Brief Biography

Luca Conti obtained the PhD in Chemical Sciences in 2015 and he is currently an independent researcher at the Department of Chemistry "*Ugo Schiff*" of the University of Florence. His research interests focus on various topics of Inorganic Chemistry, spanning from the synthesis of luminescent systems for the recognition and sensing of targets of environmental and biological relevance to the development of photoresponsive metal complexes for application in the biomedical field. His scientific production, Luca Conti is author of 39 scientific papers, includes relevant studies on the use of Ru(II) polypyridyl complexes as photoactive prodrugs in photodynamic therapy (PDT) and in photoactivated chemotherapy (PACT) and, more recently, on the potential of the "*photorelease antimicrobial therapy*" approach in the design of novel and effective antibacterial agents. Besides, Luca Conti is also actively involved in editorial activities and various scientific divulgation projects.

Ru(II) polypyridyl complexes and light: a powerful combination in the design of novel photoresponsive compounds with biological activities

Photodynamic therapy (PDT) is attracting a growing interest in the design of novel and effective antitumoral and antibacterial agents. Among the main advantages that this therapeutic approach provides, there is the possibility to achieve a precise spatio-temporal control over the drug activation, thus permitting to localize the cytotoxic effects and to considerably lower the most crucial drawbacks incurring with commonly employed drugs.[1]

Among the numerous of inorganic compounds that have been studied as photosensitizers (PSs) for PDT, Ru(II)-polypyridyl complexes (RPCs) represent an interesting class of compounds whose rich chemical-physical repertoire makes them appealing photoresponsive tools. In this lecture we will see how the chemical structures of these metal complexes can be optimally modified to finely tune some key properties for PDT. As an example, the introduction of highly charged polyamino-macrocycles into Ru(II)-scaffolds can be exploited not only to improve their solubility in physiological media, a key prerequisite for their biological application, but even to strengthen their interaction with biological targets, such as DNA and proteins. Another crucial feature that an ideal PS should possess is to being able to efficiently sensitize the formation of reactive oxygen species (ROS). To this aim, inorganic scaffolds can be enriched with one or more π-expansive ligands, boosting the ROS production of the resulting complexes and shifting their absorption profiles towards the red.[2] Herein, a series of RPCs, whose performances as PSs are rationalized on the basis of their peculiar design, are presented along with the analysis of their biological behavior, evaluated on different types of cancer and bacterial cell lines.

The insertion of hindered ancillary ligands into RPCs featuring distorted octahedral architectures will be also considered. Indeed, this strategy has been conveniently employed to impart RPCs a different mechanism of photoactivation, *i.e.* the release of photoactive ligands rather than the production of ROS, thus overcoming the classical reliance of PDT on molecular oxygen. In this respect, we recently demonstrated that strained RPCs could serve as optimal photocages for different analogues of metronidazole, a mainstay drug in the treatment of anaerobic bacterial infections and can be of use to realize novel antibacterial agents, whose effectiveness is unleashed following irradiation and under the therapeutically relevant hypoxic conditions.[3]

The aim of this lecture is to demonstrate that Ru(II)-polypyridyl complexes represent an intriguing and versatile molecular platform to realize a wide variety of photoresponsive compounds, opening the way to the development of novel anticancer as well as antibacterial agents.

References:

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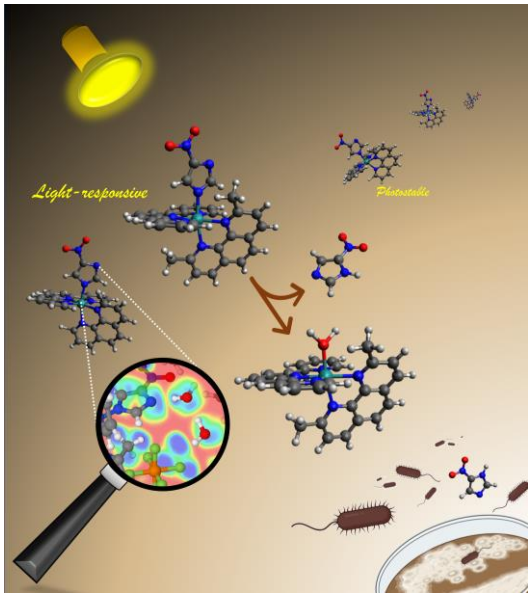
[2] G. E. Giacomazzo, M. Schlich, L. Casula, L. Galantini, A. D. Giudice, G. Pietraperzia, C. Sinico, F. Cencetti, S. Pecchioli, B. Valtancoli, L. Conti, S. Murgia, C. Giorgi, *Inorganic Chemistry Frontiers,* **2023**, DOI: 10.1039/D2QI02678C.

[3] G. E. Giacomazzo, L. Conti, C. Fagorzi, M. Pagliai, C. Andreini, A. Guerri, B. Perito, A. Mengoni, B. Valtancoli, C. Giorgi, *Inorganic Chemistry,* **2023**, in press. DOI: 10.1021/acs.inorgchem.3c00214.



Scheme 1 : Mechanism of action for RPCs with antibacterial photoinduced activity