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^{99}Mo/^{99m}Tc radioisotope generator based on adsorption of ^{99}Mo (VI) onto zirconium selenomolybdate as column matrix

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Abstract

Zirconium selenomolybdate-^{99}Mo gel was prepared by adsorption of ^{99}Mo onto inactive zirconium selenomolybdate gel matrix. The batch equilibration method was used for investigation of the interaction between ^{99}Mo (VI) radionuclide and the zirconium selenomolybdate gel matrix in HCl acid solutions. The apparent capacity of zirconium selenomolybdate for ^{99}Mo(VI) was determined by dynamic method and was found to be 0.13 mmol/g. ^{99}Mo/^{99m}Tc radioisotope generators of the elution mode was prepared based on adsorption of ^{99}Mo radiotracer, of low specific activity, onto chromatographic columns packed with 2g zirconium selenomolybdate gel matrix. The radioactivity of ^{99m}Tc was eluted with 0.9% NaCl solution each 24 h at a flow rate 0.5 ml/min. The eluted ^{99m}Tc radioactivity was of high yield and quality over the period of investigation.

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1. Introduction

In nuclear imaging processes, ^{99m}Tc($t_{1/2}$ = 6.01 h) is most commonly used isotope because of its suitable nuclear characteristics; short half-life, emission of mono energetic gamma--rays(140 keV), absence of beta emission and 90% of its decay by isomeric transition to ^{99}Tc and 10% by internal conversion[1-5]. Labeled molecules with ^{99m}Tc, for example, ^{99m}Tc-MDP and ^{99m}Tc-sestamibi are used for bone and cardiac scanning, respectively. They are also used for visualization of kidney, liver and lung [1, 2]. Technetium-99m can be directly produced in cyclotron via proton bombardment of natural target of molybdenum, ^{100}Mo (p, 2n) $^{99m\mathrm{Tc}}$ [6, 7]. Technetium-99m is generally produced indirectly via ^{99}Mo/^{99m}Tc generator systems as it is the decay product of ^{99}Mo ($t_{1/2}$ = 65.94 h). There are three processes of production of ^{99}Mo: ^{235}U(n,f)^{99}Mo, ^{98}Mo(nγ)^{99}Mo and cyclotrons via ^{100}Mo(p,2p)^{99}Mo and ^{100}Mo(p,pn)^{99}Mo[8-11]. The difference among the proposed chromatographic generators concerns the column material and the source of the parent, ^{99}Mo [3, 4, 12-16]. The main source of ^{99m}Tc is radioisotope generators of chromatographic column type based on alumina loaded with fission ^{99}Mo. Silica gel, hydrous titanium oxide, hydrous zirconium oxide and manganese oxide were investigated as a column matrix for fission ^{99}Mo/^{99m}Tc radioisotope generators [17]. In developing countries, the production of high specific activity (tens thousands of Ci/g) ^{99}Mo is limited as it needs highly expensive hot cells in addition to complex multi-step separation of fission ^{99}Mo which generates considerable amounts of radioactive waste [18]. To meat the global increasing demand of ^{99}Mo [19] and to overcome the shortcoming of production of fission ^{99}Mo, neutron activation ^{99}Mo of low specific activity (< 10 Ci/g) was used for preparation of ^{99}Mo/^{99m}Tc radioisotope generator. Simple equipments are needed for processing of neutron activation ^{99}Mo with producing of limited radionuclidic contamination and low radioactive waste. Solvent extraction, sublimation, and chromatographic ^{99}Mo/^{99m}Tc generators are types of generators based on neutron activation ^{99}Mo. Chromatographic column ^{99}Mo/^{99m}Tc generators include (i) adsorption of ^{99}Mo on high capacity sorbent such as nanocrystalline alumina, poly zirconium and poly titanium compound and (ii) incorporation of neutron activation ^{99}Mo into gel matrices via precipitation reaction of Ti, Zr, Al, Ce, Sn and Mg and molybdate-^{99}Mo solution. Zirconium molybdate, zirconium phosphomolybdate, 6-tungstocerate, 12-molybdocerate, zirconium silicomolybdate, cerium molybdate, cerium (IV) tellurium molybdate, stannic molybdate and alumina molybdate were used as base materials for preparation of gel ^{99}Mo/^{99m}Tc generators using the post and pri-irradiation methods [20-33]. To overcome some of the drawbacks of the previous two methods (degradation of the irradiated gel, production of undesirable radionuclides, decrease the elution yield due to reduction of Mo(VI) and Tc(VII) and high loss of ^{99}Mo activity due to multi-step procedure), labeling of inactive gel matrix with neutron activation ^{99}Mo via isotope exchange reactions was used [34,35].

