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การเตรียมเซอร์โคเนียมโมลิบเดตเจลเจนเนอร์เรเตอร์

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บทคัดย่อ

วิธีการเตรียม ^{99m}Tc gel generator ในรูปของ zirconium molybdate gel โดยอาศัย ^{99}Mo ที่ได้จากการอาบรังสีนิวตรอนในเครื่องปฏิกรณ์ฯ zirconium molybdate gel เตรียมได้จากสารละลาย zirconium oxychloride pH 1.6 กับสารละลาย ammonium molybdate pH 3-5 ในอัตราส่วนโมล zirconium กับโมล molybdenum 1:1 และมีค่า water content 7 - 8 % ^{99m}Tc generator ที่เตรียมจาก zirconium molybdate gel ขนาด 1-1.5 กรัม จะสามารถให้ elution efficiency โดยเฉลี่ยประมาณ 77 % และได้ปริมาณรังสีของ ^{99m}Tc ใน 3 มิลลิลิตรแรกของการชะล้างด้วยน้ำเกลือ 10 มิลลิลิตร ปริมาณของ zirconium และ molybdenum ในตัวชะล้างเกือบทั้งหมดมีค่าน้อยกว่าค่าที่ยอมรับได้ นอกจากนี้ยังสามารถเตรียม ^{99m}Tc gel generator ขนาด 100 mCi ที่ได้ผลดีทั้งในด้าน elutability และ stability

PREPARATION OF ZIRCONIUM MOLYBDATE GEL GENERATOR

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ABSTRACT

A procedure for preparation of ^{99m}Tc generator based on conversion to zirconium molybdate gel of ^{99}Mo produced by neutron activation was reported. The gel was prepared from zirconium oxychloride solution pH 1.6, ammonium molybdate solution pH 3-5 and mole ratio of Zr : Mo 1:1 which had water content about 7 - 8 %. Small generators containing 1-1.5 g of gel were eluted with average efficiencies of 77 % and the activity peak in the first 3 ml of 10 ml of saline solution. The amount of Mo and Zr in eluates were below the acceptance limit. The gel generators of activity about 100 mCi were prepared and had the good performance in elutability and stability.

1. Introduction

Technetium-99m(^{99m}Tc),one of the most important radioisotopes in nuclear medicine, is used for over 85 % of all the diagnostic in vivo medical application of radioisotopes. It is an ideal radioisotope in organ imaging because it posses excellent physical properties . Many methods are known to produce ^{99m}Tc from the parent ^{99}Mo. Most of the commercial ^{99m}Tc medical generators, are still produced based on column chromatography over aluminium oxide which adsorbed ^{99}Mo obtained from fission products of ^{235}U. This type of generator has several disadvantages which limit its practical application. The major one is the limitation of the adsorption capacity for molybdate ions (20 mg. per gram of alumina)[1] which requires the use of ^{99}Mo of high specific activity. In the countries which do not have a nuclear reactor with sufficient neutron flux and technology to handle fission products of ^{235}U, it is almost impossible to prepare chromatographic generators suitable for medical use. Hence,there has been a strong need to develop a new ^{99}Mo-^{99m}Tc generator which would retain the advantage of ease of operation but at the same time utilize ^{99}Mo of low or medium specific activity which could be produced in medium neutron flux reactors. The concept of the zirconium molybdate gel generator was first developed by EVANS et al.[2], the low specific activity ^{99}Mo produced from ^{98}Mo(n, τ) ^{99}Mo reaction was formed into zirconium molybdate gels and used as a column matrix material. The gels were obtained as amorphous precipitates by mixing aqueous solutions of ammonium molybdate and zirconium oxynitrate. The gel contained approximately 25% of molybdenum. The properties of the gels were varied by the preparation conditions such as the pH of molybdate and zirconium solutions,the mole ratio of molybdenum and zirconium, the order of mixing molybdenum and zirconium and the aging, washing and drying conditions of the precipitates.

This paper describes the investigation of production of ^{99m}Tc generators based on gel elution,the optimization of the parameters and conditions of the zirconium molybdate gel and the characterization of the gels are performed.

2. Experimental

2.1 Preparation of zirconium molybdate gel

Zirconium oxychloride solution 0.1 M

Zirconium oxychloride solution was prepared by dissolving 32.225 g or $ZrOCl_2.8H_2O$ in 1000 ml of distilled water.

