


Mechanochemically synthesized mesoporous alumina: a smart new-generation sorbent for preparation of chromatographic $^{188}\text{W}/^{188}\text{Re}$ generator

Rubel Chakravarty^{1,3}  · Jitendra Bahadur² · Sharad Lohar¹ · Sachin Jadhav¹ · Debasis Sen² · Sudipta Chakraborty^{1,3}

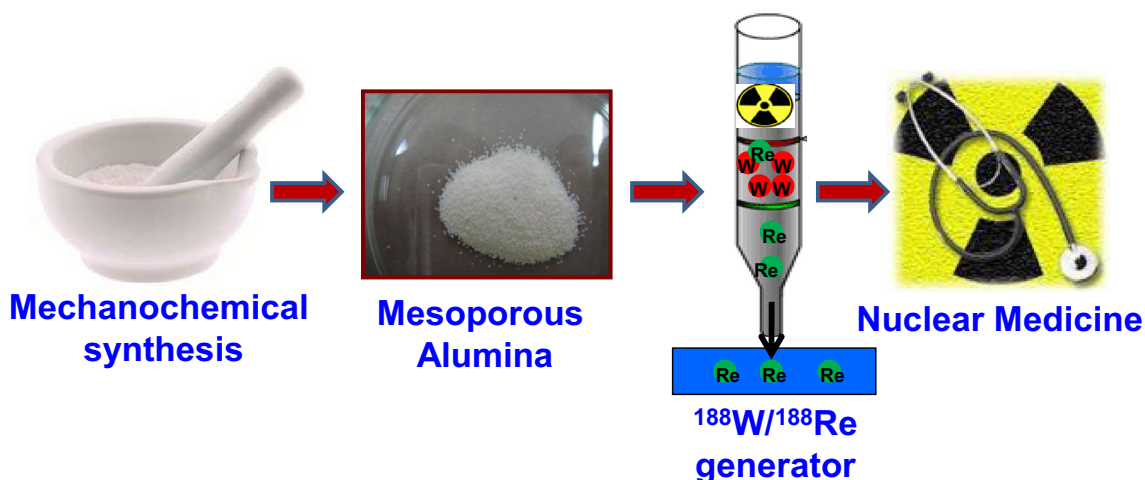
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Abstract

In an effort towards affordable availability of chromatographic $^{188}\text{W}/^{188}\text{Re}$ generators for widespread clinical use, we report the mechanochemical synthesis of mesoporous alumina as an advanced sorbent material for preparation of the generator. The synthesized material exhibits remarkably high sorption capacity (550 ± 12 mg W/g), which is adequate for preparation of clinical-scale generators using low specific activity (LSA) ^{188}W produced in medium flux research reactors. Sorption of ^{188}W in mesoporous alumina follows Freundlich adsorption isotherm and pseudo second order kinetics, indicating that the process is chemisorption. A clinical-scale (~ 14.0 GBq) $^{188}\text{W}/^{188}\text{Re}$ generator was developed and its performance was evaluated over a period of 6 months. Rhenium-188 could be consistently obtained from the generator with high yield ($> 80\%$) and it met all the requirements for clinical use. The present strategy is expected to increase the scope of separation chemistry for availing clinical-grade ^{188}Re for the benefit of millions of cancer patients world over.

Graphic abstract



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✉ Rubel Chakravarty, rubelc@barc.gov.in; rubelchakravarty@gmail.com | ¹Radiopharmaceuticals Division, Bhabha Atomic Research Centre, Trombay, Mumbai 400085, India. ²Solid State Physics Division, Bhabha Atomic Research Centre, Trombay, Mumbai 400085, India. ³Homi Bhabha National Institute, Anushaktinagar, Mumbai 400094, India.



