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Characterization of Re/99Tc KYCAR Complexes for Radiopharmaceuticals

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Radiopharmaceuticals are very powerful diagnostic tools for evaluation of a host of medical conditions. These drugs are labeled with radioactive isotopes which are utilized to create pictures of areas of interest through absorption of the drug. They are currently in high demand due to their ability to image areas that traditional imaging devices cannot. The main differences between radiopharmaceuticals and other imaging methods are how the tissue in question is imaged and how the information is obtained. The radioisotope 99mTc, with a half-life of 6.01 hour and a 140 keV gamma emission, is central to many radiopharmaceutical compounds. This isotope is easily obtained from a 99Mo- 99mTc generator, through beta decay and column chromatography separations. Very little technetium, less than 6 ng, is need to label the pharmaceuticals for use in-vivo. Another radioisotope 188Re is also important due to its ability to be used for therapy while being tracked throughout the body. One of the main reasons there is interest in rhenium pharmaceuticals is the chemical similarity between it and technetium. The 188Re isotope also has a considerably short half–life of approximately 17 hours and has emission energy of 155 KeV. The 188Re isotope is separated from 188W- 188Re generator, analogously to the 99Mo- 99mTc generator.

Radiotherapy gives radiopharmaceuticals a huge advantage by their ability to destroy rapidly growing cells. The ligand used in this work is a pentapepetide macrocyclic ligand. This ligand, also called KYCAR (lysyl-tyrosyl-cystyl-alanyl-arginine), has been designed for the possible application for tumor imaging for breast cancer. Ligands are chosen based on their in-situ biological behavior, and are used in the complexation with technetium and rhenium. Understanding and exploiting technetium and rhenium chemistry can provide insight into the reaction mechanisms and coordination chemistry of these compounds. The exploration of various oxidation states as a function of the ligands used and the reaction conditions can help develop novel radiopharmaceuticals. The investigations of the manipulation of oxidation states have the possible application to simplify the synthesis of the pharmaceutical. The versatility of the oxidation states of these metals leads to numerous possibilities in developing new radiopharmaceuticals. The coordination chemistry and reaction mechanisms must be efficiently characterized to ensure the reproducibility of the radiopharmaceutical. The current study focuses on technetium and rhenium complexes with peptides. These complexes have become increasing interesting for their use in diagnostic and therapeutic radiopharmaceuticals. The characterization of the complexation of Tc(V), and Rh(V) with the pentapeptide KYCAR (lysyl-tyrosyl-cystyl-alanyl-arginine) will be discussed. Complexes will be characterized by High Purity Liquid Chromatography (HPLC), UV-Visible Spectroscopy, Proton NMR, Circular Dichroism (CD), Electrospray Ionization Mass Spectroscopy, Single-crystal x-ray diffraction, and x-ray absorption fine structure spectroscopy, to compare them to current radiopharmaceuticals. Information on the underlying reactions and coordination will be discussed.

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