358

NEW TUMOR DIAGNOSIS RADIOPHARMACEUTICAL 99m-Tc(V)-DMS : BASIC STUDIES AS FOR CLINICAL APPLICATION. H.Masuda, N.Hata, A.Yokoyama, H.Saji, H.Ohta, K.Endo, K.Torizuka. Faculty of Pharmaceutical Sciences and School of Medicine, Kyoto University.

A polynuclear complex of 99m-Tc(V) Dimercaptosuccinate [Tc(V)-DMS] holding a pentavalent metal core, TcO_4^{3-}, alike PO_4^{3-}, has presented high accumulation in tumor cells. Its great potential for clinical use as an agent for tumor diagnosis, called for the formulation of an easy to label kit form. A kit form was designed as follows : DMS dissolved in $NaHCO_3$ solution was deaireted and the appropriate amount of $SnCl_2$ prepared in 0.1 N HCl added, and the mixture with required additives was lyophilyzed. This new kit demonstrated marked stability with shelf life up to 6 months at 4°C. The agent prepared by this kit, showed similar in vitro and in vivo behavior as that Tc(V)-DMS, previously reported (1). On the other hand, this agent showed slow blood clearance, a phenomenon to hinder a wide clinical use. Thus, in order to achieve a tumor/tissue ratio within a proper tenure for clinical application, the use of various chelating agents was screened. Among them, the post administration of citrate indicated the highest ability to decrease rapidly the blood activity level. Usefulness of Tc(V)-DMS prepared by this formulation and the post administration of citrate is now being tested in clinical studies.

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359

Tc-99m LABELED PROTEIN USING BIFUNCTIONAL CHELATING AGENT (VI): LABELING CONDITIONS FOR A STABLE Tc-99m-HSA. Y. Arano, Y. Magata, A. Yokoyama, H. Saji and K. Torizuka. Faculty of Pharmaceutical Sciences and School of Medicine, Kyoto University, Kyoto.

In Tc-99m labeling reaction of HSA using bifunctional chelating agent (BCA), the reaction is hindered by a great portion of reduced Tc-99m seized by the aminoacid residue present on the protein surface, followed by a slow transfer toward the chelating moiety of the BCA attached to the protein. While another portion of the reduced technetium hydrolyzes and breaks down to TcO_4^- or TcO_2.

In a search for a workable solution, in a di-thiosemicarbazone containing BCA, elongation of the chain between the chelating site and the protein coupling site has shown some improvement. In the present paper optimization of the labeling parameters are pursued. Using the stannous chloride method, a study of the labeling reaction at pH 3.4 with the reducing agent prepared in various different solvents, in the presence or absence of antioxidants were conducted.

The labeling of HSA coupled to this BCA was achieved with high efficiency as a well deairated solution of stannous chloride (10^{-4} M) in the presence of ascorbic acid (10^{-2} M) was used. A very selective binding to the chelating moeity, as well as, a lower lost of reduced technetium trapped by the aminoacid residue were procured. This formulation showed an improved in-vivo behavior and better feature than the well known I-131-HSA.

360

SEARCH FOR BRAIN PERMEABLE CHEMICAL FORM OF GLUCOSONE 1,2-bis(THIOSEMICARBAZONE)(GBT): Tc-99m-GBT, Cu-62-GBT. K.Horiuchi, A. Yokoyama, Y. Arano, S. Sano, A. Yamada, Ch. Tanaka, H. Saji, N. Tamaki and K. Torizuka. Faculty of Pharmaceutical Science and School of Medicine, Kyoto University, Osaka College of Pharmacy.

Among the various bifunctional chelating agents designed in our laboratory, GBT has been synthesized and labeled with Tc-99m under very restricted condition. Since favourable brain uptake has been limited, for characterization of target specific Tc-complex, exploration of GBT complexes with copper, a metal with more defined chemical characteristic is attempted.

Generator produced 99m-TcO_4^- and 62-$CuCl_2$, were used for the labeling of GBT. Chemical character was analyzed by HPLC, TLC and electrophoresis and the biological implications tested in mice and rabbit.

Analytical studies revealed the labeling of a stable Cu-62-GBT at pH 4.6 to 5.5. An increase of neutral complex formation was observed as the pH was raised. A phenomenon reflected on the partition coefficient and mice brain uptake. Biodistribution, scintigraphic and PCT images of Tc-99m-GBT, Cu-62-GBT with different charge, stability, lipophilicity are presented and their implication discussed. Basis for understanding the plausible Tc chemical form involved is explored.

361

A NEW APPRORCH OF DEVELOPMENT A RADIOTRACER FOR ESTIMATION OF BRAIN MAO ACTIVITY IN VIVO. Osamu Inoue,Toshiyoshi Tominaga and Toshio Yamasaki. National Institute of Radiological Sciences,Chiba.

We designed and evaluated a new method for estimation of brain MAO activity in vivo based on a metabolic-trapping radiotracer. We selected N-methyl labeled(C-14)N-methylphenylethylamine(MPEA) as a prototype of this radiotracer,because MPEA was expected to pass through the blood-brain barrier,and the labeled metabolite-C-14 methylamine should be trapped in the brain because of its cationic charge.In fact, C-14MPEA rapidly entered into the brain and was metabolized to C-14 methylamine by both forms of MAO in the brain.Whereas,unmetabolized C-14 MPEA itself was found to be eliminated fast from the brain.When mice were pretreated with a vrious dosage of MAO inhibitors(Clorygyline and 1-deprenyl),the whole brain radioactivity at 2 hr after i.v. of C-14 MPEA significantly decreased in a dosage (MAOI)-dependent way.The production rate of labeled methylamine in the brain seemed to be almost proportional to MAO activity remaining.These results indicated C-11MPEA has a high potency for in vivo estimation of brain MAO activity.We synthesized C-11 labeled MPEA with a high radiochemical yield within a short period.