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1 Introduction

Radionuclide generators continue to play an imperative role in providing radioisotopes for use in nuclear medicine. Efficiency, reliability, safety and cost-effectiveness are the key parameters that govern the development of next-generation radionuclide generators for regular usage in clinical context. To a large extent, progress in design of improved radionuclide generators is dependent on the advancements in separation science and technology [1]. Owing to its simplicity and convenience to use in hospital radiopharmacies, the column chromatographic separation technique has found the widest application in development of radionuclide generators. Basically, the ‘heart’ of any column chromatographic separation process is the sorbent and hence progress in this field is related to evolution of materials chemistry towards synthesis of advanced sorbent materials.

Synthesis of advanced sorbent materials with high capacity and improved performance towards development of radionuclide generators has now become a continuing object of research with potential for clinical translation [2]. In this regard, sorbent materials with regular and relatively large mesopores tend to become indispensable. There have been numerous reports of synthesis of mesoporous materials over the last several years [3–7]. Driven by the need for new, cleaner, scalable, highly efficient and more sustainable synthetic methodologies, solid state mechanochemical approaches for synthesis of mesoporous materials has seen a reawakening during the past few years [8, 9]. These techniques have not only been demonstrated as feasible alternatives to conventional solution-based syntheses, but they have also received consideration for their ability to enable high mesoporosity and thus develop novel sorbents for radionuclide generators. The solid-state synthesis route is easily amenable for scale up for synthesis of large quantities of sorbents required for the preparation of multiple radionuclide generators in order to meet the demands of the nuclear medicine community.

Rhenium-188 ($T_{1/2} = 16.9$ h, $E_{\text{max}} = 2.12$ MeV, 155 keV γ -ray) is an established therapeutic radioisotope that can be obtained in a no-carrier-added (NCA) form via $^{188}\text{W}/^{188}\text{Re}$ generator for preparation of a wide variety of radiopharmaceuticals [10]. The parent ^{188}W can be produced with adequate specific activity by double neutron capture i.e. $^{186}\text{W}(n,\gamma)^{187}\text{W}(n,\gamma)^{188}\text{W}$ reaction on enriched ^{186}W target in high flux research reactors

($> 10^{15}$ n·cm⁻²·s⁻¹) [10]. There are only very few operational high flux research reactors in the world. As a result, the widespread and cost-effective availability of clinically useful $^{188}\text{W}/^{188}\text{Re}$ generators is compromised. In order to enhance the scope of utilization of ^{188}Re in clinical domain, it is essential to utilize relatively LSA ^{188}W produced in medium flux research reactors for the preparation of $^{188}\text{W}/^{188}\text{Re}$ generators. According to the International Atomic Energy Agency—Research Reactor Database (IAEA-RRDB), there are more than 50 operational medium flux research reactors world over and they are located in good geographical distribution to meet the supply logistics [11]. Utilization of LSA ^{188}W produced in these research reactors mandates the need for high capacity advanced sorbent materials for preparation of clinically useful $^{188}\text{W}/^{188}\text{Re}$ generators. In the past, many high capacity sorbent materials such as polymeric zirconium compound, polymeric titanium oxychloride, synthetic alumina, polymer embedded nanocrystalline titania, nanocrystalline zirconia and nanocrystalline alumina, etc., have been reported for preparation of chromatographic $^{188}\text{W}/^{188}\text{Re}$ generators [10, 12–19]. Despite their high sorption capacity, most of these generators used high specific activity ^{188}W produced in high flux research reactors. In fact, the development of clinical-scale generators using LSA ^{188}W produced in medium flux reactors is yet to commence in commercial settings.

In this study, we report the synthesis of mesoporous alumina sorbent by solid state mechanochemical approach and its utilization as a chromatographic sorbent in preparation of $^{188}\text{W}/^{188}\text{Re}$ generator using LSA ^{188}W produced in a medium flux research reactor. The sorption characteristics of the material were investigated and conditions were optimized for chromatographic separation of ^{188}Re from ^{188}W . Detailed quality assessment tests were carried out over a period of 6 months to analyze the suitability of ^{188}Re obtained from the $^{188}\text{W}/^{188}\text{Re}$ generator for clinical use. To the best of our knowledge, this is the first study on detailed investigation of tungsten-sorption characteristics of mesoporous alumina and its utilization as a chromatographic sorbent for preparation of a clinical-scale $^{188}\text{W}/^{188}\text{Re}$ generator using ^{188}W produced in a medium flux research reactor.

