

## Titanium Molybdate Gels as Matrix of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ Generators

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This work deals with  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generators produced from titanium  $^{99}\text{Mo}$ -molybdate, first synthesized and then irradiated. This method avoids the use of special equipment for the synthesis of radioactive material and reduces the process time which usually is at least 7 h. The effect of four parameters of titanium molybdate gel synthesis on the performance of  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generators and some physico-chemical properties of these gels were evaluated: gel irradiation, titanium solution concentration, effect of the washing gels, and their drying temperature. The data reveal that: (1) the irradiation of the titanium molybdate gels did not influence significantly the generator performance, (2) the dehydration of titanium molybdate gels, the presence of occluded salt in the gel during drying, and the washing of the gels after drying improved the diffusion of the  $^{99\text{m}}\text{TcO}_4^-$  ions and thus the generator performance, and (3) the gels had a three-dimensional structure with cavities which allowed the diffusion of the  $^{99\text{m}}\text{TcO}_4^-$  ions inside the gel and were directly connected with the performance of the titanium  $^{99}\text{Mo}$ -molybdate  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generators.

### 1. Introduction

The development of new techniques to produce radioactive generators is of great importance in nuclear medicine, considering that radioisotopes such as  $^{99\text{m}}\text{Tc}$ , which are widely used as diagnostic agent, are mainly produced by generator systems.<sup>1,2</sup> In these systems, the  $^{99}\text{Mo}$  is normally adsorbed onto an alumina column and the less strongly bound  $^{99\text{m}}\text{TcO}_4^-$  is eluted with isotonic saline solutions at intervals. However, these generators present an inherent disadvantage: the limited adsorption capacity of alumina for Mo(VI) requires the use of very high specific activities of  $^{99}\text{Mo}$  ( $\sim 10^3$  TBq/g).<sup>2-4</sup> To avoid this drawback, alternative methods of generator preparation using low or medium specific activities have been proposed and developed. In particular, the incorporation of  $^{99}\text{Mo}$  into insoluble precipitates is the most studied procedure. Amorphous materials formed for the junction of molybdates with atoms like zirconium, titanium, cerium, thorium, tin, etc. have been examined as  $^{99\text{m}}\text{Tc}$  generator matrices.<sup>2-19</sup> In this case, the content of Mo inside the matrix is about 30% and it is possible to use low or medium specific activities of  $^{99}\text{Mo}$  ( $\sim$  Bq/g).<sup>2,20</sup> Considering that the properties of these generators depend basically upon their preparation conditions, factors as the pH of  $^{99}\text{Mo}$ -molybdates, the molar ratios of X:Mo (X = Zr, Ti, Th, etc.), the concentrations, the order of reactive addition, the drying temperature of the final product, etc., must be carefully studied and determined to reproduce the properties of the gel generators.<sup>2-19</sup>

Our laboratory has developed and evaluated the gel formulation of zirconium molybdate gels and its effect on the performance of  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator.<sup>16,18</sup> The results have shown the technical viability of these  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  gel type generators. However, the highest  $^{99\text{m}}\text{Tc}$  elution efficiencies attained have been about 82%. In addition, the synthesis of these gels using  $^{99}\text{MoO}_3$  requires the use of specialized installations in order to handle radioactive materials and at least a period of 7 h processing time.<sup>16,18</sup> In order to simplify the production process of these  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  gel type generators and taking advantage of

our previous experience with the zirconium molybdate generators, we propose in this work to develop a generator based on titanium-molybdate gels which can be irradiated after being synthesized. The short half life of the only radioisotope produced for the titanium,  $^{51}\text{Ti}$  ( $t_{1/2} = 5.79$  m), during the irradiation of the titanium molybdate gels and the analogue chemical properties of the titanium and the zirconium make feasible the preparation of titanium-molybdate  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generators by this approach.

Vanaja et al.<sup>8</sup> and Nieto and Osso<sup>21</sup> have reported the preparation of a  $^{99\text{m}}\text{Tc}$  generator using neutron irradiated titanium molybdate. The preparation conditions of the titanium molybdates in both works were different: Vanaja et al used  $\text{TiCl}_4$ , and suggests that (1) the irradiation of the gels induced the reduction of  $^{99\text{m}}\text{TcO}_4^-$  directly or via Ti(III), formed by reduction of Ti(IV), (2) the decomposition of the gel forms soluble Mo species if the gels are irradiated at neutron fluence more than  $2 \times 10^{13}$  n  $\text{cm}^{-2}$   $\text{s}^{-1}$ , and (3) the yields of  $^{99\text{m}}\text{Tc}$  depends on the water content of the titanium molybdate<sup>8</sup>; while Nieto and Osso synthesized the gels from  $\text{TiCl}_3$  and  $\text{TiO}_2$ , obtaining best results with  $\text{TiCl}_3$ : a yield of  $^{99\text{m}}\text{Tc}$  about 75% and a good quality  $^{99\text{m}}\text{Tc}$ .<sup>21</sup>

In order to explain the influence of the preparation conditions of the gels on the generator performance, systematic studies on titanium  $^{99}\text{Mo}$ -molybdate gel  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generators were done in this work. The effect of five parameters of titanium molybdate gel synthesis on the  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator performance were evaluated: concentration of the titanium (IV and III) solutions, Ti:Mo molar ratios, effect of the gels washed and the drying temperature, and irradiation of the titanium molybdate gels. The gel physico-chemical properties were also determined in order to establish the connection among the chemistry of the reactant solutions, the gel properties, and the generator performance.

### 2. Experimental Section

**2.1. Preparation of titanium molybdate gels.** The titanium molybdate gels were prepared by adding molybdate solution (80 drops  $\text{min}^{-1}$ ) to  $\text{TiCl}_4$  or  $\text{TiCl}_3$  solutions. The molybdate solutions were prepared from  $\text{MoO}_3$  (1 g) which is

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dissolved in 2 M NH<sub>4</sub>OH. The pH of this solution is then adjusted to 4.5 by adding 4 M HCl. The TiCl<sub>3</sub> (10% wt Sigma Aldrich) solutions were dissolved in H<sub>2</sub>O and 6 M HCl. The TiCl<sub>4</sub> solutions were prepared dissolving TiCl<sub>4</sub> (99% purity FLUKA) in HCl. The dilution was performed in a N<sub>2</sub> atmosphere by means of a special device. This solution was then dissolved in concentrated HCl and the titanium concentration was quantified by spectrophotometric measurements with hydrogen peroxide at 410 nm.<sup>22-24</sup>

The gel was stirred and the pH value was adjusted with 7 M NH<sub>4</sub>OH and dried in the air for 1 day at 40 – 60 °C using an infrared lamp and for a period of 20 h at 40 °C in a stove. The resulting gel was crushed in an agate mortar. One portion of this gel was placed on a funnel to be washed using 200 mL of distilled water and then dried in a stove for 24 h at 40 °C. The gels were synthesized in duplicate at different conditions and four parameters were evaluated: concentration of the titanium solution (series A and E4), Ti:Mo molar ratios (series B), the effect of the washed gels (series C, E), and the drying temperature (series D). Table 1 shows the preparation conditions of titanium molybdate gels for each series.

