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A New ^{99m}Tc Generator using Cerium (IV) Oxide as an Adsorbent for ^{99}Mo

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ABSTRACT

In this research, a new technetium-99m generator has been developed with addition of Cerium oxide to alumina column. The adsorption behaviors of ^{99}Mo in the form of molybdate and ^{99m}Tc in the form of pertechnetate on CeO_2/Al_2O_3 was investigated and showed that the adsorption capacity of molybdate on this generator is higher than usual generator using Al_2O_3. Ceric ions were selected as an additive for the alumina because of their powerful oxidizing character and led to considerable yield. ^{99m}Tc is eluted with 0.9% NaCl and radionuclidic, radiochemical and chemical purities of the eluate were checked. This generator has a great potential as compared to the traditional alumina generators.

Keywords: Generators; technetium-99m; molybdenum-99; Cerium (IV) oxide

INTRODUCTION

Radioisotope ^{99m}Tc is an artificial element which does not exists in nature. Perrier and Segre [1] discovered it in 1937 from molybdenum which have been irradiated by deuterons in the cyclotron of the University of California at Berkeley. It remained more or less only a scientific curiosity till the late 1960 decade when its potential for the use in nuclear medicine was recognized. When it is necessary to obtain three-dimensional dynamic images of organs or tissues of patients, the SPECT (single photon emitter computed tomography) technique is used [2,3]. ^{99m}Tc with the decay photons of 140,5 keV, 6,01h half-life and practically no corpuscular radiation were found to be almost ideal for nuclear medicine, specially SPECT technique. However, for the routine use of ^{99m}Tc, a reliable production route was needed.

The relatively short half-life, favourable in the application, is a drawback in the supply of the users distant from the production site. This logistic problem is solved by the introduction of the ^{99}Mo/^{99m}Tc generators. The concept of the radionuclide generators is not new. Already in1920,Failla patented the first one(^{226}Ra/^{222}Rn) for the production of ^{222}Rn. Principally, it is based on the effective separation of a decaying, longer-lived, parent and the daughter of shorter half life. The obtained daughter radioisotope should be in a pure radionuclidic and radiochemical form. After the separation, the precursor, by decay, generates a new supply of the daughter. So, instead of a short lived daughter, the longer-lived parent, bond onto a suitable substrate, is transported. The separation is performed by the end user, often very distant from the production site.

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In the literature the generators are often named as "cows" as the daughter is "milked" from its parent. In an $^{99}Mo/^{99m}Tc$ generator, the daughter ^{99m}Tc ($T_{1/2}$ = 6.01 h) is separated from its parent radioisotope ^{99}Mo ($T_{1/2}$ = 66,0 h). Thus an easy and inexpensive access of ^{99m}Tc was created. Its use has grown dramatically ever since, with an expected growth of about 5-10% per year. At present, about 90% of all scintigraphic examinations is performed by ^{99m}Tc. There are several routes for the production of ^{99}Mo which apply nuclear reactions both in nuclear reactor and cyclotron. The separation of ^{99m}Tc is performed by using ion exchange, extraction, sublimation, etc. These topics, covered by several reviews [4,5], are beyond the scope of this article. The current ^{99m}Tc production system is based on the chromatographic $^{99}Mo/^{99m}Tc$ generator in which ^{99}Mo is obtained by uranium fission via the nuclear reaction $^{235}U(n, f)^{99m}Zr\rightarrow\ldots{}^{99}Mo$. For practical reasons it is sometimes denoted as $(n, f)^{99}Mo$ and is, in the form of molybdate ions ($^{99}MoO_4^{2-}$), loaded on alumina in the generator column.

^{99m}Tc produced by the decay, passes readily into the saline solution (0.9% NaCl) and is thus in the form of pertechnetate $^{99m}TcO_4$ separated from molybdenum as the solution is drawn out of the column. The generator should fulfill certain requirements for the use in nuclear medicine. One of the most important is the efficiency of the separation of ^{99m}Tc from ^{99}Mo. To ensure the high and stable elution yield, several procedures were tested based on the modifications of the adsorbent layer. Using suitable material and different amount of adsorbent such as aluminum oxide [6], charcoal [7], ferric hydroxide [8], manganes dioxide [9], or zirconium oxide [10] and their adsorption capacities with respect to ^{99}Mo have been studied. This paper presents the preparation of new generator with modification of alumina using cerium dioxide which shows rather good ^{99}Mo adsorption capacity than alumina. Beside we show in our study that ^{99m}Tc activities obtained from this new column chromatographic generator, is greater than commercial and typical alumina generator. This generator presents some features that make it easy to prepare and to operate.

