Inorganic and Radiopharmaceutical Chemistry

Isabel Rego Santos

The main goal of the Inorganic and Radiopharmaceutical Chemistry Group is the design, synthesis and characterization of novel specific radiopharmaceuticals for non-invasive molecular imaging of targeted macromolecules and biological processes associated with different pathologies. The use of some of these probes for therapy, by using β or Auger emitters, produced at the RPI, is also one of our goals.

This group is multidisciplinary, combining expertise on the synthesis and characterization of organic, compounds and inorganic and organometallic complexes of *d*- and *f*-elements, as well as on radiochemistry and radiopharmacology. Such a combination, unique in the country, allows the synthesis of compounds at the macroscopic level and their characterization in the solid state and in solution. The expertise and infrastructures, implemented and maintained by the group, also allow the synthesis of the corresponding radioactive compounds and their characterization and biological evaluation, using nuclear techniques and animal models. During 2004, our animal house has been improved and, since November, we are able to perform studies with cell lines and with tumour bearing mice models.

The expertise and infrastructures of the group enable basic and applied-oriented research in modern Radiopharmaceutical Chemistry, an important topic in life science. This justifies our participation as a partner in National and International research projects and the support of a Pharmaceutical Company. Our know-how on chemistry, radiochemistry and radiopharmacy, and our facilities, are used to provide training and education to undergraduate, graduate and post-graduate students.

In summary, the main achievements during 2004 were the following:

I. Halogen-Based Radiotracers: Following our previous work with estradiol analogues, the radiosynthesis and characterisation of some 17α-(*p*-[^{125}I]iodophenylethynyl)estra-1,3,5(10),6-tetraene-3,17β-diols has been carried out. The evaluation of these novel radioligands as ER binding radiopharmaceuticals is underway.

II. Metal *d*- and *f*- Based Radiotracers: We pursued the synthesis and characterization of novel bifunctional pyrazolyl containing chelators and we studied their coordination chemistry towards the fac-$[M(CO)_3]^+$ (M=Re, Tc) moieties. Some of these chelators have been tested with success for the labelling of tumor-seeking peptides and for preparing complexes potentially useful as DNA metallointercalators.

For targeting EGFR, several quinazoline derivatives have been prepared and their coupling to pyrazolyl containing ligands is underway. Structure/activity relationships were established for Re and Tc complexes anchored by heterofunctionalized phosphines or by soft scorpionates bearing a (2-methoxyphenyl)piperazine pharmacophore. The excellent *in vitro* binding properties found for the scorpionate complexes, led us to synthesize and evaluate ^{11}C-labelled mercaptoimidazoles as radioligands for PET imaging of $5HT_{1A}$ receptors.

For lanthanides, we concluded our studies with cyclic polyamines having a pyridine moiety. We pursued studying the chemistry, radiochemistry and biological behaviour of ^{153}Sm and ^{166}Ho complexes with [14]aneN4 macrocycles having different pendant arms.

III. Training: At the graduation level, the group has taught, in a regular way, radiopharmacy at the Escola Superior de Tecnologias da Saúde de Lisboa (ESTeSL) and at the Faculty of Pharmacy/University of Lisbon. Students from ESTeSL and from Escola Superior de Tecnologias da Saúde do Porto (ESTeSP) have also been trained in our laboratories, during two weeks.

At the post-graduate level we organized and supported the Master Course *Biomedical Inorganic Chemistry: Diagnostic and Therapeutical Applications*, which started in September 2004 with thirty students. This Master is running in collaboration with the University of Lisbon (UL) (Faculties of Sciences, Pharmacy and Medicine), Hospital Garcia da Orta and Instituto Português de Oncologia/Lisboa. For such collaboration a specific protocol has been established. We also collaborated in a Teaching Program organized by ITQB/UNL and in the Master Course *Pharmaceutical and Therapeutical Chemistry*, organized by the Faculty of Pharmacy/UL. Physicians from the Instituto Português de Oncologia have also been trained in our group.

At the International level, we participated in the European Radiopharmacy Course, INSTN. We are partners in the EC shared COST RTD ACTION, Virtual Radiopharmacy (VIRAD)/V Framework Program and in the Coordination Action on Education and Training in Radiation Protection/VI Framework Program.

We also have trained several young scientists, funded by FCT grants, namely BIC, PhD and Post-Doctoral researchers. Our expertise has also been provided to some Nuclear Medicine Centers, to the Portuguese Medicines Evaluation Agency and IAEA.

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Research Team

Researchers

- I. SANTOS, Principal Researcher/Agregação
- A. PAULO, Auxiliary Researcher
- J.D.G.CORREIA, Invited Aux. Researcher
- M.P.C.CAMPELLO, Auxiliary Researcher
- M.C. MELO e SILVA, Auxiliary Researcher
- C.FERNANDES, Research Assistant
- L.GANO, Auxiliary Researcher
- F.MARQUES, Auxiliary Researcher
- P.RAPOSINHO, Auxiliary Researcher

Students

- L. MARIA, Post-Doctoral, FCT Grant
- S. ALVES, PhD student, FCT Grant
- R.GARCIA, PhD student, FCT Grant
- R. VITOR, PhD student, FCT Grant
- E.PALMA, BIC student
- S. LACERDA, BIC student
- C. XAVIER, PhD student, since November

Technical Personnel

- A. RODRIGUES*, Technical of 1st class
- E. CORREIA, Technical of 1st class

Funding (€)

Research Projects:	90.762,40
Services:	8.120,50
Total:	**98.882,90**

Publications

Patents:		1
Books:		2
Journals:		10 and 7 in press
Conf. Communications:		22
Other publications:		1
Theses:	MSc	1

* Technical assistance to the Group and to the Chemistry Department Ventilation System