**2.2. Irradiation of titanium molybdate gels and preparation of <sup>99</sup>Mo/<sup>99m</sup>Tc generators.** The gels were irradiated for 2 h at a neutron fluence of about 1.61×10<sup>13</sup> n cm<sup>-2</sup> s<sup>-1</sup> in the Triga Mark III Reactor (Mexico). After irradiation, about 1.5 g of titanium <sup>99</sup>Mo-molybdate gels (~4.9 MBq/g) were added into a glass column (12 mm × 70 mm) containing a bed of acid alu-

mina (1 g). The column was finally washed with 50 mL of saline solution and eluted every 24 h using 0.9% NaCl for 1 week.

**2.3. Elution of generators and eluate analysis.** The <sup>99</sup>Mo and <sup>99m</sup>Tc activities were measured in a CRC-10R Capintec dose calibrator and an HPGe detector (Canberra 7229P) coupled to a PC-multichannel analyzer (ACUSPECT-A, Canberra). Elution profiles were obtained by collecting 250 µL fractions of 0.9% NaCl solution. The radiochemical purity of the <sup>99m</sup>Tc eluate was determined by paper chromatography using 1 CHR (Whatman®) paper as solid phase and 85% methanol as mobile phase. The R<sub>f</sub> of <sup>99m</sup>TcO<sub>4</sub><sup>-</sup> was 0.66–0.72. Titanium, molybdenum, and aluminium concentrations in eluates were determined by the hydrogen peroxide method measured at 420 nm and 470 nm by the thiocyanate method, and at 535 nm by the aluminon method, respectively.<sup>23-26</sup>

**2.4. Gel characterization.** Gels characterization was achieved by X-ray diffraction (XRD), scanning electron microscopy (SEM), thermogravimetry, infrared spectrometry, and neutron activation analysis (NAA). The X-ray diffraction patterns were obtained on a Siemens D500 diffractometer for 1 h, and scanned from 2.5° to 70° with steps of 0.02°. SEM imaging was performed by means a Philips XL30. Digital images were obtained at 3000X magnifications in randomly selected fields. The thermogravimetric analyses were performed using a Phillips unit at a heating rate of 10 °C min<sup>-1</sup> under a nitrogen atmosphere. The infrared measurements were

**TABLE 1: Preparation conditions of titanium molybdate gels**

Series	Gel	Ti:Mo	T(°C)	pH molybdates	TiCl <sub>4</sub> (M)	pH gel	washing
A	A1	1:1	40	4.5	0.83	5.4	yes
	A2	1:1	40	4.5	0.56	5.4	yes
	A3	1:1	40	4.5	0.3	5.4	yes
	A4	1:1	40	4.5	0.10	5.4	yes
B	B1	1:1	40	4.5	0.83	5.4	yes
	B2	1:2	40	4.5	0.83	5.4	yes
	B3	2:1	40	4.5	0.83	5.4	yes
	B4	1:1	40	4.5	0.56	5.4	yes
	B5	2:1	40	4.5	0.56	5.4	yes
C	C1	2:1	40	4.5	0.83	5.4	no
	C2	2:1	40	4.5	0.83	5.4	yes
	C3	1:1	40	4.5	0.56	5.4	no
	C4	1:1	40	4.5	0.56	5.4	yes
	C5	1:1	40	4.5	0.3	5.4	no
	C6	1:1	40	4.5	0.3	5.4	yes
D	D1	1:1	40	4.5	0.56	5.4	yes
	D2	1:1	100	4.5	0.56	5.4	yes
	D3	1:1	200	4.5	0.56	5.4	yes
	D4	1:1	400	4.5	0.56	5.4	yes

Series	unwashed	washed	Ti:Mo	T(°C)	pH molybdates	TiCl <sub>3</sub> (M)	pH gel
E1	E1A	E1LA	1:1	40	4.5	0.35/HCl	1
	E1B	E1LB	1:1	40	4.5	0.35/HCl	5.9
	E1C	E1LC	1:1	40	4.5	0.35/HCl	8.5
	E1D	E1LD	1:1	40	4.5	0.35/HCl	9.0
E2	E2A	E2LA	1:1	40	4.5	0.35/H <sub>2</sub> O	5.8
	E2B	-	1:1	40	4.5	0.35/H <sub>2</sub> O	8.5
	E2C	E2LC	1:1	40	4.5	0.35/H <sub>2</sub> O	9.0
E3	E3A	E3LA	1:1	40	4.5	0.35/HCl	5.9
	-	E3LB	1:1	150	4.5	0.35/HCl	5.9
	-	E3LC	1:1	400	4.5	0.35/HCl	5.9
E4	E4A	E4LA	1:1	40	4.5	0.35/HCl	8.5
	E4B	E4LB	1:1	40	4.5	0.35/H <sub>2</sub> O	8.5
	E4C	-	1:1	40	4.5	0.7/HCl	8.7

taken on a Nicole Magna-IR<sup>Tm</sup> spectrometer 550 with the samples pressed in KBr pellets.<sup>16</sup>

The gel concentrations of titanium and molybdenum were determined by means of instrumental neutron activation analysis (INAA). The procedure described in previous works was used in the Mo determination.<sup>20</sup> In the case of titanium, 20 mg of each gel and  $\text{TiO}_2$ , used as reference material, were irradiated in the Triga Mark III reactor at a neutron fluence of about  $1.65 \times 10^{12} \text{ n cm}^{-2} \text{ s}^{-1}$  for 30 s. Titanium was determined by the 330 keV  $\gamma$ -ray of  $^{51}\text{Ti}$  by means of a coaxial HPGe detector (7229P, CANBERRA).

### 3. Results

**3.1. Acid-base behavior of titanium molybdate gels.** The  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generators performance depends on gel physico-chemical properties and thus on their preparation conditions. In particular, the gel pH can benefit or damage the formation of indissoluble gels. Our experiments showed that the gels prepared with 0.83 M  $\text{TiCl}_4$  formed indissoluble gels without the need to fix their pH, whereas the gels prepared at other  $\text{TiCl}_4$  concentrations had to adjust their pH values to induce precipitation. Figure 1 shows the typical acid-base behaviour of the titanium molybdates prepared in this work. The shape of the curve is similar to that of a strong acid and indicates that the gel can perform as a strong-acid cation exchanger. It is important to consider that the ammonium ions ( $\text{NH}_4\text{Cl}$ ) were already present in the system before adding the ammonium hydroxide to the gel, as a result of the dissolution of the molybdenum oxide. The presence of the ammonium chloride results in a lower and slightly more sloping curve in the early titration stages.<sup>27</sup> However, the pH change produced by the presence of this salt is less drastic in the strong-acid exchanger.

