ISMEC 2024

International Symposium on Thermodynamics of Metal Complexes

ACTA OF THE INTERNATIONAL SYMPOSIA ON METAL COMPLEXES

June 10th to 13th
Nice, France

ISMEC 2024

International Symposium on Thermodynamics of Metal Complexes

UNIVERSITÉ CÔTE D'AZUR

Institut de Chimie de Nice

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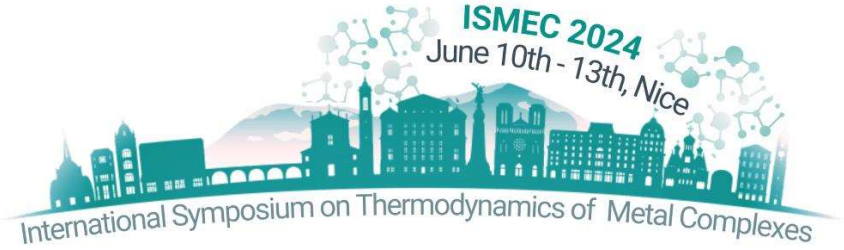

Acta of the International Symposium on Thermodynamics of Metal Complexes

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ISMEC GROUP SERIES
VOLUME: 13
YEAR: 2024
SYMPOSIUM EDITION: XXXIV
https://www.ismecgroup.org/ismec-acta/

ISSN: 2239-2459

UNIVERSITÉ CÔTE D'AZUR

Institut de Chimie de Nice

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I S Me C
International Group for the Thermodynamics of Complexes

The **Acta of the International Symposia on Metal Complexes** (ISSN: 2239-2459) are published annually online by the **ISMEC Group**.

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Foreword

On behalf of the International Scientific Committee and the Local Organizing Committee, it is our great pleasure to welcome you to Nice for the 2024 edition of the International Symposium on Thermodynamics of Metal Complexes (ISMEC 2024).

Since its inception in 1972, ISMEC has grown from its roots as the annual meeting of the Italian "Gruppo di Termodinamica dei Complessi" into a globally recognized congress. Each year, researchers from around the world come together to share their latest findings, foster collaboration, and promote the advancement of knowledge in the field of thermodynamics of metal complexes.

ISMEC 2024 continues this proud tradition by offering a scientific program that highlights the most recent advances in the thermodynamics and kinetics of coordination processes. Our symposium will explore a wide range of topics within analytical, biomedical, environmental, inorganic, and physical chemistry. Main topics include:

- Complexation thermodynamics and kinetics
- Solution equilibria and coordination chemistry
- Complexation processes in supramolecular chemistry
- Metal-based reactivity and catalysis
- Metal-complex interactions with biomolecules
- Metals in diseases: transport, homeostasis, and toxicity
- Metal-based drugs: diagnosis and therapy
- Metal complexes of environmental and biological interests
- Nanostructured metal complexes
- Analytical methods and sensors based on complexation equilibria
- Computer methods for equilibrium analysis

These topics not only underscore the diversity and depth of the chemistry of metal complexes, but also reflect the innovative research being conducted by our community. ISMEC 2024 will feature a series of plenary lectures, oral presentations and poster sessions, providing ample opportunities for participants to exchange ideas, present their research, and form new collaborations.

We are confident that ISMEC 2024 will be a stimulating and rewarding experience for all attendees. We encourage you to engage fully with the program, take advantage of the networking opportunities and enjoy the vibrant city of Nice.

Welcome to ISMEC 2024! We look forward to your contributions and to a fruitful and inspiring conference.

Sincerely,

Maria Rosa Beccia
Chair of the Organizing Committee of ISMEC 2024

Montserrat López-Mesas
President of the ISMEC Group

Nice, June 2024

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PROGRAM

	Monday 10th	Tuesday 11th	Wednesday 12th	Thursday 13th	
09:00		Plenary Lecture 2 *Xavier Gaona*	Plenary Lecture 3 *Stephen Butler*	Plenary Lecture 4 *Christelle Hureau*	09:00
10:00		Session 2 - Experimental and computer methods for complexation equilibria analysis *Chair: Demetrio Milea*	Session 3 - Analytical methods and sensors based on complexation equilibria *Chair: Vieri Fusi*	Session 5 - Metal-based drugs: diagnosis and therapy *Chair: Tarita Biver*	10:00
10:45		Coffee break	Coffee break	Coffee break	10:45
11:15		Keynote Lecture 2 *Philippe Guilbaud*	Keynote Lecture 3 *Eleonora Macedi*	Keynote Lecture 4 *Trinidad Arcos Lopez*	11:15
11:45		Session 2 - Experimental and computer methods for complexation equilibria analysis *Chair: Silvia Berto*	Session 4 - Supramolecular chemistry and nanostructured metal complexes *Chair: Enrique Garcia- España*	Session 5 - Metal-based drugs: diagnosis and therapy *Chair: Gaëlle Creff*	11:45
12:30		Lunch	Lunch	Lunch	12:30
13:00	Registration				13:00
14:00		ISMEC group meeting	Social Event Visit of Chagall Museum	Keynote Lecture 5 *Jalila Simaan*	14:00
14:30				Session 6 - Metal-complex interactions with biomolecules *Chair: Magdalena Rowińska-Żyrek*	14:30
15:00	Opening Ceremony	Session 2 - Experimental and computer methods for complexation equilibria analysis *Chair: Marilena Tolazzi*			15:00
15:15	Plenary Lecture 1 *Montserrat Filella*				15:15
15:45				Book presentation - *M. Meyer & D.M. Milea*	15:45
16:00		Coffee break		Coffee break	16:00
16:15					16:15
16:30	Session 1 - Metal complexes of environmental and biological interest *Chair: Eva Enyedy & Alicia Dominguez Martin*	Poster session		Pulidori Award *Maurizio Remelli - Lisa Rita Magnaghi*	16:30
17:00				ISMEC 2025 & Closing Ceremony	17:00
17:30	Keynote Lecture 1 *Maya Engel*		Free time		17:30
18:00	Welcome party				18:00
19:30			Banquet Negresco Hotel		19:30
20:00					20:00

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	Chair: Vieri Fusi		
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17:30	Free time		
19:30	**Banquet**	**Negresco Hotel**	
00:00	End of day 3		

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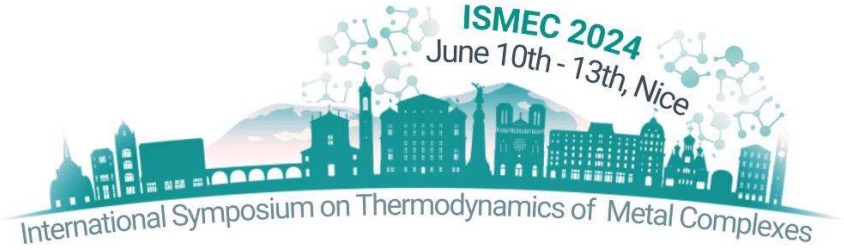
Plenary Lectures



Germanium in aqueous solution, a nice example of the intricacies of the chemistry of hydrolysed chemical elements

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Germanium (Ge) is a chemical element in group 14 of the periodic table whose economic importance and use is growing due to its critical technological applications in polymerisation catalysis, infrared optics and fibre optic systems. Germanium, although relatively little studied compared to other chemical elements such as lead, mercury or arsenic in terms of environmental and toxicological aspects, had already received attention in certain scientific communities in the past, in particular in oceanography and geochemistry. In both cases because of its similarity to silicon: in the first case because it is taken up by diatoms and has been proposed for use in paleoclimatic studies [1] and, in the second, because it provides a tool for studying the weathering of silicates [2].

The only stable oxidation state of germanium in aqueous solution is IV; the element exists as the neutral species $Ge(OH)_4$ over a wide pH range. Germanium is also present in natural systems as monomethyl and dimethyl Ge.

Despite countless rather debatable claims and publications on this subject in the recent past (e.g. the book *Miracle Cure: Organic Germanium* [3]), Ge has no proven biological function in any known organism, and no beneficial pharmacological effects associated with the ingestion of Ge compounds are scientifically recognised. It is important to note the complete misunderstanding of what is meant by "organic germanium" that plagues the literature relating to the element's magical properties.

In this communication, our recent work on germanium [4–8], both in laboratory experiments and in environmental systems, will be presented and discussed. It will be shown that only a thorough understanding of the behaviour of an element in solution can allow us to interpret field results and to critically evaluate the analytical methods used to obtain them.

In particular, the following will be discussed:

- the results of our recent study in which equilibrium constants have been determined for Ge(IV) complexes with about 50 low molecular weight organic ligands, mainly bidentate oxygen and/or nitrogen donors,
- the surprising inertness of some systems such as germanium poly(aminocarboxylates), which makes them intractable by conventional continuous potentiometric titrations,
- the first results on the aqueous equilibria of methylated germanium species,
- the interpretation of speciation measurements in lakes of contrasting physico-chemical characteristics in the light of the above results.

References:

[1] R.A. Mortlock, C.D. Charles, P.N. Froelich, M. Zibello, J. Saltzman, L.D. Burckle, J.D. Hays, *Nature* **1991**, 351, 220–223. doi:10.1038/351220a0.

[2] V.M. Goldschmidt, *Naturwissenschaften* **1926**, 14, 295–297. doi:10.1007/BF01503585.

[3] A. Kazuhiko, *Miracle Cure. Organic Germanium*. Japan Publications: Tokyo, **1980**.

[4] M. Biver, M. Filella, *Monatsh. Chem*. **2018**, 149, 461–465. doi:10.1007/s00706-017-2131-5.

[5] A. García-Figueroa, M. Filella, T. Matoušek, *Talanta* **2021**, 225, 121972. doi:10.1016/j.talanta.2020.121972.

[6] M. Filella, T. Matoušek, *Appl. Geochem.* **2022**, 143, 105352. doi:10.1016/j.apgeochem.2022.105352

[7] M. Filella, P.M. May, *Appl. Geochem.* **2023**, 155, 105631. doi:10.1016/j.apgeochem.2023.105631

[8] M. Biver, M. Filella, *Inorg. Chem.* **2024**, 63, 2470–2485. doi:10.1021/acs.inorgchem.3c03640.

Aquatic chemistry and thermodynamics of radionuclides: applications to repository science and environmental studies

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Safety concepts regarding the disposal of nuclear waste in underground repositories generally rely on a combination of engineered and geological barriers that minimize the potential release of radionuclides from the containment-providing rock zone and transport through the biosphere. The presence of water (*e.g.*, groundwater and pore water of repository rocks), however, can alter the engineered barrier system, dissolve radionuclides, and facilitate radionuclide transport that, over millennia, may allow small fractions of water-soluble radionuclides to permeate to the biosphere. Thus, while barrier systems aim to prevent or hinder water from contacting the waste, the possible intrusion of aqueous solutions must be considered for several safety case scenarios impacted by the long-term evolution of a repository.

Solubility and sorption phenomena arise as important processes controlling the chemical behavior of radionuclides and other key elements relevant to such repositories and their safety assessment. For many radionuclides, solubility limits are reached only after release from the disposed waste products close to the disposal locations, where the expected maximal concentrations are highest. It is then often the solubility of a secondary phase, precipitated after the dissolution of a primary phase in the waste matrix, that controls the maximum transportable radionuclide concentration close to the disposal location. Complexation with inorganic and organic ligands present in the waste, in the technical barriers or in the intruding groundwater may also contribute to radionuclide mobilization.

In the context of nuclear waste disposal, actinides represent the main contributors to the radiotoxic inventory in a repository in the long term. Because of their specific electronic configuration, several oxidation states of actinides (+III to +VII) can exist in aqueous solution. This imposes a differential chemical behaviour as a function of the boundary redox conditions. Beyond the actinides, an accurate description of the aquatic chemistry of fission (*e.g.*, ^{99}Tc, ^{79}Se, ^{93}Zr, ^{129}I) and activation (*e.g.*, ^{63}Ni, ^{94}Nb) products is also relevant in specific repository concepts, involving both high level (HLW) and low and intermediate level (L/ILW) radioactive wastes. Moreover, research in the context of repository science extends beyond the radionuclides, for instance including chemotoxic elements expected in the repository (*e.g.*, Be) or key major elements like Fe, which is massively present in the repository (e.g., as

container material, for construction purposes, etc.) and will strongly impact the redox boundary conditions.

In this contribution, examples on recent studies at KIT–INE on the radionuclide solubility, complexation and thermodynamic description will be presented, including actinides (^{242}Pu, ^{237}Np), fission and activation products (^{99}Tc, ^{95,93}Nb) and chemotoxic elements (^{9}Be). In connection with these experimental studies, this contribution will make the link with the comprehensive reviews dedicated to the aquatic chemistry and thermodynamics of radionuclides and other elements of relevance in the context of nuclear waste disposal, a series of reference volumes developed within the Thermochemistry Database project of the Nuclear Energy Agency (NEA-TDB) of the OECD (*e.g.*, [1-3]). These critical reviews summarize the very significant progress achieved in this field within the last decades, whilst highlighting data gaps and most relevant limitations in the existing thermodynamic models.

Acknowledgements: *Some of the studies in this contribution were partly funded by SKB (Sweden) and ONDRAF-NIRAS (Belgium). The research leading to some of these results received funding from the European Union's European Atomic Energy Community's (Euratom) Horizon 2020 Programme (NFRP-2014/2015) under grant agreement, 662147—Cebama, and by the German Federal Ministry of Economics and Technology (BMWi) under the project of VESPA.*

References:

[1] I. Grenthe, J. Fuger, R.J.M. Konings, R.J. Lemire, A.B. Muller, C. Nguyen-Trung, H. Wanner, Chemical Thermodynamics of Uranium (vol. 1), Elsevier, North Holland, Amsterdam, 1992.

[2] W. Hummel, G. Anderegg, L. Rao, I. Puigdomènech, O. Tochiyama, Chemical Thermodynamics of Compounds and Complexes of U, Np, Pu, Am, Tc, Se, Ni and Zr with Selected Organic Ligands (vol. 9), Elsevier, North Holland, Amsterdam, 2005.

[3] I. Grenthe, X. Gaona, A.V. Plyasunov, L. Rao, W.H. Runde, B. Grambow, R.J.M. Konings, A.L. Smith, E.E. Moore, Second Update on the Chemical Thermodynymics of Uranium, Neptunium, Plutonium, Americium and Technetium (vol. 14), Nuclear Energy Agency of the OECD (NEA), 2020.

Anion Binding and Sensing with Luminescent Lanthanide Probes

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The design of molecular probes that selectively bind and sense anions in aqueous media is a key challenge in supramolecular chemistry. The ability to distinguish between biological phosphate anions (*e.g.* ATP, ADP, AMP) will underpin exciting new sensing tools for biological, clinical and drug discovery research. However, this is very challenging due to similarities in anion structure, size and charge. Luminescent lanthanide probes, particularly of europium(III) and terbium(III), offer unique photophysical properties that are very valuable for sensing and imaging in biological media. However, only a small number of lanthanide probes have been developed that exhibit sufficiently high anion selectivity to be utilised in biological applications.

I will present our progress in the development of lanthanide probes, which utilise macrocyclic ligands functionalised with multiple recognition motifs. These probes are capable of recognising target phosphate species with high selectivity and sensitivity in 100% aqueous media.[1-5] We have established key design principles to create lanthanide complexes that engage their anionic target through a combination of metal-ligand coordination, hydrogen bonding and reversible boronate formation (Figure 1). I will discuss our efforts to translate these selective lanthanide probes into improved bioassays and cellular imaging tools. By doing so, we aim to drive advancements in biomedical research and expedite drug discovery efforts.

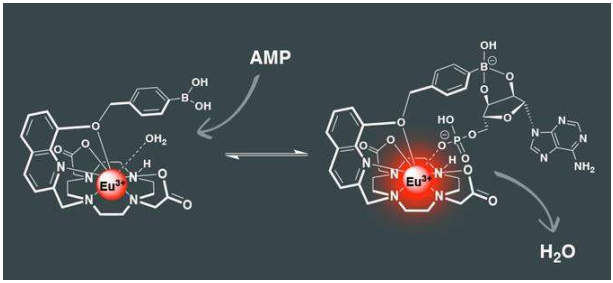

Figure 1. Macrocyclic europium(III) complex designed for multisite recognition of adenosine monophosphate (AMP), producing intense and long-lived red emission.

References:

[1] S. H. Hewitt, G. Macey, R. Mailhot, M. R. J. Elsegood, F. Duarte, A. M. Kenwright and S. J. Butler, *Chem. Sci.*, **2020**, 11, 3619–3628.

[2] S. E. Bodman, C. Breen, S. Kirkland, S. Wheeler, E. Robertson, F. Plasser, S. J. Butler. *Chem. Sci.*, **2022**, 13, 3386–3394.

[3] A. Cataldo, K. Norvaisa, L. Halgreen, S. E. Bodman, K. Bartik, S. J. Butler, and H. Valkenier. *J. Am. Chem. Soc.*, **2023**, 145, 16310–16314.

[4] M. L. Shipton, F. A. Jamion, S. Wheeler, A. M. Riley, F. Plasser, B. V. L. Potter, S. J. Butler, *Chem. Sci.*, **2023**, 14, 4979–4985.

[5] S. E. Bodman, C. Breen, A. R. Hambleton, S. J. Butler and H. Willcock, *Chem. Commun.*, **2024**, 60, 284–287.

Consequences of metal-peptide interactions in Alzheimer's Disease & some strategies to prevent them

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Alzheimer (AD) is a multifactorial disease where two key events have been linked to the etiology of the disease: (i) the self-assembly process of the Alzheimer-related amyloid-β (Aβ) peptides leading to the deposits of the Aβ amyloids in the senile plaques detected in AD patients' brains [1] and (ii) oxidative stress.[2] Metal ions (copper, zinc and iron) have been found in the senile plaques in abnormally high level. They can modulate the self-assembly of the Aβ peptides and Aβ-bound copper ions can catalyze the production of Reactive Oxygen Species. They are thus key players in the pathology.

During the talk, I will give an overview of the approaches we have developed during the last years to (i) understand at the molecular level how metal ions are linked to the fate of the disease [1-4] and to (ii) overcome their deleterious effects by copper-targeting molecules [4] and modulators of Aβ peptides self-assembly.[6]

References:

[1]. Atrian-Blasco, E.; Gonzalez, P.; Santoro, A.; Alies, B.; Faller, P.; Hureau, C., Cu and Zn coordination to amyloids: a chemistry of pathological importance ? Coord. Chem. Rev. **2018**, 371, 38-55.

[2]. Cheignon, C.; Tomas, M.; Bonnefont-Rousselot, D.; Faller, P.; Hureau, C.; Collin, F., Oxidative stress and the amyloid beta peptide in Alzheimer's Disease. Redox Biology **2018**, 14, 450-464.

[3]. V. Borghesani, B. Alies, C. Hureau, Eur. J. Inorg. Chem. **2018**, 7-15.

[4]. E. Falcone, C. Hureau, Chem. Soc. Rev. **2023**, 52, 6595-6600.

[5]. Esmieu, C.; Guettas, D.; Conte-Daban, et al., Copper-Targeting Approaches in Alzheimer's Disease: How To Improve the Fallouts Obtained from in Vitro Studies. Inorg. Chem. **2019**, 58, 13509-13527.

[6]. DeCremoux, L. and coworkers, in prep.

Acknowledgments

The ERC StG 638712 ('aLZINK') and ANR SUPRAMY are acknowledged for financial supports. The past and current researchers who have contributed to the results that will be shown are also warmly thanked.

Keynote Lectures

How Organic Matter Modulates Heavy Metal-Soil Mineral Interactions

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The interactions between soil minerals and heavy metals are pivotal in biogeochemical processes. Soil minerals like clays and oxides have the ability to bind heavy metals, thereby influencing their mobility and bioavailability in the environment. Heavy metals undergo various processes such as aggregation, dissolution, complexation, and precipitation, which are regulated by solution conditions like pH, ionic strength, redox status, and organic matter content. Organic matter, consisting of a diverse array of organic compounds, often exhibits strong affinities to soil mineral surfaces. Coating of mineral surfaces by organic matter can either inhibit or enhance the reactivity of both the organic compounds and the soil minerals, impacting their interactions with heavy metals. Because organic compounds act as effective chelators for many heavy metals, this leads to complex interactions among soil minerals, organic matter, and heavy metals under environmental conditions. We will present several examples highlighting how the composition of organic matter governs the mechanisms and kinetics of heavy metal-soil mineral interactions, with a specific focus on ferrihydrite, an iron oxyhydroxide mineral, in both field and laboratory experiments. Utilizing micro- and nanoscale techniques such as TEM, XAS, Mössbauer spectroscopy, and XPS, we aim to characterize heavy metal speciation and bonding environment to elucidate their reactivity and environmental fate.

Molecular Dynamics Studies of the Separation of Uranium(VI) Using Organic Solvents or Solid Supports

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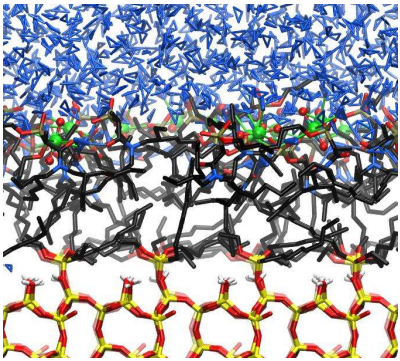
In the front end of the nuclear fuel cycle, uranium is usually separated by solvent extraction processes. These processes are very efficient for the separation of uranium from concentrated effluents. For the recovery of the uranium in low-concentration solutions, separation using solid supports is much more promising. In both kinds of separation processes, bifunctional ligands of the amidophosphonate family can be used to recover selectively the uranium(VI) cation. However, despite several experimental studies, the mechanisms involved in its extraction are still not well understood at the molecular level in both kinds of processes. In this study, we used classical molecular dynamics to model organic phases and solid/liquid interfaces with amidophosphonate bifunctional ligands to better understand the separation process for both systems.



First, we developed new force fields parameters for the actinyl(VI) cations, using the 12-6-4 formalism [1], which is efficient to take into account polarization effects of the media by the cations.[2] This new force field parameters allowed us to perform molecular dynamic simulations ranging from a hundred to a thousand of nanoseconds, simulations times that were essential for the equilibration of the systems simulated here.

Organic phases containing an amidophosphonate extractant and uranyl(VI) cations were simulated at concentrations representative of the experimental conditions. The organization of these extractants and the speciation, with and without uranium, were then described, with a validation of the results using experimental data. The role of the organic functions of the amidophosphonate molecule has been highlighted: the molecule can extract uranium without fully dehydrating it thanks to a network of hydrogen interactions in the complexes.[3] Finally, representative molecular models of solid supports were designed. Essential information was obtained on two key points: i) the structuring of solid/liquid interfaces with and without uranium, and ii) the speciation of uranium at these surfaces.

References:

[1] Moreno Martinez, D.; Guilbaud, P.; Guillaumont, D. Force Field Parameterization of Actinyl Molecular Cations Using the 12-6-4 Model. Chem. Inf. Model. 2022, 62 (10), 2432–2445

[2] Li, P.; Roberts, B. P.; Chakravorty, D. K.; Merz, K. M. Rational Design of Particle Mesh Ewald Compatible Lennard-Jones Parameters for +2 Metal Cations in Explicit Solvent. J. Chem. Theory Comput. 2013, 9, 2733−2748.

[3] Moreno Martinez, D.; Acher, E.; Vatin, M.; Dourdain, S.; Guillaumont, D.; Guilbaud, P.; The Journal of Physical Chemistry B 2021 125 (38), 10759-10771

Polyazaligands as tools for sensing

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The design of receptors able to selectively recognize and bind specific guests is a challenging and dateless target. Due to their easy functionalization and tunable topology, polyaza scaffolds are useful to this purpose, moreover they provide high solubility in aqueous solution.

Both open-chain and macrocyclic compounds could provide favourable properties. On one hand, open-chain polyamine ligands ensure flexibility, allowing for the accommodation of metal cations with different sizes and coordination geometries. Polynuclear complexes can form when the ligand features multiple aza-binding sites, and the distance between the metal centres can be tuned to have them cooperate or not in the formation of the active site [1]. Moreover, a preorganized polyaza-metal complex can become a metallo-receptor for additional guests [2–4]. On the other hand, macrocyclic polyamine ligands ensure high complex stability and selectivity towards the target metal cations, thanks to the preorganization provided by the stiffened system [5]. The insertion in the aza-ligands of chromophores or fluorophores can signal the occurred interaction with the guest [6,7]. The optical active group can be linked to the polyamine through a simple spacer or could be part of the macrocycle, forming a cyclophane [8–10] (Figure 1).

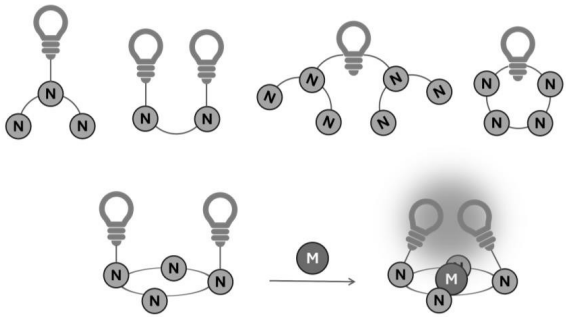

***Figure 1**: Scheme of possible polyaza-ligands and example of metal ion complexation*

Our group has long been working on polyaza-ligands to be used as receptors for guests of different nature. In this contribution, some examples of open-chain, macrocycle or cyclophane polyamine ligands are reported, to show their peculiar behaviour towards selected metal ions.

References:

[1] M. Formica, G. Ambrosi, V. Fusi, L. Giorgi, M. Arca, A. Garau, et al., New J. Chem. 2018, 42, 7869–7883.

[2] E. Macedi, L. Giorgi, M. Formica, P. Rossi, D. Paderni, P. Paoli, V. Fusi, Chempluschem 2023, 88, e202200364.

[3] P. Rossi, E. Macedi, M. Formica, L. Giorgi, P. Paoli, V. Fusi, Chempluschem 2020, 85, 1179–1189.

[4] D. Paderni, L. Giorgi, E. Macedi, M. Formica, P. Paoli, P. Rossi, V. Fusi, Dalt. Trans. 2021, 50, 15433.

[5] A. Garau, L. Lvova, E. Macedi, G. Ambrosi, M. C. Aragoni, et al., New J. Chem. 2020, 44, 20834–20852.

[6] D. Paderni, D. Lopez, E. Macedi, G. Ambrosi, A. Ricci, et al., Inorganica Chim. Acta 2023, 549, 121400.

[7] D. Paderni, E. Macedi, L. Lvova, G. Ambrosi, M. Formica, et al., Chem. - A Eur. J. 2022, 28, e202201062.

[8] D. Paderni, G. Barone, L. Giorgi, M. Formica, E. Macedi, V. Fusi, Dalt. Trans. 2023, 3716–3724.

[9] D. Paderni, L. Giorgi, M. Voccia, M. Formica, L. Caporaso, E. Macedi, V. Fusi, Chemosensors 2022, 10, 188.

[10] G. E. Giacomazzo, D. Paderni, L. Giorgi, M. Formica, L. Mari, R. Montis, et al., Molecules 2023, 28, 2031.

Redox reactivity of non-classical copper-protein complexes: Implications in physiological and pathological processes

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Due to its reactivity and catalytic functions, copper is an essential cofactor in metalloproteins. Copper proteins are classified by their function and spectroscopic features, e.g. type 1 Cu and Cu_A sites are electron transfer centers, binuclear and trinuclear Cu sites for oxygen activation and reduction, and tetranuclear Cu_Z sites for N_2O reduction [1]. However, several proteins associated with neurodegenerative and degenerative diseases, such as prion (PrP^C), alpha-synuclein (AS) and γ-crystallin proteins, can coordinate Cu ions, but the resulting complexes are not classical sites with specific electron transfer or reactivity functions [2-4]. This presentation will discuss and contrast the biophysical details of copper coordination to PrP^C, AS and γ-crystallin proteins and their impact on reactivity, providing critical insights to understand the physiological and pathological implications of these proteins.

PrP^C is a 209 amino acids cell-surface glycoprotein that is anchored to the cell membrane by a glycosylphosphatidylinositol. The misfolded isoform of PrP^C is named prion scrapie (PrP^{Sc}) and is associated with a set of rare and fatal neurodegenerative disorders affecting humans and other mammalian species. PrP^C is expressed primarily in the central nervous system (CNS) and has been associated with a role in metal homeostasis [5]. PrP^C coordinates up to six Cu^{2+} ions in the N-terminal region, whose anchor sites are the histidine residues at positions 61, 69, 77, 85, 96 and 111; its Cu^{2+} coordination is highly dependent on Cu concentration and pH. Interestingly, the His111 site contains two adjacent methionine residues at positions 109 and 112, where the thioether groups of these methionines act as ligands in Cu^+ coordination and promote redox reactivity at this site (Figure 1).

On the other hand, AS is a 140 amino acids protein that is predominantly expressed in the presynaptic terminals of CNS neurons. AS aggregation is associated with synucleinopathies, a group of neurodegenerative disorders whose hallmark is cytoplasmic inclusions known as Lewy bodies. The proposed physiological functions of AS include uptake, storage and recycling of neurotransmitter vesicles, auxiliary chaperone at synapses as well as maintenance of dopamine levels [5]. AS can coordinate copper ions with high affinity, the binding sites are located at the N-terminal region, a site involving the first six residues of AS (MDVFMK); and the other site around the only His residue of AS, His50. The first site contains two methionine residues involving in the Cu^+ coordination (Figure 1).

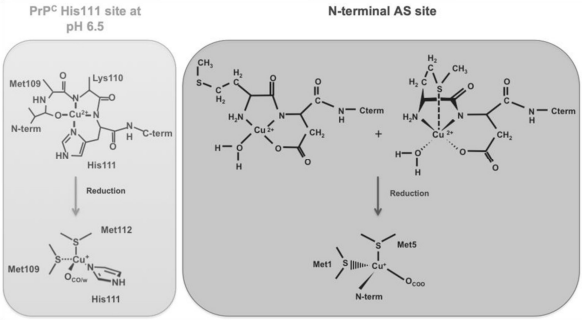

Figure 1. Comparison of Cu^{2+} and Cu^{+} coordination between the complex formed at pH 6.5 at the His111 site of PrP^{C} and the N-terminal site of AS protein.

Finally, γ-crystallins, proteins found mainly in the lens, are among the more stable proteins in the human body. The formation of nonamyloid aggregates of γ-crystallins contributes to light-scattering in a cataractous lens. Cu^{2+} ions can cause nonamyloid aggregation of human γ-crystallins *in vitro*. The mechanism for Cu-induced aggregation of γ-crystallins involves metal-bridging, formation of disulfide-bridged dimers and oligomers, protein unfolding, and Cu^{2+} reduction to Cu^{+} at expense of protein oxidation [4].

These proteins linked to various neurodegenerative and degenerative diseases can coordinate copper ions and exhibit a coordination and reactivity that differs from the classical Cu metalloprotein sites. A discussion and comparison of these three systems will be presented, contributing to the understanding of the physiological and pathological aspects of these proteins.

References:

[1] T. Arcos-López, N. Schuth, L. Quintanar, *Transition Metals and Sulfur – A Strong Relationship for Life*, Berlin, Boston: De Gruyter, **2020**, pp. 51-90. DOI: 10.1515/9783110589757-009

[2] T. Arcos-López, et al. *Inorg. Chem.* **2016**, 55, 6, 2909–2922

[3] N. González, T. Arcos-López, et al. *J. Neurochem*. **2019**, DOI: 10.1111/jnc.14721

[4] G. Palomino-Vizcaino, et al. *J. Am. Chem. Soc.* **2023**, 145, 12, 6781–6797

[5] Y. Posadas, V. E. López-Guerrero, T. Arcos-López, et al. *Comprehensive Inorganic Chemistry III (Third Edition),* Elsevier, **2023,** pp. 575-628

ISMEC 2024
June 10th - 13th, Nice
International Symposium on Thermodynamics of Metal Complexes

From the study of copper containing enzymes to the development of bioinspired catalysts

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Lignocellulosic biomass (composed mainly of polysaccharides and lignin) is increasingly considered as a renewable feedstock to produce bio-sourced chemicals, biomaterials and advanced biofuels. One important step in the valorisation of biomass components into valuable products consists in size reduction of the polymeric recalcitrant components. LPMOs are copper-containing enzymes produced by some bacteria and fungi, among a consortium of enzymes that act collectively to degrade recalcitrant polysaccharides such as cellulose or chitin [1]. LPMO enzymes were shown to oxidatively cleave polysaccharide chains. Notably, LPMOs catalyse the hydroxylation of a strong C-H bond (> 95 kcal/mol) at the glycosidic linkage (either at C1 or C4) leading to glycosidic bond cleavage using either O_2 (and electrons) or H_2O_2 (**Figure 1**) [2]. LPMO active centre is constituted of a mononuclear copper ion ligated by an unusual "histidine-brace" motif consisting of two histidines residues including the *N*-terminal histidine bound in a bidentate fashion.

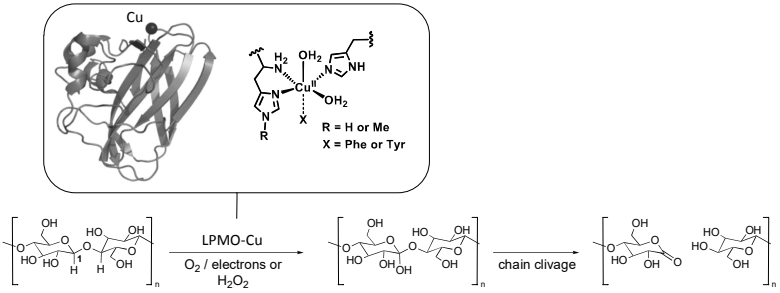

Figure 1: C1 oxidation of cellulose catalysed by LPMO. Structure of a LPMO (PDB ID 6T5Z) with surface exposed copper active-site [3].

Our group combines studies on the enzymatic system to the development of bioinspired copper complexes [3-7]. In particular, we have produced and characterized bacterial LPMOs and evaluated the effect of mutations of active site residues on the physicochemical properties and the reactivity of the enzymes. We have also prepared and characterized bioinspired complexes to get insight into mechanistic pathways allowing strong C-H bonds activation by copper systems. Following this interdisciplinary approach, several functional bioinspired catalysts were prepared and proof-of-concept that bioinspired complexes can oxidatively promote polysaccharide depolymerization was obtained.

