A. Ferro-García, C. Moreno-Castilla, Activated carbon surface modifications by adsorption of bacteria and their effect on aqueous lead adsorption, *J. Chem. Technol. Biotechnol.* 76 (2001) 1209-1215. [4] G.R. Mettam, L.B. Adams, in: B.S. Jones, R.Z. Smith (Eds.), *Introduction to the Electronic Age*, E-Publishing, Inc. New York, 2009, pp. 281–304.

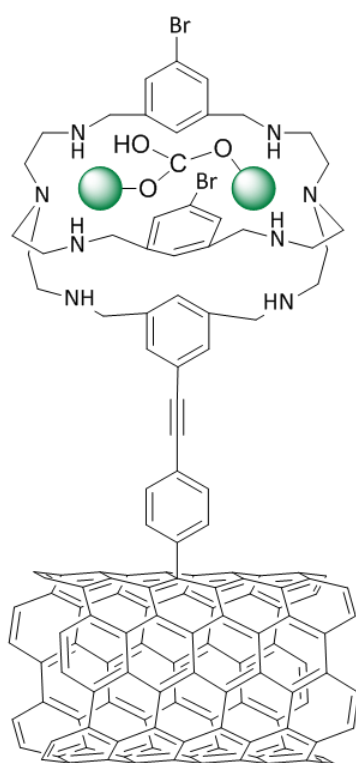
Synthesis and Immobilization of Metallo-organic Structures to Capture and Convert CO₂

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Cascade complexes are formed stepwise by reaction of ligands with metal ions, which may in turn bind small molecules. Polyaza ligands have shown their versatility in creating, after coordinating two or three 3d cations, depending on their topological properties, a small cavity to bind anions. Nelson's cryptands[1] provide an example of a dynamic structure with useful applications, demonstrated by their ability to capture and convert CO₂ to carbonate following their coordination to two metal ions. On the other hand, the electrochemical reduction of CO₂ to other products with well-defined molecular catalysts has selectively produced compounds such as CO, formic acid, methane and methanol.[2] One of the strategies for catalytic CO₂ reduction is based on carbon nanotubes functionalisation through covalent grafting of metal complexes. Here we explore the conversion of CO₂ into CO by carbon nanotubes modified with Co(II) cryptates (Figure 1) that can capture CO₂ from the atmosphere. The syntheses of different Co(II) cryptates were performed under N₂ and CO₂ atmosphere. The new species characterised by FTIR, elemental analysis, and XPS. The redox properties of both the complexes and the modified carbon nanotubes were studied by cyclic voltammetry. The behaviour of the new materials under exposure to a CO₂ saturated atmosphere was investigated in aqueous medium.

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References

- [1] Y. Dussart, C. Harding, P. Dalgaard, C. McKenzie, R. Kadirvelraj, V. McKee and J. Nelson, *J. Chem. Soc., Dalton Trans*, 2002, 1704-1713.
- [2] A. Maurin and M. Robert, *J. Name*, 2013, 00, 1-3.

Nanoassemblies for magnetic hyperthermia

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Heat dissipation by magnetic materials when exposed to alternating magnetic fields, known as magnetic hyperthermia, is an emergent and promising technique, which has been explored as a therapy for cancer treatment in combination with radiation- and/or chemo-therapy. It has been predicted that the best nanoheaters should be obtained by tailoring the magnetic properties of core-shell type structures.¹

In this work, a different route to obtain magnetic nanomaterials with enhanced magnetic hyperthermia performance was investigated. Nanoassemblies of different magnetic nanoparticles (NP) were obtained using a seed-mediated growth method. The first nanoparticles (named as core) were prepared by an established procedure in gelatinous medium². Afterwards, the second magnetic material was precipitated in the presence of the core nanoparticles, using a rotating system to facilitate the homogeneous coverage of the core nanoparticles. Different combinations of Fe₃O₄ and MnFe₂O₄ were used to prepare these NP nanoassemblies. After a full structural and magnetic characterization, induction heating measurements under an AC magnetic field were performed in optimized non-adiabatic conditions³. The results show a clear enhancement of the specific energy dissipation for these nanoassemblies when compared with each kind of nanoparticles. Finally, cytotoxicity and uptake assays of these nanoassemblies were performed on human breast (MDA-MB-231) and colon (Caco-2) cancer cell lines, indicating that the composition and ratio of the materials affect their cellular uptake, with MDA-MB 231 internalizing more NP than Caco-2 cells. All samples are nontoxic for concentrations below 1.8 mg mL⁻¹.

These results point to these materials as good candidates for magnetic hyperthermia applications.

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References

- [1] M. S. Carrião, A. F. Bakuzis, *Nanoscale*. 8 (2016) 8363.
- [2] A. F. Alves, S. G. Mendo, L. P. Ferreira, M. H. Mendonça, P. Ferreira, M. Godinho, M. M. Cruz, M. D. Carvalho, *J. Nanopart. Res.* 18 (2016) 27.
- [3] S. G. Mendo, A. F. Alves, L. P. Ferreira, M. M. Cruz, M. H. Mendonça, M. Godinho, M. D. Carvalho, *New J. Chem.* 39 (2015) 7182.

π - Chem & Go! π -Stack on DNA and go to the best place

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The interaction of the $[\text{Mo}(\eta^3\text{-C}_3\text{H}_5)\text{Br}(\text{CO})_2(\text{phen})]$ metal complex synthesized in our group [1] with DNA has been studied at computational level by docking, semiempirical methods including dispersion, QM/MM and DFT. The $[\text{Mo}(\eta^3\text{-C}_3\text{H}_5)\text{Br}(\text{CO})_2(\text{phen})]$ metal complex exists as two main isomers in solution. Indeed, in one isomer phenanthroline (phen) is coordinated in the equatorial plane (EqEq), whereas in the other one N of phen is coordinated in an equatorial position and the other N in an axial one (EqAx). Although the EqEq structure is more stable, there is not a great difference between the energy of the isomers and we studied both systems, EqEq and EqAx, interacting with DNA to explain the experimentally found cytotoxicity.[1] We also took into account two different modes of interaction with DNA, that is, groove binding and intercalation, since such competition has been recently described in the bibliography for metal complexes with flat ligands interacting with DNA.[2-4] PM6-DH2 hamiltonian and QM/MM methods by using M11L/6-31+G(d,p):AMBER were calibrated with the intercalated 1n37 structure of PDB and were observed to perform excellently. On the other hand, for the $[\text{Mo}(\eta^3\text{-C}_3\text{H}_5)\text{Br}(\text{CO})_2(\text{phen})]$ metal complex, it is observed that the system prefers the intercalation via minor groove than through the major groove. Moreover, once the bases experimented the rise movement to allocate the metal complex, the groove binding mode became unstable and the intercalation more likely.

Acknowledgements

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References

- [1] D. Bandarra, M. Lopes, T. Lopes, J. Almeida, M. S. Saraiva, M. Vasconcellos-Dias, C. D. Nunes, V. Félix, P. Brandão, P. D. Vaz, M. Meireles, M. J. Calorda, *J. Inorg. Biochem.* 104 (2010) 1171-1177.
- [2] A. Mukherjee, R. Lavery, B. Bagchi, J. T. Hynes, *J. Am. Chem. Soc.* 130 (2008) 9747-9755.
- [3] W. D. Sasikala and A. Mukherjee, *Phys. Chem. Chem. Phys.* 15 (2013) 6446-6455.
- [4] D. Franco, A. V. Vargiu, A. Magistrato, *Inorg. Chem.* 53 (2014) 7999-8008.

Phenolic compounds extraction and sugars characterization in Algerian honeys

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The aim of this work is the characterization of sugars and phenolic compounds existing in samples of honeys from different regions of Algeria. Phenolic compounds, products of the secondary metabolism of plants, are present in honey and they represent a significant source of active substances with multiple therapeutic effects. Sugars represents 95 to 99% of the honey dry matter^[1].

Eighteen honeys were extracted with Amberlite XAD-2 according to the method described by Ferreres et al. 1994^[2]. Phenolic compounds extracts were obtained and analysed by thin-layer chromatography (TLC). Plates were eluted with, first acetone/chloroform (1:9) and then chloroform/methanol/water (5:5:1). The TLC profile at UV light 254nm varied with the floral origins of honeys. The comparison with standards suggests the presence of gallic, caffeic and vanillic acid. Flavonoids present in the extract were visualized by spraying the plate with aluminium chloride methanolic solution (5%) and then observing it at UV light 336 nm^[3]. The revelation with the aluminium chloride solution and observation under UV light clearly shows various fluorescent yellowish spots indicating the presence of flavonoids. Rf of quercetin was identical to one of the major spots in all samples, indicating the presence this flavonoid.

Majority sugars were characterized by NMR. NMR spectra of honeys only shows peaks between 5.5-3.0 ppm corresponding to the main sugars, glucose and fructose, in almost identical proportion.

These results confirm that honey besides being mainly a source of glucose and fructose also contains a multitude of phenolic compounds.

Acknowledgements

Support for this work was provided by FCT through UID/MULTI/00612/2013 and PEst-OE/QUI/UI0612/2013.

References

- [1] G. Berreta, P. Granata, M. Ferrero, M. Orioli, R.M. Facino. Standardization of antioxidant properties of honey by a combination of spectrophotometric/ fluorimetric assays and chemometrics. *Analytica Chimica Acta*. 533 (2005) 185–191.
- [2] F. Ferreres, F.A. Tomás-Barberán, C. Soler, C. Garcia-Viguera, A. Ortiz, F. Tomas-Lorente. A simple extractive technique for honey flavonoid HPLC analysis. *Apidologie*. 25 (1994) 21-30.
- [3] M.J. Amiot, S. Aubert, M. Gonnet, M. Tacchini. Les composés phénoliques des miels : étude préliminaire sur l'identification et la quantification par familles. *Apidologie*. Springer Verlag. 20 (1989) 115-125.

Optimization of the extraction of tannins from chestnut bark and sumac leaves

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Tannins were defined by Horvath (1981) as "Any phenolic compound of sufficiently high molecular weight containing sufficient hydroxyls and other suitable groups (i.e. carboxyls) to form effectively strong complexes with protein and other macromolecules under the particular environmental conditions being studied" [1]. Their name is derived from the French word "tannin", a tanning substance that helps turning relatively fragile animal skins into more durable materials like leather [2].

In the past, vegetable tannins were the main tanning agent used in the process, but the complexity and time involved led to the development of mineral tanning agents, like chrome instead. However, this process has a negative environmental impact [3], so it is important to try to bring back the traditional method and extract tannins from renewable vegetable sources.

In this work, we extract tannins from chestnut bark and sumac leaves, varying the time of the extraction: 24 hours, 72 hours and 1 week, and the solvent: water and a solution of water:ethanol 1:1. Using UV-Vis spectroscopy we obtained and compare the spectra of all extracts, which allow verifying that the tannins extracted from sumac leaves are tannic acid. We also assessed the quantity of tannins present in each extract, using the Folin method referred by Hagerman [4], and conclude that a higher period of extraction led to a higher presence of phenolic compounds. Since complete drying of the extracts is a lengthy process, yields of the extraction process will be presented in the poster.

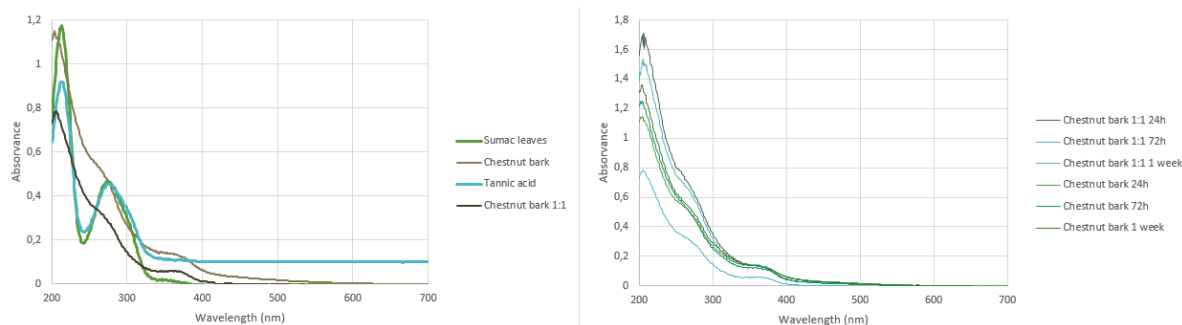


Figure 1: UV-Vis spectra of the 24h extractions and tannic acid (A) and UV-Vis spectra of the chestnut bark extractions

Acknowledgements

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References

- [1] J.J Halvorson, J.M Gonzalez, A.E Hagerman, J.L Smith, *Soil Biology & Biochemistry*. 41 (2009) 2002-2010
- [2] P.K Ashok, K. Upadhyaya, *Journal of Pharmacognosy and Phytochemistry*. 1 (2012) 45-50
- [3] A. Ojgaard, *Carryology* 2016. <http://www.carryology.com/insights/chrome-vs-vegetable-tanned-leather/> (accessed on 6 May 2017)
- [4] A.E Hagerman, *The Tannin Handbook*, 2011. <http://www.users.miamioh.edu/hagermae/> (accessed on 6 May 2017)

Grapevine subtilase family characterization: first clues of their involvement in grapevine resistance against *Plasmopara viticola*

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Grapevine (*Vitis vinifera* L.) is currently the most important fruit plant cultivated worldwide due to its economic importance in the wine industry, however highly susceptible to downy mildew disease, caused by *Plasmopara viticola*. Our previous studies in this pathosystem have highlighted the role of a subtilase presenting a high constitutive expression in a resistant *V. vinifera* cultivar and a high increase in the first hours after infection with *P. viticola*. Studies in other plants systems have highlighted subtilase participation in response to biotic and abiotic environment stimulus. In tomato leaves the expression increase of a subtilase (P69) was observed after citrus exocortis viroid infection and in *Arabidopsis* a subtilase gene (SBT3.3) which expression rapidly increases during innate immunity activation was identified. We have performed a characterization of the grapevine subtilase gene family and identified 97 proteins, encoded by 82 genes. The family is phylogenetically divided into 6 groups and the proteins are predictably located in apoplast, cell wall or extracellular region [1]. Considering the homology with the *Arabidopsis* subtilases, a nomenclature for the grapevine subtilase members are proposed [2]. Fourteen grapevine subtilases presented either high homology to tomato P69C, *Arabidopsis* SBT3.3 and are located near the Resistance to *Plasmopara viticola* (RPV) locus. Expression studies performed in this pathosystem, indicate that some of grapevine subtilases are actively participating in the defence response against *P. viticola* [1]. Two of them have already been cloned and the first tests for recombinant protein expression are underway. These results are the first step in the direction of the establishment of these subtilases as candidates for introgression in breeding programs, as an alternative to the excessive use of pesticides.

