

$^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ Gel Generator Based on the ^{99}Mo -Zr Gel Technology with ^{99}Mo Obtained by Irradiation at Nuclear Reactor

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In this paper a new type of generator, named $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ gel generator, is presented. It is based on a polypropylene column filled with zirconium-molybdenum matrix, ^{99}Mo -Zr; the raw material is ^{99}Mo obtained by nuclear reaction $^{98}\text{Mo}(n, \gamma)^{99}\text{Mo}$ at nuclear reactor. The advantages of the $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ gel generator are: the radionuclide ^{99}Mo obtained by (n, γ) nuclear reaction is less expensive than ^{99}Mo obtained by separation from fission fragments; the $\text{Na}^{99\text{m}}\text{TcO}_4$ solution obtained by elution from $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ gel generator has chemical, radiochemical and radionuclidic purity higher than the classic generator with alumina column; in this case the alpha, beta-gamma fission fragments are not present; ^{99}Mo binding is much stronger in zirconium-molybdenum matrix (in this matrix bounds are chemical), than in classical generator where ^{99}Mo are absorbed on the alumina column (interactions are physical).

Key words: $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ gel generator; radiopharmaceutical products; radiodiagnosis

Radioisotopes generators continue to play an important role in nuclear medicine. $^{99\text{m}}\text{Tc}$ obtained from $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator is used in more than 80% of the clinical diagnostic scintigraphic studies. The parent radionuclide ^{99}Mo for this generator is obtained by two methods. The first one is neutron irradiation by a (n, γ) type nuclear reaction from ^{98}Mo stable isotope which has a natural abundance of 23.75%. The second method is by separation from ^{235}U fission products as a “carrier free” product with high specific activity.

The β^- disintegration of ^{99}Mo led to both $^{99\text{m}}\text{Tc}$ and ^{99}Tc , according to the decay scheme presented in figure 1 [1]:

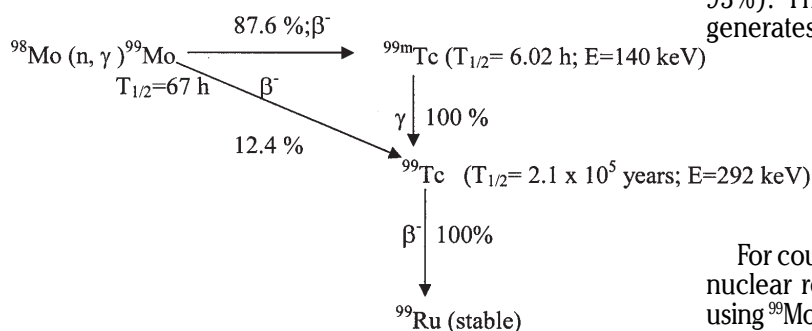


Fig.1 Decay of ^{99}Mo and $^{99\text{m}}\text{Tc}$

$^{99\text{m}}\text{Tc}$ radioisotope results from β^- disintegration of ^{99}Mo (with a probability of 87.6%) and has 67 h half life. Both nuclear properties and physiological action of $^{99\text{m}}\text{Tc}$, allow the expansion of its application in nuclear medicine. We must notice the fact that extremely low quantities of $^{99\text{m}}\text{Tc}$ (about 1 ng) present in the eluate from generators with activity of 370 MBq (10 mCi) means that its potential toxicity for the organism is very low, being practically neglectable. Also it is predictable that in the eluted pertechnetate it is possible to exist traces of stable molybdenum and ^{99}Mo (with maximum allowed limit of 0.1% from the total activity of the eluate) but it has a lower toxicity comparing to other radionuclides. The lethal dose molybdenum as sodium molybdate is 117 mg/kg body weight in rats for intraperitoneal administration and 248

mg/kg body weight in mice fir intravenous administration. The biological half live of ^{99}Mo is estimated to be of 20 days, 80% of the ^{99}Mo activity being placed in the liver [2-5].

