



ISSN 1110-0451



(E N S A)

Selective Separation of no Carrier added Sc-47 from Reactor Irradiated Ca Using Zirconium Vanadate Gel for Nuclear Medical Applications

M. A. Gizawy ^{a, b}, M. I. Aydia ^{a, c*}, H. A. Shamsel-Din ^{a, b}, K.M. El-Azony ^c

^(a) Radioisotopes Production Facility (RPF), Second Research Reactor (ETRR-2), Egyptian Atomic Energy Authority, Cairo, Egypt.

^(b) Labelled Compounds Department, Hot Labs Center, Egyptian Atomic Energy Authority, Cairo, Egypt.

^(c) Radioactive Isotopes and Generator Department, Hot Labs Center, Egyptian Atomic Energy Authority, Cairo, Egypt.

ARTICLE INFO

Article history:

Received: 15th Apr. 2021

Accepted: 1st July 2021

Keywords:

Scandium-47; Calcium-47;

Theranostics,

Reactor produced

radioisotopes,

Ion exchange

chromatography,

Zirconium Vanadates.

ABSTRACT

Various concentrations of HCl or HNO₃ on Zirconium Vanadate (ZrV) gel as an ion exchanger were studied by batch technique to determine the K_d values of ⁴⁷Ca(II) and ⁴⁷Sc(III) ions. A small chromatographic column packed with ZrV gel for ⁴⁷Sc(III) separation based on a high elution yield with high purity from the point of view chemical, radiochemical and radionuclidic. The maximum elution yield of ⁴⁷Sc (88 ± 2.2%) was obtained using 60% acetone-0.2 M HCl as an eluent. The ⁴⁷Sc was separated with acceptable radionuclidic purity (> 99.98±0.001%) and radiochemical purity (99.9±0.09%), in addition to a very low concentrations of Ca⁺² (0.05 ppm) which is lower than the permissible level (10 ppm) for medical applications, particularly for the labelling of pharmaceutical compounds.

INTRODUCTION

Scandium-47 is a promising candidate that can be used for therapeutic applications in low-energy beta-particle therapy ($E_{\beta^-} = 440.7$ keV, $I_{\beta^-} = 68.4\%$; 600.1 keV, $I_{\beta^-} = 31.6\%$) that is primarily aimed for the small tumors [1, 2]. In addition, the ⁴⁷Sc half-life is short ($T_{1/2} = 3.35$ d) and would be motivated to label small organic molecules. Separation of ⁴⁷Sc radionuclide with a high purity is a primary issue for labelling a variety of pharmaceuticals that have biological applications [3, 4]. Two different neutron-induced reactions based on neutron energy were used to produce ⁴⁷Sc [5-8]. Fast neutrons with energy greater than 1 MeV were used via ⁴⁷Ti(n,p) reaction for the ⁴⁷Sc production [9], while thermal neutrons ($E_n = 0.025$ eV) used via the ⁴⁶Ca(n, γ)⁴⁷Ca $\xrightarrow{\beta^-}$ ⁴⁷Sc reaction [2]. Calcium contains six stable isotopes of natural abundance, such different radionuclides can be produced by irradiation using thermal neutrons as seen in Scheme (1). Scandium and calcium radioisotopes have not been detected by gamma-analysis of the irradiated calcium target, with the exception of ⁴⁷Sc and ⁴⁷Ca radionuclides [8]. The induced proton reaction to the enriched ⁴⁸Ti target could

also be used to produce ⁴⁷Sc via (p, 2p) reaction, but unfortunately ⁴⁶Sc ($t_{1/2} = 83.79$ d) was co-produced with a high level associated with ⁴⁷Sc [10]. Despite the physical and nuclear properties of ⁴⁷Sc, which refers to its potential to be used as a theragnostic agent, there are different factors that hindered the production of ⁴⁷Sc, such as the high cost of the enriched target [7]. Several separation methods have been performed on the irradiated natural calcium target to achieve a high separation yield for ⁴⁷Sc with high radiochemical, radionuclidic and chemical purity based on solvent extraction such as tributyl phosphate [11] and ion exchange technique using different exchangers [12-22]. Synthetic inorganic ion exchangers are still more widely used due to their substantial advantages over organic resins [23, 24]. They are characterized by their higher thermal stability at elevated temperatures and resistance to high radiation doses, as well as their selectivity to some ions, which are properties that appear to lack organic resins. In comparison with organic ion-exchangers, synthetic inorganic ion exchangers have a high sensitivity to radionuclides and work over a broad pH range [25-29].

The current study concerns the use of zirconium vanadate (ZrV) as an inorganic sorbent for the effective ^{47}Sc separation technique from the neutron irradiated natural calcium target with excellent yield and chemical form valid for radiolabelling. Then, comparing the results obtained with the literature results in order to show the validity of this procedure.

Experimental

Chemicals

Zirconium oxychloride ($\text{ZrOCl}_2 \cdot 2\text{H}_2\text{O}$) from Sigma-Aldrich and sodium vanadate (99.98%) from Merk, both of AR grade, were bought without further purification. Other chemical reagents used in this study were of analytical purity and were used without further purification. Double distilled water was used to prepare all solutions.

Instrument

Several techniques were used to investigate the chemical structure of the ZrV gel. The FTIR spectrum of ZrV gel was studied in the $400\text{-}4000\text{ cm}^{-1}$ range to identify the functional groups in the ZrV gel. The X-ray diffractometer (XRD) (X-lab Shimadzu X-6000) used a wavelength of 1.54 \AA , Cu-K α for quantitative and qualitative analysis. High-purity germanium detector (HPGe), γ -ray spectrometer (GX2518 model, Canberra, USA) connected to a multi-channel analyzer used to detect radionuclides impurities in the final product. Inductive coupled plasma-atomic emission spectroscopy (ICP-AES) is used to determine calcium impurity in the eluted ^{47}Sc after ensuring its decay.

Preparation of ZrV matrix

Both zirconium oxychloride and sodium vanadate were used in the AR grade. Amorphous ranges of zirconium vanadate were prepared according to Roy's method [27] by the following steps: A drop by drop of 100 ml sodium vanadate solution (0.1 M) was added to 50 ml of zirconium oxychloride solution (0.1 M) by continuous stirring and dissolved in 2 M HCl. The mixture solution was water-diluted to 1 litre, and then allowed to settle for 24 hours. Several times the precipitate was washed with deionized water, then filtered and washed again with hot water to remove the excess chloride. The pH of the final solution moved slightly to the acidic medium at about pH 4.

^{47}Sc and ^{47}Ca radiotracers

Approximately 1 g of natural CaCO_3 was weighed accurately and encased in thin aluminum foil that was

wiped with acetone-moistened cotton and air-dried prior to use. The sample of CaCO_3 target was inserted in an aluminium container, enclosed and tested for leakage, and then irradiated for 24 hours in the 22 MW water-cooled Egyptian Research Reactor (ETRR-2) with a thermal neutron flux of approximately $1.8 \times 10^{14}\text{ n/cm}^2\cdot\text{S}$. The radioactive target was decided to leave for 3 days to decay short-lived radionuclides and then dissolved in 5 ml of 0.1 M HCl acid. The solution was changed to steam by heating and was almost dry, and finally dissolved in 10 ml of deionized water. All scandium and calcium radioisotopes that could be produced and were discussed in Scheme.1.

Chemical species produced in the aqueous solutions based on chemical equilibrium diagrams

Chemical structure evaluation based on preparation solution evolution was modeled using chemical equilibrium diagrams [30] to give perspective into the available cation and anion species at the beginning of the reaction in order to interpret the sorption behavior of calcium and scandium species at a specific pH onto ZrV matrix.

Acid-base titration of ZrV gel

100 mg ZrV gel specimens were placed in 25 ml glass bottles, divided into two sets and equilibrated with different volumes of 0.1 M NaCl & 0.1 M HCl in the first set and 0.1 M NaCl & 0.1 M NaOH in the second set with preserving an ionic strength equal to 0.1 M and a total volume of 10 ml in each bottle and left overnight at 25°C . The pH value was measured in each bottle and plotted against the concentration of H^+ (meq) per gram of ZrV gel in the first set and the concentration of OH^- (meq) per gram of ZrV gel in the second set showing the acid-base titration curve for ZrV gel.