Acknowledgements

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References

- [1] Figueiredo, J., Costa, G. J., Maia, M., Paulo, O. S., Malhó, R., Sousa Silva, M., & Figueiredo, A. (2016). *Frontiers in Plant Science*, 7, 1783. doi.org/10.3389/fpls.2016.01783
- [2] Figueiredo, J., Maia, M., Sousa Silva, M. and Figueiredo, A. (2017) *Frontiers in Plant Science*, 8, 716. doi: 10.3389/fpls.2017.00716

Grapevine leaves metabolic characterization for a resistance biomarker discovery

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Grapevine (*Vitis vinifera* L.) is the most widely cultivated and economically important fruit crop in the world, mainly due to the wine industry [1]. Unfortunately, all *V. vinifera* cultivars widely used for wine making are susceptible to fungal associated diseases, like downy and powdery mildews, which cause a massive damage and destruction of the plant, resulting in high financial costs compromising the economy of many countries. The current strategies are the intensive application of powerful pesticides, with high environmental impacts. Alternatively, a promising approach is the development of breeding programs combining wild *Vitis* species (resistant to pathogens) and *V. vinifera* (susceptible) towards the development of new cultivars with good berry quality and a high degree of resistance. However, this last approach takes years to accomplish and the majority of the resulting hybrids did not succeed in the market since they are unsuitable for the production of high quality wines [2,3]. The identification of biomarkers that allow a quick and easy identification of the young plants resistance characteristics would give a new hope for the wine industry.

Metabolic biomarkers are an advantageous in this particular problem, since plants contain a unique metabolome that change upon pathogen infections and allow a better understanding of the innate resistance/susceptibility of cultivars. We developed a metabolite extraction method for grapevine leaves [4], performed a large scale metabolic characterization using Fourier Transform Ion Cyclotron Resonance MS (FTICR-MS) and identified several metabolic entities that enable a constitutively discrimination between resistant and susceptible plants.

Acknowledgements

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References

- [1] Organisation of Vine and Wine, "2016 OIV Statistical Report on World Vitiviculture," 2016.
- [2] D. Buonassisi *et al.*, *Euphytica*, vol. 213, no. 5, May 2017.
- [3] S. L. Toffolatti, G. Venturini, D. Maffi, and A. Vercesi, *BMC Plant Biol.*, vol. 12, no. 1, p. 124, 2012.
- [4] M. Maia *et al.*, *EuPA Open Proteomics*, vol. 12, pp. 4–9, Sep. 2016.

Metabolic characterization of *V. vinifera* cv. Trincadeira upon *Plasmopara viticola* infection

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One of the most widely cultivated and economically important fruit crops in the world is grapevine (*Vitis vinifera* L.), where Europe's wine industry represents 40% of the world production (Organisation of Vine and Wine, 2016) [1]. In Portugal, one of the most important and widely used cultivar is *Vitis vinifera* cv. Trincadeira. However, it is susceptible to many fungal infections, of which downy mildew is one of the most threatening [2]. Downy mildew is caused by the biotrophic oomycete *Plasmopara viticola* (Berk. et Curt.) Berl. et de Toni affecting the leaves, shoots and fruits, reducing berry quality and yield, with significant production losses. To prevent infection the use of powerful fungicides continues to be the most widely used strategy for pathogen control, another alternative is the development of new hybrid grapevines that combine good berry quality and high degree of resistance.

Since plants have a unique metabolome that change upon pathogen infection [3], in this study, we have characterized the metabolome of *V. vinifera* cv. Trincadeira leaves after inoculation with *Plasmopara viticola*. Metabolites were analysed by Fourier Transform Ion Cyclotron Resonance MS (FTICR-MS), following a previously developed method [4]. This approach allowed the identification of several metabolic entities that, not only may differentiate infected from non-infected grapevine leaves, but also discriminate among different stages of infection.

Acknowledgements

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References

- [1] Organisation of Vine and Wine. 2016. 2016 OIV Statistical Report on World Vitiviniculture,.
- [2] Gessler, C., I. Pertot, and M. Perazzolli. 2011. *Phytopathol. Mediterr.* 50: 3–44.
- [3] Ali, K., F. Maltese, A. Figueiredo, M. Rex, A. M. Fortes, E. Zyprian, M. S. Pais, R. Verpoorte, and Y. H. Choi. 2012. *Plant Sci.* 191–192: 100–107
- [4] Maia, M., F. Monteiro, M. Sebastiana, A. P. Marques, A. E. N. Ferreira, A. P. Freire, C. Cordeiro, A. Figueiredo, and M. Sousa Silva. 2016. *EuPA Open Proteomics* 12: 4–9.

Expression of subtilases involved in grapevine resistance to *Plasmopara viticola*

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One of the most important fruit plant cultivated worldwide is grapevine (*Vitis vinifera* L.), mainly due to its economic importance in the wine industry. It is however highly susceptible to downy mildew caused by the oomycete *Plasmopara viticola*. This pathogen affects the leaves, shoots and berries in susceptible *V. vinifera* cultivars, resulting in great losses in entire vineyards. The current disease control strategies include the massive use of fungicides, which are very prejudicial to human health [1]. A deeper understanding of the resistance mechanisms is crucial to define alternative control methods.

Subtilisin-like proteases (subtilases) belong to a large group of serine proteases present among all groups of organisms such as archaea, bacteria, eukarya, fungi and yeast [2]. We have previously characterized the grapevine subtilase gene family, highlighting the involvement of some subtilases in *P. viticola* resistance [3]. Recent studies in *Arabidopsis* and tomato have identified a prosystemin as the subtilase SBT3. The systemin is involved in the octadecanoid pathway for jasmonic acid (JA) biosynthesis [4]. In the present work we have analysed by qPCR the expression of 6 subtilase genes that were previously shown to be upregulated after *P. viticola* inoculation, in two *Vitis* genotypes (*V. vinifera* Pinot noir (susceptible) and *V. riparia* (resistant)), after elicitation with JA and salicylic acid. Our results show that 2 subtilases were upregulated after JA elicitation. We have thus selected these enzymes for further functional characterization. We aim to unravel the structure and function of these subtilases and their involvement in grapevine resistance to *P. viticola*, to gain a more comprehensive knowledge on their role in plant immunity, thus contributing to the development of alternative strategies for fungal diseases' control.

Acknowledgements

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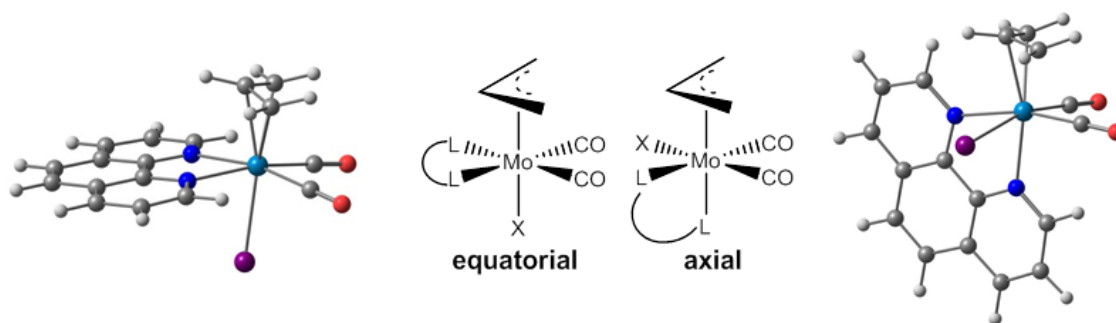
References

- [1] Gessler, C., I. Pertot, M. Perazzolli. *Phytopathol. Mediterr.* 50 (2011) 3–44.
- [2] Siezen, R.J., W.M. de Vos, J.A Leunissen, B.W Dijkstra. *Protein Eng.* 4(1991) 719–737
- [3] Figueiredo, J., Costa, G. J., Maia, M., Paulo, O. S., Malhó, R., Sousa Silva, M., & Figueiredo, A. (2016). *Frontiers in Plant Science*, 7, 1783. doi.org/10.3389/fpls.2016.01783
- [4] Ryan CA. *Biochimica et Biophysica Acta.* 1477 (2000) 112–121.

Seven-coordinate allylic Mo(II) complexes: structure, bonding and CO₂ reduction

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The allylic complexes $[\text{Mo}(\eta^3\text{-C}_3\text{H}_5)(\text{CO})_2\text{X}(\text{LL}')]]$ were reported in the 1960s,[1,2] and can be described as pseudo-octahedral, assuming that the centroid of the allyl group corresponds to one ligand. A search in the Cambridge Crystallographic Data Base [3] has shown that two main isomers, equatorial and axial, are usually observed. They are depicted in Figure 1 for $[\text{Mo}(\eta^3\text{-C}_3\text{H}_5)(\text{CO})_2\text{Br}(\text{phen})]$ (phen = 1,10 phenanthroline) in a scheme and a 3-D representation. The experimentally determined structure (single crystal X-ray diffraction) is the equatorial one. In both isomers the facial arrangement of the two carbonyl and the allyl centroid is observed, the exo conformation of the allyl being also preferred. This complex is fluxional in solution. Both isomers are detected, as well as the exo conformer of the equatorial isomer. We analyze the structural preferences of this family of formally seven-coordinate Mo(II).[4] We also report the activity of the 1,10-phenanthroline and dipyridophenazine derivatives in CO₂ electroreduction.



Two isomers of $[\text{Mo}(\eta^3\text{-C}_3\text{H}_5)(\text{CO})_2\text{Br}(\text{phen})]$.

Acknowledgements

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References

- [1] H. tom Dieck, H. Friedel, *J. Organomet. Chem.* 14 (1968) 375.
- [2] C. G. Hull, M. H. B. Stiddard, *J. Organomet. Chem.* 9 (1967) 519-525.
- [3] C. R. Groom, I. J. Bruno, P. Lightfoot, S. C. Ward, *C. Acta Cryst.* B72 (2016) 171-179.
- [4] M. J. Calhorda, P. J. Costa, *Coord.Chem. Rev.* (2017), <http://dx.doi.org/10.1016/j.ccr.2016.12.010>

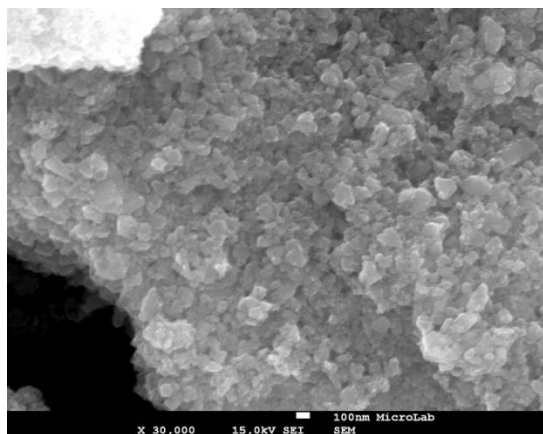
Novel TiO₂-MoO₃ nanocomposites for the selective oxidation of benzyl alcohol to benzaldehyde

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Heterogeneous photocatalysis is currently recognized as one of the most promising, advanced and environment friendly technologies due to its excellent advantages such as clean, effective, energy-saving, and low cost. Selective photocatalytic oxidation of aromatic alcohols to aldehydes is of great relevance regarding the importance of those compounds (e.g., benzaldehyde) as raw materials for the synthesis of many useful chemicals, such as dyes, resins, fragrances and drugs.

Titanium oxide (TiO₂) has raised a great deal of interest on the scientific community due to its photocatalytic activity, chemical stability, nontoxicity and low cost. However, it presents a critical drawback: the wide band gap of TiO₂ makes only possible the use of the ultraviolet fraction of the solar light (the highest and cheapest source of radiation). Therefore, great efforts have been made for improving its photocatalytic efficiency. Similarly, molybdenum trioxide (MoO₃) is also attractive due to its unique structural, electronic and optical properties. MoO₃ can present band-gap energies in the range of 2,9 to 3,1 eV and it is broadly employed in electrochromic and photochromic devices. In this study, new photocatalytic materials were prepared by combination of TiO₂ and MoO₃ particles. Nanocrystalline particles and nanocomposites were prepared using a hydrothermal approach and were subsequently characterized in terms of their structural, morphological, and electronical/optical properties. Materials were tested in the simulated solar-light-driven selective oxidation of benzyl alcohol to benzaldehyde in acetonitrile, in which the TiO₂-MoO₃ nanocomposites exhibited higher values of selectivity and yield comparing to the isolated components.



SEM image of TiO₂-MoO₃ nanocomposite particles

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Design of new urea and thiourea-based receptors for anion recognition

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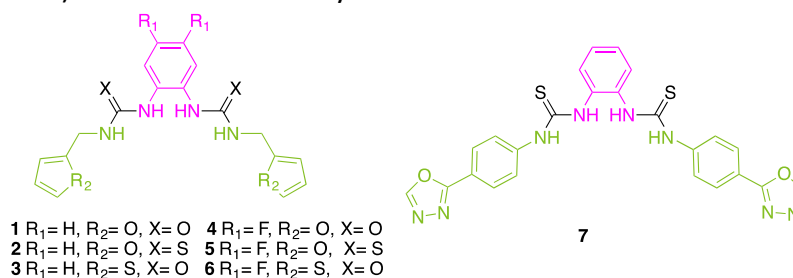
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Ion transport across the phospholipid cell membranes is crucial to several biological processes, such as nerve conduction and homeostasis maintenance.¹ A combination of protein ion channels embedded in the membrane establishes and controls the ion concentrations inside and outside the cell.¹ The dysfunction of these channels is currently linked with the occurrence of serious pathologies, including types of male infertility and the prominent cystic fibrosis (CF), caused by a defective transmembrane transport of the chloride and bicarbonate anions.¹ Most of the current treatments for CF aim to manage the disease symptoms, while the cure remains a challenge. Therefore, the development of drug-like transporters with potential to be applied as replacement therapeutics for malfunctioning channels is an imperative demand.

During the last decade, an increasing number of synthetic anion transporters have been synthesised.²⁻⁴ In this context, here we present the syntheses of new oligo(thio)ureas receptors containing two heteroaromatic recognition units linked by an *ortho*-phenylene rigid linker. The ability of these synthetic receptors to bind, in solution, with halides (F⁻, Cl⁻, Br⁻, and I⁻) was investigated using ¹H NMR titration experiments in DMSO-*d*₆.

The strongest binding affinities was found for chloride anion probably due to its best matching size of the receptor cavity which allowed maximizing the number of hydrogen bonds between the anion and the bis-(thio)ureas units of the receptors. The urea receptors gave higher binding constants than the corresponding thioureas. However, the thiourea **7** also has a high binding constant probably due to the presence of the oxadiazole rings. The presence of the fluorine atoms in the aromatic ring of the receptors (**4** and **5**) increases the affinity for chloride anion.



Scheme 1: Representation of the synthetic receptors.

