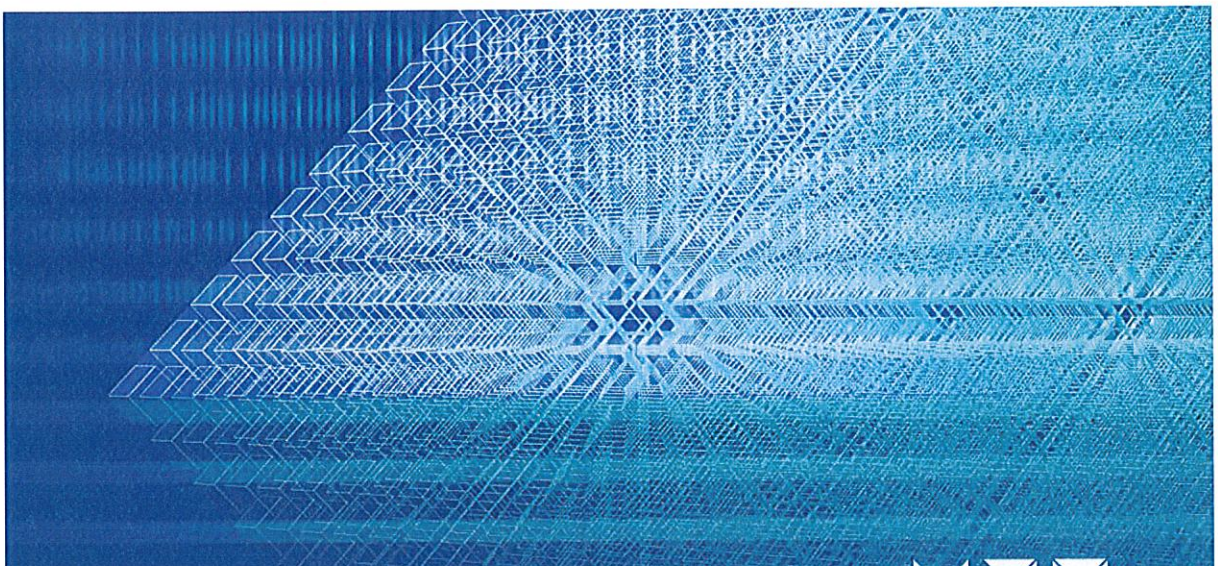

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# Therapeutic Radionuclide Generators: $^{90}Sr/^{90}Y$ and $^{188}W/^{188}Re$ Generators

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# FOREWORD

Rapid progress in preclinical and clinical research realized over the past two decades has stimulated broad interest in the use of radionuclides for targeted therapy of cancer and for other therapeutic applications using unsealed sources. The use of radiopharmaceuticals labelled with short lived radioisotopes for these applications has advantages such as higher rates of dose delivery and shorter hospital stays. Wider use of targeted therapy using radiopharmaceuticals requires the reliable availability of cost effective products of short lived radionuclides from dependable sources and suppliers. The use of short lived radionuclides is thus often restricted to places with local production of these radionuclides or places that are well connected to production facilities. An important additional strategy is the use of radionuclide generator systems that utilize parent radionuclides with long physical half-lives of months or years. The daughter can be extracted from these radionuclide generators at periodic intervals to obtain short lived radionuclides for formulation of therapeutic radiopharmaceuticals. Hence, there is great interest in developing technologies for therapeutic radionuclide generators.

To address this need, the IAEA implemented a coordinated research project (CRP) on the development of generator technologies for therapeutic radionuclides. This publication is based on the work carried out at participating institutions in several Member States aimed at developing generator prototypes using various separation techniques. The two radionuclide generators described in this publication are based on $^{90}Sr/^{90}Y$ and $^{188}W/^{188}Re$ generator systems. Strontium-90 has a physical half-life of over 28 years, and $^{188}W$ has a physical half-life of 69 days. Radionuclide generators prepared from these long lived parents can serve as convenient production systems to provide the therapeutic radioisotopes $^{90}Y$ and $^{188}Re$ on a routine basis. By adapting the technologies described in this publication, $^{90}Sr/^{90}Y$ and $^{188}W/^{188}Re$ generators can be fabricated for cost effective production of $^{90}Y$ and $^{188}Re$ for radiopharmaceutical preparation.

The IAEA thanks all the participants in the CRP for their contributions to this publication and F.F. Knapp, Jr., for his valuable help in editing this report. The IAEA officer responsible for this publication was M.R.A Pillai of the Division of Physical and Chemical Sciences.