Acknowledgement: The authors acknowledge the financial support of ECOS-NORD (project M17P01), Region-Sud PACA (EJD) and ANR (ANR-22-CE07-0032-03 & ANR-23-CE43-0012)

References:

[1] Z. Forsberg, M. Sørlie, D. Petrović, G. Courtade, F. L. Aachmann, G. Vaaje-Kolstad, B. Bissaro, Å. K. Røhr, V. G. Eijsink, *Curr. Opin. Struct. Biol*. **2019**, 59, 54–64

[2] B. Wang, Z. Wang, G.J. Davies, P.H. Walton, C. Rovira, *ACS Catal* **2020**, 10 (21), 12760–12769

[3] A. Munzone, B.E. Kerdi, M. Fanuel, H. Rogniaux, D. Ropartz, M. Réglier, A. Royant, A.J. Simaan, C. Decroos, *FEBS J.* **2020**, 287 (15), 3298–3314

[4] R.J. Gómez-Piñeiro, M. Drosou, S. Bertaina, C. Decroos, A.J. Simaan, D.A. Pantazis, M. Orio, *Inorg. Chem*. **2022**, 61(20), 8022-8035

[5] A.L. Concia, A. Munzone, M.C. Kafentzi, A. Kochem, M. Réglier, C. Decroos, A.J. Simaan, in Series on Chemistry, Energy and the Environment: Volume 5 "Bioinspired Chemistry: From Enzymes to Synthetic Models"; Wordpress Sc. **2019**, pp 185-263

[6] A.L. Concia, M.R. Beccia, M. Orio, F.T. Ferre, M. Scarpellini, F. Biaso, B. Guigliarelli, M. Réglier, A.J. Simaan, *Inorg. Chem*. **2017**, 56 (3), 1023–1026

[7] R. Leblay, R. Delgadillo-Ruíz, C. Decroos, C. Hureau, M. Réglier, I. Castillo, B. Faure, A. J. Simaan, *ChemCatChem*, **2023**, 15, e202300933

ISMEC 2024 Pulidori Award

Exploiting Principal Component Analysis (PCA) to reveal temperature, buffer and metal ions' role in neuromelanin (NM) synthesis by dopamine (DA) oxidative polymerization

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Neuromelanin (NM) plays a well-established role in neurological disorders pathogenesis; the mechanism of action is still discussed and the investigations in this field are limited by NM's complex and heterogeneous composition, insolubility, and low availability from human brains. An alternative can be offered by synthetic NM obtained from dopamine (DA) oxidative polymerization; however, a deep knowledge of the influence of both physicochemical parameters (T, pH, ionic strength) and other compounds in the reaction media (buffer, metal ions, other catecholamines) on DA oxidation process and, consequently, on synthetic NM features is mandatory to develop reliable NM preparation methodologies. To partially fulfil this aim, the present work focuses on defining the role of temperature, buffer and metal ions on both DA oxidation rate and DA oligomer size. DA oxidation in the specific conditions is monitored by UV-Vis spectroscopy and Principal Component Analysis (PCA) is run either on the raw spectra to model the background absorption increase, related to small DA oligomers formation, or on their first derivative to rationalize DA consumption. After having studied three case studies, 3-Way PCA is applied to directly evaluate the effect of temperature and buffer type on DA oxidation in the presence of different metal ions. Despite the proof-of-concept nature of the work and the number of compounds still to be included in the investigation, the preliminary results and the possibility to further expand the chemometric approach represent an interesting contribution to the field of in vitro simulation of NM synthesis.

Oral Presentations

FIRST-ROW TRANSITION METAL COMPLEXES WITH SCORPIONATE- OR PINCER-TYPE POLYPYRAZOLE LIGANDS AS BIOMIMETIC MODELS

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Here, we present the series of first-row transition metal complexes with polypyrazole, *N*-scorpionate: tris(3,5-dimethylpyrazol-1-ylmethyl)amine (L) or *N*-pincer: bis(1-(3,5-dimethylpyrazolyl)methyl)amine (L') type ligands. The obtained complexes are compounds of Cu(II), Co(II), Zn(II), Fe(II) and Fe(III) with structural diversity. They show monomeric: **$[Cu(NCS)_2(L')]$**, **$[Fe(NCS)_2(L)]\cdot CH_3CN$**, dimeric: **$[Fe_2(\mu\text{-}Cl)_2L_2][BPh_4]_2\cdot 2CH_3CN$**, **$[FeLCl(\mu\text{-}O)FeCl_3]\cdot CH_3CN$** as well as cationic-anionic structures: **$[Zn(NCS)L]_2[Zn(NCS)_4]$**, **$[CuClL]_2[CuCl_4]$** and **$[CoClL][CoCl_3L'']$**. All the complexes were fully characterized using structural, spectroscopic and magnetic methods supported by quantum chemical calculations.

Due to the fact that scorpionate-type ligands, analogous to polypyrazole ligands introduced by Trofimenko [1] are a good choice as ligands for the synthesis of complexes with potential enzymatic activity, we have tested our complexes as functional enzyme models. The presented first-row transition metal complexes have been tested as biomimetics in three different reactions (Fig. 1), namely:

1) **$[Cu(NCS)_2(L')]$** and **$[Zn(NCS)L]_2[Zn(NCS)_4]$** complexes as inhibitors of xanthine oxidase (XO) [2]. Both compounds acted as mixed-type inhibitors for XO, and the differences in the activity of the complexes were confirmed by a molecular docking study.
2) **$[CuClL]_2[CuCl_4]$** and **$[CoClL][CoCl_3L'']$** as catechol oxidase (CO) mimetics. Interestingly, from the tested complexes, only Cu(II) one possesses catalytic activity in the oxidation of 3,5-di-tert-butylcatechol. Moreover, catalytic results obtained for the Cu(II) complex revealed that the solvent's nature significantly affects its catecholase activity, and the results are in agreement with the theoretical studies.

3) **$[Fe(NCS)_2(L)]\cdot CH_3CN$**, **$[Fe_2(\mu\text{-}Cl)_2L_2][BPh_4]_2\cdot 2CH_3CN$** and **$[FeLCl(\mu\text{-}O)FeCl_3]\cdot CH_3CN$** as mimetics of RPE65 protein. The complexes were tested in the reaction with retinyl acetate as a potential catalysts for cis-retinoids synthesis. The changes in the electronic structure of the central metal ions were tracked during the reaction using XAS measurements with the synchrotron radiation and supported with quantum chemical calculations.

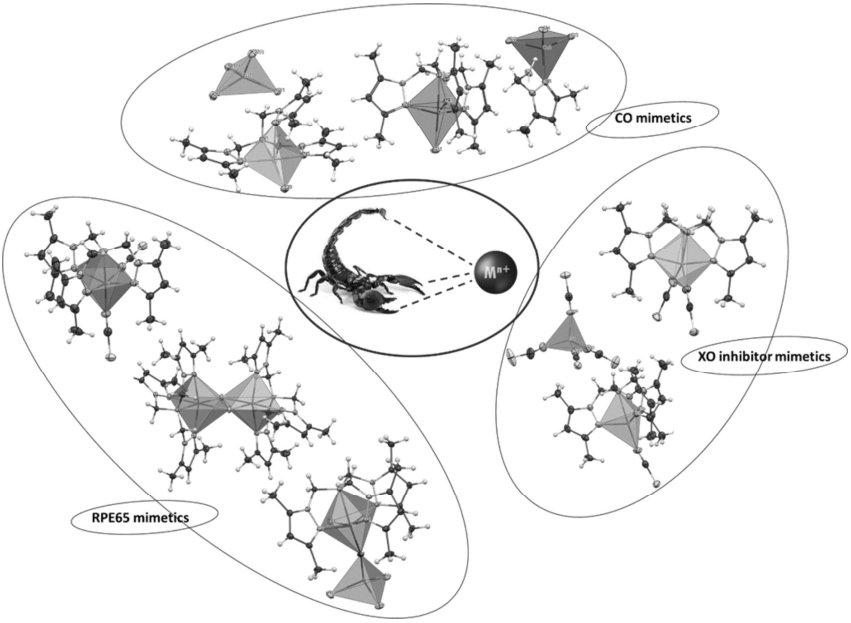

Fig. 1. Tested as biomimetics first-row transition metal complexes.

This work was financially supported by the National Science Centre, Poland, Grant No. 2020/39/B/ST4/01952

References:

[1] S. Trofimenko, *J. Am. Chem. Soc.*, **1967**, 89, 6288.

[2] J. Masternak, M. Zienkiewicz-Machnik, K. Kazimierczuk. B. Barszcz, *Polyhedron*, **2018**, 142, 93.

The influence of Cu(II) and Zn(II) ions on the thermodynamics properties, structure, stability and antimicrobial activity of salivary histatins

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Antimicrobial Peptides (AMPs) are essential components of the hosts' non-specific immune response; they are known for their small size and positive charge, typically consisting of 5 to 100 amino acid residues. Their primary role is to combat microorganisms by either killing them or inhibiting their growth. AMPs are garnering attention as potential therapeutics due to their effectiveness against microbes, with minimal instances of microbial resistance observed. Some AMPs display altered antimicrobial activity or mechanisms of action upon binding with metal ions such as Cu(II) and Zn(II). This interaction can hinder microbial survival and virulence by depriving them of essential metal ions, in a phenomenon called "nutritional resistance." Metal ions may also enhance antimicrobial effectiveness by modifying the peptide's charge or structure.[1] Histatins, small, cationic peptides, expressed in the saliva of humans and higher primates have particular antimicrobial activity against the fungal strain *Candida albicans*.[2]

We delve into the relationship between coordination chemistry and antimicrobial activity of Cu(II) and Zn(II) complexes of histatin 3 and histatin 5, as well as their hydrolysis products: N-terminal fragments (histatin 3-4 and 5-8) and C-terminal fragments (histatin 4 and histatin 8). Cu(II) typically coordinates in an albumin-like binding mode, except for histatin 4, which lacks the ATCUN motif. Zn(II) can bind to up to three His imidazole groups in all of the studied AMPs. The antimicrobial efficacy of histatins and their metal complexes is notably affected by pH, with higher activity observed at pH 5.4 compared to pH 7.4.

Additionally, both the complexes and individual ligands demonstrate greater efficacy against Gram-positive bacteria than Gram-negative ones. In most cases, Zn(II) coordination moderately enhances the histatin antimicrobial potency. Furthermore, histatin 3-4 and histatin 5-8, upon binding Zn(II) ions, undergo significant changes in their secondary structure.[3] This effect, as shown by SAXS, is much more visible in the case of the Zn(II)-histatin 3-4 complex, compared to the Zn(II)-histatin 5-8 complex.

References:

[1] D. Łoboda, H. Kozłowski, M. Rowińska-Żyrek, *New J. Chem.* **2018**, 42, 7560-68.

[2] H. Du, S. Puri, A. McCall, H.L. Norris, T. Russo, M. Edgerton, *Front. Cell. Inf. Microbiol.*, **2017**, 7, 41.

[3] E. Dzień, J. Wątły, A. Kola, A. Mikołajczyk, A. Miller, A. Matera-Witkiewicz, D. Valensin, M. Rowińska-Żyrek, *Dalton Transactions*, **2024**, 53, 1-10.

Recovery of critical metals from LCO battery cathodes through a polymer inclusion membrane with ionic liquid [P_{66614}][Dec]

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Lithium-ion batteries (LIBs) are the most employed energy-storage systems in modern electric vehicles which are considered crucial for achieving the objectives of "carbon neutrality" and reduce "carbon peaking". The proper disposal of used LIBs is vital for effective resource management and avoiding environmental pollution associated with the uncontrolled release of toxic materials contained [1]. A significant weight fraction of LIBs consists in the so-called Critical Raw Materials (CRMs) [2], presenting a high supply risk and price variability, in particular: cobalt, lithium, graphite etc. Over the past few years, the research on sustainable processes for safe treatment and material recovery from spent LIBs has been intense. Among the different material recovery technologies, hydrometallurgical recycling is attractive due to the low energy and resource consumption and high purity of the recycled metals. Liquid-liquid separations based on ionic liquids (ILs) as receiving hydrophobic phases have gained significant attention for their potentially high selectivity as well as the superior characteristics with respect to volatile organic solvents, VOCs (low volatility, safety, chemical and thermal stability, recyclability)[3]. One of the strategies to reduce the quantities of the ILs, which are relatively expensive with respect to VOCs, is to immobilize them into a supporting polymeric membrane to manufacture the so called polymer inclusion membranes (PIMs). Besides the economic advantage of the use of low volumes of ILs, extraction and stripping occur in a single step [4], thus making PIMs suitable for a scale up of the processes.

In this work we prepared and characterized a PIM membrane based on PVC and IL [P_{66614}][Dec] for separation of Li and Co from lithium – cobalt oxide (LCO) cathode. First, the battery from mobile phone was discharged and dismantled. The cathode was scratched from a current collector and leached in aqua regia for metal content determination. For the separation experiment, the cathode was leached in HCl and appropriate conditions (contact time, metal loading, acid molarity) for leaching were determined. After leaching, the solution

was diluted and poured into one compartment of the separation cell (Figure 1). For stripping, H_2O was utilized. Metal content in Feed and Strip phase for kinetics and separation study was determined by ICP-OES, and absorption spectra was collected by UV-VIS.

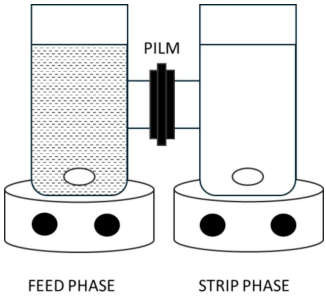

Figure 1. Setup for separation of cobalt from lithium. The volume of each compartment is 100 ml, contact surface with the membrane 28.27 cm^2, stirring speed 700 rpm.

Acknowledgements: AM&AK acknowledge the PhD programme on Green topics (Action IV.5, DM 1061/2021, cycle XXXVII) carried out with co-financing from the European Union - ESF REACT-EU, PON Research and Innovation 2014-2020, UniUD. MT&MS acknowledge the Italian Ministry for University and research for funding: PRIN2022 "Wastezilla" (2022HYH95P).

References:

[1] Or T., Gourley S. W. D., Kaliyappan K., Yu A., Chen Z., *Carbon Energy* **2020**, 2, 6–43.
[2] European Commission, Study on the critical raw materials for the EU **2023** – Final report https://data.europa.eu/doi/10.2873/725585, 2023.
[3] Lei Z., Chen B., Koo Y. M., Macfarlane D. R., *Chem. Rev.* **2017**,117, 6633–6635.
[4] Fajar A. T. N., Kubota F., Firmansyah M. L., Goto M. *Ind. Eng. Chem. Res.* **2019**, 58 (49), 22334 – 22342.

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Complexation of environmental interest analytes with pyridoxal polyamine derivatives.

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One of the biggest problems facing chemistry arises from the increasing pollution of the environment. Supramolecular complexes offer a new and efficient way for the monitoring and removing of many pollutant substances [1]. Polyamines have been chosen as recognition units since it is possible to modulate their binding affinities by changing the pH. Furthermore, the addition of pyridoxal moieties to these polyamines induces fluorescence, which together with their lack of toxicity and solubility in aqueous solution allows the development of potential sensors for species of environmental interest. Here, the synthesis, acid base behaviour and heavy metal (Hg^{2+}, Cd^{2+}, Pb^{2+} and UO_2^{2+}) coordination chemistry of two polyamines containing pyridoxal as the sensing unit have been studied by potentiometric, NMR, fluorescence and UV-Vis techniques.

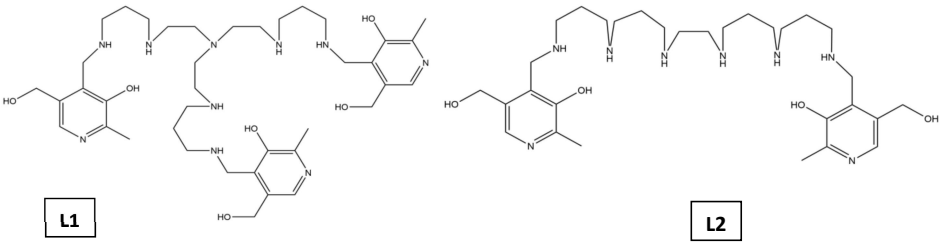

Figure 1: Structures of L1 and L2

References:

[1] M. T. Albelda, J. C. Frías, E. García-España, H. Schneider. Supramolecular complexation for environmental control. Chem. Soc. Rev., **2012**, 41(10), 3859-3877.

How metal ions rule and rock the world of antimicrobial peptides

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The activity of antimicrobial peptides (AMPs), potential treasure troves for finding new, effective classes of antibiotics, can be significantly affected by the coordination of Zn(II) and Cu(II). In the dozens of complexes that we have had a closer look at, we have discovered several ways in which metals may enhance the antimicrobial potency of AMPs: (i) Cu(II) binding induces the formation of an α-helix in the PvHCt peptide from shrimp, making it active even against methicillin-resistant *Staphylococcus aureus*; (ii) Zn(II) coordination triggers structural and morphological changes and enhances the antifungal activity of human amylin analogues [1] and that of the peptides from the shepherin group (from the plant *Capsella bursa pastorsis*) [2] - the formed fibrils can act as needles, physically damaging the fungal cell wall or membrane; (iii) metal coordination may also have a simple effect on the local chare and/or structure of the AMP.

Acknowledgements
The authors thank the National Science Centre (UMO2017/26/E/ST5/00364) for support.

References:

[1] Dudek D., Dzień E., Wątły J., Matera-Witkiewicz A., Mikołajczyk A., Hajda A., Olesiak-Bańska J., Rowińska-Żyrek M., Zn(II) binding to pramlintide results in a structural kink, fibril formation and antifungal activity, Scientific Reports, 2022, 12, 20543/1-20543/8

[2] Wątły J., Szarszoń K., Mikołajczyk A., Grelich-Mucha M., Matera-Witkiewicz A., Olesiak-Bańska J., Rowińska-Żyrek M., Zn(II) Induces Fibril Formation and Antifungal Activity in Shepherin I, An Antimicrobial Peptide from *Capsella bursa-pastoris*, Inorganic Chemistry, 2023, 62, 19786-19794

[3] Dzień, E., Wątły, J., Kola, A., Mikołajczyk, A., Miller, A., Matera-Witkiewicz, A., Valensin, D., Rowińska-Żyrek, M. Impact of metal coordination and pH on the antimicrobial activity of histatin 5 and the products of its hydrolysis. Dalton Transactions, 2024, 53, 1-10.

Exploring the thermodynamics of metal-peptide complexes: unveiling promising perspectives for antimicrobial innovation

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The global identification of antibiotics as crucial tools in fighting infectious diseases is undeniable. However, the rise of antimicrobial resistance among various microorganisms demands a reevaluation of their utility. Antimicrobial peptides have emerged as promising alternatives to conventional antibiotics. These peptides exhibit bioactivity through diverse mechanisms, including the interaction with metal micronutrients. One such example is the human antimicrobial peptide calcitermin, which has been previously investigated by our research team. Our aim was to assess its ability to chelate metals and its effectiveness against a range of pathogens *in vitro* [1,2].

From this perspective, we conducted a systematic study of calcitermin derivatives. By introducing chemical modifications to the native sequence, we aimed at understanding the influence of divalent Cu(II) and Zn(II) ions on the stability, coordination, and antimicrobial activity of the resulting complexes. Among various derivative, we investigated the calcitermin mutants A7R and A8R, wherein the alanine residues at positions 7 and 8 were substituted with arginines, known to enhance antibacterial activity. Additionally, the A7H analogue has been considered, to obtain a chelating sequence with four histidines in alternate position. Notably, the affinity for metal binding not only increases with the number of histidines but is also higher for histidines separated by a single amino acid rather than separated by several amino acids or in consecutive order [3].

Through a comprehensive approach involving potentiometric titrations, mass spectrometry, UV-Vis spectrophotometry, circular dichroism, and electronic paramagnetic resonance, we delved into the formation equilibria and coordination chemistry of these complexes. Antimicrobial assays were also performed to assess the bioactivity of the compounds against a broad spectrum of microorganisms, revealing the pivotal role of metal ions.

This work highlights the significance of characterizing the thermodynamic properties of metal-peptide complexes in solution. The obtained results serve as a foundational step toward the development of novel metal-based antimicrobial agents.

Financial support of the National Recovery and Resilience Plan (NRRP), Mission 4 Component 2 Investment 1.1 – NextGenerationEU (PRIN PNRR 2022 - P2022EMY52) and of the Polish National Science Centre (UMO-2020/37/N/ST4/03165) is gratefully acknowledged.

References:

[1] D. Bellotti, M. Toniolo, D. Dudek, A. Mikołajczyk, R. Guerrini, A. Matera-Witkiewicz, M. Remelli, M. Rowińska-Żyrek, Dalton Trans., 2019, 48(36), 13740-13752.

[2] M. D'Accolti, D. Bellotti, E. Dzień, C. Leonetti, S. Leveraro, V. Albanese, E. Marzola, R. Guerrini, E. Caselli, M. Rowińska-Żyrek, M. Remelli, Sci. Rep., 2023, 13, 18228.

[3] J. Watly, E. Simonovsky, R. Wieczorek, N. Barbosa, Y. Miller, H. Kozlowski, Inorg. Chem., 2014, 53, 6675-6683.

Interactions of the Aspf2 zincophore from *Aspergillus fumigatus* with its zinc transporter, ZrfC

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Aspergillus fumigatus is a well-adapted saprophytic and opportunistic fungal pathogen, that invades the lungs of immunosuppressed patients and causes invasive pulmonary aspergillosis. To survive in the host, *A. fumigatus* produces many small airborne spores and uses a highly specified Zn(II) transport mechanism based on the peptide zincophore, Aspf2 and the zinc transporter, ZrfC. This mechanism of Zn(II) uptake is one of the critical aspects of fungal virulence and survival, and distinguishes fungal cells from mammalian ones. Consequently, it is a good starting point to design a highly specific antifungal drug.

After the invasion of the host cells, *Aspergillus fumigatus* secretes an extracellular zincophore Aspf2, which is released into surrounding host cells, where it binds Zn(II) and delivers it to the fungal pathogen through physical interaction with the ZrfC transporter. The most probable Zn(II) binding site on Aspf2 is its *C*-terminal region, PNCHTHEGGQLHCT, and on the ZrfC transporter – the MNCHFHAGVEHCIGAGESESGSSQ fragment. At pH 7.4, both fragments coordinate Zn(II) via two histidine imidazoles and two cysteine thiolates with the $\{2N_{im}, 2S^{-}\}$ binding mode [1, 2]. The ZrfC fragment coordinates Zn(II) with higher affinity than the Aspf2 fragment, which allows efficient Zn(II) transport from the zincophore to the transporter [2]. Moreover, the same fragments also have a high affinity for another metal ion essential for fungi, Ni(II), that can compete with Zn(II) for its binding sites. In this case, however, even in a theoretical situation in which equimolar amounts of both metals would be available, the Aspf2 zincophore strongly prefers to bind Zn(II) over Ni(II). At around physiological pH, more than 85% of the PNCHTHEGGQLHCT fragment is coordinated to Zn(II). It shows that the $\{2N_{im}, 2S^{-}\}$ binding mode, typical for zinc fingers, is more tempting for Zn(II) than for Ni(II). The situation is different in the case of the MNCHFHAGVEHCIGAGESESGSSQ fragment, where more than 58% of the sequence prefers to bind Ni(II), making transporter selectivity much more complicated.

References:

[1] K. Garstka Kinga, A. Hecel, H. Kozłowski Henryk, M. Rowińska-Żyrek, *Metallomics* **2022**, 14, mfac042

[2] K. GarstkA, G. Potoczniak, H. Kozłowski, M. Rowińska-Żyrek, *Dalton Transactions* **2024**, 53, 2848-2858

Ga^{3+}- hydroxypyrone complexes: from solution studies to biological activity

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Targeting iron uptake systems can significantly impact the antimicrobial cargos, since the pathogenic microbes produce Fe-scavenging molecules that sequester iron from their extracellular environment and transporting proteins. In this context, the complexation studies were carried out in aqueous solution between Fe^{3+} and Ga^{3+} with hydroxypyrone molecules: Ga^{3+} is able to mimic Fe^{3+} behavior, although inert in the physiological conditions; hydroxypyrones, in particular kojic acid derivatives, are very promising chelators for the treatment of hard metal ions [1, 2]. Hence, the joined use of potentiometry and spectrophotometry techniques has allowed the determination of the different species involved in the equilibria. In particular, Fe^{3+} complexation was investigated firstly, and after that Ga^{3+} one for evaluating the similarities between these two metal ions.
The results indicated the formation of 2:3 metal:ligand complexes, differently protonated, starting at high acidic pH in the presence of both metal ions. The stability constants calculated for Ga^{3+} system have shown a good similarity with those calculated for Fe^{3+}.
The characterization of solid-state complexes by NMR spectroscopy and mass spectrometry confirmed the 2:3 stoichiometry.
Lastly, biological test revealed the promising activity of Ga^{3+}-complexes against *A. fumigatus* and gram-negative bacteria.

References:

[1] L. Toso *et al*., *Journal of Inorganic Biochemistry* **2013**, 127, 220-231.
[2] R. Cappai *et al*., *New Journal of Chemistry* **2018**, 42, 8050-8061.

PyES and libeq, tools for a unified framework for equilibrium data treatment

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There is currently a great need for software and tools for the treatment and analysis of thermodynamic equilibrium data. Actual available solutions, while still being an indispensable tool in the hand of expert chemists devoted to the study of equilibrium problems, are slowly fading in the realm of abandoned development, loosing compatibility with modern systems, and being relegated to a niece and unexplored field. As such it is of uttermost importance to keep developing and updating these tools that should be fully considered laboratory equipment on par with the instrumentation required to obtain the raw data.

An effort on this sense has already been made in the context of the COST Action NECTAR[1] by producing PyES[2], an open-source software for the simulation of titrations and species distribution. The developed application has been shaped in its current form with the aim of showing how a modern solution can lower the barrier to entry for the study of thermodynamic equilibrium, minimizing the effort required to describe and investigate chemical systems even when considering the effects of ionic strength and the formation of precipitates. By allowing the manipulation of files through a graphical user interface, even less experienced users can approach the idea of "chemical speciation" and introduce in their research the insight that such approach can provide. In the last development cycle the possibility of stability constants refinement from potentiometric titration data has also been added. This, with the intent of adding more target experimental sources in the future, opens to the possibility of making PyES a one-stop and unified solution for the study of thermodynamic equilibrium.

With the aim of simplifying the collaboration to the project and to assure its continuity in time the work has been split in two twin endeavours: libeq[3], a Python library that aims to be a one stop solution for the treatment of thermodynamic data, and PyES, a graphical front-end that allows to use the functions exposed by libeq without the need of any programming language.

With the separation of the core logic from how its results are presented to the users it has been possible to simplify the code and introduce a more robust way of considering the effect of activity coefficients on the equilibrium[4]. Moreover, encapsulating all the code required for solving the equations of thermodynamic equilibrium in a standard and standalone Python library opens to the possibility of not only having an installable software that can be run locally, but also creating online interfaces usable from any web-capable machine.

References:

[1] "NECTAR COST," available at https://www.cost-nectar.eu/index.html.
[2] L. Castellino, E. Alladio, S. Bertinetti, G. Lando, C. De Stefano, S. Blasco, E. García-España, S. Gama, S. Berto, D. Milea, *Chemometrics and Intelligent Laboratory Systems,* **2023**, 104860.
[3] "libeq," available at https://www.github.com/kastakin/libeq.
[4] J. Carrayrou, C. Bertagnolli, M. Fahs, *AIChE Journal,* **2022**, *68*, e17391.

Octadentate chelates based on bispidines for use in nuclear medicine

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Theragnostic has shown in the last decade a growing interest by the scientific community. This work aims at developing true theragnostic probes for radioimmunotherapy and positron emission tomography (PET) imaging based on Tb(III) radioisotopes (^{152}Tb (β^+), ^{161}Tb (β^-))[1] or Sc(III) radioisotopes (^{43}Sc (β^+), ^{44}Sc (β^+), ^{47}Sc (β^-)).[1,2] Based on the high kinetic inertness of bispidine chelates,[3] two novel octadentate chelators substituted with either pyridine-phosphonate ($H_6\mathbf{L^1}$) or picolinate ($H_4\mathbf{L^2}$) subunits have been synthesized and their physico-chemical properties were studied.

Thermodynamic stability constants of the bispidine-chelators and their corresponding complexes of Tb(III) or Sc(III) were determined by potentiometric, UV-visible absorption titration and emission spectrophotometry. Luminescence quantum yields of the Tb(III) complexes were measured according to conventional procedures.[4] The kinetic inertness of those complexes were studied by adding them either to an aqueous solution and $ZnCl_2$ aqueous solution at different pH or to PBS and mouse serum.

Despite their apparent similarity, these two octadentate ligands differ in their most stable conformation, namely chair-chair conformation for $H_4\mathbf{L^2}$ and chair-boat conformation for $H_6\mathbf{L^1}$.[5] Those conformation has been confirmed by NMR studies and the physico-chemical results. The luminescence properties of the isolated Tb(III) complexes have shown the formation of nona-coordinated complexes with one water molecule completing the Tb(III) inner-sphere but no crystalline structure could be obtained with either Tb(III) or Sc(III) complexes. The first radiolabelling tests on ^{44}Sc were carried out with the $H_4\mathbf{L^2}$ ligand and the results showed good complexation under mild conditions.

To conclude, the resulting data of this study showed that picolinate is a better subunit for the complexation of Tb(III) or Sc(III) with bispidine structure. The high kinetic inertness of [Tb($\mathbf{L^2}$)], the good radiolabeling of the ^{44}Sc with $H_4\mathbf{L^2}$ and the bifunctionalization of $H_4\mathbf{L^2}$ pave the way for the development of inert and bioconjugated probes for theragnostic applications.

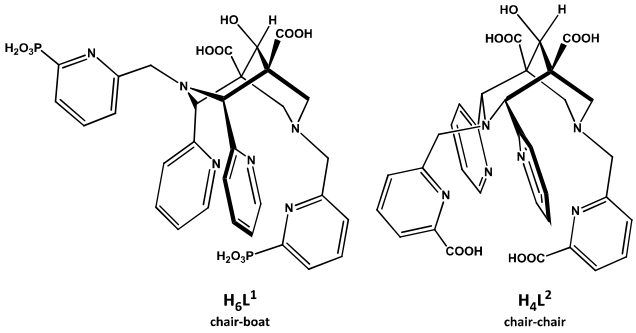

Figure 1: 3D structure of ligand H_6L^1 (left) and H_4L^2 (right).

References:

[1] E. May, M. Thoennsen, *Atomic Data and Nuclear Data Tables* **2013**, 99, 1-21.

[2] R. Mikolajczak, S. Huclier-Markai, C. Alliot, F. Haddad, D. Szikra, V. Forgacs, P. Garnuszek, *EJNMMI Radiopharm. Chem.* **2021**, 6, 19.

[3] D. Ndiaye, M. Sy, A. Pallier, S. Même, I. de Silva, S. Lacerda, A. M. Nonat, L. J. Charbonnière, É. Tóth, *Angewandte Chemie International Edition* **2020**, 59, 11958–11963.

[4] B. Valeur, M. N. Berberan-Santos, Molecular Fluoresence: Principles and Applications., 2nd edition, Wiley **2001**.

[5] T. Legdali, A. Roux, C. Platas-Iglesias, F. Camerel, A. M. Nonat, L. J. Charbonnière, *J. Org. Chem.* **2012**, 77, 11167–11176.

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Vanadium-containing ionic liquids

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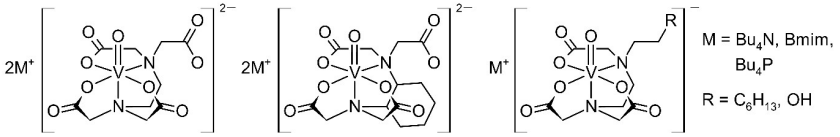
Transition-metal-containing ionic liquids (TM-ILs) have been extensively studied since a strong magnetic field response was discovered for paramagnetic [Bmim][$FeCl_4$] [1]. TM-ILs are usually classified as task-specific, as their role goes beyond that of a solvent. Transition metals present in the cation or anion catalyze various reactions used for organic synthesis, and industrially relevant processes [2]. Furthermore, they were found to be suitable precursors for the electrodeposition of transition metals [3]. Magnetic TM-ILs have been thoroughly scrutinized, leading to their use in the fields of analytical microextraction [4]. Although ILs containing first-raw transition metals have been deeply scrutinized, only a few studies have dealt with vanadium. They contain vanadium in the form of vanadate [5] and molybdovanadate anions [6].

This study deals with stabilized anionic oxidovanadium(IV) complex ligands ethylenediaminetetraacete (edta) and its congeners 1,2-diaminocyclohexanetetraacetate (dcta), *N*-octylethylenediaminetriacetate (oedta) and hydroxyethylethylenediaminetriacetate (heedta). As counter ions, common cations of tetrabutylammonium (Bu_4N), 1-butyl-3-methylimidazolium (Bmim) and tetrabutylphosphonium (Bu_4P) are used (Scheme 1).



Scheme 1: prepared ionic liquids with vanadium present in the anionic part.

Vanadium-containing ILs were prepared from oxidovanadium(IV) sulfate and the edta congeners in an aqueous solution. In the first step, coordination of the polydentate ligands proceeds to give stable anionic complexes, isolated in the form of barium salts. In a second step, the series of ILs was prepared by cation exchange. The final product and barium intermediates were characterized by analytical methods including elemental analysis and

mass spectrometry. The content of vanadium, barium, and phosphorus was determined by ICP-OES spectroscopy.

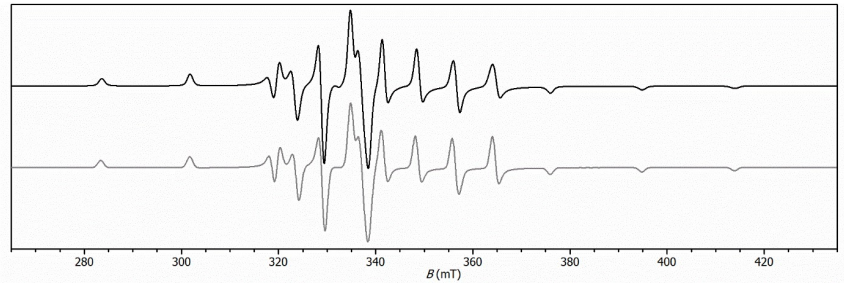


Figure 1: frozen solution EPR spectrum of $[Bu_4N]_2[VO(oedta)]$ collected at 123 K (top) and its computer simulation (bottom).

