FINAL REPORT

CONTRACT NUMBER : 5647/R1/RB

TITLE OF PROJECT: " Studies on the production of Technetium - 99m Generators based on gel elution".

INSTITUTION: Nuclear Center "RACSO" Lima - Perú . Instituto Peruano de Energía Nuclear.

CHIEF SCIENTIFIC INVESTIGATOR: Manuel Castro

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DESCRIPTION OF RESEARCH CARRIED OUT

ABSTRACT

Technetium-99m Generator based on TiMo elution has been carried out. The gel matrix was prepared by mixing non irradiated molybdate with Titanium Chloride solution.

Conditions of preparing and drying TiMo were evaluated as a function of elution yield. Thus, pH and water content were found highly criticals for reproductiveness of the results.

Non-elutable form of Tc-99m can be oxidized treating the target after irradiation with $K_2Cr_2O_7$ 0.001M solution. During several experiments the columns were soaked with this oxidizing solution for one hour and afterwards the TiMo was washed with 150 ml physiological saline. Daily elutions were done with 10 ml of NaCl 0.9%.

Cooling water reactor during irradiation quartz ampoules has been estudied. To study this effect, one group of samples were irradiated in aluminium caps air-tight screw and another one was irradiated in drilled caps with six holes to permit water reactor recirculation around quartz ampoules.

By combination $K_2Cr_2O_7$ target treatment and cooling TiMo during irradiation is possible to get yields of Tc-99m near to 76 % .

The radiochemical purity was > 99% and Al content < 10 ppm , Cr < 0.05 ppm , Mo < 20 ppm , Ti was no detected . Biological scans practiced in animals have been considered satisfactories.

PREPARATION OF THE SAMPLES.

The matrices of Titanium Molybdate were prepared by the precipitation carried out by mixing aqueous Ammonium Heptamolybdate solution with Titanium Oxychloride solution according the following procedure.

1.- Preparation of the Titanium Oxychloride Solution.

As we know, Titanium (IV) Chloride is too corrosive. so handling it must be very careful using N_2 current and sealed fighty the mother flask. For experiments, 5 ml of $TiCl_4$ is added to 44.5 ml of water dropwise with continous stirring.

2.- Preparation of the Ammonium Heptamolybdate.

7.80 g of MoO_3 is dissolved by adding slowly 50 ml NH_4OH: 25% (5 portions of 10 ml for each time).

3.- Gel preparation.

The Titanium Oxychloride solution is mixed with Ammonium Heptamolybdate. The gel produced is accompanied for heat production in a typical exthermic reaction. The precipitate obtained is filtered through a whatman paper washed several times with bidistillate water and dried at 80°C for 6 hours till the moisture content is near to 10%.

The samples thus obtained were manually crushed and sieved to 100 - 150 mesh.

Finally the Titanium Molybdate is stored air tight in dry atmosphere at room temperature.

Facilities and irradiation conditions.

TiMo was irradiated in the RP-10 Reactor (Nuclear Center RACSO-Lima) at a neutron fluxes of 1-2 x 10^{13} n/cm^2 s during 8 hours. The average power level of the reactor during all irradiations was 7 Mw. However is necessary to say that in the best positions of the core exist fluxes near to 3.5 x 10^{14} n/cm^2 s.

According the Schedule Reactor Operation for radioisotope production, the reactor operates once a week during 8 hours every friday. Water cemperature in the core at 7 Mw is 34° C.

Samples irradiation.

The TiMo in the form of particle size of 100 - 150 mesh were prepared for irradiation. TiMo targets were closed in the aluminium container air-tight sealed and the weight material was 4 g.

In our work several irradiations have been carried out putting TiMo in quartz ampoules inside of drilled caps to permit water reactor recirculation around them.

Column preparation and elution of generator.

The TiMo after irradiation is transfered over 2 grams of acid alumina (sieved and selected and previously treatment with HCl 0.01 N) in a generator column with sintered glass disc at the botton. The column is filled with wool glass and washed with 150 ml of 0.9% NaCl.