# Chapter 20

# PREPARATION OF INORGANIC POLYMER SORBENTS AND THEIR APPLICATION IN RADIONUCLIDE GENERATOR TECHNOLOGY

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**Abstract**

Adsorbents based on poly zirconium compound (PZC) and poly titanium compound (PTC) were synthesized for the preparation of $^{188}W/^{188}Re$ generators. The chemical composition, molecular structure and physicochemical characteristics of these adsorbents were investigated. The adsorption properties of PZC and PTC sorbents in different tungstate solutions and the elution performance were investigated. Tungsten adsorption capacities of about 520 mg of tungsten per gram of PZC and 515 mg of tungsten per gram of PTC and a $^{188}Re$ elution yield greater than 80% for both PZC and PTC sorbents were achieved. A $^{188}Re$ eluate concentration process was developed by eluting $^{188}Re$ from the tandem system of $^{188}W$-PTC–alumina columns with two different concentrations of saline solution, which gave a concentration factor of about 6. The technology developed can be used for the preparation of clinically applicable $^{188}W/^{188}Re$ generators using low specific radioactivity $^{188}W$ produced in medium flux research reactors.

## 20.1. INTRODUCTION

Tungsten-188 is produced via the $^{186}W$ (nn,$\gamma$) $^{188}W$ reaction using high neutron flux reactors, which are available in only a handful of countries around the world. However, $^{188}Re$ generators can be produced using imported $^{188}W$ solution, provided that an appropriate generator technology is used. The literature contains studies of $^{99m}Tc$ generator technologies using gel or zirconium/titanium polymer based sorbents to produce $^{188}W/^{188}Re$ radionuclide generators [20.1–20.5]. Here, zirconium and titanium inorganic polymer sorbents were studied for the preparation of $^{188}W/^{188}Re$ generators.

## 20.2. MATERIALS AND METHODS

### 20.2.1. Preparation of PZC and PTC sorbents

PZC and PTC sorbents were synthesized from isopropyl alcohol (iPrOH) and anhydrous metallic chloride under strictly controlled reaction conditions. A given amount of anhydrous metallic chloride ($ZrCl_4$ for PZC; $TiCl_4$ for PTC) was carefully added to different amounts of iPrOH. The temperature of the reaction mixtures immediately reached 96–98°C for iPrOH-$ZrCl_4$ and 92–94°C for iPrOH-$TiCl_4$, where it was maintained. Solutions were stirred gently using a magnetic stirrer in open air until they became viscous. As the reaction temperature increased, a water soluble gel (the intermediate precursor) was formed at 129–131°C for the PZC sorbent and at 111–113°C for the PTC sorbent. The water insoluble, solid PZC or PTC materials of particle sizes from 0.10 to 0.01 mm were formed by maintaining the reaction temperature at 141–142°C (30 min) for PZC and at 124–126°C (45 min) for PTC. The preparation conditions for the different batches of the synthesized PZC and PTC samples are summarized in Tables 20.1 and 20.2.

TABLE 20.1. CONDITIONS FOR THE CHEMICAL SYNTHESIS OF DIFFERENT PZC SAMPLES

| Sample | $ZrCl_4$ weight (g) | Volume of isopropyl alcohol (mL) | Reaction temperature at final stage (°C) |
|---|---|---|---|
| $PZC_1$ | 50 | 40 | 141–142 |
| $PZC_2$ | 50 | 80 | 141–142 |
| $PZC_3$ | 50 | 100 | 141–142 |

TABLE 20.2. CONDITIONS FOR THE CHEMICAL SYNTHESIS OF DIFFERENT PTC SAMPLES

| Sample | $TiCl_4$ weight (g) | Volume of isopropyl alcohol (mL) | Reaction temperature at final stage (°C) |
|---|---|---|---|
| $PTC_1$ | 40.7 | 40 | 124–126 |
| $PTC_2$ | 40.7 | 80 | 124–126 |
| $PTC_3$ | 40.7 | 100 | 124–126 |

### 20.2.2. Investigation of the chemical composition, structure and physicochemical properties of the PZC and PTC sorbents