Batch experiment

The effect of the initial concentrations of HCl or HNO_3 on the absorption behavior of $^{47}\text{Sc}(\text{III})$ and $^{47}\text{Ca}(\text{II})$ ions on ZrV matrix was studied by equilibrating 100 mg of the exchanger with 10 ml of various concentration of HCl or HNO_3 with 300 μl of radioactive tracers of ^{47}Sc and ^{47}Ca in 25 ml glass bottles shaken at 25°C in a thermostat shaker (140 rpm). Solutions were jolted for 24 hours, then the shaker stopped and the solid phases settled down. One ml of the aqueous phase was withdrawn and radioactivity was measured for ^{47}Sc and ^{47}Ca . The K_d value of $^{47}\text{Sc}(\text{III})$ and $^{47}\text{Ca}(\text{II})$ from HCl or HNO_3 solution to ZrV matrix was calculated using the following equation:

$$K_d = (A_o - A_e) \times V/A_e \times m \quad (\text{ml/g})$$

Where (A_o) and (A_e) are the aqueous phase counting rates before and after equilibration, respectively, (V) is the aqueous phase volume (10 ml) and (m) is the matrix weight (100 mg of ZrV). All measurements were repeated in triplicate, estimating the average values of K_d .

⁴⁷Sc separation via column technique

The glass column (10 cm long \times 0.5 cm inner diameter) was first filled with 0.001 M HNO_3 , followed by the addition of 600 mg of the prepared ZrV matrix to obtain a bed volume of about 1 ml. After the particles of the exchanger were settled down in the column, the quartz wool was located on the top of the exchanger to prevent any disruption of the packed column surface. The radioactive tracers of ^{47}Sc and ^{47}Ca in 0.001 M HNO_3 were passed through the loading column, followed by a 10 ml mixture of 0.2 M HCl with 60 % acetone solution for ^{47}Sc elution. In symmetrical glass bottles, both ^{47}Sc and ^{47}Ca radionuclides were radiometrically measured the flow rate passing through the column is 0.5 ml/min and equal amounts of the effluent were gathered.

Quality control on the separated ⁴⁷Sc

The eluted ^{47}Sc in aqueous solution (60% acetone in 0.2M HCl) was heated to almost dry, then dissolved in

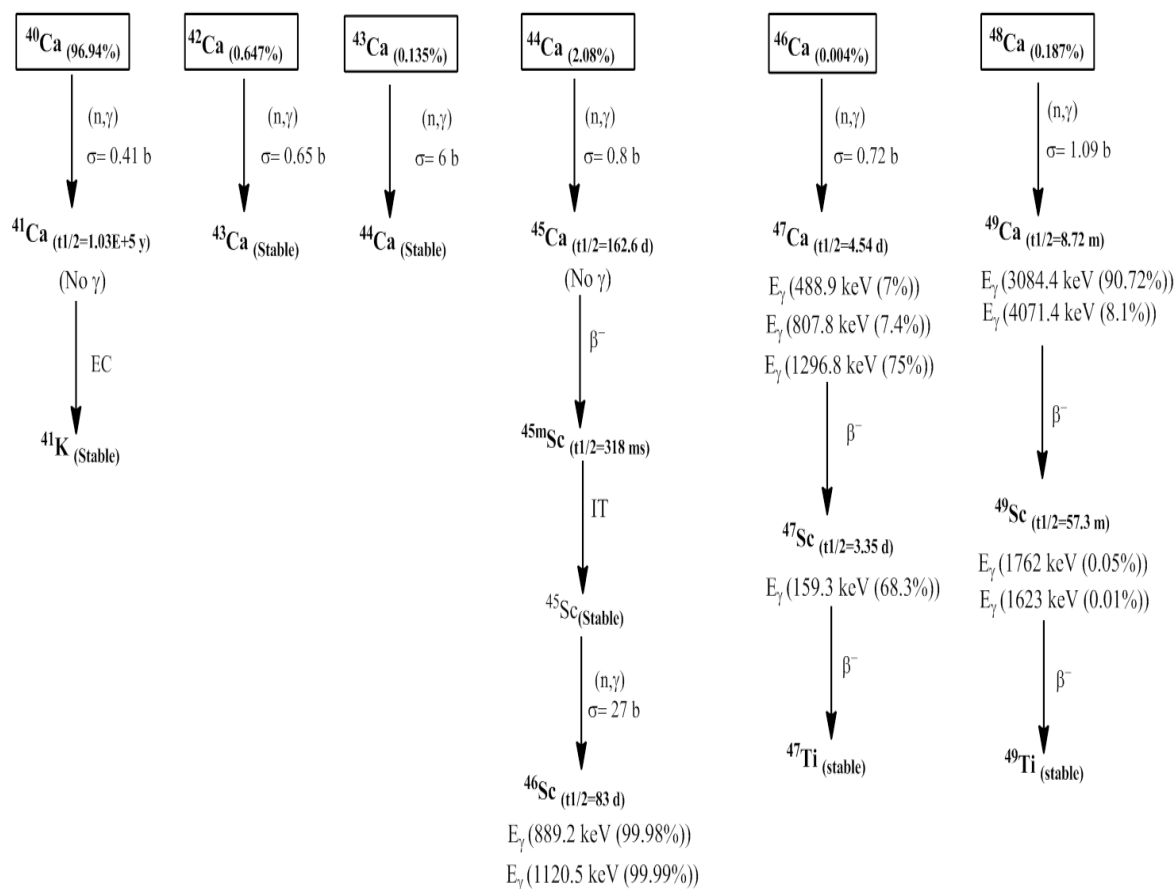
500 μl of deionized water to perform quality control tests.

Radiochemical purity

The radiochemical purity of the $^{47}\text{Sc}(\text{III})$ was evaluated using two strips of Whatman No.1 moving up paper chromatography. A solution mixture 1:1 ratio of dilute acetic acid in water was used as a developer for the first strip and for the second strip a saline solution used (0.9% NaCl solution) [31]. The radioactive solution ($\sim 10 \mu\text{l}$) was spotted at the indicated point using a syringe needle and the strip was then placed in a jar containing about 2 ml of the above-mentioned solvent. After the solvent was developed to a specific front position, the strip was allowed to dry, snip into 0.5 cm pieces and counted separately using the gamma-scintillation counter. The R_f was then calculated for each solvent employed.

Chemical purity

The eluted solution was left for a suitable time to ensure the decay of ^{47}Sc and other long-lived scandium radionuclides, such as ^{46}Sc ($t_{1/2} = 83.8 \text{ d}$), then a sample was analyzed using inductively coupled plasma atomic emission spectroscopy (ICP-AES) to determine the calcium ion impurity concentration.



Scheme. (1): Irradiation Scheme of natural calcium target by thermal neutrons for the production of scandium radioisotopes

Radionuclidic purity

After the elution process, the separated ^{47}Sc was directly measured using the HPGe detector connected to multichannel analyzer (γ -analysis) to detect any radionuclide impurity. Furthermore, the purity of ^{47}Sc was determined as a function of time by measuring its gross radioactive gamma decay.

RESULTS AND DISCUSSION

FT-IR spectrum

The FT-IR spectrum of prepared ZrV gel is shown in Fig. 1. and the vibrations are listed in Table (1). The

broad absorption band 3000-3700 cm^{-1} corresponds to O-H in adsorbed water molecules and intermolecular hydrogen bonds. The sharp peak was assigned to the H-O-H bending at 1621.7 cm^{-1} . The vibration of metal-OH could be attributed to the emerging peak at 1402 cm^{-1} [32]. The perception of the characteristic vanadate peaks, in accordance with Geng et al. 2014[33], is that of the intense, broad band with weak shoulder resolution at the peaks of 984.3, 817 and 703 cm^{-1} correlate to the symmetrical and asymmetrical stretching/bending V-O vibrations. The Zr-O stretch vibration is shown in the 435.75 cm^{-1} band [27].

