2nd European NECTAR Conference

Lisbon, August 25th - 27th, 2021

BOOK OF ABSTRACTS

COST ACTION CA18202

NECTAR – Network for Equilibria and Chemical Thermodynamics Advanced Research

cost
EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

COST is supported by the Horizon 2020 Framework Programme of the European Union

The 2nd European NECTAR Conference is three-days meeting, held in Lisbon, organized within the activities of COST Action CA18202 (NECTAR – Network for Equilibria and Chemical Thermodynamics Advanced Research).

After the success of the 1st European NECTAR Conference, held last year in Belgrade, we decided to keep the format of our annual NECTAR meeting, joining the Management Committee (MC), Core Group (CG) and Working Group (WG) meetings, together with a classical conference. This format allows NECTAR's WG members and other eminent scientists to share and disseminate latest results within the scopes of our COST Action while, simultaneously, discussing about the management and development of the Action itself.

As such, more than a scientific workshop, the 2nd European NECTAR Conference represents a moment of joyful reencounter, invigorating in-person scientific discussion and deepened engagement, all this with the outstanding "Lisbon light" as host and one of the most beautiful European cities as background.

This book collects the abstracts of main communications from attendees, hoping that it can serve as stimulus for fruitful scientific discussion and future collaborations.

Demetrio Milea

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	2nd NECTAR Conference Programme		
	25th August	26th August	27th August
8:30 - 9:00		Registration	Registration
9:00 - 9:20		OC8 Olga IRANZO	Individual WGs Meetings
9:20 - 9:40		OC9 Carlos BERNARDES	
9:40 - 10:00		OC10 J. Carlos LIMA	
10:00 - 10:20		OC11 Laura RODRÍGUEZ	
10:20 - 10:40		OC12 Andrea MELCHIOR	
10:40 - 11:00		OC13 Carmelo SGARLATA	
11:00 - 11:20		Coffee Break	Coffee Break
11:20 - 11:40		OC14 Demetrio MILEA	Individual WGs Meetings
11:40 - 12:00		OC15 Josef HAMACEK	
12:00 - 12:20	Registration	OC16 Emanuele ZANDA	
12:20 - 12:40		OC17 Vladimir SLADKOV	
12:40 - 13:00		OC18 Montserrat FILELLA	
13:00 - 15:00		Lunch Break	Lunch Break
15:00 - 15:20	Opening Ceremony	OC19 Sabriye AYDINOĞLU	WGs Summary Managers Summary Core Group Meeting
15:20 -15:40	OC1 Péter BUGLYÓ	OC20 Guido CRISPONI	
15:40 -16:00	OC2 Rosita CAPPAI	OC21 Matteo TEGONI	
16:00 - 16:20	OC3 Emel YILDIZ	OC22 Arunas RAMANAVICIUS	
16:20 - 16:40	Coffee Break	Coffee Break	Coffee Break
16:40 - 17:00	OC4 Sławomir POTOCKI	Posters Session	MC Meeting and Closing Ceremony
17:00 - 17:20	OC5 Kamila STOKOWA-SOŁTYS		
17:20 - 17:40	OC6 Nádia RIBEIRO		
17:40 - 18:00	OC7 Adoracion QUIROGA		

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CONFERENCE PROGRAMME

Wednesday 25th

15:00 - 15:20 ***Opening Ceremony***

Chairperson: Maria Amelia SANTOS - *Universidade de Lisboa, Portugal*

15:20 - 15:40 **OC1** - Donor atom preference of metal ions with biological relevance to construct heterobimetallic complexes having likely hypoxia activation
Péter BUGLYÓ - *University of Debrecen, Hungary*

15:40 - 16:00 **OC2** - Solution equilibrium studies of 3-hydroxy-4-pyridinones as oxo-vanadium(IV) chelators
Rosita CAPPAI - *University of Cagliari, Italy*

16:00 - 16:20 **OC3** - Synthesis of metal complexes of ligands which containing acridine derivatives and curcumin with Al(II), Fe(III), Fe(II) ions and İnvestigation of β -amyloid Interactions
Emel YILDIZ - *Çukurova University, Turkey*

16:20 – 16:40 *Coffee Break*

Chairperson: Ełżbieta GUMIENNA-KONTECKA - *University of Wroclaw, Poland*

16:40 - 17:00 **OC4** - The impact of His mutations on the stability of Zn(II) – SmtB and -BigR4 α-5 domain complexes
Sławomir POTOCKI - *University of Wrocław, Poland*

17:00 - 17:20 **OC5** - Cu(II) and Fe(II) binding by peptides constituting fragments of *F. nucleatum* outer membrane proteins
Kamila STOKOWA-SOŁTYS - *University of Wrocław, Poland*

17:20 - 17:40 **OC6** - 8-Hydroxyquinoline benzohydrazide Schiff bases: coordination to Cu^{II} and $V^{IV}O$ and binding to biomacromolecules
Nádia RIBEIRO - *Universidade de Lisboa, Portugal*

17:40 - 18:00 **OC7** - Metallodrugs: Tautomer's coordination, speciation in solution and biological activity
Adoracion G. QUIROGA - *Universidad Autónoma de Madrid, Spain*

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Thursday 26th

Chairperson: Matteo TEGONI - *University of Parma, Italy*

09:00 - 09:20 **OC8** - Tuning the properties of Cu(II) N,N,O-chelating complexes for enhanced cytotoxic activity
Olga IRANZO - *Aix Marseille Université, France*

09:20 - 09:40 **OC9** - Thermodynamics of organic crystalline materials
Carlos BERNARDES - *Universidade de Lisboa, Portugal*

09:40 - 10:00 **OC10** - Multi-equilibria of the *flavylium* family: impact on their performance in DSSCs
J. Carlos LIMA - *Universidade Nova de Lisboa, Portugal*

10:00 - 10:20 **OC11** - Supramolecular assemblies based on weak intermolecular interactions. Study of their weak contacts and resulting properties and applications.
Laura RODRÍGUEZ - *Universitat de Barcelona, Spain*

10:20 - 10:40 **OC12** - Thermodynamic and structural and aspects of Ln(III) complexes with N-donor heteroaromatic ligands and their interaction with bio-analytes
Andrea MELCHIOR - *Università di Udine, Italy*

10:40 - 11:00 **OC13** - Determining the driving forces of molecular recognition equilibria in solution
Carmelo SGARLATA - *Università degli Studi di Catania, Italy*

11:00 - 11:20 *Coffee Break*

Chairperson: Michel MEYER - *Université Bourgogne–Franche-Comté, France*

11:20 - 11:40 **OC14** - Open-source software for species concentration calculation and potentiometric data analysis
Demetrio MILEA - *Università degli Studi di Messina, Italy*

11:40 - 12:00 **OC15** - Determination of binding affinities with Flow-Induced Dispersion Analysis: the case of synthetic affibodies
Josef HAMACEK - *Center for Molecular Biophysics, France*

12:00 - 12:20 **OC16** - Complexation of Th(IV) and U(VI) with a new tetrahydroxamic acid by affinity capillary electrophoresis
Emanuele ZANDA - *Laboratoire de Physique des 2 Infinis Irène Joliot Curie, France*

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12:20 - 12:40	**OC17** - Polynuclear metal hydrolysis species or colloidal particles? Vladimir SLADKOV - *Laboratoire de Physique des 2 Infinis Irène Joliot Curie, France*
12:40 - 13:00	**OC18** - On data loss and accessibility Montserrat FILELLA - *University of Geneva, Switzerland*
13:00 - 15:00	*Lunch Break*
Chairperson:	Tarita BIVER - *University of Pisa, Italy*
15:00 - 15:20	**OC19** - The method validation study of Favipiravir by HPLC Sabriye AYDINOĞLU - *Çukurova University, Turkey*
15:20 - 15:40	**OC20** - A smart spectrophotometric method for the analytical determination of total iron concentration Guido CRISPONI - *Università di Cagliari, Italy*
15:40 - 16:00	**OC21** - Developing designed copper – histidine sites in protein and peptides with redox catalytic behavior Matteo TEGONI - *University of Parma, Italy*
16:00 - 16:20	**OC22** - Towards Microorganism-based Microbial Fuel Cells Arunas RAMANAVICIUS- *Vilnius University, Lithuania*
16:20 - 16:40	*Coffee Break*
16:45 - 18:00	***Poster Session***
19:30 - 23:30	***Conference Dinner*** ***Restaurante D' Bacalhau (Parque das Nações EXPO, Lisboa)***

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Friday 27th

09:00 - 11:00	***Individual WGs meetings***
11:00 - 11:20	*Coffee Break*
11:20 - 13:00	***Individual WGs meetings***
13:00 - 15:00	*Lunch Break*
Chairperson:	Demetrio MILEA - *Università degli Studi di Messina, Italy*
15:00 - 16:20	***WGs Summary***
	Managers Summary
	Core Group Meeting
16:20 - 16:40	*Coffee Break*
16:40 - 18:00	***MC Meeting***
	Closing Ceremony

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Oral Communications

Donor atom preference of metal ions with biological relevance to construct heterobimetallic complexes having likely hypoxia activation

Linda BÍRÓ, [a] Etelka FARKAS, [a] Imre NAGY, [a] Sándor NAGY, [a] András OZSVÁTH, [a] Attila C. BÉNYEI, [b] Péter BUGLYÓ [a]

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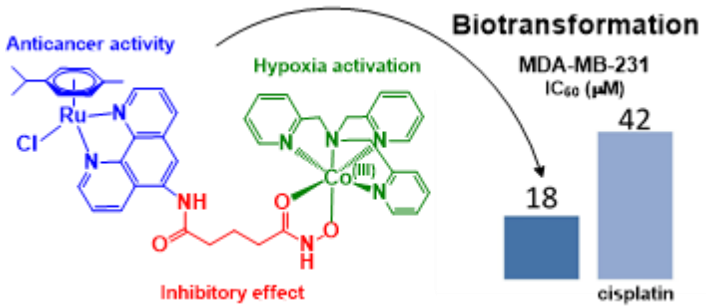
Ambidentate ligands may serve as useful building blocks for heterobimetallic complexes with various properties. In an ongoing project to develop cobalt(III)-platinum group metal (Co/PGM) complexes with likely hypoxia activation and selective anticancer activity various ligands incorporating separate O and N donor sets have synthesized and characterized. Although a $[Co(4N)]^{3+}$ ion (4N = tripodal 4N donor (tren, tpa) or 2x2N (phen, bpy, en, ampy)) with two vacant coordination sites is considered as a hard metal entity while PGMs are known to behave as soft metal ions their preference to coordinate to the above chelating sets needs to be explored for the successful synthesis of the desired Co/PGM complexes or to foresee the fate of the prepared solids after administration.