EPR spectroscopy allowed us to follow the vanadium(IV) species upon synthesis. It proves the high stability of anionic complexes in water and in coordinating solvents. Very similar EPR parameters observed for complexes bearing edta, oedta and heedta prove virtually the same coordination sphere of vanadium(IV) atom. Figure 1 shows an anisotropic spectrum $[Bu_4N]_2[VO(oedta)]$ measured in frozen solution that reveals the axial symmetry of the SOMO orbital. The lower values of the HFC constant in the dtca complexes are ascribed to the geometrical constrain caused by the cyclohexane ring.

Selected vanadium-based ILs were tested on catalytic activity. They exhibit improved activity toward ring-opening copolymerization of epoxide resin with cyclic anhydrides.

References:

[1] S. Hayashi, H. Hamaguchi, *Chem. Lett.* **2004**, 33 (12), 1590.

[2] R. Giernoth, *Angew. Chem. Int. Ed.* **2010**, 49 (16), 2834-2839.

[3] J. Sniekers, P. Geysens, T. V. Hoogerstraete, L. Van Meervelt, J. Fransaer, K. Binnemans, *Dalton Trans.* **2018**, 47 (14), 4975-4986.

[4] L. Qiao, Y. Tao, H. Qin, R. Niu, *J. Chromatogr. A* **2023**, 1689, 463771.

[5] A. Branco, J. Belchior, L. C. Branco, F. Pina, *RSC Adv.* **2013**, 3 (48), 25627-25630.

[6] E. Rafiee, M. Kahrizi, *J. Mol. Liq.* **2016**, 218, 625-631.

The authors acknowledge the financial support from the Czech Science Foundation (GACR No. 22-05244S).

Speciation and redox-properties study of n-hydroxycoumarins complexes with copper(II) and vanadium(IV/V) metal ions

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Please use Calibri, Coumarins are a class of naturally occurring compounds with interesting biological features. This family of compounds comprise several 1,2-benzopyrone derivatives that in the recent years have been intensely studied as drug candidates. In particular, the role and implications of natural and synthetic coumarins have been investigated in human biology due to their great therapeutic potential. Their biological properties include anticancer, antimicrobial, antiviral, anti-inflammatory, neuroprotective and antioxidant activities.

Several studies highlighted the role of coumarins as antioxidant agents. The antioxidant activity is not only based on direct scavenging of reactive oxygen and nitrogen species (RONS) but is also linked to other mechanisms. These latter include *i)* the chelation of Fenton-active metal ions and *ii)* the inhibition of RONS-producing enzymes. The mechanisms involved in the antioxidant activity of coumarin derivatives appears to be complex and synergistic. Furthermore, biological properties of coumarins can be radically changed combining the coumarin moiety with metal ions [1].

n-Hydroxylated coumarin derivatives show pronounced antioxidant activity and moderate metal binding abilities [2]. The study of their interaction with biological relevant metal ions (especially redox-active metals) represents an interesting approach to further elucidate the implications of coumarin derivatives in biological fluids.

In this work, simple n-hydroxylated coumarins as 3-hydroxycoumarin, 4-hydroxycoumarin and 6,7-hydroxycoumarin were studied in combination with copper(II) and vanadium(IV/V) metal ions.

Copper plays an essential role in human physiology. An excess or lack of this metal could be associated with pathological states: its chelation could therefore represent a possible

therapeutic strategy [3]. Nevertheless, copper is involved also in the functioning of a series of redox active metalloenzyme and therapeutical compounds as antioxidant metalloenzymes mimics [4].

Oxovanadium(IV) and vanadium(V) represent the most biological relevant vanadium oxidation states [5]. Vanadium(IV/V) compounds showing a plethora of biological activities have been studied and characterized. Anyway, the distribution and the interconversion between V(IV) and V(V) in biological fluids still remains an interesting research topic.

Due to the interesting biological and redox properties of coumarin derivatives and the cited metal ion, the speciation of Cu(II), V(IV) and V(V) with the above mentioned n-hydroxylated coumarins was studied in aqueous solution at 25 °C and 0.2 $mol \cdot L^{-1}$ in $KCl_{(aq)}$.

Potentiometric and UV-Vis spectrophotometric titrations were exploited to investigate the metal-ligand system over a wide pH range, including physiological pH 7.4. When interaction between the two components was observed the metal complexes were characterized, the stoichiometries were elucidated and their formation constants were refined. Other spectroscopic techniques as NMR and EPR spectroscopy were exploited to extensively study the considered system. The redox behavior of the metal-ligand system was investigated by voltammetric techniques and antioxidant assays.

References:

[1] Ł. Balewski, S. Szulta, A. Jalińska, A. Kornicka, *Front Chem* **2021** 9.

[2] T. Filipsk, M. Íha, K. Macáková, E. Anzenbacherová, J. Karlíková and P. Mladnka, *Curr Top Med Chem* **2015**, 15.

[3] M. C. Catapano, J. Karlíčková, V. Tvrdý, S. Sharma, A. K. Prasad, L. Saso, A. K. Chhillar, J. Kuneš, M. Pour, V. S. Parmar and P. Mladěnka, *Journal of Trace Elements in Medicine and Biology*, **2018**, 46, 88–95.

[4] C. Policar, J. Bouvet, H. C. Bertrand and N. Delsuc, *Curr Opin Chem Biol*, **2022**, 67.

[5] D. C. Crans and P. B. Chatterjee, in *Comprehensive Inorganic Chemistry II (Second Edition): From Elements to Applications*, Elsevier Ltd, **2013**, vol. 3, pp. 323–342.

ISMEC 2024
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Lanthanide complexation by phenanthroline carboxamides

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Coordination chemistry is the basis of neutral solvent extraction, whose aim is to separate one or several particles from an aqueous mixture by contacting it to an immiscible organic phase containing selective molecules. The reaction then follows a two-steps mechanism, with first the selective coordination of the targeted particles by the organic molecules at the interface, and then the transfer of the formed neutral complexes to the organic phase.

Recently, research on the mutual separation of lanthanides has gained a renewed interest considering the increasing industrial demand for highly pure materials. The main focus is on designing new molecules and/or developing new processes that are more efficient than the phosphor-based organic acids commonly in use. Among the newly developed families, the phenanthroline carboxamides are particularly promising.[1–7] Indeed, high separation factors of adjacent light lanthanides could be reached in optimized conditions.[8,9] Both the mono- (PTA) and di-carboxamides (PTdA) were studied (Figure 1, left), as they present different coordinating sites (tridentate vs tetradentate, respectively). The different coordination induces differences in selectivity among the lanthanides (Figure 1, right), even though in both cases a preference for the light Lns is observed.

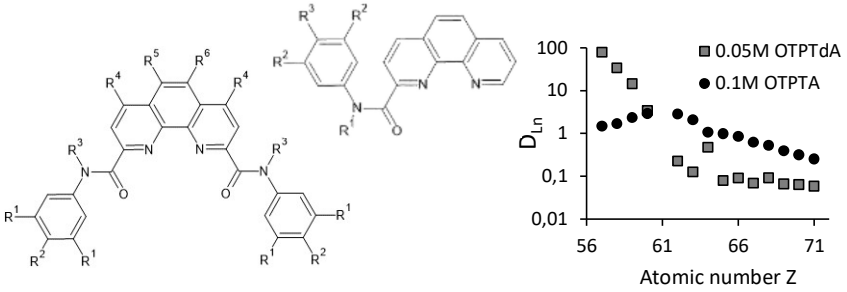

Figure 1: Left: Phenanthroline dicarboxamides (PTdA) and monocarboxamides (PTA) Right: Ln distribution ratios vs the Ln series; octyl-tolyl ligands diluted in chloroform, aqueous phase 0.1 M HNO_3 1 M HNO_3 7 ppm of each Ln

In all studied systems, a maximum of extraction appeared with PTA, for which the preferred extracted light Ln depended on the amide substituents of the extractant and on the diluent. This is due to a variation of the ideal matching size between the Ln ionic radii and the cavity formed by ligands and anions around the metal; the size of this cavity is mainly based on the position of the carboxamide oxygen, itself dependent on the amide substituents and their interactions with the outer sphere.

More advanced studies showed an unexpected modification of the selectivity along the lanthanide series depending on the chosen counter-ion[7]. This behaviour occurred for both PTA and PTdA, and spectroscopic techniques (UV-Vis, EXAFS) were used to investigate these changes. The resulting trends for five inorganic anions with PTA are displayed in Figure 2. The above-mentioned preference for the light Ln in a nitrate medium reverses in sulfate, chloride and nitrite media, for which an increase in D_{Ln} all along the series is observed. Perchlorate medium follows a similar trend, although a maximum appears around Dy. We also observed a change in the stoichiometry of the complexes depending on the counter-ion, *i.e.* three PTA for perchlorate anions but only two for nitrate and chloride anions. The different extraction trends were eventually explained by a change in the coordination depending on the location of the counter-ion in the organic phase, inducing a different ligand stoichiometry. The polarity of the diluent was also found to impact the selectivity through a better stabilization of the anion.

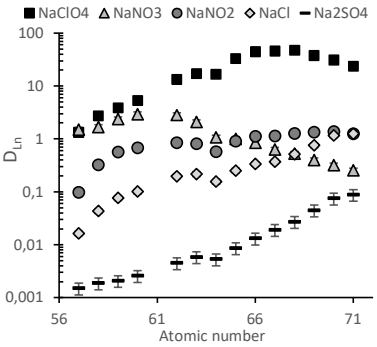

Figure 2: Ln distribution ratios vs the Ln series, 0.1 M PTA in chloroform, 1 mM HX and 1 M NaX (0.1 M $NaClO_4$) and 7 ppm of each Ln

This finding paves an interesting new way of optimizing the separation by a careful choice of the {diluent, counterion} pair.

[1] Alyapyshev, *et al.*, *RSC Adv.* **2016**, *6* (73), 68642–68652. DOI: 10.1039/C6RA08946A.
[2] E. M. Archer, *et al.*, *Solvent Extr Ion Exch* **2023**, *41* (6), 697–740. DOI: 10.1080/07366299.2023.2239866.
[3] D. Merrill, R. D. Hancock, *Radiochimica Acta* **2011**, *99* (3), 161–166. DOI: 10.1524/ract.2011.1805.
[4] N. J. Williams, *et al,. Inorg. Chem.* **2009**, *48* (16), 7853–7863. DOI: 10.1021/ic900737q.
[5] N. Tsutsui, *et al.*, *ANAL. SCI.* **2020**, *36* (2), 241–245. DOI: 10.2116/analsci.19P275.
[6] M. Simonnet, *et al.*, *Inorg. Chem.* **2021**, *60* (17), 13409–13418. DOI: 10.1021/acs.inorgchem.1c01729.
[7] M. Simonnet, *et al.*, *Solvent Extr Ion Exch* **2020**, *38* (4), 430–440. DOI: 10.1080/07366299.2020.1744806.
[8] M. Simonnet, *et al., Solvent Extr Ion Exch* **2023**, *41* (7), 857–867. DOI: 10.1080/07366299.2023.2248189.
[9] K. R. Johnson, *et al.*, *JACS Au* **2023**, *3* (2), 584–591. DOI: 10.1021/jacsau.2c00671.

How terminal protection affects the chemical and biological properties of the antimicrobial calcitermin

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The discovery of antibiotics changed modern medicine, both drastically reducing the severity of many bacterial diseases, and allowing spectacular progress in other fields, such as chemotherapy, surgery, and organ transplant. However, the abuse and misuse of these excellent drugs has led to an increase of antimicrobial resistance (AMR), a phenomenon which occurs when microorganisms learn to adapt and grow in the presence of previously effective medications. AMR would require the continuous discover and introduction of new antibiotics, but, unfortunately, in the last decades, the investments in this field have been highly insufficient to face the clinical and financial burden due to AMR [1].

Antimicrobial peptides (AMPs) represent a promising base for developing new drugs since they present a broad spectrum of activity and a scarce attitude to induce antimicrobial resistance. In fact, their activity can be exerted through different mechanisms of action such as the interaction with cell membranes and the innate immune response termed "nutritional immunity". AMPs act as mediators of the immune defence through the sequestration of metallic nutrients such as Zn^{2+}, Cu^{2+}, Mn^{2+} or Ca^{2+}, interfering with the homeostasis of the pathogenic cells [2]. On the other hand, AMPs present the drawback of a metabolic instability since they are subject to degradation by both human and pathogenic proteolytic enzymes.

Calcitermin is a human, 15-amino acid, antimicrobial peptide (VAIALKAAHYHTHKE), corresponding to the C-terminal domain of calgranulin C, a pro-inflammatory protein of the S100 family [3]. It presents an effective metal-binding domain with three alternated histidine residues (His9, His11 and His13) and the free terminal amino and carboxyl groups. Several studies showed an increased microbicide activity when Zn^{2+} and Cu^{2+} ions are present in the culture medium. Our research group have recently determined the stability of this calcitermin in human plasma which corresponds to a half-life of 18 minutes [4]. In order to extend this lifetime, i.e. to obtain a better proteolytic resistance, without losing the antimicrobial properties, several strategies can be employed. To increase the resistance towards exo-peptidases (enzyme that catalyse the cleavage of the terminal peptide bonds), the chemical

modification of one or both the peptide ends can be applied. To this aim, we protected the amino- and carboxyl-termini of calcitermin by acetylation and amidation respectively [4], obtaining the following derivatives: Ac-VAIALKAAHYHTHKE, Ac-VAIALKAAHYHTHKE-NH_2 and VAIALKAAHYHTHKE-NH_2. Of note, the introduction of such terminal protection preserves the metal binding site of calcitermin, corresponding to the histidine motif –HxHxH-.

We investigated the complex-formation equilibria of these mutants with Zn^{2+} and Cu^{2+} by means of different experimental techniques: mass spectrometry, potentiometry, UV-Vis spectrophotometry, circular dichroism and electron paramagnetic resonance. In addition, the peptide stability in human plasma was determined by HPLC and the antimicrobial activity towards different potential pathogens has also been investigated.

The results show that with both copper and zinc, the most stable complexes are always those formed by the native calcitermin, throughout the explored pH range, suggesting an evident contribution of the amino and carboxyl termini. As expected, the acetylation of the N-terminal confers a much longer half-life with respect to peptides with free amino terminus. Interestingly, the formation of both copper and zinc complexes almost doubled the half-life of calcitermin in human plasma. Finally, encouraging results have been obtained for the Zn^{2+} complexes of the protected peptides against *Candida albicans.*

References:

[1] D. M. P. De Oliveira, B. M. Forde, T. J. Kidd, P. N. A. Harris, M. A. Schembri, S. A. Beatson, D. L. Paterson and M. J. Walker, *Clin. Microbiol. Rev.*, **2020**, 33.

[2] D. Dudek, H. Kozlowski and M. Rowinska-Zyrek, *NJCh,* 2018, 42.

[3] A. M. Cole, Y. H. Kim, S. Tahk, T. Hong, P. Weis, A. J. Waring and T. Ganz, *FEBS Lett.*, **2001**, 504, 5-10.

[4] M. D'Accolti, D. Bellotti, E. Dzień, C. Leonetti, S. Leveraro, V. Albanese, E. Marzola, R. Guerrini, E. Caselli, M. Rowińska-Żyrek, M. Remelli, *Scientic reports*, **2023**, 13 (1), 18228.

Scandium(III) hydrolysis and complexation studies with desferrioxamine B

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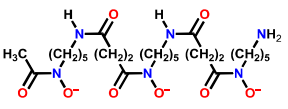
Scandium exists only in the trivalent oxidation state in aqueous solutions, with coordination numbers (CN) equal to 3, 6, 7, 8, and 9. Crystal structures containing the $[Sc(H_2O)_x]^{3+}$ (x = 6–9) hydrated cations have been described [1]. Owing to the d^0 electronic configuration and rather small ionic radius (0.745 Å for CN = 6), scandium(III) is a hard Lewis acid sharing some common features with aluminum and lanthanides, among them the high affinity for oxygen donor ligands, but it shows a stronger tendency to undergo hydrolysis and polycondensation reactions even at low pH [2]. The free aqua ion is only stable in acidic solutions (pH < ~2.5), while scandium exhibits an amphoteric character at high pH values. Besides mononuclear $[Sc(OH)_x]^{(3-x)+}$ hydrolyzed species with x = 1–4, olation promotes the formation of polynuclear hydroxides, although clear evidence has only been provided for two species, the $[Sc_2(OH)_2]^{4+}$ dimer and $[Sc_3(OH)_5]^{4+}$ trimer.

In nature, scandium is found as a single, NMR active, isotope (^{45}Sc, I = 7/2) of rather high receptivity (0.302 with respect to ^1H). Although the quadrupolar moment is responsible for line broadening that increases upon symmetry lowering, ^{45}Sc NMR spectroscopy turns out to be a valuable technique for probing the chemical environment as the chemical shifts span a wide range of ca. 350 ppm (from –100 to 250 ppm with respect to $Sc(ClO_4)_3$ in 1 M $HClO_4$ [3].

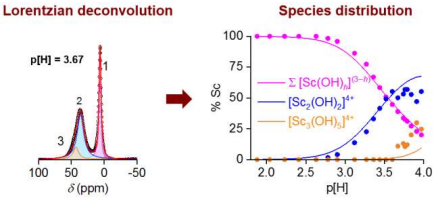
Over the last decade, the coordination chemistry of scandium(III) has experienced an upsurge in interest, spurred by the possibility to use ^{44}Sc ($T_{1/2}$ = 3.97 h) in positron emission tomography (PET) and the β^- emitting isotope ^{47}Sc ($T_{1/2}$ = 3.35 d) in radiotherapy [3]. Moreover, the possibility to generate in a cyclotron ^{44m}Sc that decays into ^{44}Sc with emission of soft γ rays with a half-life ($T_{1/2}$ = 2.44 d) that is compatible with the pharmacokinetics of antibodies, paves the way towards an *in vivo* $^{44m}Sc/^{44}Sc$ generator. Hence, $^{44/44m}Sc$ together with ^{47}Sc is considered as a most promising radioimmunotheranostic pair in oncology. Radiopharmaceuticals incorporating bifunctional chelators derived from either the

octadentate linear $DTPA^{5-}$ (diethylene-triamine-*N*,*N*,*N*′,*N*′′,*N*′′-pentaacetate) or the macrocyclic $DOTA^{4-}$ (1,4,7,10-tetraazacyclo-dodecane-1,4,7,10-tetraacetate) binders have been tested. However, as efficient radiolabeling of $DOTA^{4-}$ can only be achieved at elevated temperatures, usually above the denaturation point of proteins and thus of antibodies, bioconjugates made thereof are restricted to oligopeptides. Thus, the search for mild-labeling alternative bifunctional chelators that provide in vivo stability is ongoing.



Desferrioxamine B (DFO), the emblematic hexadentate trishydroxamic siderophore excreted by *Streptomyces* bacteria, is an authorized drug for treating iron or aluminum overloads in humans, but is also entitled as the "gold standard" for chelating another positron emitter, $^{89}Zr^{4+}$ [4]. Currently, ^{89}Zr-labeled DFO immunobioconjugates are the only constructs that have been translated for human applications. Our on-going work intends to evaluate the potency of DFO to bind efficiently Sc^{3+} *in vitro* before envisaging *in vivo* tests. The presentation will focus on:

- The implementation of ^{45}Sc NMR spectroscopy for investigating the hydrolytic behavior of Sc^{3+} in aqueous media;



- The speciation study of the Sc^{3+}/DFO^{3-} system by combining ^{1}H, ^{13}C, and ^{45}Sc NMR spectroscopic measurements.

Acknowledgements:

Authors thank the CNRS and the French Grant Agency ANR (project n° ANR-21-CE19-0037) for financial support, and the French Embassy in the United States for a Chateaubriand fellowship to A.H.

References:

[1] On-line Cambridge Structural Database, https://www.ccdc.cam.ac.uk/.

[2] P. L. Brown, C. Ekberg, *Hydrolysis of Metal Ions*. Wiley-VCH: Weinheim, **2016**, Vol. 1.

[3] R. Kerdjoudj, M. Pniok, C. Alliot, V. Kubicek, J. Havlickova, F. Rosch, P. Hermann, S. Huclier-Markai, *Dalton Trans.* **2016**, *45*, 1398–1409.

[4] R. Raavé, G. Sandker, P. Adumeau, C. B. Jacobsen, F. Mangin, M. Meyer, M. Moreau, C. Bernhard, L. Da Costa, A. Dubois, V. Goncalves, M. Gustafsson, M. Rijpkema, O. Boerman, J.-C. Chambron, S. Heskamp, F. Denat, *Eur. J. Nucl. Med. Mol. Imaging* **2019**, *46*, 1966–1977.

A novel phenantroline- coumarine based fluorescence sensor for Cd(II) and Hg(II)

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The public safety and environmental preservation prompt the interest of scientific communities towards the detection of harmful environmental analytes, such as heavy metal ions. The presence of heavy metal ions in the environment represents a major concern because of their toxicity for human life and ecosystem. Among the various metal ion-based pollutants, mercury and cadmium ions stand out as a leading contaminant to both human health and environment. The presence of cadmium in soil and water is attributed to agricultural practices and to industrial activities. Consequently, exposure to cadmium, also through the food chain, can result in various health issues, including anemia, abdominal pain, neurological disorders, and others. Another important chemical pollutant is the mercury, whose presence stems from both natural and anthropogenic sources. Through high bioaccumulation and bio-amplification factors, the mercury compounds end up in the food chain and even small amounts of mercury in the body can cause long-term and irreversible damage to human health.

For these reasons, there is a growing need to develop new sensors, for metal ion pollutants, characterized by high sensitivity. In this field, fluorescence based chemosensors are very interesting.

We have designed a novel phenanthroline-coumarin fluorescence sensor (HL) for the detection of cadmium and mercury. From our studies, it became apparent that our sensor behaves as a ratiometric sensor towards cadmium and as a turn-on fluorescence sensor towards mercury, demonstrating strong specificity for both metals (fig.1).

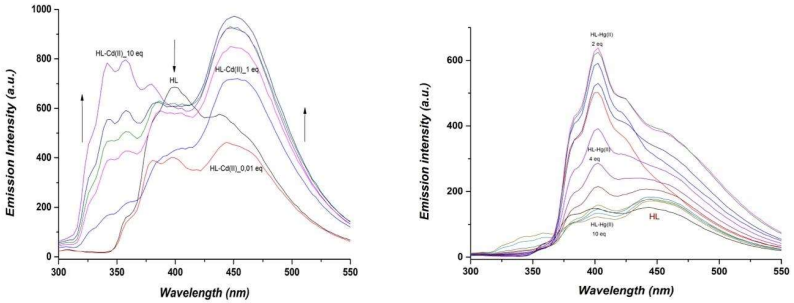

Fig.1. Changes of the fluorescence spectra of HL upon titration by Cd(II) in CH_3CN/H_2O. λexc = 282 nm, Exc slit = 5 nm, Em slit = 5 nm, Scan rate = 384 nm/min, Ave time = 0,5 s, Data interval = 3,2 nm, PMT = 885 (left), and by Hg(II) (7,07x10-4 M) in CH_3CN/H_2O. λexc = 282 nm, Exc slit = 5 nm, Em slit = 5 nm, Scan rate = 384 nm/min, Ave time = 0,5 s, Data interval = 3,2 nm, PMT = 700 (right).

References:

[1] RSC Adv., 2021, 11, 29632

[2] Journal of Luminescence 183 (2017) 315–321

[3] RSC Adv., 2016, 6, 23169

Green synthesis of biomass-derived Carbon Quantum Dots for metal ion sensing: optimization, characterization, and binding affinity studies

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Since the discovery of Carbon Quantum Dots (CQDs) in 2004 [1], interest in these materials has increased over the past two decades. CQDs are photoluminescent carbonaceous nanomaterials characterized by a particle size smaller than 10 nm and the presence of hybridized sp^2 carbon and oxygen-containing groups on their surface. The existence of these functional groups makes CQDs prone to interaction with metal cations, leading to the quenching of photoluminescence even at low metal concentrations. Consequently, extensive research has been conducted on the potential application of CQDs in metal ion sensing, often showing good selectivity [2].

Moreover, the synthesis of CQDs from green sources, like biomasses, presents a promising alternative for waste management, allowing for the reuse of agricultural and food industry wastes. This approach has gained significant attention due to the biocompatibility and cost-effectiveness of the starting materials [3]. Among the various preparation strategies, the hydrothermal method is the most common and environmentally friendly approach, involving the heating of a water suspension of the precursor in an autoclave for a certain amount of time [4].

In this study, biomass-based CQDs were synthesized using citrus waste lyophilized bergamot pomace as a precursor. Following optimization of the synthesis parameters, CQDs were obtained by employing 200 mg of lyophilized pomace in 25 mL of water, heated in a Teflon vessel within a stainless autoclave at 210 °C for 9 hours. The resulting product underwent purification via dialysis for 48 hours and filtration through a 0.22 µm filter. Subsequently, the photoluminescence properties of the CQDs were investigated, alongside particle size evaluation through Transmission Electron Microscopy and surface group analysis using ATR-FTIR spectroscopy. The quantum yield was determined using quinine sulfate as a reference.

Potentiometric titrations were also conducted to aid in the determination of surface groups capable of interacting with metal cations and their respective protonation constants [5]. Finally, the ability of the CQDs obtained from lyophilized bergamot pomace to interact with different metal cations was examined. Copper, dysprosium and neodymium, exhibited the best capability to quench the luminescence of the CQDs. They are classified as Critical Raw Materials, whose recovery is of utmost importance in the technological industry [6]. Their interaction was further investigated through spectrofluorimetric titrations, enabling the determination of binding ability through the Stern-Volmer equation [7].

Aknowledgement: We thank MUR: PNRR - Missione 4, Componente 2, Investimento 1.1 - Bando Prin 2022 - Decreto Direttoriale n. 104 del 02-02-2022. Project title: "Wastezilla: Recycled waste biomass for efficient recovery of critical elements". CUP: J53D23007540006 – project code: PRIN_2022HYH95P_001.

References:

[1] X. Xu, R. Ray, Y. Gu, H.J. Ploehn, L. Gearheart, K. Raker, W.A. Scrivens, *J. Am. Chem. Soc.* **2004**, 126 (40), 12736–12737.

[2] X. Gao, C. Du, Z. Zhuang, W. Chen, *J. Mater. Chem. C* **2016**, 4 (29), 6927–6945.

[3] S. Mathew, B. Mathew, *Inorg. Chem. Commun.* **2023**, 156, 111223.

[4] M. Palacio-Vergara, M. Álvarez-Gómez, J. Gallego, D. López, *Talanta Open* **2023**, 8, 100244.

[5] Z. Wang, Y. Xie, Z. Lei, Y. Lu, G. Wei, S. Liu, C. Xu, Z. Zhang, X. Wang, L. Rao, J. Chen, *Anal. Chem.* **2019**, 91 (15), 9690–9697.

[6] M. Grohol, C. Veeh, Study on the Critical Raw Materials for the EU 2023: Final Report; Publications Office of the European Union, 2023.

[7] J.R. Lakowicz, Principles of Fluorescence Spectroscopy; Ed.; Springer US: Boston, MA, **2006**.

A combined theoretical/spectroscopic study on the ring-opening mechanism in a prototype rhodamine-based fluorescent dye for pH sensing

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Monitoring pH in strongly acidic solutions is of relevant importance in many applications. An accurate pH measurement in environments with high and/or variable ionic strength, requires a continuous calibration of the glass electrode often in matrices difficult to mimic. In similar conditions, a device able to signal the acidity of the solution in easy and fast way is a convenient alternative method. Several pH fluorescent probes have been developed, given their remarkable advantages in terms of selectivity, sensitivity, low-cost, simple operations and real time monitoring [1-3]. Anyway, since most pH probes reported in literature are used to monitor pH values higher than four, it remains a challenge to detect pH in extremely acidic conditions.

Rhodamine derivatives have been largely employed for the detection of several analytes and to monitor pH, but few of them could be used at pH lower than 3. At pH ≥ 7, the rhodamine amide derivatives in their spirolactam form, are not absorbing or emitting in the visible range. However, metal or proton ion(s) binding in specific site, induce a structural change from the spirocyclic to the ring opening-form, giving rise to a strong fluorescence emission and a visible absorption. Despite the high number of prepared rhodamines, the response of the sensor strictly connected to the spirolactam opening, remains not fully understood. Also the presence of multiple basic groups, i.e. amines and/or substituted amines, in the backbone of the molecule, could play a relevant role, since they may vary the pH at which the spirolactam opens, but this process is often unconsidered.

We prepared a fluorescent chemosensor (RhO-L3) that could be used to monitor the pH in a wide range of proton concentration, from mmolar to molar range, exploiting its strong UV-Vis absorption and emission (Figure 1). This hybrid platform presents multiple basic sites and it has been chosen as suitable prototype sensor able to interact with the proton in different ways.

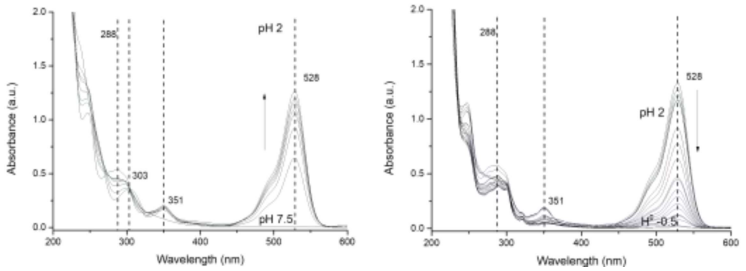

Figure 1. Selected absorption spectra recorded during the spectrophotometric titration of **RhO-L$_3$**, from pH 7.0 to 2 (a) and from 2 to H^0 -1. (CH3CN-H2O 4:1, ligand concentration 2.5x10-5 M, ionic strength 0.001 M KCl, T 298 K).

References:

[1] A. Black, B. White, C. Green, D.-W. Brown, *Journal* **Year**, volume (issue), 10-15. Y. Chen, Analytical Biochemistry 2021, 612, 113900, doi:10.1016/j.ab.2020.113900.

[2] M. Oggianu, C. Figus, S. Ashoka-Sahadevan, N. Monni,; D. Marongiu, M. Saba, A. Mura, G. Bongiovanni, C. Caltagirone, V. Lippolis, et al. RSC Advances 2021, 11, 15557–15564, doi:10.1039/d1ra02695j.

[3] T. Pivetta, S. Masuri, M.G. Cabiddu, F. Isaia, E. Cadoni, New Journal of Chemistry, 2019, 43(30), pp. 12032–12041

Selective Pd(II) metal complexes for the design of supramolecular hybrid Pd(II)-DNA arrays

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DNA nanotechnology takes advantage of the properties of this biomolecule, mainly water solubility and self-recognition, to assemble supramolecular motifs with enhanced physicochemical properties that feature novel applications [1]. In this context, DNA metallization is one of the most successful strategies promoting physicochemical properties that are not intrinsic to DNA, for instance conductivity, catalytic activity, magnetism, and photoactivity [2]. To design and predict the formation of tailored metalated DNA-structures, a comprehensive knowledge of their intimate structure is required, including the supramolecular recognition by non-covalent intermolecular interactions; however, the crystallization and crystal structure determination of DNA is not an easy task. Therefore, solution studies become essential to comprehensively explain the equilibria that certainly exists in such systems and complement the available solid-state data.

Results will show how Pd(II) metal complexes can be successfully accommodated throughout DNA homopolymers yielding a double-stranded DNA structure, forming a continuous one-dimensional metal array (Figure 1). On one hand, the metal complex [Pd(Cheld)(CH3CN)] (Cheld=chelidamic acid) self-assembles with single-stranded polydeoxyadenosine (dA15) or polydeoxydeazaadenosine(ddA15) [3]. On the other hand, the metal complex [Pd(Aqa)(DMSO)] (Aqa=8-amino-4-hydroxyquinoline-2-carboxylic acid) self-assembles with a single-stranded polydeoxycytosine (dC15) [4], both cases yielding the formation of a supramolecular Pd-DNA hybrid structure. Such palladium(II)-mediated base pairs in a continuous DNA array (Figure 1) are fully characterized by a combination of different solution techniques including UV-Vis spectroscopy, circular dichroism, mass spectrometry and NMR spectroscopy.

Competitive binding assays using circular dichroism titration experiments and isothermal titration calorimetry measurements demonstrate the preferential binding of Pd-Aqa to cytosine compared to Pd-Cheld. The key aspects that drive metal ion coordination within the nucleoside moieties as well as the most relevant molecular recognition aspects will be discussed, trying to rationalize the rational design of strategic metal complexes to build future metal-based DNA nanowires.

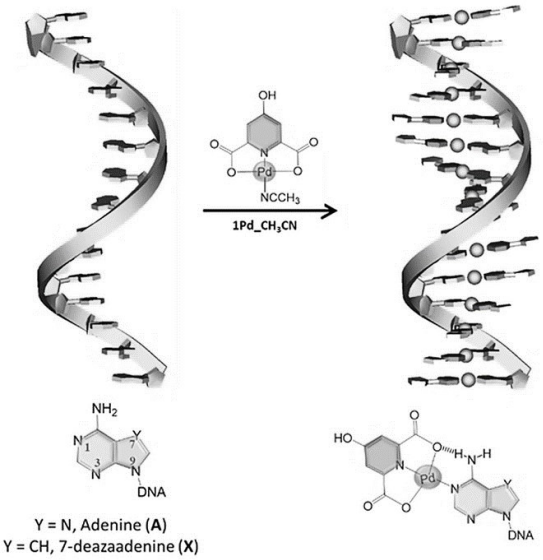

Figure 1: Scheme of the formation of palladium-mediated base pairs. Adapted from reference [3].

Acknowledgements: Financial support from Spanish Ministerio de Ciencia e Innovación (projects PID2020-120186RB-I00 and PID2022-138479NB-I00), Junta de Andalucia (project P20_00702). University of Granada (A-FQM-465-UGR18), and Junta de Andalucía (FQM-293 and FQM-283) is gratefully acknowledged.

References:

[1] X. Dai, Q. Li, A. Aldalbahi, L. Wang, C. Fan, X. Liu, *Nano Lett*. **2020**, 20, 5604–5615.

[2] Z. Chen, C. Liu, F. Cao, J. Ren, X. Qu, *Chem. Soc. Rev.* **2018**, 47, 4017–4072.

[3] A. Pérez-Romero, A. Domínguez-Martín, S. Galli, N. Santamaría-Díaz, O. Palacios, J.A. Dobado, M. Nyman, M.A. Galindo, *Angew. Chem. Int. Ed*. **2021**, 133(18) 10177-10182.

[4] A. Pérez-Romero, M. Cano-Muñoz, C. López-Chamorro, F. Conejero-Lara, O. Palacios, J. A. Dobado, M. A. Galindo, *Angew. Chem. Int. Ed.* **2024**, 63, e202400261.

