AN EVALUATION OF A NEW BIFUNCTIONAL HEPATOBILIARY SCANNING AGENT 99m-Tc-PC (PC: 3,3'-BIS(N,N-DI(CARBOXYMETHYL)-AMINOMETHYL)-O-CRESOLPHTHALEIN)

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Based on the so called bifunctional compound concept, PC, an IDA derivative, structurally similar to BSP, was labeled with the dinuclear 99m-Tc spieces. This new 99m-Tc radiopharmaceutical is rapidly cleared from the blood by the liver and rapidly excreated through the common bile into the duodenum.

The percentage of 99m-Tc-PC(61 %), excreated into the bile within the first hour after the administration, was similar to that reported for 99m-Tc-HIDA (65 %) but lower than the 131-I-BSP(77 %).

Binding of the tested compounds with plasma and the liver cytoplasmic proteins is analyzed by Sephadex G-50, T.L.C. and the ultrafiltration. 99m-Tc-PC bindings is higher as compared with 99m-Tc-HIDA but similar to that of BSP. Further, the percentage of 99m-Tc-PC recovered from the bile decreased significantly as compared with that of 99m-Tc-HIDA, when BSP is simultaneously administered. This result suggested that 99m-Tc-PC and BSP probably shared a similar transport path way.

Thus, the similar behavior in vivo of the newly developed agent and BSP, reflect the similar structure involved. Also the presence of a stable binding with 99m-Tc species in an effective state is estimated. These features are the most desirable ones for the future use of 99m-Tc-PC in the clinical field.

CHEMICAL CHARACTER OF 99m-Tc LABELED RADIOPHARMACEUTICALS AND ITS IN VIVO BEHAVIOR: 99m-Tc-Pen(COMPLEX II)

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In the labeling reaction of 99m-Tc-penicillamine (Pen), introduced as a cholescintigraphic agent, various Tc-Pen complexes have been detected depending upon the labeling condition, mainly the amount of $SnCl_2$ and pH. Sephadex column chromatography(SCC) of the labeling solution has individualized complexes such as Complex I (35-50 min), Complex II(15-25 min) and polymerized complexes(9-15 min) against a free pertechnetate elution time of 100 to 140 min. Nevertheless hepatobiliary excretion has been restricted to Complex I and Complex II and their pharmacokinetic were completely different, behaving as different compound. Their chemical state has been postulated as the molecule of Pen coordinated with a tetravalent mononuclear and dinuclear Tc state in Complex I and Complex II, respectively.

The reaction involving Complex I has been already published. Complex II formation reaction is studied by using 99-TcO_4^- (10^{-4} M) and carrier free 99m-TcO_4^- in the presence of 10^{-2} M Pen. The effect of the reducing agent is screened and a correlation between the elution pattern on SCC and the absorption spectra of every fraction is studied.

Maximum absorption spectra of the fraction eluted as Complex II is registered at 475-480 nm with molar absorptivity of about 13000. This datum is higher than the value observed for Complex I (4600 at 420 nm). The best Tc/Sn mole ratio for the complex with maximum absorption at 480 nm (Complex II) is 1 : 3 at pH 1.5. These results lead us to postulate the formation of Complex II in which Pen is coordinated with a tetravalent dinuclear Tc state. In fact, analysis of data obtained in kinetic studies corroborated with the criteria and dinuclear Tc state is the chemistry of Mo complexes. Moreover, the formation of Complex II was also observed in the reaction of Pen with a tetravalent Tc species, $TcCl_6^{2-}$ at pH 0.5 in the absence of $SnCl_2$. Basic implication of $SnCl_2$ in the complicated chemistry of Tc labeling reaction could be outlined and the role of this agent not only on the reduction of TcO_4^- but also on the hydrolysis of the reduced Tc species leading to the formation of dinuclear complex is discussed.