2 Experimental

Enriched (99.9% in ^{186}W) tungsten oxide was purchased from Isoflex, Russia. All other chemicals were purchased from Sigma-Aldrich and used as received.

Mesoporous alumina was synthesized by mechanical grinding of aluminum isopropoxide and glucose taken in different molar ratios (1:1, 1:1.25, 1:1.5, 1:1.75 and 1:2) in an agate mortar at room temperature for 1 h. After grinding, the reaction mixture was calcined in a furnace at 500 °C for 2 h. The lump obtained after calcination was crushed and sieved to get free flowing particles of 50–100 mesh size. The detailed procedure for optimization of the synthesis protocol and thorough characterization of the synthesized material are described in the Supporting Information.

For understanding the sorption of tungsten on mesoporous alumina synthesized under the optimized conditions, ^{187}W produced via ^{187}W reaction by irradiation of natural tungsten oxide powder in the Dhruva reactor at a flux of $1 \times 10^{14} \text{ n.cm}^{-2}.\text{s}^{-1}$ for 7 d was used as radiotracer. For this, neutron irradiated ^{187}W powder was dissolved in 4 M NaOH solution in presence of few drops of 30% H_2O_2 to convert it into $[\text{}^{187}\text{W}]\text{Na}_2\text{WO}_4$. The distribution coefficients (K_d) values of tungstate and perrhenate ions for the sorbent matrix were measured at different pH, using ^{187}W and ^{188}Re as radiotracers, as per the procedure described in the Supporting Information. Sorption studies were carried out both by batch equilibration method as well as under dynamic (column flow) condition. In batch equilibration method, an accurately weighed amount of sorbent (50 mg) was taken in a stoppered glass conical flask and equilibrated with 10 mL of the tungstate solution of varying concentration (1, 2.5, 3.7, 5.6, 7.4 mg W / mL), spiked with $\sim 370 \text{ kBq}$ (10 μCi) of ^{187}W for 4 h at pH 3. Subsequently, the contents were filtered and the activity of the filtrate was compared with that of the standard solution taken from the equilibrium mixture before incubation with the sorbent. Similarly, kinetic studies were carried out by taking 3.7 mg W/mL solution (pH ~ 3) spiked with $\sim 370 \text{ kBq}$ (10 μCi) of ^{187}W and sorption capacities were determined at different time intervals as described above. The dynamic sorption capacity was determined by passing 10 mg W/mL solution spiked with $\sim 370 \text{ kBq}$ (10 μCi) of ^{187}W through a chromatographic column packed with 1 g of mesoporous alumina at a flow rate of 1 mL/min, as per the reported procedure [9].

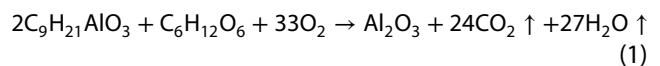
The theoretical specific activity of ^{188}W produced by double neutron capture reaction on ^{186}W target at different flux conditions was calculated by simplified Bateman equations as detailed in the Supporting Information.

Under the optimized conditions, ^{188}W was produced by irradiation of enriched (99.9% in ^{186}W) tungsten oxide (1.25 g) at a flux of $1.5 \times 10^{14} \text{ n.cm}^{-2}.\text{s}^{-1}$ for 6 months. Post irradiation, the neutron irradiated $^{186}\text{WO}_3$ powder was converted to $[\text{}^{188}\text{W}]\text{Na}_2\text{WO}_4$ by dissolving it in 20 mL of 4 M NaOH containing few drops of 30% H_2O_2 . The $^{188}\text{W}/^{188}\text{Re}$ generator was prepared by taking 4 g of mesoporous alumina in a chromatographic column placed in a lead shielded assembly. The activity was loaded in the column by passing ^{188}W solution (14.1 GBq, 100 mL at pH ~ 3) through the column at a flow rate of 1 mL/min. Rhenium-188 was regularly eluted from the $^{188}\text{W}/^{188}\text{Re}$ generator in saline solution [0.9% NaCl (w/v) solution prepared in deionized water] and the performance of the generator was evaluated over a period of 6 months. The details regarding preparation of the $^{188}\text{W}/^{188}\text{Re}$ generator and its quality control are provided in the Supporting Information.