This contribution will summarize some of our latest results obtained on ambidentate chelating ligands with various (N,N) and (O,O) chelating sets using the combination of pH-potentiometry, NMR and ESI-TOF-MS techniques [1-8].

References:

[1] S. Nagy, A. Ozsváth, A. Cs. Bényei, E. Farkas, P. Buglyó, *Molecules*, **2021**, *26,* 3586

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[4] I. Nagy, G. Ferenczik, L. Bíró, E. Farkas, A. C. Bényei, P. Buglyó, *Polyhedron,* **2020***, 190,* 114780
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[6] I. Nagy, E. Farkas, J. Kasparkova, H. Kostrhunova, V. Brabec, P. Buglyó, *J. Organomet. Chem.,* **2020**, *916,* 121265
[7] A. Ozsváth, L. Bíró, E. M. Nagy, P. Buglyó, D. Sanna, E. Farkas, *Molecules*, **2019**, *24*, 3941
[8] A. Ozsváth, E. Farkas, R. Diószegi, P. Buglyó, *New J. Chem.,* **2019**, *43*, 8239-8249

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Solution equilibrium studies of 3-hydroxy-4-pyridinones as oxovanadium(IV) chelators

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Hydroxypyridinones (HPs) are considered very good building blocks for the design of metal chelating agents. Actually, thanks to their high affinity and selectivity, they form thermodynamically stable complexes with hard metal ions in aqueous media promoting their application in both biological and medical fields. Moreover, they show chelating properties towards vanadyl cation, especially suitable for enhancing insulin mimetic activity, being so a good candidate for the treatment of type II diabetes mellitus [1].

In the frame of this work we present oxovanadium(IV) complexes of tetradentate ligand (KC21) with 3,4-HP arms N-attached to an aminomethanetrispropionic acid backbone, previously studied for Fe^{3+} and Al^{3+} cations, and with the corresponding mono 3,4-HP (L5) [2, 3].

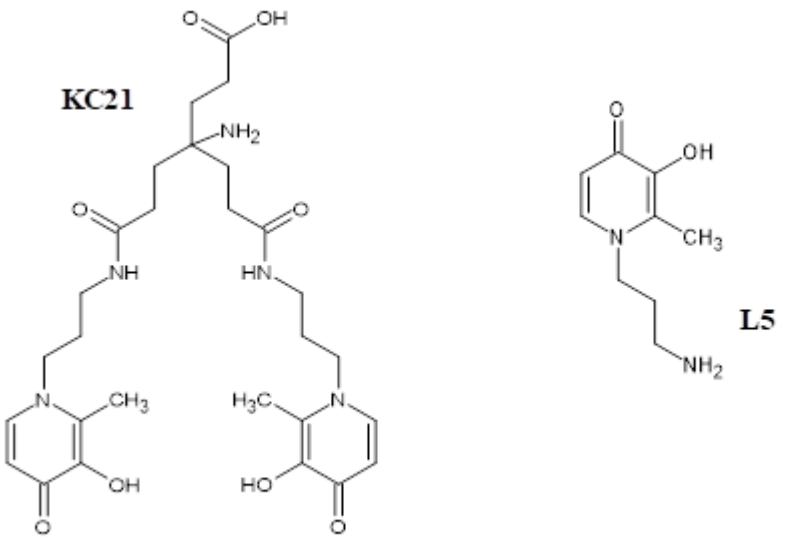

Figure: 3-hydroxy-4-pyridinones under study: KC21, tetradentate HP and L5, mono HP.

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The chemical systems were studied by potentiometric and UV-spectrophotometric titrations at 25°C and 0.1 M NaCl ionic strength and speciation models were drawn up by HyperQuad and HypSpec taking into account the hydrolysis constant at used experimental conditions.
The coordination model shows the formation of 1:1 VO^{2+}-ligand complex in case of KC21 and 1:2 in case of mono where two HP moieties are linked in the equatorial plane of the vanadyl cation coordination sphere.

References:

[1] S. Berto, E. Alladio, P. G. Daniele, E. Laurenti, A. Bono, C. Sgarlata, G. Valora, R. Cappai, J. I. Lachowicz, V. M. Nurchi, *Molecules* **2019**, 24, 3768-3786.
[2] V. M. Nurchi, R. Cappai, K. Chand, S. Chaves, L. Gano, G. Crisponi, M. Peana, M. A. Zoroddu, M. A. Santos, *Dalton Trans.* **2019**, 48, 16167-16183.
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Synthesis of Metal Complexes of Ligands Which Containing Acridine Derivatives and Curcumin with Al (II), Fe (III), Fe (II) ions and İnvestigation of Beta Amyloid Interactions

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Alzheimer's occurs with the loss of neurons and synapses in some parts of the central nervous system; It is a disease that shows symptoms such as decreased cognitive functions, self-care deficiencies, neuropsychiatric and behavioral disorders [1]. The interaction of different metal complexes with Aß also limits the binding of disordered metal ions such as Fe, Cu and Zn through competition for the same amino acid residues. In addition, metal complexes can be designing with additional activity activated by external stimuli, thus providing therapeutic selectivity [2].

In this study, as a continuation of the two studies which conducted by our group [3, 4], it was aimed to synthesis of heteroleptic metal complexes of Acridine derivatives and Curcumin ligands (with Al (III), Fe (III) and Fe (II) salts) by conventional method under in vitro conditions and then investigate its therapeutic properties in Alzheimer's disease by looking at whether it prevents beta amyloid accumulation at in vivo conditions. For this purpose, 9-aminoacridine-curcumin-Al (III) complex was synthesized (Figure 1). Characterization studies and pharmacology applications are continuing.

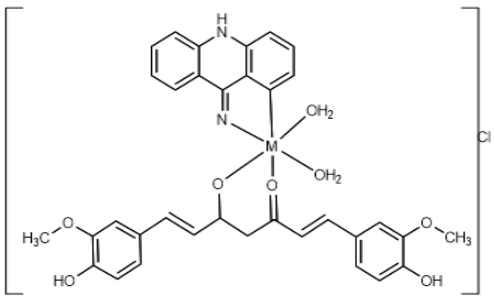

Figure: 9-aminoacridine-curcumin AI(III)

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References:

[1] S. Gilman, *Alzheimers disease*, **1997**, 40(2):230-45.
[2] L. M. F. Gomes, J. C. Bataglioli, T. Storr, *Coordination Chemistry Reviews*. **2020**, 412.
[3] N. Bicer, E. Yildiz, AA. Yegani, F. Aksu, *New Journal of Chemistry*, **2019**, 42(10):8098-8104.
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The impact of His mutations on the stability of Zn(II) – SmtB and -BigR4 α-5 domain complexes

Anna ROLA,[a] Robert WIECZOREK,[a] Marta MARTENKA,[a] Karolina KRZYWOSZYŃSKA,[b] Henryk KOZŁOWSKI,[b] Sławomir POTOCKI[a]

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The increasing number of antibiotic-resistant pathogens has become one of the major health problems of modern times, not excluding *Mycobacterium tuberculosis* infections [1, 2]. One of the possible response of the mammalian immune system to mycobacterial infection is the increase of zinc(II) concentration in phagosomes to a toxic level [3]. The mycobacterial SmtB protein belongs to the family of ArsR/SmtB transcription regulators which in the presence of high concentrations of metals, dissociate from DNA and activate the expression of metal efflux proteins.

In this work, we focus on α5 zinc(II) binding domains of SmtB/BigR4 proteins (the latter being the SmtB homolog from non-pathogenic *M. smegmatis*) and two mutants of BigR4, taking a closer look at the coordination modes and thermodynamic properties of their zinc(II) complexes. Ligand sequences studied in this project are given below:

L1 – Ac-101DHHLAHIVVDAIAHASEDRR120 (BigR4)
L2 – Ac-101DHALAHIVVDAIAHASEDRR120 (mutant 1)
L3 – Ac-101DHHLAHIVVDAIAAASEDRR120 (mutant 2)
L4 – Ac-116DHHLAHIVLDAVAHAGEDAI135 (SmtB)

Like in other metal-sensitive proteins, domains are composed *i.e.* of carbocyclic acid and imidazole containing side chains [4, 5]. The study points out the specificity of metal-ligand interaction and describes the effect of mutations on the coordination properties of studied systems. Stabilities of zinc(II) complexes were determined by potentiometry and coordination sites were determined by NMR experiments and DFT calculations. The comparison of complex stabilities reveals that the Zn(II)-BigR4 species are more stable than the Zn(II)-SmtB complexes, and His mutations strongly affect the stability of complexes and coordination modes of the metal ion [5]. Exchanging one of the histidines into alanine causes, surprisingly, an increase in the stability of zinc(II) complexes with the studied domain (L2), which was confirmed by potentiometric and DFT methods (Figure 1). This work can be considered as a bioinorganic introduction to the search for new strategies in *M. tuberculosis* treatment based on zinc(II)-sensitive mechanisms in bacterial cell survival.

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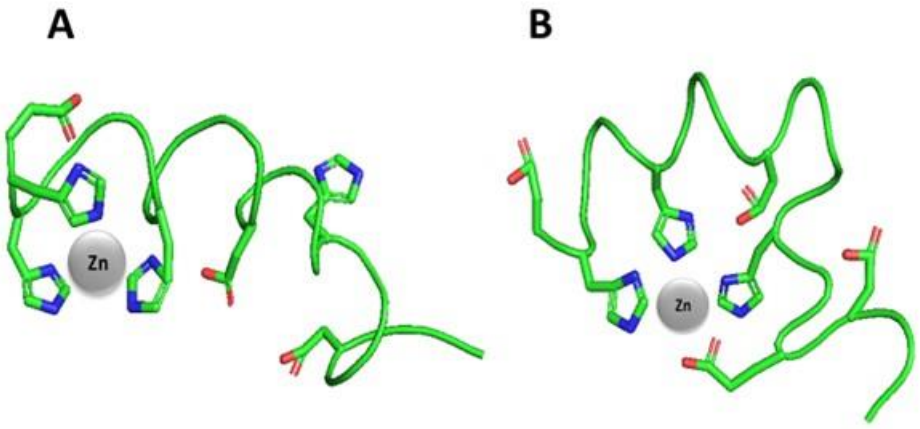

Figure 1. Postulated coordination of zinc(II) in L1 (A) and L2 (B) complexes at physiological pH (7.20). In both cases, three imidazole groups are involved; in L1 to complete tetrahedral coordination water molecule is bound; in the case of L2, involvement of Glu and Asp residues has been observed.

