463

Tc-99m(Sn)-N-PYRIDOXYL-5-METHYLTRYPTOPHAN: A NEW HEPATOBILIARY IMAGING AGENT. H. Ueda, M. Kato-Azuma and M. Hazue. Research & Development, Technical Department, NIHON MEDI-PHYSICS CO., LTD., Takarazuka.

Recently, we have introduced Tc-99m(Sn)-N-pyridoxyl-5-methyltryptophan[Tc-PMT] as a result of our intensive investigation to overcome some disadvantages associated with thus far reported Tc-99m labeled hepatobiliary imaging agents. Our current investigation is based on:(a) catalytic hydrogenation of the imine moiety of the corresponding pyridoxylidene-5-methyltryptophan, (b) preparation of Tc-99m-labeled agent by the stannous reducing method.

The in vivo distribution studies in rats and rabbits revealed:(1) the fast blood clearance and hepatic uptake, (2) the rapid hepatobiliary transit, (3) the low renal excretion, and (4) no intestinal re-absorption. Furthermore, the biliary excretion of Tc-PMT was much more resistant than that of Tc-PI or -EHIDA to the intervention of bromosulfophthalein[BSP]. The toxicity studies on PMT and final injectable solution showed a wide margin of safety for the proposed human dose.

The establishment of prolonged stability for the Tc-complex allows us to produce the radiopharmaceutical in its ready to inject Tc-99m-labeled form.

The clinical trials [IND] of this agent are now in progress.

464

Tc-99m HMDP: DEVELOPMENT OF A NEW BONE IMAGING AGENT. M. Hayashi, K. Takahashi and M. Hazue. Technical Department, NIHON MEDI-PHYSICS CO., LTD., Takarazuka.

For bone imaging agents, the important factors are high affinity to bone and rapid clearance from blood and soft tissues. Furthermore, we think that the most favorable property is the specificity to a lesion such as tumor. These properties mentioned above depend on the choice of chelate compounds and, therefore, many investigators have so far made efforts to survey new chelate compounds. When a new compound is employed in radiopharmaceuticals, the design of formulation is essentially important to get pharmaceuticals of good effectiveness.

HMDP, a new bone imaging agent, has high affinity to bone but HMDP dose concentration has to be maintained low enough, since HMDP forms colloidal particles with serum Ca^{2+} ions and accumulates in reticuloendthelical systems. Concerning the level of Sn^{2+}, lower levels of Sn^{2+} are generally acceptable. Then, in case the labeling efficiency decreases with increasing radioactivity, we have to use a stabilizer to prevent the radiolysis.

Based on these findings, the formulation of the radiopharmaceuticals are decided. Moreover, it was found in this study that pH of the radiopharmaceutical solution affected in vivo metabolism.

465

INDIUM CHLORIDE(In-111); DEVELOPMENT OF BONE MARROW SCANNING AGENT. K. Takahashi, M. Hayashi, M. Hazue. Technical Department, NIHON MEDI-PHYSICS CO., LTD., Takarazuka

Indium-111 decays by electron capture with a 67.44 hr physical half life and it emits two gamma rays in a very high abundance: 0.17 MeV-89% and 0.24 MeV-94%. Therefore, In-111, which has these excellent physical characteristics, is a suitable nuclide for use in radiopharmaceuticals.

In 1973, Lilien et al reported that In-111 is transported into erythroid precussors in a manner similar, if not identical, to iron, and then In-111 chloride is useful for bone marrow scanning agent.

The toxicity and biodistribution of In-111 were investigated, and the routine production systems were established, and now clinical evaluation is under way.

The acute toxicity studies on final injectable solution revealed a wide margin of safety for proposed human dose. The biodistribution studies in rats revealed that In-111 chloride accumulated in bone marrow. In the autoradiography in mice, it was observed that bone marrow uptake was higher than uptake in other tissues. From these results obtained in animal studies, the usefulness of In-111 chloride as a bone scanning agent was proven.

466

DEVELOPMENT OF I-123-o-IODOHIPPURATE (I-123-OIH). T. Sanada, H. Matsushima and M. Hazue. Research & Development, Technical Department, NIHON MEDI-PHYSICS CO., LTD., Takarazuka.

Since I-131 was introduced as a nuclear medical indicator, I-131-o-iodohippurate (I-131-OIH) has been used widely for measuring effective renal plasma flow. But, I-131 decays by β-emission with a 8.05 day half-life, giving a 82% 365keV gamma photon. It is unsuitable for clear imaging and also gives high radiation dose to patients.

On the contrary, I-123 is a cyclotron-produced isotope emitting γ-rays of energy 159 keV and having a half-life 13.0 h. It has quite suitable radionuclidic properties for in vivo diagnosis. Therefore, we developed a reproducible and efficient production method of OIH labeled with I-123, which was the modification of the radioiodination by isotopic exchange under molten state reported by Elias et al. Biodistribution in rats and rabbits indicated that I-123-OIH was quite stable in vivo as well as in vitro, and that the blood clearnace ratio and the excretion ratio from the kidneys were quite similar to those of I-131-OIH.

Meanwhile, the radiation doses from the administration of I-123-OIH were calculated on the basis of the distribution data in animals and human using the MIRD method. Compared with I-131-OIH, the use of I-123-OIH provides reduction in radiation dose. Clinical evaluation of I-123-OIH is now under way.