Acknowledgements

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References

- [1] a) A. Vankeerberghen, H. Cuppens, J.-J. Cassiman, *Journal of Cystic Fibrosis* 1 (2002) 13; b) F.M. Ashcroft, *Ion Channels and Disease*, Academic Press, San Diego, 1st ed., 1999, vol. 1.
- [2] V.B. Bregovic, N. Basaric, K. Mlinaric-Majers, *Coord. Chem. Rev.* 295 (2015) 80–124.
- [3] N. Busschaert, C. Caltagirone, W.V. Rossom, P.A. Gale, *Chem. Rev.* 115 (2015) 8038–8155.
- [4] C. Jia, W. Zuo, D. Zhang, X.-J. Yang, B. Wu, *Chem. Commun.* 52 (2016) 9614–962

The effect of metallic ions presence on the structural, optical and photocatalytic properties of modified metal-titanate nanotubes

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Pharmaceuticals and personal care products (PPCPs), which include pharmaceutical drugs, cosmetics, food supplements and other personal care products, have become essential for human life. Unfortunately, their disposal after use has become very problematic. They are extremely resistant to conventional treatments and, even at very low concentrations, they may impose toxicity at all biological hierarchy levels. For instance, certain pharmaceuticals, like antibiotics, may cause irreversible change to micro-organisms genome, creating new resistances to their action. Several approaches have been proposed to overcome this dramatic environmental problem, but the definitive answer to solve this issue is far from being found.

The use of nanocrystalline semiconductors as photocatalysts, on the treatment of wastewaters, has generated great interest. TiO_2 has been the most extensively used semiconductor in the removal of a large number of organic pollutants from water systems. However, TiO_2 has a major drawback in processes associated with solar photocatalysis due to its wide bandgap (3.2 eV), and high recombination rate of photo-generated carriers. Therefore, the synthesis of TiO_2 -based materials, e.g. titanate nanotubes (TNT), with a broader range of light absorption and a lower charge recombination rate would be an important achievement towards the development of successful photoactive materials.

This work is in line with this concern and reports the synthesis of nanocrystalline TNT-based materials modified by transition metals, by using an ion-exchange (TNT/M) and doping (M-TNT) processes. The transition metals selected for this study were Cu, Mn and Ni. The influence of the transition metal position in the TNT structure on the optical and photocatalytic properties of the materials was studied. The photocatalytic activity of the samples was investigated using the terephthalic acid (TA) as probe molecule to study the catalytic production of hydroxyl radical ($\bullet\text{OH}$). The results show that either M-TNT or TNT/M modified samples are better catalysts than the pristine TNT, being the photocatalytic performance dependent on the transition metal used and on its position in the TNT crystalline structure.

Acknowledgements

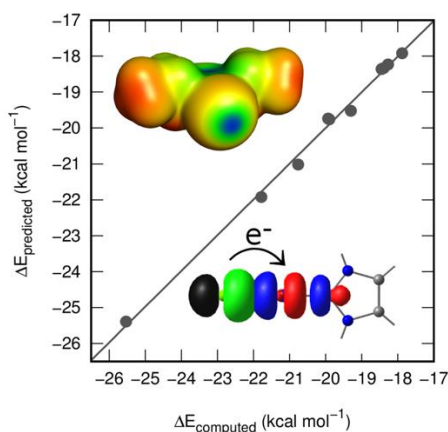
Support for this work was provided by FCT through UID/MULTI/00612/2013, PEst-OE/QUI/UI0612/2013 and IF/01210/2014 projects.

Tuning ion-pair halogen bonds towards efficient anion receptors in solution

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Halogen bonds (XB) are highly directional, attractive interactions involving a halogen atom (X) and a Lewis base (B), in a complex type $R-X\cdots B$ ($X = \text{Cl}, \text{Br}$ or I). The nature of this specific type of non-covalent interaction has been predominantly explained by the existence of a localized electrophilic region at X, named σ -hole, while evidence for significant contributions from charge-transfer have been the subject of intense discussion recently. XBs have found widespread application, amongst other fields, in anion recognition in solution.^[1,2] In particular, the charged haloimidazolium or halotriazolium motifs are shown to establish very strong XBs with anions in competitive aqueous media. In this communication, we investigate this class of ion-pair systems by quantum mechanical methods discussing the key roles of solvent and substituents on the XB nature and strength, and their implications for the design of efficient anion receptors working in solution.^[3]



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References

- [1] T.M. Beale, M.G. Chudzinski, M.G. Sarwar, M.S. Taylor, *Chem. Soc. Rev.* 42 (2013), 1667-1680.
- [2] A. Brown, P.D. Beer, *Chem. Comm.* 52 (2016), 8645-8658.
- [3] R. Nunes, P.J. Costa, *Chem. Asian J.* 12 (2017), 586-594

Revisiting the reactions of *t*-BuX (X = Br, I) with monoalcohols: a mechanistic analysis through numerical integration and nonlinear regression methods

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Solvolytic reactions are probably the most studied reactions, whether in organic solvents, in water, or in aqueous–organic mixtures. Reactions of tertiary alkyl halides, substituted tosylates, and adamantyl chloride derivatives, among others, have been systematically used as model reactions to probe, discuss, and characterize pure, mixed, and borderline behaviours involving S_N1 , S_N2 , E1, and E2 mechanisms [1]. Since the pioneering work by Hughes and Ingold in 1935 [2], the reactions of tertiary alkyl halides, and in particular of tertiary butyl halides, *t*-BuX, with hydroxylic solvents have been thoroughly investigated and commonly considered to follow first-order kinetics. However, most of the published studies were limited to the only generally acknowledged meaningful reaction step, *viz.* the solvolysis reaction, in which *t*-BuX is consumed to produce the halogen acid, HX. Gonçalves, Martins, and Simões (GMS) have nevertheless shown that the whole kinetic picture is much more complex than this and proposed in the early '90s a multistep mechanism involving the putative influence of various subsequent reaction steps beyond the initial solvolysis process [3].

The aim of this work was to quantitatively test, through the use of numerical integration (4th order Runge-Kutta method) associated with nonlinear regression (Levenberg–Marquardt method) the GMS mechanism for the reactions of *t*-BuX with monoalcohols, and to provide a reliable way to obtain accurate values for all involved rate constants. All kinetic experiments were followed by conductimetry at several temperatures, during extended periods of time. Maximum acid concentration was obtained by potentiometric titration using an Ingold glass electrode suited for non-aqueous media. Concentration vs. time curves for the intermediate species, HX, were derived from *G* vs. *c* calibration curves [1]. The use of the referred combined mathematical approaches permitted the rigorous computation of the rate constants of the relevant kinetic steps described by the GMS mechanism, and confirmed the predicted distinct behaviours of the solvolyses of *t*-BuX with primary, secondary and tertiary alcohols (Fig. 1) [1].

Acknowledgements

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References

- [1]R. Elvas-Leitão, F. Martins, *Int. J. Chem. Kin.*, 49, 2017,100-111.
- [2]E. D Hughes, C. K. Ingold, *J. Chem. Soc.* (1935) 244–255.
- [3]R.M.C. Gonçalves, F. Martins, A. Simões, *An. Quim.*, 88, 1992, 417-420

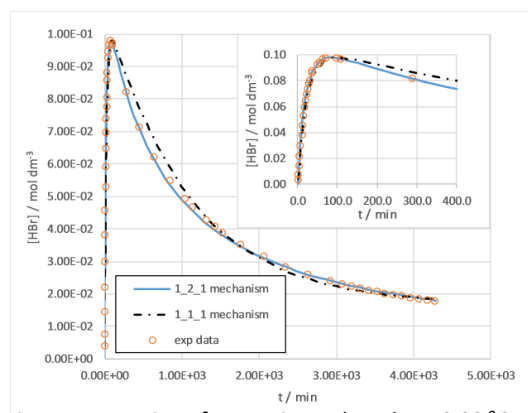


Figure 1- Reaction of *t*-BuBr in methanol at 50.00 °C

Electrochemical versus Chemical synthesis of polydopamine films for the construction of enzymatic biosensors

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The development of electrochemical enzyme biosensors is a growing field to achieve portable, fast and reliable devices needed for chemical analysis in the sampling site [1]. To overcome problems regarding stability of immobilized enzymes, bio-inspired materials such as polydopamine films (PDA) are being explored to covalently bind target biomolecules through the latent reactivity of quinone groups [2]. Most of the reported studies of PDA concern the chemical polymerization of dopamine in alkaline oxygenated solutions. However, the chemical synthesis does not allow an precise control of the oxidation state of the films compromising their reactivity towards amine groups, and therefore the covalent binding of biomolecules. To overcome this limitation, electropolymerization of dopamine [3] arises as a promising alternative.

In this work, PDA films prepared by chemical and electrochemical oxidation of dopamine on glassy carbon electrodes were characterized by optical, morphological and electrochemical techniques (e.g. ellipsometry, water contact angle, atomic force microscopy and cyclic voltammetry), and their surface properties compared. In general, thinner films with higher electroactivity are achieved by fast electrochemical synthesis, revealing a higher density of quinone groups, in contrast to the films prepared by chemical oxidation. The catalytic performance of the enzyme electrodes was assessed by chronoamperometry and cyclic voltammetry toward the oxidation of 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic) acid diammonium salt (ABTS). The results reveal a great potential application of these biocompatible polymeric matrices in novel biosensing devices.

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References

- [1] S. Alegret, A. Merkoçi, *Comprehensive Analytical Chemistry - Electrochemical Sensor Analysis*, Elsevier, Netherlands, 2006.
- [2] Y. Lui, K. Ai, L. Lu, *Chem. Rev.* 114 (2014) 5077-5115.
- [3] F. Bernsmann, J. Voegel, V. Ball, *Electrochimica Acta* 56 (2011) 3914–3919.

Structural Stability and Molecular Organization of Yeast Sphingolipid-enriched Membrane Domains

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The backbone of all major sphingolipids in yeast and filamentous fungi is phytoceramide. Its sphingoid base, phytosphingosine, differs from that usually found in mammals by the addition of a hydroxyl group to the 4-ene, which may be a crucial factor for the different properties of membrane microdomains among those organisms. Recently, we have disclosed the presence of sphingolipid-enriched domains in the plasma membrane of *Saccharomyces cerevisiae* in exponential phase [1], which were not found in mammals. Hence, the study of the biophysical properties of phytosphingolipids is relevant, since it helps to understand the importance of sphingolipid hydroxylation in the formation of gel domains *in vivo*. In this work, binary mixtures of N-stearoyl-phytoceramide (PhyCer) with palmitoyl-oleoylphosphatidylcholine (POPC) were studied. Steady-state and time-resolved fluorescence of membrane probes, X-ray diffraction, atomic force microscopy and confocal microscopy were employed. As for other saturated ceramides, highly rigid gel domains start to form with just ~5 mol% PhyCer at 24°C. However, PhyCer gel-enriched domains in coexistence with POPC-enriched fluid present additional complexity, since their properties (maximal order, shape and thickness) change at specific POPC:PhyCer molar ratios, suggesting the formation of highly stable stoichiometric complexes with their own properties. A POPC/PhyCer binary phase diagram, supported by the different experimental approaches employed, is proposed with complexes of 3:1 and 1:2 stoichiometries, stable at least from ~15 °C to ~55 °C, providing mechanisms for *in vivo* formation of sphingolipid-enriched gel domains, that may account for stable membrane compartments and diffusion barriers in yeast membranes [2].

Acknowledgements

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References

- [1] Aresta-Branco, F., Cordeiro, A.M., Marinho, H.S., Cyrne, L., Antunes, F., and de Almeida, R.F.M. (2011) Gel domains in the plasma membrane of *Saccharomyces cerevisiae*: highly ordered, sphingolipid-enriched, ergosterol-free lipid rafts. *J. Biol. Chem.* 286: 5043.
- [2] Marquês, J.T., Cordeiro, A.M., Viana, A.S., Herrmann, A., Marinho, H.S., de Almeida, R.F.M. (2015) Formation and properties of membrane ordered domains by phytoceramide: role of sphingoid base hydroxylation. *Langmuir*, 31: 9410.

Biochemical and biophysical studies of sphingolipids from *Saccharomyces cerevisiae* plasma membrane

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The plasma membrane of the yeast *Saccharomyces cerevisiae* has a similar composition in ergosterol and also sphingolipids, although with smaller variety, to that of pathogenic fungi, being ergosterol the main classical target of antifungal agents¹. In addition, *S. cerevisiae* sphingolipid-biosynthetic mutants, such as *ipt1Δ*, unable to synthesize the sphingolipid mannosyl-diinositolphosphorylceramide, M(IP)2C, show greater antifungal resistance^{2,3}. Both strains share equal content in ergosterol and therefore, the mechanisms of resistance may involve the highly-ordered sphingolipid-enriched domains discovered in our laboratory⁴.

For the reasons above, it is important to study the sphingolipid influence in the plasma membrane organization of *S. cerevisiae*. To this end, we are isolating each complex sphingolipid class present in that organism to perform a biophysical characterization and compare it with biophysical properties observed in living cells. Before that it is, however, necessary that the sphingolipid extraction from yeast cells is optimized. After obtaining the total lipid extracts, the lipids have to undergo mild alkaline hydrolysis to eliminate glycerophospholipids. The sphingolipid extracts thus obtained are then analyzed by thin layer chromatography.

Regarding lipid extracts obtained by the Fölch method, it was possible to identify mannosyl-inositolphosphorylceramide (MIPC), in both wt and *ipt1Δ* extracts. The impossibility to detect M(IP)2C may be due to low extraction and/or revelation efficiency of this highly polar lipid and consequently additional methods were attempted. No differences in glycerophospholipids and ergosterol contents between the two strains were observed.

Preliminary biophysical studies with several sphingolipid biosynthetic mutants were performed in living cells, revealing sphingolipid-dependent changes of plasma membrane organization.

Acknowledgments

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References

- [1] Castelli, M. V. et al. Novel antifungal agents: a patent review (2011 - present). *Expert Opin. Ther. Pat.* 24, 323–338 (2014).
- [2] François, I. E. J. A. et al. Membrane rafts are involved in intracellular miconazole accumulation in yeast cells. *J. Biol. Chem.* 284, 32680–32685 (2009).
- [3] Leber, A., Fischer, P., Schneiter, R., Kohlwein, S. D. & Daum, G. The yeast *mic2* mutant is defective in the formation of mannosyl-diinositolphosphorylceramide. *FEBS Lett.* 411, 211–214 (1997).
- [4] Aresta-Branco, F. et al. Gel domains in the plasma membrane of *Saccharomyces cerevisiae*: highly ordered, ergosterol-free, and sphingolipid-enriched lipid rafts. *J. Biol. Chem.* 286, 5043–5054 (2011).