Before elution the column is sealed with a rubber closure and aluminium cap. Tc-99m elutions are done with 10 ml of saline solution and measured in a Capintec dose calibrator. Mo-99 activity in the column and eluate were measured and compared with the theoric values.

Eluate analysis.

Elution yield was calculated by measuring the Tc-99m activity in the eluate and expressing the yields as percentage of the Mo-99.

Mo-99 and others radionuclides impurities were checked using a Ge-Li detector. Molybdenum content was determineted spectrophotometrically. Aluminium was measured also by colorimetryc method.

Radiochemical purity was done by paper chromatography using Whatman No.1

EVALUATION RESULTS

TABLE 1-A

EFEECT OF TiMo HUMIDITY ON ELUTION EFFICIENCY OF Tc-99m

Sample	Water Content (%)	% Yield Tc-99m	uCi Mo-99 / mCi Tc-99m
1A	7.71	14.9	0.015
2A	8.34	9.8	1.65
3A	9.55	53.2	7.35
4A	10.04	63.1	8.33
5A	12.77	12.5	1.35
6A	13.21	7.6	1.04
7A	13.76	12.3	9.09
8A	14.30	13.8	1.18
9A	14.40	32.2	0.016
10A	15.41	12.3	4.5

Comments:

From Table 1 ,we can observe, that exist good separation yield for samples which the percentage water content is between 9-10 % . TABLE 1-B lists the effect of differents pH on elution efficiency in a new experimental serie. Results confirm prior tendency.

TABLE 1-B

Sample	Water Content (%)	% Yield Tc-99m	uCi Mo-99 / mCi Tc-99m
1B	4.2	12.3	1.2
2B	6.1	22.6	4.1
3B	7.5	31.3	2.6
4B	9.2	60.1	4.3
5B	10.5	67.1	4.2
6B	12.4	39.4	11.3
7B	14.5	19.7	11.4
8B	17.7	8.9	10.1

TABLE 2-A

EFFECT OF PH ON ELUTION EFFICIENCY OF Tc-99m

Sample	PH	% Yield Tc-99m	Non Active Mo Content (ppm/ml)
1A	4.4	9.8	10
2A	5.1	14.1	10
3A	6.3	16.3	20-25
4A	6.6	12.3	25-30
5A	7.4	29.1	25-30
6A	8.8	67.2	40
7A	9.5	53.5	38
8A	10.0	56.2	38

Comments:

For the last three samples, the corresponding yield is good, however the non active Molybdenum content is too high. The values showed above for samples 3 to 8 are average of 2 experiments.

A new serie of experiments have carried out lately confirm similar tendency (See table 2-B).

TABLE 2-B

Sample	PH	% Yield Tc-99m	Non Active Mo Content (ppm/ml)
1B	6.0	12.5	35
2B	7.0	32.6	36
3B	8.0	66.2	42
4B	9.0	65.8	36
5B	10.0	51.4	34

EFFECT OF OXIDIZING AGENT

It is well know that the existing non elutable form of Tc-99m can be oxidizing using differents agents; so it is possible increase the elution efficiency soaking the column by an oxidizing solution. In our experimental work, different concentrations of Potasium Dichromatic were putted inside the column sealed at the bottom with a rubber. Thus the chromic solution and Titanium Molybdate are in contact during one hour. Before elutions the column is washed with 150 ml of saline solution. At the beginning the eluate has a blue color, being transparent after the first 50 ml of elution. Daily elutions are done with 10 ml of physiological solution. Experimental results are shown in Tables 3 and 4.