Molybdenum trioxide solution 0.2 M

Molybdenum trioxide solution was prepared by dissolving 28.8 g of MoO_3 in 3 M NH_4OH, adjusting pH to 4 with 5 M HNO_3 and make volume to 1000 ml.

Precipitation of ZirconiumMolybdate Gel

The zirconium oxychloride solution was stirred vigorously at room temperature and the molybdate solution was slowly added dropwise to the stirred zirconiumawolution. After leaving overnight, the precipitate was filtered by suction and dried at 80 °C for 6 hours. The dried products were crushed and sieved to obtain grain size between 150–500 μm and determined water content from weight loss of the gel at 100 °C for 24 hours.

2.2 Preparation of Zirconium Molybdate Gel Generator

The generator was prepared by adding 1–1.5 g of zirconium molybdate gel to a glass column (0.8 cm in diameter and 5 cm height) with sintered glass frit (G-4) and glass microfiber filter at the bottom end of the column. The column was washed with 50 ml of saline solution. The ^{99m}Tc was eluted daily with 10 ml of saline solution at a constant rate of 1.0 ml/min. The elution efficiency and elution profile of the ^{99m}Tc were determined.

2.3 Preparation of Higher Activity Zirconium Molybdate Gel Generator

The higher activity of zirconium molybdate gel generators were prepared from irradiated 8.76 g of MoO_3 for 39 hours (Tue = 12 hrs, Wed = 6 hrs, Thu = 6 hrs and Fri = 15 hrs) at thermal neutron flux $2x10^{13}$ $n.cm^{-2}.sec^{-1}$. The irradiated MoO_3 target was dissolved in 3 M. ammonium hydroxide solution and the solution was adjusted to pH 4.0 with 5 M nitric acid. The volume of the solution was made to 300 ml and slowly added dropwise to the stirred zirconium oxychloride solution which was prepared from dissolving 19.35 g of zirconium oxychloride in 600 ml of distilled water. The white precipitate was formed. After leaving overninght, the precipitate was filtered and dried at 80 °C for 6 hours. The dried gel was crushed and sieved to obtained the grain size between 150-500 μm. The 10 g of the gel was packed into the column. The generator performance and the ability of labelling with in vivo kits were determined.

2.4 Gel Analysis

The water content of the gels were determined from the weight loss by drying at 100 °C for 24 hours. The zirconium and molybdenum mole ratio of the gels were analysed by X-ray fluorometry. The structure of the gels were characterized by X-ray diffractometry.

2.5 Eluate Analysis

The elution efficiencies were determined by measuring the ^{99m}Tc gamma activity in the eluate and expressing the yield as a percentage of the calculated total ^{99m}Tc activity determined from the ^{99}Mo activity at equilibrium. The zirconium content of eluates were determined by the arsenazo III method[3]. The molybdenum contents were determined by the thiocyanate method[4].

2.6 Experimental Conditions

The gels were prepared under different conditions in order to study the effect of the gel preparation on the generator performance.

Initially inactive zirconium molybdate gels were prepared to study the stability of the gel by determination of Mo and Zr breakthrough and the characterization of the gels were performed.

The radioactive zirconium molybdate gels were prepared by adding $Na_2{}^{99}MoO_4$ as a tracer to study the generator performance. The effect of pH of the molybdate solution, Zr:Mo mole ratio and water content were also studied.

The small zirconium molybdate gel generators were prepared from the irradiated MoO_3

to study the generator performance.

The higher activity of zirconium molybdate gel generators were also prepared to study the generator performance and the ability of labelling with in vivo kits.

3. Results

Zirconium molybdate gel prepared by this method was translucent yellow glassy solid. The inactive gels were prepared to study the stability of the gels by determination of Mo and Zr breakthrough. Table 1. shows effect of pH of molybdate solution on Mo, Zr breakthrough and water content of the gels. The gels prepared from molybdate solution pH 3-5, zirconium solution pH 1.6 and mole ratio of Zr:Mo 1:1 seemed to have a good stability which the amount of Mo and Zr breakthrough were below the acceptance limit (Mo < 5 ppm [5] and Zr < 5 ppm[6]). The water content of the gels were in the range of 7-8 %. Table 2 shows the effect of Zr:Mo mole ratio on Mo,Zr breakthrough and water content of the gels. The result showed no significant difference in the stability of the gels prepared from molybdate solution pH 4, zirconium solution pH 1.6 and varied Zr:Mo mole ratio 1:1.1, 1:1.2, 1:1.1 and 1.2:1. The molybdenum and zirconium breakthroughs were lower than the acceptance limit and the water contents were about 8 %. The structure of the prepared gels are amorphous as shown in Table 3.

