Ph D in Chemistry

Other Research Projects for Cycle XXIX (2014 – 2016)

1) Title: Development of breath analysis procedures as diagnostic tools for pathologies and environmental exposure to pollutants.

Proposer Dr. Pierluigi Barbieri (e-mail: barbierp@units.it), Department of Chemical and Pharmaceutical Sciences.

Project description

The study program is aimed at developing robust methods for the sampling and analysis of metabolites and volatile organic compounds from human breath.

Volatile focusing and thermal desorption as well as solid phase micro-extration from optimised sampling on inert bags are options that will be compared as pretreatment before gas-cromatographic and mass spectrometric studies. Preconcentration of VOCs mixtures on tailored nanostructured devices will be considered for maximizing detectability of specific compounds on portable micro-gc.

Comparison of procedures with on line breath MS analysis will be performed thanks to national scientific partners. A complementary study will focus on breath condensate.

Applications that will be covered range from disease diagnosis to assessment of environmental pollution exposure.

References

Andrea Mazzatenta, Mieczyslaw Pokorski, Sergio Cozzutto, Pierluigi Barbieri, Vittore Veratti, Camillo Di Giulio "Non-invasive Assessment of Exhaled Breath Pattern in Patients with Multiple Chemical Sensibility Disorder" Advances in Experimental Medicine and Biology, 2013, Volume 756, 179-188

Mònica Alonso, Juan M. Sanchez "Analytical challenges in breath analysis and its application to exposure monitoring" TrAC Trends in Analytical Chemistry, Volume 44, March 2013, 78-89

Altomare, D.F., Di Lena, M., Porcelli, F., Trizio, L., Travaglio, E., Tutino, M., Dragonieri, S., Memeo, V., De Gennaro, G. "Exhaled volatile organic compounds identify patients with colorectal cancer", British Journal of Surgery 2013, 100 (1) , pp. 144-150

2) Title: ARTIFICIAL IONOPHORES

Proposer: prof. PAOLO TECILLA –Department of Chemical and Pharmaceutical Sciences

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Research programme:

Artificial ionophores are synthetic molecules able to promote the transport of ions and/or polar molecules across a biological membrane thus mimicking the action of natural occurring ion channels and carriers. The interest in this research is twofold: on one hand to get insight on the molecular basis of recognition and transport, and on the other hand to get control of the biomedical relevant processes. For example, several genetic diseases, the most known being cystic fibrosis, involve chloride channel impairments and current therapeutic leads comprise artificial ionophores able to restore the chloride transport process [1].

Ion transport across phospholipid membrane is a typical supramolecular function involving dynamic recognition of the substrate during the whole translocation process. Therefore, the design of artificial ionophores requires a careful balance of several factors from binding affinity to lipophilicity. We have been involved for some time in the design of artificial ionophores developing amphipathic molecules based on steroid, calixarene and other organic scaffolds [2, 3]. More recently we have started a research program aimed to design metal organic nanopores derived from the self-assembly of porphyrin ligands with proper metal fragments.[4] Within the project the candidate will identify and synthesize new ionophores and will study their activity on liposomes with particular regard to the definition of the structure/activity correlation in order to investigate the mechanism of action. The best found ionophores will be tested for biological activity and in sensing applications in a collaborative work.

[1] A. P. Davis, D.N. Sheppard, B.D. Smith *Chem. Soc. Rev.* **2007**, *36,* 348–357.

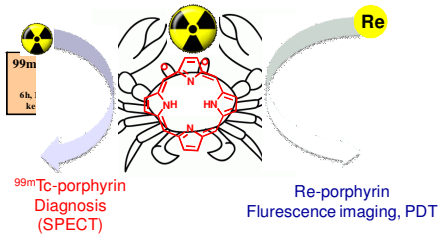
[2] N. Maulucci, F. De Riccardis, C. B. Botta, A. Casapullo, E. Cressina, M. Fregonese, P. Tecilla, I. Izzo *Chem. Commun.* **2005**, 1354-1356.

[3] L. Simeone, D. Milano, L. De Napoli, C. Irace, A. Di Pascale, M. Boccalon, P. Tecilla, Daniela Montesarchio, *Chem. Eur. J.* **2011**, *17*, 13854 – 13865.