Acknowledgement:

Financial support by the National Science Centre (UMO-2017/26/D/ST5/00372) is gratefully acknowledged.

References:

[1] World Health Organization, *Global tuberculosis report 2020*, **2020**.
[2] J. Wątły, S. Potocki, M. Rowińska-Żyrek, *Chemistry-A European Journal*, **2016**, 22, 15992-16010.
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Cu(II) and Fe(II) binding by peptides constituting fragments of *F. nucleatum* outer membrane proteins.

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Fusobacterium nucleatum is one of the most abundant Gram-negative anaerobic bacteria, part of the gut and oral commensal flora, generally found in human dental plaque. Its presence could be associated with various human diseases, including, e.g., periodontal, angina, lung and gynecological abscesses [1, 2]. It has been proven that *F. nucleatum* migrates from its primary site of colonization in the oral cavity to other parts of the body and is actively involved in colorectal carcinogenesis. An overwhelming number of sources show a fairly close correlation between colorectal cancer and the presence of *F. nucleatum* [3]. The basic mechanism contributes to the adhesion of bacterial cells to the intestinal epithelium. Therefore, examination of outer membrane proteins properties is essential for understanding bacterial pathogenesis.

Numerous *F. nucleatum* outer membrane proteins are able to chelate metal ions. Herein, complexes with peptides constituting HmuU protein fragments are discussed. We have shown that these peptides bind iron(II) and/or copper(II) ions and form thermodynamically stable complexes. At large intestine physiological pH (around 6.8) cupric ions are bound by four nitrogen donor atoms (amino group and three amides from the peptide bond) deriving from the N-terminal sequence of HmuU. In the case of ferrous ions, most probably sulphur donor atom is also involved in the binding. Based on the potentiometric titrations performed in anaerobic conditions and in the presence of one-electron reductant (ascorbic acid) we have shown that Fe(II) ions form three complexes with peptide MKYRI-NH_2. In the case of the second studied ligand, Ac-AGACF-NH_2, it reduces cupric ions and further studies are needed to characterize Cu(I) binding. However, studies of ferrous coordination were possible. The experiments were performed in the presence and absence of ascorbic acid. Obtained results indicate that ascorbic acid does not affect the overall stability constants of the Fe(II) complexes with the peptides (similar values were calculated in both cases). The overall stability constants are given in Table 1. Moreover, in the presence of hydrogen peroxide or ascorbic acid all studied complexes generate more reactive oxygen species (ROS) than free metal ions. It means, that these peptides increase the prooxidative activity of cupric and ferrous ions. We have shown, that one of the most abundant ROS is hydroxyl radical. This is the most reactive free radical which may destroy all kind of biologically important macromolecules. Performed studies indicate that the nascent hydroxyl radical caused DNA relaxation and degradation (Fig. 1). All these facts suggest that proteins present on the bacterial outer-membrane enhance the production of ROS which may be involved in the carcinogenesis process.

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Table 1. Thermodynamic parameters for deprotonation and Fe(II) complex formation of fragment of HmuU, in aqueous solution. T = 25 ◦C, I =0.1 M (KCl). Standard deviations are given in parentheses.

L = Ac-AGACF-NH_2; Asc = ascorbate		
	log β	pK_a
H_2Asc	15,36(2)	4,11
HAsc	11,25(1)	11,25
FeHAsc	13,68(5)	8,19
FeAsc	5,49(5)	–
$FeAsc_2$	10,30(3)	9,19
$FeH_{-1}Asc_2$	1,11(4)	–
HL	8,784(3)	8,784
FeL	3,83(3)	8,71
$FeH_{-1}L$	-4,88(4)	8,97
$FeH_{-2}L$	-13,85(3)	9,44
$FeH_{-3}L$	-23,29(2)	-

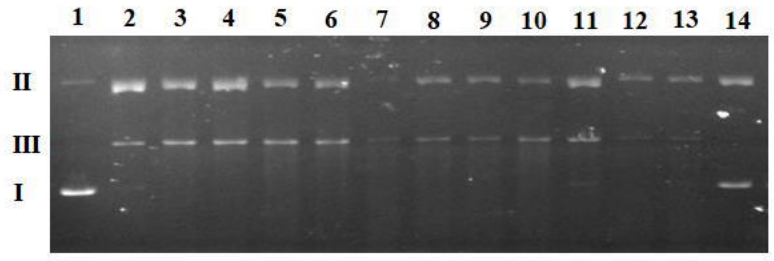

Figure 1. Agarose gel electrophoresis of plasmid DNA cleavage by Fe(II)–Ac-AGACF-NH_2 at pH 6.8 in the presence of 500 μM H_2O_2.

Lane 1. Control reaction, plasmid DNA. Lane 2. plasmid + 10 μM Fe(II), Lane 3. plasmid + 10 μM complex, Lane 4. plasmid + 25 μM Fe(II), Lane 5. plasmid + 25 μM complex, Lane 6. plasmid + 50 μM Fe(II), Lane 7. plasmid + 50 μM complex, Lane 8. plasmid + 100 μM Fe(II), Lane 9. plasmid + 100 μM complex, Lane 10. plasmid + 250 μM Fe(II), Lane 11. plasmid + 250 μM complex, Lane 12. plasmid + 500 μM Fe(II), Lane 13. plasmid + 500 μM complex, Lane 14. plasmid + 500 μM ligand

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COST Action CA18202, NECTAR – Network for Equilibria and Chemical Thermodynamics Advanced Research,
supported by COST (European Cooperation in Science and Technology).

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8-Hydroxyquinoline benzohydrazide Schiff bases: coordination to Cu^{II} and $V^{IV}O$ and binding to biomacromolecules

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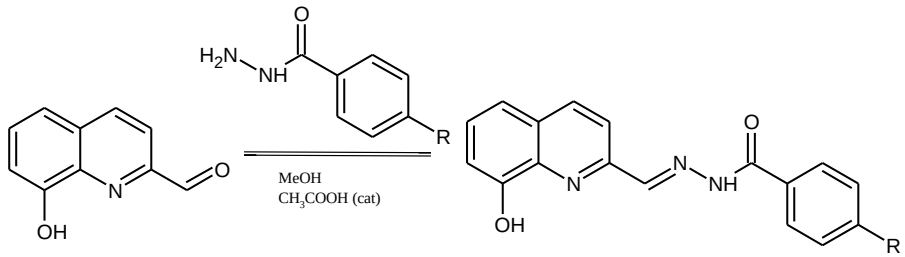
8-Hydroxyquinoline (8HQ) has structural and electronic features that make it an excellent metal ion binder. Derivatization of this molecule in position 2 with additional chelating groups is a suitable strategy for the development of new ligands for attaining more robust metal complexes [1]. The strong ability to chelate metal ions allied with appropriate lipophilic properties may make 8HQ derivatives good candidates for pharmaceutical applications, namely in anticancer therapy [2, 3]. Lanthanide complexes with Schiff bases (SBs) derived from 8-hydroxyquinoline-2-carboxaldehyde were found to possess DNA binding properties, although several other cell death mechanisms were proposed [4, 5]. Considering these data, a new family of Schiff base compounds was synthetized from condensation of 8HQ-2-carboxaldehyde with benzohydrazides bearing different substituents at the *para* position (Scheme 1).



	R
H_2L^1	H
H_2L^{2A}	F
H_2L^5	OCH_3
H_2L^6	NH_2

Scheme 1: Synthesis of the Schiff-base ligands derived from 8-hydroxyquinoline-2-carboxaldehyde and substituted benzohydrazides.

The compounds were coordinated to copper(II) and oxidovanadium(IV) ions and characterized by the usual analytic techniques. Cu^{II} complexes have a 1:1 L:M stoichiometry with the ligands acting as dianionic, tetradentate chelates, except for $[Cu(HL^1)(AcO)]$ (AcO^- stands for acetate). The $V^{IV}O$ complexes have 2:1 stoichiometry, with the SBs behaving as monoanionic, bidentate chelates, except for $[VOL^1]$. The compounds were studied for their interaction with *calf thymus* DNA by UV-Vis absorption with temperature variation and steady-state fluorescence emission. The measurement of absorption spectra with increasing temperature allows the determination of the DNA melting temperature in the presence of the

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compounds, while fluorescence emission quenching assays of ethidium bromide intercalated into DNA by addition of the compounds were used to investigate their ability to displace the probe. In spite of the examples found in the literature, these compounds were found to have none or weak interactions with DNA.

The compounds ability to bind bovine serum albumin (BSA), a carrier protein present in substantial amounts in cell culture media and a model for the human variant, was also evaluated. The use of BSA site markers in fluorescence competition studies showed that the studied compounds prefer site I, with binding constants in the order of 10^5 M^{-1}, which were calculated with the computer program HypSpec2014®.

Overall, the results suggest that the compounds will be able to reach cells protected in the hydrophobic environment of albumin and any cytotoxic effect that might be observed will not depend of a direct interaction with DNA.

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Acknowledgements:

This work was supported by Fundação para a Ciência e Tecnologia (FCT) (projects UIDB/00100/2020, UIDP/00100/2020, PTDC/QUI-QIN/0586/2020 and grant SFRH/BD/135797/2018). NR acknowledges COST Action CA 18202 for STSM 48102.

