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≪Technical Report≫ Preparation of ^{99m}Tc Ferric Hydroxide Macroaggregates for Lung Perfusion Studies

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Abstract

^{99m}Tc Ferric Hydroxide Macroaggregates for Lung Perfusion Studies were prepared from home made Na $^{99m}TcO_4$ which was extracted by methyl ethyl ketone from low activity ^{99m}Mo. Particle size was in between 20 and 60μ. Rabbit and human body tests gave excellent results.

요 약

낮은 방사능의 ^{99m}Mo으로 부터 methyl ethyl ketone으로 추출하여 제조된 Na $^{99m}TcO_4$를 가지고 폐검진에 사용되고 있는 ^{99m}Tc Ferric Hydroxide Macroaggregates를 제조하였으며 여러 pH 범위에서 입자의 크기와 수가 변하는 모양을 검토하였고 pH 6-7에서 평균입자의 크기가 scanning에 가장 적당한 20~60μ이었다. 토끼와 인체에 주사하여 좋은 결과를 얻었다.

1. Introduction

At present two radiopharmaceutical agents are used for visualization of pulmonary blood perfusion. The first and most widely used agent is ^{131}I macroaggregated serum albumin (^{131}I-MAA). Iodine-131 decays with a half-life of 8.05 days emitting β-particles and 264-KeV γ-ray of which abundance is 82%. The radiation dose limits the maximum amount of ^{131}I that can be given and a relatively long time. is required for each lung scan.

More recently ^{113m}In ferric hydroxide particles were introduced as a lung scanning agent. The 390-KeV γ-ray emission from ^{113m}In is relatively difficult to collimate for use with the gamma camera.

^{99m}Tc has the favorable physical characteristics of high photon yield, low radiation dose and an easily collimated 140-KeV γ-ray emission. It decays with a half-life of 6 hrs.

As the lung scanning agent, the preparation of ^{99m}Tc Ferric Hydroxide Macroaggregates (^{99m}Tc-$Fe(OH)_3$-MA) was recently reported by Boyd *et al*[1].

To utilize the advantages of ^{99m}Tc for lung scanning, we have prepared ^{99m}Tc-lablled Ferric Hydroxide Macroaggregates from ^{99m}Tc ($^{99m}TcO_4^-$) which is produced by the extraction method using methyl ethyl ketone[2,3] and the discussion on the results is presented below.

2. Experiment

(1) Reagents

a) 248 mg $FeSO_4 \cdot 7H_2O$ dissolved in 50 ml pyrogen-free water; added 1 ml of 5% H_2SO_4;

stored under refrigeration.

b) 20 mg $SnCl_2.2H_2O$ dissolved in 10 ml cold pyrogen-free water; stored under refrigeration.

c) 10 g gelatin dissolved in 100 ml cold pyrogen-free water; heated in water bath at 85°C; sealed in 10 ml penicillin bottle; stored under refrigeration.

d) 1 ml human serum albumin (250 mg/ml) diluted with 24 ml cold pyrogen-free water; stored under refrigeration.

e) 1 ml of 4 N NaOH diluted with 19 ml pyrogen-free water to give 0.2 N NaOH; stored under refrigeration.

f) isotonic saline solution.

(2) Procedure

The ^{99m}Tc-pertechnetate in 4 ml isotonic saline solution was placed in a penicillin bottle with a Teflon-coated magnet: 1 ml $FeSO_4$ (1 mg Fe^{2+} per ml) and 0.5 ml $SnCl_2$ solution (1.2 mg Sn^{2+} per ml) were added and the solutions were then mixed on a magnetic stirrer. The pH of the solution was raised to 6-7 by the rapid addition of 0.2 N NaOH.

The suspension of green $Fe(OH)_2$ was transferred into a centrifuge tube and spun for 1 minute at 2000 rpm. The supernate was drawn off and discarded. The residue was resuspended in 6 ml of isotonic saline, and the mixure was centrifuged again for a further 1 minute at 2000 rpm. The supernate was drawn off and discarded.

The residue was transferred in 7 ml saline to a penicillin bottle to which was then added 2 ml gelatin solution (10 wt. %) and 0.5 ml $SnCl_2$ solution (1.2 mg Sn^{2+} per ml). The final pH of the solution was adjusted to pH 6.5-7.5 by the addition of 0.12 ml of 0.2 N NaOH. 0.25 ml of the human serum albumin solution (10 mg per ml) was added to the penicillin bottle which was capped and sealed. The penicillin bottle was autoclaved at 132°C for 6 minutes.

The bottle was then cooled under running water, shaken vigorously to disperse the clumped precipitate and was freezed in the refrigerator to improve the stability of solution during the transportation. The same experiment was performed at several pH ranges.

Radioactivity was checked with the 4π-ionization chamber with D. C. -Amplifier (Rank Nucleonics and Controls, England), the particles were sized and numbered in a haemocytometer grid using optical microscopy (Fig. 1).

^{99m}Tc-$Fe(OH)_3$-MA was injected into the rabbit and human body (Fig. 2, 3, 4).

Free $^{99m}TcO_4^-$ content was determined by the paper chromatography in 95% methanol.