The zirconium and titanium contents were analysed by the gravimetric method of ignition of the sorbent samples at 1200°C for 2 h. The $ZrO_2$ and $TiO_2$ were weighed, and the zirconium and titanium contents were calculated. The carbon, hydrogen and oxygen contents of the PZC and PTC samples were determined by thermal decomposition of the sorbents on a Perkin Elmer 2400 II instrument. The chlorine content of the sorbents was analysed by thermal decomposition of the samples. The decomposed HCl product was trapped in an alkaline solution and the $Cl^-$ content was determined by ion chromatography. Thermal analysis of the sorbent samples was carried out using an MB-7H derivatographer instrument with an $N_2$ gas flow rate of 50 mL/min and a heating rate of 10°C/min. Potentiometric titration of PZC and PTC samples was carried out with 0.1 g of PZC or PTC sorbent samples in 60 mL of 0.1M NaCl solution. The titration solution was 0.1M NaOH solution.

Infrared spectra of sorbent samples were recorded on a Brucker-IFS 48, Carlo Erba-GC 6130 instrument. X ray diffraction patterns of sorbent samples were recorded on a Rigaku Miniflex diffractometer with a CuK$\alpha$ ray and CuNi filter at 40 KV/20 mA.

### 20.2.3. Adsorption and elution patterns of $^{188}W/^{188}Re$ generators

A radioactive $^{188}W$ solution with a concentration of 25.6 mg W/mL at pH7 was added to the PZC or PTC sorbent samples (0.75 g weight), which were then gently shaken in a water bath at 50°C overnight. After shaking, the samples were allowed to stand and a portion of clear supernatant solution was removed to measure the $^{188}W$ radioactivity. The remaining solution was decanted to obtain the solid sorbent portion. These solid PZC or PTC samples were packed on 8 mL glass columns and washed with 50 mL of water followed by 10 mL of saline. Activity levels of 5–10 mCi of $^{188}W$ were used in all column experiments. Elution yield, $^{188}W$ breakthrough and tungsten elemental content were determined for each elution.

### 20.2.4. PZC or PTC sorbent based $^{188}Re$ elution concentration systems

Investigation of the $^{188}Re$ concentration process was carried out by eluting $^{188}Re$ from the $^{188}W$-PTC column with a 0.005% saline solution; this eluate was passed through a small alumina column where all $^{188}ReO_4^-$ was retained. The $^{188}ReO_4^-$ was subsequently eluted with a small volume of physiological saline.

## 20.3. RESULTS AND DISCUSSION

### 20.3.1. Synthesis and specification of PZC and PTC sorbents

Both the PZC and the PTC sorbents were light brown in colour and changed to white when soaked in water. These particles swelled in water and were hydrolyzed to give an acidic solution, while the solid matrix of the sorbents remained insoluble. The volume of swollen PZC was 1.25 and that of the PTC bed was 1.35 times that of the dry gel. The adsorption capacities of both PZC and PTC sorbents decreased with an increase of the reaction temperature, whereas an increase of the molar ratio of the reactants (isopropyl/$MeCl_4$) resulted in a higher degree of swelling of sorbent particles in aqueous solution. This swelling phenomenon favoured diffusion of the tungstate ions into the solid matrix of the sorbents during the adsorption process. However, the swelling of particles also gives rise to a decrease of their mechanical stability. For further investigations, the PZC2 and PTC2 sorbent samples were used owing to their favourable stability.

### 20.3.2. Chemical composition and molecular formula of PZC and PTC sorbents

The results of chemical and thermal analysis are given in Tables 20.3 and 20.4. Based on these results, the molecular structure of the PZC and PTC sorbents was calculated. The molecular weight (including organic residue) was determined to be M = 5901.3. Organic residue in the PZC molecule was equivalent to 9.63% of the PZC molecular weight, as was seen with thermal analysis. Because the organic substance in this formula was attributed to a residual organic by-product of the chemical synthesis reaction and was completely released from the polymer matrix in aqueous solution, the segment unit of the real polymer compound is assumed to have the following formula: $[Zr_{15}(OH)_{30}Cl_{30}(ZrO_2)\cdot 126\ H_2O]_n$.