According to Figure 1, the "apparent" pK of the titanium molybdate gel is about 1.8, which is considered as the acid-base equilibrium of the gel and the ammonium chloride, and a capacity of  $10.7 \text{ meq g}^{-1}$  gel. The acid-base behavior of titanium molybdate gels could thus be expressed by reaction (1):



The neutralization of the charges by the increased pH values causes the decrease of zeta potential and the increase of the electrolytic concentration in the solution. Thus, both effects promote the flocculation of the titanium molybdates. The intrinsic precipitation of the gel prepared from 0.83 M  $\text{TiCl}_4$  can be then explained by the ionic strength of the system which is sufficient to allow to the particles to approach each other and

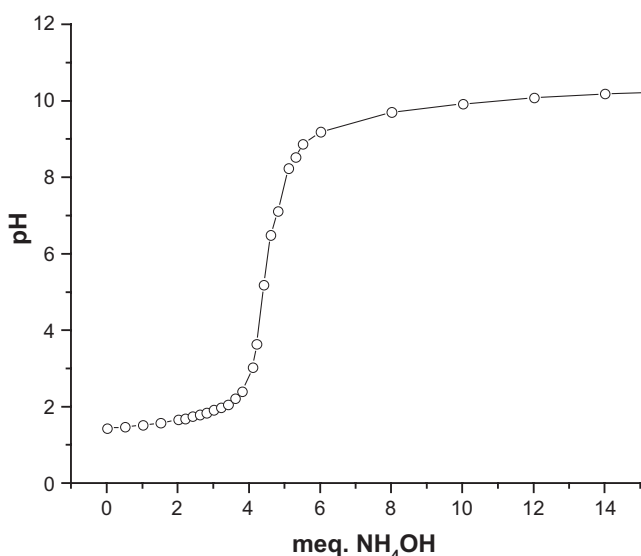


Figure 1. Acid-base behavior of titanium molybdate gel.

aggregate, whereas in the case of the gels prepared with  $\text{TiCl}_4$  concentrations of less than 0.83 M, this ionic strength has to increase by the addition of the  $\text{NH}_4\text{OH}$  solutions to induce the precipitation of the gels. In order to allow the precipitation of the gels and to simplify the interpretation of the results, the gels pH was fixed to 5.4 by adding  $\text{NH}_4\text{OH}$  solutions. Under these conditions the ionic strength was about 1.

**3.2. Performances of  $^{99}\text{Mo}$ -molybdate titanium generators.** Table 2 shows the performances of the titanium  $^{99}\text{Mo}$ -molybdate gel generators obtained for the series A, B, C, D, and E. These data are the average of six elutions performed on each generator.

**3.2.1. Effect of the Ti(IV) concentration (Series A).** An increase of the  $\text{TiCl}_4$  concentration during the preparation of gels causes the augmentation of the elution efficiency and the decrease of the eluate pH values. All these gels showed  $^{99}\text{Mo}$  breakthroughs of more than 0.1% (see Table 2). The gels prepared at higher  $\text{TiCl}_4$  concentrations presented higher  $^{99}\text{Mo}$  breakthroughs. The radiochemical purity was more than 90% except for the gel prepared at a higher  $\text{TiCl}_4$  solution concentration which presented 44% of radiochemical purity. The elution volumes ( $\sim 3 \text{ mL}$ ) and the Al contents ( $< 10 \text{ ppm}$ ) of the  $^{99\text{m}}\text{Tc}$  eluates were not changed by the variation of  $\text{TiCl}_4$  concentration during the preparation of the gels.

**3.2.2. Effect of the Ti:Mo molar ratio (Series B).** An increase of the Ti in the Ti:Mo molar ratio of the gels produced the decrease of efficiency and  $^{99}\text{Mo}$  breakthroughs at the two  $\text{TiCl}_4$  concentrations used (see Table 2). However, these decreases presented different rates in each  $\text{TiCl}_4$  concentration. At 0.83 M  $\text{TiCl}_4$ , efficiency and  $^{99}\text{Mo}$  breakthroughs were reduced in 60% and 95%, respectively, regarding the best efficiency (82%) and its Mo breakthrough value (0.13%), while at 0.56 M  $\text{TiCl}_4$  the decreases were about 20% and 60%, respectively. The increase of Ti produced also an increase of radiochemical purity in the case of the 0.83 M  $\text{TiCl}_4$  solutions, and a decrease when the 0.56 M  $\text{TiCl}_4$  solutions were used. The gels prepared with 0.83 M  $\text{TiCl}_4$  solutions always presented the lowest radiochemical purity ( $< 65\%$ ). The eluate pH values tended to 7.4 when the Ti:Mo molar ratio was 2:1 and increased to 7.7 at Ti:Mo molar ratio of 1:1 and a 0.56 M  $\text{TiCl}_4$  solution concentration. At a Ti:Mo molar ratio of 1:2, the efficiency decreased and the  $^{99}\text{Mo}$  breakthroughs increased about 35% and 97%, respectively, regarding gel values with 1:1 molar ratio and 0.83 M  $\text{TiCl}_4$  solution. The elution volume and the Al content were similar to those of series A: 3 mL and less than 10 ppm, respectively.

**3.2.3. Effect of the washed gel (Series C).** The washing of the gels before drying and irradiation produced a decrease of elution efficiency,  $^{99}\text{Mo}$  breakthroughs, and elution volume; and increase of pH values and radiochemical purity. The elution efficiency decreased to 35% after washing the gel, except for the gel prepared with 0.56 M  $\text{TiCl}_4$  which presented an opposite behavior and its efficiency increased by 15%. These efficiencies were, in all the cases, relatively low ( $\sim 30\text{--}70\%$ ). The washing of the gels reduced the  $^{99}\text{Mo}$  breakthroughs between 55% and 95%, improving considerably the  $^{99\text{m}}\text{Tc}$  eluate radionuclide purity. Nevertheless only the gel prepared with a Ti:Mo molar ratio of 2:1 is within the limits established by the Pharmacopeia ( $< 0.015\% \text{ }^{99}\text{Mo}$ ).<sup>28</sup> The eluate pH values of the unwashed gels were more acidic than their washed homologues which tended toward pH values between 7.4 and 7.8. The elution volume was reduced about 30% in the washed gels remaining at about 3 mL. The radiochemical purity was appreciably improved with the washing of the gels, it increased from 2 to 90% in the gel prepared with 0.3 M  $\text{TiCl}_4$ , but it was reduced in the gel prepared with Ti:Mo molar ratio of 2:1 from 90 to 65%.

