E. Radiopharmaceuticals

Chemical and Biological Studies on $^{99m}$Tc-DMS—Formation of Various Tc-DMS Complexes
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Various Tc-dimercaptosuccinate (Tc-DMS) complexes were prepared using both $^{88}$Tc and carrier $^{88}$Tc. A yellow complex (Complex I) was obtained at low concentration of Sn(II), and a purple complex (Complex II) with a large excess amount of Sn(II). Potentiometric titration of Sn(II)-DMS indicates the formation of a 1:1 complex alone, which can be utilized as a reducing agent of TcO$_4^{-}$. The absorption spectra suggests that there is little possibility of a mixed metal complex of Tc-Sn-DMS. Potentiometric and radiometric titrations were used for the determination of the technetium valence state. It was found that pertechnetate is reduced to the IV state, which is due to the formation of Complex I. The formation of Complex II is increased as the amount of Sn(II) as well as the molar ratio of Sn(II)/Sn(IV) is increased or the TcO$_4^{-}$ concentration decreased. Maximum Complex II formation was observed at the $^{99m}$TcO$_4^{-}$ only concentration level. Complex II showed the highest kidney uptake, and it is suggested that the Complex II might be a Tc(III)-DMS.

Studies on the Tumor Uptake of $^{99m}$Tc-Labelled Compounds:
Affinity of Metal Polymer for Tumor Cells
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The affinity of Ga-citrate for tumor cells has often been reported and the polymer character of this complex is also known. So, we predicted that a molecular size and charge of polymer might be an important factor considered on tumor localization. Based on this consideration, the affinity of various $^{99m}$Tc polymer complexes for tumor was studied.

Different polymer complexes of Tc were chosen, and their affinities for Ehrlich ascites tumor cells were investigated in vitro. In various Tc polymer analyzed, such as $^{99m}$Tc-citrate, $^{99m}$Tc-PPi and $^{99m}$Tc-DMSA, a similar degree of accumulation as Ga-citrate was observed. In every labeling preparation, a severe control of every variable was necessary because even with the same ligand small variation resulted in a great difference on tumor cell uptake. Besides, complexes with a molecular size and charge resembling Ga-citrate appeared to contain higher affinity for tumor cells.

Once high uptake complexes were defined in vitro, distribution studies were accomplished with tumor bearing mice. A great variety of phenomena was then observed such as accumulation in stomach or blood clearance rate. So, it is likely that different degree of decomposition of polymers occurs in vivo. Thus, the present results showed that $^{99m}$Tc polymer complexes resembling Ga-citrate in a molecular size and charge are available in the tumor diagnosis if they are made stable after injection in the body.