Metal adsorption on functionalised mesoporous silica: isothermal titration calorimetry (ITC) applied to solid-liquid systems

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The rapid growth of industry and human activity led to the generation of large amounts of wastewater contaminated with hazardous metals, such as Cd or Pb, which are a great threat to the environment and may have serious consequences for all living organisms [1]. In this work, a material (SBA-GSH) based on mesoporous silica SBA-15 and glutathione (GSH), a biologically relevant ligand, has been developed [2]. GSH is the main source of non-protein thiols in cells, known for its ability to bind metal ions [3]. Therefore, the developed material showed good adsorption capacities for several metal ions such as Cd(II) (1,03 $mmol_{Cd}.g^{-1}$) or Pb(II) (0,70 $mmol_{Pb}.g^{-1}$), lower affinities for Cu(II) and a selectivity for Pb(II).

Isothermal titration calorimetry (ITC) appeared as a good technique to get information on both the adsorption thermodynamics and competition effects in this system [4, 5]. In this work, we used ITC to investigate the mechanism of adsorption of three metal ions: Cd(II), Cu(II) and Pb(II) on SBA-GSH. Results allowed to better understand the nature of the interactions involved in the adsorption mechanism. In particular, it was found that Cd(II) adsorption relied mainly on physical contributions while Cu(II) and Pb(II) adsorption was shown to be chemically driven [6].

References:

[1] C. Femina Carolin, P. Senthil Kumar, A. Saravanan, G. Janet Joshiba, Mu. Naushad, *Journal of Environmental Chemical Engineering* **2017**, 5 (3), 2782-2799.
[2] C. Gourmand, C. Bertagnolli, J. Brandel, V. Hubscher-Bruder, A. Boos, *Industrial & Engineering Chemistry Research* **2022**, 61(23), 8188-8203.
[3] A. Devez, E. Achterberg, M. Gledhill, Metal Ion-Binding Properties of Phytochelatins and Related Ligands. In *Metallothioneins and Related Chelators : Metal Ions in Life Sciences*, A. Sigel, H. Sigel, R. K.O. Sigel, Eds. De Gruyter: Berlin, Boston, **2009**, Vol. 3, pp 441-481.
[4] M.-A. Ahmad, B. Prelot, J. Zajac, *Thermochimica Acta* **2020**, 694, 178800.
[5] B. Prelot, M. Araïssi, P. Gras, F. Marchandeau, J. Zajac, *Thermochimica Acta* **2018**, 664, 39-47.
[6] C. Gourmand, C. Bertagnolli, B. Prelot, A. Boos, V. Hubscher-Bruder, J. Brandel *Dalton. Trans.* **2024**, 53, 3690-3701.

Novel Fret based chemosensor for the recognition of Norfloxacin in aqueous solution

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The presence of antibiotics in water ecosystems has emerged as a significant environmental concern due to their potential adverse effects on ecological balance and human health. In this scenario, the widespread distribution of antibiotics in aquatic environments, coupled with their persistence, leads to continuous exposure to these compounds, which contributes to the development of multidrug resistance, undermining the effectiveness of traditional antibiotic treatments.[1] Among antibiotics, norfloxacin, commonly used to treat urinary infections, stand out as commonly detected pollutant, originating from various sources including pharmaceutical manufacturing and improper disposal of medications. In response to the urgent need for efficient and low-cost detection methods, we present the development of the novel chemical sensor N5CP *(figure 1)*, for the selective recognition of norfloxacin in water solution.

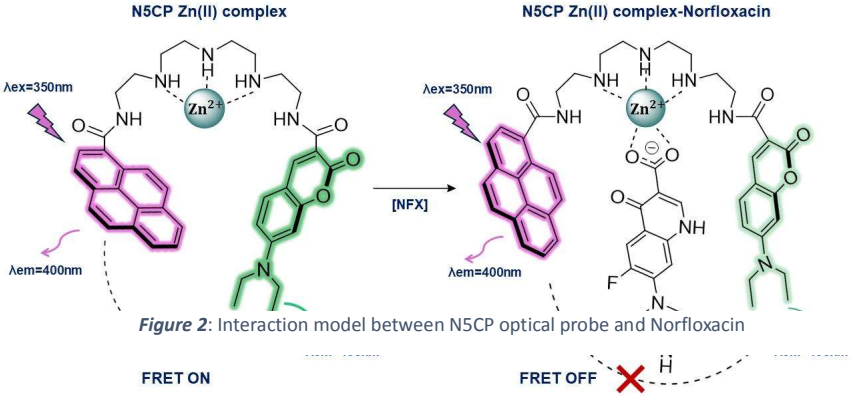

Figure 2: Interaction model between N5CP optical probe and Norfloxacin

Figure 1: Interaction model between optical probe N5CP and Norfloxacin

The optical probe was designed using a receptor-spacer-fluorophore modular approach.[2] The receptor unit incorporates a polyamine moiety known for its ability to form stable metal complexes with transition metals. These coordinated metals serve as anchoring points for the anionic head of the analytes, resulting in highly stable complexes. Among transition metals, we focused on Zn(II), which typically forms fluorescent metal complexes with ligands and can readily expand its coordination sphere, facilitating binding with the anionic group of norfloxacin.[3] Concerning the fluorophore units, we opted for a Förster resonance energy transfer (FRET) pair consisting of pyrene as the donor and 7-diethylaminocoumarin as the acceptor.[4] This choice allows us to utilize energy transfer process as a monitoring channel for detecting the targeted analyte. After synthesis and complete characterization of N5CP Zn(II) complex, sensing capability towards selected compounds belonging to different classes of antibiotics, including penicillins and cephalosporins, were tested by fluorescence titrations, evaluating the variation in energy transfer by excitation at λ=350 nm for increasing concentrations of the antibiotic. The interaction between the probe and the analyte generally led to a decrease in energy transfer, likely caused by the insertion of the antibiotic between the pair of fluorogenic units, followed by their spatial separation. Spectrofluorimetric titrations were used to determine the stability constants of complexes with the various antibiotics.

This study uncovers that the fluorescent receptor N5CP displays good sensing and selectivity properties for norfoxlacin over the other tested antibiotics, making it a promising optical probe for the detection of fluroquinolones over other classes of antibiotics normally spread in aquatic environments.

References:

[1] M. Kumar et al., *Environ. Int.*, **2019**, 124, 448-461.
[2] B. Valeur, I. Leray, *Coord. Chem. Rev.,* **2000**, 205, 3-40.
[3] D. Prabha et al., J *Chem Sci*, **2021**, 133, 1-12.
[4] L. Wu et al., *Chem. Soc. Rev.*, **2020**, 49, 5103-5640.

Anticancer 8-hydroxyquinoline derivatives targeting multidrug resistant cancer cells and their interaction with essential metal ions

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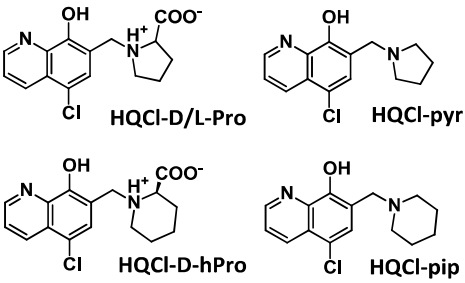
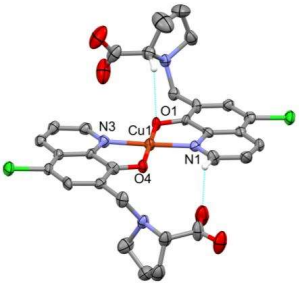
Drug resistance in chemotherapy is one of the major drawbacks and development of compounds to overcome resistance is a rather challenging task. 8-Hydroxyquinoline (HQ) derivatives are well-known for their wide range of pharmacological properties and among them we can find derivatives capable of targeting multidrug resistant (MDR) cancers [1,2]. Collateral sensitivity, the phenomenon whereby resistance to one drug is accompanied by a paradoxical increase in sensitivity to a second drug, is gaining attraction as a promising new strategy to guide the rational design of combination therapies. We hypothesized that the incorporation of the CH_2-N subunit and a halogen substituent at positions 7 and 5 on the HQ backbone plays an important role in their MDR-selective toxicity [2,3]. It is also suggested that the MDR-selectivity of certain Mannich base HQ derivatives is related to their interaction with endogenous metal ions such as iron and copper [3,4]. Certain HQ derivatives have been reported to induce a pronounced depletion of iron levels in the P-glycoprotein-expressing MDR cancer cells, leading to cell death [4].

Herein, studies on the interaction of five selected MDR-selective Mannich base HQ derivatives with iron(II), iron(III) and copper(II) are presented in terms of solution speciation and redox properties of the complexes formed.





The stability and structure of the complexes in solution were studied by UV-visible, circular dichroism and electron paramagnetic resonance spectroscopy, and their electrochemical properties were characterized by cyclic voltammetry and spectroelectrochemistry. The pysico-chemical properties of the iron and copper complexes are compared with those of the non-MDR-selective HQs in order to identify differences in their solution chemical behaviour and cytotoxic activity.

Acknowledgements

Project no TKP2021-EGA-32 has been implemented with the support provided by the Ministry of Culture and Innovation of Hungary from the National Research, Development and Innovation Fund, financed under the TKP2021-EGA funding scheme. The “Lendület” Programme (HUN-RES Hungarian Research Network, LP2019-6/2019) is also acknowledged.

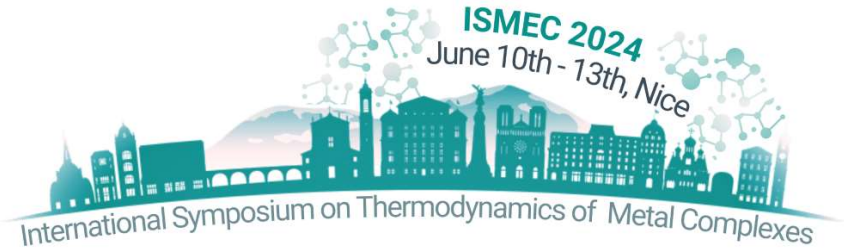
References:

[1] M. Cserepes, D. Türk, S.Z. Tóth, V.F.S. Pape, A. Gaál, M. Gera, J.E. Szabó, N. Kucsma, G.Y. Várady, B.G. Vértessy, C. Streli, P.T. Szabó, J. Tovari, N. Szoboszlai, G. Szakács, *Cancer Res*. **2020**, 80, 663-674.

[2] V.F.S. Pape, R. Palkó, S. Tóth, M.J. Szabó, J. Sessler, G. Dormán, É.A. Enyedy, T. Soós, I. Szatmári, G. Szakács, *J. Med. Chem.* **2022**, 65, 7729-7745.

[3] V.F.S. Pape, A. Gaál, I. Szatmári, N. Kucsma, N. Szoboszlai, C. Streli, F. Fülöp, É.A. Enyedy, G. Szakács, *Cancers* **2021**, 13, 154.

[4] V.F.S. Pape, N.V. May, G.T. Gál, I. Szatmári, F. Szeri, F. Fülöp, G. Szakács, É.A. Enyedy, *Dalton Trans.* **2018**, 47, 17032-17045.



New PET imaging agent based on 64-Cu bispidine antibody conjugates: From synthesis to *in vivo* evaluation

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Enhancing the detection of Multiple Myeloma (MM) represents a critical challenge for optimizing its management. Current clinical imaging methods rely mostly on Positron Emission Tomography (PET) using non-specific radiotracers like ^{18}F-FDG. These radiotracers are employed to monitor tumor activity [1], but in some cases, they fail to capture the plasma cell population due to low cellular proliferation. In this study, we aim to develop a novel immunoPET radiotracer enable to detect specifically the tumor-associated antigen (TAA) CD38 overexpressed on the surface of malignant MM cells.

For this purpose, bispidine-anti CD38 monoclonal antibody (mAb), labelled with 64-Cu is used as a radiotracer. 64-Cu is an ideal radioisotope due to its β^+ decay with high energy and long half-life ($t_{1/2}$ =12.7h) [2], offering logistical advantages that align well with the pharmacokinetics of mAb. Also, the bispidine chelators demonstrate promising characteristics as pre-organized ligands for forming Cu (II) complexes, as well as appropriate by their thermodynamic stability and excellent kinetic inertness in biological media [3,4]. Series of conjugates have been developed and i*n vitro* studies have been achieved to validate the affinity for CD38$^+$ cell lines. One promising conjugate with a specific degree of conjugation (DOL) of 8, which did not affect its specificity toward CD38 antigen, has been injected *in vivo* to evaluate pharmacokinetics and biodistribution.

These promising results mark the initial steps toward the first development of a novel 64-Cu bispidine-based radiotracer, specifically targeting malignant MM cells. This endeavor holds the potential to enhance the quality of monitoring for MM patients.

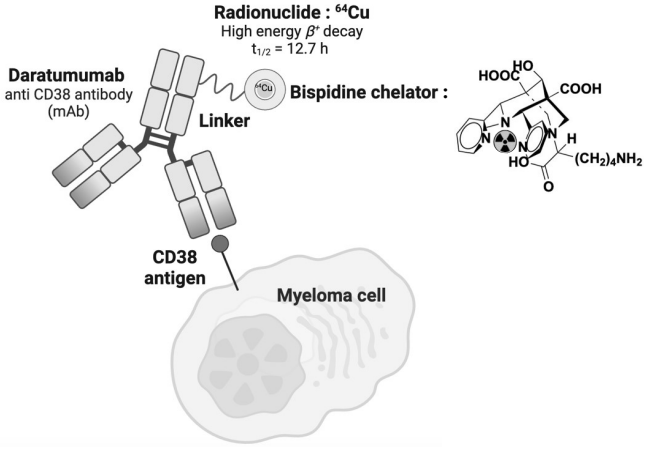

Figure 1: Structure of the mAb-bispidine immunoconjugate specifically targeting myeloma cell. (Created with BioRender.com)

References:

[1] E. Zamagni, F. Patriarca, C. Nanni, B. Zannetti, E. Englaro, A. Pezzi, P. Tacchetti, S. Buttignol, G.Perrone, A. Brioli, L. Pantani, C. Terragna, F. Carobolante, M. Baccarani, R. Fanin, S. Fanti, M. Cavo, Blood **2011**, 118 (23), 5989-5995.

[2] W. Wei, Z. T. Rosenkrans, J. Liu, G. Hang, Q-Y. Luo, W. Cai, Chemical Reviews **2020**, 120 (8), 3787-3851.

[3] A. Roux, R. Gillet, S. Huclier-Markai, L. Ehret-Sabatier, L. J. Charbonnière, A. M. Nonat, Organic & Biomolecular Chemistry **2017**, 15 (6), 1475-1483.

[4] D. Ndiaye, M. Sy, A. Pallier, S. Même, I. de Silva, S. Lacerda, A. M. Nonat, L. J. Charbonnière, E. Tóth, Angewandte Chemie International Edition **2020**, 59 (29), 11958-11963.

Evaluation of the role of cysteines in the copper coordination and metal induced aggregation of human γD crystallin

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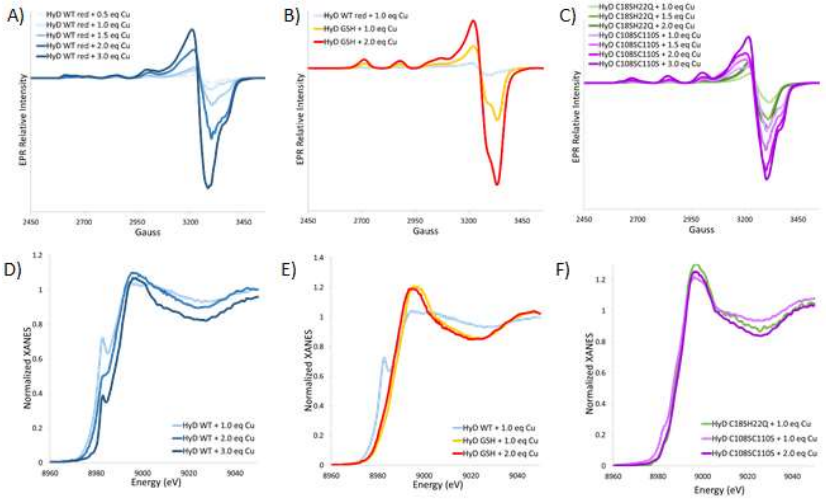
Cataracts are the main cause of blindness in the world, and are caused by the formation of high molecular weight protein aggregates in the lens, which cause light scattering and loss of transparency [1]. Human γD crystallin (HγD) is one of the most abundant proteins in the lens and one of the most stable proteins in the human body; however, *in vitro* studies have shown that Cu(II) can induce its non-amyloid aggregation by different mechanisms, including metal bridging [2, 3], disulfide bond formation [2-4], unfolding of the N-terminal domain [2, 3] and formation of a tyrosyl radical due to the reduction of Cu(II) to Cu(I) [3], suggesting copper may play an important in role cataract formation. HγD crystallin possesses 6 cysteine residues, which could be involved in copper coordination and Cu(II) reduction. Here we evaluate the role of cysteines in HγD in copper induced aggregation, Cu(II) to Cu(I) reduction and copper coordination. To elucidate the copper coordination sites in HγD crystallin and their role in the aggregation mechanism, the glutathionylated protein (HγD GSH), as well as cysteine mutants were analyzed by Electron Paramagnetic Resonance (EPR) and copper X-Ray Absorption (XAS).

Cys18, Cys41 and Cys110 were identified as glutathionylation sites in HγD crystallin *in vitro* by Tandem Mass Spectrometry (MS/MS). Aggregation assays of HγD WT and HγD GSH showed that glutathionylation decreases Cu(II) induced aggregation, as well as disulfide bond formation. EPR and XAS of HγD WT showed reduction of Cu(II) to Cu(I) and the formation of



Cu(I) complexes. XAS spectra shows a peak at 8983 eV, characteristic of linear or trigonal Cu(I) species. Furthermore, EPR spin quantification indicates that the first equivalent of Cu(II) is reduced to Cu(I), while at higher equivalents, excess copper remains as Cu(II). On the contrary, EPR and XAS spectra of HγD GSH showed no reduction of Cu(II) to Cu(I), since no Cu(I) species were observed by XAS and no decrease in spin quantification was shown by EPR. These results indicate that glutathionylation of HγD prevents the reduction of Cu(II) to Cu(I) *in vitro*, and that cysteines are involved in this redox process. Mutation of Cys residues also decreases or prevents the reduction of Cu(II) to Cu(I). The double mutation C108SC110S prevents reduction to Cu(I), since no Cu(I) species are observed by XAS and there is no decrease in spin quantification by EPR, confirming the involvement of Cys108 and Cys110 in the redox process. C18 also participates in the formation of Cu(I) species, since the C18S mutation avoids the Cu(II) to Cu(I) reduction and decreases the spin quantification by half.

Figure 1. EPR spectra of A) HγD WT at 0.5, 1.0, 1.5, 2.0, and 3.0 eq of Cu(II), B) HγD GSH at 1.0 and 2.0 eq of Cu(II) and C) HγD C18SH22Q and HγD C108SC110S at 1.0, 1.5 and 2.0 eq of Cu(II). D) XAS spectra of HγD WT at 1.0, 2.0 and 3.0 eq of Cu(II); E) HγD GSH at 1.0 and 2.0 eq of Cu(II), and F) HγD C18SH22Q at 1.0 and HγD C108SC110S at 1.0 and 2.0 eq of Cu(II). No

Cu(I) species are observed in the glutathionylated protein and C18SH22Q and C108SC110S mutants.

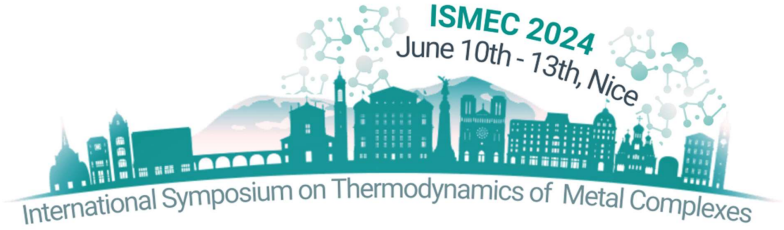
References:

[1] Moreau K. L., & King, J. A. *Trends in molecular medicine*, **2012**, 18(5), 273–282.

[2] Quintanar, L., Domínguez-Calva, J. A., Serebryany, E., Rivillas-Acevedo, L., Haase-Pettingell, C., Amero, C., & King, J. A. *ACS Chemical Biology*, **2016**, 11(1), 263–272.

[3] Palomino-Vizcaino, G., Schuth, N., Domínguez-Calva, J. A., Rodríguez-Meza, O., Martínez-Jurado, E., Serebryany, E., King, J. A., Kroll, T., Costas, M., & Quintanar, L. *Journal of the American Chemical Society*, **2023**, 145(12), 6781–6797.

[4] Ramkumar, S., Fan, X., Wang, B., Yang, S., & Monnier, V. M. *Biochimica et Biophysica Acta. Molecular Basis of Disease*, **2018**, 1864(11), 3595–3604.



MCTs as new potential targets in oncology: a preliminary investigation in nuclear medicine exploiting both fluorine and copper.

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MCT1 is a membrane protein responsible for the transport of lactate normally expressed in healthy tissues. However, in some cancer lines its expression results dysregulated and allows the establishment of the "Warburg effect". This mechanism explains the aggressive character of specific tumoral types and allows MCT1 to be a potential target for theranostic applications in oncology [1]. To date, only few molecules acting as inhibitors for MCT1 are known [2], and the interaction of some of them with MCT1's pocket has been elucidated by Xray crystal data [1]. Some of these are Diclofenac and 7ACC2, a Coumarin derivative. Coumarins are natural phyto-compounds known since the 19th century, their scaffold has attracted the attention of synthetic and medicinal chemists for decades and showed a large variety of biological activities [3]. One of the recently developed MCT1 inhibitor (7ACC2), that reached clinical trials, is a coumarin derivative [2]. Starting with preliminary docking calculations, the structure of 3-carboxy,7-hydroxycoumarin and Diclofenac was modified to retain a high affinity for the protein structure and to insert an additional specific moiety that allows the radiolabelling with Fluorine-18. ^{18}F is "the working horse" in the everyday clinical PET, however, being ^{18}F a pure positron emitter, its applications are limited to diagnosis. Inserting a bifunctional chelator (BFC) to the targeting structure opens up to theranostics if a proper element is choosen, such as copper that has a variety of isotopes useful for both diagnosis and therapy (^{61}Cu, ^{64}Cu, ^{67}Cu). The selected bifunctional polyazamacrocycle no3py [4] was conjugated on the targeting vector using a PEG chain long enough to reduce the impact of the metal complex on MCT.

References:

[1] V. L. Payen, E. Mina, V. F.Van Hée, P. E. Porporato, P.Sonveaux, *Mol. Metab*., **2020**, 33, 48.

[2] S. Puri, K. Juvale, *Eur. J. Med. Chem*., **2020**, 199, 112393.

[3] N. Wang, et al., *Cell*, **2021**, 184, 370-383.

[4] A. Guillou et al., *Eur., J. Inorg. Chem*., **2017**, vol. 18, 2435–2443

ISMEC 2024
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International Symposium on Thermodynamics of Metal Complexes

How protonation states modulate biological activity in Ir(III) Biscyclometallated Complexes with Imidazophenanthroline Ligands

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Two Ir(III) biscyclometallated complexes, **[Ir1]Cl** and **[Ir2]Cl**, with the formula $[Ir(C^N)_2(N^N)]Cl$, where C^N = 2-phenylpyridinate and N^N = L1 or L2, were synthesized and characterized (Fig. 1). The imidazophenanthroline ligands differ in the substituent on the imidazole N atom (N-R), with L1 containing N-H and L2 containing N-Ph. The presence of an acidic proton in **[Ir1]Cl** leads to different protonation states in the cellular pH range compared to **[Ir2]Cl**, which not only affects their photophysical properties but also their intracellular compartmentalization. Consequently, their potential as photosensitizers for cancer photodynamic therapy and as binders of G-quadruplexes is strongly affected.

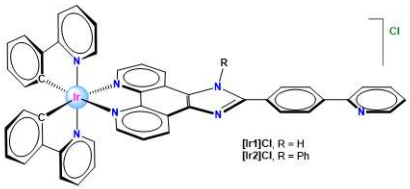

Fig. 1: Molecular structure of **[Ir1]Cl** and **[Ir2]Cl**.

[Ir1]Cl exhibits pH-sensitive emission due to deprotonation of its N-H group, while **[Ir2]Cl** is less affected by pH due to the absence of acidic protons. The complexes display large Stokes shifts and long excited state lifetimes indicative of phosphorescence. Both complexes exhibit self-aggregation properties in aqueous solution, which enhance their emission intensity, demonstrating the phenomenon of aggregation-induced emission enhancement (AIEE), a desired property for bioimaging and therasnostic fluorescent probes [1].

At physiological pH, **[Ir1]Cl** adopts its neutral form due to the loss of the N-H proton, whereas **[Ir2]Cl** preserves its monocationic character. Photocytotoxicity tests on A549 cells show that in the dark, the cytotoxicity of **[Ir1]Cl** is low, while the cytotoxic activity of **[Ir2]Cl** is

very high. Upon irradiation with blue light, both complexes show photo-induced activation, with PI values > 14 and 3, respectively. Evaluation of singlet oxygen ($^1O_2$) production indicates that **[Ir1]Cl** is a more efficient photosensitizer than **[Ir2]Cl**, correlating with their respective photo-indexes.

Regarding their mechanism of action, we have shown that **[Ir1]Cl** and **[Ir2]Cl** are successfully internalized by A549 cancer cells and exhibit differential intracellular distribution patterns, with **[Ir1]Cl** selectively accumulating in lysosomes and **[Ir2]Cl** showing a less specific localization, mainly in mitochondria. Their intracellular localization can also be related to the different protonation states of these derivatives at the cellular pH range. Indeed, we postulate that the diffusion and accumulation of **[Ir1]$^+$** into lysosomes are favoured by a change in its protonation state from the neutral form, **[Ir1]**, predominant at the neutral pH of the cytoplasm (pH ≈ 7.2-7.4), to the cationic form, **[Ir1]$^+$**, prevailing at the acidic pH of lysosomes (pH ≈ 4.5-5.5) [2].

Moreover, both complexes effectively stabilize G-quadruplex structures, particularly those with antiparallel topology. In fact, **[Ir2]Cl** induces a higher thermal stabilization of the mitochondrial G4 sequence mt9438 compared to **[Ir1]Cl**. Thus, we hypothesize that **[Ir2]Cl** could exert its cytotoxic activity by causing mitochondrial dysfunction, whereas **[Ir1]Cl** affects lysosomal integrity.

References:

[1] H. Wang, Q. Li, P. Alam et al., *ACS Nano*. **2023**, 17 (15), 14347–14405.

[2] C. Liu, X. Liu, X. Ge et al. *Dalton Trans.* **2020**, *49* (18), 5988–5998.

Zinc(II), Gallium(III) and Indium(III) pyridinecarboxylates - composition, speciation in aqueous solution and potential biotherapy

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The world of microorganisms surrounds us every day, while many of them help us and contrary many harm. Even those that help us can seriously endanger our health after their proliferation. Therefore, it is generally known that maintaining the balance of all physiological processes in organisms is essential for their life. However, it is a real fact that this balance is very fragile and often disturbed. People (but also animals and plants) are either attacked by pathogens or beneficial microorganisms' proliferation. Similarly, the internal body imbalance involves abnormal cells proliferation (the otherwise healthy cells) and they gradually become harmful to the body. As already mentioned many times, the most common diseases of civilization (after cardiovascular diseases) are precisely infections and cancers. That is the reason why it is necessary to support the investigation and research of these diseases and look for ways to treat them. In addition to many drugs based on organic compounds, one possible and promising approach is to include metal ions in potential drugs. This procedure has already been used successfully several times [1, 2] and therefore new combinations are still being sought. In addition to known coordination compounds of ions Ag, Cu, Zn, Pt, Ru, Pd, etc recently, compounds based on Ga, Gallium(III) maltolate (GaM) and tris(8-quinolinolato)Ga(III)(KP46) [3] have been successfully moved into clinical studies. This discovery naturally aroused the interest of scientists to apply In(III) compounds as potential antimicrobial and cytotoxic drugs. In the contribution, we will present the results obtained by solution experiments, solid phase methods and bioevaluation [4].

ACKNOWLEDGEMENTS

This work was supported by Slovak grant agencies VEGA 1/0037/22, 1/0268/24, KEGA 007UPJŠ-4/2024.

References:

[1] J. Liang, D. Sun, Y. Yang, M. Li, H. Li, L. Chen, *European Journal of Medical Chemistry* **2021,** (224), 113696.
[2] A. Cotia, H. A. Oliveira Junior, J. Y. Matuoka, Í. Boszczowski. *Antibiotics* **2023,** (12), 935.

[3] X. X. Peng, S. Gao, J. L. Zhang, *European Journal of Inorganic Chemistry* **2022,** e202100953.
[4] M. Rendošová, R. Gyepes, S. Sovová, D. Sabolová, M. Vilková, P. Olejníková, M. Kello, B. Lakatoš, Z. Vargová, *Journal of Biological Inorganic Chemistry* **2023,** (28), 591-611.

Exploring the Potential of Lycorine in Alleviating Amyloid β Toxicity and Its Interaction with Copper Ions

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Lycorine (LYC) is an active alkaloid initially extracted from Narcissus pseudonarcissus and commonly found in various Amaryllidaceae plants. It belongs to the same family as galantamine, which is the active component of a drug used for the early stages of Alzheimer's disease. Like galantamine, LYC exhibits the capability to alleviate induced amyloid β (Aβ) toxicity in differentiated SH-SY5Y cell lines [1]. Additionally, we have demonstrated weak electrostatic interaction between LYC and the N-terminal region of Aβ [1]. This region of Aβ is also implicated in binding with Cu(II)/Cu(I), forming complexes pivotal in reactive oxygen species (ROS) production [2-4].

This investigation delved into the interaction between Aβ and LYC, both in the presence and absence of copper ions, utilizing the N-terminal Aβ peptide comprising the initial 16 residues. NMR analysis unveiled that Aβ can simultaneously engage with Cu(II) and LYC, as previously observed with other molecules [5, 6]. While the binding mode of Cu(II) remains unaltered in the presence of LYC, LYC association is favored upon the formation of an Aβ–Cu(II) complex. Furthermore, UV-VIS studies showcased LYC's capacity to disrupt the catalytic activities of Aβ–Cu(II) complexes [6].

Acknowledgements: Financial support by MIUR-PRIN 2022RCRWE5 and CIRMMP is gratefully acknowledged.

References:

[1] A. Kola, S. Lamponi, F. Currò, D. Valensin, *Int. J. Mol.* **2023**, 24 (3), 2500.
[2] G. De Gregorio, F. Biasotto, A. Hecel, M. Luczkowski, H. Kozlowski, D. Valensin, *J. Inorg. Biochem.* **2019**, 195, 31-38.
[3] E. A.-Blasco, P. Gonzalez, A. Santoro, B. Alies, P. Faller, C. Hureau, *Coord. Chem. Rev.* **2018**, 375, 38-35.
[4] H. Kozlowski, M. Luczkowski, M. Remelli, D. Valensin, *Coord. Chem. Rev.* **2012**, 256, 2129-2141.
[5] R. De Ricco, D. Valensin, S. Dell'Acqua, L. Casella, C. Hureau, P- Faller, *Chembiochem*, **2015**, 16, 2319-23128.
[6] A. Kola, G. Vigni, D. Valensin, *Inorganics,* **2023**, 11, 443.

Molecular recognition within [Cu(N-(R)-iminodiacetate)(creatinine)(H_2O)] complex molecules is determined by the nature of R non-coordinating arms.

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Creatinine (crea) is a planar five-membered heterocyclic bioligand, first elucidated in a review by M. Mitewa [1]. As a ligand, crea provides solely its N-heterocyclic donor atom. Furthermore, the adjacent O-keto and a $–NH_2$ exocyclic groups can cooperate with the metal-N(crea) bond through interligand hydrogen bonding interactions. Only eight Cu(II)-crea complexes have been documented [2-4]. In mixed-ligand metal molecules, the Cu-N(crea) bond is reinforced by one or two interligand hydrogen bonds.

This work delves into the molecular recognition of 'copper(II) chelate-crea' looking at eleven novel [Cu(N-(R)-iminodiacetate)(crea)] molecules, featuring a variety of non-coordinating R groups. As tridentate chelators, iminodiacetates offer two terminal O-(metal bonded carboxylate) atoms as suitable H-acceptors.

All eleven newly synthesized compounds conform to the general formula [Cu(N-(R)-IDA)(crea)(H_2O]·nH_2O (n = 0.5-3) wherein (a) the Cu(II) consistently adopts a distorted square-pyramidal coordination geometry (type 4+1), (b) the O-aqua atom acts as distal donor, and (c) the molecular recognition Cu(N-(R)-IDA)-creatinine entails a highly effective cooperation involving the Cu-N(crea) coordination bond along with an interligand H-bonding interaction. These H-bonds can manifest as either (crea)N-H···O(carboxylate, IDA-like) for family 1 or (crea)N-H···O(aqua, distal) for families 2 and 3. Such structural revelations prompt us to inquire about the origin of these three families, focusing our attention in the distinct α = P(1)/P(crea) values. In family 1 (comprising four compounds, N-benzyl-IDAs- see Figure 1), there are α ranges from 37° to 40°. The most illustrative example is shown in the figure

below. In clear contrast, family 2 (consisting of three compounds, N-phenethyl-IDAs, α = 73°-78°) and family 3 (comprising three compounds, N-alkyl-IDAs, α = 81°-89°) progressively approach a P(1)/P(crea) dihedral angle indicative of perpendicularity (α = 90°).

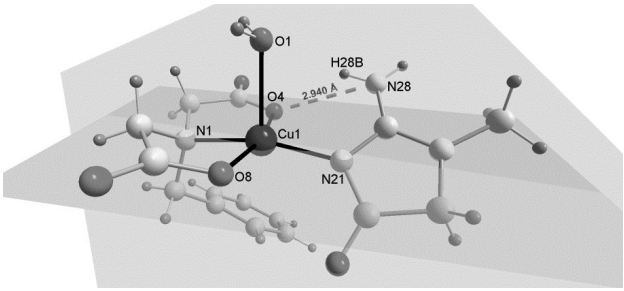

Figure 1. Mean planes to estimate α = 39.9° in (1).