The classic $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator consists of one polypropylene column filled with alumina - Al_2O_3 . The sodium molybdate - $\text{Na}_2^{99}\text{MoO}_4$ is adsorbed on this column. The sodium pertechnetate - $\text{Na}^{99\text{m}}\text{TcO}_4$ is eluted from the column with 0.9% sodium chloride solution. The ^{99}Mo for the classic $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator is obtained by separation from fission products resulted after irradiation of a uranium target (of natural composition or enriched in ^{235}U up to 89-93%). The separation technology is expensive and generates large quantities of radioactive wastes.

For countries with developing economies which have a nuclear reactor a more adequate technology is the one using ^{99}Mo obtained by thermal neutron irradiation at nuclear reactor of natural molybdenum enriched in ^{98}Mo targets. This technology is cheaper and generates fewer radioactive wastes so the generator based on this technology is an “ecological” one.

In this paper we propose the obtaining of a new type of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator, named $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ gel generator, based on a polypropylene column filled with the ^{99}Mo -Zr gel, using ^{99}Mo obtained by irradiation at Triga – Pitesti (Romania) nuclear reactor as raw material.

Experimental part

Molybdenum trioxide targets preparing and irradiation

In order to obtain ^{99}Mo radionuclide, we prepared targets containing 6 g molybdenum trioxide - MoO_3 each (with naturally isotopic composition and chemical purity >99%). Each 6 g molybdenum trioxide - MoO_3 portion was

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conditioned in aluminum tube (ϕ 10 x 50 mm, purity >99) as inner packaging and then in a second aluminum tube (ϕ 12 x 60 mm, purity >99) as exterior packaging forming the irradiation block. The irradiation blocks were tightly closed by welding in electron beam. The targets, prepared as described, were irradiated at Triga – Pitesti nuclear reactor for 7 days, with neutron flux between 5×10^{13} n/cm²s and 10^{14} n/cm²s.

The first performed studies aimed to establish the Mo:Zr optimum ratio in ⁹⁹Mo-Zr gel preparation because the quantity of ⁹⁹Mo fixed into the gel matrix and ⁹⁹Mo stability in the gel depend on this ratio. We prepared ⁹⁹Mo-Zr gel samples with Mo and Zr quantities adequate for the following Mo:Zr ratios: 1:1; 1:1.25; 1:1.5.

The irradiated molybdenum trioxide - MoO₃ targets (of natural isotopic composition and chemical purity >99 %) were dissolved in 3M sodium hydroxide – NaOH solution, under stirring and heating, resulting a sodium molybdate solution - Na₂MoO₄. This solution was clarified adding 1-2 drops of oxygenated water - H₂O₂.

Separately, we prepared a 0.25 M zirconyl chloride - ZrOCl₂ solution, by dissolving the adequate quantity of zirconyl chloride – octahydrate - ZrOCl₂ · x 8 H₂O in distilled water. Over the sodium molybdate solution - Na₂MoO₄ we added the zirconyl chloride - ZrOCl₂ solution and adjusted pH value to 4 - 4.5, resulting the ⁹⁹Mo-Zr gel. The ⁹⁹Mo-Zr gel was vacuum filtered after a few minutes. After filtering, the gel was dried in hot air flow for 4 - 6 h at 100°C.

The dried gel was crushed by adding cold 0.9% sodium chloride – NaCl solution over the hot gel. The resulting fragments were dried again in hot air flow for 2 - 4 h at 100°C. The sequence of these operations is presented in figure 2; the laboratory installation used for the experiment is presented in figure 3.

The radioactive gel grains obtained were placed in the polypropylene column (with the following dimension: ϕ 20 x 85 mm) of the gel generator. In figure 4, we present the scheme of ⁹⁹Mo/^{99m}Tc gel generator.