The aim of the present work is to evaluate the elution performance of ^{99m}Tc from zirconium selenomolybdate chromatographic columns loaded through adsorption of ^{99}Mo onto zirconium selenomolybdate for the preparation of ^{99}Mo/^{99m}Tc radionuclide generators.

2. Experimental

Chemicals

The all chemicals used in our work were of A. R. grade.

Instruments

Identifications and measurements of the activity were done by a multichannel analyzer, which has a high-purity germanium coaxial detector (p-tyype) of “GX2518” model, Canberra, USA. The germanium detector is coupled with one unit containing a multichannel analyzer, amplifier and power supply (Inspector 2000 model, Canberr Series, made in USA). A UV-VIS spectrophotometer (Shimadzu, UV-160 A model, Japan) was used for determination of Mo (VI) and Zr (VI) contents in the ^{99m}Tc eluates. PH values of solutions were measured using a pH-meter with a microprocessor (Hanna Instruments pH211 model, Portugal). An analytical balance (A&D Engineering Inc., AND HR-202 model, USA) having dual range (42 g/0.01 mg, 210 g/0.1 mg) was used for weighing.

Radiotracer of ^{99}Mo

For preliminary studies, carrier-free ^{99}Mo was obtained by elution of Mon-Tek ^{99}Mo/^{99m}Tc generator (Monrol Nuclear Products Industry and Trade Inc. made in Turkey) after 25 days from its calibration date (loaded with 20 GBq of ^{99}Mo on its calibration date) with 2M NaOH solution. The ^{99}Mo eluate solution was passed through 0.45 micro-millipore filter to retain any possible contained alumina particles. Then, ^{99}Mo solution was diluted with HCl solution to the desired pH value.

For preparation of the generators, fission ^{99}Mo solution was obtained from Radioisotoope Production Facility (RPF) ETRR-II sample of NaOH of pH 13 containing 100 mCi ^{99}Mo was used as radiotracer.

Preparation of zirconium selenomolybdate gel matrix

0.25 M Mo (VI) was prepared by dissolving 3.025 g $Na_2MoO_4.2H_2O$ in a small portion of distilled water with addition of 5 ml of ^{99}Mo solution along with a few drops of 30% H_2O_2. The obtained sodium molybdate solution was warmed to destroy the excess of H_2O_2 and then cooling to room temperature before adjusted to pH about 4.5 using 2M HNO_3 solution. The volume of the Mo (VI) solution was completed to 50 ml with distilled H_2O. 0.25M Zr(IV) was prepared by dissolving 5.062 g $ZrOCl_2.8H_2O$ in a small portion of distilled water and then completed to 62.5 mL, after that it was heated just to 60 °C, then left to cool to room temperature ~ 25 °C. 0.2M Se (IV) solution was prepared by dissolving 3.224 g H_2SeO_3 in a small portion of distilled water and then completed to 50 ml. Mixture with 1.55:0.5:1.25 Zr(IV):Se(IV):Mo(VI) molar ratio were prepared by adding Mo(VI) solution dropwise to stirred Se(IV) solution and, then, Zr(IV) solution was added dropwise to the Mo(VI)-Se(IV) mixture. The pH of ZSM gel mixture solution was adjusted to the desired pH (~5.0) using 2M Na_2CO_3 solution. The formed precipitate was digested in the mother solution for 24 h at room temperature before phase separation by centrifugation. After separation, the resulting precipitate was washed several times with distilled water until the washing filtrates were free from chloride ions, dried at 50 °C for 24 h and pulverized to the desired particles size.