EXPERIMENTAL

All chemical used were analytical grade and solution were prepared by using redistilled water. Fission-produced ^{99}Mo is purchased as molybdate in 0.2N NaOH. The solution is acidified and the aliquot of desired activity is adsorbed in the column. ^{99}Mo-^{99m}Tc column chromatographic generators were prepared by loading (n , *f*) ^{99}Mo in a glass column (0.6 cm dia. × 8 cm long), which was filled with 0.2 (gr) of CeO_2 (E-Merck) mixed with 1.8 (gr) preconditioned alumina (90 active, acidic, 70-230 mesh ASTM, E-Merck) or in the form of thin layer in the middle of the column. other generator was filled with 2 (gr) acidic alumina (90 active, 70-230 mesh ASTM, E-Merck) for comparison studies. The generators are eluted daily (interval between two subsequent elutions: 24 h), and the ^{99m}Tc activities measurements were performed by using radioisotopes calibrator (Capintec ARC-120).

RESULTS AND DISCUSSION

The constructions of $^{99}Mo/^{99m}Tc$ generators differ from one producer to another. Common to them all is the column containing alumina with adsorbed $(n, f)^{99}Mo$. The elutions of ^{99m}Tc are performed by saline (0.9% NaCl) which is passed through the column by the action of vacuum The problem of low or reduced elution yield is one of the major problems with the generators based on $(n, f)^{99}Mo$. It happens that the elution yield (i.e. the retention of ^{99m}Tc on the column) varies for no obvious reason. However, the main reason are the complex chemical, physicochemical and radiochemical processes in the column. $^{99}Mo/^{99m}Tc$ generator is a heterogeneous system. Due to its very high specific activity, fission-produced ^{99}Mo is adsorbed in a very limited volume of the adsorbent. The self irradiation doses due to the decay of ^{99}Mo could be very high. In the presence of water, highly reactive oxidation and reduction agents and free radicals are formed.

Cifka [11] showed that the elution yield depends on the valence state of technetium. Heptavalent technetium is readily eluted, but reduced forms remain firmly bond to alumina. It is supposed that the hydrated electrons are the species responsible for the reduction and thus for the

decrease of the elution yield. Therefore, any method of ensuring stable and high elution yields should be based on the prevention of the reduction of Tc(VII). Using cerium(IV) oxide as an oxidizing agent could overcome this problem and preserved the ^{99m}Tc in it's higher oxidation state and then led to higher elution yield.

Designing a new in-house generator using one column, filling with new column material modifier such as cerium dioxide, can lead to comparable results. This new generator has high efficiency and low ^{99}Mo breakthrough compared with the same ones acidic or nonacidic alumina columns generators (Table 1).

The results show that the generators containing new column material (especially in mixing form) appear to be technically and commercially viable source of ^{99m}Tc. From the glass columns containing cerium dioxide, ^{99m}Tc was eluted with 0.9 % NaCl. About 85% of the available ^{99m}Tc is eluted with 7 (mL) of saline. The fractionated elution profile of mixing column shows that over 90% of collected ^{99m}Tc activity was eluted using 3 (mL) of eluate (Fig. 1). The elution curve and cumulative yields of ^{99m}Tc which obtained from the generator, displayed in Figure 2. Technetium-99m can be eluted in a well ; ~ 80% of ^{99m}Tc, corresponding to 94% against the final yield of 84.73 %, could be collected in the first 3 (mL) of effluent at elution rate of 3 (mL/min).

Table 1. Performance evaluation of ^{99m}Tc efficiency and ^{99}Mo breakthrough of C-ACG systems

Decay time (h)	Practical yields (%) of C-ACG [a]		^{99}Mo measurements of eluates (%)	
	Mixing form [b]	Thin-layer form [c]	Mixing form	Thin-layer form
6.5	89	91	1.5×10^{-4}	5×10^{-4}
30.5	85	83	1.5×10^{-4}	2×10^{-4}
54.5	86	81	2×10^{-4}	1×10^{-4}
78.5	87	82	8×10^{-4}	2×10^{-4}

[a] ^{99m}Tc activitiy obtained in 7 mL of eluate as % of ^{99m}Tc activity expected on the generators in elution pH of 5-6.
[b] Elution rate was 3 mL /min , [c] Elution rate was 0.8 mL /min

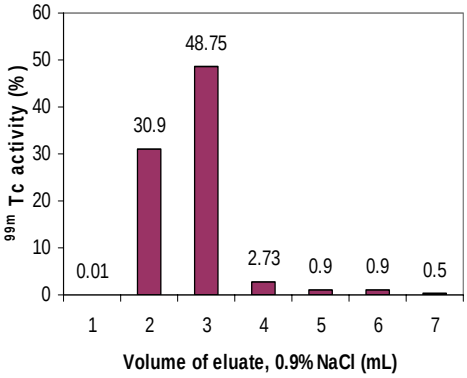

Fig.1. Elution curve of ^{99m}Tc.