To ascertain the decisive influence of the non-coordinating N-(R)-IDA arms on α dihedral angle values, we '*designed*' the compound [Cu(alida)(crea)(H_2O)]·2H_2O, where alida = N-allyl-IDA or N-(H_2C=CH-CH_2)-IDA). In this particular instance, the partial unsaturation of the N-allyl-IDA arm results in α = 60.7° (a value intermediate to those of family 1 and of families 2 and 3). Notably, in this compound, the interligand H-bond (crea)N-H···O(aqua, distal) aligns with those included in families 2 and 3, but not in family 1 (which exhibit a (crea)N-H···O(carboxylate, proximal) interligand H-bond).

In conclusion: Based in all novel structural results, we conclude that the non-coordinating (benzyl, phenethyl or alkyl) R-arm of the N-(R)-IDA chelators, within the studied copper(II) complex molecules, delineate three distinct structural families. These delineations establish boundaries within which the development of newly designed compounds is also feasible.

References:

[1] M. Miewa, *Coord. Chem. Rev.* **1995**, 140, 1-25. https://doi.org/10.1016/0010-8545(94)01122-R

[2] A. Castiñeiras, D. Choquesillo-Lazarte, J. M. González-Pérez, R. Carballo, J. Niclós-Gutiérrez**,** *Z. Anorg. Allg. Chem.* **2006**, *632*, 845-850. http://dx.doi.org/10.1002/zaac.200500459

[3] M. Tribet, B. Covelo, A.G. Sicilia-Zafra, R. Navarrete-Casas, D. Choquesillo-Lazarte, J.M. González-Pérez, A. Castiñeiras, J. Niclós-Gutiérrez, *J. Inorg. Biochem.* **2005**, *99*, 142-1432. http://dx.doi.org/10.1016/j.jinorgbio.2005.03.012

[4] A. García-Raso, J.J. Fiol, B. Adrover, P. Tauler, A. Pons, I. Mata, E. Espinosa, E. Molins, *Polyhedron* **2003**, *22*, 3255-3264. http://dx.doi.org/10.1016/j.poly.2003.07.013

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Designing artificial metalloenzymes exploiting the Spy technology: study of a Cu(II)-Spy construct and perspectives

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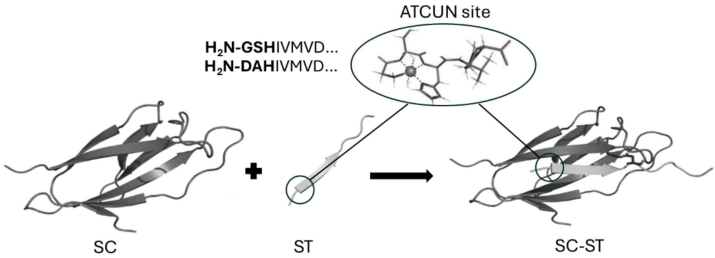
Metalloproteins promote several among the most complex biomolecular processes in Nature. The expanding demand for synthetic catalysts displaying enzyme-like activity is moving toward the development of ARTificial metalloenZYMES (ARTZYMES).[1] Protein redesign and de novo design are the two major strategies for the development of Artzymes, both having potentiality and drawbacks concerning the introduction of metal binding sites in a construct. Within the redesign approach, the so called 'Trojan horse' strategy involves the covalent or supramolecular grafting of a metal complex to a biomolecule,[2] to obtain the introduction of a metal ion into a known protein scaffold.

We present here the original incorporation of a transition-metal binding site specifically designed on a small peptide component (SpyTag), onto a Spy-protein construct, thereby providing the Spy protein with a selective binding site for metal ions (**Scheme 1**).



Scheme 1. Representation of the SpyCatcher (SC)-SpyTag (ST) construct, with ATCUN metal binding sites introduced in the ST sequence.

The Spy protein, redesigned by Howarth and colleagues,[3] comprises two components: a small beta-sandwich SpyCatcher (SC) protein component (ca. 110 residue), and the SpyTag (ST) peptide (13-16 residues). SC and ST incubated together in buffered aqueous solutions at neutral pH interact rapidly and selectively to form an isopeptide bond between a Lys (SC) and an Asp residue (ST).

We redesigned the ST sequence by introducing an ATCUN sequence onto the Tag peptides. The ATCUN (Amino Terminal Cu and Ni binding site) fragment, characterized by a H_2N-Xxx-Xxx-His sequence at the N-terminus, is known for its ability to bind Cu(II) and Ni(II) ions.[4] Additionally, the SC sequence was modified mutating two His residues into Gln to reduce the possibility of copper binding while preserving hydrogen bond interactions between residues.

We were able to demonstrate that three different SpyTag-ATCUN peptides exhibit high binding affinity for Cu(II). Additionally, we confirm that the specific binding of Cu(II) at the ATCUN site of the ST sequence occurs in the presence of one equivalent of copper when SC is bound to ST. We observed this behaviour both with short ST peptides and when the ST sequence is expressed at the N-terminus of a natural protein, such as Thioredoxin. This engineered construct serves as an interesting proof-of-concept for novel metalloproteins, wherein the SpyTag peptide establishes the initial metal coordination sphere, while the SpyCatcher protein potentially contributes to the second coordination sphere.

Starting from these results, this solid SC-ST metal binding construct could be employed studying its reactivity with different metals, as well as different metal binding groups with both natural and unnatural amino acids, introduced in the ST sequence via solid-phase peptide synthesis.

Project ART2HYDROGEN “Artificial enzymes for the photocatalytic production of hydrogen in photosynthetic bacteria” funded under the National Recovery and Resilience Plan (NRRP), Mission 2 Component 2 Investment 3.5 - Call for tender No. 4 of March 23, 2022 of Italian Ministry of Ecologic Transition funded by the European Union – NextGenerationEU. Project code RSH2A_000009, Concession Decree 445 of December 29, 2022 adopted by the Italian Ministry of Environment and Energy Security.

References:

[1] F. Yu, V. M. Cangelosi, M. L. Zastrow, M. Tegoni, J. S. Plegaria, A. G. Tebo, C. S. Mocny, L. Ruckthong, H. Qayyum, V. L. Pecoraro, *Chemical Reviews* **2014**, 114, 3495-3578.

[2] Y. W. Lin, *Molecules* **2019**, 24, 2743.

[3] B. Zakeri, J. O. Fierer, E. Celik, E. C. Chittock, U. Schwarz-Linek, V. T. Moy, M. Howarth, *Proceedings of the National Academy of Sciences of the United States of America* **2012**, 109.

[4] B. K. Maiti, N. Govil, T. Kundu, J. J.G. Moura, *iScience* **2020**, 23, 101792.

Effect of amide methylation on the speciation and catalytic behaviour of copper(II) peptide complexes: "the cherry on the cake"

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Peptide frameworks constitute a very attractive and versatile platform for the development of metal catalysts because they can provide multiple donor atoms in a single molecule and in a chiral environment. In addition, they have structural and chemical diversity (possibility of using both proteinogenic and non-proteinogenic amino acids and peptide backbone modifications), accessible chemical synthesis by well-established solid-phase methodologies and water solubility.

Inspired by copper-containing enzymes that participate in a variety of O_2-processing reactions acting either as oxygenases or as oxidases,[1] we have been developing a family of His-containing peptides capable of coordinating copper(II)[2-3] and fine-tuning its properties for different chemical transformations. We have shown how the introduction of different degrees of conformational constrains in the peptide backbone and recently, amide methylation,[3] have a drastic effect on the formation, speciation and properties of the copper(II) species. In this communication, we will present these data and the oxidation catalytic properties of these complexes with special emphasis on sulfoxidation, an important oxidation reaction in the high-value added chemical industry. We will show how amide methylation not only fine-tuned speciation but also positively impacted the catalytic behaviour of the copper(II) peptide complexes.

References:

[1] E.I Solomon, D.E. Heppner, E.M. Johnston, J.W. Ginsbach, J. Cirera, M. Qayyum, M.T. Kieber-Emmons, C.H. Kjaergaard, R.G. Hadt, and L. Tian, *Chem. Rev.*, **2014**, 114, 3659-3853.

[2] a) A. Fragoso, P. Lamosa, R. Delgado, O. Iranzo, *Chem. Eur. J.*, **2013**, 19, 2076-2088; b) A. Fragoso, T. Carvalho, P. Rousselot-Pailley, M.M. Correia dos Santos, R. Delgado, and O. Iranzo, *Chem. Eur. J.*, **2015**, 21, 13100-13111.

[3] A. Hautier, T. Carvalho, D. Valensin, A.J. Simaan, B. Faure, P. Mateus, R. Delgado, and O. Iranzo, *Dalton Trans.*, **2019**, 48, 1859-1870.

Malten and Maltonis-Pd^{2+} complexes as binding and biological tools

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Our group has long been working on bis-maltol polyamines, developing different compounds that possess both antineoplastic activity and peculiar coordination properties towards metal cations in aqueous solution. So far, the most effective compounds of the bis-maltol polyamines series are Malten (N,N'-bis((3-hydroxy-4-pyron-2-yl)methyl)-N,N'-dimethylethylendiamine, **L1**) and Maltonis (4,10-bis[(3-hydroxy-4-pyron-2-yl)methyl]-1,7-dimethyl-1,4,7,10-tetraazacyclododecane, **L2**), both possessing two maltol units symmetrically spaced by either a linear or macrocyclic polyamine, respectively (Fig. 1). [1-4] They both have a molecular mechanism of action that may involve the interference with the chromatin structure, causing a dose-dependent reduction in cell survival in the neoplastic models studied associated with activation of cell cycle arrest and apoptosis.

They were also studied for their ability to bind transition metal ions involving in the coordination both the maltol and polyamine fragments, resulting in preorganized structures when suitable cations are used (Cu^{2+} for Malten, Co^{2+} for Maltonis). These preorganized complexes behave as metallo-receptors in aqueous solution towards hard species, such as alkali, alkaline-earth and rare earth metal ions, that are notably promptly lodged in the oxygen-rich area formed by the convergence of maltol moieties. [5-6]

Here, the binding properties of the two ligands towards Pd^{2+} metal ion was investigated both in aqueous solution and in the solid-state (Fig. 1). The ability of the Pd-complexes to act as host towards hard metal cations was investigated as well as their evaluation as efficient biological agents.

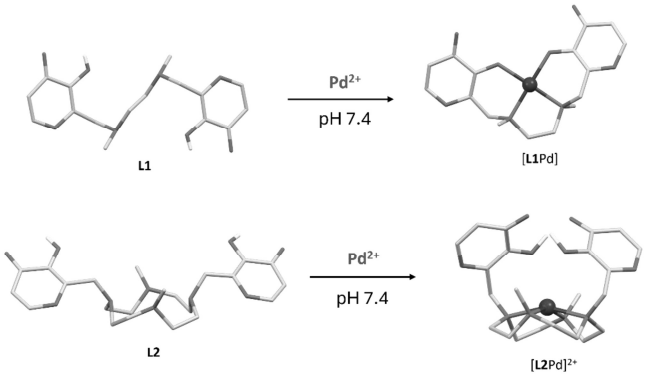

Figure 1: Schematic representation of the [**L1**Pd] and [**L2**Pd]$^{2+}$ complexes formation.

References:

[1] S. Amatori, I. Bagaloni, E.Macedi, M. Formica, L. Giorgi, V. Fusi, M. Fanelli, *British Journal of Cancer* **2010**, 103 (2), 239-248.

[2] E. Macedi, D. Paderni, M. Formica, L. Conti, M. Fanelli, L. Giorgi, S. Amatori, G. Ambrosi, B. Valtancoli, V. Fusi, *Molecules* **2020**, 25 (4), 943.

[3] L. Giorgi, G. Ambrosi, D. Paderni, L. Conti, S. Amatori, F. Romagnoli, P. Rossi, M. Formica, E. Macedi, C. Giorgi, P. Paoli, M. Fanelli, V. Fusi, *New Journal of Chemistry* **2021**, 45, 2659-2669.

[4] S. Amatori, G. Persico, F. Cantatore, M. Rusin, M. Formica, L. Giorgi, E. Macedi, F. Casciaro, A. E. Provenzano, S. Gambardella, R. Noberini, T. Bonaldi, V. Fusi, M. Giorgio, M. Fanelli, *Cancer Gene Therapy* **2023**, 30, 671-682.

[5] E. Borgogelli, M. Formica, V. Fusi, L. Giorgi, E. Macedi, M. Micheloni, P. Paoli, P. Rossi, *Dalton Transactions* **2013**, 42, 2902-2912.

[6] C. Benelli, E. Borgogelli, M. Formica, V. Fusi, L. Giorgi, E Macedi, M. Micheloni, P. Paoli, P. Rossi, *Dalton Transactions* **2013**, 42, 5848-5859.

The project is funded by the European Union - NextGenerationEU - National Recovery and Resilience Plan M4-C2-I1.5 under the Italian Ministry of University and Research (MUR) National Innovation Ecosystem grant ECS00000041 - VITALITY - CUP: H33C22000430006

Poster Presentations

ISMEC 2024
June 10th - 13th, Nice
International Symposium on Thermodynamics of Metal Complexes

Sorbent materials as carriers of key nutrients for soil amendment

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Adsorption is a surface phenomenon of passive capture of a certain solute. The process itself can be described in terms of equilibrium between a solid dispersed in a solution interacting with species dissolved in that solution [1-3].

Adsorption has been described in numerous articles as a valid technique to be used in decontamination processes taking into account the mechanism of action described above. However, it does not have to be considered simply as a decontamination technique. As it is an equilibrium process where a species in solution is retained on the surface of a solid, it is possible to select adsorbent materials that are capable of interacting and retaining significant amounts of key elements in the development of plants, in such a way that these adsorbent materials, once loaded with these key elements, can be used as soil amendments where the sorbent materials progressively release these nutrients so that they can be used by plants.

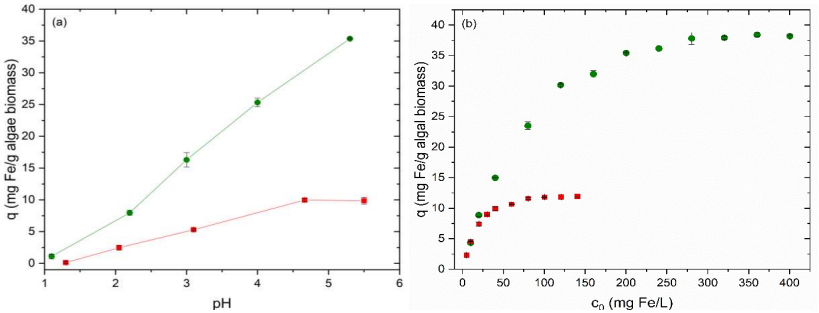

Figure 1. On the left-hand side pH dependence of Fe sorption by clean *Ulva ohnoi* biomass (●) and clean *Gracilaria cornea* biomass (■). On the right-hand side q vs C_0 for Fe(II) adsorption by biomass of *U. ohnoi* (●) and *G. cornea*

We present the study carried out using two types of biomass from marine algae that have been used in a first step to retain Fe(II) on their surface. Once the material has been loaded with iron, the adsorption process was completed simultaneously retaining phosphate. Both adsorption processes have been studied by analysing critical parameters such as the pH of the medium, the contact time and the concentration of the adsorbate used.

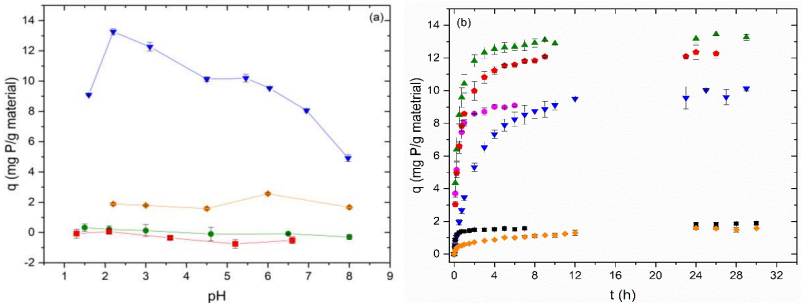

Figure 2. On the left, pH dependence of P sorption by U-NF (▼) G-NF (♦), clean *U. ohnoi* biomass (●) and clean *G. cornea* biomass (■). On the right, q vs C_0 for P adsorption by U-NF and G-NF

These sorbents loaded with both iron and phosphate are being tested to show their effect upon plants growth.

Acknowledgements

Authors want to thank Agencia Española de Investigación for the financial support through the research project PID2020-117910GB-C22/AEI/10.13039/501100011033 and Xunta de Galicia for the project ED431B 2022/40

References:

[1] P. Lodeiro, M. Martínez-Cabanas, R. Herrero, J.L. Barriada, T. Vilariño, P. Rodríguez-Barro, M.E. Sastre de Vicente, A Systematic Analysis and Review of the Fundamental Acid-Base Properties of Biosorbents, in: G. Crini, E. Lichtfouse (Eds.) *Green Adsorbents for Pollutant Removal: Fundamentals and Design*, Springer International Publishing, Cham, **2018**, pp. 73-133.

[2] P.X. Sheng, Y.-P. Ting, J.P. Chen, L. Hong, Sorption of lead, copper, cadmium, zinc, and nickel by marine algal biomass: characterization of biosorptive capacity and investigation of mechanisms, *J. Colloid Interface Sci.*, **2004**, 275, 131-141.

[3] B. Volesky, *Sorption and Biosorption*, BV Sorbex, St. Lambert, Quebec, **2003**.

Kynurenic acid: the coordination properties of the tryptophan metabolite towards Fe^{3+} and Ga^{3+}

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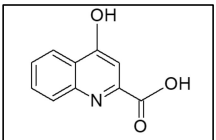

Scheme 1. Chemical structure of Kynurenic acid (KynA).

Among the 20 amino acids involved in protein synthesis, tryptophan (Trp) is one of the essential mammalian amino acids. It is well-known that Trp metabolism plays a vital role in the healthy function of the nervous and immune systems and the mechanisms linked to the gut-brain axis. At least 95% of human-ingested Trp is metabolized via the kynurenine pathway to a series of neuroactive metabolites, among which quinolinic acid and kynurenic acid (KynA) have been widely studied due to their association with inflammation and diverse inflammatory diseases. Furthermore, Trp metabolites (TrpMs) are closely related to neurodegenerative disorders, such as Alzheimer's Disease, depression, and schizophrenia, but also cancers, mainly colorectal cancer. Most of these diseases result from the fact that gut microbiota can also regulate the kynurenine pathway, leading to its abnormal activation and, thus, alternations of the balance between TrpMs [1,2]. Moreover, metal homeostasis is crucial in the good quality of the intestine microbial community since it is known that dietary metal ions have the potential to change the distribution and function of the microbiota [3]. Our recent work was focused on chemical speciation studies of TrpMs in aqueous solution, in particular, of 8-hydroxyquinoline-2-carboxylic acid (8-HQA) [4,5], recently reported as a regulator on bacterial abundance and diversity in the midgut of *S. littoralis* larvae, mainly due to its iron chelation properties [6]. For that purpose, we performed a detailed characterization of its protonation processes in human blood plasma conditions as well as of its coordination properties towards several biologically relevant metal ions, such as $Fe^{2+/3+}$, MoO_4^{2-} and even Ga^{3+} [4,7].

Considering the other important TrpMs already mentioned, the KynA, despite its potential relation with neurodegenerative diseases due to its ROS scavenging ability and Fe^{3+} complex formation, a complete understanding of its chemical speciation is still lacking. As such, we present herein the study of the binding ability of KynA towards Fe^{3+} and Ga^{3+}. Each KynA/M^{3+} system was investigated separately in $KCl_{(aq)}$ at I = 0.2 mol·dm^{-3} and T = 298.15 K by UV-Vis spectrophotometric titrations. The results obtained suggest the formation of mainly one metal complex for both studied systems, i.e. $[M(KynA)_2H_2]^-$, containing a protonated hydroxyl group in the investigated pH range (2.3 – 9.0). Based on the stoichiometry of the formed complex, it seems that KynA mainly acts as a bidentate ligand, with the hydroxyl group in 4 position not being involved in complexation and, thus, remaining in its protonated form even during complex formation. Lastly, the relative stabilities of formed metal complexes were compared with those formed by its isomer, i.e., 8-HQA, in terms of the influence of the hydroxyl group position on its activity. As expected, the different position of the hydroxylate in KynA vs 8-HQA determines a different coordination behaviour of the two ligands, as well as a different nature and stability of formed complexes.

Acknowledgements:

The authors would like to thank the financial support from the National Science Centre (NCN), Poland, under the research project number 2020/39/B/ST4/03060. DM acknowledges financial support under the National Recovery and Resilience Plan (NRRP), Mission 4, Component 2, Investment 1.1, Call for tender No. 1409 published on 14.9.2022 by the Italian Ministry of University and Research (MUR), funded by the European Union – NextGenerationEU– Project Title Efficient Sequestration of Metal Ions from Aqueous Systems for Green and Sustainable Applications - AquaGreen – CUP J53D23014430001- Grant Assignment Decree No. 1409 adopted on 14/09/2022 by the Italian Ministry of University and Research (MUR).

References:

[1] H.-l. Zhang, A.-h. Zhang, J.-h. Miao, H. Sun, G.-l. Yan, F.-f. Wu, X.-j. Wang, *RSC Advances* **2019**, 9, 3072-3080.

[2] M. Platten, E.A.A. Nollen, U.F. Röhrig, F. Fallarino, C.A. Opitz, *Nat Rev Drug Discov.* **2019**, 18, 379-401.

[3] C.A. Lopez, E.P. Skaar. *Cell Host & Microbe* **2018**, 23, 737-748.

[4] S. Gama, M. Frontauria, N. Ueberschaar, G. Brancato, D. Milea, S. Sammartano, W. Plass, *New J. Chem.* **2018**, 45, 8062-8073.

[5] A. Baryłka, A. Bagińska-Krakówka, L. Zuccarello, F. Mancuso, G. Gattuso, G. Lando, C. Sgarlata, C. De Stefano, B. Godlewska-Żyłkiewicz, D. Milea, S. Gama, *Thermochim. Acta* **2023,** 730, 179615.

[6] T. Mazumdar., S. Hänniger, S. P. Shukla, A. Murali, S. Bartram, D. G. Heckel, W. Boland, *Front. Microbiol* **2023,** 14, 1-10.

[7] K. Arena, G. Brancato, F. Cacciola, F. Crea, S. Cataldo, C. De Stefano, S. Gama, G. Lando, D. Milea, L. Mondello, A. Pettignano, W. Plass, S. Sammartano, *RSC Advances* **2019**, 9, 3072-3080.

Chemical mechanisms in radioecology : cesium and uranium accumulation in bivalve mollusks

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Of all the environmental compartments that serve as outlets for various metal contaminants, the oceans can be considered the ultimate receptacle for rivers and watersheds. Therefore, the oceans may act as a long-term reservoir (i.e., source) for pollution such as metals and radionuclides. Indeed, the marine environment has often been monitored as a marker of pollution. In the specific case of metal trace radionuclides, such as cesium and uranium, their origin in seawater is essentially anthropogenic (atmospheric nuclear testing, waste management, mining activities, accidental releases, etc.). Most radioecological studies in marine ecosystems have aimed at mapping and inventorying ultra-trace radionuclides, their propagation and accumulation areas in specific compartments (e.g. water and marine organisms). It is also known that the transfer of pollutants to living organisms is strongly dependent on their bioavailability. In the marine system, mollusks, especially mussels, are widely used to better understand radioactive pollution because of their ability to filter large volumes of seawater and for their sedentary nature. Main goal is to understand cesium(I)[1] and uranium(VI)[2] accumulation, distribution and speciation[3] in mussels Mytilus galloprovincialis using a model ecosystem. This methodology can also be used to understand the interaction of cesium and uranium with the biomolecules of the target organs. From a broader point of view, this research will provide basic information on U and Cs transfer constants to living organisms and ecotoxicity.

References:

[1] M. A. Ashraf; S. Akib ,M. Jamil Maah, I. Yusoff, K. S. Balkhair, Critical Reviews in Environmental Science and Technology, 2013, 44(15), 1740– 1793.

[2] M. Krmpotić, M. Rožmarić, D. Barišić, Journal of Environmental Radioactivity, 2015, 144, 47-51.

[3] M. Maloubier, P. L. Solari, P. Moisy, M. Monfort, C. D. Auwer, C. Moulin,. Dalton Trans, 2015, 44 (12), 5417–5427.

Design and study of metal complexes with tetrabranched peptide systems as surrogates of superoxide dismutase

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Enzymes offer numerous advantages as catalysts, such as selectivity and stereocontrol. However, their practical use is constrained by various limitations, including low thermal stability, low tolerance to diverse experimental conditions, and expensive processes of preparation and purification. To address these challenges, the development of enzyme mimics aims to mitigate these weaknesses.

Enzyme mimics (EMs) are typically developed to replicate the binding and catalytic functions of natural enzymes, employing two primary methods: either mimicking enzyme activity through metal complexes with comparable properties, or reproducing the structure of the enzyme active site by means of suitable functional groups, such as oligopeptides [1,2].

Our approach in designing novel enzyme mimics integrates both strategies and relies on synthetic branched peptides to generate a previously unexplored category of EMs. A biocompatible central scaffold serves as the core of the EM structure, to which various oligopeptides can be attached (one for each maleimide chain, Figure 1) [3,4].

In this work we aimed at replicating the catalytic sites of metalloenzymes by introducing specific amino acid sequences capable of binding active metal ions. For instance, various surrogates of Cu/Zn-SOD, Fe/Mn-SOD, and Ni-SOD can be synthesized. Thermodynamic, spectroscopic and structural studies of single peptides and/or tetrabranched systems and their

metal complexes (e.g. Cu, Mn, Ni) will be carried out, together with the investigation of their redox behaviour and catalytic activity.

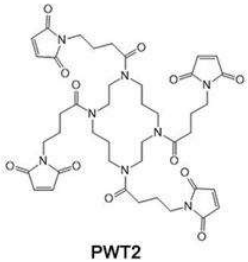

Figure 1. Schematic representation of the designed EMs scaffold.

Financial support of the National Recovery and Resilience Plan (NRRP), Mission 4 Component 2 Investment 1.1 – NextGenerationEU (PRIN PNRR 2022 - P2022EMY52) is gratefully acknowledged.

References:

[1] E. Kuah, S. Toh, J. Yee, Q. Ma and Z. Gao, 2016, 22, 8404-8430.

[2] M. Tegoni, Eur. J. Inorg. Chem., 2014, 2014, 2177-2193.

[3] M. Perinelli, R. Guerrini, V. Albanese, N. Marchetti, D. Bellotti, S. Gentili, M. Tegoni and M. Remelli, J. Inorg. Biochem., 2020, 205, 110980-110993.

[4] G. Calo, A. Rizzi, C. Ruzza, F. Ferrari, S. Pacifico, E. C. Gavioli, S. Salvadori and R. Guerrini, Peptides, 2018, 99, 195-204

Potentiometric data processing: analysis of software for optimization of protonation constants

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A critical evaluation of the software actually available for the analysis of potentiometric data was conducted, in order to identify the strengths and weaknesses of each of program and to use this knowledge for the development of the new IT products. With this aim, five software HYPERQUAD [1], SUPERQUAD [2], BSTAC [3], ReactLab™ pH PRO [4], and KEV [5], have been considered. An artificial dataset composed of six different titration curves, simulated by the PyES program [6], for a hypothetical hexaprotic acid, was processed with the aim of optimizing the six protonation constants. Moreover, the data analysis was carried out including some errors in the input data from different sources, as some calibration parameters, the total analytical concentration of reagents and ionic strength variations during titrations, in order to stress their impact on the refined parameters. The protonation constants were determined and the obtained results were analysed and discussed.

The investigation showed that the differences on the protonation constants estimated by the different software are not significant, although the minimisation approach used by the different software are not the same. The tested software presents several differences, such as the type of interface and the refinement possibilities. Only few software allow for a complete treatment of input data, i.e., optimization of calibration parameters, introduction of constrains between the total concentrations to be refined, management of the ionic strength variations that occur during the titration. The analysis of the perturbed dataset was useful to quantify the impact of some common errors on the protonation constant values. In particular, the effect of ionic strength fluctuation was discussed. It has a not negligible impact, especially for chemical systems involving highly charged metal cations and/or polyelectrolyte ligands when investigated at rather low ionic strengths. Nevertheless, among the evaluated software, the management of the ionic strength fluctuations is only implemented in two programs, the freeware but not widely spread BSTAC and the commercially available ReactLab™ pH PRO package. It should be noted that the approach proposed by the two software for the definition of the activity coefficients is quite different. The process of ionic strength correction into the general minimization algorithm needs further work to be improved in order to make the software able to properly manage the variation of the ionic strength during each titration. This possibility would open new perspectives in the field of solution complexation thermodynamics and might profoundly change some firmly established experimental practices.

References:

[1] P. Gans, A. Sabatini, A. Vacca, *Talanta* **1996**, 43, 1739–1753

[2] P. Gans, A. Sabatini, A. Vacca, *J. Chem. Soc. Dalton Trans.* **1985**, 1195–1200

[3] C. De Stefano, P. Mineo, C. Rigano, S. Sammartano, *Ann. di Chim.* **1993**, 83, 243–262

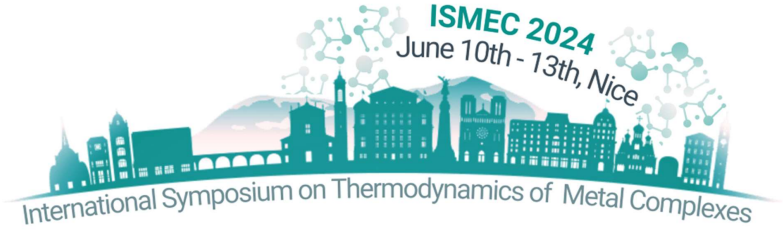
[4] P. King, M. Maeder, S. Clifford, https://jplusconsulting.com/, **2023**. (Accessed 23 November 2023)

[5] A.N. Meshkov, G.A. Gamov, *Talanta* **2019**, 198, 200–205

[6] L. Castellino, E. Alladio, S. Bertinetti, G. Lando, C. De Stefano, S. Blasco, E. García-España, S. Gama, S. Berto, D. Milea, *Chemometr. Intell. Lab. Syst*. **2023**, 239, 104860

Acknowledgements:

This publication is based upon work from COST Action CA18202 NECTAR — Network for Equilibria and Chemical Thermodynamics Advanced Research, supported by COST (European Cooperation in Science and Technology, www.cost.eu, https://cost-nectar.eu/).



Recovery of critical metals from exhausted batteries. Forcing equilibrium chemistry out of its comfort zone.

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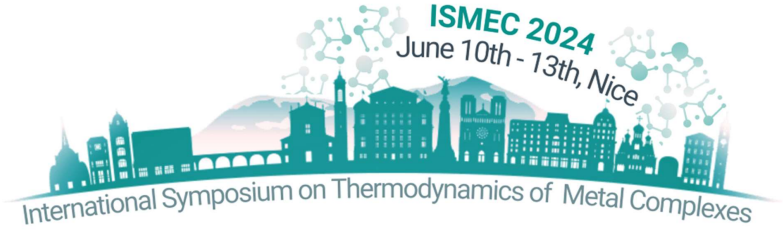
The rapid growth in demand for lithium-ion batteries (LIBs) is posing challenges in the management of end-of-life (EoL) systems and the supply of critical raw materials (CRMs), especially Li, Ni, Co and Mn. Such challenges can be addressed by collecting and recycling spent LIBs through economically and environmentally sustainable processes and by enabling the transition to a circular economy vision based on the use of secondary raw materials [1]. These processes involve the metallurgic approaches to recover the critical metals. The state-of-the-art recovery methods employed for metal extraction are chemical in nature: pyrometallurgy (using high-temperature furnaces to reduce the metal oxide components to metal alloys), and hydrometallurgy. The latter approach is based on the treatment of the black powder coming from the mechanical treatment of the dismantled batteries to recover metals by leaching with mineral acids and reducing agents and subsequent precipitation in the salt form [2]. However, these processes are highly energy-consuming, exploiting harsh conditions and producing toxic materials, so resulting in drastic environmental drawbacks [3]. New, greener routes need to be explored to return such critical raw materials into a more sustainable circular economy [2]. Among them, the application of organic acids is gaining even more attention due to the combination of good recovery efficiency, low cost, environmental benefit and reduced energy demand [4].

A preliminary screening on systems such as citric, oxalic and formic acid, in combination with reducing agents, demonstrated their suitability as greener alternatives to classical inorganic acids, even at low process temperatures, for the hydrometallurgical recycling of lithium-ion batteries.

The results obtained during the first year of the PhD project of A. Bianchi's PhD project demonstrated that, for instance, a quantitative recovery of all the metal ions, including Co(II), is achieved with an optimized procedure applied to xxx mg of oxide material in xx mL of xxx acid higher after xx min of shaking a T=xx C, with no effect of the oxidising agent.
(data covered by a patent)



The conditions, i.e. ligand concentration higher than 1M, while rather common in hydrometallurgy, are definitively far away from the typical domain of equilibrium chemistry. Nevertheless, many questions were raised in this early stage step that, in one way or another, all deal with the typical items of equilibrium chemistry. What is the role of the organic acid nature? Is the complexing properties of these acids the real driving force of dissolution? The cooperative effect of an oxidizing agent seems important only at lower T.

To try to rationalize at least some of these challenging findings, we proposed a pilot attempt to provide a method to explore the equilibrium chemistry. As a model system, we started with citric acid (H_3Cit), and Co(II) and Ni(II) as metal ions. In detail, two sets of potentiometric titrations have been performed, the first in canonical experimental conditions (at millimolar level) and the second mimicking the conditions of the hydrometallurgical process (H_3Cit ~ 1 mol dm^{-3}; Co(II) ~ 0.2 mol dm^{-3}). In both measurement sets, no background salt was added into the measurement cell, causing a relevant ionic strength variation upon NaOH addition, causing deprotonation of citric acid. Calibration of the electrode system (glass half-cell with double junction reference electrode) was tested both in internal and external conditions. The results of the analysis of potentiometric measurements at low ionic strength were used to validate our results by comparison with reference literature data [5] and have a reference for data analysis at high concentrations. Data analysis of the latter measurements was very challenging and was done taking advantage of the feature of BSTAC4 software to analyse data, also considering the variation of activity coefficients during measurements.

References:

[1] Ferrara C., Ruffo R., Quartarone E., Mustarelli P., *Adv. Energy Sustainability Res*., **2021**, 2100047.

[2] Harper, G.; Sommerville, R.; Kendrick, E.; Driscoll, L.; Slater, P.; Stolkin, R.; Walton, A.; Christensen, P.; Heidrich, O.; Lambert, S.; Abbott, A.; Ryder, K.; Gaines, L.; Anderson, P. *Nature* **2019**, 575 (7781), 75–86.