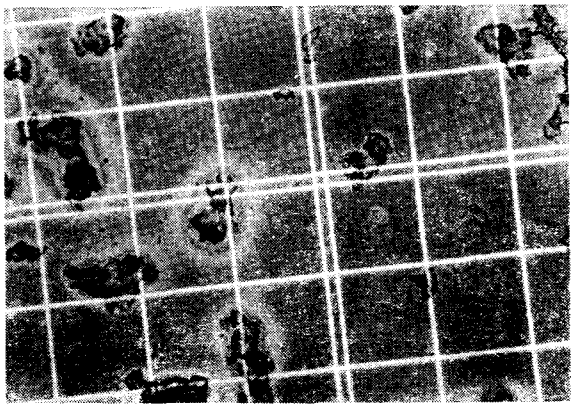

Fig. 1. Photomicrographs of ^{99m}Tc-Fe $(OH)_3$-MA. Sizes are in the range of 20-60μ (small square is 50×50μ)

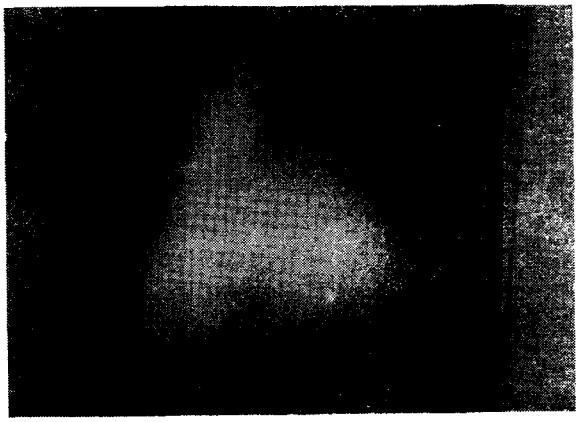

Fig. 2. Lung scintigraph for rabbit. (Courtesy Seoul University Hospital)

Table 1. Experimental data at several pH ranges

pH range	Activity of $^{99m}TcO_4^-$ used (mCi)	Activity of ^{99m}Tc-$Fe(OH)_3$-MA (mCi)	Yield (%)	Content of free $^{99m}TcO_4^-$ (%)	Particle size (μ)
4—5	21	15	75	1.3	5—50
6—7	43	32	74	1.4	20—60
9—10	34	25	74	1.5	30—150

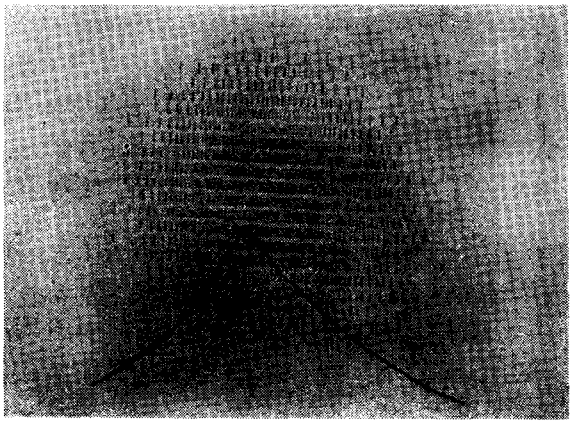

Fig. 3. Lung scan for racbit with ^{99m}Tc-$Fe(OH)_3$-MA. (Courtesy Radiological Research Institute.)

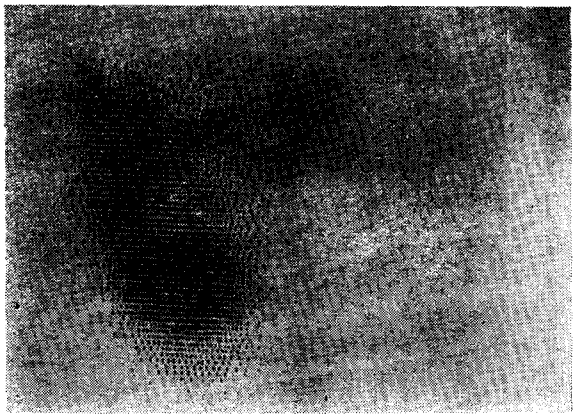

Fig. 4. The right lung scan for a man with ^{99m}Tc-$Fe(OH)_3$-MA. (Courtesy Seoul University Hospital)

3. Results and Discussion

(1) Table 1. shows the yield, content of free $^{99m}TcO_4^-$ and microscope observation at several pH ranges.

Yield was over 74%; Particle size range was 20-60μ; Content of $^{99m}TcO_4^-$ was less than 1.5%; Desired ^{99m}Tc-$Fe(OH)_3$-MA was formed at pH 6-7.

Over pH 6-7, number of particles was increased but some of the particles were larger than 100μ and below pH 6-7, number of particles was decreased remarkably.

It is known that the particles of 20-60μ are excellent for perfusion scan, the smaller particles ($<10\mu$) are accumulated into the liver and the larger particles ($>100\mu$) can not be used.

(2) The stirring through the process and cracking after centrifugation were important to control the particle size below 100μ.

(3) In order to get the desired particle size, gelatin solution must be added with a homogeneous state. For this purpose, gelatin solution must be warm and shaken before adding.

(4) Vigorous shaking after the autoclaving and freezing in refrigerator were required to prevent dissolution into free $^{99m}TcO_4^-$ and flocculation.

References

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