TABLE 3

EFFECT OF OXIDIZING AGENT ON ELUTION EFFICIENCY

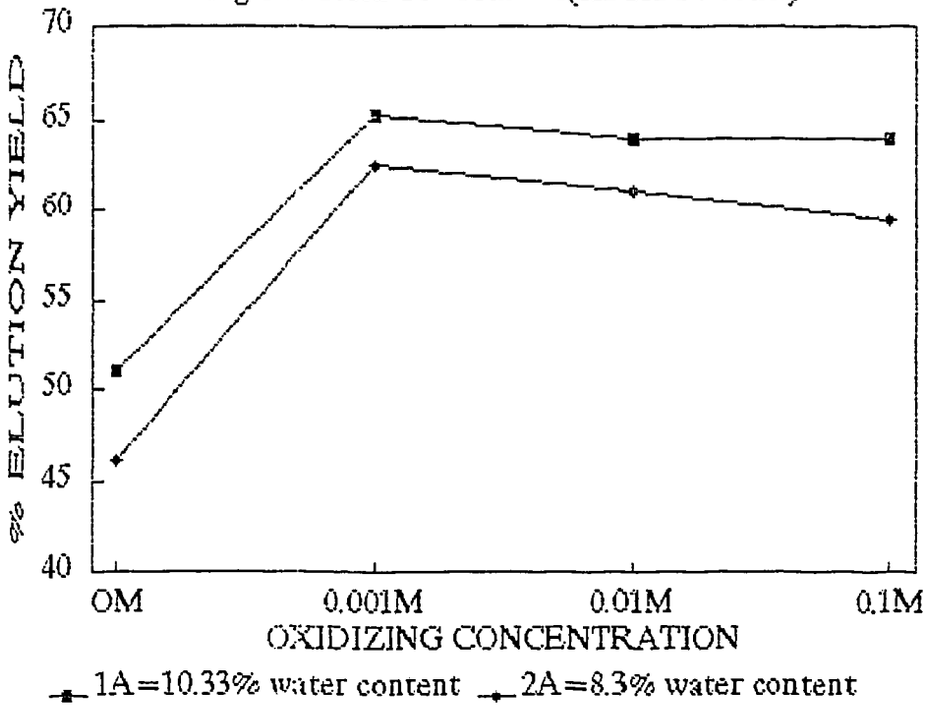
Sample Water content (%)		$K_2Cr_2O_7$ conc/%Yield Tc-99m			
		0 M	0.001 M	0.01 M	0.1 M
1A	10.33	51.1	65.3	64.0	64.0
2A	8.3	46.2	62.5	61.0	59.5
S A M P L E S		A1	A2	A3	A4

Comments:

Results shown in Table 3 are the average of three experiments. The effect of $K_2Cr_2O_7$ 0.001M improve the elution efficiency for samples 1A and 2A . Samples A2 are shown the best values among different concentrations . More experiments were done maintaining constant the oxidizing concentration. See Table 4 and fig 1,2.

EFFECT OF OXIDIZING AGENT ON ELUTION EFFICIENCY

Fig.1 % Yield Tc−99m = f(K2Cr2O7 conc.)



EFFECT OF K2Cr2O7 0.001M ON ELUTION

Fig. 2 % Yield Tc−99m = f (Sample water content)