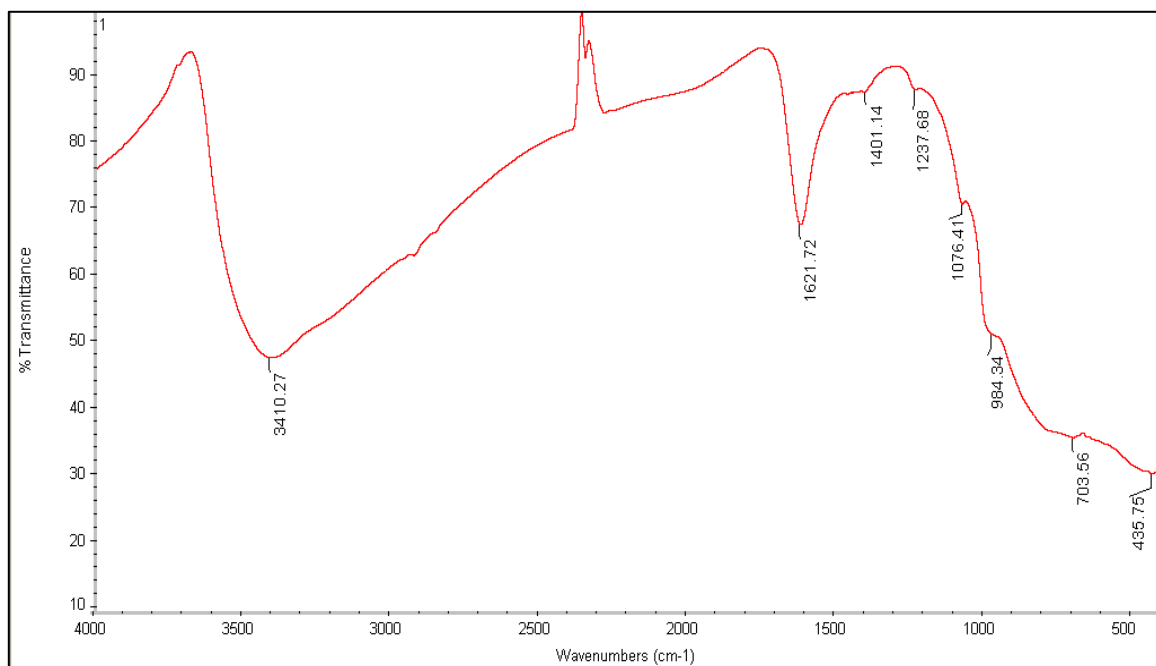


Fig. (1): FT-IR spectrum of zirconium vanadate (ZrV).

Table. (1): FT-IR vibrations of prepared zirconium vanadate

Peak assignment	Positions of the FT-IR band (cm^{-1})
(H-O-H) stretching/bending	3410, 1622
(V-OH), (Zr-OH) bending	1401
(V-O) stretching/bending	984, 817
(V-O) stretching	703
(Zr-O) stretching	436

X-ray diffraction (XRD) analysis

The amorphous structure (AS) of ZrV gel was confirmed by the XRD analysis as shown in **Fig. 2**. In some cases, AS is much better than the crystal structure (CS) in which the diffusion of eluent is more widespread in the amorphous material than in the crystalline material, resulting in an increase in the yield of elution [27]. From the other side, AS is more chemically stable, resulting in a high purity of ^{47}Sc eluate [34].

Titration curve of ZrV

The pH plays an important role in the uptake and nature of the ZrV sorbent. **Fig. 3** shows that ZrV has a point of zero charge (PZC) at pH 4.8. PZC implies that

the surface charge density (SCD) is equal to zero. The literature stated that PZC for ZrO_2 was located in the range 4 to 8, while vanadate was found at pH 4.2 [34, 35]. The ZrV sorbent has a point of zero pH titration at pH 5.5. The amphoteric sorbent is known to have a positively charged surface at pH values lower than its PZC and to have a negatively charged surface at pH values greater than its PZC. ZrV behaviour in the acid medium was observed to act as an alkaline substance, so the pH increased higher than the blank curve as shown in **Fig. 3**, may be due to the release of OH^- ions in the solution from ZrV gel. While ZrV gel acts as an acidic substance in the alkaline medium due to a lower pH value than a blank curve due to the release of H^+ ions from the ZrV gel.

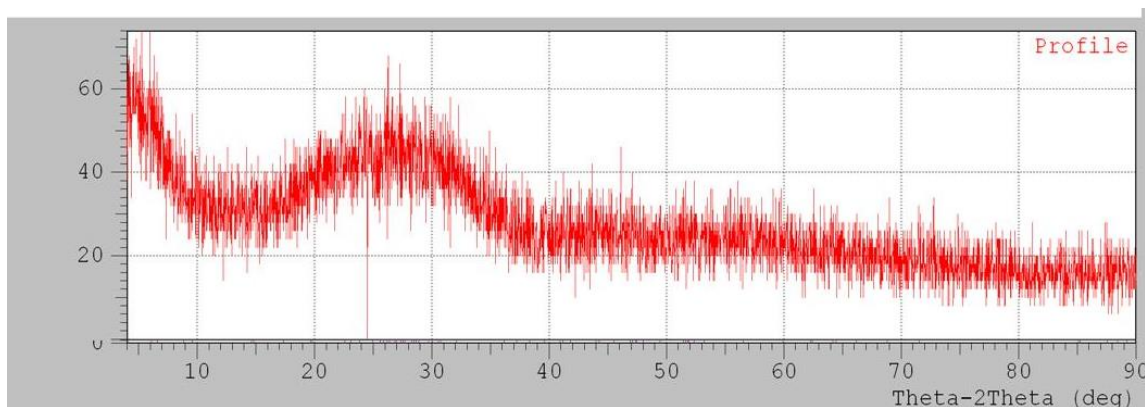


Fig. (2): XRD pattern of ZrV gel

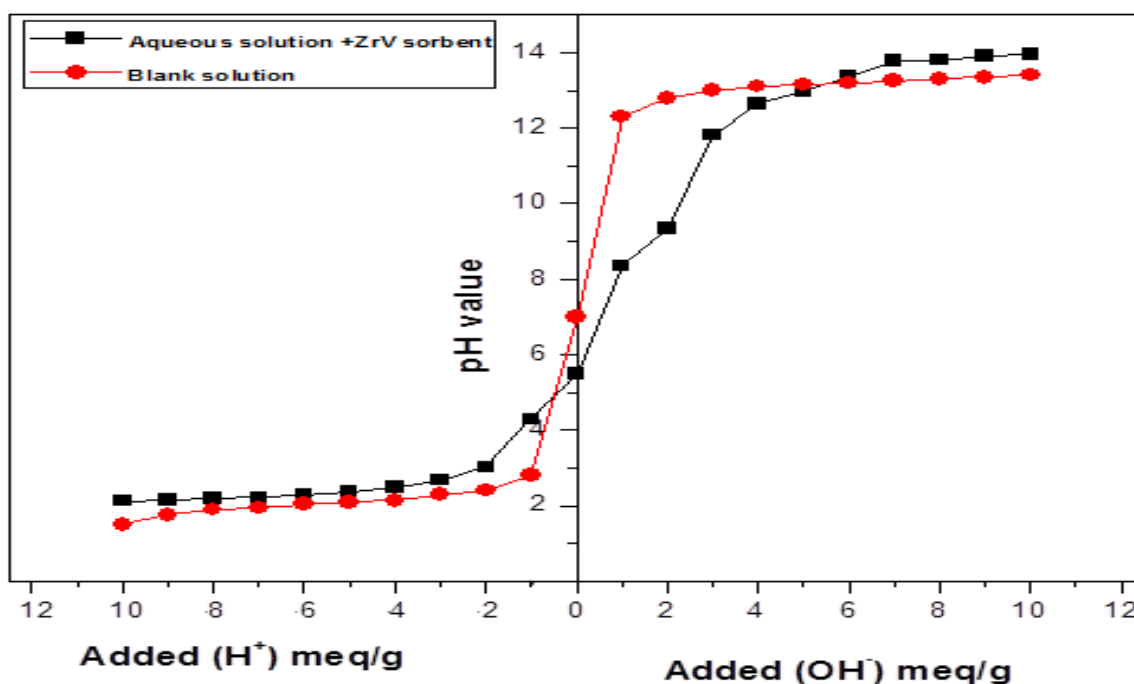


Fig. (3): Acid-base titration curve of ZrV

Chemical species of Ca(II) and Sc(III) in aqueous solution using chemical equilibrium diagrams

Fig. 4 and 5., represent aqueous species of Ca(II) and Sc(III) at different pHs, where pH ranges from 2 to 12 using chemical equilibrium diagrams [30]. Ca^{2+} is dominant with the presence of a further contribution of H^+ ions at pH 1, which decreases by increasing pH to pH 5. $\text{CaCl}(\text{OH})_2$ starts to form at pH2 and increases

by an increase in pH up to pH 9 as shown in **Fig. 5** . While Sc^{3+} is dominant with the existence of $\text{Sc}(\text{OH})_2^+$ and H^+ species only at pH 1-2 range as shown in **Fig. 5** ., where H^+ ions decreased with an increase in the other contributions of $\text{Sc}(\text{OH})_2^+$, $\text{Sc}_2(\text{OH})_2^{4+}$ and $\text{Sc}_3(\text{OH})_5^{4+}$ ions by increasing the pH from 2 to 4.5, $\text{Sc}(\text{OH})_3$ precipitate is formed higher than pH 4.5.

