

# Technetium and Rhenium (I and V) Complexes for Radiopharmaceutical Applications

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## Abstract

The chelation of technetium and rhenium has been explored to create complexes for radiopharmaceutical applications. Two  $^{99m}\text{Tc}$  (I) radiopharmaceuticals have been created that seek to target somatostatin receptors (SSTRs), which are commonly overexpressed on neuroendocrine tumor tissues. The complexes use tridentate, bifunctional chelating agents (BFCAs) to chelate the  $^{99m}\text{Tc}(\text{CO})_3^+$  core while tethering it to an antagonist somatostatin receptor-seeking peptide (sst<sub>2</sub>-ANT).

The histidine-derived tridentate BFCAs used either an [N,S,N] or an [N,S,O] donor system to form complexes with  $^{99m}\text{Tc}/\text{Re}(\text{CO})_3^+$ . The non-radioactive Re complexes were synthesized to verify the products made on the radiotracer level as well as determine receptor-binding affinity. *Fac*- $[\text{Re}(\text{CO})_3(\text{NSN-sst}_2\text{-ANT})]^+$  and *fac*- $[\text{Re}(\text{CO})_3(\text{NSO-sst}_2\text{-ANT})]$  both exhibit low nanomolar affinities for somatostatin receptor subtype two (SSTR2), as determined in AR42J cells. The radio-tracer products *fac*- $[\text{Re}(\text{CO})_3(\text{NSN-sst}_2\text{-ANT})]^+$  and *fac*- $[\text{Re}(\text{CO})_3(\text{NSO-sst}_2\text{-ANT})]$  both exhibited high in vitro stability during challenges in cysteine, histidine, and mouse serum. Mouse biodistribution and imaging studies were also performed to determine the pharmacokinetic properties of each complex.

Lastly, complexation of Re and Tc using a tetradentate diphosphinedithiol (DPDT) ligand was explored in order to determine whether or not the reducing abilities of the P<sub>2</sub>S<sub>2</sub> donor system would aid in the stability of rhenium in the +5 oxidation state. Synthesis of ReO(DPDT) led to the formation of a highly stable Re (V) complex, which remained stable in oxidative environments over a period of 5 months. Macroscale reactions using the DPDT ligand to synthesize the  $^{99}\text{Tc}$  counterpart led to the formation of Tc (III) complexes directly from Tc (VII).