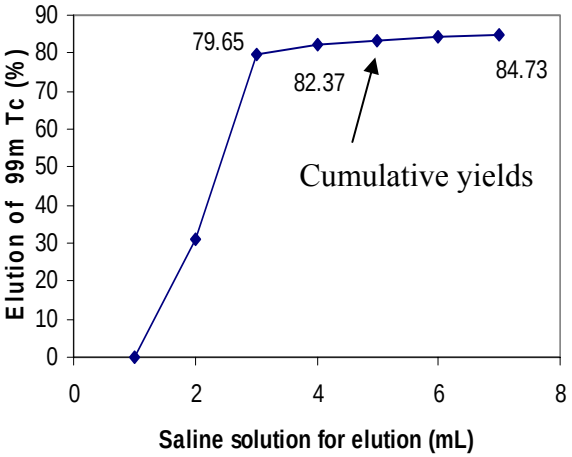

Fig.2. Elution profile of 99mTc from generator.

Figure 3 shows the results of milking ^{99m}Tc from the generators. More than 82% of ^{99m}Tc can be milk each time from cerium dioxide-alumina column generator (C-ACG) against 75% in typical generator based on alumina (ACG) until 273 (h), though the yields almost decreased slightly with time elapsed. Evaluation of differences in ^{99m}Tc recoveries can be observed in Table 2. It was also found that $0.1\text{-}0.8 \times 10^{-5}$ % of ^{99}Mo was accompanied with ^{99m}Tc eluted since the column including ^{99}Mo was washed with 10 (mL) of saline after loading molybdate and before milking the generator. Rates of elutions show that the pertechnetate is weakly sorbed by columns, whereas molybdate is very strongly adsorbed. ^{99}Mo content of ^{99m}Tc eluates was tested and it was found to be less than 10^{-3} % (Table 1).

Table 2. Comparison evaluation between a Typical generator for ^{99m}Tc based on alumina column(ACG) and generator using cerium dioxide-alumina column(C-ACG)

^{99m}Tc growth time (h) [a]	^{99m}Tc activity GBq (mCi)			^{99}Mo breakthrough (%)		Practical yield (%) [b]	
	Expected	ACG	C-ACG	ACG	C-ACG	ACG	C-ACG
9.5	4.44 (120.2)	3.55 (96.2)	3.9 (105.5)	1×10^{-4}		80	88
33.5	5.47 (148)	4.21 (114.5)	4.53 (122.6)	1×10^{-4}	0.5×10^{-4}	77	83
57.5	4.25 (115)	3.3 (89.3)	3.5 (94.5)	1.5×10^{-4}	0.5×10^{-4}	77	83
81.5	3.3 (89.4)	2.56 (69.3)	2.7 (73.4)	3×10^{-4}	1×10^{-4}	77	82
177.5	1.2 (32.6)	0.98 (26.5)	1.05 (28.6)	2×10^{-4}	1×10^{-4}	81	88
201.5	0.94 (25.6)	0.7 (18.8)	0.75 (20.1)	1×10^{-3}	1×10^{-4}	74	79
225.5	0.72 (19.7)	0.53 (14.5)	0.6 (15.7)	5×10^{-4}		73	80
249.5	0.56 (15.3)	0.42 (11.6)	0.45 (11.9)	2×10^{-4}	1×10^{-4}	76	78
273.5	0.44 (11.9)	0.32 (8.83)	0.35 (9.64)	1×10^{-4}	1×10^{-3}	74	81

[a] Loading of (n , *f*) ^{99}Mo was done so as to obtain a ~ 4.5 GBq ^{99m}Tc generator.
[b] ^{99m}Tc activity recovered in final eluate as % of ^{99m}Tc activity expected on the generator at the time of elution.

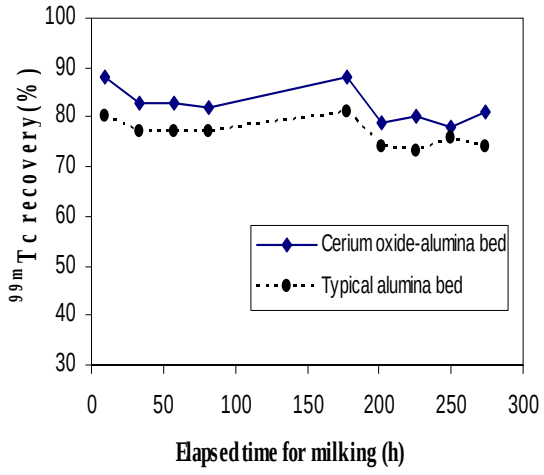

Fig.3. Milking of ^{99m}Tc from generators, 7mL of isotonic saline, pH=5.

CONCLUSION

The results show that the generators containing pure alumina as adsorbent are not reliable. In the experiment modification of the adsorbent was tested. Fission-produced ^{99}Mo was adsorbed either in the alumina and in the mixture of Al_2O_3 + CeO_2. Comparing this new generator with commercial available ones, it needs to be mentioned that the mixture has some advantages over Al_2O_3 as far as elution yield is increase. Beside this, the following quality control tests such as radionuclidic identification, radiochemical, chemical purity and biological control shows that ^{99m}Tc eluate of this adsorbent is suitable for medical applications. However, for a possible routine use of this procedure further investigations are needed.

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