Metallodrugs: Tautomer's coordination, speciation in solution and biological activity

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Cisplatin is the most widely known anticancer drug but its use in clinic presents adverse side-effects which has fueled research and development of new metallodrugs with different metals and/or ligands searching for a relationship between the structure of the drug and the biological activity[1]. It has not been until recently when the speciation studies in solution have started showing its importance.[2] This importance results from the role played by the possible generated species which may have greater persistence, different locations in the body, or even affect other metabolic sequences that are not the primary target of the initial drug. This phenomenon also increases in complexity when coordinating solvents (DMSO) are used.[4]
In this work, we introduce two thiosemicarbazone Pd(II) complexes, in which the ligands coordinate in two tautomeric forms.[4] Their stability in aqueous solution, DNA interaction studies and excellent cytotoxic activity against a series of cancer cell lines prompted us to continue studying these systems with a new design in which we varied the substituent group but maintained the core of the heterocyclic thiosemicarbazone. The tautomeric equilibrium of the new ligand has shown a very intense dependence on the pH of the solution, and the reactivity of the complexes in DMSO and aqueous solution changed dramatically (Figure 1).

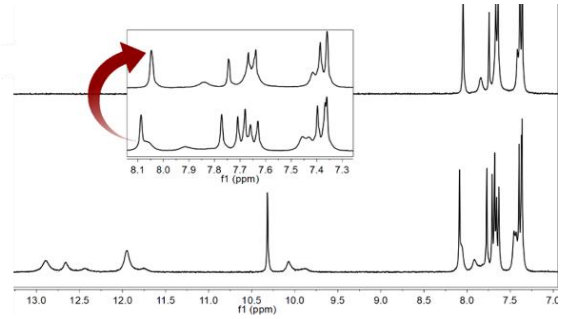

Figure 1: pH dependence of the ligand tautomeric form in solution, monitored by ^{1}H NMR.

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This contribution 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).

COST is supported by the Horizon 2020 Framework Programme of the European Union

Tuning the properties of Cu(II) N,N,O-chelating complexes for enhanced cytotoxic activity

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During the last 30 years, Ru, Ir, Pd, Fe or Cu complexes have appeared as promising alternatives to overcome the drawbacks encountered with Pt compounds in cancer therary [1]. Among them, Cu complexes have awakened strong interest as potential therapeutic agents [2]. Two important features make Cu attractive for this purpose: (i) its nature as a physiological metal, which may imply fewer side effects than other exogenous metals, and (ii) its Cu(II)/Cu(I) redox pair, which can promote reactive oxygen species (ROS) generation [3]. The production of ROS is not only reported to cause cellular damage, but also to offer a putative discrimination between healthy and cancer cells [4].

In this context, we have recently designed and synthesized a family of Cu(II) complexes, based on tridentate *N,N,O*-donor salphen-like ligands [5]. The complexes were characterized using different methods, and electrochemical studies indicated that they undergo Cu(II)/Cu(I) redox cycling in biological conditions (**Figure 1**). Cytotoxicity studies revealed that they are active against two different cancer cell lines (HeLa and MCF7 cells), and further analysis in HeLa cells highlighted a high ROS generation inside cells.

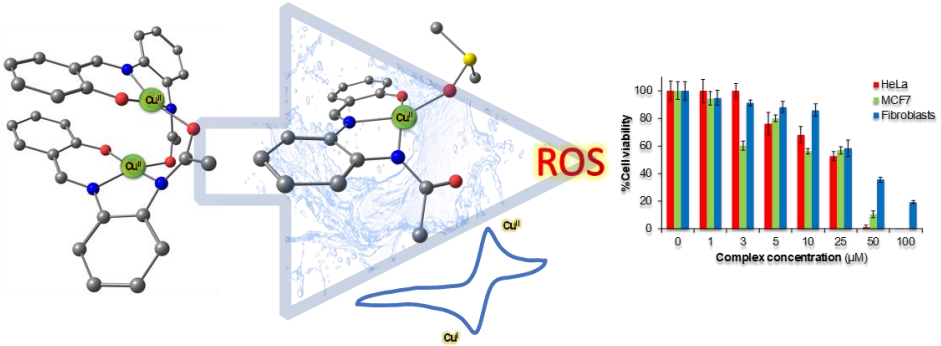

Figure 1. Schematic representation of the Cu(II) complexes and their cytotoxic activity.

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Despite these promising data, solubility issues were encountered and this prompted us to modify the ligands to improve their solubility, while maintaining the same Cu(II) coordination environment, as well as to improve their cellular uptake. In this communication, we will present the strategies pursued to attain these goals and their effect in the *in vitro* cytotoxic properties of the corresponding Cu(II) complexes.

Acknowledgments: MINECO-FEDER (Project BIO2015-67358-C2-2-P and RTI2018-098027-B-C22), *Ministerio de Educación, Cultura y Deporte* (FPU grants to QP and SGC) and Servei d'Anàlisi Química (UAB) and Spectropole facilities (AMU) for allocating instrument time and mass spectrometry analysis.

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This contribution 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).

COST is supported by the Horizon 2020 Framework Programme of the European Union

Thermodynamics of Organic Crystalline Materials

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The control of the organization of the molecules in the solid-state is a key feature to tune the properties of a material with an application in view. Indeed, organic compounds can often be prepared with different tridimensional arrangements in the solid-state, a phenomenon is known as polymorphism, where each crystal phase can exhibit significant differences in its physical properties (e.g., color, solubility, and fusion temperature). Additionally, it is possible to change the materials by crystallizing a compound with other organic moieties (conformers), to form multicomponent materials. A key aspect in the development of these materials is the study of their kinetic and thermodynamic stability. For example, (i) during the development stages of these substances (e.g., active pharmaceutical ingredients, dyes, explosives), it is necessary to evaluate if a given phase is more stable than another at a given temperature and pressure, or (ii) determine if a multi-component material is stable relative to its precursors. In this work, an overview of different experimental and theoretical techniques to investigate the kinetic and thermodynamic stability of solid materials will be presented.

Acknowledgements:
This work was supported by Fundação para a Ciência e Tecnologia (FCT), Portugal (projects PTDC/QUI-OUT/28401/2017, LISBOA-01-0145-FEDER-028401, UIDB/00100/2020, and UIDP/00100/2020). The author also acknowledges COST Action CA18202, NECTAR.

Multi-equilibria of the flavylium family: impact on their performance in DSSCs

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Dye-Sensitized Solar Cells (DSSCs) are photovoltaic devices based on the sensitization of wide band-gap semiconductor electrodes with dyes absorbing visible light. The first reported DSSC using a natural anthocyanin displayed a conversion yield of 0.56%, paving the way for sustainable DSSCs.[1] Unfortunately the natural anthocyanins which are present in present in many flowers and fruits an many related synthetic derivaties (usually called flavylium salts), display strong colors only at acidic pH values. At neutral pH values a multiequilibria involving the colorless forms of hemiketal and chalcones leads to the loss of color (Figure 1)[2] compromising the role of absorbing visible radiation from the sun when used as DSSC sensithizers.

Pyranoanthocyanins are a class of related dyes that are present in mature red wines. The resistance of pyranoanthocyanins to hydration grants this family of compounds, closely related to anthocyanins, increased color stability in the whole pH range increasing the potential of this family as photosensitizers in bio-inspired DSSCs. [3-5]

An additional strategy to stabilize these colorants at neutral pH is the use of electron donor groups that lower the positive charge density ant shift the hydration reaction to higher pH values, thus stabilizing the colored species with respect to the colorless hydration products. In some cases this strategy leads to remarkable results in DSSCs performance for this class of dyes.[6]

In this work, several bio-inspired derivatives of anthocyanins are applied as dye sensitizers in DSSCs. The efficiency of the DSSCs, performance of dyes and the relation with the forms in equilibrium available for anchoring TiO_2 electrode is analyzed.

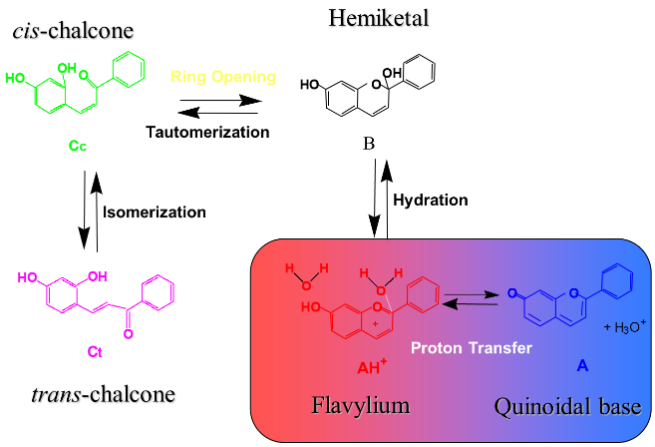

Figure 1. Multiequilibria of the dyes of the anthocyanin family at moderately acidic pH values.

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COST Action CA18202, NECTAR – Network for Equilibria and Chemical Thermodynamics Advanced Research,
supported by COST (European Cooperation in Science and Technology).

COST is supported by the Horizon 2020 Framework Programme of the European Union

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Acknowledgments:
This work was supported by the Associate Laboratory for Green Chemistry - LAQV which is financed by national funds from FCT/MCTES (UIDB/50006/2020).

This contribution 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).

COST is supported by the Horizon 2020 Framework Programme of the European Union

Supramolecular assemblies based on weak intermolecular interactions. Study of their weak contacts and resulting properties and applications.

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Supramolecular systems are based on molecular assemblies that are held together by intermolecular interactions rather than by covalent bonds. These interactions are well known, such as π–π stacking, hydrogen bonding or C-H···π interactions. Neverthteless, in the case of some heavy metals, such as gold and platinum, M···M interactions play a key role on the resulting supramolecular assemblies. Thus, the presence of these metals in the chemical structure of the individual molecules increases the possibilities of geometry modification and they affect also on the resulting luminescence.[1-3]

The photophysical properties of heavy-metal complexes have been intensely studied in the last two decades due to their fascinating versatility as well as the promising potential for technological applications in very different research fields such as optoelectronics, biological activity, chemosensors, mechanochromism, materials etc. All these properties are based on the study of the luminescence characteristics of these type of compounds, which often depend dramatically on the presence of metal-metal interactions.

In our research group we have developed in the last years a large number of luminescent supramolecular systems containing Au(I) and Pt(II)/Pt(IV) as heavy metal atoms.[4] We are mainly interested on exploring how modification of the ancillary ligands affects the resulting properties in different fields such as luminescence, molecular recognition, anticancer activity, metallogels formation and solubility in water among others.

An overview of some of the conclusions obtained in our group is shown in this communication together with some selected applications (Figure 1).