**3.2.4. Effect of the drying temperature of the gels (Series D).** The increase of the gel drying temperature had the follow-

TABLE 2: Performance of  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  gel generators based on titanium molybdate- $^{99}\text{Mo}$ 

Gel		$^{99\text{m}}\text{Tc}$ elution Efficiency (%)	$^{99}\text{Mo}$ Breakthrough (%)	Eluate volume (mL)	$^{99\text{m}}\text{Tc}$ Radiochemical purity (%)	$\text{Al}^{3+}$ (ppm)	%Ti	%Mo	pH Eluate	
gels prepared from Ti(IV) solutions										
TiCl <sub>4</sub> (M)										
A1	0.83	<b>82.4</b>	0.132	2.8	44.51	<10	-	-	7.1	
A2	0.56	69.0	0.113	3.0	95.40	<10	19.90	38.12	7.8	
A3	0.3	42.1	0.249	3.0	90.14	<10	21.30	36.56	7.8	
A4	0.100	55.8	0.171	3.0	97.42	<10	20.08	38.35	7.8	
Ti:Mo TiCl <sub>4</sub> (M)										
B1	1:1	0.83	<b>82.4</b>	0.132	2.8	44.51	<10	-	-	7.1
B2	2:1	0.83	32.6	<b>0.006</b>	3.0	65.66	<10	24.02	24.99	7.4
B3	1:2	0.83	53.5	0.246	3.5	71.36	<10	15.24	35.42	6.1
B4	1:1	0.56	69.0	0.113	3.0	95.40	<10	19.90	38.12	7.8
B5	2:1	0.56	55.5	0.046	3.0	77.40	<10	3.36	8.60	7.5
C1	2:1	0.83	52.8	0.121	5.2	90.36	<10	24.02	24.99	7.3
C2	2:1	0.83	32.6	<b>0.006</b>	3.0	65.66	<10	-	-	7.4
C3	1:1	0.56	58.4	0.254	4.3	77.16	<10	-	-	6.5
C4	1:1	0.56	69.0	0.113	3.0	95.40	<10	19.90	38.12	7.8
C5	1:1	0.3	62.2	0.768	4.3	2.64	<10	21.30	36.56	5.3
C6	1:1	0.3	42.1	0.249	3.0	90.14	<10	22.34	36.56	7.8
T(°C)										
D1	40	65.4	0.313	3.6	82.01	<10	19.90	38.12	5.1	
D2	100	75.2	0.109	3.3	83.15	<10	-	-	4.7	
D3	200	82.7	0.037	5.0	81.60	>10	-	-	4.4	
D4	400	90.2	0.009	4.7	86.17	<10	-	-	4.3	
gels prepared from Ti(III) solutions										
	<b>Gel pH</b>	<b>TiCl<sub>3</sub> (M)</b>	<b>unwashed</b>							
E1A	1	0.35/HCl	<b>94.8</b>	<0.0001	4.7	89.53	<10	19.90	39.05	4.8
E1B	5.9	0.35/HCl	90.1	<b>0.0046</b>	4.0	74.82	<10	19.60	43.35	4.4
E1C	8.5	0.35/HCl	72.8	0.0028	4.5	47.02	<10	15.75	32.60	4.4
E1D	9.0	0.35/HCl	64.7	0.0182	3.8	76.15	<10	17.20	35.75	4.4
	<b>Gel pH</b>	<b>TiCl<sub>3</sub> (M)</b>	<b>washed</b>							
E1LA	1	0.35/HCl	95.7	0.0130	3.8	92.54	<10	-	-	5.5
E1LB	5.9	0.35/HCl	95.4	<0.0001	3.7	94.15	<10	-	-	5.9
E1LC	8.5	0.35/HCl	94.3	0.0167	4.0	94.89	<10	-	-	5.7
E1LD	9.0	0.35/HCl	94.6	0.0090	3.8	76.51	<10	-	-	6.0
	<b>Gel pH</b>	<b>TiCl<sub>3</sub> (M)</b>	<b>unwashed</b>							
E2A	5.9	0.35/H <sub>2</sub> O	80.2	0.0266	4.5	95.57	<10	18.62	30.47	4.6
E2B	8.5	0.35/H <sub>2</sub> O	67.5	0.0419	4.0	96.36	<10	15.23	31.52	4.5
E2C	9.0	0.35/H <sub>2</sub> O	69.2	0.0152	4.1	94.56	<10	27.15	31.85	4.4
	<b>Gel pH</b>	<b>TiCl<sub>3</sub> (M)</b>	<b>washed</b>							
E2LA	5.9	0.35/H <sub>2</sub> O	92.7	<0.0001	3.9	96.35	<10	-	-	6.3
E2LC	9.0	0.35/H <sub>2</sub> O	93.5	0.0210	3.9	67.09	<10	-	-	6.5
	<b>Gel pH</b>	<b>T(°C)</b>	<b>washed</b>							
E3LA	5.9	40	95.4	<0.0001	3.7	94.15	<10	19.60	43.35	5.9
E3LB	5.9	150	95.0	0.0066	3.7	72.00	<10	26.25	38.49	6.6
E3LC	5.9	400	95.5	0.0042	3.6	62.24	<10	28.39	38.79	6.4
	<b>Gel pH</b>	<b>TiCl<sub>3</sub> (M)</b>	<b>unwashed</b>							
E4A	8.5	0.35/HCl	72.8	0.0028	4.5	47.02	<10	15.75	32.60	4.4
E4B	8.5	0.35/H <sub>2</sub> O	67.5	0.0419	4.0	96.36	<10	15.23	31.52	4.5
E4C	8.7	0.7/HCl	88.5	0.0008	4.4	52.10	<10	33.35	27.37	4.7

ing effects on the generator performance: rise of the elution efficiency and the elution volume, reduction of the  $^{99}\text{Mo}$  breakthroughs and the eluate pH values, and no significant effect on the radiochemical purity.

**3.2.5. Gels prepared from Ti(III) solutions (Series E).** Series E comprises the titanium  $^{99}\text{Mo}$ -molybdate generators prepared from  $\text{TiCl}_3$  solutions. The effect of four synthesis parameters on the generator performance was evaluated: the gel pH, the Ti (III) concentration, the washing, and drying temperature of the gel.