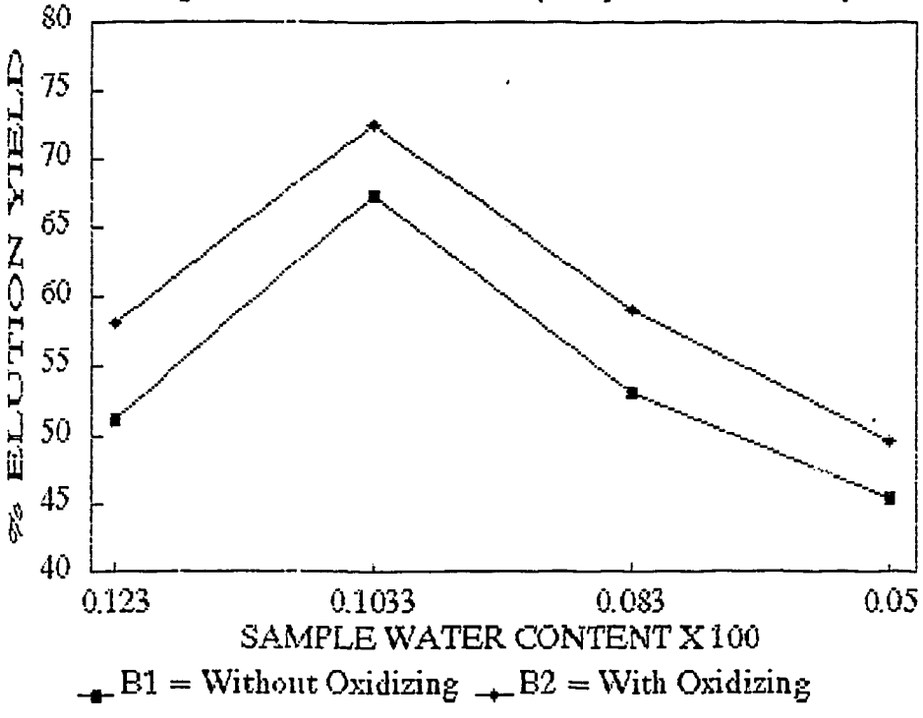


TABLE 4

EFFECT OF $K_2Cr_2O_7$ 0.001M ON ELUTION

Sample Water content (%)		% Yield Tc-99m		uCi Mo-99 / mCi Tc-99m	
		without oxidizing	with oxidizing		
1B	16.2	34	39	7.9	7.5
2B	14.1	39	46	6.6	6.6
3B	12.3	51	58	3	2.9
4B	10.33	56	81	1	1
5B	10.33	51	72	0.8	0.7
6B	10.33	52	69	0.6	0.6
7B	10.33	57	68	0.1	0.2
8B	8.3	53	59	0.1	0.1
9B	5.0	50	53	2	2.1
10B	5.0	41	46	2.1	2.1
S A M P L E S		B1	B2	B1	B2

Comments:

Yields percent showed in Table 4 are an average of daily elutions for each sample . The corresponding values for samples with 10.33% of water content confirm the requirement of prevent the reduction of Technetium forms in the gel matrix putting a chromic solution.

COOLING REACTOR WATER DURING IRRADIATION QUARTZ AMPOULES

Many factors occuring during irradiation in the reactor cause serious changes of the matrix properties,till now usually characterized by the change of the Technetium-99m yield. Their influence seems on the first glance quite unclear, but a critical evaluation can explain all those factors by one common effect. It is the produced heat that increases the local temperature in the matrix, followed by loss of structural water, which causes destruction of the zeolitic structure of the matrix. This causes the substantional decrease of the Tc-99m yield.

To study this effect we have irradiated samples putting the matrix in a sealed quartz ampoules . A group of samples were irradiated in aluminium caps air-tight screw and other group was irradiated in drilled caps with six holes (4mm of diameter each one) to permit water reactor recirculation.

We can see the results in Table 5.

Comments:

From Table 5 we can conclude that it is possible improve the elution efficiency by water reactor recirculation through the aluminium cap.

Both samples C1 and C2 were soaked with chromic solution.

TABLE 5

EFFECT OF REACTOR WATER RECIRCULATION ON QUARTZ AMPOULES

Sample Water content (%)		Elution	% Yield Tc-99m		Mo-99 content per mCi Tc-99m (uCi)
			Al caps sealed	Drilled caps	
1C	10.3	1 2 3	60 60 62	71 71.4 71.5	0.5-1.1
2C	8.3	1 2 3	56 55.4 55.3	61 61.5 62	0.6-1.3
3C	5.0	1 2 3	39 40 39	42 42.5 42.5	1.0-1.5
4C	9.2	1 2	61 61	69 70	2.5-3.5 2.6-2.9
5C	10.5	1 2	62.5 63	70.5 71.1	2.9-3.9 3.0-3.9
S A M P L E S			C1	C2	

BIOLOGICAL SCAN WITH RADIOPHARMACEUTICALS

Biological scans by using radiopharmaceuticals labelled with Tc-99m eluted from Gel generator were done in animals.The imagens obtained are qualified as very good for medicals of the Nuclear Medice Department of Neoplasics Deseases Hospital where was carry out the corresponding Study.

For the last experiment,previously we have done a new serie of irradiations under conditions considered optimum till now. In all cases we got reproductiveness in the results.

