

Title	Metal-based Radiopharmaceuticals
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Project description:

Radiodrugs (RDs) are compounds harboring a radioactive element to be used either in diagnosis and/or treatment of diseases. The paradigmatic leading nuclide in SPECT imaging is Tc-99m; new metals (Cu-64, Ga-67, Lu-177, others) have recently gained momentum, especially in the theranostic selective targeted delivery of radio-drug to the tumor site and simultaneous scintigraphic monitoring of the delivery itself. Our research concerns the recognition, development and optimization of new metal-based radiopharmaceuticals to be used in SPECT/PET diagnosis as well as in therapy. As a viable example of our approach to the development of new RPs we remind the strategy of the indirect labelling (optimised for Tc-99m RDs), performed using the $[M(N)(PNP)]^{2+}$ technology within the classical BFCA approach. Selected BFCAs such as Cys or DOTA/NOTA ligands can be conjugated by chemical methods to a suitable biological vector (e.g., peptides) and then incubated with the selected radionuclide (interested readers will find in literature examples describing this paradigm with respect to, for example, In-111 or Ga-68). Obtained derivatives are then investigated by ESI-MS to identify the modification sites, whereas to optimize radiochemical yield the influence of the manifold reaction parameters, such as reagent concentrations, reaction time, pH and temperature are investigated. Radiochemical purity of products will be determined using HPLC analysis. In vitro stability can also be assessed by HPLC methods after incubation at 37 °C with fresh human serum, cysteine, glutathione or EDTA solutions at time points ranging from 0.5 to 24 h. Chemical identity of desired products will be ascertained using cold analogues in the solid state by X-ray diffraction techniques.

Publications:

Baron, Marco; Tubaro, Cristina; Basato, Marino; Ahmed Isse, Abdirisak; Gennaro, Armando; Cavallo, Luigi; Graiff, Claudia; **Dolmella, Alessandro**; Falivene, Laura; Caporaso, Lucia (2016). Insights into the Halogen Oxidative Addition Reaction to Dinuclear Gold(I) Di(NHC) Complexes. CHEMISTRY-A EUROPEAN JOURNAL, Vol. 22, p. 10211-10224, doi:

Nicola Salvarese, **Alessandro Dolmella**, Fiorenzo Refosco, Cristina Bolzati (2015). Reactivity of the $[M(PS)_2]^+$ Building Block (M = ReIII and $^{99m}\text{TcIII}$; PS = Phosphinothiolate) toward Isopropylxanthate and Pyridine-2-thiolate. INORGANIC CHEMISTRY, vol. 54, p. 1634-1644, ISSN: 0020-1669, doi: 10.1021/ic502632h -Impact Factor 4.794

Collaborations/Network:

Dr. Cristina Bolzati, ICMATE-CNR, Padova; PhD Nicola Salvarese, ICMATE-CNR, Padova; PhD Laura Melendez-Alafort, DISCOG, Padova; Prof. Antonio Rosato, DISCOG, Padova.

Research funding: =