Physico-chemical characteristics of a novel diphenylphosphinomethyl derivative of ketoconazole

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Concern regarding the development of resistance to any of the few antifungal drugs available has been growing in the last decade [1]. Although we are able to define certain mechanisms of drug resistance, continued efforts for a deeper understanding of the cellular and molecular mechanisms as well as the clinical components of antifungal resistance is very important.

The overall goal of the project is to study new ketoconazole derivatives as antifungal agents targeting sphingolipids in plasma membrane. Ketoconazole is a synthetic imidazole antifungal drug approved by FDA in 1981 [2]. This drug was the only antifungal available for treatment of systemic fungal infections caused by yeasts for the following ten years. Nowadays, it is mainly used in a variety of formulations for topical applications. Since one of the molecular mechanisms of resistance to azoles is based on alterations in the plasma membrane composition [3], a better understanding of it is essential to the prompt and efficient treatment of patients with invasive mycoses and to improve the outcome of such infections. It is important to study the interactions of the new ketoconazole derivatives with sphingolipids, which are major lipid components of the cell plasma membrane of eukaryotes, but unlike glycerophospholipids, are structurally very different among fungi and humans. It makes them a molecular target for fungal infections treatment which is much less exploited than other membrane components, such as ergosterol, or cell-wall components.

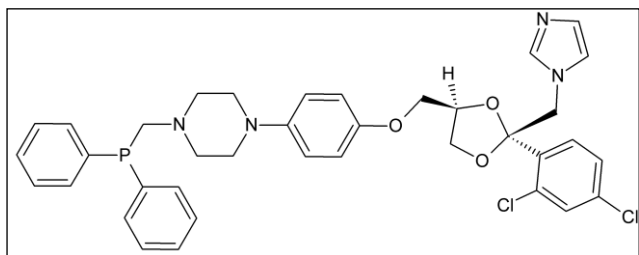


Figure 1. Schematic view of the diphenylphosphinomethyl derivative of ketoconazole

Herein we present the synthesis and characteristics of the first compound - the diphenylphosphinomethyl derivative of deacetylated ketoconazole. The identity of the new synthesized compound was confirmed by NMR spectroscopy. Obtained phosphine, similarly to ketoconazole, is soluble in a wide range of solvents and rather insoluble in water. Importantly, its solutions are air-stable for at least several hours. The compound

shows a strong luminescence with its maximum at 360-375 nm (depending on the solvent) upon excitation 290-300 nm. TD-DFT calculations showed that the first transition involves mostly its piperazine moiety and directly bound phenyl ring.

Currently, we are starting to investigate its interactions with membrane model systems of fungal and mammalian membranes as well as with other models of cellular targets. This will allow us to get important insights into the structural basis and functional significance of the membrane lipid domains for the development of new antifungal agents.

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[1] Centers for Disease Control and Prevention, Antifungal Resistance (2014) October 23, Available from: <http://www.cdc.gov/fungal/antifungal-resistance.html>

[2] Gupta, A.K., Daigle, D., and Foley, K.A. (2015) *Expert Opin Drug Saf*, 14: p. 325-334.

[3] Francois, I.E., Bink, A., Vandercappellen, J., Ayscough, K.R., Toulmay, A., Schneiter, R., van Gysegem, E., Van den Mooter, G., Borgers, M., Vandenbosch, D., Coenye, T., Cammue, B.P. and Thevissen, K. (2009) *J Biol Chem*, 284: 32680-32685; Mukhopadhyay, K., Prasad, T., Saini, P., Pucadyil, T.J., Chattopadhyay, A. and Prasad, R. (2004) *Antimicrob Agents Chemother*, 48: 1778-1787.

Lysosomal-mimicking vesicles: a valuable tool to explore the effect of sphingosine abnormal accumulation on membrane biophysical properties

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Artificial membranes have been widely used to unveil specific lipid-lipid and lipid-protein interactions in complex cellular systems. In this work, we developed a new synthetic biosystem that more closely resembles the lysosome – the lysosome-mimicking vesicles (LMVs), displaying internal acidic pH and external neutral pH. The LMVs were used to further understand how the sphingosine (Sph) abnormal accumulation in Niemann Pick type C1 (NPC1) impacts lysosomal membrane structure and biophysical properties. To this end, ternary 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC)/Sphingomyelin (SM)/Cholesterol (Chol) mixtures with, respectively, low and high Chol/SM levels (NPC1 phenotype) were prepared. The effect of Sph on the membrane permeability and biophysical properties was then evaluated by fluorescence spectroscopy, electrophoretic and dynamic light scattering. Our results showed that Sph has the ability to cause a shift in vesicle surface charge, increase the packing properties of the membrane and promote a rapid increase in membrane permeability. These effects are enhanced in NPC1-LMVs, i.e., containing higher levels of Chol and SM. Overall, the results suggest that lysosomal accumulation of these lipids, as observed under pathological conditions, might significantly affect lysosomal membrane structure and integrity, and therefore disturb cellular homeostasis.

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Assessing lipophilicity of plant polyphenolic compounds: different experimental approaches

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Polyphenols are wide spread phytochemicals, occurring naturally in many edible plants. They are known to exert several bioactivities, such as anti-inflammatory, anti-oxidant, and antibacterial [1]. However, their interaction and affinity for lipid bilayers is largely unknown, even for quercetin, a widely studied polyphenol [2]. Their bioactivities, in particular anti-oxidant, have been linked to a direct interaction with membrane lipids [2], which, is dependent on their partition to lipid bilayers, i.e. their lipophilicity.

In this work, we used an array of techniques, including different fluorescence spectroscopy approaches, cyclic voltammetry, and air/water tensiometry. The work concerned rosmarinic acid (RA), caffeic acid (CA), chlorogenic acid (CGA) and quercetin. Membrane/water partition coefficients for well defined lipid systems [3] (POPC and POPC:Cholesterol (1:1) at 23°C) were obtained using intrinsic fluorescence properties, including anisotropy and lifetime, of the compounds. Values of 5.1×10^2 and 1.1×10^4 were estimated for the $K_{p_{popc/water}}$ of RA and quercetin, respectively, and of 1.6×10^2 and 2.2×10^3 for the $K_{p_{popc:chol/water}}$. The values for RA are consistent with its air/water partition. Due to their low lipophilicity, it was not possible to estimate CGA and CA partition coefficient values. The redox process of the phenolic compounds was monitored by cyclic voltammetric measurements, which confirmed that RA and quercetin have the highest affinity for a membrane environment. Molecular dynamic simulations show that, unlike quercetin [2], the three phenolic acids locate preferentially near the lipid/water interfacial region of the bilayer.

In sum, combining the results obtained from different techniques, the relative lipophilicity of the compounds could be established and from the fluorescence spectroscopy approaches it can also be concluded that cholesterol when added to a fluid bilayer weakens polyphenol-membrane interactions.

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References

- [1] B.Halliwel, J.Rafter, A. Jenner, *Am. J. Clin. Nutr.* 81 (2005) 268–276.
- [2] P.Kosinova, K.Berka, M.Wykes, M.Otyepka, P.Trouillas, *J. Phys. Chem. B* 116 (2012) 1309–1318.
- [3] R. F. M. de Almeida, A. Fedorov, M. Prieto, *Biophys. J.* 85 (2003) 2406–2416.

Sphingolipid-enriched versus ergosterol-enriched domains in *Saccharomyces cerevisiae*

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Recently, we have disclosed the presence of sphingolipid-enriched domains in the plasma membrane of *Saccharomyces cerevisiae* in exponential phase. These domains differ immensely from the prototypical lipid domains both in composition, given that they are ergosterol-depleted, and biophysically, as they are highly rigid gel domains, and not liquid ordered domains [1]. We hypothesize that these sphingolipid-enriched gel domains should be related to yeast membrane compartment containing Pma1 or MCP. Alternatively, these gel domains may act as diffusion barriers contributing to the spatial-temporal stability of membrane compartments in yeast, which contrasts with the small size and highly dynamic nature of lipid rafts in mammalian cells. We have also been focused on which structural features contribute to structural stability of gel domains and how important they are for the action of antifungal agents.

The presence of these gel domains does not preclude the existence of ergosterol-enriched membrane domains in the budding yeast. In fact, ergosterol is thought to co-localize with the membrane compartment containing Can1, or MCC. Thus, we assessed the usefulness of several membrane probes usually employed for cholesterol-enriched domains in mammalian cells to characterize ergosterol-dependent biophysical properties in yeast membranes [2]. We have identified potential-sensitive dyes as the most useful, and started to address the structural and functional interplay between ergosterol-enriched and sphingolipid-enriched domains in yeast, investigating the biophysical properties of the plasma membrane of the wild type and of mutant cells with deletions in genes involved in ergosterol and sphingolipid biosynthetic pathways.

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References

- [1] Aresta-Branco, F., Cordeiro, A.M., Marinho, H.S., Cyrne, L., Antunes, F., and de Almeida, R.F.M. (2011) Gel domains in the plasma membrane of *Saccharomyces cerevisiae*: highly ordered, sphingolipid-enriched, ergosterol-free lipid rafts. *J. Biol. Chem.* 286: 5043.
- [2] A.E.P. Bastos, H.S. Marinho, A.M. Cordeiro, A. Soure, R.F.M. de Almeida (2012) Biophysical properties of ergosterol-enriched lipid rafts in yeast and tools for their study. *Chem. Phys. Lipids*, 165: 577

Natural caffeic acid ester derivatives affect lipid bilayers surface and human cells cytoskeleton organization

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One of the most wide spread class of phytochemicals are phenolic acids, which occur naturally in coffee, herbal infusions and several other edible plant sources [1]. Like flavonoids and other polyphenols, phenolic acids have beneficial health effects such as anti-inflammatory, antioxidant and antibacterial [2]. However, their mechanism of action is illusive. Particularly, their effect on the structure and dynamics of lipid bilayers is poorly studied. This work aims to characterize phytochemical-membrane interactions using both liposomes and the retinal pigmented epithelial human cell line (RPE-1).

The effect of caffeic acid (CA) and two CA esters, rosmarinic acid (RA) and chlorogenic acid (CGA), was studied in different liposome models. Each liposome model presents a different lipid phase behaviour at 23°C, Liquid Disordered (Ld), Liquid Ordered (Lo) and Ld/Lo coexistence, representative of human cell membranes. Quercetin was also used as a positive control since its interactions with lipid bilayers are well characterized [3,4]. As phenolic acids have low lipophilicity we proceeded to the evaluation of their effects on several biophysical properties of the liposomes using two fluorescent probes with superficial membrane location, in the lipid/water interface, where these compounds are expected to localize. Phenolic acids effects on model membranes order and hydration were negligible even at high concentrations. RA and CGA interact superficially with the membrane changing hydration water and polar headgroups orientation, possibly altering H-bonding patterns due to their own groups with H-bonding ability. Quercetin, the positive control, had large effects, especially in more ordered systems, even at concentrations below 100 µM.

In RPE-1 cells, RA, CA and CGA (100 µM) seemed not to affect global membrane order and dynamics after 2 and 8 h of exposure. However, the cell cytoskeleton was considerably affected showing alterations resembling those caused by oxidative stress. Interestingly, we observed the production of H₂O₂, ranging from 6.6 to 16.2 µM in the cell culture medium after 8 h incubation with the phenolic compounds. As the effects on the cytoskeleton may be linked to membrane caveolae, further studies targeting caveolin-1 and membrane specific domains will be prosecuted.

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References

- [1] M.N. Clifford, *J. Sci. Food Agric.* 80 (2000) 1033-1043.
- [2] P. Falé, L.L. Ascensão, M.L. Serralheiro, *Food Funct.* 4 (2013) 426-431.
- [3] J.T. Marquês, A.S. Viana, R.F.M. de Almeida, *Langmuir* 30 (2014) 12627-12637.
- [4] P. Košinová, K. Berka, M. Wykes, M. Otyepka, P. Trouillas, *J. Phys. Chem. B* 116 (2012) 1309-1318.

Role of endogenous VIP VPAC₁ receptor activation during hypoxia and interictal-like activity induced in vitro by 0mM-Mg²⁺ in LTP expression in the rat hippocampus

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VIP, a known modulator of synaptic transmission present in hippocampal interneurons, was recently shown to inhibit long-term potentiation in the CA1 area of the rat hippocampus through activation of VPAC₁ receptors (1). VIP release is triggered by electrical activity, VIP receptors are enhanced in TLE patients (2) and VIP promotes neuronal survival in the absence of electrical activity (3), a situation observed during hypoxic depression. In this work, we investigated the influence of VPAC₁ receptor activation during brief hypoxia (HPX) or in vitro interictal-like activity (ILA) to the subsequent expression of LTP in the CA1 area of the hippocampus.

Extracellular electrophysiological recordings of field-excitatory post-synaptic potentials (fEPSPs) evoked by electrical stimulation were used to access synaptic transmission in hippocampal slices obtained from male Wistar rats (6-7-week-old). HPX was induced by 3 min superfusion with 95% N₂-5% CO₂ (normoxia: 95% O₂-5% CO₂). In vitro ILA was induced by 30 min superfusion with aCSF containing no 0mM MgCl₂ and 6mM KCl (normal: 1mM MgCl₂ and 3mM KCl). LTP was induced by theta-burst stimulation (TBS, five 100Hz bursts, 4 stimuli, separated by 200 ms) and potentiation of fEPSP slope evaluated 50-60 min after LTP induction. The selective VPAC₁ antagonist PG 97-269 was used to block endogenous VPAC₁ receptor activation during both insults. ANOVA was used to evaluate the statistical differences between control and test groups.

TBS in control slices caused a long-lasting enhancement in fEPSP slope by 29.0±2.9% (n=7). Hypoxia (3 min) caused a brief but marked decrease in fEPSP slope that returned to basal values 30 min after hypoxia. This recovery was not complete (89.0±1.8%) when hypoxia occurred in the presence of 100nM PG 97-269. TBS-induced LTP was enhanced to 44.9±1.3% (n=4) and 43.8±1.3% (n=4) when induced 30 min and 60 min after hypoxia, respectively. This enhancement was not observed in slices subjected to hypoxia in the presence of PG 97-269 (100nM). Following 30 min interictal-like activity induced by 0mM Mg²⁺ aCSF, TBS-induced LTP was impaired to 17.9±2.3% (n=3) and 24.8±1.5% (n=3) induced 30 min and 60 min after interictal-like activity, respectively. When interictal-like activity was induced in the presence of 100nM PG 97-269, this impairment was not observed (n=3).

These results suggest that activation of VPAC₁ receptors by endogenous VIP during brief hypoxia contributes to a subsequent facilitation of LTP induction. In contrast, activation of VPAC₁ receptors during interictal-like seizures may contribute to the inhibition of LTP that follows this insult.

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References

- [1] Cunha-Reis, D et al., *J Mol Neurosci*, 2010. 42: 278; [2] de Lanerolle NC et al., *Br Res*, 1995. 686: 182-93; [3] Brenneman et al., *Proc Natl Acad Sci U S A*. 1986 83: 1159-62.

