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DEVELOPMENT OF IMP LABELED WITH I-123.

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Superior radiopharmaceutical for brain imaging has been long hoped for in the field of nuclear medicine. Radiopharmaceuticals for brain imaging generally used are Tc-99m pertechnetate, Tc-99m-DTPA, Tc-99m-glucoheptonate, etc., but they are only taken up in brains in which the blood-brain barrier(BBB) is destroyed. N-Isopropyl-p-iodoamphetamine hydrochloride(IMP) which was developed by Winchell et al in 1980 is accumulated in brains with normal BBB. Based on this information, we have widely investigated its production as radiopharmaceutical, and succeeded in constant preparation of I-123 labeled IMP. I-123 labeled IMP is produced by the exchange reaction between cold IMP HCl and I-123, and the labeling yield is about 90%. Biodistribution in rats is shown below. The brain uptake of I-123 IMP becomes maximum at 1hr and remains constant till 3hr after i.v. injection. Sufficient safety was confirmed by acute toxicity test. Metabolism in animal and quality control were investigated. Presently, clinical trials of I-123 IMP are undergoing.

$^{123}$I-IMP Biodistribution in Male Rats (%/organ)

| | 5min | .5hr | 1 hr | 3 hr | 6 hr | 13 hr | 26 hr | 39 hr |
|---|---|---|---|---|---|---|---|---|
| Brain | 1.61 | 2.30 | 2.47 | 2.24 | 2.21 | 1.35 | 0.33 | 0.12 |
| Lungs | 13.78 | 7.26 | 6.17 | 6.76 | 6.01 | 3.24 | 0.78 | 0.27 |
| Liver | 13.02 | 23.37 | 21.62 | 14.96 | 11.56 | 7.03 | 3.46 | 1.50 |
| Blood* | 0.13 | 0.27 | 0.15 | 0.16 | 0.28 | 0.24 | 0.15 | 0.06 |
| Urine | 0.20 | 0.76 | 2.61 | 4.84 | 14.88 | 35.69 | 62.00 | 78.12 |

(* injected dose %/ml)

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DEVELOPMENT OF Tc-99m GENERATOR

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The advantage of Tc-99m generator is the ready availability of Tc-99m pertechnetate on site. But there were a number of problems observed in commercially available generators. Some of the problems associated with the alumina column type Tc-99m generator are Mo-99 break-through, aluminum contamination in the eluates and low Tc-99m elution efficiency. To solve these problems, the preparation of alumina column is very important.

On the basis of an oversea technical " know how" for this alumina column preparation, a compact and simple generator system,having following characteristics, was developed.

1. Automated assembly line, which has been developed for generator construction, makes the elution test of all generators possible.
2. The elution efficiency is highly stable even after repeated elutions, and high purity Tc-99m pertechnetate can be obtained.
3. Using the eluate from this generator, Tc-99m labeled diagnostic agents with high labeling efficiency can be obtained.
4. In order to minimize mechanical problems, simple unit structure is adapted.
5. Saline and collection vials can be observed from the front and the elution process can be checked.
5. Thick lead provides sufficient shielding, however secondary shield may be used for further radiation protection.

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BASIC STUDIES ON THE APPLICATION OF LIPOSOMES TO DIAGNOSTIC IMAGING AGENTS.

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In recent years, liposomes, microscopic phospholipid vesicles, have been recognized as potential carriers of therapeutic agents and they are also expected to deliver radiotracers as scanning agents. We have attemped to apply liposomes to diagnostic imaging agents. Multilamellar vesicles(MLVs)and small unilamellar vesicles(SUVs) were prepared by the standard methods and encupsulated Ga-67. Their diagnostic potentialities were studied in animals with damaged liver, damaged heart or tumor.

Accumulation of Ga-67-MLVs in the liver damaged with carbon tetrachloride was lower than that of the normal one. On the other hand,accumulation of Ga-67-MLVs and Ga-67-SUVs in the heart damaged with isoproterenol was 3-4 times higher than that in the normal one. In tumor bearing rodents Ga-67-SUVs was preferentially concentrated in tumor and tumor uptake of Ga-67-SUVs was much higer than that of Ga-67-citrate. Tumor to blood ratio obtained with Ga-67-SUVs was also superior to that with Ga-67-citrate.

These results suggested the possible application of liposomes to diagnostic imaging agents for damaged liver,damaged heart and tumor.

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THE DEVELOPMENT OF AUTOMATED SYNTHESIS SYSTEMS FOR COMPOUND LABELLED WITH SHORT LIVED RADIOISOTOPES.

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We are developing automated synthesis systems for labelled compounds with short-lived radioisotopes, that are produced by a compact cyclotron.

The important features of these design are as follows.

1. Automated control from target preparation to end of synthesis.
2. Facilities for maintenance.

Automated synthesis systems and these attachments that we are developing are as follows.

1. Production system for radioactive gas.
   This produces radioactive gases labelled with $^{11}$C,$^{15}$O, or $^{18}$F
2. Supply system of radioactive inhalation gas.
   The concentration of radioactive gas is kept constant, at the same time quality of gas is tested.
3. Automated precursor synthesis systems
   These systems synthesize [C-11]HCN, [C-11]$CH_3I$ and [C-11]HCHO as precursors for various [C-11]radiopharmaceuticals.