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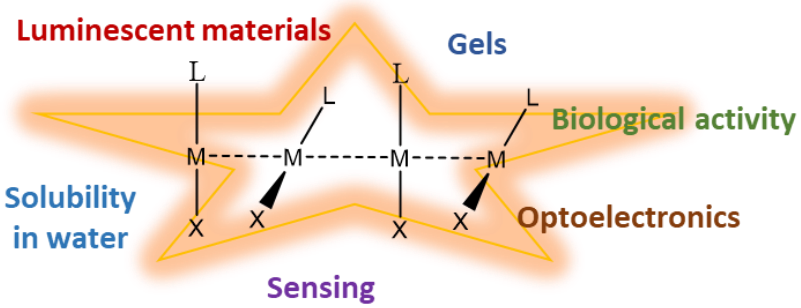

Figure 1. Schematic representation of some selected applications developed in our group with supramolecular assemblies.

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This contribution 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).

COST is supported by the Horizon 2020 Framework Programme of the European Union

Thermodynamic and structural and aspects of Ln(III) complexes with N-donor heteroaromatic ligands and their interaction with bio-analytes

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Lanthanide ions (Ln^{3+} = Sm^{3+}, Eu^{3+}, Tb^{3+}, Yb^{3+}…) complexes have been extensively studied as luminescent sensors for cell imaging and bio-sensing [1]. The long emission lifetimes of Ln^{3+} ions are favorable for reducing interference from light scattering or autofluorescence in complex microenvironments such as cells, tissues or animals *via* time-gated detection [2]. Complexes of Ln^{3+} ions present an efficient intramolecular energy transfer from a donor state (usually triplet) of the coordinated organic ligand (*antenna*) to the acceptor excited states of Ln^{3+} ion giving rise to an efficient Ln^{3+} excitation, bypassing the Laporte-forbidden nature of the *f* - *f* transitions. The large energy shift between absorbed and emitted light and the narrow emission bands allow to separate the emission from the short-lived background fluorescence.

Eu^{3+} complexes with ligands based on the *trans*-1,2-diaminocyclohexane (DACH) backbone and containing one or two heteroaromatic moiety have been studied recently [3-6].

The ligands considered (Figure 1) are: bpcd = N,N′-bis(2-pyridylmethyl)-DACH-diacetate; bQcd = N,N'-bis(2-quinolinmethyl)-DACH-diacetate; b*iso*Qcd = N,N'-bis(2-isoquinolinmethyl)-DACH-diacetate; PyC3A = N-picolyl-N,N',N'-DACHtriacetate; QC3A = N-quinolyl-N,N',N'-DACH-triacetate; *iso*QC3A = N-isoquinolyl N,N',N'- DACH-triacetate.

In these ligands, the nature of the heteroaromatic groups can be systematically changed, thus allowing to tune the emission properties of the complexes in solution. Furthermore, ligand stereochemistry can be easily defined by selecting the DACH with the desired configuration.

The ligand structure and donor properties have also an effect on the species formed in solution, in particular the number of acetate groups and the nature of the heteroaromatic groups tune the stability of the 1:1 complexes. Different heteroaromatic groups have also an effect on the optical detection of several bio-analytes: hydrogen carbonate, lactate, citrate, and bovine serum albumin (BSA).

In this contribution the thermodynamics both of complex formation and of the interaction with several bio-analytes are discussed. Structural aspects are obtained both from spectroscopic information (luminescence emission spectra) and DFT calculations.

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COST Action CA18202, NECTAR – Network for Equilibria and Chemical Thermodynamics Advanced Research,
supported by COST (European Cooperation in Science and Technology).

COST is supported by the Horizon 2020 Framework Programme of the European Union

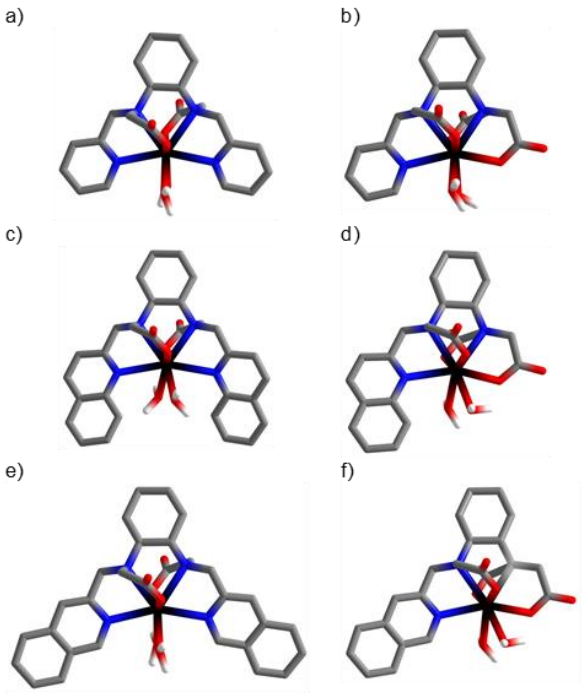

Figure 1. Structures of (a) [Y(*trans*-O,O-bpcd)$(H_2O)_2]^+$; (b) Y(*trans*-O,O-PyC3A)$(H_2O)_2$; (c) [Y(*trans*-O,O-bQcd)$(H_2O)_2]^+$; (d) Y(*trans*-O,O-QC3A)$(H_2O)_2$; (e) [Y(*trans*-O,O-*iso*bQcd)$(H_2O)_2]^+$; (f) Y(*trans*-O,O-*iso*QC3A)$(H_2O)_2$. H atoms attached to carbons are omitted for clarity.

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This contribution 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).

COST is supported by the Horizon 2020 Framework Programme of the European Union

Determining the Driving Forces of Molecular Recognition Equilibria in Solution

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Non-covalent, weak interactions are major tools used in supramolecular and coordination chemistry to oversee molecular recognition and self-assembly processes for the design and synthesis of intriguing structures such as molecular capsules, cages, flasks and nano-containers [1]. By mimicking the active sites of enzymes, synthetic assemblies are able to isolate proper guest molecules from the surrounding media and promote chemical reactions in a controlled fashion. The dramatic differences between the bulk solvent and the inner space of a molecular container provide the "thermodynamic boost" to guest complexation which cannot be driven only by structural complementarity or fitting between host and guest [2]. Consequently, the determination of complex species and thermodynamic parameters for molecular recognition, self-assembling, host-guest encapsulation, micellar aggregation and related phenomena is a key point for the rational design and efficient application of nano-containers in solution.

The entropic and enthalpic driving forces for guest binding to supramolecular receptors in solution are very different, which significantly complicates their determination. The advantageous use of complementary techniques, such as NMR, UV−vis/fluorescence and isothermal titration calorimetry (ITC), enables the disentanglement of multiple host-guest interactions. Data collected by each technique measure different components of the host−guest equilibria and together provide a complete picture of the solution thermodynamics. However, the analysis of the data is often puzzled by the variety of responses given by each different technique and by a series of mutually linked equilibria usually occurring is solution.

We developed a procedure for the simultaneous refinement of multiple parameters (ΔG, ΔH and ΔS) by handling different observables through a weighted non-linear least-squares analysis of a constrained model [3, 4]. By applying this procedure to different sets of observables, each looking at different components of multiple and often competing host–guest equilibria, the binding constants as well as the enthalpy and entropy change for the interior and multiple exterior guest binding to a supramolecular receptor were determined.

Furthermore, a new general-purpose computer program for the simultaneous determination of both standard enthalpy of reaction and binding constant values from data obtained by ITC was also developed [5]. The program does not impose limits on the complexity of the chemical systems that can be treated, including competing ligand systems, or on the quantity of experimental data to be analyzed. The chemical system is defined in terms of species of given stoichiometry rather than in terms of binding models (e.g. independent, cooperative,

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etc.). Many titration curves may be treated simultaneously. The program can also be used as a simulation program for experiment design. Typical applications are the study of ligand protonation, host-guest reactions, metal-ligand complexation and competition reactions.

The abovementioned data refinement tools have been successfully applied on our recent work on the molecular recognition of charged guests by metal-ligand clusters [6], calixarene receptors bearing polar functionalities [7, 8] as well as on the formation of anion-templated capsules and compartments [9] or supra-amphiphiles and micellar aggregates [10] in aqueous solution. A combination of different datasets from NMR, UV-vis and/or ITC titrations allowed for the deconvolution of the host-guest equilibria and the determination of the species formed in solution. In particular, ITC data allowed for splitting the Gibbs free energy term into the ΔH and ΔS components thus unveiling the different and often opposing forces, not expressed in the logK value, driving guest recognition and self-assembly processes [11].

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This contribution 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).

COST is supported by the Horizon 2020 Framework Programme of the European Union

Open-source software for species concentration calculation and potentiometric data analysis

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This work lays within in the activities of the WG4 of the NECTAR COST Action, which is the WG devoted to the development of tools, services and facilities for the NECTAR community. The aim of the work is to develop new versions of the BSTAC4 and ES4 software [1-2]. BSTAC4 is a software dedicated to the analysis of potentiometric data developed many years ago [1-2], which shows particularly useful features: i) it allows the simultaneous optimization of the formation constants and of the components concentrations; ii) it allows handling calibration data, allowing the refinement of acidic and basic junction coefficients, as well as electrode slope; iii) it can process many titrations together, also conducted at different ionic strengths; iv) it allows using constrains on total concentration of the components; v) it can refine the coefficients of an extended Debye–Hückel equation and optimize formation constants at different ionic strengths; vi) it is based on a robust mathematical approach. ES4 instead allows plotting the distribution of the species diagrams and simulating potentiometric titrations of a known chemical system. It can treat heterogeneous solutions and can take into account the variation of the ionic strength of the system as a function of pH or during the titration process. The actual version of the two software is available for free by a simple request to its authors, but it is not user friendly and it is no longer compatible with actual PC and operating systems, still working in a DOS environment. In this line, we are working on the development of new versions maintaining all the good characteristics of the original versions but improving their usability. The new versions show interactive input pages that are organized with clear captions in order to help the inexpert users. In the new BSTAC the titration curves can be uploaded as .xlsx or .cvs files. In the output pages, all the results of the calculations are visible: the optimized parameters with the corresponding uncertainties, as well as the results obtained at each iteration are shown. Both software provide the concentrations of the species for each titration point. The new ES4 also shows the percentage species distribution and the adjusted formation constants as a function of the ionic strength. These data can be exported as a convenient excel file.