The radioactive gels were prepared by adding $Na_2{}^{99}MoO_4$ as a tracer to study the performance of the generator. Table 4 shows the performance of radioactive gels. The prepared gels had elution efficiency about 45 % and the Mo and Zr contents were lower than the acceptance limit. The pH of the molybdate solution which varied in the range 3-5 did not change significantly the elutability and stability of the generator. The effect of varying Zr:Mo mole ratios on the elutability and stability of the gels is shown in Table 5. The Zr:Mo mole ratio 1:1 showed a good result in the stability of the gel although the elutability was rather lower than the others. Table 6. shows effect of water content on gel characteristics. When the water content increased the elution efficiency increased significantly but the Mo breakthrough was higher than the acceptance limit. The water content of less than 12.9 % gave good results in both elutability and stability.

The small zirconium molybdate gel generators were prepared from irradiated MoO_3 to study the characteristics of the generator. Table 7. shows performance of zirconium molybdate gel generator prepared from irradiated MoO_3 and alumina bed was used to reduce Mo content in the eluate. Gels prepared from varying pH of the molybdenum solution in the range of 3-5 did not show significant difference in the elution efficiency. The average elution efficiency of the gels were 77 % and the Mo contents were below 1 ppm. The elution profile of zirconium molybdate gels is shown in figure 1. Almost all of the ^{99m}Tc activity was eluted in the first 3 ml of 10 ml. saline solution. The performance of generators with higher activity were shown in Table 8. The zirconium molybdate gel generators of activity about 100 mCi of ^{99}Mo were eluted with saline solution and the elution efficiency were in the range of 70 - 82 %. The Mo and Zr content in the eluate were very low which could not be detected.

The ability of radiopharmaceuticals labelling was checked by labelling in vivo kits eg. DTPA and MDP with ^{99m}Tc which was eluted from the gel generators. The labelling efficiency were found to be more than 90 %.

Table 1 Effect of pH of molybdate solution on Mo,Zr breakthrough and water content in zirconium molybdate gel.

Conditions:

- pH of Zirconium oxychloride solution = 1.6
- Zr:Mo mole ratio = 1:1

Molybdate sol^{n} pH	pH of mixing	Mo content (ppm)	Zr content (ppm)	Water content (%)
3	1.04	< 5	ND	7.5
4	1.04	< 5	ND	7.1
5	1.10	< 5	ND	7.6
6	1.36	>> 5	ND	7.7
7	2.15	>> 5	ND	8.3
8	3.02	>> 5	ND	7.4
9	8.75	>> 5	ND	7.3

ND-Non Detectable

Table 2 Effect of Zr:Mo mole ratio on Mo and Zr breakthrough and water content in zirconium molybdate gel.

Conditions :

- pH of zirconium oxychloride solution = 1.6
- pH of molybdate solution = 4

Zr : Mo mole ratio	pH of mixing	Mo content (ppm)	Zr content (ppm)	Water content (%)
1 : 1.1	1.31	< 5	ND	8.6
1 : 1.2	1.35	< 5	ND	7.9
1.1 : 1	1.29	< 5	ND	7.7
1.2 : 1	1.26	< 5	ND	8.8

ND-Non Detectable

Table 3 Gel analysis, to characterize the gels by X-ray fluorescence and X-ray diffraction.

Conditions :

- pH of zirconium oxychloride solution = 1.6
- pH of molybdate solution = 4.0

	Gel analysis	
Zr : Mo mole ratio	X-ray fluorescence	X-ray diffraction
1.2 : 1	1.255 : 1	amorphous
1.1 : 1	1.193 : 1	amorphous
1 : 1	1.088 : 1	amorphous
1 : 1.1	1 : 1.012	amorphous
1 : 1.2	1 : 1.113	amorphous

Table 4 Performance of radioactive zirconium molybdate gel.

Conditions :

- Zr : Mo mole ratio = 1:1
- pH of zirconium oxychloride solution = 1.6
- Added $Na_2{}^{99}MoO_4$ as a tracer

Molybdate solution pH	Elution efficiency(%) mean $\pm$ s.d ; n=3	Mo content (ppm)	Zr content (ppm)
3	46.9 $\pm$ 2.0	< 5	ND
4	43.3 $\pm$ 1.7	< 5	ND
5	44.7 $\pm$ 2.8	< 5	ND

ND-Non Detectable

Table 5 Effect of Zr:Mo mole ratio on the elutability and stability of the radioactive gels.