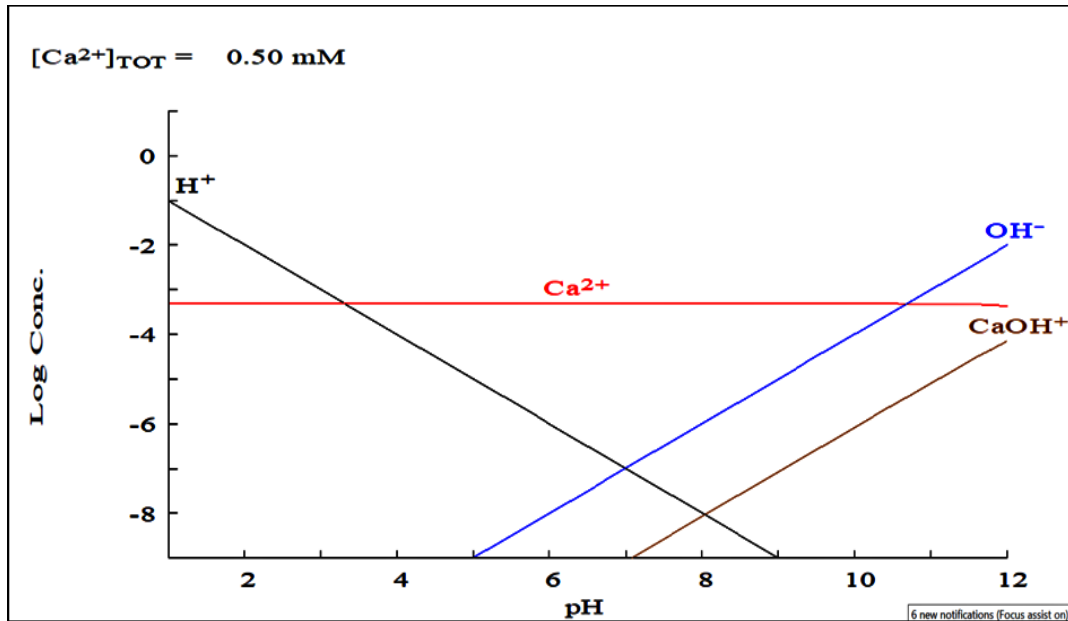


Fig. (4): Calcium species in 0.5 mM Ca(II) in aqueous solution as a function of pH

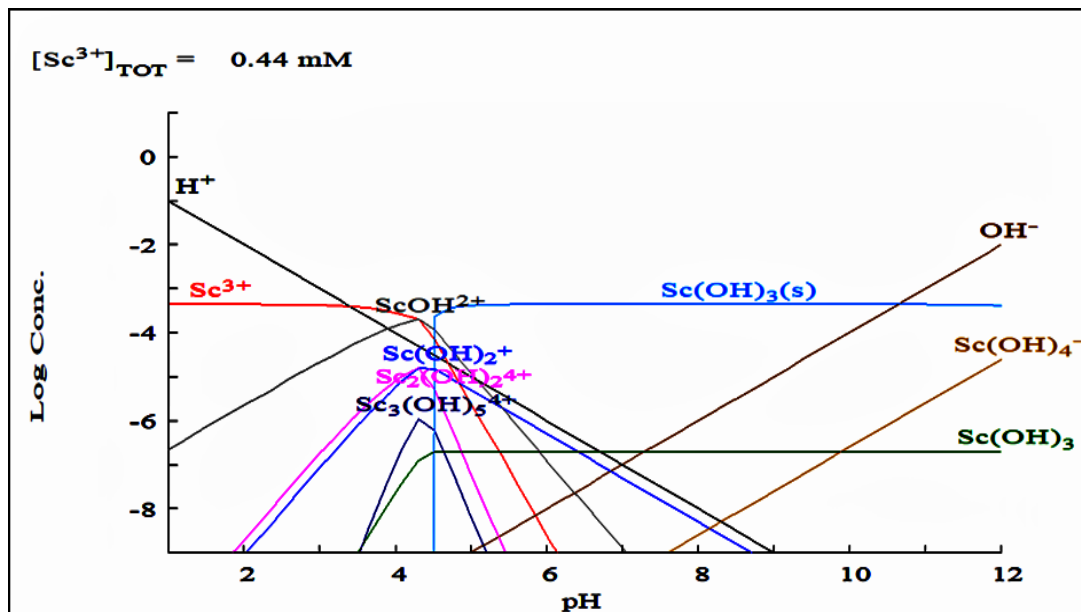


Fig. (5): Scandium species in 0.44 mM Sc(III) in aqueous solution as a function of pH

Effect of HNO₃ and HCl concentrations on K_d of Sc³⁺ and Ca²⁺ using ZrV matrix

The variation of K_d values of ⁴⁷Sc(III) and ⁴⁷Ca(II) ions as a function of HNO₃ or HCl concentration using the ZrV matrix is demonstrated in **Fig. 6**. The results showed that ⁴⁷Sc(III) was strongly adsorbed from the range 0.001-0.01M of HNO₃ or HCl to the ZrV matrix, higher and lower of these concentrations, the K_d of ⁴⁷Sc(III) decreased, while ⁴⁷Ca(II) was weakly adsorbed to the full range of HNO₃ or HCl concentrations and its K_d values were relatively constant. Sc(III) may be formed as ScCl(OH)₂, Sc(OH)₃ and Sc(OH)₄ species at pH >4 as shown in **Fig. 5**., as a result of the presence of Ca²⁺ ions in the reaction mixture, the final solution pH increases to 8 in water, [36], but in the presence of low concentration of HNO₃ or HCl (0.01-0.001M), the exist of Ca²⁺ ions shift solution pH to 3-5. These formed species have a high uptake towards the ZrV matrix, which acts as an anion exchanger based on its surface that carries positive charge in the acidic medium as seen in titration curve in **Fig. 3**., as well as the chemical reaction that could be achieved between ZrV matrix and ScCl(OH)₂. K_d values, then decreased at a high concentration of HNO₃ or HCl (>0.1M) may be due to the pH of reaction mixture being shifted to a lower pH (pH 1-2) at a high concentration of acids forming H⁺ and Sc³⁺ ions, which are less reactive to the ZrV matrix acting as an anion exchanger in an acidic medium as seen in the titration curve **Fig. 3**. On the other hand, the K_d values of Sc³⁺ decreased at low concentration of HNO₃ or HCl (<0.001 M), which may be due to the hydrolysis and precipitation of Sc³⁺ that begins at pH > 5 [37, 38]. In addition to, K_d values using nitric acid are higher than hydrochloric acid values, which may be attributed to lower nitrate anion hydration energy than the chloride anion hydration energy [39].

Performance of ⁴⁷Sc elution

Fig. 7. displays the elution curve of ⁴⁷Sc(III) and ⁴⁷Ca(II) at 0.5 ml/min flow rate, from 600 mg ZrV matrix packed in a column of 5 mm inside diameter using 60%

acetone-0.2 M HCl as an eluent. It is clear that the concentration of acid has a high effect on the effectiveness of the ZrV matrix as a sorbent material. The most suitable concentration of HCl or HNO₃ for ⁴⁷Sc (III) retention, which coincided with ⁴⁷Ca (III) elution, is 0.001 M. The acid concentration greater than 0.5 M contributes to the partial dissolution of the ZrV matrix as seen in **Table (2)**, which also indicates the elution yield of ⁴⁷Sc using various eluents. The elution yield of ⁴⁷Sc increased from 40 to 55% by increasing the HNO₃ concentration from 0.1 to 0.5 M and, in the case of HCl, the elution yield of ⁴⁷Sc decreased from 64 to 59% by increasing its concentration from 0.2 to 0.5 M. The rise concentration of HCl, or HNO₃ above 0.5 M resulted in the partial dissolution of the ZrV matrix, giving a pale yellow color in the ⁴⁷Sc eluate. Also, the elution yield using HCl, HNO₃ or ammonium acetate does not provide the appropriate results. Elution yield increased to approximately 88±2.2% in about 5 ml solution of 60% acetone-0.2 M HCl, due to acetone is quickly water miscible [40, 41]. The low concentration of HCl (relatively low concentration due to the high concentration having a deleterious effect on the ZrV matrix) with different ratios of the acetone concentration is studied to form the hydration field around the Sc cation that is sufficiently weakened to allow the chloride anions to replace the water in the coordinating shell, where the non-volatile organic matter metal chloride complex is formed [42], in order to elute ⁴⁷Sc from ZrV matrix. Therefore, scandium-chloride complex may be formed in anion form in acetone-HCl mixture solution and increased the stability of [ScCl₄]⁻ in the presence of two acetone molecules as shown in the **Fig.8**.