In the case of the unwashed gels, the increase of the gel pH caused a decrease of the elution efficiency and the radiochemical purity, and an increase of the  $^{99}\text{Mo}$  breakthroughs. High Ti(III) concentrations promoted higher elution efficiencies, and lower  $^{99}\text{Mo}$  breakthroughs and radiochemical purities. The medium used in the preparation of Ti(III) solutions also induced a variation in the generator performance. The gels prepared from  $\text{TiCl}_3$  solutions diluted in  $\text{H}_2\text{O}$  present lower elution efficiencies and higher  $^{99}\text{Mo}$  breakthroughs and radiochemical purities than those prepared with HCl. The volume required to eluate the  $^{99\text{m}}\text{Tc}$  in these generators is about 4 mL with pH of around 4.4.

The washed gels improve considerably the elution efficiencies of the generators and the radionuclide and radiochemical purity of the  $^{99\text{m}}\text{Tc}$  eluates. In general, these parameters are not affected by the variation of the gel pH, the Ti(III) concentration, or the drying temperature of the gel. These generators have elution efficiencies higher than 90%,  $^{99}\text{Mo}$  breakthroughs lower than 0.01%, radiochemical purities higher than 94%, and eluate pH of about 6. Accordingly, the titanium  $^{99}\text{Mo}$ -molybdate gels prepared from  $\text{TiCl}_3$  solutions and washed before being irradiated present the best performance of all generators and can be used in nuclear medicine.

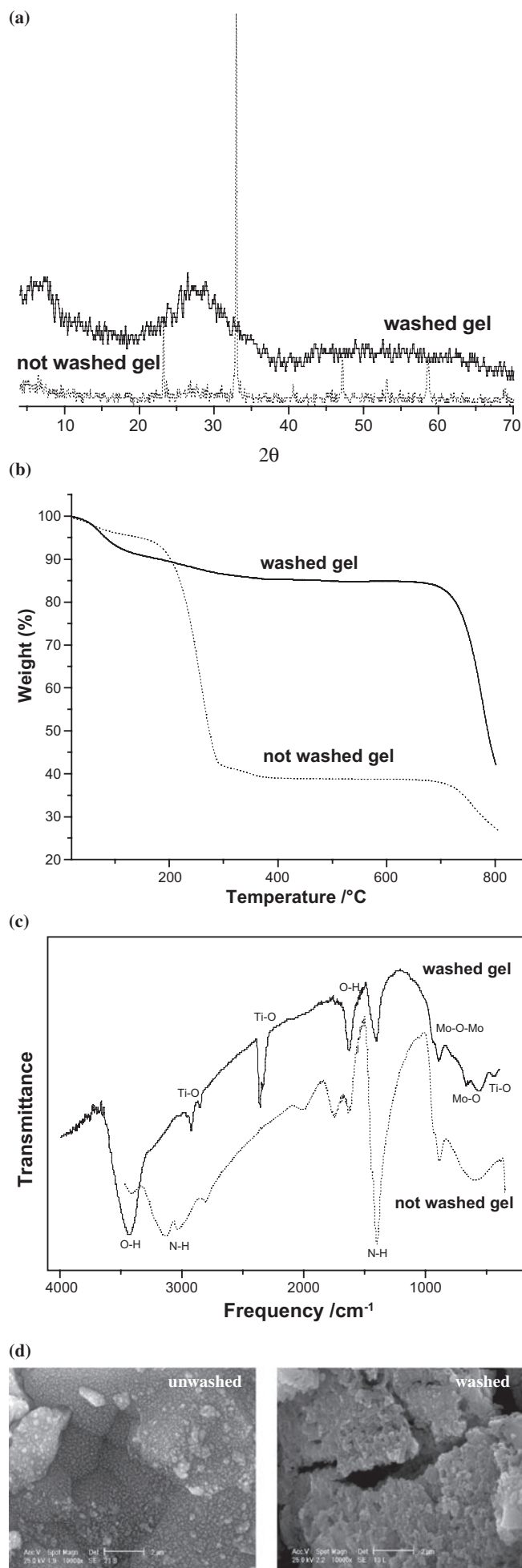
**3.3. Characterization of molybdate titanium gels.** The previous analysis of generator performance as a function of the conditions of gel preparation had shown that the Ti concentration, the Ti:Mo molar ratio, the washing of the gel, and the drying temperature changed the generator performance. In the present section, the effect of these parameters on some physico-chemical properties of the gels was discussed.

**3.3.1. Effect of gel washing.** The analysis of the X-ray diffraction patterns of washed and unwashed titanium molybdate gels (see Figure 2a) showed the presence of an amorphous structure and a crystalline system identified as ammonium chloride. This means that the ammonium chloride formed during the gel synthesis remained in the gel if the latter was not washed.

The thermogravimetric analysis of washed and unwashed titanium molybdate gels (see Figure 2b) showed that the non washed gel suffers a first weight-loss of approximately 5% at 50 °C while the washed gel loses about 15% at 70 °C. In this first step, the gels lost weight by the elimination of water. In the case of the washed gel, an anhydrous gel was formed after the water loss, which was stable until the decomposition of the gel at about 770 °C. The unwashed gel had a large weight-loss (~ 55%) at about 250 °C by the decomposition of ammonium chloride. Later it presented a slight weight-loss at about 345 °C, probably caused by the elimination of intramolecular water, forming the anhydrous gel, and at 775 °C the gel is destroyed. It is important to note that more than 60% of the unwashed gel weight corresponds to the ammonium chloride.

In general, the gels lose between 60 and 78% weight in the washing and this loss increases with an increase of the  $\text{TiCl}_4$  concentration used for the preparation of the gel. The analysis of the washing water showed the presence of ammonium chloride as the principal component and Ti traces (~ 200 ppm). The bulk of this salt was removed with about 40 mL of water which had pH between 4.5 and 5.