Conditions :

- pH of zirconium oxychloride solution = 1.6
- pH of molybdate solution = 4.0
- Added $Na_2{}^{99}MoO_4$ as a tracer

Zr : Mo mole ratio	Elution efficiency(%) mean ± s.d.;n=3	Mo content (ppm)	Zr content (ppm)
1.2 : 1	84.2 ± 2.5	> 5	ND
1.1 : 1	74.2 ± 2.6	> 5	ND
1 : 1	68.9 ± 1.1	< 5	ND
1 : 1.1	70.1 ± 1.2	> 5	ND
1 : 1.2	68.0 ± 1.2	> 5	ND

ND-Non Detectable

Table 6 Effect of water content on gel characteristics.

Conditions :

- pH of zirconium solution = 1.6
- pH of molybdate solution = 4.0
- Zr : Mo mole ratio 1:1
- Added $Na_2{}^{99}MoO_4$ as a tracer

Water content (%)	Elution efficiency(%) mean ± s.d.;n=3	Mo content (ppm)	Zr content (ppm)
20.8	80.9 ± 0.4	≥ 5	ND
15.8	66.5 ± 0.9	≥ 5	ND
12.9	65.4 ± 1.3	≥ 5	ND
10.5	66.6 ± 0.5	< 5	ND
8.7	68.9 ± 1.1	< 5	ND

ND-Non Detectable

Table 7 Performance of zirconium molybdate gel generator prepared from irradiated MoO_3

Conditions :

- pH of zirconium solution = 1.6
- Zr : Mo mole ratio = 1:1
- using alumina bed for absorbing Mo breakthrough

Molybdate solution pH	Elution efficiency(%) mean ± s.d.;n=4	Mo content (ppm)	Zr content (ppm)
3	77.7 ± 4.8	0.6 ± 0.2	ND
4	77.4 ± 5.5	0.4 ± 0.3	ND
5	77.1 ± 4.6	0.3 ± 0.1	ND

ND-Non Detectable

Table 8 Performance of Radioactive Zirconium Molybdate Gel Generator

Conditions :

- pH of zirconium solution = 1.6
- pH of molybdate solution = 4
- Zr : Mo mole ratio = 1:1
- Weight of ZrMo gel 10 g.
- Safety column 2 g Al_2O_3

Column no.	Elution no.	^{99}Mo in column (mCi)	Decay time (hr)	^{99m}Tc in eluate (mCi)	Elution eff. (%)	Mo content (ppm)	Zr content (ppm)
1	1	102.5	24	57.9	81.5	ND	ND
	2	79.7	24	45.5	82.3	ND	ND
	3	61.9	24	35.2	82.0	ND	ND
2	1	120.0	18	57.5	70.4	ND	ND
	2	99.3	24	56.8	78.1	ND	ND
	3	77.2	25	44.0	78.6	ND	ND