TABLE 20.3. CHEMICAL COMPOSITION OF PZC SORBENT

| Element | Cl | H | Zr | O | $H_2O$ | (H + O + C) Organic |
|---|---|---|---|---|---|---|
| Content (% weight) | 17.90 | 0.505 | 24.92 | 8.74 | 38.31 | 9.63 |
| Atomic ratio | 1.87 | 1.87 | 1 | 2 | 7.83 | (Not calculated) |

TABLE 20.4. CHEMICAL COMPOSITION OF PTC SORBENT

| Element | Cl | H | Ti | O | $H_2O$ |
|---|---|---|---|---|---|
| Content (% weight) | 18.965 | 0.535 | 43.87 | 29.33 | 7.3 |
| Atomic ratio | 0.584 | 0.584 | 1.0 | 2.001 | 0.443 |

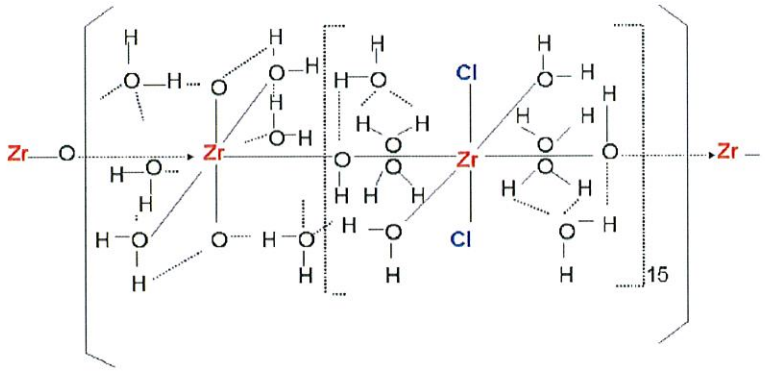


*FIG. 20.1. Proposed arrangement of atoms in PZC polymer.*

The proposed steric arrangement of atoms in the PZC molecule is shown in Fig. 20.1.

The ion exchange capacity derived from the above chemical formula offers an adsorption capacity of 517.1 mg of tungsten per gram of PZC by assuming that tungstate ions are adsorbed on PZC in the form of $WO_4^{2-}$. In addition, it is assumed that one molarity of $WO_4^{2-}$ ion consumes 2 equivalents of ion exchange capacity of PZC and PTC sorbents (one equivalent of $WO_4^{2-}$ ion is 91.92 g). This type of strong adsorption suggests a covalent bond between tungstate ions and the zirconium metal atom.

The molecular formula of the PTC sorbent was calculated to be $[Ti_{40}\,Cl_{80}\,(OH)_{80}\,(TiO_2)_{97}{\cdot}60H_2O]_n$. The proposed molecular structure of PTC is depicted in Fig. 20.2.

The chlorine content of the PTC sorbent is 5.35 millimole per gram of PTC sorbent (18.96% of chlorine element in 1 g of PTC). This is equivalent to the ion exchange capacity of 5.35 meq per gram of PTC sorbent and consequently offers a very high adsorption capacity of 491.8 mg of tungsten per gram of PTC by assuming that the tungstate ions are adsorbed on PTC in the form of $WO_4^{2-}$, and that one molarity of $WO_4^{2-}$ ion consumes 2 equivalents of ion exchange capacity of PTC sorbent. This type of strong adsorption gives a covalent bond between molybdate or tungstate ions and the titanium metal atom.

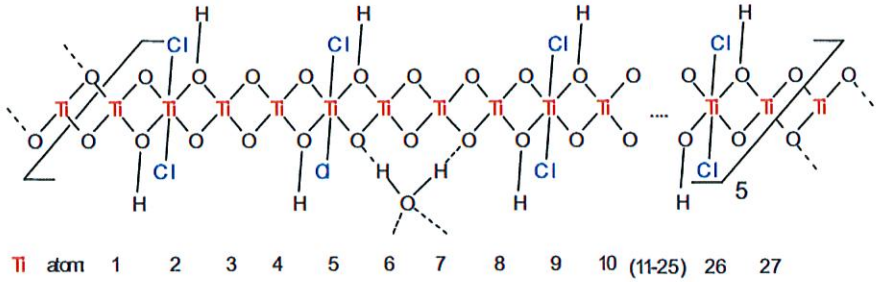


*FIG. 20.2. Proposed arrangement of atoms in PTC polymer.*

The adsorption capacity of both sorbents was varied depending on the temperature, reaction time and gel ageing process before the solid PZC and PTC polymers were formed. The actual adsorption of PZC and PTC sorbents, which is to some extent higher than the values mentioned above, accounted for the non-covalently adsorbed tungstate ions and/or for adsorption of small amounts of polytungstate ions. These polyanions could be formed at the beginning stage of adsorption owing to the strongly acidic medium resulting from the hydrolysis of the -Zr-Cl (or -Ti-Cl) groups of the backbone of the PZC or PTC molecules. These types of weak adsorption of the polytungstate ions result in higher tungstate breakthrough when loaded with high tungstate concentration. The infrared adsorption patterns of PZC and PTC are given in Table 20.5.