The infrared spectra of the washed and unwashed gels are



**Figure 2.** Washing effect of titanium molybdate gels in (a) X-ray diffraction patterns, (b) thermograms, (c) infrared spectra, and (d) morphology.

presented in Figure 2c to confirm the presence of the ammonium group in the unwashed gel and its disappearance in the washed gel. Ammonium displays strong N–H stretching bands in the region of 3300–3500  $\text{cm}^{-1}$  which are located in the same region as those for the O–H bands and a sharp bending band at 1400  $\text{cm}^{-1}$ . It is important to note that the region assigned to the aqueous bending of the unwashed gel is slightly shifted toward lower frequencies. The infrared spectrum of the washed gel loses the 3110 and 3027  $\text{cm}^{-1}$  stretching bands of the N–H bond and the 2800, 1650, and 1400  $\text{cm}^{-1}$  bands emerge, which express the Ti–O, O–H, and Mo–O groups, respectively.<sup>16,29-31</sup> The absorption band at 1750  $\text{cm}^{-1}$  which disappears completely in the washed gel may be assigned to the different arrangement of the Mo–O bond when the ammonium chloride is present at high concentrations. This analysis was also supported by the previously reported spectra of  $\text{Na}_2\text{MoO}_4$ ,  $(\text{NH}_4)_6\text{Mo}_7\text{O}_{24}$ ,  $\text{TiO}_2$ , and  $\text{MoO}_3$  obtained in the same experimental conditions as the gels.<sup>16,31,32</sup>

Figure 2d shows the SEM images of the unwashed and washed gels. In the unwashed gels, the ammonium chloride salt is embedded into the gel and this presents a typical amorphous morphology, while the washed gel is formed as flakes or layers with an appearance similar to clay.

**3.3.2. Effect of the drying temperature on the gels.** The analysis of the change in the X-ray powder pattern during the heating of the gel shows (see Figure 3a) that in the gels heated at 40 and 100 °C the ammonium chloride was the only crystalline phase identified in the diffractograms. At 400 °C, the ammonium chloride disappeared and the gel tended to crystallize incipiently, although its amorphous nature was not eliminated. This fact agrees with the SEM images shown in Figure 3b. At 100 °C the ammonium chloride was distributed inside

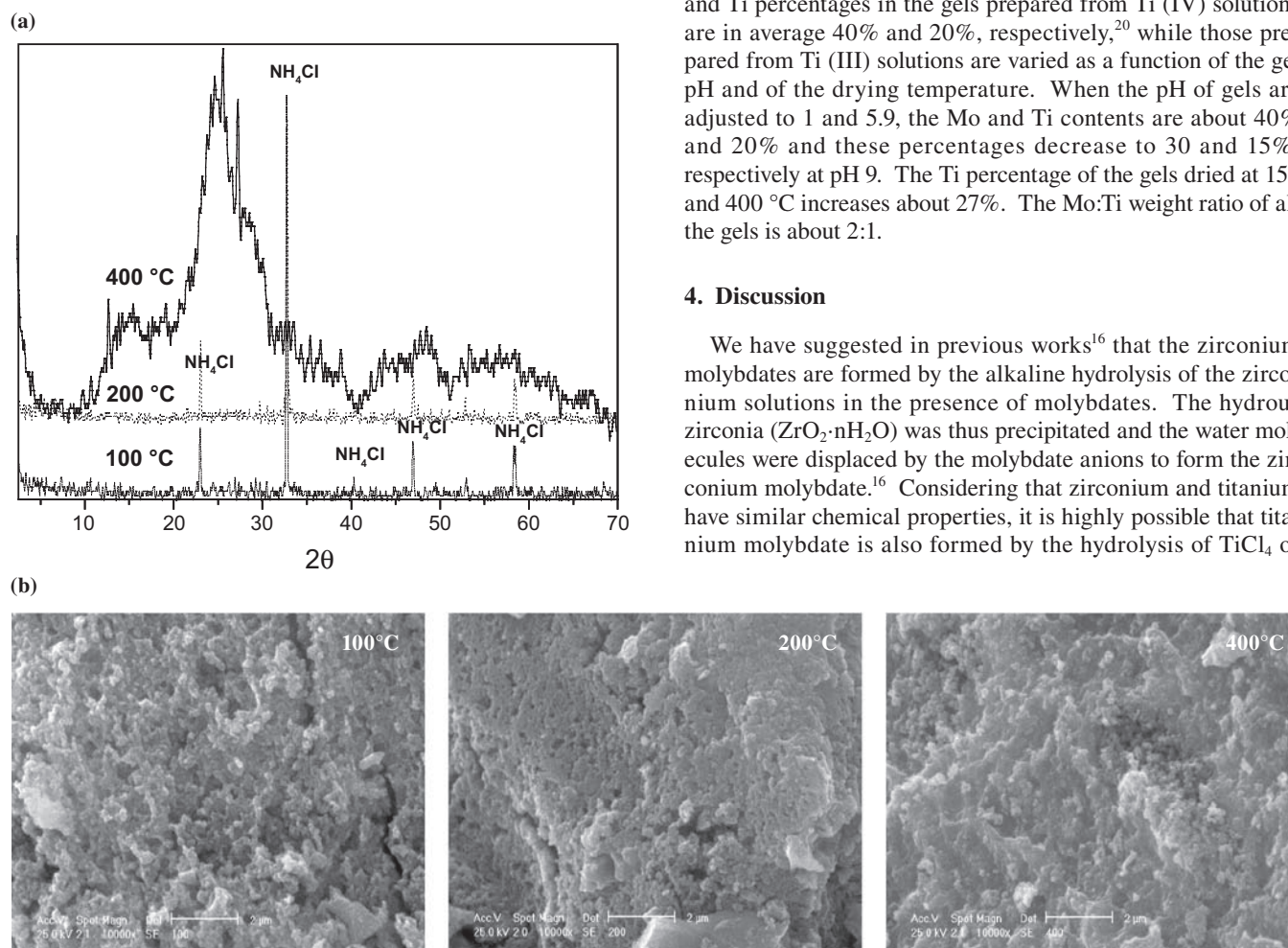
the gel (white particles in the image), and at 200 °C the pores got closer and salt particles were less visible. The morphology of these gels presented a layer or a flake shapes as we have described previously. At 400 °C the gel morphology was similar to that of glass, without the presence of the ammonium chloride particles. The infrared spectra of these gels were similar to those presented in Figure 2c. In particular, the “fingerprint” region was not affected by the drying temperature.

**3.3.3. Effect of gel irradiation.** It is known that the irradiation of the inorganic materials can modify their structure and properties depending on the irradiation conditions.<sup>32</sup> Figure 4a shows the evident transformation of the gel morphology caused by irradiation. The gel prepared with the higher Mo concentration tended to form a glazed structure when it was irradiated, while the gel irradiated and prepared at Ti:Mo = 2:1 molar ratios presented a morphology similar to that of clay, where the atoms were arranged as piled up sheets. In the case of the gel prepared at 1:1 molar ratio, the irradiation also caused a glazed appearance in the gel but less than that of the 1:2 gel. In this matter, the amorphous nature of the gel was mainly caused by the molybdenum. On the other hand, the infrared spectra (Figure 4b) of the irradiated and unirradiated gel (Ti:Mo = 1:1) present practically the same functional groups, however the 2915 and 2850, 692, 562, and 440  $\text{cm}^{-1}$  bands, assigned to the Ti–O group, disappear in the spectrum of the irradiated gel. Thus the irradiation of the gel causes an arrangement change of the Ti–O and Mo–O groups, where the presence and disposition of the Mo–O groups is dominant. In fact, the “fingerprint” region shape of the irradiated gel is very similar to that of the  $\text{MoO}_3$  spectrum.<sup>16</sup> Concerning the change of the X-ray diffraction patterns, the both gels (Ti:Mo = 1:1), irradiated and unirradiated, present an amorphous structure.