The elution of sodium pertechnetate - Na^{99m}TcO₄ from the ⁹⁹Mo-Zr gel column was performed using 0.9 % sodium chloride – NaCl solution and the eluate was collected in the evacuated vial after it passed through an alumina - Al₂O₃ filled column (safety column), which retained ⁹⁹Mo

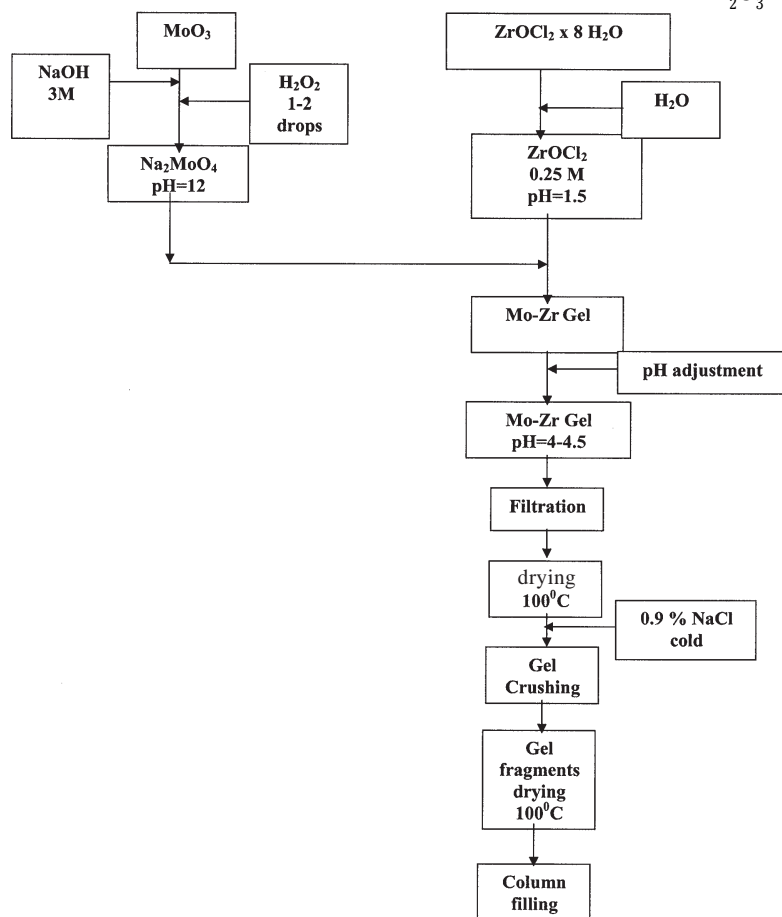


Fig. 2 Steps of Mo-Zr gel preparation process

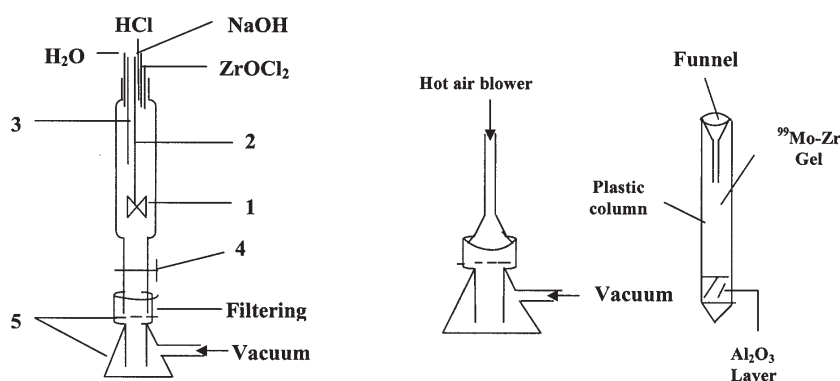


Fig. 3 Laboratory installation for ⁹⁹Mo-Zr gel preparation
1- Reaction vessel, 2- Stirrer, 3- pH probe, 4- Tap, 5- Vacuum filtering system