Table (3), demonstrated the different ion exchangers used to separate ⁴⁷Sc³⁺ from ⁴⁷Ca²⁺ based on the elution yield and the purity of the eluted ⁴⁷Sc [2, 42]. It was observed that the separation process on the ZrV matrix also provides the highest yield and purity of ⁴⁷Sc elution by comparing it with other exchangers using different methods.

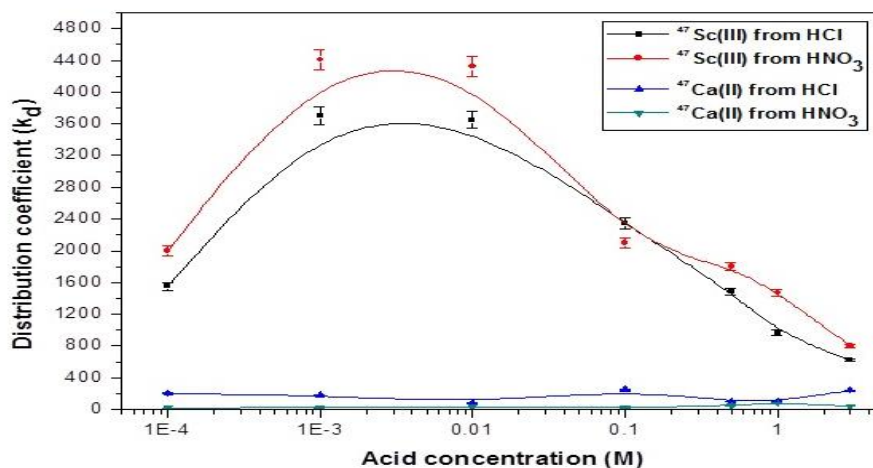


Fig. (6): Variation of the K_d values of ⁴⁷Sc(III) and ⁴⁷Ca(II) ions from different concentrations of HCl and/or HNO₃ to the ZrV matrix.

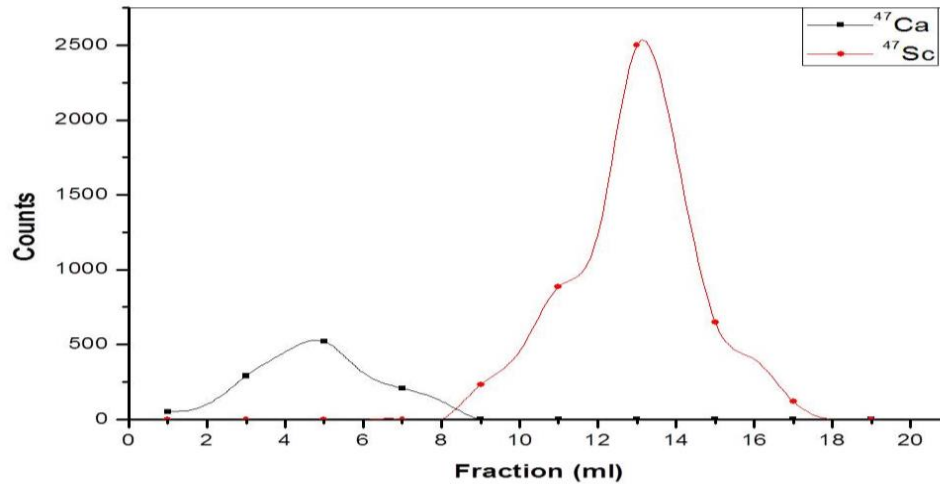


Fig. (7): Elution curve of $^{47}\text{Ca}(\text{II})$ and $^{47}\text{Sc}(\text{III})$ using 600 mg (ZrV) column (5 mm i.d) at flow rate 0.5 ml/min.

Table (2): The elution yield of ^{47}Sc from the ^{47}Sc -ZrV matrix using column dimensions (10 cm length 0.5 cm ID), 600mg ZrV, and different eluents at flow rate 0.5 ml/min.

Eluents	^{47}Sc elution yield (%)
0.1 M HNO_3	40 ± 2.0
0.5 M HNO_3	55 ± 2.5
1 M HNO_3	Partially dissolving ZrV matrix
0.2 M HCl	64 ± 3.0
0.5 M HCl	59 ± 2.8
1 M HCl	Partially dissolving ZrV matrix
40% acetone in 0.2M HCl	70 ± 3.5
50% acetone in 0.2M HCl	75 ± 4.0
60% acetone in 0.2M HCl	88 ± 2.2
70% acetone in 0.2M HCl	75 ± 4.5

Table (3): Comparison of radioscandium separation methods from calcium targets

Matrix	Elution yield (%)	Ca concentrations in the eluted ^{47}Sc product (ppm)	References
DOWEX 50	80.00	< 1	[35]
Chelex 100	85.00	< 1	[20, 37]
UTEVA extraction resin	79.00	< 1	[20]
Filtration (0.2 μm)	96.00	< 1	[20]
P (AA-AN)-NPs CuO composite	78 ± 1.2	0.05	[38]
ZrV (this work)	88 ± 2.2	0.05	

Reaction mechanism

Roy et al., 2002 [29] described ZrV as an inorganic ion exchanger and has a chemical formula, namely $ZrO_2 \cdot V_2O_5 \cdot 2H_2O$. **Fig. 8**, reveals the proposed chemical

reaction between the ZrV matrix and the proposed $ScCl(OH)_2$ species for absorption of ^{47}Sc on ZrV matrix followed by an elution using 60% acetone-0.2 M HCl with high elution yield.