Distribution coefficient studies (K_d)

The distribution coefficients (K_d) for ^{99}Mo (VI) ions between the zirconium selenomolybdate gel matrix HCl acid solution were determined by the static batch equilibration technique. 0.1g amounts of zirconium selenomolybdate (m) was shaken with 10 ml (V) 10^{-4}M ^{99}Mo (VI) solutions in a shaker thermostat for ≥ 24 h. The radioactivity of ^{99}Mo in solution at equilibrium (A_e) was compared with standard sample (A_i) and the corresponding distribution coefficient values were calculated from the equation:

$$K_d = \frac{A_i - A_f}{A_f} \times \frac{V}{m} \ (ml/g)$$

Dynamic studies

2g zirconium selenomolybdate were packed into a glass column (0.6 cm i.d) with a stopcock wool piece as support. The zirconium selenomolybdate bed matrix was conditioned with 100 HCl acid solution (pH 5). Then, 50 ml of 10^{-2}M ^{99}Mo(VI) solution(pH) was passed through the column at a flow rate 0.5 ml/min. Counting rates of the initial solution and different effluent fractions were measured. The breakthrough capacity of ^{99}Mo(VI) ions was calculated from the following equation:

$$Capacity = \frac{C_o \times V_{50\%}}{W} mmol/g$$

Where; C_o is the initial metal ion concentration of the ^{99}Mo (VI) (M), $V_{50\%}$ is the effluent volume (ml) at C/C_o = 0.5 and W is the weight of zirconium selenomolybdate column matrix.

Preparation of the ^{99}Mo/^{99m}Tc generator

Chromatographic column of 2g zirconium selenomolybdate matrix packed in glass column (0.6 cm i.d.) and fitted at the bottom with glass wool was used conditioned with 100 HCl acid solution (pH 5) and loaded with ^{99}Mo(VI) by passing 0.01M ^{99}Mo-molybdate solution (pH 5) through it. The generated ^{99m}Tc was then eluted with saline solution (0.9% NaCl) and equal eluate volumes were collected for radiometric and chemical analysis.

To identify and determine the contribution of foreign radionuclidic contaminants present in the eluate, it was radiometrically analyzed directly after elution using a multichannel analyzer. The radionuclidic purity of ^{99m}Tc eluate was investigated by following its radioactive decay with respect to time and plot of the corresponding decay curve.

Whatman no. 1 chromatographic paper and a mixture of 85% methanol + 15% H_2O as developing solvent were used for determination of the radiochemical purity of the eluted ^{99m}Tc by ascending paper chromatography. The distribution of the activity along the chromatogram was traced using the gamma-ray spectrometer to calculate R_f value.

The possible impurities of Zr and Mo in ^{99m}Tc eluates were determined spectrophotometrically at wave lengths of 665 nm (arsenazo III method) and 465 nm (thiocyanate method), respectively [36-38]. pH values of the eluate solutions were determined using the pH-paper.

3. Results and discussion

Distribution coefficient studies (K_d)

Batch equilibration method was used for the investigation of the interaction of ^{99}Mo (VI) (10^{-4} M) in HCl acid solutions on zirconium selenomolybdate gel matrix. Figure 1 displays the K_d values of ^{99}Mo(VI) from chloride media on the adsorbent dried a function of the pH of the solution. It is observed that the adsorption of ^{99}Mo(VI) on zirconium selenomolybdate increases with increasing the pH of the solution and reaches maximum at p ~ 5 then decreases.

In such type of ^{99}Mo/^{99m}Tc radioisotope generator, one of the most affecting factors on the activity level of the generated radionuclide (^{99m}Tc) is the uptake capacity of the parent radionuclide(^{99}Mo) on the zirconium selenomolybdate gel material. It can be concluded from Fig. 1 that HCl acid solution (pH 5) is the optimum for loading ^{99}Mo(VI) onto the column matrix. Figure 2 clarified the ^{99}Mo (IV) breakthrough curve from 2g zirconium selenomolybdate chromatographic column (0.6 cm, i.d) using feed solution of 1×10^{-2} M ^{99}Mo (VI) HCl acid (pH 5), which passed through the column bed at a flow rate 0.5 mL/min. Gradual breakthrough of ^{99}Mo (VI) takes place in the first 20 ml effluent after which sudden breakthrough takes place. The uptake of ^{99}Mo (VI) reached to the saturation after passing 50 mL of the feed solution onto zirconium selenomolybdate column. The capacity was determined by substituting the effluent volume (mL) corresponds to 50% of the ^{99}Mo breakthrough in equation (2). The uptake value was found to 0.13 mmol ^{99}Mo (VI)/g of zirconium selenomolybdate**.**

Figure 3 clarified the elution profile of ^{99}Mo/^{99m}Tc radioisotope generator which is a relation between the average percent radioactivities of ^{99m}Tc eluates versus eluent volume at a flow rate of 0.5 mL/min. The ^{99m}Tc radioactivity is concentrated in the first 4 mL of saline solution with the maximum at the third mL of the eluate. The elution yield of the eluted ^{99m}Tc radioactivity was found to be 80.7±1.3% in 10 mL of saline solution as eluent.

