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Radiopharmacy/Radiochemistry: Therapy - Alpha-Beta Emitters

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Room: Poster Exhibition Area

P438 New indazolebisphosphonates for bone targeted radiotherapy: synthesis, radiolabeling, in vitro and in vivo studies

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Bisphosphonates (BPs) are ligands for radioactive metal complexes used for imaging and therapeutic applications. The last BPs generation are heterocyclic nitrogen containing side chain such as risedronate and zoledronate. The aim of this study is to obtain new BPs derived from indazole with high biological and radiopharmaceutical potential activities. We report the synthesis and characterization of new indazolebisphosphonates (IDZBPs) substituted at different C- or N- positions of indazole rings, with the side chain with different lengths (1 to 5 carbon atoms from the bisphosphonate function to the nitrogen atom of the ring). IDZBPs are suitable for complexation with ^{153}Sm and the low energy electron emitters ^{177}Lu and ^{47}Sc. Radiochemicals tagged with low energy electron emitters are preferred because they are more likely to deliver a therapeutic dose to the bone and spare the bone marrow. Hydroxyapatite experiments, have shown that the highest binding values were obtained with [hydroxyl(1H-indazol-3-yl)methanediyl]bis(phosphonic acid) and [hydroxyl(1-methyl-1H-indazol-3-yl)methanediyl]bis(phosphonic acid) complexed by ^{153}Sm, ^{177}Lu and ^{46}Sc. These selected potential radiopharmaceuticals were submitted to biodistribution studies. In experiments, we use the scandium radioisotope ^{46}Sc, instead of ^{47}Sc because ^{47}Sc is produced using fast neutrons via the reaction ^{47}Ti (n,p)^{47}Sc, which is not easily accessible to us, while ^{46}Sc is producing by direct neutron irradiation of scandium. ^{153}Sm and ^{177}Lu were respectively produced by direct neutron irradiation of enriched samarium (98%) and natural lutetium oxides. A slight change between the two ligands - the free N-H position substituted by a methyl group - results in a distinct radiopharmacokinetic. These experiments confirm that a single change in the chemical structure plays a decisive role in binding to hydroxyapatite, as well in bone uptake. *Acknowledgements:* This work was carried out in the frame of Marie Curie Action for the Transfer of Knowledge, contract No. MTKD-CT-2004-509224, European Commission, FCT- Portuguese Foundation for Science and Technology (FEDER and POCI/QUI/55508/2004)and Ministry of Science and Higher Education of Poland 7T09A07320.

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