Good agreement was found between these results and the infrared absorption data of the $ZrO_2 \cdot xH_2O$ and $TiO_2 \cdot xH_2O$ samples. The organic trace amount retained in the PZC and PTC, detected at 2900 $cm^{-1}$, is assigned to

TABLE 20.5. INFRARED ADSORPTION OF PZC AND PTC SORBENTS

| Wave number ($cm^{-1}$) | Intensity | Chemical bond characteristics | Specified group |
|---|---|---|---|
| 3353 | Very strong (broad) | $\nu$ (OH) | OH in Zr-OH, Ti-OH and in $-CH_2-CH(OH)-CH_3$ |
| 3300 | Very strong | $\nu(OH_3^+)$ | |
| 2900 | Very strong | $\nu$ (CH) | $-CH_2-CH_2-$ |
| 2900 | Weak | $\nu(H_3O^+)$ | |
| 1619 | Medium | $\delta(H_2O)$ | |
| 666 | Medium | $\nu$ (Zr-O) | |

organic by-products of the chemical synthesis reaction, but not to the isopropyl alcohol reactant. X ray diffraction analysis results showed an amorphous structure of the PZC and PTC sorbents.

### 20.3.3. Behaviour of PZC and PTC sorbents in the aqueous solution

The results of potentiometric titrations of PZC and PTC sorbents are shown in Fig. 20.3. An ion exchange capacity of 5.65 meq $H^+$ per gram of PZC was found at pH11. This amount is equivalent to 5.65 meq $Cl^-$ per gram of PZC and agrees with the chlorine content of PZC found in the thermal analysis mentioned above. There is good agreement between the ion exchange capacity values as estimated by titration results and the molecular formulas of the PZC and PTC compounds.

The behaviour of PZC in aqueous solution can be summarized as follows: PZC sorbent is hydrolyzed, but not dissolved, in aqueous solution and gives an acidic solution (pH1.6) in water. This PZC product is mainly composed of (-ZrO-) and (-$ZrO^+Cl^-$-) groups bonded together. The HCl formed during hydrolysis makes the water strongly acidic.

In open air, the PZC adsorbs water molecules from the humid environment and a very strong acidic medium is formed in the PZC particles. This acidity destroys the -ZrO-$(ZrO)_n$-ZrO- bonds and, after three weeks of standing in open air at room temperature, makes the PZC sorbent soluble in water. The PZC sorbent contains a minor quantity of unidentified organic compounds (2.53% carbon, 1.96% hydrogen and 5.14% oxygen). This organic substance is released when PZC adsorbent is hydrolyzed in aqueous solution.

Potentiometric titration of PTC sorbents gave similar results: 5.35 meq $H^+$ per gram of PTC capacity was found for PTC sorbent at pH11. The hydrolysis property of the PTC sorbent is similar to that of the PZC sorbent.

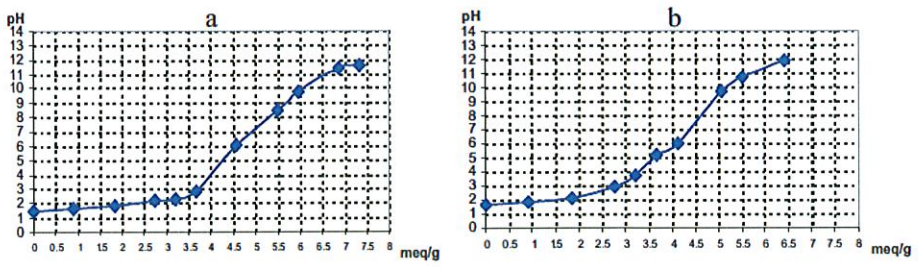


*FIG. 20.3. Potentiometric titration curve of PZC (a) and PTC (b) sorbents.*

### 20.3.4. Tungsten adsorption and $^{188}$Re elution performance of PZC and PTC sorbents

Tungsten adsorption capacity and other characteristics of PZC and PTC samples versus adsorption time are given in Table 20.6. Rhenium-188 elution profiles using PTC and PZC columns loaded with 1 g of sorbents are shown in Figs 20.4 and 20.5, respectively. These studies demonstrate that the sorbents fulfill the requirements in use for preparation of chromatographic $^{188}$W/$^{188}$Re generators.