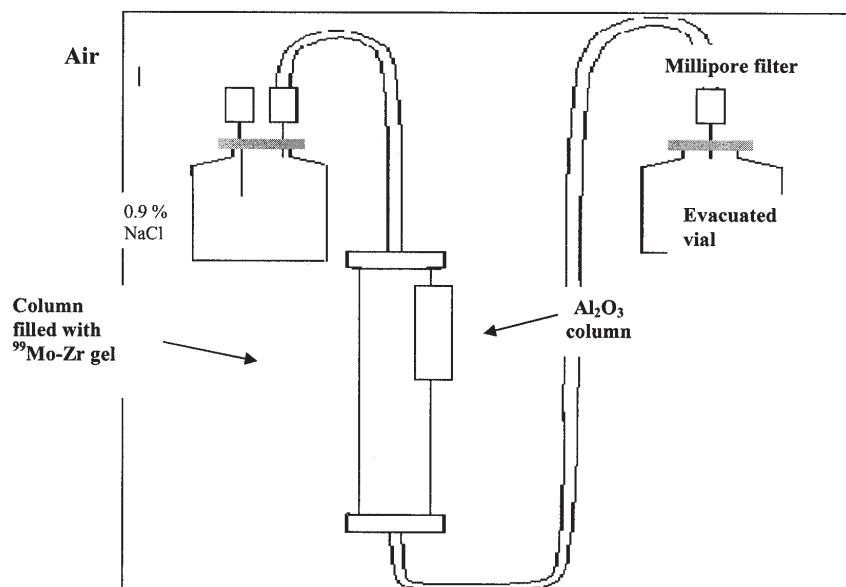


Fig. 4 The $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ gel generator structure

traces and ensured high radionuclidical purity of the eluate, and through a Millipore filter which ensured the eluate sterility.

The whole system was placed in adequate lead protection container.

In the study of the physico-chemical and radiochemical characteristics of ^{99}Mo -Zr gel and gel generator, we used adequate physico-chemical and radiochemical methods.

The quantity of ^{99}Mo linked to Zr in ^{99}Mo -Zr solid matrix (^{99}Mo -Zr gel) was determined by atomic absorption spectroscopy, using an Avanta Sigma spectrophotometer with a molybdenum lamp. The granulometric analysis for granulation determination of ^{99}Mo -Zr gel and medium size gel particle evaluation were performed using the DLS method using a Zatasizer type apparatus from Malven. The radionuclidical purity of the $^{99\text{m}}\text{Tc}$ eluted from the column filled with $\text{Mo}:\text{Zr}=1:1.25$ gel was determined by gamma spectroscopy using a multichannel gamma spectrometer Ortec Digibase type with a Maestro 32 Emulation type analyser. For the calibration, we used ^{137}Cs and ^{241}Am radionuclides with well known energy spectra and decay schemes.

Radiochemical purity of the eluate was determined by ascendant chromatography method, on Whatmann paper, using as developer 0.9 % NaCl solution.

For the IR spectral study of the ^{99}Mo -Zr gels we used a FT/IR Iasco-4200 spectrophotometer and Philips PW-140 diffractometer (Bragg-Brenato geometry) with PW-1050 goniometer using $\text{Cu-K}\alpha$ radiation in the domain $2\theta=10-100$ for X rays diffraction measurements.

Thermal analysis measurements were performed using a Q-1500 D (MOM-Budapest) thermo balance with digital data acquisition. We used a linear heating program (10K x min^{-1} heating speed), followed by free cooling of the system, in static atmosphere; we used alumina crucibles, the DTA signal was measured against Al_2O_3 standard.

Radioactivity measurements of the samples with $^{99\text{m}}\text{Tc}$ were performed using a scintillation detector, in 4π geometry coupled with NK-350 type monochannel gamma spectrometer.