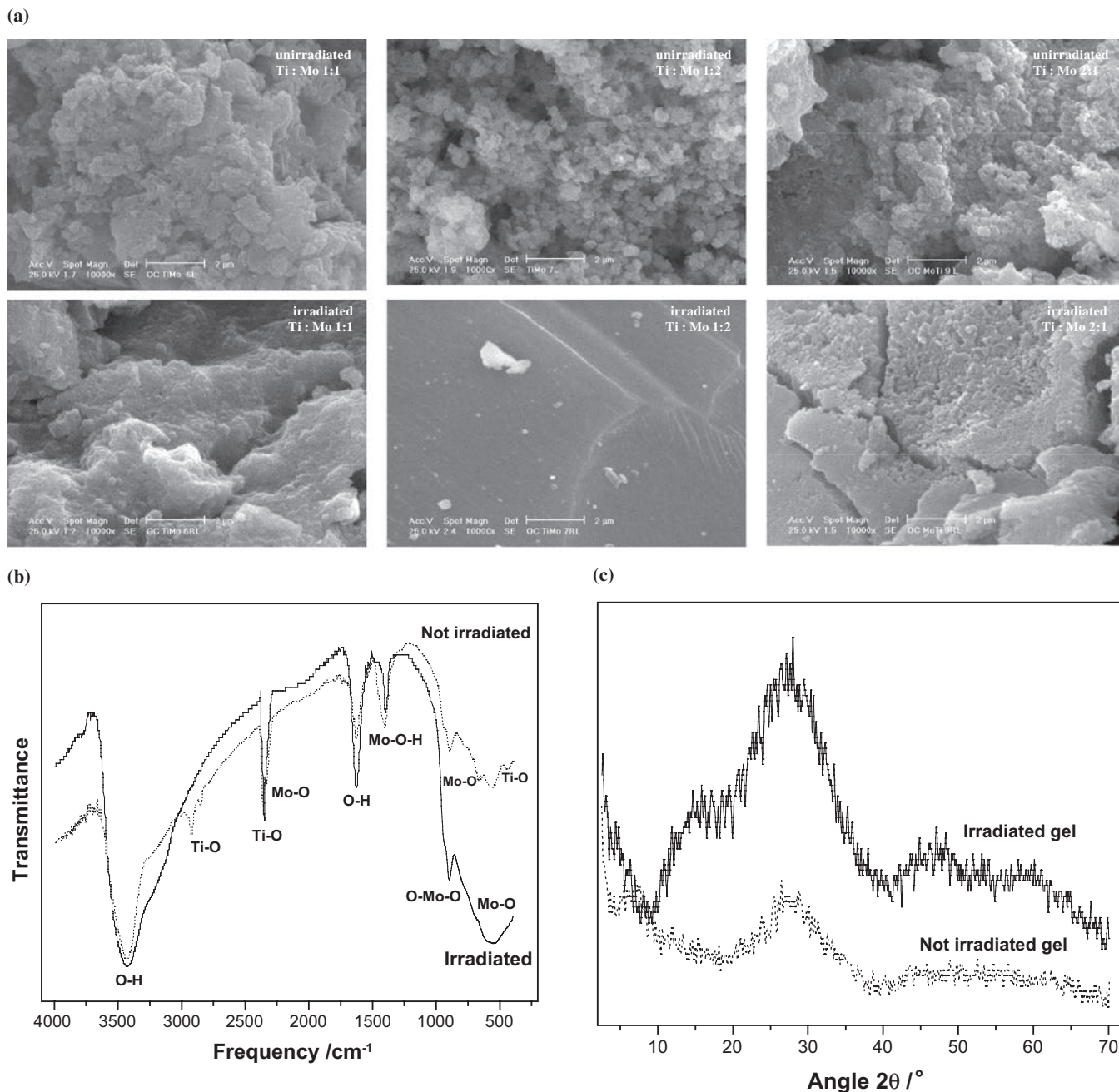
The results of neutron activation analysis show that the Mo and Ti percentages in the gels prepared from Ti (IV) solutions are in average 40% and 20%, respectively,<sup>20</sup> while those prepared from Ti (III) solutions are varied as a function of the gel pH and of the drying temperature. When the pH of gels are adjusted to 1 and 5.9, the Mo and Ti contents are about 40% and 20% and these percentages decrease to 30 and 15%, respectively at pH 9. The Ti percentage of the gels dried at 150 and 400 °C increases about 27%. The Mo:Ti weight ratio of all the gels is about 2:1.

## 4. Discussion

We have suggested in previous works<sup>16</sup> that the zirconium molybdates are formed by the alkaline hydrolysis of the zirconium solutions in the presence of molybdates. The hydrous zirconia ( $\text{ZrO}_2 \cdot n\text{H}_2\text{O}$ ) was thus precipitated and the water molecules were displaced by the molybdate anions to form the zirconium molybdate.<sup>16</sup> Considering that zirconium and titanium have similar chemical properties, it is highly possible that titanium molybdate is also formed by the hydrolysis of  $\text{TiCl}_4$  or

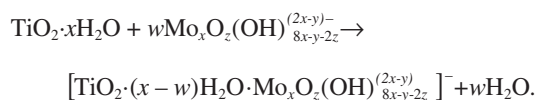


**Figure 3.** Drying temperature effect of the titanium molybdate gel in (a) X-ray diffraction patterns and (b) morphology.



**Figure 4.** Irradiation effect of the titanium molybdate gel in (a) morphology, (b) infrared spectra, and (c) X-ray diffraction patterns.