### 20.3.5. Effect of tungsten content on adsorption capacity, $^{188}$Re elution yield and tungsten breakthrough

Table 20.7 summarizes the results of the effect of the tungsten content in the solution used for adsorption by the sorbents. Adsorption of tungsten increased with increasing concentration of tungsten, indicating higher capacity at higher tungsten concentrations. However, the percentage of adsorption decreased with an increase of tungsten concentration. Tungsten breakthrough from $^{188}$W-PZC and $^{188}$W-PTC columns increased with the increasing tungsten content of adsorption solution. This is attributed to the weakly bound tungstate ion on the sorbent particle surface. Rhenium-188 elution yields showed lower yields at both low and high tungsten load concentrations with both sorbents.

TABLE 20.6. TUNGSTEN ADSORPTION CHARACTERISTICS OF THE PZC2 AND PTC2 SORBENTS

| Sorbent sample | Tungsten adsorption capacity (mg of tungsten per g of sorbent)[a] | Particle size of sorbent (mm) | Swelling in $H_2O$ (% volume) | Reaction time (min) | Re-188 elution yield (%) |
|---|---|---|---|---|---|
| PZC2-1 | 515.2 | 0.1–0.001 | 22.5 | 30 | 90.3 |
| PZC2-2 | 520.1 | 0.1–0.001 | 24.4 | 45 | 91.2 |
| PZC2-3 | 541.2 | 0.1–0.001 | 29.3 | 50 | 88.3 |
| PTC2-1 | 492.2 | 0.1–0.001 | 23.5 | 35 | 89.2 |
| PTC2-2 | 515.1 | 0.1–0.001 | 26.3 | 45 | 90.4 |
| PTC2-3 | 521.3 | 0.1–0.001 | 28.5 | 60 | 93.4 |

[a] The tungsten adsorption capacity of the PZC and PTC sorbents in tungstate solution at a concentration of 25.6 mg W/mL at pH7 (the pH of the post-adsorption solution was 4.5).

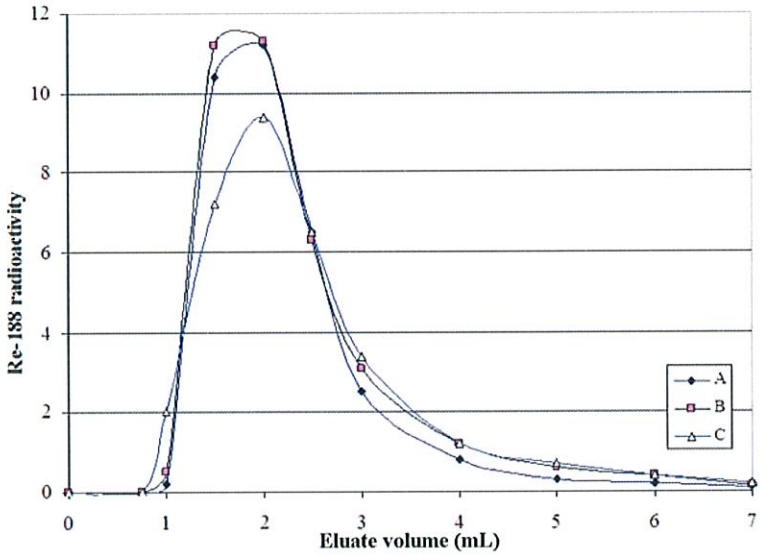


*FIG. 20.4. $^{188}$Re elution profiles of three different $^{188}$W-PTC columns loaded with 1.0 g of sorbent samples (PTC2); elution performed with 0.9% saline.*