[3] Zheng, X.; Zhu, Z.; Lin, X.; Zhang, Y.; He, Y.; Cao, H.; Sun, Z. *Engineering* **2018**, 4 (3), 361–370.

[4] Gerold E., Schinnerl C., Antrekowitsch H., Recycling 2022 7(1) 7010004

[5] Kostakis N.; Raptopolou C.P.. et al. *Inorg. Chem*. **2003**, 42 (1), 22-31

Mechanochemically-synthesised palladate complexes show cellular activity: DNA and RNA tests to help enlighten their mode of action

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The use of metal complexes as anticancer drugs became a priority sector of research since the discovery in 1965 of the cytotoxic properties of cis-platinum. Many compounds based on platinum and other metals have been synthesized since then in search of better-performing drugs. In this regard, palladium, a transition metal belonging to the same group as platinum, represents a promising candidate for new anti-tumour drugs [1]. Indenyl and allyl palladate complexes bearing N-heterocyclic carbene ligands were synthesised using a mechanochemical process; they showed excellent cytotoxicity towards ovarian cancer cell lines, anticancer activity in high-grade serous ovarian cancer (HGSOC), and inhibition of the antioxidant enzyme thioredoxin reductase (TrxR) [2]. Here, we studied the reactivity of one of these species, the indenyl palladium complex called IP-2 (Figure 1).

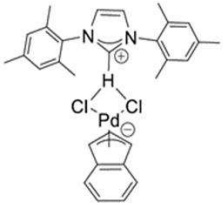

Figure 1 – The indenyl Pd(II) complex studied in this work

We have analysed the interaction between IP-2 and biosubstrates such as nucleic acids (natural DNA and synthetic RNA) and proteins (bovine serum albumin) using mainly spectrophotometric and spectrofluorimetric experiments. We will discuss the results and comment on possible selectivity, strength and binding type. These studies enable us to gain mechanistic information on the mode of action of this class of palladium metal complexes.

References:

[1] R. Czarnomysy, D. Radomska, O.K. Szewczyk, P. Roszczenko, K. Bielawsk, *International Journal of Molecular Sciences*, **2021**, 22(15), 8271

[2] T. Scattolin, I. Pessotto, E. Cavarzerani, V. Canzonieri, L. Orian, N. Demitri, C. Schmidt, A. Casini, E. Bortolamiol, F. Visentin, F. Rizzolio, S.P. Nolan, *European Journal of Inorganic Chemistry* **2022**, e20220.

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International Symposium on Thermodynamics of Metal Complexes

Eu(III)-activated luminescent biosubstrates for enhanced fluorescence microscopy

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Luminescent lanthanide complexes have attracted considerable interest in recent years across various fields ranging from materials science to biomedical applications [1]. In this study, Europium(III) complexes with ligands containing the chromophoric core of TTA (thenoyltrifluoroacetone) were employed for fluorescence labelling of both proteins and nucleic acid delivery devices within cells based on cyclodextrin sponge nanoparticles. TTA derivatives effectively coordinate Eu(III) ions and stimulate their emission in the visible spectrum at wavelengths exceeding 600 nm. Moreover, the excited state lifetimes of Eu(III) ions are much longer than those of organic fluorescent molecules present within the cellular environment, such as aromatic residues of proteins and coenzymes like NADH and FADH2. This spectroscopic characteristic enables time-gated fluorescence microscopy experiments, effectively eliminating cell auto-fluorescence background and thereby enhancing technique sensitivity.

Here, regarding protein labelling, bioconjugation to the free amino residues of proteins was utilized by reacting with the chlorosulfonic derivative of TTA. Subsequently, an excess of Eu^{3+} was added, resulting in the appearance of a pink-red fluorescence upon irradiation with a UV lamp at 365 nm (Figure 1).

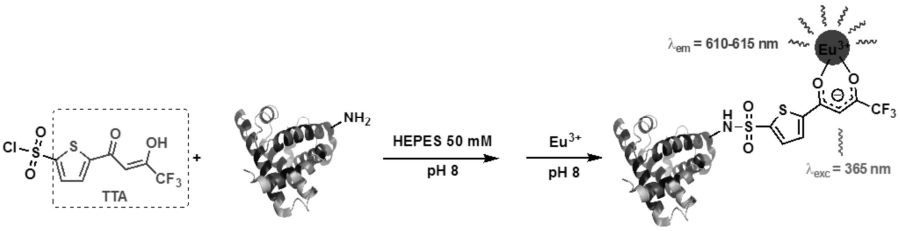

Figure 1 – The process of protein luminescent labelling using TTA derivatives able to coordinate Eu(III)

In the context of cyclodextrin nanosponges, the reaction between the same chlorosulfonic derivative of TTA and 1-adamantanamine was performed to obtain the corresponding sulfonamide derivative. This derivative forms fluorescent complexes with Eu(III) in a 1:1 stoichiometry. Subsequently, the inclusion of these adamantane derivatives within β-cyclodextrin and corresponding nanosponges was studied. Nucleic acid transport systems labelled with these complexes were developed by loading cyclodextrin nanosponges with 1-adamantanamine and a small amount of sulfonamide conjugate complexed with Eu(III). At physiological pH, the free amine groups of the included amine are protonated to form a polycationic system, which serves as a potential vehicle for nucleic acids (polyanionic systems) across the lipid bilayer [2]. In this context, fluorescent labelling with the Eu(III) complex allows observation, through time-gated fluorescence microscopy, of the actual entry of DNA into the cell.

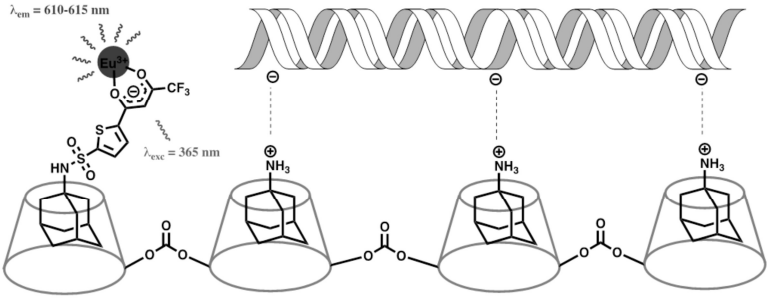

Figure 2 – Nucleic acid labelling strategy by the adamantanamine-cyclodextrin-TTA-Eu(III) luminescent system

In both cases, the luminescent systems were characterized by recording fluorescence emission spectra of the bound Eu(III) form. Additionally, the chiral environments offered by proteins and cyclodextrins were exploited to obtain circularly polarized luminescence (CPL) spectra.

References:

[1] N. Sayyadi, I. Justiniano, R. E. Connally, R. Zhang, B. Shi, L. Kautto, A. V. Everest-Dass, J. Yuan, B. J. Walsh, D. Jin, R. D. Willows, J. A. Piper, N. H. Packer, *Analytical Chemistry*, **2016**, 88(19), 9564–9571.

[2] S. Allahyari, F. Trotta, H. Valizadeh, M. Jelvehgari, P. Zakeri-Milani, *Expert Opinion on Drug Delivery*, **2019**, 16(5), 467–479.

1H-Pyrazole Metal Coordination Modulated by Polyamine Chain length in [1+1] Condensation Macrocycles with Remarkable SOD activity

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A class of metalloprotein mimetic is constituted by simple metal complex able to reproduce, at least in part, the structure, properties, or function of the active centre of given enzymes. The superoxide dismutase (SOD)[1] family of enzymes is the first biological line of defense against reactive oxygen species (ROS) produced as result of imbalances in oxygen metabolism. However, catalase enzymes are the ones finishing the cell detoxification process.

In this work we purpose the design, synthesis and characterization of three [1+1] azacyclophane macrocycles using 1*H*-pyrazole as the aromatic spacer and three polyamines with different chain lengths, the pentaamine 1,5,8,11,15-pentaazadecane (L1) and the hexaamines 1,5,8,12,15,19-hexaazanonadecane (L2) and 1,5,9,13,17,21-hexaazaheneicosane (L3). We study the SOD and catalase behaviour using the McCord-Fridovich[2] enzymatic assay and the xylenol orange method.[3] We observed that L2 and L3 binuclear cooper complexes have one on the highest antioxidant activities so far reported.[4]

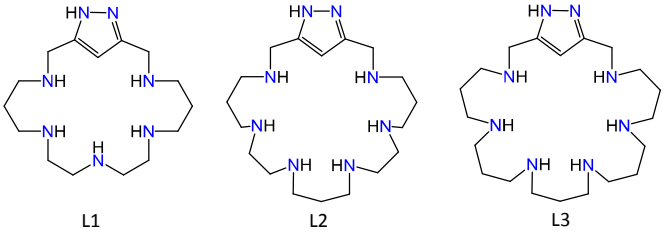

Figure 1: Ligand drawing.

References:

[1] L. Iturrino, P. Navarro, M.I. Rodríguez-Franco, M. Contreras, J. Escario, A. Martinez, M.R. Pardo, *Eur. J. Med. Chem*, **1987**, 22, 445-451.

[2] J.M. McCord, I. Fridovich, *J. Biol.Chem,* **1969**, 244, 6056-6063.

[3] C Gay, J. Collins and J.M. Gebicki. *Redox Report*. **1999**, 4, 327–328.

[4] R. Belda, S. Blasco, B. Verdejo, H. R. Jiménez, A. Doménech-Carbó, C. Soriano, J. Latorre, C. Terencio and E. García-España. *Dalton Trans*, **2013**, 42, 11194-11204.

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Designing artificial catalytic copper proteins based on the Spy technology.

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Metalloproteins promote several of the most complex biomolecular processes in Nature. The design of new metalloproteins is therefore of interest in the field of the development of new efficient biocatalysts. *De novo design* and *protein redesign* can be combined together to generate new artificial metalloproteins.[1] With this approach, a new metalloprotein (SpyComplex, ST/SC) has been engineered The Spy Complex is an artificial protein system in which a peptide (SpyTag, ST) binds to a protein (SpyCatcher, SC) through a spontaneous isopeptide bond.[2] Metal sites can be designed on the SpyTag peptide and, by recombination with SpyCatcher, an artificial metalloprotein can be obtained. Here we present a new copper protein designed using the SpyCatcher/SpyTag construct bearing a catalytic His-His site. The SC thus functionalized introduce a new specific metal site in the close proximity of a protein (SC) (which otherwise would not have it), thanks to the irreversible SpyCatcher-SpyTag recombination, in a Trojan horse approach.[2]

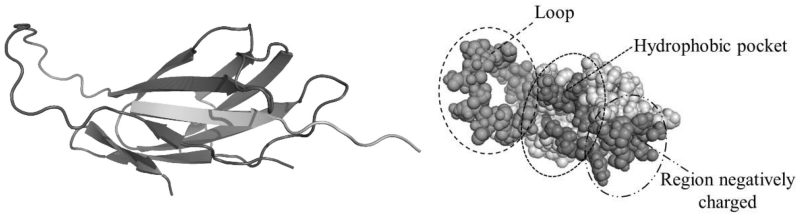

Figure 1: Left: Representation of the SC (dark grey) / ST (light gray) complex (ST/SC); Right: Representation of the SC with three key regions are highlighted: the hydrophobic pocket (where isopeptide bond is formed), the negatively charged region (where positively charged C-terminus of ST interacts with SC) and the loop

The His-His SpyTag peptide can bind copper ions in both +1 and +2 oxidation states. Cu(I/II) adducts with $(His)_2$ on the SpyTag peptide exhibit pseudocatecholase activity (Figure 2). These results have prompted us to try to achieve stereoselective oxidation of L/D-DOPA. We will present the outcomes of our efforts, along with full characterization (UV-Vis, Fluorescence, Circular Dichroism and Potentiometry) of the Cu-ST adducts.

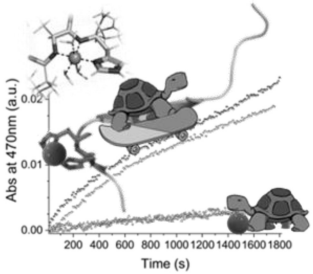

Figure 2: Schematic representation of how Cu(I/II)-SpyTag can catalyze catechol oxidation at pH 7.4.

To boost stereoselectivity in this oxidation, SpyTag-SpyCatcher adduct has been also investigate. However, despite the presence of a consensus sequence in the peptide known for its role in Spy Complex formation, we were unable to achieve SpyComplex (ST/SC) formation. Taking a step back, we will be proving that it is essential to also have charge complementary in the terminal region and we will show how this impacts stereo- and/or enantioselectivity of oxidation.

Project ART2HYDROGEN "Artificial enzymes for the photocatalytic production of hydrogen in photosynthetic bacteria" funded under the National Recovery and Resilience Plan (NRRP), Mission 2 Component 2 Investment 3.5 - Call for tender No. 4 of March 23, 2022 of Italian Ministry of Ecologic Transition funded by the European Union – NextGenerationEU. Project code RSH2A_000009, Concession Decree 445 of December 29, 2022 adopted by the Italian Ministry of Environment and Energy Security.

*Project "**Bando di Ateneo per la Ricerca 2022**" – A Way Towards Artificial Metalloenzymes - University of Parma*

Finanziato dall'Unione europea NextGenerationEU
MINISTERO DELL'AMBIENTE E DELLA TUTELA DEL TERRITORIO E DEL MARE
UNIVERSITÀ DI PARMA

References:

[1] F. Yu, V. M. Cangelosi, M. L. Zastrow, M. Tegoni, J. S. Plegaria, A. G. Tebo, C. S. Mocny, L. Ruckthong, H. Qayyum, V. L. Pecoraro, *Chemical Reviews* **2014**, 114 (7), 3495-3578.

[2] S.C. Reddington, M. Howarth, *Curr. Opin. Chem. Biol*. **2015**, 29, 94–99

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The effect of metal-porphyrins on the self-assembly of amyloid-β and amylin peptides

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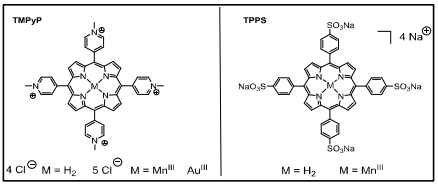
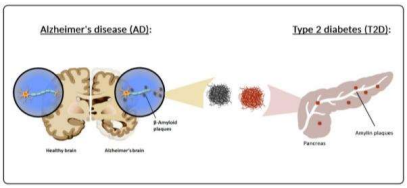
Alzheimer's disease (AD) and T2 diabetes (T2D) are key amyloid-related diseases with huge health and societal fallouts. The two diseases share a common feature, an accumulation of amyloid-β (Aβ) for AD and of amylin, also known as human islet amyloid polypeptide (hIAPP), for T2D, which are linked to the aetiology of the diseases [1]. Previous works have demonstrated that porphyrins can interact with the self-assembly of amyloid peptides such as Aβ [2], amylin [3, 4] and insulin [5]. In the present work, we will show that anionic and cationic porphyrins have a different impact on these two peptides self-assembly. The data include ThT fluorescence assays, UV-visible, NMR, transmission electron microscopy (TEM), atomic force microscopy (AFM) and circular dichroism (CD) analysis. We will show evidences that multi-cationic porphyrins (but not anionic) modulate Aβ self-assembly and that, conversely, multi-anionic porphyrins (but not cationic) modulate amylin self-assembly [6].





Acknowledgments:

The authors acknowledge financial support from ANR (projectMASAI-CE44).

References:

[1] Wells, C. Brennan, S. Keon, M. Ooi, L, Int. J. Biol. Macromol. **2021**, 181, 582–604.

[2] Fan, Y. Wu, D. Yi, X. Tang, H. Wu, L. Xia, Y. Wang, Z. Liu, Q. Zhou, Z. Wang, J, ACS Omega **2017**, 2 (8), 4188– 4195.

[3] Wu, J. Yin, X. Ye, H. Gao, Z. Li, H, Int. J. Biol. Macromol. **2021**, 167, 141–150.

[4] Wu, J. Zhao, J. Yang, Z. Li, H. Gao, Z, Chem. Res. Toxicol. **2017**, 30 (9), 1711–1719.

[5] Nath, S. Roy, P. Mandal, R. Roy, R. Buell, A. K. Sengupta, N. Tarafdar, P. K, Chem. – Asian J. **2021**, 16 (23), 3931–3936.

[6] Brison, A.; Pratviel, G.; Hureau, C. Concentration-dependent modulation of Aβ self-assembly using a series of tunable porphyrins: a structure-activity relationship. *In preparation.*

Analysis of microplastics in marine sediment samples

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Microplastics are small particles of plastic material generally measuring few millimeters or micrometers. This very small waste can enter the environment and food, resulting dangerous for ecosystems and human health. Moreover, microplastics can enter the food chain of fauna and reach the food on our table. The presence of microplastic is associate to environmental pollution by human's activities. Microplastics persist in the environment in large quantities, especially in marine and aquatic ecosystems [1-3]. For all these reasons there is an urgent need to develop low-cost, fast, green and accurate extraction and analysis methods in samples characterized by various matrices. We set-up an analytical method to study the content of microplastics in sea and lagoon sediments by using a direct immersion ultrasonic extractor. Thanks to this equipment the solvent volume, sonication time and energy consumption are reduced, as well as the acoustic pollution. Gas chromatography coupled with mass spectrometry was used for the identification and quantitation of the analytes.

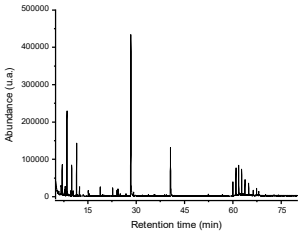

Figure 1. Chromatogram of the extract of a sea sediment sample (GC-MS).

References:

[1] Chin J Anal Chem, 2017, 45(3), 348–356.
[2] Anal. Methods, 2017, 9, 1512
[3] Marine Pollution Bulletin, 160 (2020), 111667

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Synthesis and thermodynamic properties of metal complexes for the preparation of atomically precise catalysts for the ORR reaction

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The Oxygen Reduction Reaction (ORR) is one of the most important reactions both in life processes and in artificial energy conversion systems, for example fuel cells [1,2]. This reaction is characterized by a very slow kinetics, so that the use of a catalyst is fundamental to make the reaction profitable, and Pt-based electrocatalysts have the best catalytic performance to date, Pd-ones being a close second [3,4]. Unfortunately, the scarcity and the high price of Pt, and of so-called Platinum Group Metals (PGM), prevents the widespread use of PGM-catalyst in daily human activities that require an energy supply. Nonetheless, the importance of fuel cells, which are a green substitute for the internal combustion engine, pushes us to find different ways to overcome the previously mentioned problem. To replace platinum and other PGMs of similar cost, different strategies have already been implemented, for example the use of different non-noble metals or the use of non-metal or atomically precise electrodes. Atomically precise electrocatalysts are of special interest due to their high atomic utilization efficiency, special electronic structure and homogeneous distribution of active centres [5]. We reported that the atomically precise catalyst based on the Pd(II) complex of the ligand L1 (Figure 1) effectively promotes the ORR reaction in alkaline media with performance similar to that of commercial Pt electrodes [6]. L1 consists of a cyclen structure (cyclen = 1,4,7,10-tetraaza-cyclododecane) functionalized with lateral arms bearing electron poor pyrimidine groups. The cyclen structure ensures stable coordination of the catalytic metal centre (Pd(II)) while the pyrimidine groups are used to anchor the complex on MWCNTs via spontaneous adsorption under environmentally friendly conditions (water, room temperature, unprotected atmosphere). Based on these results, we synthesized two new ligands (L2 and L3, Figure 1) that are similar to L1 but contain one or two oxygen donors, instead of nitrogen donors, to explore new selectivity patterns toward metal ion coordination and for the construction of atomically precise catalysts for ORR. We report here preliminary results on the coordination properties of L2 and L3.

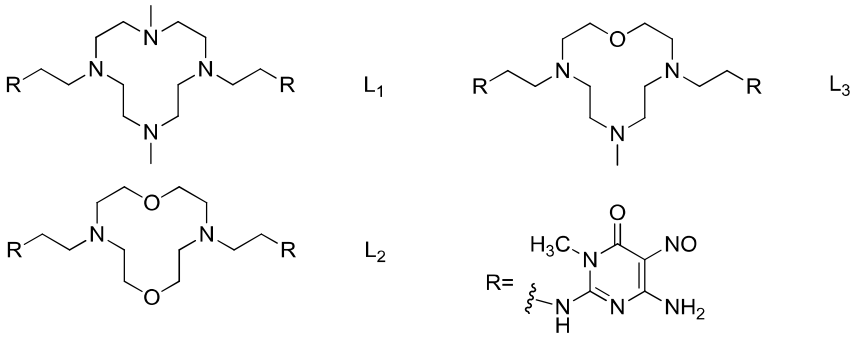

Figure 1. The ligands of this study.

References

1) G. Hoogers and F. Kreith, Eds., *Fuel Cell Technology Handbook*, CRC Press, Boca Raton, 2002.

2) B.C.H. Steele and A. Heinzel, *Nature*, 2001, **414**, 345–352.

3) X. He, S. Minelli, A. Vertova and A. Minguzzi, *Curr. Opin. Electrochem.*, 2022, **36**, 101166.

4) J. Hou, M. Yang, C. Ke, G. Wei, C. Priest, Z. Qiao, G. Wu and J. Zhang, *EnergyChem*, 2020, **2**, 100023.

5) L. Yan, P. Li, Q. Zhu, A. Kumar, K. Sun, S. Tian and X. Sun, *Chem*, 2023, **9**, 280–342.

6) V. Monini, C. Bazzicalupi, A. Bianchi, M. Bonechi, P. Gentilesca, W. Giurlani, M. Innocenti, G. M. Romano and M. Savastano, *Dalton Trans*, 2024, **53**, 2487-2500

Harnessing Ruthenium(II) Polypyridyl Complexes and Light to design advanced photoresponsive bioactive molecules

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The development of innovative photosensitizers (PSs) that can target tumorous and bacterial afflictions with high specificity has become a major focus in the quest for more precise and controlled methods of photodynamic therapy (PDT). Among these, Ru(II)-polypyridyl complexes (RPCs) have emerged as promising candidates due to their diverse chemical-physical properties that make them ideal for PDT. The adaptable chemistry of these coordination compounds allows for fine-tuning their essential photophysical properties, maximizing their effectiveness as PSs.

This communication explores the impact influence of strategic ligand design on the photochemical and photobiological performance of RPCs, emphasising the potential for enhanced control over drug activation.

The study begins by examining bis-heteroleptic RPCs with extensive aromatic polypyridyl ligands, such as the popular benzo[i]dipyrido[3,2-a:2',3'-c]phenazine (dppn) ligand. In this arrangement, the π-expansive chelate ligands can facilitate the population of the intraligand ^{3}IL states from the ^{3}MLCT, thereby increasing the efficiency of cytotoxic oxygen species generation. [1]

Furthermore, we explored the effect of directly conjugating an organic chromophore onto Ru(II)-scaffolds to create bichromophoric systems. This arrangement generates an excited state energy reservoir on the long-lived ^{3}IL states of the organic chromophore, which plays a pivotal role in augmenting the generation of singlet oxygen up to 92%. [2]

Finally, this communication even introduces the approach of the photoactivated chemotherapy (PACT) to antibacterial treatment, expanding beyond traditional photodynamic therapy applications. The unique photophysical properties of RPCs are utilized to trigger the controlled release of Metronidazole-derivatives, offering a strategic method to combat antibiotic resistance by selectively activating the drug in desired locations. This approach is referred to as *Photorelease Antimicrobial Therapy* – PAT. [3, 4]

Overall, the study highlights the crucial role of ligand architecture in determining the efficiency and versatility of RPCs as PSs. This research advances the understanding of these

mechanisms, paving the way for the development of next-generation phototherapeutic agents that can address the complexities of tumor and bacterial diseases with enhanced precision and efficacy.

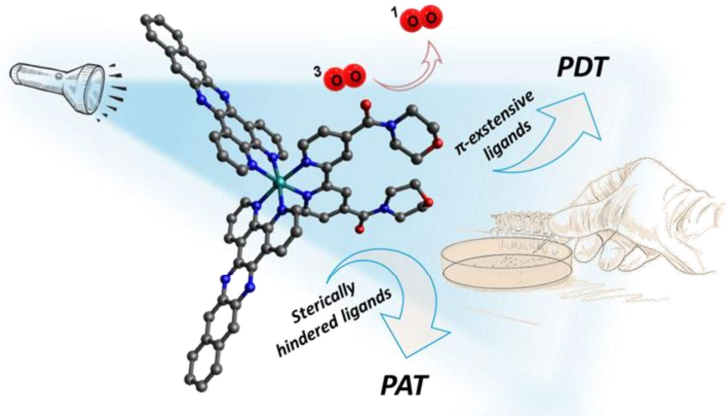

Figure 1: Ruthenium(II)-complexes as photoactivated bioactive compouds.

References:

[1] G. E. Giacomazzo, M. Schlich, L. Casula, L. Galantini, A. Del Giudice, G. Pietraperzia, C. Sinico, F. Cencetti, S. Pecchioli, B. Valtancoli, L. Conti, S. Murgia, C. Giorgi, *Inorganic Chemistry Frontiers* **2023**, 10, 3025A. Black, B. White, C. Green, D.-W. Brown, *Journal* **Year**, volume (issue), 10-15.

[2] G. E. Giacomazzo, S. Doria, A., Revilla-Cuesta, N. De Monte, M. Pagliai, G. Pietraperzia, B. Valtancoli, T. Torroba, L. Conti, M. Di Donato, C. Giorgi, *Inorganic Chemistry* **2024**, 63 (14), 6248-6259.

[3] G. E. Giacomazzo, L. Conti, A. Guerri, M. Pagliai, C. Fagorzi, P. S. Sfragano, I. Palchetti, G. Pietraperzia, A. Mengoni, B. Valtancoli, C. Giorgi, *Inorganic Chemistry* **2022**, 61 (18), 6689-6694

[4] G. E. Giacomazzo, L. Conti, C. Fagorzi, M. Pagliai, C. Andreini, A. Guerri, B. Perito, A. Mengoni, B. Valtancoli, C. Giorgi, *Inorganic Chemistry* **2023**, 62, 7716-7727.

Ga(III) hydrolysis constants: literature analysis and modeling of the dependence on medium and ionic strength

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Gallium is widely employed in plenty of fields, being crucial in many industrial and technological, as well as medical, applications [1,2]. This widespread use, together with its limited availability, concurred to include Ga(III) in the list of the *Technologically Critical Elements* (TCEs) [1]. As such, its recovery is important for the reutilization in all these applications. Many Ga properties and applications, as well as some recovery processes, take place in aqueous solutions, in which it is present as trivalent Ga species. Being Ga^{3+} a hard Lewis acid, it undergoes strong hydrolysis in aqueous solution, which deeply affects its chemico-physical parameters and reactivity. Consequently, its speciation is dominated by the formation of several hydrolytic species, both mononuclear and polynuclear, with different stability. The most common species in literature are the mononuclear $Ga(OH)^{2+}$, $Ga(OH)_2^+$, $Ga(OH)_{3(aq)}$ and $Ga(OH)_4^-$, while few other polynuclear species are reported by single authors. Collected literature values were critically analyzed in this work, evidencing that hydrolysis constants and solubility products are determined in a wide range of temperature, medium and ionic strength conditions. However, significant discrepancies were found concerning both the nature and the stability of hydrolytic species of Ga^{3+}. Furthermore, reported data at different temperatures are usually obtained in single media and ionic strengths, and *vice versa*, highlighting the necessity to perform further dedicated experiments, in order to define a correct speciation model as a function of different conditions [3-7]. As such, a reliable, simultaneous modeling of medium, ionic strength and temperature dependence of literature data on Ga^{3+} hydrolysis constants is hampered. However, considering the wide number of aqueous solution studies involving this cation, an attempt of rationalization of available data is necessary. For this reason, being most of literature hydrolysis constants of Ga^{3+} reported at T = 298.15 K in various media (e.g., ClO_4^-, NO_3^-, Cl^-, Br^-) and ionic strengths ($0 < I/mol\ dm^{-3} \leq 1.5$), these data were used for the modeling of the dependence on medium and ionic strength, and results are reported in this contribution. An Extended Debye-Hückel (EDH) type equation (Eq. 1) has been used,

$$\log \beta = \log \beta^0 - z^* \, 0.51 \left(\frac{\sqrt{I}}{1 + 1.5\sqrt{I}} \right) + CI \qquad \text{(Eq. 1)}$$

according to the "pure water model" [8,9], in which perchlorate is considered as "non interacting" with Ga^{3+}, while the dependence on medium is taken into account on the basis of weak complex formation between this cation and the anions of the supporting electrolytes (e.g., NO_3^-, Cl^-, Br^-).

Overall, obtained results allow the modeling of the mononuclear hydrolysis constants of Ga^{3+} at T = 298.15 K in a wide range of ionic strength and medium conditions, including any possible mixture of the considered anions.

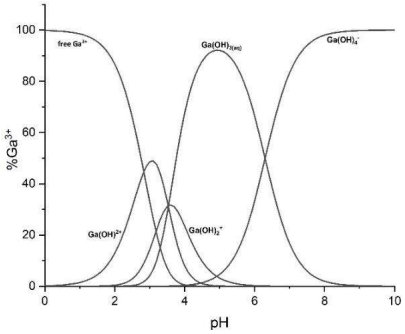

Figure 1. Distribution diagram of Ga^{3+} hydrolytic species at T = 298.15 K and I = 1 mol dm^{-3} in $NaClO_4$, (c_{Ga3+} = 1 x 10^{-6} mol dm^{-3}).

References:

[1] K. Zheng, M.F. Benedetti, E.D. van Hullebusch, *J. Environ. Manage.*, **2023**, 347, 119043.
[2] F. Kurtuldu, N. Mutlu, A.R. Boccaccini, D. Galusek, *Bioact. Mater.*, **2022**, 17, 125-146.
[3] A.E. Martell, R.M. Smith, R.J. Motekaitis, NIST Standard Reference Database 46, vers.8. Gaithersburg, 2004.
[4] D. Pettit, K. Powell, IUPAC Stability Constants Database. Academic Software: Otley, UK, 2004.
[5] P.M. May, D. Rowland, K. Murray, E.F. May, JESS, Joint Expert Speciation System, http://jess.murdoch.edu.au/jess_home.htm, accessed March 2024.
[6] C.F. Baes, R.E. Mesmer, The Hydrolysis of Cations. John Wyley & Sons: New York, **1976**.
[7] P.L. Brown, C. Ekberg, Hydrolysis of metal ions, Wiley-VCH Verlag GmbH & Co. **2016**.
[8] L. Castellino, E. Alladio, S. Bertinetti, G. Lando, C. De Stefano, S. Blasco, E. García-España, S. Gama, S. Berto, D. Milea, *Chemom. Intell. Lab. Syst.*, **2023,** 239, 104860.
[9] F. Crea,C. De Stefano, D. Milea, A. Pettignano, S. Sammartano, *Bioinorg. Chem. Appl.*, **2015**, 267985.

Metallophores as a key to understanding how bacteria withdraw and transport metal ions

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Transition metal ions are essential elements for many pathogens. These nutrients are required in significant structural and catalytic roles in many biological processes. The increasing interest in metallophores—metal chelating molecules which are excreted outside the pathogen in order to efficiently bind a given metal ion and in their interactions with appropriate metals is one of the results of the dramatic increase of antimicrobial resistance [1].

To survive in the host and succeed in competing with commensal microbes, pathogenic bacteria must maintain a steady state of zinc usage by controlling zinc distribution with zinc transporters. Bacterial cells regulate the uptake, distribution and excretion of zinc through several systems, including the Zn(II)-specific uptake system (ZnuABCD) [2-3]. For Zn(II) binding sites, histidine residues constitute the main anchoring donors forming loop structures when bound to Zn(II). The His-rich loop, present in ZnuA and ZnuD protein respectively, has a role in the capture of zinc(II), acting as a 'fishing net', which is then further delivered into other regions of the protein. Moreover, ZnuD-Cu(II) binding induces a conformational change of metal binding site to a polyproline II-like helix. To the best of our knowledge, this is the first evidence of a copper(II)-induced formation of a polyproline II-like structure in a sequence that does not contain proline residues [3].

Nickel is an essential cofactor for some pathogen virulence factors. Due to its low availability in hosts, pathogens must efficiently transport the metal and then balance its ready intracellular availability for enzyme maturation with metal toxicity concerns. HypB is one of the chaperones required for proper nickel insertion into [NiFe]-hydrogenase. *E. coli* HypB has two potential Ni(II) and Zn(II) binding sites - the N-terminal one and the so-called GTPase one. We showed that the N-terminal region binds metal ions with higher affinity than the G-domain. Moreover, the N-terminal HypB region is also more effective in Ni(II) binding than the previously studied SlyD metal binding regions [4].

The very few studies on Cu transport in bacteria have mainly focused on Cu export (in order to detoxify the microbial cell), while the mechanisms of Cu import across the outer membrane of Gram-negative bacteria and the bacterial cytoplasmic membrane have been

examined in only a few cases. A number of questions related to the structure of copper trafficking proteins remain unanswered. These questions concern both Cu(I) coordination properties and chaperone–transporter interactions. For several key players in the copper transport pathways, the identities of coordinating ligands, coordination geometries, and thermodynamic parameters remain ambiguous. Bacterial Cu transporting systems in general are far more diverse than in eukaryotes and some mechanisms of Cu uptake are limited to one group of bacteria, or even to one species. OprC is an outer membrane transporter which mediates acquisition of both reduced and oxidised ionic copper. It binds copper via an unprecedented CxxxM-HxM metal binding site, discovered recently. The interaction between novel metal binding site of OprC and its putative metallophore CopM was extensively studied.

Effective acquisition of metal ions is crucial for the survival and virulence of many pathogens, thus maintaining metal homeostasis is a critical process that must be precisely coordinated by them. To achieve this, bacteria need to use numerous of diverse metal uptake and efflux systems controlled by metalloregulatory proteins. Understanding a novel metal-acquisition mechanisms in microbes will make a significant contribution to the development and design of new therapeutics against resistant pathogens, which could be a good alternative for commonly used drugs.

Acknowledgments: The work was supported by the National Science Centre (Grant UMO-2017/26/A/ST5/00363). A.H. is supported by the Polish National Agency for Academic Exchange (Grant BPN/BKK/2022/1/00005) and Excellence Initiative – Research University Grant BPIDUB.13.2024.

References:

[1] H. Kozlowski, K. Piasta, A. Hecel, M. Rowinska-Zyrek, E. Gumienna-Kontecka, Metallophores: How do human pathogens withdraw metal ions from the colonized host. In Comprehensive Inorganic Chemistry III, Elsevier, **2023**, pp. 553-574 .