Results and discussions

The results of the studies aiming at the establishing of optimum reaction conditions and optimum $\text{Mo}:\text{Zr}$ ratio for ^{99}Mo -Zr gel formation emphasized the fact that the gel formation process is strongly influenced by numerous

factors that need to be considered in gel $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator preparation process.

The zirconyl chloride solution ZrOCl_2 must be freshly prepared just before using and added fast to the sodium molybdate solution, because zirconyl chloride can form low solubility hydroxides that led to the decrease of the effective quantity of Zr reacting with sodium molybdate and forming the Mo -Zr gel.

The pH value of reaction media plays an important role in Mo -Zr gel forming, influencing the gel chemical and crystallographic structure. When the reaction media presents a pH value in the acid domain, small quantity of molybdenum from the solution is retained and weakly bond in the zirconium molybdate matrix. For pH values in the basic domain, low solubility zirconium chloride hydroxides appear, results a large quantity of Mo -Zr gel but with small molybdenum quantity retained in the matrix. It was established that the optimum pH value for the reaction media is 4 - 4.5.

The gel drying temperature is also very important influencing the gel structure. This temperature must be between 60 and 120°C ; a temperature over 120°C leads to partial gel decomposition.

The ^{99}Mo -Zr gel is an amorphous, gelatinous precipitate with variable composition according to preparation conditions.

FT/IR and X ray diffraction spectra for the three prepared gels, with the $\text{Mo}:\text{Zr}$ ratio of $1:1$; $1:1.25$; $1:1.5$ have the same shape leading to the conclusion that all gels had a similar structure. The differences between the three samples are the result of different Zr ratios in the gel matrices.

The $\text{Mo}:\text{Zr}$ ratio leads to different polymolybdate positions on an octahedral unit around Zr, the structure being strongly influenced by the water content in the gel [6].

When Mo proportion into the gel is rising, a smaller quantity of water is retained into the matrix and the elution efficiency increases. But in this case, Mo is no longer tightly retained in the gel matrix formed, as a consequence, the $\text{Na}^{99\text{m}}\text{TcO}_4$ eluate contains larger quantities of ^{99}Mo , leading to the necessity to introduce a thin alumina Al_2O_3 layer on the bottom of the column containing ^{99}Mo -Zr gel in order to retain the ^{99}Mo from the eluate.

Because of zirconyl chloride ability to form with water low solubility hydroxides, a higher ratio of Zr, results in Zr excess not binding to Mo but forming the hydroxides and

Particle size interval	Percentage content %
<0.15 mm	30.546 %
0.15-0.4 mm	36.147 %
0.4-0.6 mm	10.094 %
0.6-1 mm	9.558 %
> 1mm	13.654 %

causing unnecessary increase in gel mass. In the same time, a higher ratio of Zr means the ^{99}Mo is better retained in the gel matrix formed, so, in the eluted pertechnetate appear smaller quantities of ^{99}Mo , but, in this case the elution yield is lower. It is obvious that the chemical structure of Mo-Zr gel is connected with the elution efficiency.

The gel structure is a sieve type structure, with pores and channels, containing a large surplus of hydroxyl groups and water molecules linked corresponding metals [7]. $^{99\text{m}}\text{Tc}$ elution from the ^{99}Mo -Zr gel depends on the gel structure, gel particle size, pore and channels distribution in the solid matrix [7, 8].

Based on the results of these preliminaries we reached the conclusion that the optimum Mo:Zr ratio is 1:1.25.

Considering this composition for the ^{99}Mo -Zr gel we passed to the physico-chemical and radiochemical characteristic determination both for the gel and the $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator based on this gel.