Figure 4, curves a and b shows the gamma-ray spectra zirconium selenomolybdate column (0.6 cm i.d.) matrix loaded with ^{99}Mo(a) and ^{99m}Tc eluates(b) measured immediately after elution. Only the energy peak of ^{99m}Tc was detected in the eluates. Radionuclidic purity of the eluates was verified by gamma-ray spectrometry and radioactive decay measurements using NaI (Tl) scintillation counter giving a half-life of ~ 6 h corresponding to ^{99m}Tc. The corresponding radionuclidic purity of ^{99m}Tc eluates was found to be ≥ 99.99%. This value is suitable according to USAEC standard requirements for ^{99m}Tc applications in nuclear medicine [18, 20, 39-42]

Figure 5 shows the obtained radiochromatogram for ^{99m}Tc eluted from zirconium selenomolybdate column matrix, loaded with ^{99}Mo (VI), with 0.9% NaCl. The peaks in the chromatograms were identified by gamma-ray spectrometric analysis. In all chromatograms only one peak at R_f ~ 0.6 due to $^{99m}TcO_4^-$[28, 43-43]. The radiochemical purity was found to be 98.1 for ^{99m}Tc eluted form zirconium selenomolybdate-^{99}Mo column. This value is in agreement with the recommended specifications for preparation of ^{99m}Tc-labelled radiopharmaceuticals [18, 20, 39, 40, and 44].

The ^{99m}Tc eluates were chemically analyzed for the presence of zirconium and molybdenum as chemically stable impurities from zirconium molybdate column matrix. The zirconium and molybdenum concentrations in the eluates were found to < 10 µg/ml. Such zirconium and molybdenum contents in ^{99m}Tc eluates are below the permitted limit for medical applications [22-24, 45]. The pH values were found to be in agreement with the recommended value [18, 20, 40, and 41].

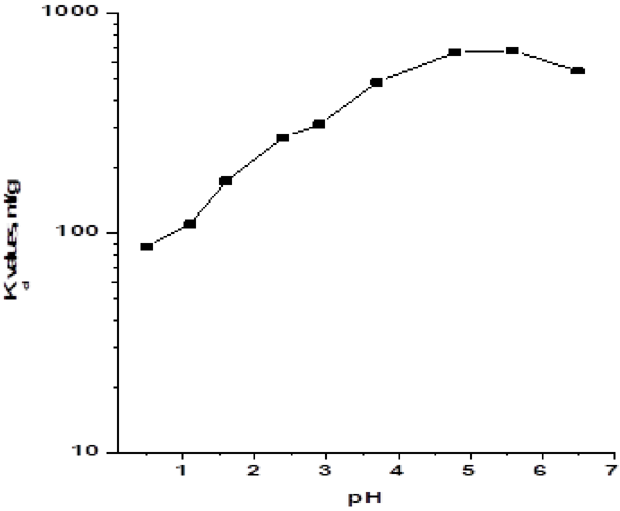


Fig (1)

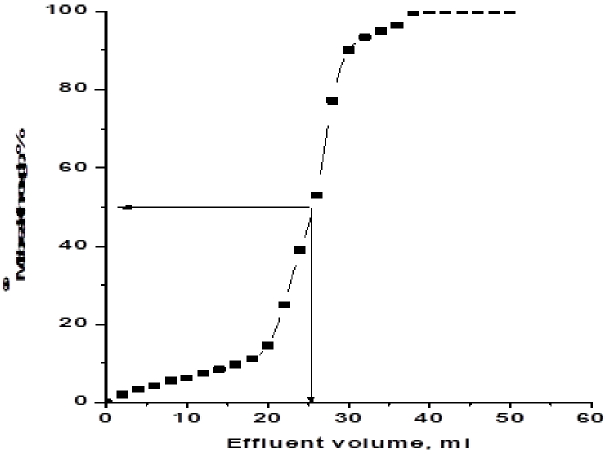
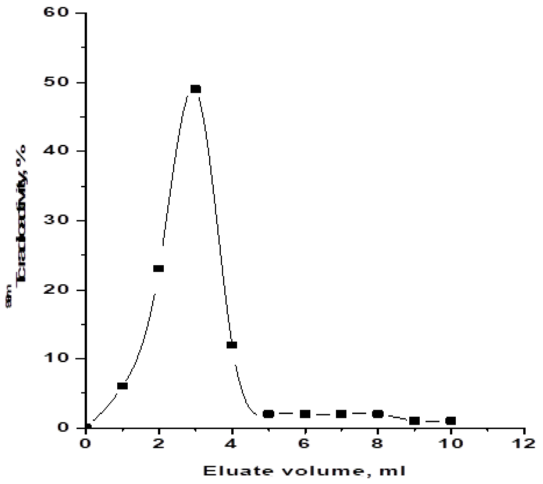