[2] A. Hecel, A. Kola, D. Valensin, H. Kozlowski, M. Rowinska-Zyrek, Inorg. Chem. **2020**, 59, 1947-1958.

[3] A. Hecel, M. Rowinska-Zyrek, H. Kozlowski, Inorg. Chem., **2019**, 58, 5932-5942.

[4] A. Hecel, A. Kola, D. Valensin, H. Kozlowski, M. Rowinska-Zyrek, Dalton Trans. **2021**, 50, 12635-12647.

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Pyclen-based ligands for the complexation of gallium(III)

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The rising cancer rates necessitate innovative detection and treatment methods. The diverse properties of metal ions play a pivotal role in numerous modalities, particularly in nuclear medicine (PET imaging and radiotherapy). Consequently, the development of effective chelators is an integral part of the development of new metal-containing drugs, to ensure safe injections by avoiding the release of free toxic metals. Polyazamacrocycles, due to their exceptional complexation properties toward a wide range of cations, are increasingly employed as chelators. The β^+ emitter ^{68}Ga [1] is valuable for PET imaging due to its short half-life ($t_{1/2}$ = 68 min), offering minimal radiation exposure. Additionally, its production via a ^{68}Ge/^{68}Ga generator offers a convenient supply.

Our group investigated the association of the pyclen macrocycle with various coordinating pendants arms to design a series of mono-*N*-functionalized pyclen derivatives (figure 1) [2].

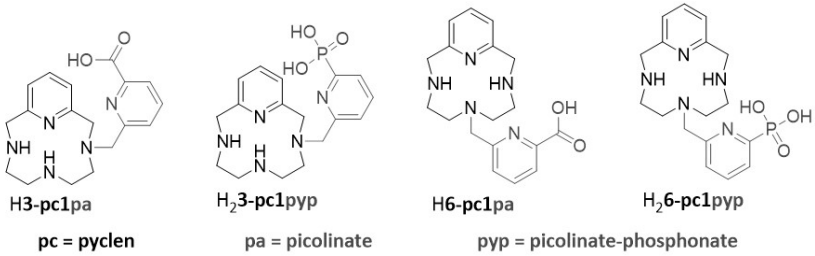

Figure 1: Series of mono-*N*-functionalized pyclen studied for the complexation of Ga^{3+}.

Noteworthy that two regioisomers, having each its peculiar properties, were systematically prepared and studied. Gallium(III) complexes were obtained and analyzed, confirming distinct behaviors influenced both by the ligand's structure and the nature of the coordinating arm. Thermodynamic constants were determined through potentiometric studies and kinetic inertness in acidic and basic conditions was evaluated. The most promising ligand, H**3-pc1pa**, was further studied for the radiolabeling with $^{68}Ga^{3+}$ where the corresponding radiocomplex was formed with quantitative yield and exhibits good stability in serum.

References:

[1] W.A.P. Breeman, E. De Blois, H. Sze Chan, M. Konijnenberg, D.J. Kwekkeboom, E.P. Krenning, *Semin. Nucl. Med.* **2011**, *41* (4), 314–321.

[2] G. Nizou, E. Molnár, N. Hamon, F.K. Kálmán, O. Fougère, O. Rousseaux, D. Esteban-Gòmez, C. Platas-Iglesias, M. Beyler, G. Tircsó, R. Tripier, *Inorg. Chem.* **2021**, *60* (4), 2390–2405.

Nanocapsules as innovative manganese-based MRI contrast agents for the visualisation of pancreatic islet beta cells: synthesis, formulation and biological studies

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In 2021, 537 million people worldwide suffer from diabetes. This chronic disease occurs when the pancreas does not produce enough insulin (type 1 diabetes), or when the body does not properly use the insulin which is produced (type 2 diabetes).[1] The cells involved in insulin production are called beta cells, and when they are defective, this leads to a reduction in the beta cells mass (BCM) contributing to diabetes.[2] It therefore seems important to be able to detect and quantify this BCM. To date, there is no diagnostic tools to monitor BCM qualitatively or quantitatively.

In this work, we aim to design nano-capsules specifically targeting beta cells and containing Mn^{2+} complexes for the non-invasive quantification of BCM by magnetic resonance imaging (MRI).

As diabetic patients can present complications such as damage to the renal system, we turned towards the use of Mn^{2+} rather than Gd^{3+}. In addition, our team has developed an excellent chelator for Mn^{2+}, a bispidine-type ligand which demonstrates excellent kinetic inertness.[3] This complex is trapped at the surface between the oil phase and the hydrophilic polyethylene glycol moieties of lipid nanocapsules to increase the local concentration of Mn^{2+} and hence enabling high contrast. To specifically target beta cells, nanocapsules will be functionalized with a vector directed against beta cell surface antigens.

Our preliminary results showed that our new Mn^{2+} functionalized nano-capsules (**Mn@LNC25**) exhibited high proton relaxivity *versus* the gold standard Dotarem® (8.31 and 4.7 $mM^{-1}.s^{-1}$ respectively at 60 MHz and 25°C, **Fig 1.A.**).[4] In addition, these nano-capsules were not toxic for insulin producing INS-1E cells (**Fig 1.B.**), indicating that the formulation is promising as innovative and safe carrier for Mn^{2+} to beta cells.

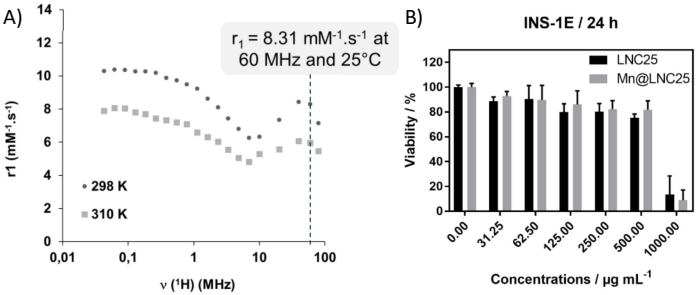

Figure 1 : A) NMRD profiles of **Mn@LNC25** in water at 298K and 310K. **B)** Effect of **Mn@LNC25** on the viability of insulin producing INS-1E cells.

References:

[1] A. Boulton, D. Magliano, E. Boyko, *IDF Diabetes Atlas | Tenth Edition*, **2021**.

[2] D. L. Eizirik, L. Pasquali, M. Cnop, *Nat Rev Endocrinol* **2020**, *16*, 349–362

[3] D. Ndiaye, M. Sy, A. Pallier, S. Même, I. de Silva, S. Lacerda, A. M. Nonat, L. J. Charbonnière, É. Tóth, *Angew. Chem. Int. Ed.* **2020**, *59*, 11958–11963.

[4] Éva Tóth, L. Helm, A. Merbach, in *The Chemistry of Contrast Agents in Medical Magnetic Resonance Imaging*, **2013**, pp. 25–81.

Cu and Zn Mobility Study from Winery Sludge for Use as Fertilizer in Vineyards

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Vineyards have historically depended on copper-based fungicides to control fungal diseases, such as Downy Mildew. The intensive use of these fungicides for more than a century has contributed to the accumulation of copper (and concomitantly zinc) in soil, water, vegetation, and winery waste, causing a serious environmental and agro-industrial problem. Lack of alternatives to fully replace Cu compounds requires the promotion of sustainable practices to reduce the environmental impact [1].

In this sense, one of the biggest challenges of sustainable agriculture in vineyards is to recycle the waste generated at the end of the winemaking process, the winery sludge (WS). This WS contains a significant amount of nutrients and organic matter which are in high demand for soil fertilisation and regeneration, however, its high Cu and Zn content hinders its application in soils.

The aim of this study is to explore winery sludge (WS) as a potential agricultural resource, focusing on its physicochemical parameters, heavy metal content and distribution throughout the WS matrix, and metal extraction approach for remediation purposes. Risk assessment was performed by employing sequential extractions schemes which revealed distinct patterns of heavy metal association within the WS matrix [2].

Metal content analysis via FP-XRF and ICP-MS methods revealed levels of copper and zinc above 100 mg/kg. More than 70% of Cu exhibited a high affinity for organic matter (OM), forming stable complexes that reduce its bioavailability and restrict its short-term mobility. In contrast, Zn showed a 26% to be bound to the iron and manganese oxides phases and 50% complexed to OM, making it more easily released to the environment.

The most effective conditions for metal extraction were achieved by using sulfuric acid (0.5 mol·L^{-1}), establishing an appropriate sludge-to-acid ratio to facilitate selective metal removal. Copper extraction reached 80%, while zinc extraction exceeded 95%.

WS matrix has been characterised through ATR-FTIR and DRX after each extraction step. Residual OM analysis in the remaining WS post-extraction revealed negligible

alteration, crucial for maintaining nutrient-rich but metal-free compositions for effective soil fertilization.

Aknowledgements:

European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie (GA: 801342, Tecniospring INDUSTRY) proposed by the Catalan Agency for Business and Competitiveness (ACCIÓ), FI-Joan Oró scholarship from the Catalonian Government and the Ministry of Science and Innovation, Spain (PID2021-124084OB-100) are kindly acknowledged.

References:

[1] E.F.S. Authority, Conclusion on the peer review of the pesticide risk assessment of the active substance disodium phosphonate, EFSA Journal 11 (2013) 3213. https://doi.org/https://doi.org/10.2903/j.efsa.2013.3213.

[2] J. Wang, X. Wang, G. Li, J. Ding, Y. Shen, D. Liu, H. Cheng, Y. Zhang, R. Li, Speciation Analysis Method of Heavy Metals in Organic Fertilizers: A Review, Sustainability 14 (2022). https://doi.org/10.3390/su142416789.

Improved Adsorption of Trace Cisplatin via Thiol-Functionalized Sponges Facilitated by Pt–S Complexation

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Cisplatin is a widely employed platinum-based cytostatic drug (Pt-CDs) in cancer therapy. After administration, 10–40% of the compound is excreted through urine of patients in 24 h, reaching the ecosystem, via the release of hospital or household wastewaters, where the compound can be found in trace amounts [1]. To effectively eliminate the trace amounts of cisplatin from aqueous solutions, a strategy involving the functionalization of a commercial cellulosic sponge has been employed.

The functionalization process was conducted via esterification with 3-mercaptopropionic acid, followed by reduction with $Na_2S{\cdot}9H_2O$ or $SnCl_2{\cdot}2H_2O$ [2-4]. This resulted in the production of thiol-functionalized sponges (TFSs), denoted as TFS_1 and TFS_2, respectively, which exhibited enhanced capabilities for trace cisplatin removal compared to the non-functionalized. The maximum removal efficiencies achieved were 95.5±0.8% for TFS_1 and 99.5±0.1% for TFS_2, highlighting the efficacy of the functionalization process.

Characterization studies using FTIR, elemental analysis, SEM-EDS, and XPS confirmed the successful grafting of thiol groups onto the sponge surfaces, facilitating Pt−S complexation during adsorption. The aqua-derivatives of cisplatin, formed through hydration, were found to complex with the thiol sites via ligand displacement. Furthermore, the presence of a Sn/SnO_2 coating on TFS_2 contributed to an enhanced adsorption process.

The adsorption kinetics followed a pseudo-second-order model, indicating a rapid process involving both diffusion and chemisorption, and showing that the adsorption is primarily controlled by the chemical bonding interactions occurring between cisplatin and thiol groups. While the Langmuir isotherm model generally described the monolayer adsorption behavior of cisplatin, the introduction of surface heterogeneity through the aggregation of Sn/SnO_2 onto TFS_2 at 343 K resulted in a better fit with the Freundlich model. The evaluation of mean free energy, derived from the Dubinin-Radushkevich

isotherm model, suggested that physisorption, including electrostatic attraction, predominated for TFS_1, while chemisorption was the dominant mechanism for TFS_2.

Form the thermodynamic parameters, the adsorption of cisplatin onto both TFS_1 and TFS_2 showed to be spontaneous. Increasing the temperature further enhanced the adsorption of cisplatin onto TFSs, as the chemisorption predominantly governed by Pt–S complexation has been proved to be an endothermic process. However, the results at 343 K, showed aggregation on the surface coverage of Sn/SnO_2 in TFS_2, decreasing the adsorption of cisplatin.

In comparison with adsorbents reported in the literature, TFSs exhibit advantages in terms of adsorption performance, adsorption kinetic characteristics, and cost-effectiveness.

Acknowledgements:

This work was carried out within the scope of the RECOPHARMA project (grant agreement #778266) under the European Community's H2020 Program H2020-MSCA-RISE 2017. D. Han acknowledges support from the China Scholarship Council (No. 201906450024).

References:

[1] Y. Roque-Diaz, M. Sanadar, D. Han, M. López-Mesas, M. Valiente, M. Tolazzi, A. Melchior, D. Veclani, *Processes* **2021**, 9 (11), 1873.

[2] D. Han, M.E. Villanueva-Tagle, M. Peña-Icart, M. López-Mesas, M. Valiente, *Journal of Hazardous Materials* **2024**, 471 (April), 134442.

[3] D. Han, M. López-Mesas, M. Luaces, Y. Enamorado, M. Sanadar, A. Melchior, M. Valiente, *Science of The Total Environment* **2023**, 891 (March), 164385.

[4] D. Han, M. López-Mesas, R. Boada, T. Farías, A.R. Lazo Fraga, M. Valiente, *Chemical Engineering Journal* **2023**, 472 (July), 144894.

Multivariate optimization of starch/glycerol/CMC films by casting deposition: towards cheap and tuneable biomaterials for metal ions sorption

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Water pollution represents a significant challenge for the scientific community, especially in the case of heavy metals, aromatic molecules and dyes contamination. [1] Focusing on the first class of pollutants, i.e. heavy metals, this sort of contamination is typical of industrial wastewaters [2] and adsorption is nowadays the most common approach researchers are opting for to remove these pollutants from industrial effluents before their discharge in groundwaters; among all the alternatives, natural polymers are undoubtedly the most interesting materials for this application, ranging from polysaccharides to chitosan, zeolites, cellulose or lignin-based materials. [1-3]

The reasons behind such a widespread diffusion of natural polymers for heavy metal sorption can be rapidly listed: (i) natural polymers are generally cheap and ensure higher biocompatibility and biodegradability than synthetic compounds, [4] (ii) several plant or animal-derived monomers show intrinsic binding affinity towards metal ions [1,3] and, last but not least, (iii) multicomponent biomaterials' properties can be appropriately tuned by changing the type and ratios of starting materials. [5] On the other side, all that glitters in not gold and it must be underlined that films made of natural polymers suffer from poor chemical and mechanical properties and high solubility, thus strongly limiting their actual applicability in real cases. [5]

In this scenario, we put in place our knowledges on chemometric tools for multivariate optimization aiming at tuning the properties of starch/glycerol/CMC films, obtained by casting deposition, to improve their chemical and mechanical properties and to achieve the goal requirements for their actual applicability. We identified the suitable range of starch, glycerol and CMC percentages, as shown in Figure 1a, in which films enough resistant to be handled and tested but exhibiting much different properties were always achieved. [5] Then, according to Mixture Design methodology, [6] the relevant compositions to be synthesized to model films' features were identified, highlighted as circles in Figure 1a, synthesized according to the optimized procedure [5] and characterized. [7,8]

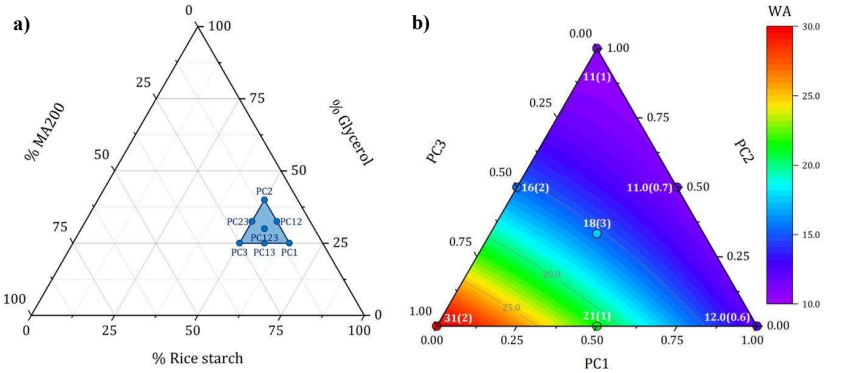

Figure 1: Suitable range of rice starch, glycerol and CMC percentages for suitable films by casting deposition (a) and example of swelling trend modelled within the identified domain (b)

Characterization measurements allowed to determine several features of the samples, mainly mechanical properties, swelling, water vapour absorption and solubility, together with thermal behaviour. [5,7,8] Each feature was then separately modelled according to Mixture Design methodology to describe and predict the trend of the property of interest in the range of main components previously defined. An example is reported in Figure 1b in the case of swelling. Finally, correlations between the modelled features were identified by means of Principal Component Analysis [9] to identify the ideal composition for heavy metal sorption in real samples.

References:

[1] G. Crini, *Prog. Polym. Sci.* **2005**, *30*, 38–70

[2] A. Gupta, V. Sharma, K. Sharma, V. Kumar, S. Choudhary, P Mankotia, B. Kumar, H. Mishra, A. Moulick, A. Ekielski, P. Kumar Mishra, *Materials* **2021**, *14*, 4702

[3] R. Sharma, P. Chandra Nath, Y. Kishore Mohanta, B. Bhunia, B. Mishra, M. Sharma, S. Suri, M. Bhaswant, P. Kumar Nayak, K. Sridhar, *Int. J. Biol. Macromol.* **2024**, *256*, 128517

[4] S. Shaikh, M. Yaqoob, P. Aggarwal, *Curr. Res. Food Sci.* **2021**, *4*, 503–520

[5] L.R. Magnaghi, M. Guembe-Garcia, V. Cerone, P. Perugini, G. Alberti, R. Biesuz, *Chemom. Intell. Lab. Syst.* **2024**, *244*, 105044

[6] J.A. Cornell, *Experiments with Mixtures : Designs, Models, and the Analysis of Mixture Data R. Green*. Wiley, **2002**

[7] X. Zhou, X. Zong, S. Wang, C. Yin, X. Gao, G. Xiong, X. Xu, J. Qi, L. Mei, *Carbohydr. Polym.* **2021**, *251*, 117100

[8] D. Gomez-Heincke, I. Martínez, M. Stading, C. Gallegos, P. Partal, *Food Hydrocoll.* **2017**, *73*, 21-29

[9] R. Bro, A. K. Smilde, *Anal. Methods*, **2014**, *6*, 2812

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Characterization of acid-base equilibria of dissolved organic matter from rivers and estuaries

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The carbon exchange with the atmosphere is controlled by the oceanic carbonate system. The ocean acts a vast reservoir storing CO_2 at depths in both organic and inorganic forms. The interrelationships between chemical, biological and physical processes play a major role in the capacity of the ocean to uptake and store atmospheric CO_2. Dissolved organic matter (DOM) is one of the key parameters of the oceanic carbonate system and acts as a bioactive carbon reservoir [1]. Besides its contribution to the storage of atmospheric CO_2 in the ocean, DOM sustains ecosystems and influences metal cycles, that are essential for primary production and agriculture. Moreover, the transport, behaviour, and fate of pollutants in the environment may also be influenced by DOM. DOM comprises a broad range of structurally complex organic compounds with a size range <0.2/0.7 µm. The diversity on the chemical composition of DOM has large implications on its accumulation, fate, physicochemical properties, and binding behaviour. Despite the heterogeneous nature of marine DOM, carboxylic acids and phenolic compounds are two of its main structural components [2, 3].

In this study the physicochemical characteristics of DOM extracted from riverine and estuarine water have been evaluated by potentiometric titrations. The proton binding capabilities of DOM extracted from Mero and Ebro Rivers (NW and NE Spain) were assessed. Several sampling locations (Figure 1) were selected to examine the changes of DOM from the source of the rivers to their outflow into the ocean (Atlantic Ocean and Mediterranean Sea, respectively).

Seasonality of DOM and its ancillary parameters in the selected study sites was also studied. The effect of ionic strength on DOM binding properties were analysed by fitting the data to the NICA-Donan model (Figure 2).

Figure 1. Sampling sites in both Mero and Ebro systems

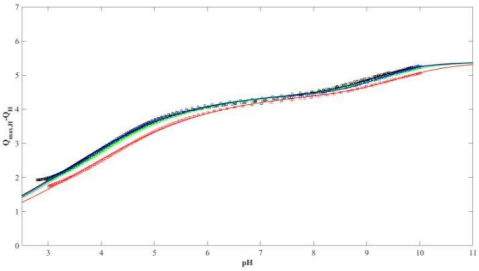

Figure 2. NICA-Donan master curve for acid-base equilibrium data in Mero river, Summer 2023.

Acknowledgements

Authors want to thank Agencia Española de Investigación for the financial support through the research projects PID2020-117910GB-C22/AEI/10.13039/501100011033 and PID2020-117910GB-C21/AEI/10.13039/501100011033 and Xunta de Galicia for the project ED431B 2022/40

References:

[1] Carvalhais, N. et al. Global covariation of carbon turnover times with climate in terrestrial ecosystems. Nature, **2014**, 514, 213–217.

[2] Repeta, D. J. Chapter 2 - Chemical Characterization and Cycling of Dissolved Organic Matter. in Biogeochemistry of Marine Dissolved Organic Matter (Second Edition). Eds. Hansell, D. A. & Carlson, C. A. Academic Press, Boston, **2015**, 21-63.

[3] Lodeiro, P. et al. Acid-base properties of dissolved organic matter extracted from the marine environment. Science of The Total Environment, **2020**,729, 138437.

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Synthesis, molecular structure, physicochemical and catalytic properties of 12-nuclear copper cluster - preliminary studies

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The design and synthesis of transition metal complexes as model compounds for metalloenzymes with oxidase activity is of increasing interest to researchers. Therefore, we have used direct synthesis to obtain a Cu(II) complex (labelled **1**) with a pyrazole derivative as a potential biomimetic of catechol oxidase activity.

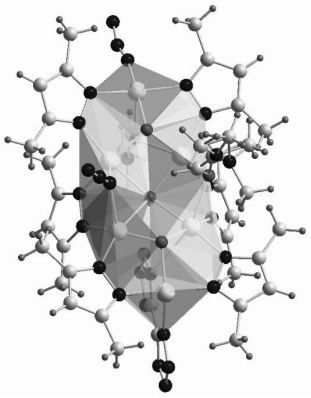

Figure 1. Copper(II) coordination spheres in the hexanuclear core of cluster **1** with polyhedra.

The molecular structure of new copper cluster **1** consists of a twelve-nuclear (dodecanuclear) Cu(II) metallic centers. The structure of multicopper complex **1** can be represented as a double cluster core consisting of two hexanuclear $\{Cu_6(\mu_4\text{-}O)(\mu_3\text{-}O)_2(\mu\text{-}\kappa N,\kappa N\text{-}L_1)_6(\mu\text{-}\kappa O,\kappa O\text{-}DMF)(\kappa O\text{-}DMF)(\mu\text{-}N_3)(N_3)\}$ fragments connected by a μ-κN,κN-5,5'-bitetrazole dianion (L_2). Additionally, all six Cu(II) ions in the core are hold peripherally by μ-κN,κN-pyrazol anion bridges (L_1). In addition, the central copper(II) ions are connected by 4 oxygen bridges (Fig. 1).

Preliminary spectroscopic and magnetic studies are also presented. The ability of the synthesised complex **1** to catalyse the oxidation of 3,5-di-tertbutylcatechol (3,5-DTBC) to 3,5-di-tertbutylquinone (3,5-DTBQ) was investigated.

References:

[1] Tripathy, R.R. Singha, S. Sarkar, S. *Journal of Coordination Chemistry* **2022**, 75 (15–16), 1967–2017.

Extraction of Eu(III) in the $[P_{66614}][Dec]$ ionic liquid: an experimental and theoretical study

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In the last two decades, Ionic liquids (ILs) have progressively emerged as a promising alternative to conventional volatile organic solvents (VOCs) in the liquid-liquid extraction processes of metal ions from waste streams. This interest is related to several advantages of ILs over VOCs: negligible vapor pressure, good thermal and electrochemical stability, high conductivity [1]. ILs are salts formed by a bulky organic cations and an organic or inorganic anions which are in the liquid state at temperatures below 100 °C. Their low melting points of ILs are mostly due to the large size of the ions and strong charge delocalization, which causes a damping of the coulombic interaction [2].

Among the different classes of hydrophobic ILs, that based on the quaternary phosphonium trihexyl(tetradecyl)phosphonium ($[P_{66614}]^+$) cation has shown potential in metal ion recovery[3] (Fig. 1). The interest in this family of ILs was due to their lower cost with respect to other popular hydrophobic ILs (e.g. the alkyl imidazolium ones) and also to the fact that being the cation highly hydrophobic due to the long alkyl chains simple and cheap anions can be used. In this way, the release of the organic cation is prevented in extraction of metals occurring through ion-exchange mechanism [3].

In this study, the $[P_{66614}]^+$ decanoate ($[Dec]^-$ IL is tested in the extraction of Eu(III) from aqueous environment. The decanoate anion can be considered as a model for a fatty acid, and thus for ILs made of biomass-derived building blocks. Eu(III) extraction up to 100% was obtained from moderately acidic solutions containing 10mM of the starting salt with 10 mins contact time. On the contrary, no extraction occurred from concentrated HCl and HNO_3 solutions. This is explained by the fact that, when in contact with strongly acidic solutions, the decanoate anion is protonated ad thus unavailable for the coordination of the metal ion. Stripping experiments using a 0.5M HNO3 solution showed a 100% recovery of Eu(III) within 3 cycles.

Luminescence spectroscopy was employed to monitor the extraction the coordination of Eu(III) in $[P_{66614}][Dec]$ and obtain the average number of coordinated water molecules (q ~ 0.5 ± 0.3). Also, extraction experiments carried out using diluted ILs solutions in toluene as receiving phases allowed to estimate an average number of ~3 coordinated $[Dec]^-$ anions (2.98 ± 0.26) to the Eu(III) cation (Fig. 1).

Density functional theory (DFT) calculations and molecular dynamics (MD) simulations allowed to obtain further structural insights on the coordination environment of Eu(III) in $[P_{66614}][Dec]$ in dry conditions and in presence of water.

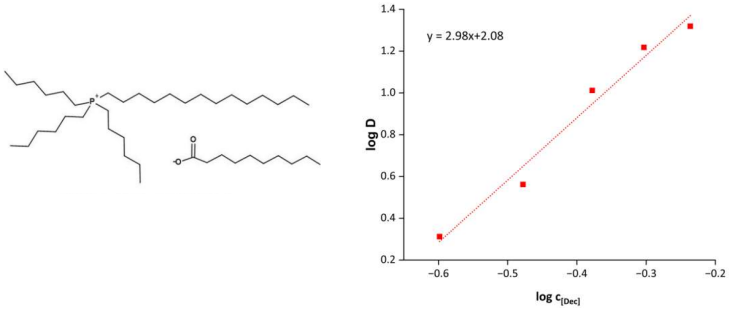

Fig. 1. Dependence of the distribution factor (logD) upon anion concentration ($logC_{[Dec]^-}$) in the organic phase.

References:

[1] V. Kaim, J. Rintala, C. He, Sep. Purif. Technol. **2023**, 306, 122699.

[2] D.R. MacFarlane, M. Kar, J.M. Pringle, The Structure of Ions that Form Ionic Liquids, in: Fundamentals of Ionic Liquids, John Wiley & Sons, Ltd, **2017**, 27–53.

[3] T. V. Hoogerstraete, S. Wellens, K. Verachtert, K. Binnemans, *Green Chem.* **2013**, 15, 919-927.

Interaction of tryptophan metabolites and their metal complexes with human serum albumin and DNA

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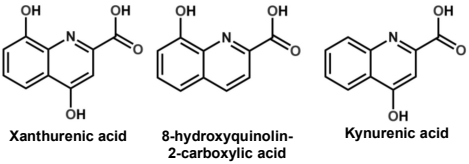
Colorectal cancer is the third most common cancer type worldwide [1]. Although there are highly developed surgical techniques for tumor removal and/or chemotherapeutics, it is still the second leading cause of cancer-related deaths [1]. There is a strong need to develop a highly effective and less toxic chemotherapeutic drug that acts through a different action mechanism from conventional compounds.

Colorectal cancer is frequently associated with the disorder of tryptophan metabolism and modified microbiota [2]. It is highly probable that microbiota and tryptophan metabolites (TrpMs) affect colorectal cancer, as TrpMs have various biological effects on the human body [3]. *E. coli* bacteria in the microbiota can also produce one of the TrpMs (kynurenic acid (KynA)) in order to control the growth of other bacteria [3].

In this study, those tryptophan metabolites are included, which can form high stability chelates with essential metal ions, namely KynA and xanthurenic acid (XA) (**Scheme 1**). As a continuation of our recent publication [4], 8-hydroxyquinoline-2-carboxylic acid (8-HQA) is also involved in these studies, as it is a structurally similar metabolite discovered in high concentration in *Noctuid* larvae, through which the larvae's gut microbiome is controlled [5,6]. Moreover, both KynA and 8-HQA showed antimigratory and antiproliferative effects on melanoma and colon cancer cells [7,8]. Previous studies showed that dietary metal ion supplements have the potential to change the composition of the microbiota [9], and the combination with bioactive metabolites may enhance this effect. For example, the antibacterial activity of 8-hydroxyquinolines on *M. tuberculosis* could be modulated by the addition of metal ions [10].

The interaction between these compounds and biomacromolecules (proteins and DNA) may explain the differences in the biological effects. During the transport of TrpMs and their metal complexes in the blood, the interaction with human serum albumin (HSA) is inevitable since it is the most abundant transporter protein in the blood. On the other hand, DNA is a classic target of anticancer drugs.



Scheme 1 The structures of ligands involved in this study

The interaction of ligands with HSA and DNA was studied using spectrofluorometric techniques supported by spectrophotometry. The studies show that only minor differences exist between the binding constants of the chosen ligands. The competition between HSA and 8-HQA/XA resulted in the dissociation of the Cu^{2+} complexes, which can be explained by the high affinity of HSA to Cu^{2+} ions. In the case of DNA, the small planar aromatic TrpMs are most probably intercalating between the DNA bases. To prove this, ethidium bromide displacement studies were performed in the presence and absence of metal ions.

Acknowledgments: The authors would like to thank the financial support from the National Science Center (NCN), Poland, under research project number 2020/39/B/ST4/03060.

References:

[1] S. Shinji, T. Yamada, A. Matsuda, H. Sonoda, R. Ohta, T. Iwai, K. Takeda, K. Yonaga, Y. Masuda, H. Yoshida, *J. Nippon Med. Sch.* **2022** 89 (3), 246-254.

[2] H.-l. Zhang, A.-H. Zhang, J.-H. Miao, H. Sun, G.-l. Yan, F.-F. Wu, X.-J. Wang, *RSC Advances* **2019**, 9, 3072-3080.

[3] M. P. Turski, M. Turska, P. Paluszkiewicz, J. Parada-Turska, G. F. Oxenkrug, *Int. J. Tryptophan Res.* **2013**, 6.

[4] A. Baryłka, A. Bagińska-Krakówka, L. Zuccarello, F. Mancuso, G. Gattuso, G. Lando, C. Sgarlata, C. De Stefano, B. Godlewska-Żylkiewicz, D. Milea, S. Gama, *Thermochim. Acta* **2023**, 730, 179615.

[5] T. Mazumdar, S. Hänniger, S. P. Shukla, A. Murali, S. Bartram, D. G. Heckel, W. Boland, *Front. Microbiol.* **2023**, 14, 1075557.

[6] S. Gama, M. Frontauria, N. Ueberschaar, G. Brancato, D. Milea, S. Sammartano, W. Plass, *New J. Chem.* **2018**,42, 8062-8073

[7] K. Walczak, E. Langner, K. Szalast, A. Makuch-Kocka, P. Pożarowski, T. Plech, *Molecules* **2020**, 25, 1655

[8] K. Walczak, E. Langner, A. Makuch-Kocka, M. Szelest, K. Szalast, S. Mariniak, T. Plech, *Int. J. Mol. Sci.* **2020**, 21, 7946.

[9] C. A. Lopez, E. P. Skaar, *Cell Host Microbe* **2018**, 23, 737-748.

[10] S. Shah, A. G. Dalecki, A. P. Malalasekera, C. L. Crawford, S. M. Michalek, O. Kutsch, J. Sun, S. H. Bossmann, F. Wolschendorf, *Antimicrob. Agents Chemother.* **2016**, 60, 5765-5776.

AGNES (Absence of Gradients and Nernstian Equilibrium Stripping) can provide free gallium (III) concentrations

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Gallium is being extensively used in technological applications. Increasing emissions to the environment classify it as an emerging contaminant. Speciation of gallium is fundamental for understanding/predicting its bioavailability and potential toxicity to biota. According to the Free Ion Activity Model and the Biotic Ligand Model, the potential toxicity of metals in water may be more correlated to their free form than to the total concentration. Continuous advances in analytical methods are needed to quantify the free fraction of Ga [1]. The electroanalytical technique AGNES (Absence of Gradients and Nernstian Equilibrium Stripping) provides direct access to the free metal ion concentration in solution via two stages: i) deposition, where a potential is applied to preconcentrate the metal inside the working electrode until the redox couple reaches Nernstian equilibrium; ii) stripping, where the concentration of the reduced metal is quantified. Free Sn, In, Zn, Cd and Pb concentrations have been measured in a variety of matrices including river, sea and estuarine waters, in wine, in systems containing humic acids or nanoparticles and soil extracts have been successfully [2-4].

The presentation will show how the electrodic irreversibility of the couple Ga0/Ga(III) can be overcome with a suitable calibration strategy. For the implementation of AGNES, the attainment of equilibrium has to be confirmed from a plateau in a "trajectory" (stabilized charges vs. deposition time) and by checking the suitable Nernstian proportionality between stabilized charges from more than one deposition potential. The speciation capability of AGNES for Ga will be assessed with the ligand phthalate and results will be compared with predicted concentrations from existing complexation models.

References:

[1] Y. Kouhail, N. Amiel, I. Dror, B. Berkowitz, *Chemosphere* **2020**, 249, 1-9.

[2] E. Companys, J. Galceran, J.P. Pinheiro, J. Puy, P. Salaün, *Curr. Opin. Electrochem* **2017**, 3, 144–162.

[3] K. Rosales-Segovia , E. Companys, J. Puy , J. Galceran, *Sci. Total Environ.* **2024**, 926, 1-10.

[4] L. Lopez-Solis, J. Galceran, J. Puy, Companys, *E. Chemosensors* **2022**, 10, 351.