Synthesis and Hepatotoxicity of Psychoactive Cathinones

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Khat (*Catha edulis*) is a plant from East Africa and Arabian Peninsula that has been consumed over centuries, due to its stimulant properties. The main psychostimulant compound present in its leaves is cathinone, a β -keto analogue of amphetamine [1]. Since cathinone is a potent central nervous system stimulant, several synthetic analogues have emerged in the market of recreational drugs as legal substitutes of illicit substances such as amphetamine, MDMA (ecstasy) and cocaine. This type of substances, known as synthetic cathinones, are the second largest group of New Psychoactive Substances (NPS) reported to EMCDDA (European Monitoring Centre for Drugs and Drug Addiction) [2,3]; just in the past ten years 103 new synthetic cathinones were found. These NPS are a public health issue, not only due to the secondary effects, such as fatal intoxication, observed in some cases, but also because of their easy availability to the general public [2,4]. Considering that these compounds are synthesized illegally in laboratories, the knowledge of a simple synthetic route that resembles the one used in those labs became important to predict new compounds appearing into the market. Moreover, it is urgent to understand how these drugs lead to liver toxicity since it is known that this organ is the main target of amphetamine-like compounds.

This work describes a two-step pathway to synthesize 20 psychoactive cathinones (fig. 1) and their characterization by NMR and GC-MS, along with the evaluation of their toxicity towards the liver cancer cell line HepG-2, considered a good model to screen the potential hepatotoxicity of new compounds. So far, the results suggest a relation between the hepatocellular toxicity of cathinones and their chemical structure, showing a toxicity enhancement with the increase of the alkyl chain length of the ketone moiety, as well as with the substitution of an Aromatic-H by a methyl group.

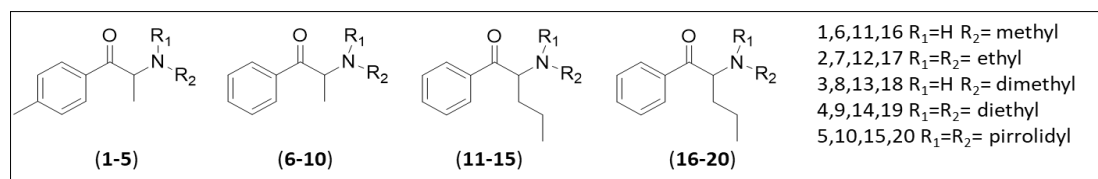


Figure 5 - Psychoactive cathinones.

Acknowledgements

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References

- [1] E. Smolianitski, E. Wolf, J. Almog, *Forensic Sci. Int.* 242 (2010) 219-27.
- [2] EMCDDA (2016), *European Drug Report 2016: Trends and Developments*, EU Publications Office, Luxembourg.
- [3] UNODC (2013), *The Challenge of New Psychoactive Substances*, United Nations Publication, Austria.
- [4] M. Coppola, R. Mondola, *Toxicology Letters* 211 (2012) 144-149.

Notes on the nature of the chemical bond in actinide di-sulfides.

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Actinide disulphide dications, AnS_2^{2+} , were produced in the gas phase for $An = Th$ and Np by ionic collisions. To provide insight into their geometric and bonding scenarios high level multiconfigurational (CASPT2) electronic structure calculations were performed to assess the structures and bonding of the new AnS_2^{2+} species obtained for $An = Th, U, Np$ and Pu to examine trends along the An series.^[1] The CASPT2 results showed that, like in the case of uranium, the new AnS_2^{2+} ions have ground states with triangular geometries, corresponding to the presence of a persulphide in the case of thorium that formally leads to a stable $Th^{IV}S_2^{2+}$ species, while a super-sulphide appears to be present in the case of U, Np and Pu , formally leading to a $An^{III}S_2^{2+}$ species. The computations also revealed that linear thioactinyl structures are higher in energy, with a difference that increases fourfold upon moving from U to Pu , apparently indicating that it will be even more pronounced for Am .

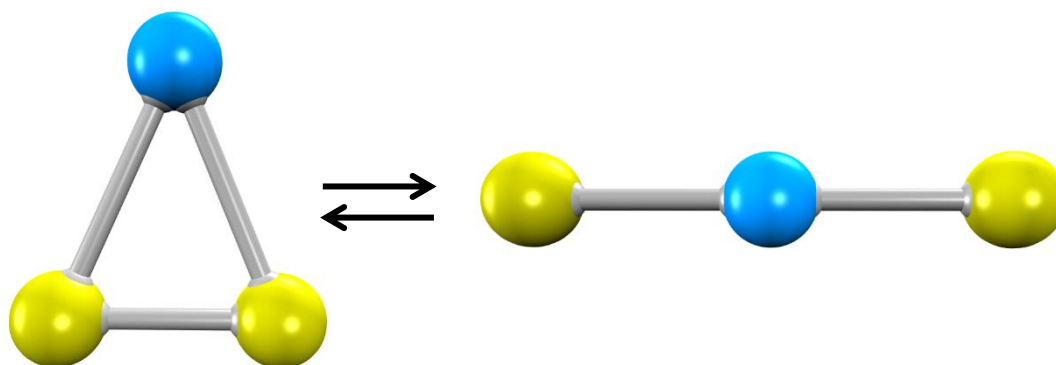


Figure 1 – Triangular or Linear? CASPT2 provides the answer.

Acknowledgements

This work was supported by FCT post-doc grant SFRH/BPD/110419/2015 and project PTDC/QEQ-QIN/3414/2014 both of which are gratefully acknowledged.

References

[1] A. F. Lucena, N. A. G. Bandeira, C. C. L. Pereira, J. K. Gibson and J. Marçalo, *Phys. Chem. Chem. Phys.*, 19 (2017) 10685-10694.

Photoactive nanoparticles supported on textile fibers for photocatalytic applications

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The implementation of new technologies for waste water treatment is of utmost importance due to the increasing demand for clean water. In this context, the development of suitable materials for pollutants removal by adsorption and/or degradation is extremely important and a promising approach relies in the use of photoactive nanomaterials. Several semiconducting nanoparticles (NPs) have shown encouraging photocatalytic results [1,2], however, due to its dimensions, their recovery is difficult and its release to the environment a common problem. A key approach to overcome this problem is the immobilisation of the NPs on surfaces retaining its activity [3].

In this work, the attachment of semiconducting NPs on textile fibers is performed by *in situ* approaches resulting in the formation of composite nanomaterials. Those were structural and morphologically characterised by several techniques such as XRD, DRS, SEM and surface area measurements. The results show the successful *in situ* synthesis and modification of synthetic fibers with bismuth oxychloride (BiOCl) and tin oxide (SnO₂) NPs. BiOCl forms a layer of sheet-like NPs on the surface whereas for SnO₂ a small amount of NPs was detected by SEM analysis. The presence of the NPs on the surface of the fibers was confirmed by DRS for SnO₂ and by XRD for BiOCl. The catalytic activity of the prepared composites was evaluated, under UV-vis light irradiation, through the photodegradation of dyes used in leather industry. The best pollutants removal was achieved using the BiOCl-synthetic composite.

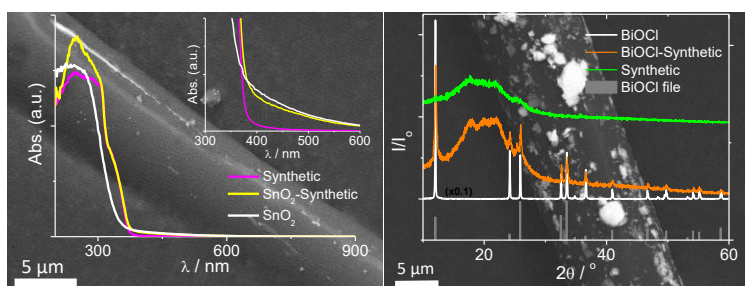


Figure. SEM images for BiOCl-synthetic and SnO₂-synthetic composites and DRS and XRD profiles.

Acknowledgements

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References

- [1] B. Barrocas, A.J. Silvestre, A. G. Rolo, O.C. Monteiro, Phys. Chem. Chem. Phys. 18 (2016) 18081-18093.
- [2] V. C. Ferreira, M. C. Neves, A. R. Hillman, O. C. Monteiro, RSC Adv. 6 (2016) 77329 – 77339.
- [3] M. Abid, S. Bouattour, D. Conceição, A. Ferraria, L. Ferreira, A. Rego, M. Vilarc, S. Boufi, RSC Adv. 6 (2016) 58957–58969.

New sugar-based molecules for infectious and neurodegenerative diseases

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The increasing average life expectancy in developed countries led to an escalating concern regarding geriatric infectious diseases. Infections in elderly populations, particularly nosocomial infections, are known to be not only more frequent but also more severe, being this susceptibility often related to neurodegenerative diseases such as dementia and Alzheimer's [1].

Alkyl 2-deoxy/2,6-dideoxy-*arabino*-hexopyranosides with a potent antimicrobial activity in some *Gram*-positive bacteria have been previously described by our research group [2] and their mechanism of action was recently unravelled (unpublished results). Additionally, promising results arising from NMR interaction studies of some of these 2,6-dideoxyglycosides with cystatin B amyloid fibrils, show their potential for neurodegenerative diseases as well.

These results motivated us to explore the chemistry and bioactivity of 2-deoxy sugars as either neuroprotective or antimicrobial candidates. Thus, new alkyl 2-deoxyglycosides and their thio analogues were synthesized, as well as alkyl 3-deoxy, 4-deoxy and 6-deoxy glycosides, aiming at a better insight of the importance of the deoxygenation pattern. The action of the lead compound on the thermotropic behaviour of phosphatidylethanolamine liposomes was investigated, leading to the proposal of the mechanism of action for this family of compounds. In parallel, 2-deoxyglycosides embodying natural neuroprotective polyphenols were also prepared, envisioning the improvement of the activity and bioavailability of such molecules.

This work clearly demonstrates the uniqueness and versatility of carbohydrates as exceptional scaffolds for medicinal chemistry applications.

Acknowledgements

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References

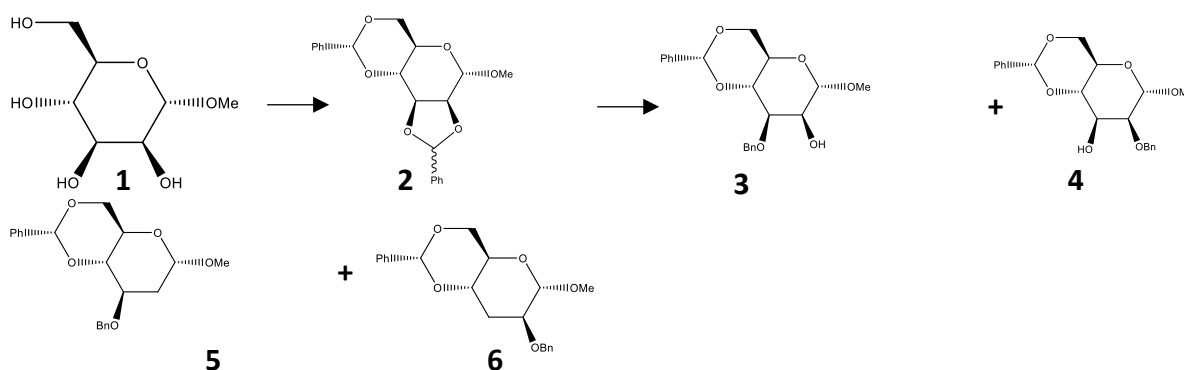
- [1] G. Gavazzi, K. H. Krause. *Lancet Infect. Dis.* 2 (2002) 659-666.
- [2] A. Martins, M. S. Santos, C. Dias, P. Serra, V. Cachatra, J. Pais, J. Caio, V. H. Teixeira, M. Machuqueiro, M. S. Silva, A. Pelerito, J. Justino, M. Goulart, F. V. Silva, A. P. Rauter. *Eur. J. Org. Chem.* 8 (2013) 1448-1459.

Investigation of acetal protected sugars

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Butyrylcholinesterase (BChE) is an enzyme that catalyses the hydrolysis of the neurotransmitter acetylcholine. Evidences point to its important role in cholinergic neurotransmission [1]. Its inhibition is, therefore, relevant for the study of its involvement in neurodegenerative diseases, in particular in Alzheimer's disease. Purine nucleosides have been reported as potent and selective inhibitors of this enzyme [2,3]. In this communication, we disclose the synthesis of selectively benzyl protected sugars, required for their future transformation in deoxy purine nucleosides, embodying remaining hydroxy groups benzylated, as these protecting groups are key structural features for the required bioactivity [2]. As described in the scheme below, the first step was to protect methyl α -D-mannopyranoside (**1**) free OH groups with two benzylidene acetal groups. The second step investigated aimed at a regioselective opening of the five-membered ring acetal in **2**, using Dibal-H as a reducing agent, to give compounds **3** and **4**. After successful isolation of both regioisomers, reaction with trimethylsilyl trifluoromethanesulfonate (TMSOTf) and tetrabutylammonium borohydride afforded the target deoxy compounds, namely the 4,6-O-benzylidene protected 2-deoxy-D-*arabino*-hexopyranoside (**5**) and the 3-deoxy-D-*arabino*-hexopyranosid in good yield.



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References

- [1] Sultan Darvesh, David A. Hopkins, Changuz Geula, Neurology of butyrylcholinesterase, *Nature Reviews Neuroscience* 2003, 4, 131-138.
- [2] Filipa Marcelo, Filipa V. M. Silva, Margarida Goulart, Jorge Justino, Pierre Sinay, Yves Blériot, Amélia Pilar Rauter, Synthesis of novel purine nucleosides towards a selective inhibition of human butyrylcholinesterase, *Bioorg. Med. Chem.* 2009, 17(14), 5106-5116.
- [3] S. Schwarz, R. Csuk, A. P. Rauter, Microwave-assisted synthesis of novel purine nucleosides as selective cholinesterase inhibitors, *Org. Biomol. Chem.* 2014, 12 (15), 2446 – 2456.

Investigation of structural features towards butyrylcholinesterase selective inhibition by purine nucleosides

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Alzheimer's disease (AD) is the most common form of senile dementia. The etiology of this complex and fatal disease is still unknown and treatment options are based mainly on inhibitors of both acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes. However, these therapeutics are not effective in preventing disease progression. While AChE activity decreases in specific brain regions as disease progresses, BChE activity is upregulated, making it an interesting target for drug discovery. Interestingly, it has been demonstrated that selective inhibition of BChE improved memory, cognitive functions and learning abilities in mice [1].