$\text{TiCl}_3$  [hydrous titanium (IV) ( $\text{TiO}_2 \cdot n\text{H}_2\text{O}$ )] for the molybdate solutions:



According to the literature, the crystalline zirconium molybdate could have the formulae  $\text{ZrMo}_2\text{O}_7(\text{OH})_2 \cdot 2\text{H}_2\text{O}$  and a three-dimensional structure built-up from regular zirconium pentagonal bipyramids [ $\text{ZrO}_5(\text{OH})_2\text{O}_2$ ] and highly distorted molybdenum octahedral [ $\text{cis-MoO}_4(\text{OH})(\text{H}_2\text{O})$ ].<sup>33-35</sup> Since zirconium is tetravalent, the lattice carries a negative electric charge: two elementary charges per zirconium atom. This charge is balanced by alkali or alkaline-earth cations which do not occupy fixed positions, but are free to move in the channels of the lattice framework. These ions act as counter ions and can be replaced by other cations.<sup>27,34-35</sup> Thus, these compounds behave as a very narrow ionic sieve. In the case of the titanium molybdate gels studied in this work, it was possible that their structures were similar to those of the zirconium molybdate

previously discussed. This assumption agreed with our NAA results which show that the Mo:Ti ratio of the gels is about 2:1. Therefore the crystalline titanium molybdate could have a formula and structure that is similar to that of the zirconium molybdate:  $\text{TiMo}_2\text{O}_7(\text{OH})_2 \cdot 2\text{H}_2\text{O}$  with a three-dimensional structure. These data were also supported by our SEM images (see Figures 2d, 3b, and 4a) which showed the presence of a three-dimensional framework with cavities in the gel. These cavities allow the diffusion of ions inside the gel and are directly connected with the performance of the titanium  $^{99}\text{Mo}$ -molybdate generators, in particular the  $^{99\text{m}}\text{Tc}$  elution efficiency and the Mo breakthrough. In addition, the infrared data show that all the gels prepared present two types of bonded water: (1) in the form of hydroxyl bonded to a Mo atom ( $1400\text{ cm}^{-1}$ ) and (2) water molecules present as hydration water inside the crystal lattice or in an adsorbed state ( $3500$  and  $1650\text{ cm}^{-1}$ ). These were congruent with the formula proposed for the crystalline titanium molybdate which contains hydroxyl groups and water molecules. In the case of the precipitated titanium molybdate gels, they could be represented by the empirical formula  $\text{TiMo}_x\text{O}_{2+3x-y}(\text{OH})_{2y} \cdot z\text{H}_2\text{O}$ .<sup>35</sup>

Our infrared spectroscopy data had shown that the titanium molybdate gels prepared at different conditions were practically constituted by the same functional groups and only variations on the intensity of the characteristic bands of each group were observed. These results proved that depending upon the preparation conditions of the gels, the titanium pentagonal bipyramids and molybdenum octahedral were packed differently in the framework, modifying the cavity sizes in the gel (see Figures 2b and 3b), its diffusion properties, and consequently the generator performance.

Considering that titanium molybdate gels act as cation exchangers, the  $^{99m}\text{TcO}_4^-$  ions produced in these generators were not exchanged, and their elution was then governed by a free diffusion mechanism.<sup>16</sup> During the elution, the  $^{99m}\text{TcO}_4^-$  ions diffused within the gel cavities. If the size of the opening was smaller than the diameter of the hydrated  $^{99m}\text{TcO}_4^-$  ion, it would stay captured in the gel and caused a decrease of the elution efficiency of the generator. According to this hypothesis, the dehydration of the gels removed the hydration water allowing a better diffusion of the  $^{99m}\text{TcO}_4^-$  ions and thus the generators prepared from these gels present higher elution efficiency (see Table 2).<sup>8</sup> The presence of occluded salt ( $\text{NH}_4\text{Cl}$ ) in the gel (non washed gels Figure 2b) appeared to be essential during drying for the retention of an open pore structure which was capable of a better free diffusion of the  $^{99m}\text{TcO}_4^-$  ions.<sup>2</sup> This fact agrees with the low efficiencies obtained in the generators prepared from Ti(IV) solutions which were washed before drying (see Table 2). On the other hand, our data had also shown that the washing of the gels after drying improved the elution efficiency and the radionuclide purity (see Table 2, series E), because the lattice cavities are free of  $\text{NH}_4\text{Cl}$  and the  $^{99m}\text{TcO}_4^-$  ions can diffuse easier across the gel.

The titanium solution concentration had an evident effect on the gel generator performance: gels prepared from diluted titanium solutions present lower efficiencies and higher  $^{99}\text{Mo}$  breakthrough than those prepared from concentrated titanium solutions. Considering that diluted solutions of tetrachloride and trichloride titanium could form from hydrolysis of oxychloride titanium, these oxychlorides may block the formation of hydrous titanium (IV) which is essential to precipitate the titanium molybdate gels. In this case, the reaction between the titanium and molybdate solutions produces a mixture of titanium molybdate with titanium and molybdate species in solution or precipitated (oxy-hydroxide phases), causing an increase of the  $^{99}\text{Mo}$  breakthrough in the eluates, especially if the gels were not washed after drying.

The amorphous materials were less perturbed by the introduction of defects due to irradiation than those related with crystal structure.<sup>36</sup> The irradiation of the titanium molybdate gels, shown in this work, did not influence appreciably the generator performance (see Table 2) although the irradiated titanium molybdate gels suffered a slight change in their morphology (amorphization), structure (arrangement of the Ti–O and Mo–O groups) and sometimes in their color (see Figure 4). These results showed the feasibility of producing gel generators based on titanium molybdate which could be irradiated after being synthesized. This approach will reduce the preparation time of gel generators and eliminates the use of specialized installations.

## 5. Conclusion

Titanium molybdate gels were amorphous materials which act as cation exchangers, and their flocculation was favored by the increase of the ionic strength. These gels could be represented by the empirical formula:  $\text{TiMo}_x\text{O}_{2+3x-y}(\text{OH})_{2y}z\text{H}_2\text{O}$  and a three-dimensional structure with cavities which allowed the diffusion of ions inside the gel. Cavity sizes were directly related to the performance of titanium  $^{99}\text{Mo}$ -molybdate genera-

tors. Depending upon the preparation conditions of the titanium molybdate gels, the titanium pentagonal bipyramids and molybdenum octahedral were packed differently in the framework, modifying the cavity sizes in the gel, its diffusion properties and so the generator performance. The dehydration of the titanium molybdate gels, the presence of occluded salt in the gel during drying and the washing of the gels after drying improved the diffusion of the  $^{99m}\text{TcO}_4^-$  ions, the elution efficiency and in general the generator performance. The irradiation of the titanium molybdate gels did not influence significantly the generator performances. It was feasible to produce titanium  $^{99}\text{Mo}$ -molybdate generators preparing first the titanium molybdate gels and later irradiating them. This approach will reduce the preparation time of the gel generators and eliminates the use of specialized installations.

Practically, all the  $^{99m}\text{TcO}_4^-$  eluates obtained from the generators prepared from gels washed before irradiation and from  $\text{TiCl}_3$  solutions satisfied the Pharmacopoeias.<sup>28</sup> The best generator performances were obtained using the gels prepared from 0.35 M HCl  $\text{TiCl}_3$  solutions, adjusted to pH 5.9, dried at 40 °C, and then washed.

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