[4] M. Boccalon, E. Iengo, and P. Tecilla, *J. Am. Chem. Soc.* **2012**, *134*, 20310−20313

3) Title: Conjugates of porphyrins with metal centers as agents for multimodal imaging and therapy.
Proposer: Prof. Enzo Alessio, Department of Chemical and Pharmaceutical Sciences
(alessi@units.it)

This research project concerns the design and modular synthesis of ruthenium- and rhenium-porphyrin conjugates as potential multimodal diagnostic and/or therapeutic (*theranostic*) agents. The concept of binding metal fragments to the periphery of a porphyrin through a chelator affords site-specific and highly stable labeling, without interference of the chromophore system. In the theranostics context, porphyrin-metal conjugates offer exciting perspectives, as both fragments might be used for imaging and/or therapy. For example, a Ru-porphyrin conjugate might combine the phototoxicity and the tumour-localization properties of the porphyrin chromophore with the cytotoxicity of the metal fragment for additive antitumour effects. At the cellular lever, porphyrin fluorescence affords the localisation of the conjugates. The conjugation with Re fragments belongs to the *matched pair strategy*, that takes advantage of the very similar chemical features of Re and Tc compounds (^{99m}Tc compounds are used as contrast agents in nearly 80% of all clinical radiodiagnostics). Thus, the *cold* Re conjugate is suitable for chemical investigation, fluorescence imaging and photodynamic therapy (PDT), whereas the *hot* ^{99m}Tc conjugate potentially suitable for bimodal molecular imaging (fluorescence and SPECT). Combining imaging modalities in a single chemical agent guarantees exact co-localisation, thus simplifying and improving image interpretation. The strict similarity between Re and Tc congeners implies also that they have very similar biodistribution (i.e. co-localisation). The ^{99m}Tc analogues will be prepared and investigated at the University of Zurich as part of an existing collaboration with the research group of Prof. Roger Alberto.



A consistent part of the project will be devoted to the development of suitable Ru(II) and Re(I) precursors. These metal ions – beside being inert and thus suitable for the preparation of robust conjugates – are diamagnetic and allow the extensive use of NMR spectroscopy for characterization. Suitable precursors will contain both ligands that are very strongly bond and inert and others that can be replaced under different conditions, thus allowing stepwise substitutions to be performed. Other desirable characteristics are a good solubility in water and a fairly simple structure or a certain degree of symmetry in order to avoid the formation of different stereoisomers upon binding to the functionalized porphyrins.

References

1. C. Spagnul, R. Alberto, G. Gasser, S. Ferrari, V. Pierroz, A. Bergamo, T. Gianferrara, E. Alessio *J. Inorg. Biochem.* **2013**, *122*, 57–65.
2. T. Gianferrara, A. Bergamo, I. Bratsos, B. Milani, C. Spagnul, G. Sava, E. Alessio *J. Med. Chem.* **2010**, *53*, 4678–4690.
3. T. Gianferrara, I. Bratsos, E. Iengo, B. Milani, A. Oštrić, C. Spagnul, E. Zangrando, E. Alessio, *Dalton Trans*. **2009**, 10742–10756.

4) Title: sviluppo di catalizzatori omogenei a base di metalli di transizione della prima serie per la copolimerizzazione controllata di CO_2 con epossidi per ottenere selettivamente policarbonati.

Proposer: Dott. Barbara Milani (e-mail: milaniba@units.it), Department of Chemical and Pharmaceutical Sciences.

Research Programme:

5) Title: Development of the LCAO B-spline computer code for the inclusion of nuclear motion effects

Proposer: Prof. Piero Decleva (decleva@univ.trieste.it) Department of Chemical and Pharmaceutical Sciences.

Research Program

The calculation of molecular photoionization parameters, cross sections and angular distributions, has been performer up to now in the fixed nuclei approximation. A very limited number of conformers, or vibration along a single normal mode, have been treated case by case. The need for a more general and automatic inclusion of vibrational motion is called upon by several recent experiments, either when treating flexible molecules which require a Boltzmann average over a large conformational space, or describing the behaviour of multimode vibrationally resolved spectra [1] which require evaluation of the cross section over a multidimensional grid around the equilibrium geometry.

The project will aim at the automatic generation of the configurations and of all parameters needed by the electronic calculations, the automatic collection of the results and calculation of Boltzmann averaged or vibrationally resolved spectra

See publications at http://www.dscf.units.it/theochem/

[1] G.A. Garcia et al., "Vibrationally induced inversion of photoelectron forward-backward asymmetry in chiral molecule photoionization by circularly polarized light"

Nature Communications 4 (2013) 2132