Our group has disclosed a new family of highly selective and potent BChE inhibitors based on a purine nucleoside scaffold, whose most active one has $k_i = 50$ nM for BChE and showed an extraordinary selectivity (selectivity factor of 340) over acetylcholinesterase inhibition [2]. These promising results encouraged us to further investigate the role of glycosyl structure and configuration in promoting activity as BChE selective inhibitor. Synthetic approaches to either different protecting groups or glycosyl deoxygenation followed by synthesis of the respective purine nucleosides are now presented affording promising analogues of the lead nucleoside, bearing a perbenzyl protected α -D-manosyl N⁷ linked to a 2-acetamido-6-chloropurine.

Acknowledgements

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References

- [1] U. Košak, B. Bru, D. Knez, R. Šink, S. Skelj, J. Trontelj, A. Pišlar, J. Šlenc, M. Gobec, M. Živin, L. Tratnjek, M. Perše, K. Sałat, A. Podkova, B. Filipek, F. Nachon, X. Brazzolotto, A. Więckowska, B. Malawska, J. Stojan, I. M. Raščan, J. Kos, N. Coquelle, J.-P. Colletier, S. Gobec, *Sci. Rep.* 6 (2016) 39495-39511.
- [2] S. Schwarz, R. Csuk, A. P. Rauter, *Org. Biomol. Chem.* 12 (2016) 2446-2456.

Exploiting the Potential of C-Glucosyl Flavonoid Analogues against Diabetes and Alzheimer's Disease

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According to the International Diabetes Federation, type 2 diabetes accounts for at least 90% of all cases of diabetes, affecting over 415 million people around the world. Family history of diabetes, unhealthy lifestyles and increasing age are known major risk factors for this metabolic disorder. On the other hand, the risk of dementia (particularly Alzheimer's disease) is up to 73% higher in people with type 2 diabetes and, therefore, the increasing incidence of Alzheimer's disease is perhaps not only a consequence of population ageing alone, but also a result of the diabetes epidemic itself.¹

The discovery of an extremely potent antidiabetic C-glucosyl isoflavone isolated from *Genista tenera*² prompted us to further explore the ability of this and other related compounds to exert antidiabetic and neuroprotective effects as well. Hence, in this communication we will present our efforts to combine key features of the flavone scaffold with the reported benefits of the sugar moiety. Aiming at the disclosure of structural requirements of flavonoid derivatives with optimal physicochemical properties against therapeutic targets such as $A\beta_{1-42}$, we have focused on the synthetic introduction of structural variations on the flavonoid core, which culminated in the development of a small library of nature-inspired flavone analogues with therapeutic potential against type 2 diabetes and Alzheimer's disease.

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References

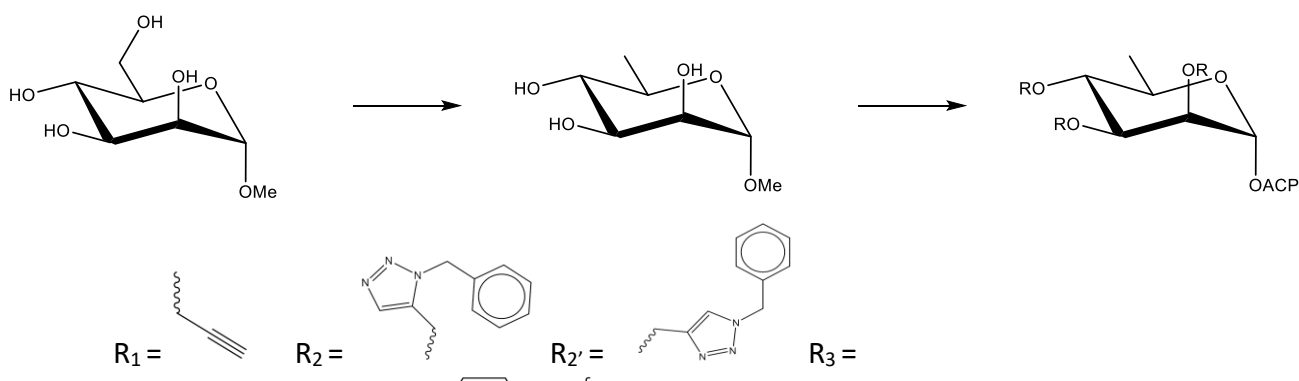
- [1] A.M. Matos, M.P. Macedo, A.P. Rauter, *Med. Res. Rev.*, 2017, DOI:[10.1002/med.21440](https://doi.org/10.1002/med.21440)
- [2] A.R. Jesus, C. Dias, A.M. Matos, R.F. de Almeida, A.S. Viana, F. Marcelo, R.T. Ribeiro, M.P. Macedo, C. Airoidi, F. Nicotra, A. Martins, E.J. Cabrita, J. Jimenez-Barbero, A.P. Rauter. *J. Med. Chem.* 2014, 57(22), 9463-9472.

Synthesis of purine nucleosides with deoxygenated sugars: exploratory chemistry of potential butyrylcholinesterase selective inhibitors

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The purpose of this work is to synthesise purine nucleosides with deoxygenated sugars as potential butyrylcholinesterase (BChE) selective inhibitors to better understand the way butyrylcholine (BCh) affects Alzheimer's Disease (AD) in the final disease stages. As of today, work has been done with different purine bases and various sugar moieties of purine nucleosides, and it was found that perbenzyl D-mannosyl moiety α -N⁷-linked to 2-acetamido-6-chloropurine (ACP) led to the best selective inhibition of BChE ($IC_{50} = 50nM$).^{1,2} As an attempt to improve and further investigate factors that promote BChE inhibition, the deoxygenation of D-mannose to D-rhamnose and subsequent protection with protecting groups such as propargyl (R_1), 1-benzyl-5-methyl-1H-1,2,3-triazole (R_2) or 1-benzyl-4-methyl-1H-1,2,3-triazole (R_2') and *p*-methoxybenzyl (R_3) groups was carried on and will be presented and discussed. Compound structure evidence was provided by NMR spectra and will also be discussed.



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References

- [1] Marcelo, F.; Silva, F. V. M.; Goulart, M.; Justino, J.; Sinaý, P.; Blériot, Y.; Rauter, A. P. *Bioorg. Med. Chem.*, 17 (2009), 5106–5116.
- [2] Schwarz, S.; Csuk, R.; Rauter, A. P. *Org. Biomol. Chem.*, 12 (2014), 2446–2456.

N-acetylgalactosamine mimetics: synthesis of potential candidates to block virus infection

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C-type lectins play important roles in both innate and adaptive immune responses. The human macrophage galactose C-type lectin (MGL) is a key physiological receptor expressed on the surface immature dendritic cells (DCs) and macrophages. MGL binds with high affinity to the terminal *N*-acetylgalactosamine (GalNAc) residues, like the Tn antigen (α -GalNAc-Ser/Thr) of mucin-like glycoproteins in a Ca^{2+} -dependent manner. MGL recognizes the mucin-like envelope glycoprotein of filovirus like Ebola, Marburg or Influenza and promotes the virus entry and infectivity [1,2]. Design of MGL inhibitors could help to block the virus entry and represents a new strategy for developing more effective antiviral drugs. Also, a wide range of organic selenides are now known as useful antioxidants, antibiotics and antiviral agents [3,4].

Within this project we have synthesized mimetics of GalNAc, namely phenyl selenogalactosides bearing imide functionality at position 2 aiming at better binders than GalNAc itself towards MGL receptor, therefore competing to the interaction between the MGL and the GP of Ebola or Marburg filovirus. The synthesized molecules will also be tested for interactions with $\text{A}\beta_{1-42}$ toxic small oligomers, and their fibrilization generating neuronal death, associated to the multifactorial Alzheimer's disease, since their structure bears functional groups able to establish π - π interactions and hydrogen bond formation, usually mandatory for binding [5].

Acknowledgements

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References

- [1] Takada, A., Fujioka, K., Tsuiji, M., Morikawa, A., Higashi, N., Ebihara, H., Kobasa, D., Feldmann, H., Irimura, T., Kawaoka, Y., (2004) Human Macrophage C-Type Lectin Specific for Galactose and *N*-Acetylgalactosamine Promotes Filovirus Entry, *J. Virology*, 78, 2943-2947;
- [2] Marcelo F., Garcia-Martin F., Matsushita T., Sardinha J., Coelho H., Oude-Vrielink A., Koller C., André S., Cabrita E. J., Gabius H.-J., Nishimura S.-I., Jiménez-Barbero (2014) J., Cañada F. J., Delineating binding modes of Gal/GalNAc and structural elements of the molecular recognition of tumor-associated mucin glycopeptides by the human macrophage galactose-type lectin, *Chem. Eur. J.* 20, 16147-16155;
- [3] Mamoru, K.; Hideharu, I. Masahiro, H. (1998) *Novel compounds, 1,3-selenazine derivatives, as antibacterial agents against Escherichia coli and Staphylococcus aureus*; *Res. Commun. Mol. Pathol. Pharmacol.*, Volume 101, 179-186;
- [4] Kirsí, J. (1983) *Broad-spectrum antiviral activity of 2-beta-D-ribofuranosylselenazole-4-carboxamide, a new antiviral agent.*; *J. Antimicrob. Agents Chemother.*, Volume 24, 353-361;
- [5] Matos A.M., Macedo M.P., Rauter A.P. (2017) *Bridging type 2 diabetes and Alzheimer's disease: assembling the puzzle pieces in the quest for the molecules with therapeutic and preventive potential.* *Med. Res. Rev* DOI:[10.1002/med.21440](https://doi.org/10.1002/med.21440).

Free copper (II) as an early Alzheimer's disease biomarker

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Free copper (II) is present in high concentration in biological fluids associated with several neurodegenerative diseases. These elevated levels of free copper cause prion protein misfolding, being associated with the onset of several of neurodegenerative disorders, and can thus be used as an early disease biomarker[1]. Copper quelating molecules bearing a fluorescent portion, but also highly soluble in biological fluids, and selective towards copper (II) in respect to other bivalent ions present in these fluids, are an important tool for early Alzheimer's diagnosis [2].

In this work, fluorescent copper quelating molecules were investigated and, in order to improve their solubility in serum and bioavailability, the insertion of a sugar portion, in a negligible part of the molecule in terms of activity and selectivity, was attempted. In addition, making use of the multifunctional capacity of the sugar, a radiolabel will be inserted in the sugar moiety. These radioligands could be employed for PET studies in animal models specific for Alzheimer's disease.

The main molecules investigated were fluorescein derivatives (Fig 1) for their known fluorescent properties, but the conjugation methodologies did not produce good yields, and other fluorescent residues were tested. The results obtained will be presented and discussed.

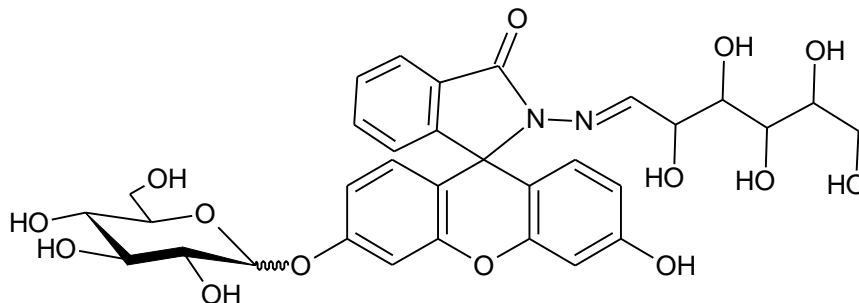


Fig. 1: Schematic representation of main target copper (II) chelating compound.

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João P. Pais acknowledges financial support from FCT through the Ph.D. grant co-sponsored by CIPAN SFRH/BDE/51957/2012.

References

- [1] Kozłowski, H., Luczkowski, M., Remelli, M., & Valensin, D., *Coord. Chem. Rev.*, 256(2012), 2129–2141.
 [2] Squitti, R., & Polimanti, R., *Am J Neurodegener Dis.*, 2(2013), 46-5

Towards the synthesis of purine nucleosides with deoxygenated sugars: Exploratory chemistry of potential selective inhibitors of butyrylcholinesterase

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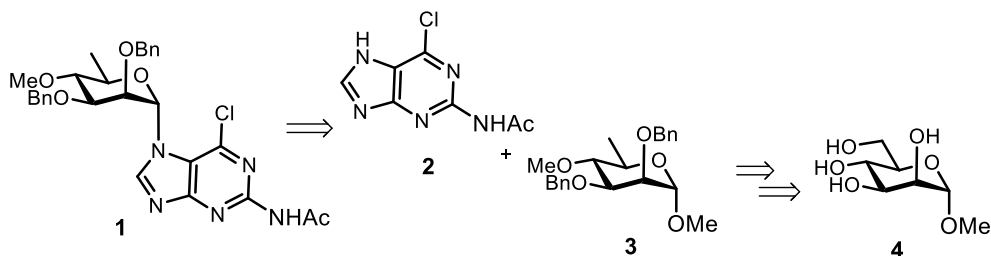
Alzheimer's is a neurodegenerative and incurable disease affecting millions of people around the world. Research has proven that, in advanced stages of this disease, butyrylcholinesterase (BChE) plays an important role as hydrolytic enzyme by destroying acetylcholine. Therefore, the selective inhibition of this enzyme is a matter of interest for the understanding of this multifactorial disease in later disease phases.

Previous work in our group has shown that D-mannosyl purine nucleosides are potent and selective BChE inhibitors, and the presence of benzyl groups on the glycosyl moiety, as well as N⁷ linkage to the purine nucleobase are required for strong BChE inactivation [1,2].

In this work, we present our efforts to synthesize a methyl 6-deoxy mannoside as a new substrate for construction of the purine nucleoside bearing O-benzyl and O-methyl substituents. This structure aims to evaluate the role of sugar substitution and 6-deoxygenation onto the selective inhibition of BChE.

Scheme 1 shows the retrosynthesis of the nucleobase **1**. In this work we describe the reaction steps carried out to transform the methyl mannoside **4** into the corresponding 2,3-di-O-benzyl-6-deoxy-4-O-methyl- α -D-mannopyranoside **3**.

The ultimate goal is to explore the contribution of the residue resulting from **3** in the selective inhibition of butyrylcholinesterase by testing the biological activity of the new purine nucleoside **1**.



Scheme 1. Retrosynthesis of purine nucleoside **1**.