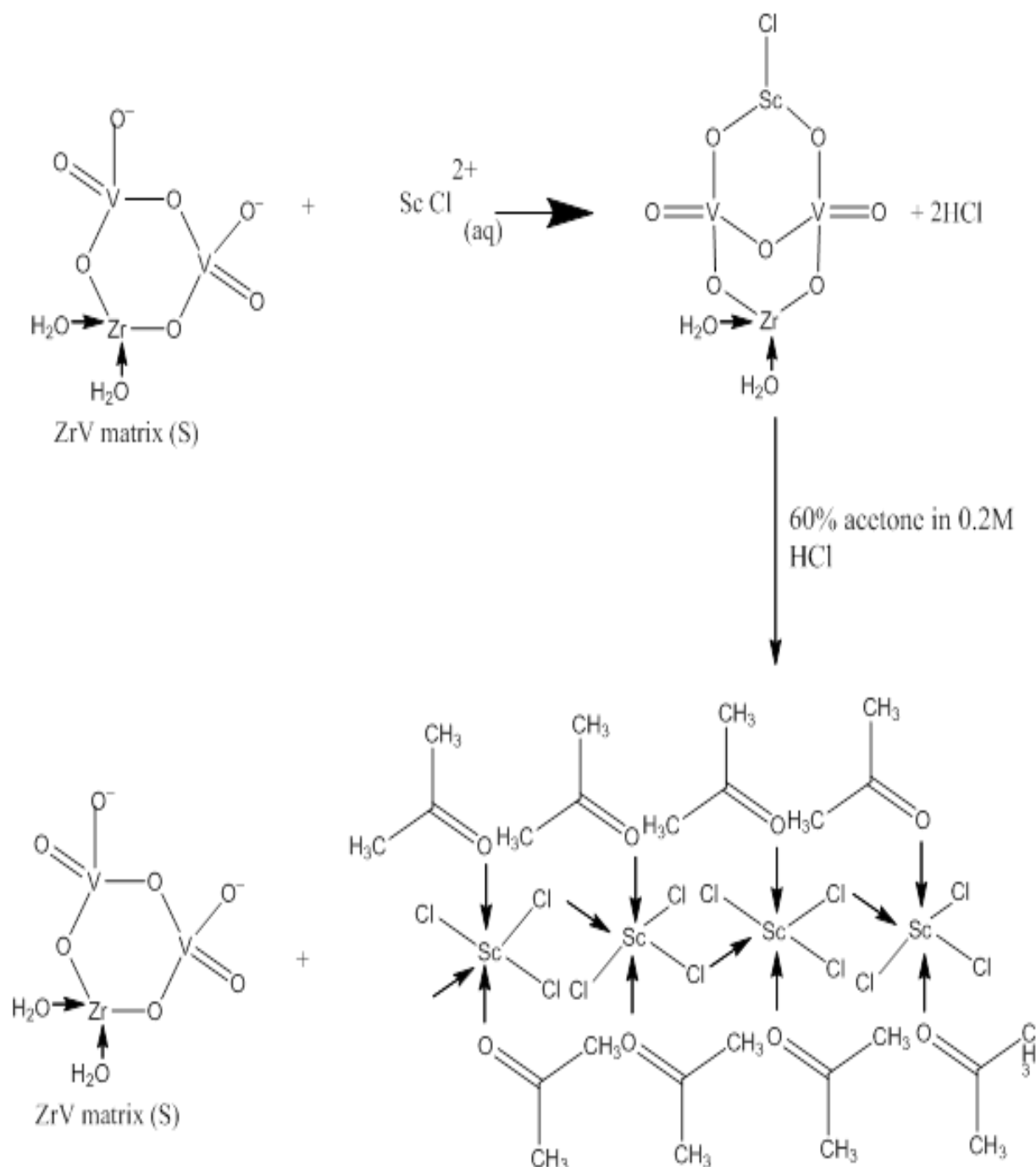


Fig. (8): Suggested mechanism for the separation of ^{47}Sc from ZrV matrix

Quality control performance on the eluted ^{47}Sc (III) Radiochemical purity

In order to investigate the radiochemical purity of the eluted ^{47}Sc , the development of the eluted ^{47}Sc solution on chromatographic paper was carried out in two different developing solvents. The radio-chromatogram in **Fig. 9(a and b)**., shows that one major peak was accomplished at $R_f = 0.1$ using saline as a mobile phase, while in the other developing solvent (acetic acid: water, 1:1 v / v) the peak was moved to the higher R_f value ($R_f \sim 1$) with the solvent front. The radiochemical purity of ^{47}Sc as Sc^{3+} ions could be evaluated to be $99.9 \pm 0.09\%$.

Chemical purity

Despite Ca is non-toxic, an excess of $^{47}\text{Ca}^{2+}$ radioactivity may have a deleterious effect, due to an increase in the undesired radioactive dose during the labelling process of pharmaceutical compounds using ^{47}Sc . Furthermore, the presence of Ca^{2+} in the eluted ^{47}Sc is more hazardous to the radiochemical yield of ^{47}Sc -pharmaceutical compounds due to its competition with $^{47}\text{Sc}^{3+}$ [43, 44]. **Table (2)**, shows that the concentration of Ca^{2+} in the decayed ^{47}Sc solution did not exceed 0.05 ppm, therefore the eluted ^{47}Sc is suitable for medical

applications, due to its value below the allowable level (10 ppm) [45]. On the other hand, for the purpose of extracting acetone from ^{47}Sc eluate, the literature data showed that dibasic potassium phosphate (K_2HPO_4), was used to separate acetone by 100%, which is also used safely as a buffering agent [46].

Radionuclidic purity

Fig. 10 (a)., showed the gamma-ray spectrum of the radioactive calcium target dissolved in 1 M HCl and measured using the HPGe detector connected to the multichannel analyzer to indicate the main gamma peaks associated with ^{47}Sc at 159.3 keV and ^{47}Ca at 488.9, 807.8 and 1296.8 keV. On the other hand, **Fig.10 (b)**., explained the ^{47}Sc gamma-peak, which was measured directly after the elution to determine the purity of ^{47}Sc radionuclide, that was found to be $> 99.98 \pm 0.001\%$. There are two main reasons for the inability to determine gamma energy lines of ^{46}Sc ($t_{1/2}=83$ d), either in the irradiated calcium target or in the eluted ^{47}Sc solution: the small cross-section of $^{44}\text{Ca}(n, \gamma)^{45}\text{Ca}$ reaction (0.8 b) and the long half-life of ^{45}Ca ($t_{1/2}=163$ d). The ^{45}Ca then decayed by beta to produce ^{45}Sc as a stable isotope with very small quantities, which will be activated again by thermal neutrons to produce ^{46}Sc that could not be determined by gamma analysis.

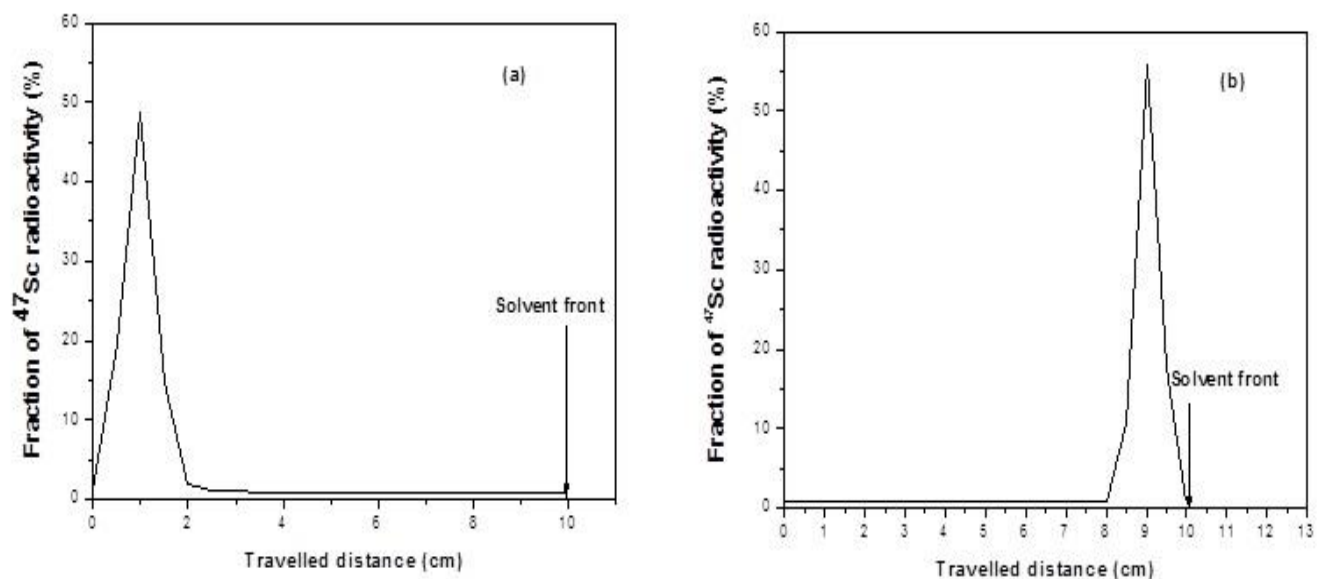


Fig. (9): The eluted ^{47}Sc radio-chromatogram using (a) saline solution (0.9% NaCl solution) and (b) acetic acid : water (1:1 v/v)

CONCLUSION

The distribution coefficients of ^{47}Sc and ^{47}Ca radionuclides between aqueous solutions (HCl or HNO_3 solution) and the ZrV gel were studied by batch technique and the results refer to loading of ^{47}Sc from 0.001M HNO_3 or HCl. The sorption process of ^{47}Sc was interpreted by studying the chemical equilibrium diagram study, which revealed that the chemical species formed as a function of pH, represented the chemical absorption. Where, the chemical reaction that could be done by two groups of hydroxides on the $\text{ScCl}(\text{OH})_2$ interacting with the two hydrogen ions (H^+) on the ZrV gel. In addition, the physical adsorption was verified by

the titration curve, which revealed the sorbent charge of ZrV (+ve charge < pH4.8) and the formed species of scandium (ScCl_4^-) as a function of pH. The elution efficiency of about $88 \pm 2.2\%$ was obtained for ^{47}Sc using 60% acetone in 0.2 M HCl. The eluted ^{47}Sc has a radionuclidic purity of $>99.98 \pm 0.001\%$ in an oxidation state (III).