3 Results and discussion

3.1 Synthesis and characterization of the sorbent

The sorbent, mesoporous alumina, was synthesized by solid state mechanochemical reaction of aluminum isopropoxide with glucose, followed by calcination at 500 °C. The glucose acted as template which could be removed during calcination leading to formation of gases which resulted in creation of mesopores in the sorbent matrix [8, 9]. The balanced chemical equation for this process can be written as:



As predicted from this equation, 2 molecules of aluminum isopropoxide reacts with 1 molecule of glucose for getting 1 molecule of aluminum oxide product. However, in order to obtain higher mesoporosity and hence higher sorption capacity of mesoporous alumina, higher amount of glucose content (than the amount predicted from the balanced chemical equation) was required in the reaction mixture. For maximizing the sorption capacity, the molar ratios of the aluminum isopropoxide to glucose in the reaction mixture were varied and the reactions were carried out under identical conditions, as detailed in the Supporting Information. Based on the mesoporosity (Figure S1, Figure S2 and Table S1) and sorption capacity (Table S2) studies, the material synthesized by maintaining aluminum isopropoxide to glucose molar ratio in the reaction mixture as 1:1.5 was identified as the optimal material for preparation of the $^{186}\text{W}/^{188}\text{Re}$ generator. The material synthesized under the optimized synthetic condition was free flowing and exhibited adequate mechanical