Quantitative determination of ^{99}Mo linked in ^{99}Mo -Zr matrix was performed by atomic absorption spectrophotometry method. We used a sample of 6 g $^{99}\text{MoO}_3$ containing 3.999 g for ^{99}Mo -Zr gel preparation, with the ratio Mo:Zr=1:1.25. We determined the content of free Mo (not linked to Zr) in the filtrate resulting after the gel filtering step of gel preparation. The quantity of free Mo determined was 0.001523 g. The percentage of Mo linked into the Mo-Zr matrix was calculated using the relation (1):

$$\% \text{Mo linked into the matrix} = \frac{3.999 - 0.001523}{3.999} \times 100 = 99.96\% \quad (1)$$

Size determination of crushed and dried ^{99}Mo -Zr gel particles was performed by sieving procedure using different size sieves and weighting of separated fractions. The results are presented in table 1.

These data led to the conclusion that most of the particles, over two thirds are smaller than 0.40 mm. This granularity of the gel introduced in the column of gel generator influences mainly the elution yield of sodium pertechnetate - $\text{Na}^{99\text{m}}\text{TcO}_4$.

Determination of ^{99}Mo -Zr gel granulation in glycerine suspension was performed by DLS, resulting three records for each studied gel. From these records, we calculated the average dimension of the particles and percentage content. We found that for the gel with the ratio Mo:Zr=1:1, there was a distribution of granulation with two generation of particles with the average diameter of 227.1 nm (93.6 %) and 41 nm (6.4 %). The gel with the ratio Mo:Zr=1:1.25 presented just one type of particles with average diameter of 93.56 nm (100%) while the gel with the ratio Mo:Zr=1:1.50 presented two types of particles with the average diameter of 204.2 nm (92.1 %) and 42.55 nm (7.9 %). So, we can conclude that decreasing of Mo:Zr ratio (with increasing Zr quantities) led to decrease of gel particles average dimension.

Elution yield dependence of the eluent nature and volume was studied for two eluents: bidistilled water and NaCl 0.9 % solution. The results are presented in figure 5.

Table 1
CRUSHED AND DRIED ^{99}Mo -Zr GEL PARTICLE SIZE DISTRIBUTION

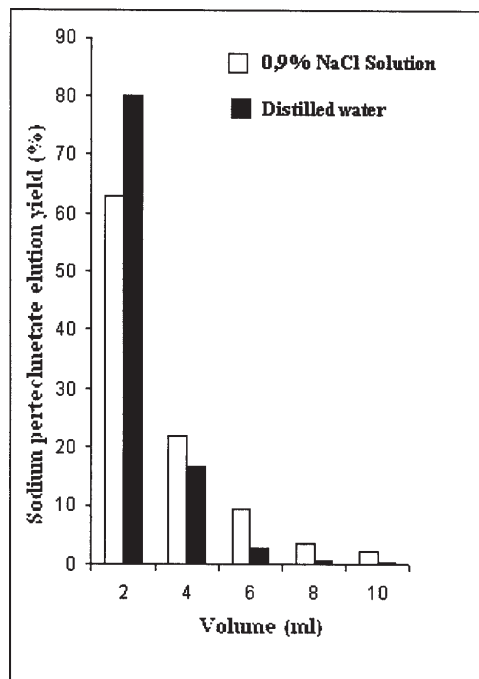


Fig. 5 Dependence of $\text{Na}^{99\text{m}}\text{TcO}_4$ elution yield of the nature and volume of the eluent

For the elution with bidistilled water, the obtained elution yields were higher than those obtained using 0.9% NaCl solution as eluent but the eluate presented lower radionuclidical purity because important quantities of ^{99}Mo were eluted together with $^{99\text{m}}\text{Tc}$ by the bidistilled water. This drawback was compensated by a safety column filled with alumina Al_2O_3 introduced into the generator (fig.4); so it was ensured the necessary radionuclidical purity for the $\text{Na}^{99\text{m}}\text{TcO}_4$ eluate. This method was also used by other authors [2-4].

Elution yield dependence of the column characteristics is presented in figure 6. We found that the elution yield depends of the gel quantity filled into the column and also of the column dimensions.