Acknowledgements

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References

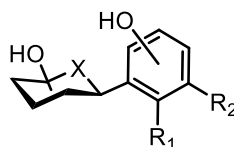
- [1] S. Schwarz, R. Csuk, A. P. Rauter, Microwave-assisted synthesis of novel purine nucleosides as selective cholinesterase inhibitors, *The Royal Society of Chemistry* 2014, 12, 2446–2456
- [2] F. Marcelo, F. V. M. Silva, M. Goulart, J. Justino, P. Sinaÿ, Y. Blériot, A. P. Rauter, Synthesis of novel purine nucleosides towards a selective inhibition of human butyrylcholinesterase, *Bioorganic & Medicinal Chemistry* 2009, 17, 5106–5116

Approaches to polyphenol C-glycosylation towards potential therapeutics for neurodegenerative diseases

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Polyphenols have shown numerous biological activities and health benefits for the treatment of neurodegenerative diseases as Alzheimer's [1] and prion diseases. [2] Both disorders are characterized neuropathologically by extracellular deposits of Abeta and PrP amyloid fibrils, respectively. [3] Previous work in our group has disclosed a C-glycosyl flavonoid, namely 8-β-D-glucopyranosylgenistein (8G), to interact with amyloid oligomers preventing aggregates formation [4]. In this work, 8G scale up optimization was carried out and 8G small analog structures have been synthesised to evaluate the minimum C-glycoside building block necessary for showing therapeutic effect. In addition, we present our efforts in the synthesis of new C-glycosyl polyphenols based on structure A designed to be decorated with different saccharide units and phenol fragments obtained by proper substitution of R₁ and R₂. (Figure 1).



Structure A

Figure 1. Scaffold for the generation of C-Glycosylated polyphenols

Acknowledgements

Support for this work was provided by the European Union's Seventh Framework Programme (FP7-PEOPLE-2013-IAPP, GA 612347)].

References

- [1] Pate, K. M.; Rogers, M.; Reed, J. W.; van der Munnik, N.; Vance, S. Z.; Moss, M. A. Anthoxanthin polyphenols attenuate Aβ oligomer-induced neuronal responses associated with Alzheimer's disease. *Neurosci Ther.* **2017**, *23*, 135-144.
- [2] Rambold A.S.; Miesbauer M.; Olschewski D.; Seidel R.; Riemer C.; Smale L.; Brumm L.; Levy. M.; Gazit E.; Oesterhelt D.; Baier M.; Becker C. F.W.; Engelhard M.; Winklhofer K.F.; Tatzelt J. Green tea extracts interfere with the stress-protective activity of PrPC and the formation of PrPSc. *J. Neurochem* **2008**, *107*, 218-229.
- [3] Eikelenboom P.; Bate C.; Van Gool W. A.; Hoozemans J.J.; Rozemuller J.M.; Veerhuis R.; Williams A.; Neuroinflammation in Alzheimer's disease and prion disease. *Glia.* **2002**, *40*, 232-239.
- [4] Jesus, A.R.; Dias, C.; Matos, A.M.; de Almeida, R.; Viana, A.S.; Marcelo, F.; Ribeiro, R.T.; Macedo, M.P.; Airoidi, C.; Nicotra, F.; Martins, A.; Cabrita, E. J.; Jiménez-Barbero, J.; Rauter, A.P. Exploiting the Therapeutic Potential of 8-β-D-Glucopyranosylgenistein: Synthesis, Antidiabetic Activity, and Molecular Interaction with Islet Amyloid Polypeptide and Amyloid β-Peptide (1-42). *J. Med.Chem.* **2014**, *57*, 9463-9472.

Why is INH-C10 more active than INH against *Mycobacterium tuberculosis*? The story so far...

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Tuberculosis (TB) was one of the top 10 causes of death worldwide in 2015. Its causative agent, *Mycobacterium tuberculosis* (*Mtb*), has become increasingly resistant to the most effective 1st line antitubercular drugs, in particular to isoniazid, INH. New INH-based compounds have been proposed to circumvent *Mtb* resistance and therefore improve drug activity. To become active against *Mtb*, INH needs to be first activated by the catalase-peroxidase KatG enzyme. Among the most promising compounds, INH-C₁₀, a new acylated INH derivative was shown to have a similar activity to INH against the *wt* strain but an activity six times higher against a *katG* S315T mutated strain [1]. We have observed that this increased activity could not be exclusively assigned to changes in the steric environment of the access channel to the heme site, since they were not found to be significant [2].

In an effort to understand the twists of INH and INH-C₁₀ in KatGs, crystallographic and kinetic studies were undertaken. Having seen no evidence of binding in the soaking experiments with INH-C₁₀ in the enzyme, kinetic assays were carried out to assess the amount of free radicals produced in the first step of the reaction of INH-C₁₀ in KatG. Results confirmed that, in *wt* KatG, this reaction was slower than that of INH, but that rate constants were similar when the S315T mutation was tested. Also, in the S315T mutant, INH-C₁₀ produced radicals faster than in the native form. We have also observed that radical formation in INH-C_x derivatives was thermodynamically less favoured (deactivated) than in INH, independently of the alkyl chain size. Recently, we also measured MIC values on two additional mutated strains, one in the same residue, but with a slightly bulkier side chain (S315N), and another one farther away from the heme pocket (D735A), to serve as a control, since such mutation should not influence the compound's activity either by steric or electrostatic effects [3]. Overall, results obtained so far suggest that, despite its smaller reactivity, the hydrophobic nature of INH-C₁₀ may promote a better trafficking through the *Mtb* membrane, leading to higher concentrations in the vicinity of KatG, thus resulting in lower MIC values.

Acknowledgements

Support for this work was provided by FCT through UID/MULTI/00612/2013.

References

- [1] F. Martins, S. Santos, C. Ventura, R. Elvas-Leitão, L. Santos, S. Vitorino, M. Reis, V. Miranda, *et al.*, *Eur. J. Med. Chem.* 81 (2014) 119-138.
- [2] V.H. Teixeira, C. Ventura, R. Leitão, C. Rafols, E. Bosch, F. Martins, M. Machuqueiro, *Mol. Pharm.* 12 (2015) 898-909.
- [3] D. Vila-Viçosa, B.L. Victor, J. Ramos, M. Viveiros, P.C. Loewen, F. Martins, M. Machuqueiro (2017) *to be submitted*.

Physicochemical and structural characterization of choline-based eutectic solvents

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The study of eutectic solvents proposed as new "green" solvents for application in chemical processes, including extraction and synthetic procedures, has been the object of many studies in recent years. Eutectic solvents are mixtures of compounds which have a melting point much lower than its individual components due, mainly, to the formation of strong intermolecular forces. These solvents are easier to prepare with higher purity and at a lower cost than ILs, and, in general, have a low toxicity. [1, 2].

However, although these solvents have become very popular due to a wide range of practical applications, there is still much work to be done, especially regarding their accurate physicochemical characterization.

In this work we have studied a set of choline chloride (ChCl)/ ethylene glycol (Eg) mixtures. These mixtures were prepared by weight in a glove box under N₂ atmosphere, and their water content was assessed by Karl-Fisher titration (Mettler Toledo Easy KfV). Their characterization was achieved in terms of various properties, studied at several temperatures, namely electrical conductivity which was determined with a Wayne Kerr B905 conductance bridge, and density and surface tension determined with an automatic Kruss K100MK2 tensiometer, using the Wilhelmy plate method. Conductivities of all mixtures increase with temperature, as expected. However the 1:2 mixture shows a peculiar behaviour when compared with all other mixtures. Both density and surface tension decrease with the increase in temperature and mole fraction of ethylene glycol, with the exception again of the 1:2 mixture which, at lower temperatures, shows a lower density than the other studied compositions. These results will be further discussed.

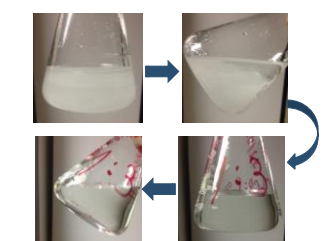


Figure 1- Preparation of eutectic solvents: top images – before heating; bottom images – final result after 2h of heating.

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References

- [1] E.L Smith, A.P Abbott, K.S Ryder, *Chem. Rev.* 114 (2014) 11060-11082.
 [2] Y. Daia, J. Spronsenb, G-J. Witkampb, R. Verpoortea, Y. H. Choia, *Anal. Chim. Acta* 766 (2013) 61-68.

Ultra-trace analysis of priority compounds in real matrices by hollow fiber microextraction (HF μ E)

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Modern sample preparation approaches aim the miniaturization of the analytical devices and easy manipulation, as well as small sample volumes and the reduction or absence of the usage of toxic organic solvents, in agreement with the green analytical chemistry principles. In 2010, bar adsorptive microextraction (BA μ E) was introduced as a novel sample enrichment technique, which operates under the floating sampling technology [1, 2]. This analytical approach presents several advantages, especially for the analysis of the most polar compounds and regarding the analytical devices used, they are easily lab made with simple and cheap materials. Furthermore, the most appropriate sorbent phases can be tuned according with the chemical characteristics of the target analytes.

In the present contribution, another enrichment concept is proposed, hollow fiber microextraction (HF μ E), which consists in the application of hollow fibers having appropriate dimensions (1.0 cm length, 1 mm inner diameter, 0.2 μ m pore size), loaded with convenient organic solvents immiscible with water. Like BA μ E, the microextraction stage also operates under the floating sampling technology and the back-extraction is performed in a 'only single liquid desorption step' with few microliters of an organic solvent inside a common glass vial insert. This approach is compatible with the auto-sampler systems currently available at the analytical labs and, therefore, can be dedicated to routine work. The performance of this novel methodology was evaluated using eighteen polycyclic aromatic hydrocarbons (PAHs) as model compounds, presenting recovery yields ranging from 14.5 \pm 8.2 % to 90.4 \pm 8.4 % and limits of detection at the ultra-trace level (2.5 - 6.0 ng L⁻¹). The proposed method was successfully applied for the analysis of the PAHs in superficial water, wastewater, soil, tea and fish liver samples, being an eco-user-friendly sorption-based microextraction alternative for ultra-trace analysis.

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References

- [1] N.R. Neng, A.R.M. Silva, J.M.F. Nogueira, *J. Chromatogr. A* 1217, 7303 (2010).
- [2] J.M.F. Nogueira, *Anal. Chim. Acta* 757, 1 (2012).

Reductive Deoxygenation of Aryl Sulfoxides catalyzed by Mo@Biochar

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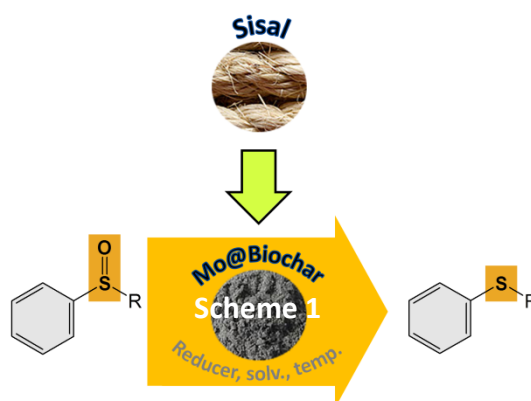
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The deoxygenation of sulfoxides is rather important from both the synthetic and the biological point of view, owing to their potential as intermediates in a variety of synthetic transformations, mainly as chiral auxiliaries for the synthesis of biologically active compounds [1]. Thus there is a continuous interest in developing new deoxygenation methods [2].

The current work aims at obtaining two new Mo@biochar materials to be tested in sulfoxides deoxygenation. The biochar support was obtained by acidic carbonization of sisal residues. The material has an acid surface, as demonstrated by the pH_{pzc} values (≈ 2), allowing it to be considered as support for two oxomolybdenum(VI) compounds, MoO₂Cl₂·2H₂O and NaMoO₄·2H₂O. The immobilized catalysts were characterized by IR spectroscopy, elemental analysis, inductively coupled plasma mass spectrometry (ICP-MS), solid state NMR, and SEM, and evaluated for their catalytic activity in sulfoxides reduction (Scheme 1).

The Mo@biochar materials acted as efficient catalysts in the heterogeneous reduction of aryl sulfoxides to the corresponding sulfides in the presence of a reducer agent, such as phenylsilane. The reaction parameters were investigated (e.g. type and loading of catalyst, temperature, solvent, reductant, acid promoter (HCl), and substrate), and total conversion into products was achieved after 4 h. This use of a carbon recycled materials as a support, besides being a clever and environmentally sustainable idea, proved to be a good strategy to develop new heterogeneous catalysts.



Acknowledgements

Support for this work was provided by FCT through UID/MULTI/00612/2013 and PEst-OE/QUI/UI0612/2013.

References

- [1] Sulfur Centered Reactive Intermediates in Chemistry and Biology, (Eds.: C. Chatgililoglu, K. D. Asmus), Nato ASI series, Plenum Press, NY, 1990.
- [2] a) A.C. Fernandes, J.A. Fernandes, C.C. Romão, L.F. Veiros, M.J. Calhorda, *Organometallics*, 29 (2010) 5517–5525, b) T.A. Fernandes, A.C. Fernandes, *ChemCatChem*, 7 (2015) 3503–3507.

Synthesis and applications of molybdenum(II) organometallic phenanthroline complexes

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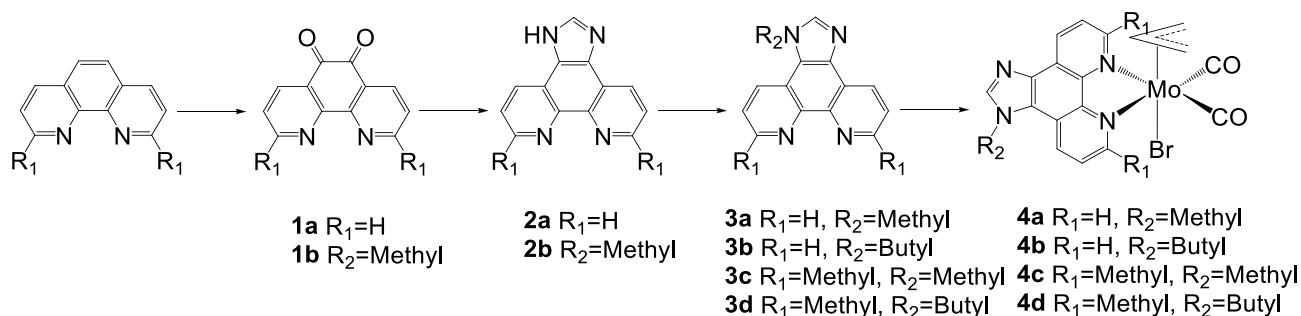
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A set of phenanthroline derivatives was synthesized from 1,10-phenanthroline and 2,9-dimethyl-1,10-phenanthroline as shown in Scheme 1.[1] These ligands reacted in inert atmosphere and at room temperature with the precursor complex $[\text{Mo}(\eta^3\text{-C}_3\text{H}_5)\text{Br}(\text{CO})_2(\text{CH}_3\text{CN})_2]$ resulting in the formation of the new family of molybdenum(II) organometallic complexes $[\text{Mo}(\eta^3\text{-C}_3\text{H}_5)\text{Br}(\text{CO})_2(1\text{-R}_1\text{-imidazo}[4,5\text{-f}]\text{-R}_2\text{-}[1,10]\text{phenanthroline})]$ (**4**, R_1 =butyl, methyl, R_2 =dimethyl, H).[2] All the ligands and complexes prepared were characterized by FTIR, ^1H and ^{13}C NMR. The new complexes prepared were used as homogeneous catalysts for the oxidation of *cis*-cyclooctene, styrene, *cis*-3-hexen-1-ol, *trans*-2-hexen-1-ol, *R*(+)-limonene, geraniol and 1-octene with TBHP (*tert*-butyl hydroperoxide) as the oxidant. The data were collected through GCMS. The effects of reaction time, temperature and amount of catalysts are discussed.