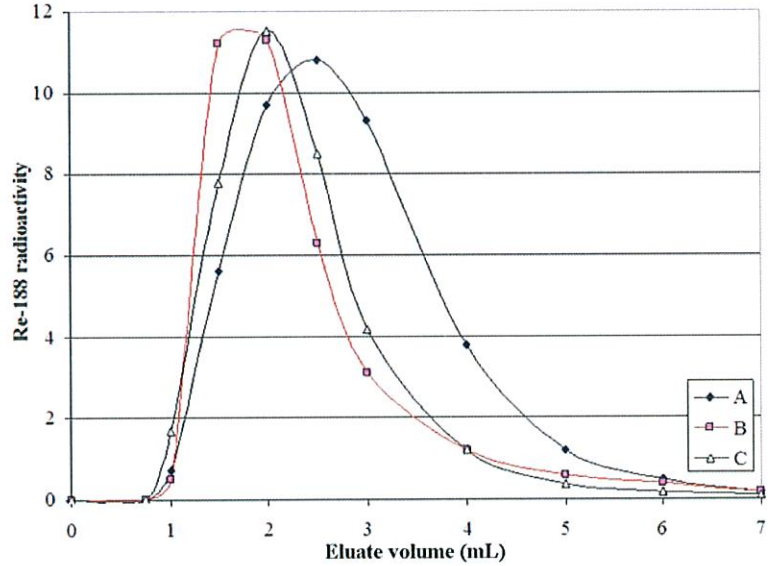


*FIG. 20.5. $^{188}$Re elution profiles of three different $^{188}$W-PZC columns loaded with 1.0 g of sorbent samples (PZC2); elution performed with 0.9% saline.*

TABLE 20.7. EFFECT OF SOLUTION'S TUNGSTEN CONTENT ON ADSORPTION CAPACITY OF SORBENT AND ON ELUTION YIELD AND TUNGSTEN BREAKTHROUGH OF Re-188 ELUATE

| Sample[a] | PZC2-1 | PZC2-2 | PZC2-3 | PZC2-4 | PTC2-1 | PTC2-2 | PTC2-3 | PTC2-4 |
|---|---|---|---|---|---|---|---|---|
| Weight of sorbent (g) | 0.20 | 0.20 | 0.20 | 0.20 | 0.20 | 0.20 | 0.20 | 0.20 |
| Volume of tungsten solution (mL) | 3.75 | 4.50 | 5.25 | 6.00 | 3.75 | 4.50 | 5.25 | 6.00 |
| Tungsten content of adsorption solution (mg of tungsten per g of sorbent) | 478.6 | 574.3 | 670.0 | 765.7 | 478.6 | 574.3 | 670.0 | 765.7 |
| Tungsten adsorption capacity (mg of tungsten per g of sorbent) | 448.0 | 520.3 | 544.7 | 601.8 | 435.7 | 515.2 | 545.1 | 595.2 |
| Adsorption percentage (%)[b] | 93.60 | 90.60 | 81.3 | 78.60 | 91.0 | 89.9 | 81.4 | 77.7 |
| Re-188 elution yield (%) | 72.50 | 85.30 | 81.20 | 79.00 | 75.1 | 86.2 | 85.6 | 81.5 |
| Tungsten breakthrough in first elution (μg of tungsten/mL) | 82.0 | 125.0 | 323.0 | 375.0 | 98.5 | 121.5 | 401.3 | 405.7 |
| Tungsten breakthrough in second–fifth elutions (μg of tungsten/mL) | 10.4 ± 0.4 | 27.1 ± 0.6 | 52.4 ± 0.7 | 60.2 ± 0.5 | 12.3 ± 0.2 | 28.2 ± 0.4 | 58.5 ± 0.5 | 65.7 ± 0.3 |

[a] PZC2 and PTC2 samples used; elution volume: 5 mL of 0.9% NaCl.
[b] Adsorption percentage (%) = 100 × (tungsten adsorption capacity/tungsten content of solution).

### 20.3.6. Effect of the composition of tungsten solution on adsorption and $^{188}$Re elution

Studies of the tungsten adsorption and $^{188}$Re elution performance of $^{188}$W-PZC and $^{188}$W-PTC sorbents in different solutions were carried out. It was found that, when NaOCl is added to the tungsten solution, both tungsten adsorption capacity and $^{188}$Re elution performance improve. Maximum tungsten adsorption capacities of about 520 mg of tungsten per gram of PZC and 515 mg of tungsten per gram of PTC were achieved. The capacities varied depending on the adsorption conditions. The adsorption of tungstate in acetate buffer solution showed a better integrity of PZC and PTC sorbent particles than did adsorption of tungsten in pure water solution of tungstate. Sterilizing the $^{188}$W-PZC and $^{188}$W-PTC columns in the autoclave reduced the elution yield of $^{188}$Re to some extent, but did not affect the tungsten breakthrough of column.