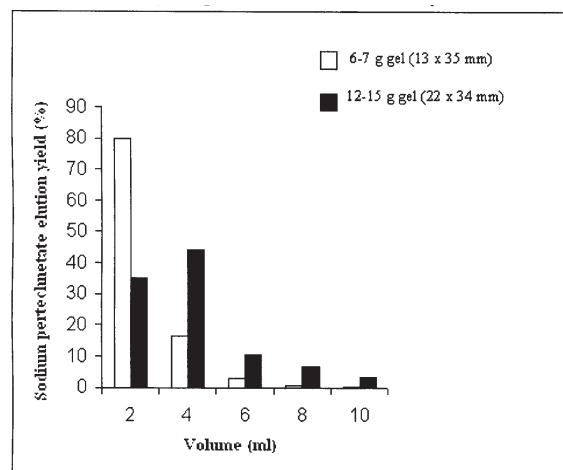


Fig. 6 $\text{Na}^{99\text{m}}\text{TcO}_4$ elution yield dependence of gel mass in the column and column dimension

The elution yield decreases with the increase of the gel mass and column diameter.

Sodium pertechnetate - $\text{Na}^{99\text{m}}\text{TcO}_4$ eluate radionuclidical purity determination was performed by gamma spectroscopy, recording the gamma spectra for the three ^{99}Mo -Zr gels with different Mo:Zr ratios. All $\text{Na}^{99\text{m}}\text{TcO}_4$ eluate samples presented a single distinct maximum. The resulted value for the gamma emission energy of $^{99\text{m}}\text{Tc}$ was 140.51 keV concordant with the literature [9]. Sodium pertechnetate eluate was practically 100% for all measured samples.

$\text{Na}^{99\text{m}}\text{TcO}_4$ eluate radiochemical purity determination was performed by ascending chromatography method, on Whatmann paper after the procedure described in the literature [10]. We used as eluent 0.9% NaCl solution. The value of radiochemical purity for all measured samples was higher than 95%.

Conclusions

The $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ gel generator presented in this paper is an alternative to the classic $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator and presents the following advantages:

-the raw material for gel preparation (^{99}Mo) is cheaper (being obtained by irradiation at nuclear reactor of natural molybdenum) than the one for the classic generator which is obtained by separation from fission fragments of ^{235}U (this separation is more expensive and generates more radioactive wastes);

- $\text{Na}^{99\text{m}}\text{TcO}_4$ eluate from the gel generator presented higher chemical, radiochemical and radionuclidical purities comparing to the classic type of generator;

-in the gel generator, ^{99}Mo is strongly bind to the gel matrix by chemical bonds, when in the classic generator ^{99}Mo is adsorbed on the alumina filling of the column by bonds of physic nature.

In the $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ gel generator, the ^{99}Mo -Zr gel presented a gelatinous amorphous structure that varies with the gel forming reaction conditions (pH, temperature, reactants concentration, stirring speed etc.). The variation in structural composition could be explained through the fact

that both Mo and Zr existence in aqueous solutions are determined by the mentioned reaction conditions.

Sodium pertechnetate elution yield from the gel generator depends of the gel structure; a structure with open pores and adequate granulation of the gel favoring the $^{99\text{m}}\text{Tc}$ elution through diffusion processes.

Zr excess (Mo:Zr = 1:1.5 or Mo:Zr = 1:1.25) in gel formation process leads to strong ^{99}Mo binding into the gel matrix, the quantity of ^{99}Mo in the eluate being extremely low (meaning very good radionuclidical purities, close to 100%), but the $^{99\text{m}}\text{Tc}$ elution yield decreases.

The values of radionuclidical and radiochemical purities obtained for sodium pertechnetate - $\text{Na}^{99\text{m}}\text{TcO}_4$ eluted from the ^{99}Mo -Zr gel generator were adequate for a radiopharmaceutical product.

Aknowlegement: The results presented in this paper were achieved in the frame of 71-124/2007 Research Contract funded by CNMP

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Manuscript received: 25.10.2010