Scheme 1 Synthesis of the molybdenum organometallic complexes **4**.

Acknowledgements

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References

- [1] A. A. Webster, S. K. K. Prasad, J. M. Hodgkiss, J. O. Hoberg, Dalton Trans. 44 (2015) 3728-3736.
 [2] M. S. Saraiva, S. Quintal, F. C.M. Portugal, T. A. Lopes, V. Félix, J. M.F. Nogueira, M. Meireles, M. G.B. Drew, M. J. Calhorda, J. Organomet. Chem. 693 (2008) 3411–3418.

Molybdenum Complexes with 2,2'-Dipyridylamine Derivatives as Catalysts in Oxidation Reactions

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New molybdenum complexes from the family $[\text{MoBr}(\eta^3\text{-C}_3\text{H}_5)(\text{CO})_2(\text{L})]$ were synthesised by reaction of the precursor $[\text{MoBr}(\eta^3\text{-C}_3\text{H}_5)(\text{CO})_2(\text{CH}_3\text{CN})_2]$ with a family of bidentate ligands derived from 2,2'-dipyridylamine, as shown in Figure 1. All new compounds prepared were characterized by FTIR, NMR of ^1H e ^{13}C as well as elemental analysis.

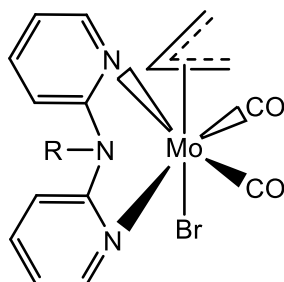


Figure 1. Molybdenum complexes from 2,2'-ddipyridylamine derivatives.

All complexes were tested as homogeneous pre-catalysts in the oxidation of olefins and sulfides, such as *cis*-cyclooctene, styrene, *cis*-3-hexen-1-ol, *trans*-2-hexen-1-ol, geraniol, methylphenylsulfide and diphenylsulfide, using hydrogen peroxide, tert-butyl hydroperoxide or cumene hydroperoxide as the oxidant. These studies were carried out to determine the influence of the length of the alkyl chains of the ligands on the complexes catalytic activity.

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References

- [1] M.S. Saraiva, S. Quintal, F.M.C. Portugal, T.A. Lopes, V. Félix, J.M.F. Nogueira, M. Meireles, M.G.B. Drew, M.J. Calhorda, *Journal of Organometallic Chemistry* 693 (2008) 3411–3418.
- [2] M.J. Rauterkus, S. Fakh, C. Mock, I. Puscasu, B. Krebs, *Inorganica Chimica Acta* 350 (2003) 355-365.

Hierarchical zeolites through surfactant assisted method as environmentally friendly catalysts for Friedel-Crafts reactions

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Friedel-Crafts acylation reactions are one of the most important routes for the synthesis of aromatic ketones that are intermediates for producing fine and speciality chemicals. Several studies show that zeolites are promising catalyst in this reactions as an alternative for homogeneous catalysts such as AlCl_3 and FeCl_3 that are harmful to the environment. However, the microporous nature of zeolites limits its application, especially when larger molecules are involved. To overcome this limitation efforts have been made to incorporate mesopores in zeolites, thus creating hierarchical materials.

In this study Y zeolite (FAU structure) was submitted to an alkaline treatment, assisted by surfactant molecules, under autogenous pressure. The effect of the experimental parameters such as: temperature, duration of the treatment, pH of the reaction mixture, base/surfactant ratio, type of base and surfactant, was investigated in order to obtain optimized catalysts. The effect of the treatments on the crystallinity was evaluated by X-ray powder diffraction, the textural characterization was made by N_2 adsorption isotherms at -196°C and the morphology of the crystals was studied by TEM and SEM.

The catalytic behaviour was investigated in Friedel-Crafts acylation of heteroaromatics using furan as substrate and acetic anhydride as acylating agent (molar ratio 1:5) at 60°C . Samples of the reaction mixture was periodically separated from the catalyst and analysed by GC to follow conversion and product yield as a function of time. Preliminary results show that optimized hierarchical Y is a more efficient catalyst since high product yield is obtained at lower reaction times. Langmuir-Hinshelwood kinetic model modified according to [2] allowed to calculate kinetic parameters showing that higher rate constant were obtained. These results indicate that the mesoporosity generated as a consequence of the surfactant assisted alkaline treatment reduces diffusional limitations and enhances the access to the acid sites of the catalyst.

Acknowledgements

Support for this work was provided by FCT through UID/MULTI/00612/2013 and PEst-OE/QUI/UI0612/2013.

References

- [1] J. Garcia-Martinez, M. Johnson, J. Valla, K. H. Li, J.Y. Ying, *Catal Sci Technol*, 2(5) (2012) 987-994.
- [2] R. Aleixo, R. Elvas-Leitão, F. Martins, A.P. Carvalho, A. Brigas, A. Martins, N. Nunes *J. Mol. Catal.* 434 (2017) 175-183.

Valorization of *Salvia sclareoides*- a contribution to the development of a new dietary supplement

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Salvia sclareoides is a plant of the Portuguese spontaneous vegetation that has demonstrated a potent cholinergic action and the ability to prevent amyloid aggregation. Aiming at the development of new food supplements based on this plant and components, it is necessary to investigate whether this species, when planted, has the same properties as the species harvested in the field. In this communication, we describe extracts preparation from plant provided by the company ERVITAL, and in collaboration with the Instituto Superior de Agronomia (ISA), the incorporation of the dry plant in sweet and salty cookies was investigated. The results obtained will be presented and discussed.

Towards the synthesis of polyphenols containing deoxy sugars: a strategy against diabetes and Alzheimer's diseases

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Polyphenols have shown therapeutic efficacy on diabetes neurodegenerative diseases such as Alzheimer's by suppression of Islet amyloid peptide IAPP and β -amyloid fibrils avoiding their cytotoxicity [1][2]. Rauter et al has synthesized the major component of Genista tenera, 8- β -D-glucopyranosylgenistein (8G), finding its therapeutic potential in amyloid events characteristic of both diseases and its antidiabetic properties have been demonstrated [3]. The aim of this work is the synthesis of a new flavonoid analog containing 6-deoxyglucose, (compound 1, Figure 1), as saccharide residue. This less polar saccharide fragment could facilitate 8G permeability properties to cross the brain barrier. Compound 1 will be subjected to biological testing for type 2 diabetes and Alzheimer's disease.

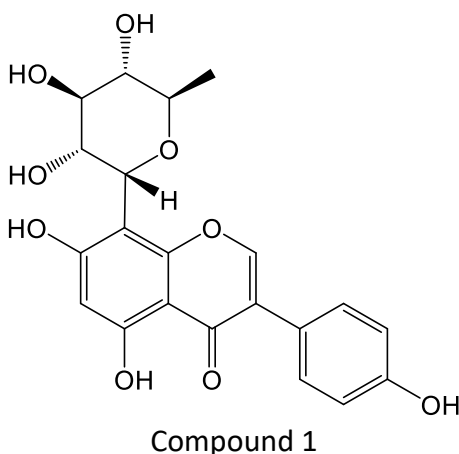


Figure 6. Structure of 8-(6-deoxy-b-D-glucopyranosylgenistein) 1

References

- [1] Chieti, F.; Dobson, C. M. Protein misfolding, functional amyloid, and human disease. *Annu. Rev. Biochem.* 2006, 75, 333-366.
- [2] Ono, K.; Hasegawa, K.; Naiki, H.; Yamada, M.; Curcumin has potent anti-amyloidogenic effects for Alzheimer's β -amyloid fibrils in vitro. *J. Neurosci. Res.* 2004, 75, 742-750.
- [3] Jesus, A.R.; Dias, C.; Matos, A.M.; de Almeida, R.; Viana, A.S.; Marcelo, F.; Ribeiro, R.T.; Macedo, M.P.; Airoldi, C.; Nicotra, F.; Martins, A.; Cabrita, E. J.; Jiménez-Barbero, J.; Rauter, A.P. Exploiting the Therapeutic Potential of 8- β -D-Glucopyranosylgenistein: Synthesis, Antidiabetic Activity, and Molecular Interaction with Islet Amyloid Polypeptide and Amyloid β -Peptide (1-42). *J. Med.Chem.* 2014, 57, 9463-9472.

Sugar Derived Carbon Spheres as Esterification Catalysts

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Carbon spheres have been used in different research fields, namely as supercapacitors, adsorbents, catalyst supports, and also as catalysts. [1] The most common synthesis strategy involves hydrothermal treatments and as carbon precursors, although various renewable biomasses have been explored, a great number of studies are based on sugar derived materials. [2]

In the studies that are being developed in our group, glucose, fructose and sucrose derived carbon spheres obtained by hydrothermal treatment at 190 °C were tested as catalysts for the esterification of acetic acid with 1-butanol. The materials have acidic surface properties, demonstrated by the presence of carboxylic acids and alcohols, estimated by the Bohem titration, and pH_{PZC} values (ca. 2.0). Besides the as synthesized materials also samples treated with concentrated H_2SO_4 were assayed. The introduction of sulfonic groups has a positive effect on the reaction yield which in the more favourable case reaches 95 % after 6 h of reaction. The results obtained so far point out the potentialities of these materials as alternatives to the commonly used strong inorganic acids.

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References

- [1] M. Wu, Y. Wang, D. Wang, M. Tan, P. Li, W. Wu, N. Tsubaki, J. Porous Mater. 23 (2016) 263-271.
- [2] R. Demir-Cakan, N. Baccile, M. Antonietti, M.M. Titirici, Chem. Mater. 21 (2009) 484-490.

Salphen inspired complexes and materials for CO₂ reduction

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The versatility of salen-type (salen = N,N – bis(salicylidene)ethylenediamine) complexes has been shown, among others, in their extensive applications in electrochemistry owing to their electrochromic,[1] sensor[2] and catalytic[3] properties. These features are complemented by their easy electropolymerisation without significant modifications of the metal environment.[4] This reaction requires that there are no substituents at the phenolate para position and the mechanism involves oxidation of the metal coordinated to the unsubstituted salphen, followed by C-C coupling. DFT calculations show the high spin density of the oxidised complex at those positions. Mono and binuclear complexes were synthesised being the later prepared by a template procedure. A template synthesis allowed the preparation of homobinuclear complexes and a newly developed stepwise procedure led to heterobinuclear complexes, with two distinct environments for the metal centres. [5,6] The compounds were characterised by FTIR spectroscopy, elemental analyses and HR-mass spectrometry. Studies with these complexes were performed on the homogeneous and heterogeneous conversion of CO₂. Modified electrodes based on metallopolymers and nafion were produced and characterised by cyclic voltammetry and the study of the morphologic properties performed by atomic force microscopy (AFM). For the CO₂ reduction, bulk electrolysis experiments were performed and gas chromatography with thermal conductivity detector was used to detect and quantify the reduction products.

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References

- [1] D. T. Whipple, P. J. A. Kenis, *The Journal of Physical Chemistry Letters*, 1 (2010) 3451.
- [2] G. W. Coates, D. R. Moore, *Angew. Chem. Int. Ed.*, 43 (2004) 6618.
- [3] J. Meléndez, M. North, R. Pasquale, *Eur. J. Inor. Chem.*, 21 (2007) 3323.
- [4] J. Qiao, Yuyu Liu, F. Hong, J. Zhang, *Chem.Soc.Rev.*, 43 (2014) 631-675.
- [5] S. Realista, A. S. Viana, B. de P. Cardoso, A. M. do Rego, P. D. Vaz, A. I. Melato, P. N. Martinho and M. J. Calhorda, *RSC Adv.*, 5 (2015) 39495.
- [6] S. Realista, P. Ramgi, Bernardo de P. Cardoso, A. I. Metalo, M. J. Calhorda, P. N. Martinho, *Dalton Trans.*, 45 (2016) 14725.

Sugar metabolism in *Metschnikowia pulcherrima* yeasts during fermentation of synthetic must

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Climate change has impacted winemaking industry by increasing sugar content in grapes that in turn lead to high-ethanol content wines [1]. In an attempt to control ethanol levels and avoid their continued growth tendency, non-conventional yeast strains can be explored as alternative fermenting organisms. The current conventional yeasts to ferment musts to wine are *Saccharomyces cerevisiae* strains, which high-fermentative capacity translates in a virtual capacity of metabolizing all present sugars into ethanol giving them very high ethanol yields [2]. Due to this fact, a higher sugar content in grape must will produce wine products with higher ethanol levels. A strategy to lower ethanol yields in wine while tackling the fermentation process, is the use of alternative fermenting microorganisms (non-*Saccharomyces* or non-conventional yeasts) [3,4]. That is the case of *Metschnikowia pulcherrima*, a yeast naturally found in grape's microflora with a key role in production of active aroma compounds in wine, with lower fermentative power, but which metabolism is yet to be studied [5,6].

In this study, a strain of *Metschnikowia pulcherrima* was grown in synthetic must media under two different sugar concentrations and had its metabolome fingerprinted by Fourier Transform Ion Cyclotron Resonance Mass Spectrometry (FT-ICR-MS). Cells and culture medium were collected, fingerprinted and compared, in a time-course experiment.

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References

- [1] B.G. Coombe, (1987). "Distribution of Solutes within the Developing Grape Berry in Relation to Its Morphology." *Am J Enol Vitic* 38(2): 120.
- [2] G.H. Fleet, S. Lafon-Lafourcade and P. Ribéreau-Gayon (1984). "Evolution of Yeasts and Lactic Acid Bacteria During Fermentation and Storage of Bordeaux Wines." *App Environ Microbiol* 48(5): 1034-1038.
- [3] van Leeuwen, C. and P. Darriet (2016). "The Impact of Climate Change on Viticulture and Wine Quality." *Journal of Wine Economics* 11(1): 150-167.
- [4] G.H. Fleet, (2003). "Yeast interactions and wine flavour." *Int J Food Microbiol* 86(1-2): 11-22.
- [5] M. Ciani, P. Morales, et al. (2016). "Non-conventional Yeast Species for Lowering Ethanol Content of Wines." *Front Microbiol* 7: 642.
- [6] P. Romano, et al. (1997). "Secondary products formation as a tool for discriminating non-*Saccharomyces* wine strains. Strain diversity in non-*Saccharomyces* wine yeasts." *Antonie Van Leeuwenhoek* 71(3): 239-242.

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