Free Sn (II) determination with AGNES (Absence of Gradients and Nernstian Equilibrium Stripping)

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Sn has important applications in food and electronic industries. Understanding the behaviour and fate of inorganic tin species is relevant in environmental studies because of their potential toxicity. There is a scarcity of works on inorganic tin speciation [1], due to the strong hydrolysis of Sn(II) and its easy oxidation to Sn(IV) [2].

The quantification of the Sn(II) free concentration in natural waters is important to the Free Ion Activity Model (FIAM), which is hegemonic in ecotoxicology. Currently, there is no commercial ion selective electrode to measure [Sn^{2+}]. Furthermore, the available methods described in the literature for the determination of low concentrations, as spectrophotometry, absorption or emission spectrometry, are considered time demanding or too expensive for most laboratories [3]. Consequently, alternative techniques such as AGNES (Absence of Gradients and Nernstian Equilibrium Stripping) can be helpful. AGNES consists of two steps: deposition, where the metal ion in solution is reduced and amalgamated into the Hg electrode until equilibrium is reached; and stripping, where the quantification of the accumulated reduced analyte is performed. AGNES has been successful in determining Zn, Cd, Pb, In, Ga free ion concentrations in a variety of matrices ranging from wine to seawater and nanoparticle dispersions [4-5].

The presentation will show how the influence of oxidation was overcome in the implementation of the different variants of AGNES to quantify the Sn(II) free fraction. The hydrolysis impact will be discussed. The results from AGNES for mixtures of Sn and EDTA will be compared with concentrations predicted by existing complexation models.

References:

[1] R.M. Cigala, F. Crea, C. De Stefano, D. Milea, S. Sammartano *et al.* , *Monatsh Chem* **2013**, 144, 761–772.

[2] R.M. Cigala, F. Crea, C. De Stefano, G. Lando, D. Milea, *et al.*, *Geochim. Cosmochim. Acta* **2012**, 87, 1–20.

[3] S. Chandra, K. Sharma, A. Kumar, *J. Chem.,* **2013**, Article ID 130372, 1-5.

[4] L. Lopez-Solis, J. Galceran, J. Puy, Companys, *E. Chemosensors* **2022**, 10, 351.

[5] K. Rosales-Segovia , E. Companys, J. Puy , J. Galceran, *Sci. Total Environ.* **2024**, 926, 1-10.

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DEVELOPMENT OF PHENANTHROLINE-BASED METAL COMPLEXES FOR TARGETING G-QUADRUPLEX DNA

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Non-canonical nucleic acid structures have attracted considerable attention in many science fields, including chemistry, biology, physics, materials and nanotechnology. They include triplexes, i-motifs, three/four-way junctions or G-quadruplexes (G4). G4 structures are formed in guanine-rich sequences, in which four guanine bases are held together by Hoogsteen hydrogen bonds to form a coplanar G-quartet, and then two or more G-quartets stack to form the G-quadruplex structure retaining sodium or potassium ions in a central core channel [1,2]. Strikingly, a large number of putative G-quadruplex forming sequences have been identified in the genomes of human and viruses, and evidences suggest their pivotal role in key biological processes such as ageing, neurodegenerative diseases and cancer [1]. Therefore, these G4 structures have been proposed as potential targets by small molecules for therapeutic intervention.

Herein, we show the synthesis of tridentate ligands containing a phenanthroline moiety and the corresponding metal complex with Zn, Cu, Ni, Mn, Pt and Pd. Some of the metal complexes adopt a square-planar geometry, which allows an efficient binding to G-quadruplex DNA structures [3]. We have studied the coordination of different metals with the ligands by mass spectrometry and UV-Vis/fluorescence spectroscopies and we are currently investigating the interaction of the metal complexes with a panel of G4s by means of FRET melting.

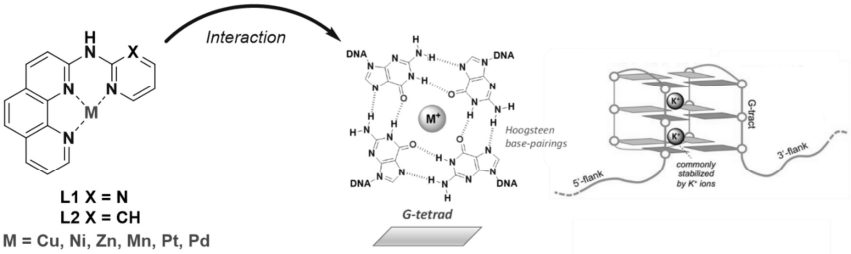
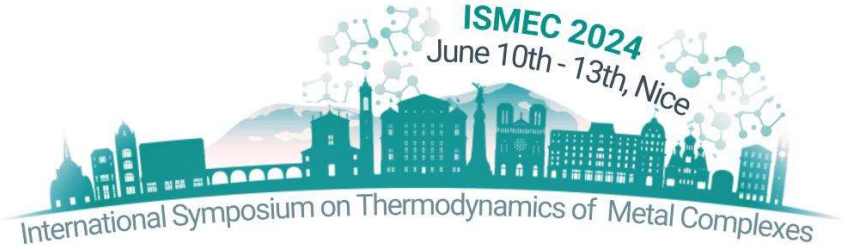


Figure 1. Metal complexes (left panel) and G-quadruplex structure (right panel).



References:

[1] D. Rhodes and H. J. Lipps, *Nucleic Acids Res*., **2015**, 43, 8627-8637

[2] N. Kosiol, S. Juranek, P. Brossart, A. Heine and K. Paeschke, *Mol. Cancer,* **2021**, 20:40.

[3] S. Bianco, C. Musetti, A. Waldeck, S. Sparapani, J. D. Seitz, A. P. Krapcho, M. Palumbo and C. Sissi, *Dalton Trans*. **2010**, 39 (25), 5833–5841.

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The unusual N(proximal),O(distal),O'(distal)-pyridine-2,6-dicarboxylate (pdc) conformation in $[Cu(pdc)(crea)(H_2O)_2]\cdot H_2O$ is mainly induced by the (primary amino, crea)N-H···O(carboxylate, pdc) interligand interaction.

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Delve into the interligand interactions within mixed-ligand complexes featuring bioligands, the synthesis, molecular and/or crystal structures, and DFT calculations of the 'inner-sphere' $[Cu(pdc)(crea)(H_2O)_2]\cdot H_2O$ (**1**) and the 'outer-sphere' $(Hcrea)_2[Cu(pdc)_2]$ complex are reported. Particular emphasis is placed on compound **1**, where an unconventional pdc chelating mode for Cu(II) is observed. Both pdc and crea are rigid-planar ligands. In **1** (see figure), the Cu(II) center exhibits an asymmetrically elongated octahedral coordination, type 4+1+1, where N-crea, both trans-O-aqua atoms, and the N-pdc atom act as proximal donors (giving bonds of ~2.00 Å). Hence, two O-carboxylate pdc donors occupy unequal trans-distal sites (Cu1-O21 2.289(2) < Cu1-O11 2.431(2) Å). Within this intricate molecule, the dihedral angle α, defined by P1 (the mean plane of four closest donors) and P(crea), is 68.4°(see figure).

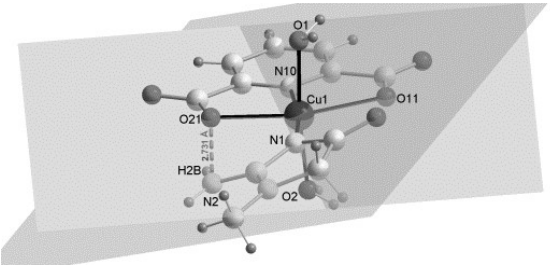

Figure. Dihedral angle α in the complex molecule of $[Cu(pdc)(crea)(H_2O)_2]\cdot H_2O$ (**1**).

The intra-molecular H-bond (crea)N2-H2B···O21(pdc, distal) [N2···O21 of 2.731(3) Å and N2-H2B···O21 angle of 152.7°] results in unequal bond lengths Cu-O21 < Cu-O11. The lack of coplanarity between the pdc and crea mean planes (dihedral angle β 20.4°) is further influenced by the intermolecular interaction N2-H2A···O2#3 (2.801(3) Å, 157.4°, #3 = x,y+1,z). These phenomena are commonly attributed to "crystal packing", which, in turn, elucidates how the complex molecule(s) form the most stable crystal lattice (also involving the water molecule). In fact, available DFT calculations provide additional quantified insights.

Discussion: To better understand the unusual role of pdc in compound **1**, selected mixed-ligands Cu(II)-pdc-imidazole(s) complexes will be considered. Imidazole (Him) or 2-ethyl-imidazole (H2Etim), without intra-molecular interligand N-H···O(pdc) interaction, are involved in closely related compounds such as [Cu(pdc)(Him)] (square planar, α 1.91°, β 0.09°) [1], [Cu(pdc)(Him)(MeOH)] (square base pyramidal 4+1, α 58.97°, β 60.17°) [2] and [Cu(pdc)(H2Etim] (H2Etim = 2-ethylimidazole, square planar, α 72.89°, β 72.38°) [3]. Imidazole ligands as well as crea are typical borderline Pearson´s bases suitable to bind Cu(II) centers (borderline Pearson´s acid, also influenced by Jahn-Teller $3d^9$ distortions) thus occupying proximal coordination sites. Interestingly, in $[Cu(pdc)(H2Etim)_3]\cdot H_2O$ (**2**) [4], the Cu(II) center displays a distorted octahedral coordination, type 2+2+2, where the two trans-shortest bonds are Cu-N(pdc) (2.002 Å) and Cu-N(H2Etim-A) (2.006 Å). A competition for the remaining two intermediate bond distances could be anticipated from the other two imidazole ligands (H2Etim-B H2Etim-C) or from two O-carboxylate pdc donors. In this struggle, once again, Pearson's criteria become relevant. Consequently, these trans positions are occupied by the two N-imidazole donors (with Cu-N bonds of 2.123 and 2.153 Å). Thus, the remaining and longest trans-distal sites are occupied by two O-pdc donors (hard Pearson`s bases) giving Cu(II)-O(carboxylate) distances of 2.233 and 2.252 Å. Once more, HSAB Pearson's criteria come into play.

Conclusion: In **1** and **2** [4], the pdc chelator adopts the unusual conformation pdc-N(proximal)+ O(distal)+O'(distal), albeit for different reasons. In **1**, the molecular recognition Cu(pdc)-crea involves an efficient cooperation between the Cu-N(crea) bond and a (crea)N-H···O(pdc) interligand interaction. That cannot be achieved in compound **2**.

References:

[1] S. Mistri, E. Zangrando, S.C. Manna, *Inorg. Chim. Acta* **2013**, 405, 331-338. https://doi.org/10.1016/j.ica.2013.06.019

[2] San-Hui Liu, Yi-Zhi Li, Qing-Jin Meng, *Acta Crystallogr.* **2006**, E61, m1183-m1184. https://doi.org/10.1107/S1600536805015564

[3] Guang-Hua Cui, Tong-Fei Liu, Xian Peng, *J. Chem. Cryst*. **2011** 41**,** 322-327. https://doi.org/10.1007/s10870-010-9881-9.

[4] N. Uzun, A.T. Colak, F.M. Emen, G. Kismali, O. Meral, M. Alpay, G.K. Cılgı, E. Şahin. J. Coord. Chem. **2015**, 68, 949-967. https://doi.org/10.1080/00958972.2014.1003371

Model peptide studies of Mn(II) binding sites as a first step to understand Mn(II) acquisition at the host-pathogen interface

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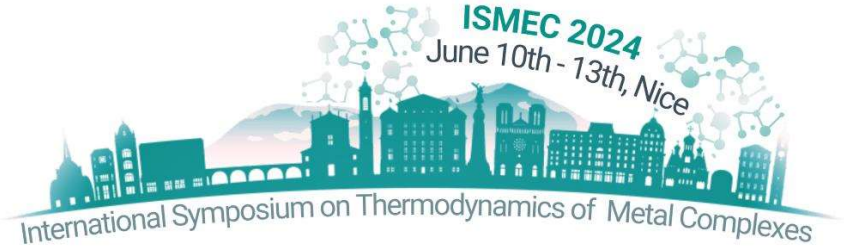
Although far less studied than iron or zinc, manganese has attracted considerable attention in recent years due to its role in almost all forms of life, especially in pathogens and in the host immune system. There is now an increasing amount of emerging evidence that the invading microbe utilizes Mn as a key micronutrient to resist the effect of host-mediated oxidative stress [1, 2]. Mn(II) plays a significant role in adaptation of pathogenic bacteria to the human host. It is obvious, host and pathogens compete for Mn(II) during infection, and genetic inactivation of Mn(II) homeostatic mechanisms decreases the ability of many bacterial species to successfully colonize and cause disease within multiple hosts. Although structural and biophysical studies provide general support for a simple competition model in which the extracellular chelator calprotectin (CP) and Mn(II)-specific uptake systems compete for the same metal on the basis of their respective affinities, there is much more to be learned about Mn(II) coordination chemistry to fully understand this process [3, 4]. In addition, there is also some evidence that Zn(II) and Fe(II) can influence Mn(II) acquisition. It is obvious that metal competitiveness is roughly governed by the intrinsic chelate thermodynamic stability - one metal can displace another metal from a metal binding site in biologically relevant proteins. The main constrains on the way to understand the Mn(II) and Fe(II) homeostasis from bioinorganic chemist point of view is a negligible number of papers concerning coordination, structure, stability, and mode of action of Mn(II)-peptide complexes.

Inspired by the unusual hexahistidine coordination site of Mn(II)-CP complex, as well as coordination spheres of most biological Mn(II) binding proteins, we have designed model Mn(II) ligands based on polyhistydyl sequences, and their alanine and aspartic and glutamic acid derivatives. Our recent results focus on the thermodynamic and structural analysis of Mn(II) complexes with model peptide ligands as well as comparison of the stability of Mn(II) complexes with Fe(II) and Zn(II) complexes, which could possibly occupy the same binding sites.



Acknowledgements

Financial support of the Polish National Science Centre (UMO-2021/43/D/ST4/01231) is gratefully acknowledged.

References:

[1] E. F. Bosma, M. H. Rau, L. A. Gijtenbeek, S. Siedler, Regulation and distinct physiological roles of manganese in bacteria, FEMS Microbiology Reviews, 2021,45, 1-16.

[2] L. J. Juttukonda, E. P. Skaar Manganese homeostasis and utilization in pathogenic bacteria, Molecular Microbiology, 2015, 97, 2, 216–22.

[3] J. P. Lisher, D. P. Gierdoc, Manganese acquisition and homeostasis at the host-pathogen interface, Frontiers in Cellular and Infection Microbiology, 2013, 3, 91, 1-15.

[4] B. Orzeł, A. Pelucelli, M. Ostrowska, S. Potocki, H. Kozłowski, M. Peana, E. Gumienna-Kontecka, Fe(II), Mn(II), and Zn(II) Binding to the C-Terminal Region of FeoB Protein: An Insight into the Coordination Chemistry and Specificity of the Escherichia coli Fe(II) Transporter, Inorganic Chemistry, 2023, 62, 18607-18624

Solvent induced selective response to metal ions of three HNBO-based chemosensors

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The research of new chemosensors able to selectively bind and signal the presence of specific metal ions in samples of biological and environmental relevance is an always growing field. Metal cations such as Mg^{2+}, Ca^{2+} and Zn^{2+} play crucial roles in the human physiology [1-5]. The development of simple and fast systems for the selective detection of metal cations in different matrices is therefore highly desirable and fluorescent chemosensors represent a suitable approach to this task, due to simplicity, reliability, velocity and low-cost [6]. For this reason a new series of ligands containing the 2-(2-hydroxy-3-naphthyl)-4-methylbenzoxazole (HNBO) fluorophore linked to polyamine scaffolds was synthesized and investigated. This fluorophore has been linked to three different amine scaffolds obtaining three fluorescent chemosensors (L1–L3, Figure 1). The ESIPT (excited-state intramolecular proton transfer) behavior was investigated in ACN and DMSO by UV–Vis spectrophotometric and spectrofluorimetric measurements, revealing the occurrence of an ESIPT process only in ACN, in the case of L1 and L2, and in both aprotic solvents, besides protic solvents (water and EtOH-water mixture), in the case of L3. The emission of L1–L3 is related to the deprotonated form of the ligand. The binding properties of L1–L3 towards Alkali, Alkaline-earth and some transition metal ions were investigated in different solvents by UV–Vis absorption, fluorescence emission and NMR spectroscopies. The fluorescence switches-ON in the presence of selected metal ions, always showing a mechanism different from ESIPT. All L1–L3 show a selectivity for Mg^{2+} in DMSO, while in ACN the selectivity of L1 and L2 shifts towards Zn^{2+} and Cd^{2+}. L3 is also able to respond to Mg^{2+} in other aprotic solvents (THF and dioxane). L1 and L3 also showed the ability to signal the presence of metal ions on a paper support (L1: Zn^{2+}; L3: Zn^{2+}, Cd^{2+} and Mg^{2+}). Therefore, L3 revealed able to signal the presence of Mg^{2+} both in solution, in different solvents, as well as on a paper support.

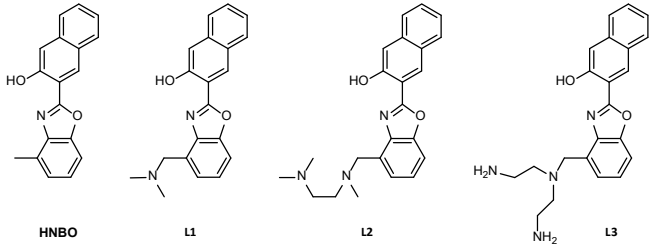

Figure 1: *Molecular structures of compounds HNBO, L1, L2 and L3*

References:

[1] C.A. Brautigam, T.A. Steitz, *Current Opinion in Structural Biology*, **1998**, 8 (1), 54–63.

[2] R. Caspi, R. Billington, I.M. Keseler, A. Kothari, M. Krummenacker, P.E. Midford, W.K. Ong, S. Paley, P. Subhraveti, P.D. Karp, *Nucleic Acids Res.*, **2020**, 48, D445–D453.

[3] K. Mubagwa, A. Gwanyanya, S. Zakharov, R. Macianskiene, *Archives of Biochemistry and Biophysics*, **2007**, 458, 73–89.

[4] P. Paoletti, C. Bellone, Q. Zhou, *Nature Reviews Neuroscience*, **2013**, 14 (6) 383–400.

[5] A.C. Alfrey, N.L. Miller, R. Trow, *The Journal of Clinical Investigation*, **1974**, 54, 1074–1081.

[6] D. Paderni, E. Macedi, L. Lvova, G. Ambrosi, M. Formica, L. Giorgi, R. Paolesse, V. Fusi, *Chemistry – A European Journal*, **2022,** 28 (49).

ISMEC 2024
June 10th - 13th, Nice
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"Bioactive Compounds: A Comparative Study of the Phytochemical Profiles of Withania somnifera and Fungi"

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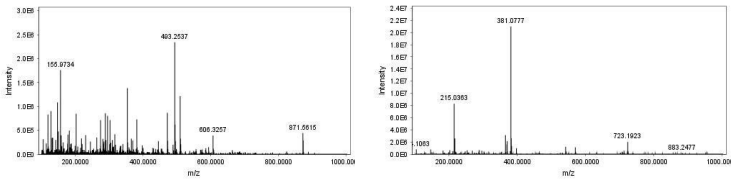
Withania somnifera (L.) Dunal, belonging to the Solanaceae family and commonly known as Ashwagandha, is a perennial herb integral to Ayurvedic medicine, India's traditional healthcare system. It is renowned for its adaptogenic, anticancer, and anti-inflammatory properties [1,2]. Originally native to India, this species has now spread globally and was recently identified in Sardinia, where it is considered an introduced species. Our study aims to perform a comparative analysis of the chemical profiles of Withania somnifera specimens found in Sardinia with other known chemotypes.

Fungi represent an exceptionally diverse group, boasting over 150,000 formally described species with estimates suggesting even greater diversity. Despite this abundance, macrofungi are largely understudied and underutilized [3,4], yet they have been a source of new compounds for pharmaceuticals, functional dietary supplements, and cosmetics. The exploration of macrofungi offers a promising avenue for the discovery of new and valuable natural compounds and therapeutic agents. We chose to focus on various species of mushroom-forming fungi from distinct ecosystems in the Mediterranean area to study their chemical compositions and biological activities.

In this work the most proper techniques for extraction (ultras-sound adssideted) and chemical analysis (GC-MS and ESI-MS) are discussed and set-up, with a green, traceable and validated approach.



A **B**

Figure 1. A) ESI-MS study of *withania* sample **B**) ESI-MS study of fungi sample

References:

[1] Orrù A et al. Alkaloids in Withania somnifera (L.) Dunal Root Extract Contribute to Its Anti-Inflammatory Activity. Pharmacology 2023;108(3):301-307.

[2] Orrù A et al. Withania somnifera (L.) Dunal root extract alleviates formalin-induced nociception in mice: involvement of the opioidergic system. Behav Pharmacol. 2016;27(1):57–68.

[3] Yadav SK et al. A mecha-nistic review on medicinal mushrooms-derived bioactive compounds: potential mycotherapy candidates for alleviating neurolog-ical disorders. Planta Med. 2020;86(16):1161-1175.

[4] Hetland G et al. Antitumor, anti-Inflammatory and antiallergic effects of Agaricus blazei mushroom extract and the related medicinal basidiomy-cetes mushrooms, Hericium erinaceus and Grifola frondosa: a review of preclinical and clinical studies. Nutrients 2020;12(5):1339.

Valorisation of waste biomasses for the recovery of *Critical Raw Materials*

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This contribution presents the preliminary results obtained using waste biomasses from the industrial food chain for the preparation of multifunctional materials possibly able to detect, bind and extract, efficiently and selectively, rare earth metal cations from aqueous solutions simulating real matrices. These metals belong to the list of "Critical Raw Materials", *i.e.* the group of materials whose recovery is considered strategic by the European Community [1]. The use of food-processing industry wastes as secondary raw materials offers a sustainable and environmentally friendly approach, that could also be useful for the rare earth metals recovery. In particular, the adsorption of neodymium and dysprosium ions in aqueous solution was studied at pH ~ 5 and t = 25°C using different waste biomasses, namely Bergamot Pomace (BP), Olive Pomace (OP) and Grape Pomace (GP), chemically pretreated at t = 30°C with H_2O and HNO_3 0.10 mol dm^{-3} [2,3] The materials were characterized employing different analytical techniques; through the FT-IR ATR spectroscopy [2], it was possible to confirm the presence of functional groups capable of interacting with the above mentioned metals. To evaluate their adsorption capacity, batch experiments were carried out on different solutions containing the metal ions (M^{3+} = Nd^{3+}, Dy^{3+}). The concentration of each M^{3+} was determined by ICP-OES [4]. The results obtained from adsorption experiments show that Langmuir equation was the best isotherm fitting model for BP, OP and GP for the rare earth metals adsorption. The adsorption equilibrium was reached within 24 hours and the kinetic of adsorption was well described by the pseudo-second order model. Then the recovery of the metals adsorbed on the biomasses was carried out using HNO_3, but the reused materials show lower performance than the starting ones, exception done for BP, which showed great reutilization capacities [4].

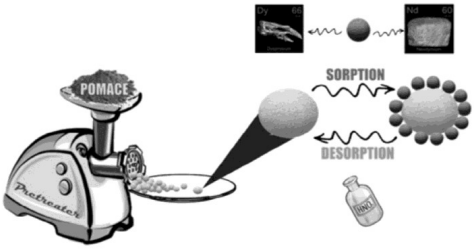

Figure 1: Graphical abstract of the studies performed on pomace.

Acknowledgements:

We thank MUR: PNRR - Missione 4, Componente 2, Investimento 1.1 - Bando Prin 2022 - Decreto Direttoriale n. 104 del 02-02-2022. Project title: "Wastezilla: Recycled waste biomass for efficient recovery of critical elements". CUP: J53D23007540006 – project code: PRIN_2022HYH95P_001 CUP: B53D23013740006- project code: 2022HYH95P_003

References:

[1] European Commission, https://eur-lex.europa.eu/legalcontent/EN/TXT/?uri=CELEX%3A52023PC0160, Accessed April **2024**.

[2] A. Irto, S.G.M. Raccuia et al. Microchem. J. **2023**, 193, 109183

[3] A. Satira et al. Appl. Sci. **2021**, 11(22), 10983.

[4] S. Cataldo et al. Environ. Sci. Pollut. Res. **2022**, 29,9023.

Thermodynamics and Kinetics of Norbornadiene MOST Systems: Old School Meets New Challenges

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MOST systems, i.e. MOlecular Solar Thermal systems for energy storage, are one of the potential contemporary answers to growing needs of clean energy. Such systems work by storing away solar energy via absorption of light at the individual molecule level, which leads to a relatively stable photoisomer. This allows the energy to be recovered later, *i.e.* on demand, as heat via chemical (*e.g.* catalyst addition) or physical (*e.g.* application of a voltage) stimuli.

In this context Norbornadiene (ND) derivatives, with their possibility of photoisomerization to Quadricyclane (QC) had previously attracted attention. A major practical limitation of this chemistry is that most of these systems were originally demonstrated in non-aqueous solvents. Another important factor to consider is the overlap between absorption spectrum of the ND derivative and solar spectrum: this simple element makes the unsubstituted ND essentially unsuitable for applications, thus demanding for attention in the functionalization of the ND core.

Our recent interest in the topic addresses both above points.

The first manifest linking point to ISMEC general interest rests in the nature of the employed catalyst: a Co(II)-porphyrin-type complex (Co-TPPC, i.e. the Co(II) complex of 5,10,15,20-tetrakis(p-carboxyphenyl)porphyrin, Figure 1).

On a second thought, it is worth noticing that both the proposition and any practical usage of this kind of systems raises a few interesting questions. A non-exhaustive relevant set of them could be: what is the speciation of the ND/QC derivative in water (assuming it has displaceable protons)? How long is the photoisomer stable? How much energy can be accumulated? If a catalyst is added, how long do we have to wait to get the stored energy back as heat?

The answers to these key questions are manifestly thermodynamic or kinetic in nature, allowing us to revisit some of the dearest themes of the conference under such an unusual light.

We will present results with a ND/QC system (Figure 1) including protonation constants (UV-Vis), conversion kinetics (^{1}H NMR), energy storage in solution (ITC), paving the way to further developments aimed at further ameliorating target chemico-physical properties of synthetic QC/ND couples.

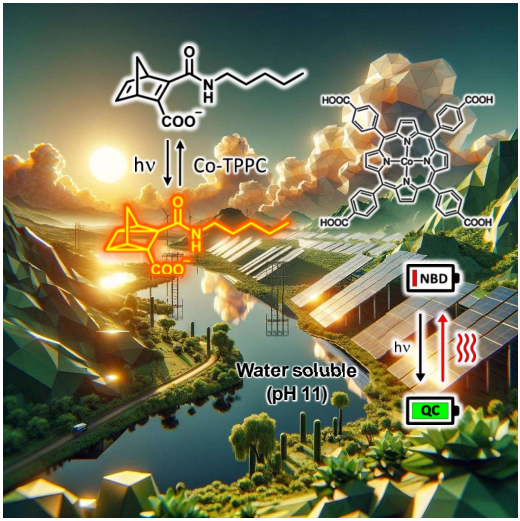

Figure 1. Our starting ND/QC MOST system, its basic working scheme and the Co-TPPC catalyst on a background suggesting potential applications. Note that a MOST-based technology would arguably better work at the individual household system level.

The author (M.S.) gratefully acknowledges the contribution of the research fund of the San Raffaele – Roma University.

Metal-bound peptidomimetics of AMP from the human saliva – coordination properties and antimicrobial activity

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Saliva serves as the primary defense mechanism against pathogenic microbes within the oral cavity. This bodily fluid harbors a unique arsenal of antimicrobial peptides (AMPs), including histatins, defensins, mucins, cathelicidins, and chemokines, which effectively combat pathogens [1]. AMPs employ diverse mechanisms to interact with pathogens, often relying on crucial interactions with metal ions for their activity [2-5]. Despite their potent antimicrobial properties, a significant drawback of antimicrobial peptides is their poor biological stability. Addressing this challenge necessitates the development of antimicrobial peptide-based peptidomimetics that are metabolically stable, non-toxic, and enhanced with metal ions.

Our recent research has focused on characterizing the coordination chemistry and biological activity of Zn(II) and Cu(II) complexes with naturally occurring salivary AMPs, as well as their D-amino acid peptidomimetics (see Table 1). Literature data show that the incorporation of D-amino acids or the replacement of L- with D-amino acids in the peptide sequence improves metabolic stability and increases antimicrobial activity [6].

Table 1. Salivary antimicrobial peptides and their peptidomimetics containing D-amino acids under investigation (small letters correspond to D-amino acids).

Name	Native sequence	Peptidomimetic
MUC7	FPNPHQPPKHPDK	FPNPHQPPkhPDK fpnphqppkhpdk
MUC7	KSHFELPHYPGL	kshfelphypgl lgpyhplefhsk
MUC7	EGRERDHELRHRRHHHQSPK	EGRERDHELRHRrhHHQSPK
Hst 5	DSHAKRHHGYKRKFHEKHHSHRGY	DSHAKRHHGYKrkFHEKHHSHRGY dshakrhhgykrkfhekhhshrgy
C-t-CCL-28	HRKKHHGKRNSNRAHQGKHETYGHKTPY	hrkkhhgkrnsnrahqgkhetyghktpy

We show that the replacement of L-amino acids with D-amino acids (in the entire sequence or in places most susceptible to enzymatic degradation) has a significant impact on the antimicrobial properties in complexes with metal ions (obtained MIC values even 15 μg/ml). Moreover, such modification results in increased resistance to proteolysis of the tested peptides. In some cases, we also noticed a different way of coordinating Cu(II) and Zn(II) ions compared to the native peptide, as well as differences in the secondary structure of the tested systems.

Our results raise hope for the potential use of these type of metal-bound peptidomimetics in the fight against pathogenic bacteria and yeasts.

Acknowledgements
J.W. acknowledges the National Science Centre (UMO-2021/41/B/ST4/02654) for financial support.

References:

[1] T. Vila, AM. Rizk, AS. Sultan, MA. Jabra-Rizk. *PLoS Pathog* **2018** 15(11), e1008058.

[2] K. Szarszoń, S. Andrä, T. Janek, J. Wątły. Insight into the chemistry, structure and the biological activity of human salivary MUC7 fragments and their Cu(II) and Zn(II) complexes. *Inorganic Chemistry* **2024** *Accepted*.

[3] K. Szarszoń, A. Mikołajczyk, M. Grelich-Mucha, R. Wieczorek, A. Matera-Witkiewicz, J. Olesiak-Bańska, M. Rowińska-Żyrek , J. Wątły. *Journal of Inorganic Biochemistry* **2024**, 253, 112476/1-112476/10.

[4] E. Dzień, J. Wątły, A. Kola, A. Mikołajczyk, A. Miller, A. Matera-Witkiewicz, D. Valensin, M. Rowińska-Żyrek. *Dalton Transactions* **2024**, 53, 1-10.

[5] J. Wątły, K. Szarszoń Klaudia, A. Mikołajczyk, M. Grelich-Mucha, A. Matera-Witkiewicz, J. Olesiak-Bańska, M. Rowińska-Żyrek. *Inorganic Chemistry* **2023**, 62, 19786-19794.

[6] J. Wątły, A. Miller, H. Kozłowski, M. Rowińska-Żyrek. *Journal of Inorganic Biochemistry* **2021**, 217, 111386/1-111386/17

In vivo speciation and molecular mechanisms of the uptake of radioactive metal ions by *A. nodosum.* Elemental interactions and biological processes.

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In the last century human activities such as accidental releases, mining, and military operations have increased the concentrations of radioactive metal ions in the environment [1]. As recipients of discharged pollutants and covering 70% of the Earth's surface, the oceans and their biotope emerged as a primary focus in environmental monitoring efforts. However, the impact of radioactive metals on marine life remains poorly understood due to their radiotoxicity and the difficulty of studying metabolic interactions.

We present here a multi-scale investigation aiming at understanding the impact of radioactive metal accumulation in the model marine macro-alga *Ascophyllum nodosum,* by describing the related uptake mechanism. We investigated the uptake and the *in vivo* speciation of the uranyl ion, UO_2^{2+}, and stable europium (Eu^{3+}), here used as an analogue of americium (Am^{3+}) because of similar ionic radii, same oxidation state and because of the too high specific activity of Am.

Contaminations experiments were performed on the *A. nodosum* specimens in closed aquaria through seawater exposure, varying concentrations from macro (10^{-5} M ^{nat}U and 10^{-7} M ^{153}Eu) to trace levels (10^{-12} M ^{152}Eu and ^{241}Am). The bioaccumulation was quantified using ICP-MS and γ-spectroscopy, while elemental distribution and speciation in algal tissues were mapped using a combination of electronic microscopy imaging (SEM), X-ray absorption spectroscopy (XAS), and X-ray fluorescence (μ-XRF).

Our results show that *A. nodosum* can bioaccumulate uranyl and europium, through different active and passive mechanisms. Specifically, UO_2^{2+} ion displayed a compartmentalization ability, with higher concentrations in the receptacles (Concentration factor: $Cf_{receptacles,\ natU}$ = 49 ± 12, $Cf_{thallus\ natU}$ = 3.1 ± 0.5). We also observed distinct speciation depending on the compartment, the gender of the alga [2], as well as the presence of bacteria living on algal external surface .

To verify the Eu/Am analogy, we conducted uptake and loss kinetics experiments with both ^{152}Eu and ^{241}Am at trace levels, which revealed similar uptake and loss kinetics for the two isotopes, suggesting chemical and biological similarities between the two. This allowed us to extrapolate speciation studies conducted on stable europium to americium. No evidence of elemental compartmentalization was found in this case ($Cf_{^{153}Eu}$ = 1086 ± 79). Our analysis suggests that alginate, the main polysaccharide in algal tissue, plays a role in Eu/Am uptake through bidentate bridging coordination.

This multiscale strategy and use of complementary spectroscopies can be useful for predicting the risk associated with contamination of living organisms, not only in the case of radioactive elements, but can also be extended to other toxic metals and related complexes.

References:

[1] H. Qin-Hong, W. Jian-Qing, W. Jin-Sheng, *Journal of Environmental Radioactivity,* **2019**, 101, 426-437.

[2] M. Zerbini; P.L. Solari; F. Orange; A. Jeanson; C. Leblanc; M. Gomari; C. Den Auwer; M.R. Beccia, *Scientific Reports*, **2024**, 14(1021), 1-13.

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