Fig (2)



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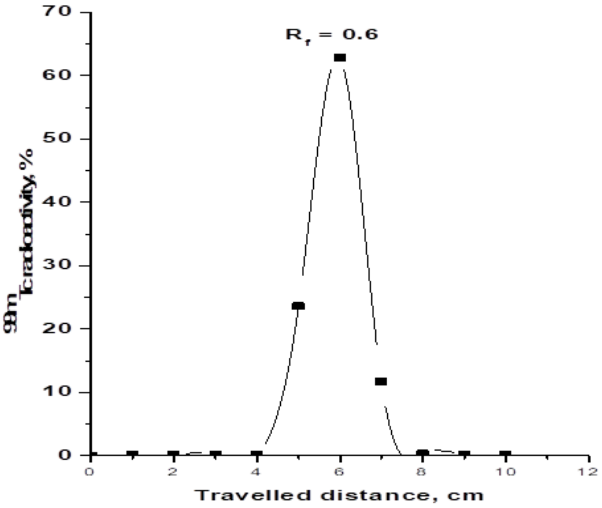

Fig (4)

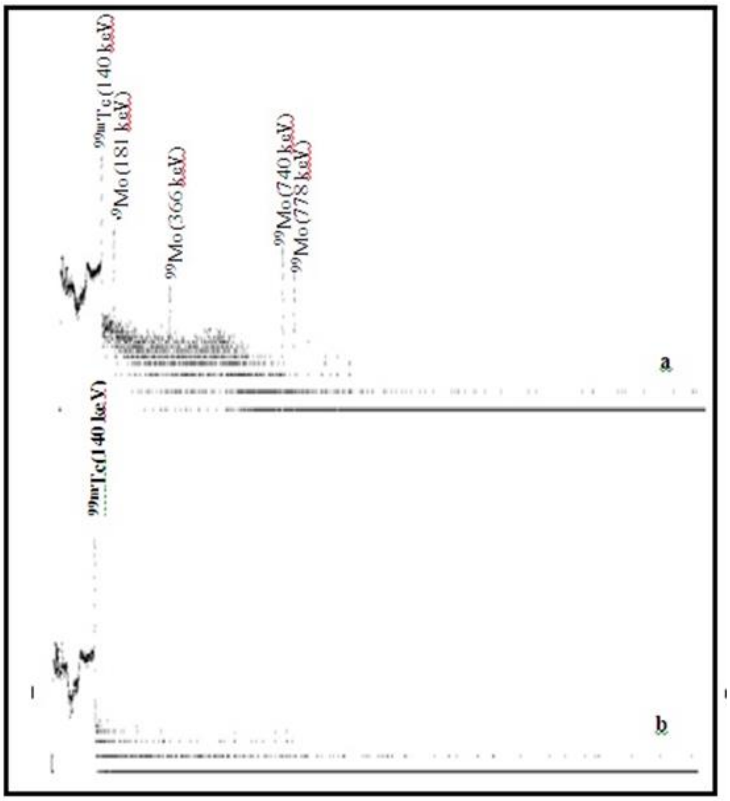

Fig (5)

4. Conclusion

The preformed zirconium selenomolybdate gel was used as a base material for ^{99}Mo/^{99m}Tc radioisotope generator. The generator was successfully prepared based on adsorption of ^{99}Mo (VI) on zirconium selenomolybdate gel matrix. The specifications of the ^{99m}Tc eluate met the requirements of the medical applications as it is eluted with satisfactory elution yield and high radiochemical, radionuclidic and chemical purity.

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