The quality control for eluate and radiopharmaceuticals labelled with Tc-99m eluted from Gel generator prepared with these TiMo gave the following set values:

	ELUATE	Tc-99m MDP	Tc-99m TSC	Tc-99m MAA
pH	6.5	-	-	-
Radiochemical Purity	99.9%	98.1	96.5%	98.2%
Mo-99	2.2 uCi / mCi Tc-99m	-	-	-
Al 3+	< 10 ppm	-	-	-
Cr 6+	0.05 ppm	-	-	-
Mo 6+	< 20 ppm	-	-	-
Toxicity	Negative	-	-	-

Whereas the Mo-99 content was relatively high in the most eluates series ,was necessary interpose a second column with 3 g of alumina between TiMo bed column and vacuum vial.The scheme is shown in Fig. 3.

Thus, reach lower the Mo-99 content in eluates until 10-15% of the initial values.(See Table 6)

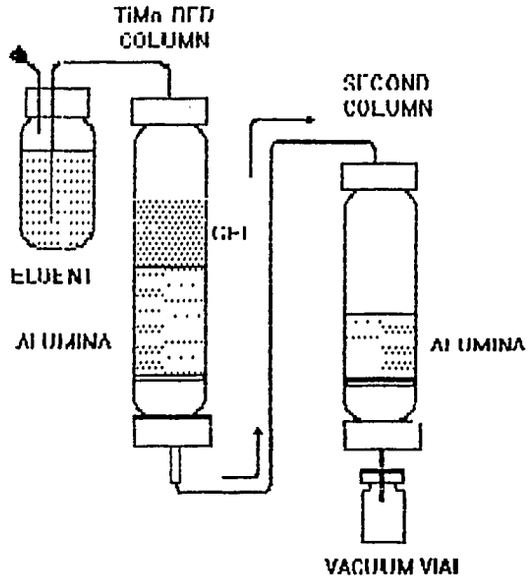


FIG. 3 A SINGLE SCHEME FOR Tc 99m PURIFICATION

TABLE 6

REDUCTION OF Mo 99 CONTENT ELUATE USING A SECOND COLUMN

SET	Eluate Mo-99 content (uCi / mCi Tc-99m)	
	TiMo bed column	Second column
1	3.1	0.30
2	2.2	0.33
3	1.2	0.18
4	1.9	0.20
5	4.8	0.14
6	8.3	0.42
7	5.0	0.22
8	6.6	0.25
9	9.1	0.72
10	6.8	0.33

BATCH LARGE PREPARATION OF TiMo TARGET

Conditions of preparing and drying TiMo, as well as samples preparation using drilled caps containing quartz ampoules have been let us get enough information in order to produce a batch large of TiMo target. Thus we have been prepared 100 g of TiMo target lately. Similar precautions in column load and soaked it with chromic solution and interposing a second column with alumina for the Tc-99m purification were achieved. See the last tests in Table No 7.

TABLE No. 7

Sample	Water content %	% Yield Tc-99m	Mo-99 content after purification x mCi Tc-99m
X1	7.5	58.1	0.083 uCi
X2	8.0	59.4	0.110
X3	8.6	66.9	0.122
X4	9.1	70.2	0.016
X5	9.4	73.4	0.093
X6	10.1	76.1	0.077
X7	10.5	76.2	0.126
X8	11.2	70.2	0.194
X9	11.5	68.8	0.223
X10	12.2	63.5	0.206

CONCLUSIONS

TiMo prepared from Titanium Tetra Chloride supplied by Aldrich Chemical Company was used in all experiments as a starting material. According experimental results,the elution efficiency is affected by Ti:Mo rate, pH of solution after reaction, humidity of the MoTi, drying temperature , oxidizing agent,etc.

The significative increase on elution efficiency when is used Potasium Dichromatic as an oxidizing agent before elution (Table 3 and 4), confirm the importance to add this agent in Generator preparation. In connection reactor water recirculation influence on targets putted in sealed quartz ampoules,new experiments have done lately in order to confirm the advantage of this varying. The utilization of a second column is necessary for reduce Mo - 99 content until reasonable limits.

The reproductiveness of the results have been confirmed preparing a new set of generators with TiMo target produced in a batch large.

On the other hand , preparation of the compact and portable generator will be possible when time irradiation of the RP-10 Reactor whether enoughly more long to produce activities of Mo-99 more than 200 mCi.

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