The development of the new version of ES4 and BSTAC4 is being done using Python programming language and it is still in progress. The software is being tested with some

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datasets, in order to find algorithm flaws and bugs. Some potentiality have to be yet developed for both. The user experience design will be further refined.

Acknowledgements:
This contribution 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).

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Determination of Binding Affinities with Flow-Induced Dispersion Analysis: The Case of Synthetic Affibodies

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Binding affinities between ligands and related macromolecular receptors (e.g., proteins) are usually invesigated with Surface Plasmon Resonance (SPR), Bilayer Interferometry (BLI), Microscale Thermophoresis (MST) or Isothermal Titration Calorimetry (ITC). In addition, Flow-Induced Dispersion Analysis (FIDA) technique [1] has been introduced relatively recently, although its basic principles were already established in 50's [2]. The method is based on measuring variations of apparent hydrodynamic radius upon addition of a ligand to a labeled receptor (fluorescence) in solution [3], which provides a binding curve for calculating K_D.

In this work, an affibody molecule was produced using solid phase peptide synthesis approach. The affinity to the targeted commercially available protein was determined using FIDA assay to check its efficiency. We will discuss the data acquisition with FIDA as well as its advantages and drawbacks. We believe that our contribution will provide a better insight into the FIDA application in binding studies, which may be of interest for NECTAR community.

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This contribution 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).

COST is supported by the Horizon 2020 Framework Programme of the European Union

Complexation of Th(IV) and U(VI) with a new tetrahydroxamic acid by affinity capillary electrophoresis

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The transfer of metal cations in soils and sediments is not only controlled by geological and physico-chemical parameters (clay and organic matter contents, pH, Eh, etc.) but also by microorganisms. The latter take part in the mobilization/immobilization of trace metals [1]. Siderophores, as natural iron-specific chelators, have to be considered in this context. These low molecular weight, water-soluble compounds are excreted by bacteria and fungi to overcome the limited bioavailability of iron under aerobic conditions (ca. 10^{-18} M at neutral pH) by dissolving iron oxohydroxides present in the soils. Because of their high affinity for hard Lewis acid cations, like Fe(III), hydroxamic siderophores are also able to effectively bind actinides (U, Th, Pu) [2-4]. The development of high affinity chelators for f-elements and the understanding of their coordination chemistry is of fundamental interest for the management and remediation of contaminated fields or the disposal of nuclear wastes [4].

This work is devoted to the complexation study of Th(IV) and U(VI) with (DFO(Me)PIPO)H_4 (Figure 1), a new hydroxamic acid obtained by coupling the 6-membered 1-hydroxypiperidine-2-one moiety [5] to the bacterial siderophore desferrioxamine B [3,4]. This compound, which contains four hydroxamic acid groups, is an effective ligand of Zr^{4+} [6], as well as actinides, such as Th^{4+} and UO_2^{2+} even at pH values of about 2.

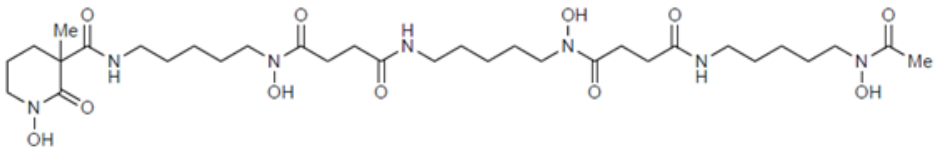

Figure 1. Structure of (DFO(Me)PIPO)H_4.

This contribution 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).

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Protonation constants of $(DFO(Me)PIPO)^{4-}$ were obtained by potentiometry and UV absorption spectrophotometry, before unravelling the speciation of the ligand in the presence of Th^{4+} and UO_2^{2+} by affinity capillary electrophoresis (ACE). This electromigration technique, which requires only a few µL of solutions, is based on the change in the electrophoretic mobility of the UV-detected analyte due to the interaction with the other species (metal or ligand) present in the electrolyte. These sets of runs were performed using $(H,Na)ClO_4$ mixtures to keep both the pH and the ionic strength (I = 0.1 M) constant. The electrophoretic mobility changes with the increasing concentrations of the reagent dissolved in the background electrolyte solution were used to assess the speciation and equilibrium constants. This method is fruitful for studying metal complex formation equilibria and gives valuable information for further modelling of their behaviour under environmental conditions [7]. Formation of 1:1 metal-to-ligand complexes was further ascertained by high-resolution ESI-MS spectrometry and circular dichroism (CD) measurements using the optically pure ligand.

Acknowledgments:
The Agence Nationale de la Recherche (ANR project PLUTON, grant N° ANR-17-CE08-0053) is gratefully acknowledged for financial support.

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This contribution 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).

COST is supported by the Horizon 2020 Framework Programme of the European Union

Polynuclear metal hydrolysis species or colloidal particles?

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This communication is in the frame of WG 1 topic "NECTAR for highly hydrolysable (HHC) and/or low-valence state (LVC) cations". Hydrolysis of metal species is very interesting and important subject. Up to our date the question of metal hydrolysis speciation is still not completely elucidated. Especially this concerns a formation of hydrolysis polynuclear species. These hydrolysis polynuclear species are often postulated to improve the fitting of experimental data obtained by potentiometric and/or spectrophotometric methods, but the confirmation of these species by other physicochemical methods is usually missing. In this communication author takes an attempt to examine this misunderstanding of metal hydrolysis speciation models. Is the terminology clear? Can the polynuclear species be considered as the colloidal particles? Do we deal with the measurements performed under equilibrium not reached? Do the systems under study have slow kinetics? Do we deal with the metastable state of the systems studied?

This contribution 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).

COST is supported by the Horizon 2020 Framework Programme of the European Union

On data loss and accessibility

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If the oft-quoted metaphor by Isaac Newton [1] "If I have seen further it is by standing on the shoulders of Giants" applies to progress in the field of equilibrium and solubility constants and their application to modelling, it can only be concluded that these shoulders are melting faster than most Swiss glaciers.

In this communication, the situation of the entire data stream will be analysed in detail. This means from the availability of original "titration data" to the accessibility of scientific papers (including the disappearance of paper journals and books in libraries and legal constraints) and non-critical and critical compilations [2]. Issues related to preservation of data in digital form will also be addressed. Although the problem is not exclusive to this scientific field [3], the author considers it particularly acute in our community. Given the proven ineffectiveness of the organizations involved so far in solving the problem (e.g., NIST, IUPAC, etc.), possible alternatives need to be discussed.

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This contribution 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).

COST is supported by the Horizon 2020 Framework Programme of the European Union

The Method Validation Study of Favipiravir by HPLC

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A simple, precise, and accurate reverse-phase high-performance liquid chromatographic technique (RP-HPLC) for the determination of Favipiravir from pharmaceutical formulation, with UV detection, was developed and validated. The method validation parameters as linearity, precision, accuracy, robustness were determined. Linearity range was determined between 0.5-100 µg/ml with regression coefficient (R^2) 0.9999. The Limit of detection (LOD) and limit of quantification (LOQ) values were evaluated as respectively 0.02 µg/ml and 0.05 µg/ml. The precision of the method was evaluated inter-day and intra-day precision studies with a relative standard deviation of less than 2%. The method robustness was investigated with alteration of flow rate, detection wavelength, and mobile phase ratio. The effect of pH on capacity factors was investigated and given in Figure 1.

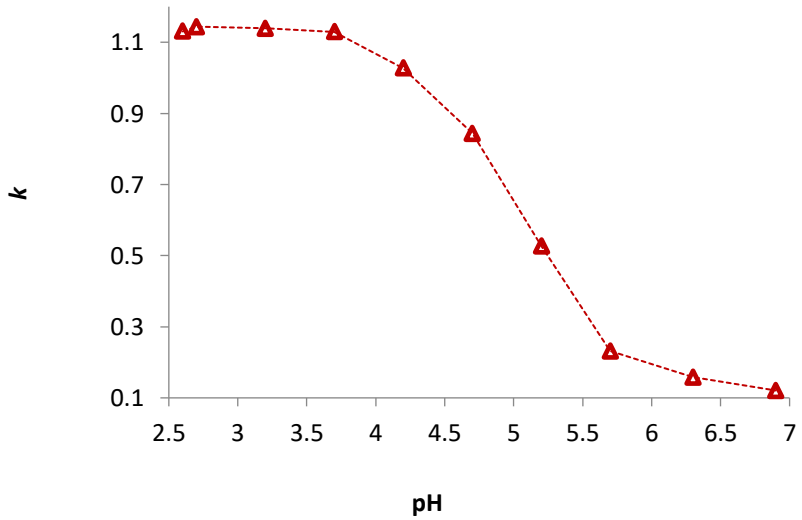

Figure 1. The effect of pH on capacity factor of FVP.

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supported by COST (European Cooperation in Science and Technology).

COST is supported by the Horizon 2020 Framework Programme of the European Union

A smart spectrophotometric method for the analytical determination of total iron concentration

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Iron, one of the most common metals in the environment, plays a fundamental role in many biological as well as biogeochemical processes, which determine its availability in different oxidation states. Its relevance in environmental, biomedical, industrial chemistry, and in many other fields has made it necessary to develop and optimize analytical techniques for its accurate determination.

Atomic absorption spectroscopy (AAS), ion chromatography (IC), inductively coupled plasma (ICP-AES and ICP-MS), controlled-potential methods, and ultraviolet-visible spectrophotometry (UV-vis) are the most used techniques.

The design and development of UV-vis spectrophotometric methods for quantitative detection has gained increasing interest among analytical chemists due to their high selectivity, cost-effectiveness, simplicity, and low detection limit. Different reagents, each one characteristic for a single iron oxidation state, have been used for. Despite the high sensitivity allowed by the use of these reagents, the methods require troublesome procedures for total iron determination.

Taking advantage of the fact that desferrioxamine B (DFO) (Fig.1), a trihydroxamic acid used since the 1970s in chelation therapy for iron overload treatment, forms a single stable 1:1 complex with iron in whichever oxidation state it can be found [1-2], a smart spectrophotometric method for the analytical determination of iron concentration was developed.