The results refer to loading of ^{47}Sc from 0.001M HNO_3 . The elution efficiency of about $88 \pm 2.2\%$ was obtained for ^{47}Sc using 60% acetone in 0.2 M HCl., with a ^{47}Sc radionuclidic purity of $>99.98 \pm 0.001\%$ in an oxidation state (III).

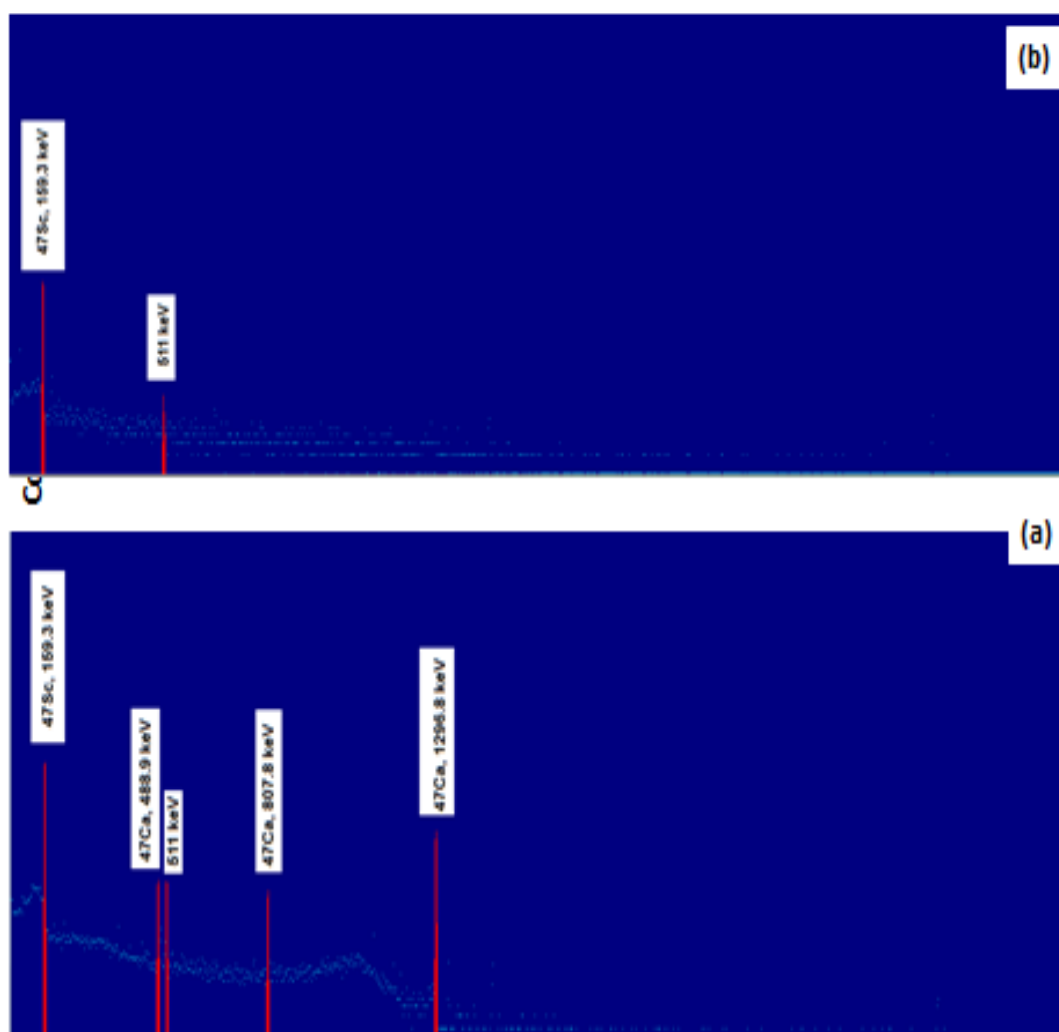


Fig. (10): Gamma-ray spectrum of (a) the dissolved irradiated natural calcium target (b) the eluted ^{47}Sc

ACKNOWLEDGMENTS

The authors are grateful to the International Atomic Energy Agency for funding our work through the IAEA Coordinated Research Project No: 20566.

REFERENCES

- [1] Domnanich, K.A., Müller, C., Benešová, M., Dressler, R., Haller, S., Köster, U., Ponsard, B., Schibli, R., Türler, A., van der Meulen, N.P., (2017). ^{47}Sc as useful β -emitter for the radiotheragnostic paradigm: a comparative study of feasible production routes. *EJNMMI radiopharm. chem.* 2 (1):5-14.
- [2] Müller, C., Bunka, M., Haller, S., Köster, U., Groehn, V., Bernhardt, P., Van der Meulen, N., Türler, A., Schibli, R., (2014). Promising prospects for ^{44}Sc -/ ^{47}Sc -based theragnostics: application of ^{47}Sc for radionuclide tumor therapy in mice. *J Nucl Med.*, 55(10):1658 – 1664.
- [3] Pietrelli, L., Mausner, L.F., Kolsky, K.L., (1992). Separation of carrier-free ^{47}Sc from titanium targets. *J. Radioanal. Nucl. Chem.* 157 (2): 335 – 345.
- [4] Majkowska, A., Neves, M., Antunes, I., Bilewicz, A., (2009). Complexes of low energy beta emitters ^{47}Sc and ^{177}Lu with zoledronic acid for bone pain therapy. *Appl. Radiat. Isot.* 67 (1): 11 – 13.
- [5] Mausner, L. F., Kolsky, K. L., Joshi, V., Srivastava, S.C., (1998). Radionuclide development at BNL for nuclear medicine therapy. *Appl Radiat Isot* 49:285–294.
- [6] Srivastava, S. C., (2011). Paving the way to personalized medicine: production of some theragnostic radionuclides at Brookhaven National Laboratory. *Radiochim Acta* 99:635–640.
- [7] Kolsky, K. L., Joshi, V., Mausner, L. F., Srivastava, S. C., (1998). Radiochemical purification of no-carrier-added scandium-47 for radioimmunotherapy. *Appl. Radiat. Isot.* 49 (12): 1541 – 1549.
- [8] Gizawy, M. A., Mohamed, N. M. A., Aydia, M. I., Soliman, M. A., Shamsel-Din, H. A., (2020). Feasibility study on production of Sc-47 from neutron irradiated Ca target for cancer theranostics applications. *Radiochimica Acta*, 108 (3): 207-215.
- [9] Gladney, E. S., Goode, W. E., (1979). Preparation of carrier-free ^{47}Sc by the $^{47}\text{Ti}(n,p)$ reaction with epithermal neutrons. *Int. J. Appl. Radia. and Isoto.*, 30 (1): 65 -73.
- [10] Srivastava S. C., (2012). Paving the way to personalized medicine: production of some promising theragnostic radionuclides at Brookhaven National Laboratory. *Semin Nucl Med.* 42(3):151– 63.
- [11] Radhakrishnan, K.P., Owens, T.C., (1972). Separation of scandium and calcium by liquid-liquid extraction using tributyl phosphate as solvent. *J. Chem. Eng. Data* 17 (4): 478 –482.
- [12] Vyas, C.K., Park, J.H., Yang, S.D., (2016). Application of extraction chromatographic techniques for separation and purification of emerging radiometals $^{44}/^{47}\text{Sc}$. *JRM* 2 (2) .
- [13] Severin, G.W., Gagnon, K., Engle, J.W., Valdovinos, H.F., Barnhart, T.E., Nickles, R.J., (2012b). ^{44g}Sc from metal calcium targets for PET. *AIP Conf. Proc.* 1509, 125 –128 .
- [14] Müller, C., Bunka, M., Reber, J., Fischer, C., Zhernosekov, K., Türler, A., Schibli, R., (2013). Promises of cyclotron-produced ^{44}Sc as a diagnostic match for trivalent β –emitters: in vitro and in vivo study of a ^{44}Sc -DOTA-folate conjugate. *J. Nucl. Med.* 54 (12):2168 –2174.
- [15] Krajewski, S., Cydzik, I., Abbas, K., Bulgheroni, A., Simonelli, F., Holzwarth, U., Bilewicz, A., (2013). Cyclotron production of ^{44}Sc for clinical application. *Radiochim. Acta* 101 (5): 333 –338.
- [16] Van der Meulen, N.P., Bunka, M., Domnanich, K.A., Müller, C., Haller, S., Vermeulen, C., Türler, A., Schibli, R., (2015). Cyclotron production of ^{44}Sc : from bench to bedside. *Nucl. Med. Biol.* 42 (9): 745 – 751.
- [17] Valdovinos, H.F., Hernandez, R., Barnhart, T.E., Graves, S., Cai, W., Nickles, R.J., (2015). Separation of cyclotron-produced ^{44}Sc from a natural calcium target using a dipentyl pentylphosphonate functionalized extraction resin. *Appl. Radiat. Isot.* 95:23 –29.
- [18] Alliot, C., Kerdjoudj, R., Michel, N., Haddad, F., Huclier-Markai, S., (2015). Cyclotron production of high purity $^{44m,44}\text{Sc}$ with deuterons from $^{44}\text{CaCO}_3$ targets. *Nucl. Med. Biol.* 42 (6):, 524 – 529.