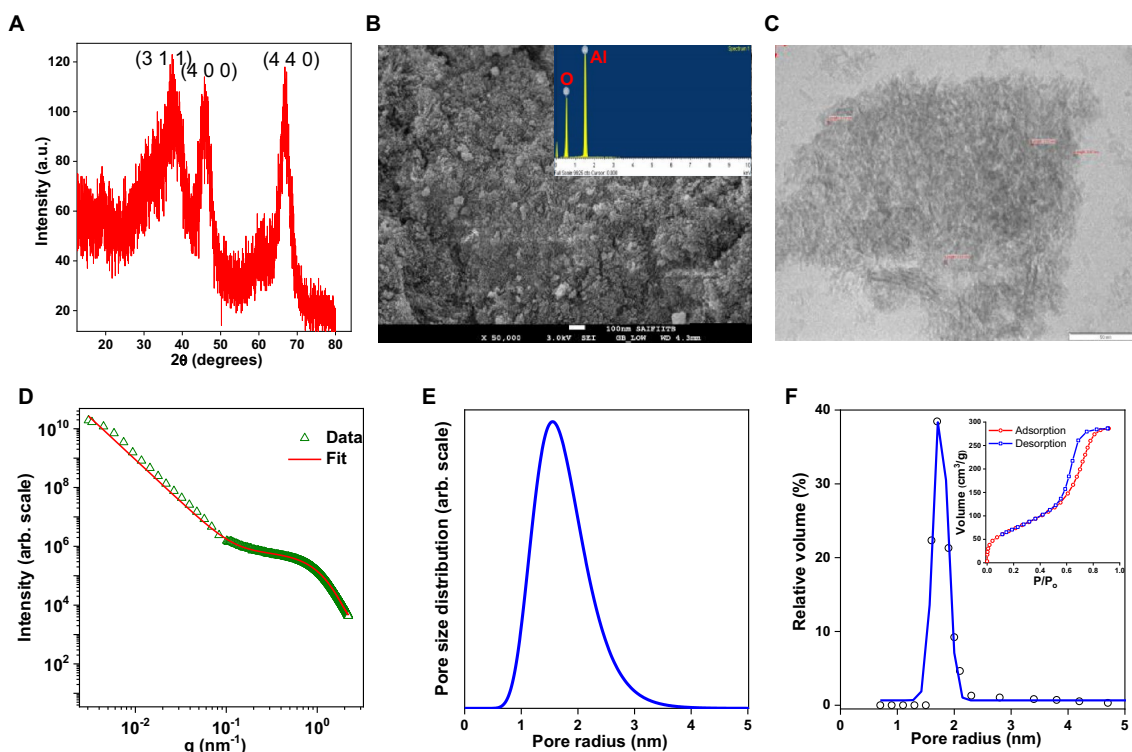


Fig. 1 Characterization of mesoporous alumina **(a)** XRD pattern, **(b)** SEM micrograph. Inset shows the EDS spectrum, **(c)** TEM micrograph, **(d)** Combined SAXS and MSANS profile. MSANS profiles are scaled to SAXS data in the overlapping q range, **(e)** Pore size distribution obtained from the SAXS-MSANS profile, **(f)** Pore size distribution from nitrogen adsorption-desorption isotherm. Inset shows the type IV isotherm

strength for use as a sorbent matrix in a chromatographic procedure.

The X-ray diffraction (XRD) pattern of mesoporous alumina indicated that the material is nanocrystalline, with peaks assigned to (3 1 1), (4 0 0) and (4 4 0) planes of cubic alumina (Fig. 1a). From the XRD pattern, the average crystallite size of the material was determined to be 2.4 ± 0.1 nm, using the standard Debye Scherrer's equation. The scanning electron microscopy (SEM) of the material showed worm-hole like structure which gives an idea that it is porous (Fig. 1b). The energy dispersive spectroscopy (EDS) showed peaks corresponding to Al and O. The SEM image of the overall particles is shown in Figure S3A. The transmission electron microscopy (TEM) of the mesoporous alumina showed that the material is nanosized but highly agglomerated (Fig. 1c). Agglomeration is essential in order to use a nanomaterial as a sorbent matrix in a chromatographic column [20]. The crystallite size of the material as evident from the TEM micrograph was in the range of 2–4 nm, which substantiated the results obtained from the XRD studies. The size distribution of the agglomerated particles as determined by laser diffraction technique is shown in Figure S3B and the mean particle size was determined to be 57.3 ± 1.6 μm .

From the SAXS-MSANS study, the pore size distribution showed that the average pore diameter of the material was 3.4 ± 0.2 nm, proving that it is mesoporous (Fig. 1e). This was further corroborated by conventional nitrogen adsorption-desorption method, which showed type IV isotherm characteristic of mesoporous materials and the average pore diameter was determined to be 3.6 ± 0.3 nm (Fig. 1f).

The porous structure of the material was investigated by combined small angle X-ray scattering (SAXS) and medium resolution small-angle neutron scattering (MSANS) techniques, using a laboratory based SAXS and nuclear reactor based MSANS facility for accessing a wide q range [8, 9]. The scattering profile did not show any diffraction peak, indicating the absence of ordered pores in the material (Fig. 1d). From the SAXS-MSANS study, the pore size distribution showed that the average pore diameter of the material was 3.4 ± 0.2 nm, proving that it is mesoporous (Fig. 1e). This was further corroborated by conventional nitrogen adsorption-desorption method, which showed type IV isotherm characteristic of mesoporous materials and the average pore diameter was determined to be 3.6 ± 0.3 nm (Fig. 1f).

The surface charge on mesoporous alumina was analyzed at different pH environments by determining the zeta potential (Table 1). Under the acidic conditions, the material showed positive zeta potential with maximum value (48.5 ± 3.7 mV) at pH 3. On increase of pH beyond 6, the zeta potential became increasingly negative. The isoelectric point was attained between pH 6 and 7.