ND-Non Detectable

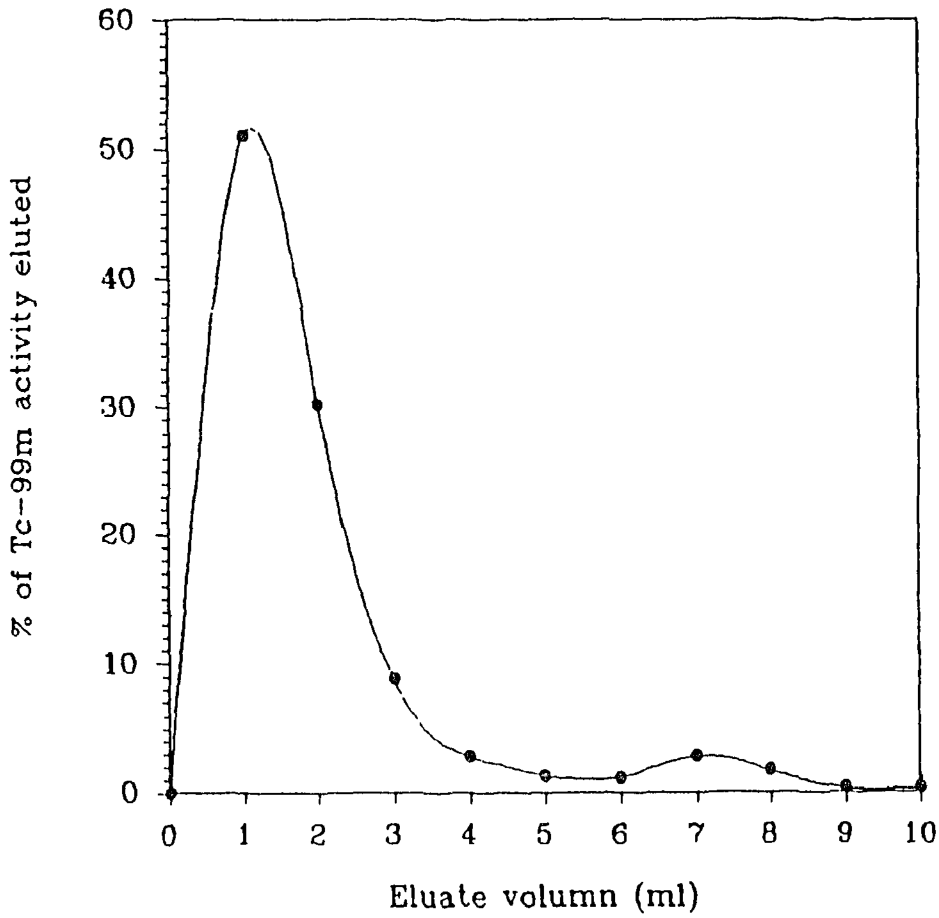

Fig. 1 Elution profile of ZrMo gel generator
(flowrate 1 ml/min, wt. of gel 2 g.)
Condition:
- pH of zirconium solution = 1.6
- pH of molybdate solution = 4
- Zr:Mo mole ratio = 1:1

4. Discussion

Zirconium molybdate gel are non stoichiometric, they are more variable than crystalline compounds which have a definite structure and composition. The amorphous zirconium molybdate gels have high ion exchange properties which are essential for the diffusion of TcO_4 in the generator matrix.[2]

The pH of molybdate solution and Zr:Mo mole ratio will effect the stability and elutability of the gels. The effects of varying the pH of molybdate solution while the pH of zirconium solution is maintained at pH 1.6 are presented in Table 1, the gels show good stability at pH of the molybdate solution from 3-5. The mole ratio of Zr:Mo 1:1 give good results which was shown in Table 5. Gels with Zr:Mo mole ratios higher or lower than ratio 1:1 have low stability due to high Mo content in the eluate, but the elutability of the gels which have Zr:Mo mole ratio 1:1 are less than the others. The formulation of the gels should be compromise between the stability and the elutability.

The water content of the gel which depends on the drying temperature and drying time will effect the stability and elutability of the gel. Table 6 indicated that the higher water content will cause the higher elution efficiency because water in the gel structure will give the similar polymerization reaction as in the acidic solution of molybdate ions. The condition of drying step in ZrMo gel preparation are very critical for getting a product of good ^{99m}Tc elution performance.[7]

The gels which were prepared under optimum conditions could be used for preparation of the gel generators. The prepared gel generators had good performance in elutability and stability. For gel generators of higher activity, The gels were prepared from the irradiated MoO_3. The specific activity of the gels were 10 mCi ^{99}Mo/g.of gel which was rather low due to the limitation of the irradiation time. The irradiation time was based on the routine operation of the reactor (Tue= 12 hrs, Wed = 6 hrs,Thu= 6hrs and Fri = 15 hrs.) which did not operate continuously.

5. Conclusion

This work on preparation of zirconium molybdate gel generator concluded that the zirconium molybdate gel could be prepared from zirconium oxychloride solution and ammonium molybdate solution with the optimum conditions as following : zirconium oxychloride solution pH 1.6, ammonium molybdate solution pH 3-5, Zr: Mo mole ratio 1:1 and drying temperature at 80^0C for 6 hours. The result gave translucent yellow glassy solid zirconium molybdate gel with water content 7-8%. The preparation of small zirconium molybdate gel generator showed that the gel had good stability and elutability which could be eluted in yield of 77.4 $\pm$ 5.5% and the Mo and Zr breakthrough were lower than the acceptance limit.

The gel generators of activity about 100 mCi were prepared and have good elutability and stability. The eluted ^{99m}Tc could be used for labelling with in vivo kits.

As a result obtained from the experiments, zirconium molybdate gel generator concept could possibly be used as one of the alternative technologies for production of ^{99m}Tc generators.

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