- [19] Kilian, K., Cheda, Ł., Sitarz, M., Szkliniarz, K., Chojński, J., Stolarz, A., (2018). Separation of 44 Sc from natural calcium carbonate targets for synthesis of 44 Sc-DOTATATE. *Molecules* 23 (7):1787-1795.
- [20] Minegishi, K., Nagatsu, K., Fukada, M., Suzuki, H., Ohya, T., Zhang, M.R., (2016). Production of scandium-43 and-47 from a powdery calcium oxide target via the nat ⁴⁴Ca (α, x)-channel. *Appl. Radiat. Isot.* 116:8–12.
- [21] Misiak, R., Walczak, R., Wąs, B., Bartyzel, M., Mieliski, J.W., Bilewicz, A., (2017). ⁴⁷Sc production development by cyclotron irradiation of 48 Ca. *J. Radioanal. Nucl. Chem.* 313 (2): 429–434.
- [22] Walczak, R., Krajewski, S., Szkliniarz, K., Sitarz, M., Abbas, K., Chojński, J., Jakubowski, A., Jastrzębski, J., Majkowska, A., Simonelli, F., Stolarz, A., (2015). Cyclotron production of ⁴³Sc for PET imaging. *EJNMMI Phys.* 2 (1):33-40
- [23] Gizawy, M.A., Aydia M.I. Abdel Monem, Islam M., Shamsel-Din H.A., Siyam T., (2019). Radiochemical separation of reactor produced Sc-47 from natural calcium target using Poly(acrylamide-acrylic acid)/multi-walled carbon nanotubes composite. *Appl. Radiat. Isot.* 150: 87–94.
- [24] Jing, Z., Zhang, G., Sun, X.F., Shi, X., Sun, W., (2014). Preparation and adsorption properties of a novel superabsorbent based on multiwalled carbon nanotubes –xylan composite and poly (methacrylic acid) for methylene blue from aqueous solution.
- [25] Harjula, R. and J. Lehto, (1987). Separation of cesium from nuclear waste solutions with hexacyanoferrate (II) and ammonium phosphomolybdate. *Solvent Extr. Ion Exch.*, 5: 343-351.
- [26] Lehto, J., R. Harjula and J. Wallace, (1987). Adsorption of cesium on potassium cobalt hexacyanoferrate (II). *J. Radioanal. Nucl. Chem.*, (111): 297-304.
- [27] Aydia, M.I., El-Said, H., El-Sadek, A.A., El-Azony, K.M. (2018). Preparation and characterization of zirconium silico W-tungstate as a base material for 188W/188Re generator. *Appl. Radiat. Isot.* 142: 203-210.
- [28] El-Said, H., El-Sadek, A.A., Aydia, M.I., El-Azony, K.M. (2018). Zirconium silicotungstate matrix as a prospective sorbent material for the preparation of ¹¹³Sn/^{113m}In generator. *J. Radioanal. Nucl. Chem.*, 317 (3): 1341–1347.
- [29] Roy K, Pal DK, Basus S, Dalia N, Susanta L., (2002). Synthesis of a new ion exchanger, zirconium vanadate, and its application to the separation of barium and cesium radionuclides at tracer. *Appl. Radiat. Isot.* 57: 471-474.
- [30] Puigdomenech, (2013). Make equilibrium diagrams using sophisticated algorithms (MEDUSA). Inorganic chemistry, Royal Institute of Technology, Stockholm, Sweden. [Http://www.kemi.kth.se/medusa](http://www.kemi.kth.se/medusa).
- [31] Chakravarty, R., Chakraborty, S., Ram, R., Dash, A. (2017). An electroosmotic approach to separate ⁴⁷Sc from neutron-activated ⁴⁶Ca target for use in cancer theranostics. *Sep. Sci. Technol.* 52(14): 2363-2369.
- [32] Sharma, H. K., Sharma, N., (2013). Synthesis and structural characterization of tin(IV)molybdotungstate-A heteropolyacid salt. *Der Chem. Sin.* 4: 182-189.
- [33] Geng, Y., Zhang, P., Kuang, S., (2014). Fabrication and enhanced visible-light photocatalytic activities of BiVO₄/Bi₂WO₆ composites. *RSC Adv* 4:46054–46059.
- [34] Kosmulski, M., (2009). pH-dependent surface charging and points of zero charge. IV. Update and new approach. *J. Colloid and interface Sci.* 337 (2): 439-446.
- [35] Muhammad, S., Hussain, S. T., Waseem, M., Naeem, A., (2012). Surface charge properties of zirconium dioxide. *Iranian J. Sci. Tech.* A4: 481-486.
- [36] Hussain, J., Tariq Jan, M., Korchef, A., Touaibi, M., (2020). Effect of pH and temperature on calcium carbonate precipitation by CO₂ removal from iron-rich water, *Water and Environment Journal*, 34: 331-341.
- [37] Baes, C. F., Mesmer R. E. (1976). *The Hydrolysis of Cations*, Wiley Interscience, New York, NY, USA.
- [38] Das, S, Behera, S.S., Murmu, B.M., Mohapatra, R.K., Mandal, D., Samantray, R., Parhi, P.K., Senanayake, G., (2018). Extraction of scandium(III) from acidic solutions using organo-

- phosphoric acid reagents: A comparative study
Sep. Pur. Tech., 202: 248–258.
- [39] Vyas, C. K., Joshirao, P. M., Manchanda, V. K. (2014). Perchloric acid a promising medium for the chromatographic separation of ^{90}Y from ^{90}Sr . Sep. Purif. Technol. 124: 179-188.
- [40] Robinson, J.W.,(1960). Effect of organic and aqueous solvents on flame photometric emission and atomic absorption spectroscopy. Anal. Chim. Acta 23: 479-478.
- [41] El-Azony, K. M.(2011). Improving the separation of Cu(II) from Zn(II) based on an anion exchanger for the preparation a $^{62}\text{Zn}/^{62}\text{Cu}$ generator. Appl. Radia. and Isoto., 69 (9):1176-1180.
- [42] El-Azony, K.M., I. smail Aydia M., El-Mohty, A.A.,(2011). Separation of Cr(III) from Cr(VI) by Triton X-100 cerium(IV) phosphate as a surface active ion exchange J .Radioanal. Nucl. Chem., 289 (2): 381-388.
- [43] Mousa, A. M., Abdel Aziz, O. A., Al-Hagar, O. E. A., Gizawy, M. A., Allan, K. F., Attallah, M. F.,(2020). Biosynthetic new composite material containing CuO nanoparticles produced by *Aspergillus terreus* for ^{47}Sc separation of cancer theranostics application from irradiated Ca target. Appl. Radia. and Isoto., 166: 109389-109396.
- [44] Martell A, Smith,R, Motekaitis,R. NIST Critically Selected Stability const-ants of Metal Complexes Database,(2004)
<http://www.nist.gov/srd/nist46.cfm>
- [45] Galle, P., Masse, R. (Eds.),(1982). Radionuclides Metabolism and Toxicity. Masson, Paris.
- [46] Xie, S., Song, W., Fu, C., Yi, C., Qiu, X.,(2018). Separation of acetone: from a water miscible system to an efficient aqueous two-phase system. Separ. Purif. Technol. 192: 55–61.