### 20.3.7. $^{188}$Re concentration for $^{188}$W-PZC or $^{188}$W-PTC generator

Since low specific activity $^{188}$W was used in the above studies, the $^{188}$Re obtained required post-elution concentration. The $^{188}ReO_4^-$ concentration process was carried out by eluting $^{188}$Re from the $^{188}$W-PZC and/or $^{188}$W-PTC columns with a dilute (0.005%) saline solution. The $^{188}$Re eluate collected was then passed through a small alumina column where all the $^{188}ReO_4^-$ was retained; the $^{188}ReO_4^-$ was then eluted from the alumina column with a small volume of physiological saline. Results of these studies are presented in Table 20.8 and Figure 20.6. A concentration factor greater than 6 was achieved with this concentration technique.

## 20.4. CONCLUSION

The PZC and PTC sorbents for the preparation of chromatographic $^{188}$W/$^{188}$Re generators were synthesized and their chemical composition and molecular structure were determined. Tungsten adsorption capacities of about 520 mg of tungsten per gram of PZC and 515 mg of tungsten per gram of PTC, and a $^{188}$Re elution yield greater than 80% were achieved with both PZC and PTC sorbents. A $^{188}$W breakthrough of 0.015% and tungsten element breakthrough of less than 5 µg of tungsten per millilitre were found in the $^{188}ReO_4^-$ eluate. A $^{188}$Re concentration process was developed by eluting $^{188}$Re from the tandem system of $^{188}$W-PTC–alumina columns with different concentrations of saline solutions. A concentration factor greater than 6 was achieved with this concentration technique.

TABLE 20.8. ELUTION PERFORMANCE OF $^{188}$W-PTC COLUMN WITH $^{188}$Re CONCENTRATION SYSTEM

| First column (W-188-PTC column) elution (0.005% NaCl eluant) | | | |
|---|---|---|---|
| Eluant volume (mL) | Re-188 elution yield (%) | Re-188 radioactivity retained on alumina column (mCi) | Tungsten breakthrough in the eluate |
| 20 | 0 | 5.5 mCi (91.6% of Re-188 radioactivity of W-188-PTC column) | Not detected |

| Second column (alumina) elution (0.9% NaCl eluant) | | | | |
|---|---|---|---|---|
| Re-188 radioactivity and elution yield | Re-188 radioactivity retained on alumina column (mCi) | Tungsten breakthrough in the eluate | Eluant volume (mL) | Concentration factor |
| 5.0 mCi (83.0% of Re-188 radioactivity of W-188-PTC column) | 0.5 | Not detected | 3 | 6.7 |

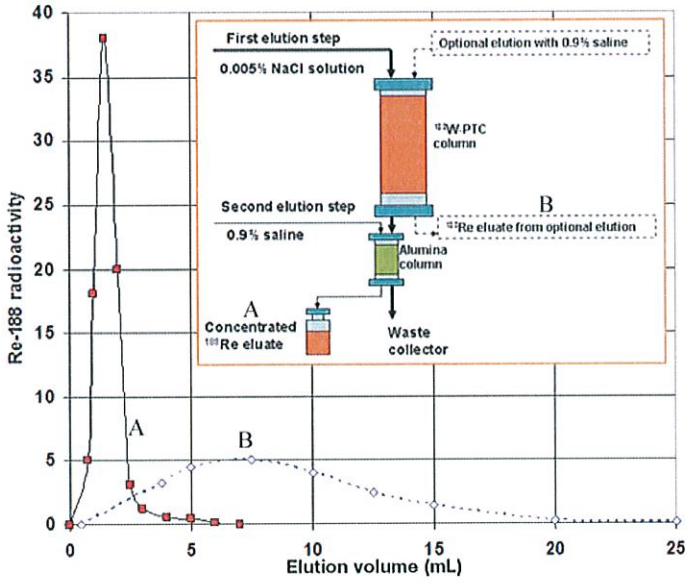


*FIG. 20.6. Concentration system and elution profiles: (A) elution profile from the alumina column after concentration; (B) elution profile from the PTC column without concentration; PTC sorbent weight: 4 g; alumina weight: 1.5 g; tungsten weight loaded onto PTC column: 2.1 g; $^{188}$W radioactivity: 6 mCi.*

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Radionuclide generators are efficient means to enhance the availability of short lived radioisotopes used in medicine and industry. Technologies for the preparation of $^{90}Sr/^{90}Y$ and $^{188}W/^{188}Re$ generator systems developed through an IAEA coordinated research project are presented in this publication. Analytical methods that are essential for evaluating the safety of radionuclides used in therapy are also described. By adapting the technologies described in this publication, these generators can be fabricated to cost effectively provide $^{90}Y$ and $^{188}Re$ for basic research and radiopharmaceutical preparation.

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