Table 1 Variation in zeta potential of mesoporous alumina and the K_d values of tungstate and perrhenate ions at different pH

Medium	Zeta potential ^a (mV)	K_d^a	
		Tungstate	Perrhenate
pH 1	23.2 ± 1.8	89,211 ± 2313	252 ± 12
pH 2	47.6 ± 4.2	231,415 ± 3141	212 ± 23
pH 3	48.5 ± 3.7	487,564 ± 2199	151 ± 22
pH 4	40.7 ± 2.9	377,567 ± 1877	125 ± 18
pH 5	31.7 ± 1.9	74,512 ± 1223	87 ± 13
pH 6	22.7 ± 2.6	19,784 ± 1458	45 ± 11
pH 7	-17.9 ± 1.4	11,754 ± 1476	13 ± 6
pH 8	-19.5 ± 1.8	2436 ± 177	8.7 ± 2.3
pH 9	-27.1 ± 2.2	811 ± 78	4.5 ± 1.6
pH 10	-33.9 ± 2.8	512 ± 37	3.2 ± 0.7
Saline	7.6 ± 1.5	15,521 ± 231	0.2 ± 0.1

^aAverage of three independent measurements with standard deviation is presented

3.2 Sorption characteristics of mesoporous alumina

In order to understand the sorption characteristics of mesoporous alumina, the distribution coefficients (K_d) of tungstate and perrhenate ions were determined at different pH and the results are summarized in Table 1. Under all conditions, the K_d values for tungstate ions are much higher than that of perrhenate ions, indicating the high affinity of the sorbent towards tungstate ions. The maximum K_d value was obtained at pH 3, indicating that this is the most favorable condition for sorption of ^{188}W in the generator column. At pH < 6, tungstate ions polymerize to form highly negative polytungstate $[\text{HW}_6\text{O}_{21}]^{5-}$ ions [21]. It is pertinent to note that the zeta potential to the sorbent was maximum positive at pH 3, resulting in high sorption of negatively charged $[\text{HW}_6\text{O}_{21}]^{5-}$ ions on mesoporous alumina. In saline solution, the K_d value for tungstate ions is appreciably high (15,521 ± 231) and that for perrhenate ions is negligibly low (0.2 ± 0.1). Therefore, saline is a suitable medium for selective elution of ^{188}Re from the generator column.

The uptake of polytungstate ions on mesoporous alumina under acidic conditions is expected to occur in two steps. The first step is due to electrostatic attraction of negatively charged polytungstate ions on the positively charged surface of alumina under acidic conditions. In the second step, thermodynamically stable complexes of tetrahedrally coordinated aluminum atoms and WO_4^{2-} tetrahedrons are formed, resulting in strong binding as evident from the high K_d values [22]. On the other hand, perrhenate ions cannot form complex with the alumina matrix and therefore manifests low K_d values.

The tungstate sorption isotherm was analyzed at room temperature (298 K) by the following three models [23]:

Langmuir model:

$$q_e = \frac{Q_0 \cdot bC_e}{1 + bC_e} \quad (2)$$

A linear form of this equation is:

$$\frac{C_e}{q_e} = \frac{1}{Q_0 \cdot b} + \frac{C_e}{Q_0} \quad (3)$$

where, Q_0 and b are Langmuir constants that are related to the maximum sorption capacity and sorption energy, respectively.

Freundlich model

$$q_e = K_F C_e^{1/n} \quad (4)$$

Equation (4) can be rewritten as:

$$\log q_e = \log K_F + \frac{1}{n} \log C_e \quad (5)$$

where, K_F is Freundlich constant and n is Freundlich exponent (dimensionless).

Dubinin–Radushkevich (D–R) Isotherm

$$\ln q_e = \ln X_m - \beta \varepsilon^2 \quad (6)$$

where, X_m is the maximum sorption capacity, β is the activity coefficient related to the mean sorption energy, and ε is the Polanyi potential, which can be written as