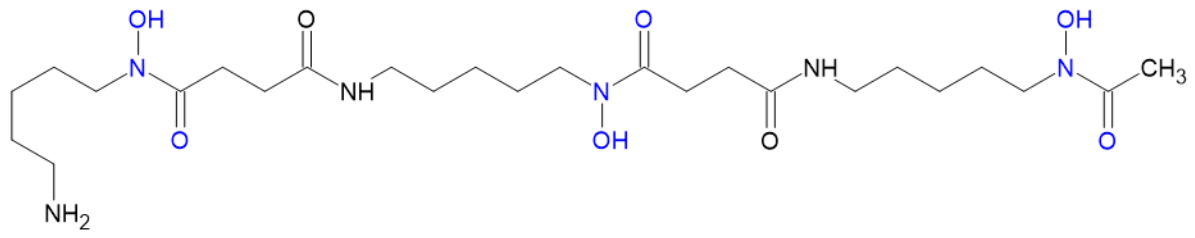

Figure 1: Molecular structure of DFO with the three iron chelating groups highlighted in blue.

In particular, the full compliance with the Lambert-Beer law (Fig.2), the range of iron concentration, the influence of pH, and the interference of other metal ions have been taken into account [3].

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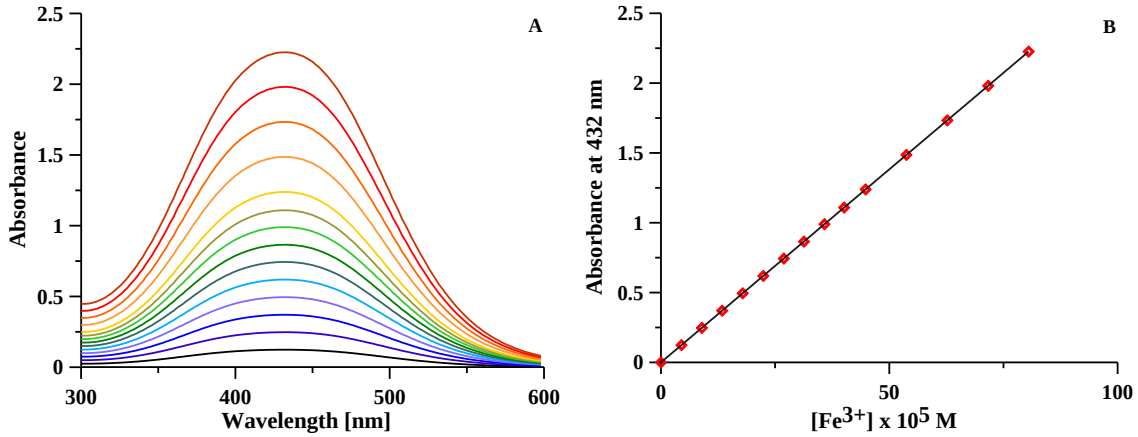

Figure 2: **A**) Spectra of 14 Fe^{3+}-DFO solutions at constant concentration [DFO] = 1.6 x 10^{-3} M and iron concentration ranging from 4.5 x 10^{-5} M to 8 x 10^{-4} M. (**B**) Calibration plot at 432 nm; regression line calculated for a straight line through the origin is reported as a continuous line.

The proposed method was validated in terms of LoD, LoQ, linearity, precision, and trueness, and has been applied for total iron determination in natural water certified material and in biological reference materials such as control human urine and control serum [4].

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COST Action CA18202, NECTAR – Network for Equilibria and Chemical Thermodynamics Advanced Research,
supported by COST (European Cooperation in Science and Technology).

COST is supported by the Horizon 2020 Framework Programme of the European Union

Developing designed copper – histidine sites in protein and peptides with redox catalytic behavior

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A new copper protein based on the SpyCatcher/SpyTag construct was designed.[1] This construct has been redesigned from a domain of a fibronectin binding protein from *Streptococcus pyogenes*. This protein consists of a 10.5 kDa β-barrel protein (SpyCatcher, Figure 1, green) and it binds covalently an oligopeptide (SpyTag, Figure 1, blue) through the formation of an isopeptide bond between an Asp and a Lys residues. The SpyTag peptide that we have designed bears: i) a GSH peptide sequence at the N-terminus for copper(II) binding; ii) a IVMVD fragment for the binding to SpyCatcher; iii) a thioredoxin (Trx) domain from *E.coli* at the C-terminus. Both SpyCatcher and SpyTag wave also been mutated to exclude any His residue other than that at the ATCUN site of Tag (GSH), expressed in *E. coli* and purified through chromatography.

The adducts of copper(II) with both components of the construct (i.e. Catcher and Tag) were studied by absorption and CD spectrophotometric data: in the presence of 1 eq. of Cu(II) the involved metal binding site is ATCUN.

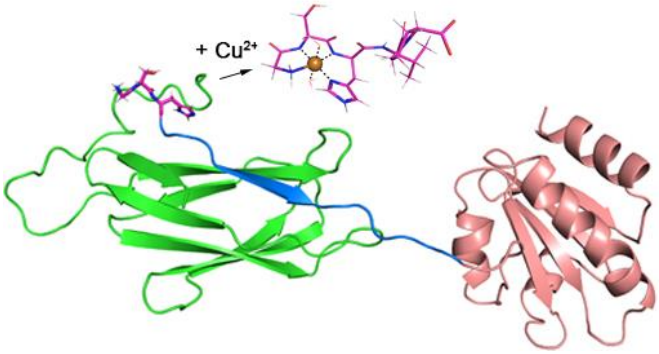

Figure 1: Representation of the SpyCatcher/SpyTagTrx construct. A representation of the ATCUN binding site of Cu(II) is shown.

We have evaluated the catalytic behaviour of the Cu(II)/SpyCatcher/SpyTag adduct toward hydrolysis of *p*-nitrophenyphosphate (pNPP) and toward cleavage of plasmid DNA strands in the presence of ascorbate. As it concerns the cleavage of DNA strands, contrarily to what reported in the literature for other ATCUN peptide the presence of Cu(II) coordinated to

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the SpyTag ATCUN site seems to protect against the appearance of nicked DNA plasmids. Even more complex observations relate with the phosphoesterase activity against pNPP: although fastest rates of hydrolysis were observed for the protein species in the presence of Cu(II), the apo-proteins also exhibit a non-innocent behaviour with respect of this reactivity.

Besides the study of the redesigned copper protein, within this COST action we started to evaluate the speciation and reactivity toward oxidation reactions of copper(II) peptides bearing one His-His tandem site and an additional third histidine residue. While the speciation and the reactivity of copper(II) bound to tandem His-His site is relatively well known, little is known about the role of a third histidine residue.[2,3]

Based on the sequence or fragment R3 of the neuroprotein tau we have designed four peptide sequences that bear a tandem (His)2 site and one additional His in positions -2, -4 and -6. Speciation and spectroscopic characterization of copper(II) adducts with these peptides have been carried out. Also, the reactivity of the peptides toward the oxidation of 3-methylcatechol was studied and will be discussed.

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COST Action CA18202, NECTAR – Network for Equilibria and Chemical Thermodynamics Advanced Research,
supported by COST (European Cooperation in Science and Technology).

COST is supported by the Horizon 2020 Framework Programme of the European Union

Towards Microorganism-based Microbial Fuel Cells

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This presentation focuses on the overview of microbial amperometric biosensors and microbial biofuel cells and shows the way how very similar principles are applied for the design of both types of these bioelectronics-based devices [1]. Some attention will be payed to thermodynamic aspects of charge transfer and spontaneousity of chemical/electrochemical reactions in biofuel cells [1]. The most of microorganism-based amperometric biosensors shows poor specificity, but this drawback can be well exploited in the design of microbial biofuel cells because this enables to consume wider range of chemical fuels [2]. The efficiency of the charge transfer is among the most challenging and critical issues during the development of any kind of biofuel cells [3]. In the most cases particular redox mediators and nanomaterials are applied for the facilitation of charge transfer from applied biomaterials towards biofuel cell electrodes [4]. Some improvements in charge transfer efficiency can be achieved by the application of conducting polymers (CPs), which can be used for the immobilization of enzymes and in some particular cases even for the facilitation of charge transfer [2,4,5]. In this presentation charge transfer pathways and mechanisms, which are suitable for the design of biosensors and in biofuel cells are discussed. The ways for the modification of cell-wall/membrane by conducting polymers in order to enhance charge transfer efficiency of microorganisms, which can be potentially applied in the design of microbial biofuel cells, are outlined [3-5]. The biocompatibility-related aspects of conducting polymers with microorganisms are overviewed.

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COST Action CA18202, NECTAR – Network for Equilibria and Chemical Thermodynamics Advanced Research,
supported by COST (European Cooperation in Science and Technology).

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COST Action CA18202, NECTAR – Network for Equilibria and Chemical Thermodynamics Advanced Research,
supported by COST (European Cooperation in Science and Technology).

COST is supported by the Horizon 2020 Framework Programme of the European Union

Poster Communications

Modelling the solubility and the acid-base properties of Cinchomeronic acid in aqueous media and binding ability towards Cu^{2+} and Co^{2+}

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Cinchomeronic acid (3,4-pyridinedicarboxylic acid, CA) is one of the six isomers of pyridine carboxylic acid.[1] In general pyridine carboxylic acids act as chelating agents of elements such as chromium, zinc, manganese, copper, iron, and molybdenum in the body. They are also used as intermediate to produce pharmaceuticals and metal salts for the application as nutritional supplements. The metal complexes of biologically important ligands are sometimes more effective than free ligands. Despite its importance few data are reported in literature about some thermodynamic aspects, such as their acid-base behaviour and their solubility, as well as their interactions with biologically and environmentally relevant metal cation. For this reason, here we report results on a potentiometric investigation on its protonation constants in different ionic media, ionic strength ($0.1 \leqslant I/\text{mol L}^{-1} \leqslant 1$), and temperatures, NaCl, (from 283.15 to 318.15K), KCl (at 298.15K) and in Tetraethylammonium iodide (Et_4NI, at 298.15K). Finally, stability constants for the species of Co^{2+} and Cu^{2+} are reported at T = 298.15 K and were determined by potentiometric titrations at different ionic strengths in KCl ($0.1 \leqslant I/\text{mol L}^{-1} \leqslant 1$). The dependence of the protonation and stability constants on ionic strength and temperature was analysed by both a Debye–Hückel type equation and the SIT (Specific ion Interaction Theory) approach. The different values of $\log K_i^H$ obtained in the three ionic media were interpreted in terms of formation of weak complexes between CA and the cations of the supporting electrolytes. To have a better picture of its thermodynamic behaviour the total solubility, the solubility of neutral species of CA was determined in NaCl and KCl at 298.15 K at various ionic strengths, Setschenow and activity coefficients of the neutral species were also computed.

Acknowledgments: This contribution 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).

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Dicarboxylato platinum(II) complexes containing dimethyl sulfoxide and triazolopyrimidine as potential anticancer agents: synthesis, structural and biological studies in solution

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Chemotherapy is one of the leading pillars of cancer treatment. Nevertheless, therapy results are often unsatisfactory to patients. Additionally, according to observations and prognoses, there is a growing tendency in cancer occurrence. For that reason, platinum-based drugs currently used in anticancer therapy require constant improvements.

From the historical point of view, *cis*-diamminedichloridoplatinum(II) was the first platinum-based anticancer agent used to treat various types of human cancer, including ovarian, head and neck, or lung and testis tumors [1,2]. Unfortunately, side effects resulting from its toxicity, e.g., neurotoxicity, nephrotoxicity, ototoxicity, limit the dose administered to patients [3,4]. Moreover, its therapeutic effectiveness is reduced by drug resistance and undesirable chemical or physical properties such as poor water solubility and significant reactivity towards glutathione [1,5]. Overcoming these clinical drawbacks in cisplatin-based chemotherapy poses a challenge in the process of more effective and less toxic platinum-based anticancer drugs development. One of the methods of platinum(II) compounds designing is focused on modifying the pharmacokinetics of cisplatin by replacing the stable ammine ligands with other non leaving N-donor groups and/or by replacing chloride ions with other ion groups, for example, chelating carboxylate, which exhibit lower toxicity [6-10].

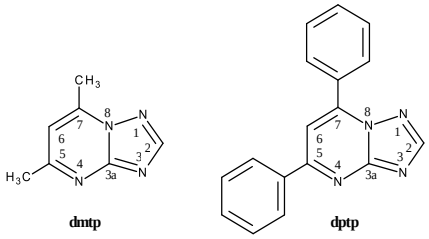

Fig. 1. The heterocyclic ligands (dmtp and dptp) with IUPAC ring-numbering system

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Following this research line, four dicarboxylato platinum(II) complexes of the general formula [Pt(R(COO)$_2$)(dmso)(N-donor)], where: R(COO)$_2$ – cyclobutane-1,1-dicarboxylato or malonato, dmso – dimethyl sulfoxide, N-donor – 5,7-dimethyl-1,2,4-triazolo [1,5-*a*]pyrimidine (dmtp) or 5,7-diphenyl-1,2,4-triazolo[1,5-*a*]pyrimidine (dptp) (Fig.1) have been synthesized and structurally characterized with the use of multinuclear magnetic resonance (^{1}H, ^{13}C, ^{15}N, ^{195}Pt). The NMR parameters unambiguously confirmed the square-planar geometry of Pt(II) in a solution with monodentate N(3)-bonded 5,7-disubstituted-1,2,4-triazolo[1,5-*a*]pyrimidine, monodentate and S-bonded dimethyl sulfoxide, and O,O-chelating dicarboxylato. The obtained platinum(II) complexes exhibit: **i)** higher susceptibility to hydrolysis, **ii)** lower toxicity and affinity to glutathione in comparison with cisplatin and carboplatin, **iii)** ability to interact with albumin and generate reactive oxygen species in the A549 cell line. Additionally, it is noticed that two lipophilic platinum(II) complexes: (3) [Pt(mal)(dmso)(dptp)] and (4) [Pt(CBDC)(dmso)(dptp)] display the most gratifying *in vitro* antiproliferative activity. Above and beyond, these promising coordination compounds exhibit lower toxicity towards normal cells and anticancer activity comparable to cisplatin.

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COST Action CA18202, NECTAR – Network for Equilibria and Chemical Thermodynamics Advanced Research,
supported by COST (European Cooperation in Science and Technology).

COST is supported by the Horizon 2020 Framework Programme of the European Union

Small antioxidant amino-nanozymes able to disaggregate Huntington's inclusion bodies

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Huntington disease is known as one of the most devastating neurological pathologies that modern societies faces nowadays. Some of the key issues underlying the generation of such neurological ailment are the formation of Huntingtin aggregates in cerebellum, dyshomeostasis and chelation of Cu^{2+} by the mutant Huntingtin fibrils, and oxidative stress.[1,2] Up to date, very little success has been achieved in the treatment of Huntington disease.

In this work we report a novel amino-nanozyme based on the anchorage of a tetraaza-macrocycle onto the surface of boehmite nanoparticles. By means of potentiometric methods we determine the capacity of the macrocycle to quantitatively subtract Cu^{2+} from medium, while using McCord-Fridovich assays and *in vitro* mitochondria oxidative stress evaluations we figure out the notably high antioxidant activity of the resulting complexes. Furthermore, we also show the capacity of the amino-nanozymes to significantly reduce the mutant Huntingtin deposits in cells.

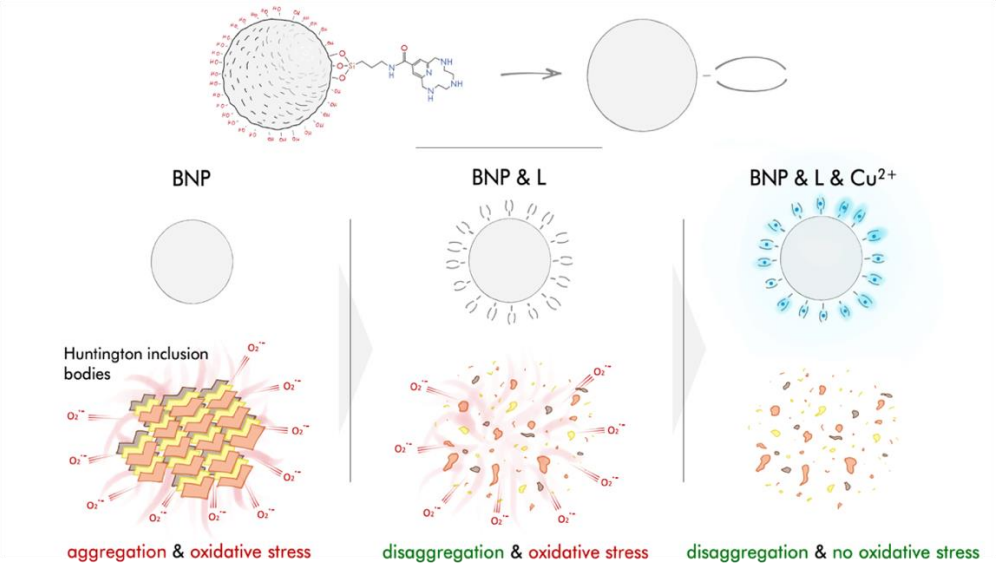

Figure 1. Schematic representation of the antioxidant and disaggregating activity of the systems.

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This contribution 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).

COST is supported by the Horizon 2020 Framework Programme of the European Union

Thermodynamic and structural aspects of adsorption of pharmaceutical drugs by carbon nanomaterials from molecular dynamics simulations

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Pharmaceutical compounds received a great deal of attention in the last two decades as their appearance in the water cycle was detected at relatively high concentrations[1]. Consequently, the long-term exposure of living organisms to low levels of such compounds or their metabolites has generated an increasing concern. Numerous specific water treatment methods have been proposed, but they are not completely efficient and the treatment of large volumes of liquid is required. Adsorption of drugs on a suitable materials has the advantage of a low operation cost, low energy demand and easy implementation [2]. After use, the adsorbent materials can be regenerated, and the concentrated pollutant efficiently degraded *in situ* by other methods.

In this contribution, the interaction of two common drugs, the non-steroidal anti-inflammatory Diclofenac (DCF, Scheme 1) and the fluoroquinolone antibiotic Ciprofloxacin (CFX, Scheme 1) which is commonly detected in surface waters and soil at relatively high concentrations [1,3]. To date, carbon-based adsorbent materials resulted to be the attractive in water treatment due to their high affinity for drugs, high loading capacity and ability to be regenerated. Some examples include: activated carbons, graphite, carbon nanotubes (CNT), graphene (G), graphene oxide(GO) and G/CNT composites.

In this contribution, the adsorption of CFX by CNT and DCF by G and GO and is studied by molecular dynamics (MD) simulations and the results compared with available thermodynamic data [5,6]. At neutral pH DCF is present in the deprotonated form only, while CFX is present as neutral or zwitterionic form Free energy calculations based on umbrella sampling technique allowed to determine the ΔG of adsorption which results negative and close to the values obtained from experimental data.

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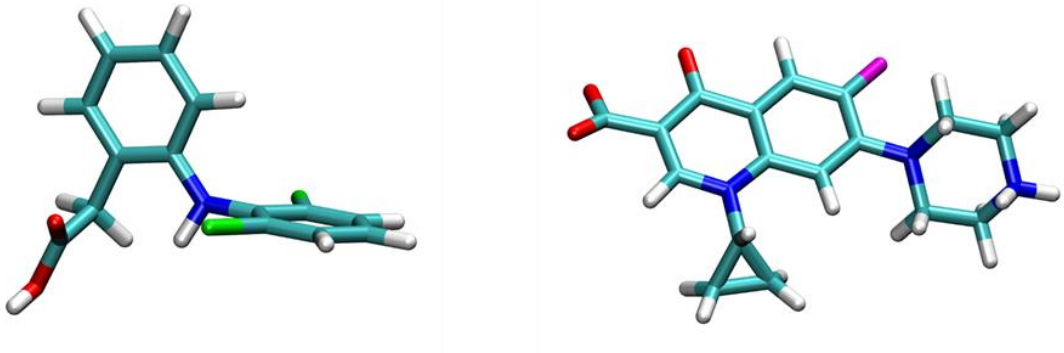

Scheme 1. Diclofenac (left) and (zwitterionic) Ciprofloxacin (right)

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BETTINELLI, Marco, OC12

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BOLCHI, Angelo, OC21

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CARUSO, Alessia, OC21

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This contribution 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).

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PEÑA, Quim, OC8

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supported by COST (European Cooperation in Science and Technology).

COST is supported by the Horizon 2020 Framework Programme of the European Union

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