$$\varepsilon = RT \ln \left(1 + \frac{1}{C_e} \right) \quad (7)$$

where, R is the universal gas constant [expressed in units of kJ/(mol.K)] and T is the temperature (in K). In all these models, q_e is the amount of tungstate ions adsorbed on mesoporous alumina at equilibrium (expressed in terms of mg/g), C_e is the equilibrium concentration of metal ions (expressed in terms of mg/L). From the fittings (Fig. 2a, Figure S4), it could be inferred that the equilibrium data could be fitted well with Freundlich model with $R^2 = 0.99$, which implied that adsorption occurred on a heterogeneous surface, where the adsorption energy exponentially reduced with decrease in number of adsorption sites [24]. The values of K_F and $1/n$ were determined to be 47.01 mg g⁻¹(mg L⁻¹)^{-1/n} and 0.24, respectively. Because the value of $1/n$ is less than unity, it indicates a favorable adsorption [23].

The kinetics for tungstate sorption by mesoporous alumina was analyzed at room temperature (298 K) by two kinetic models [23].

Pseudo-first-order reaction

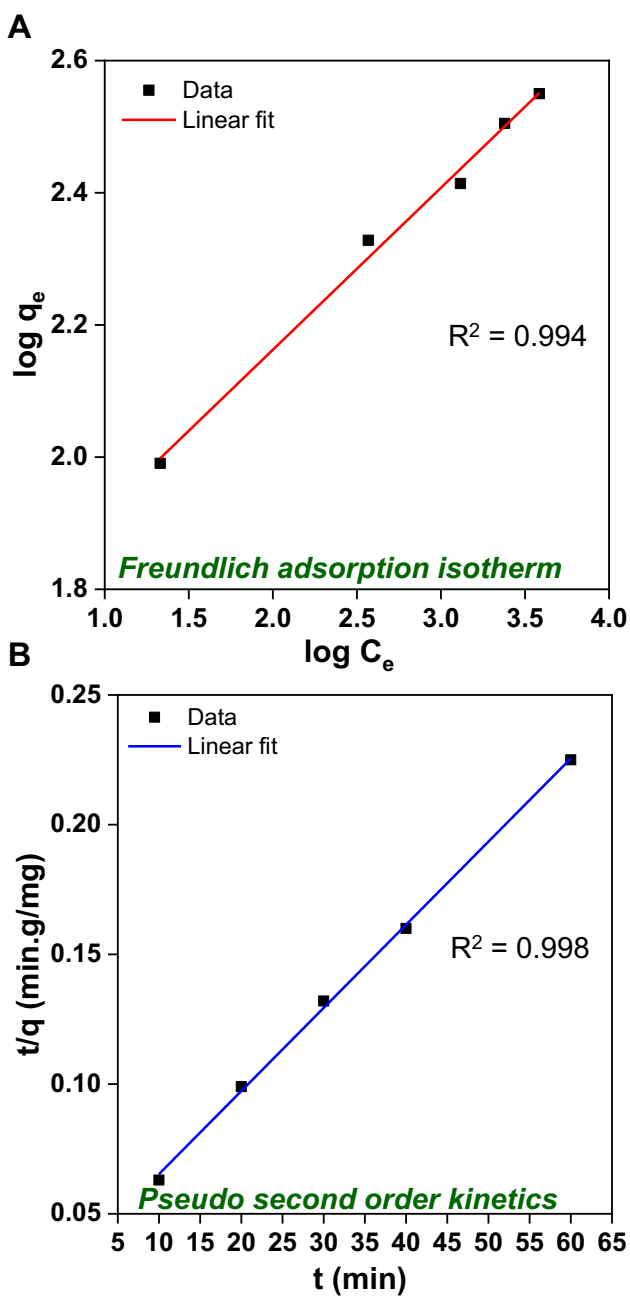


Fig. 2 Sorption of tungstate ions on mesoporous alumina. (a) Freundlich adsorption isotherm plot, (b) Pseudo second order kinetics plot

$$\log (q_e - q) = \log q_e - \frac{k_1 t}{2.303} \tag{8}$$

Pseudo-second-order reaction

$$\frac{dq}{dt} = k_2 (q_e - q)^2 \tag{9}$$

where, k_1 and k_2 are the rate constants for the pseudo-first-order and pseudo-second-order reactions respectively, q_e

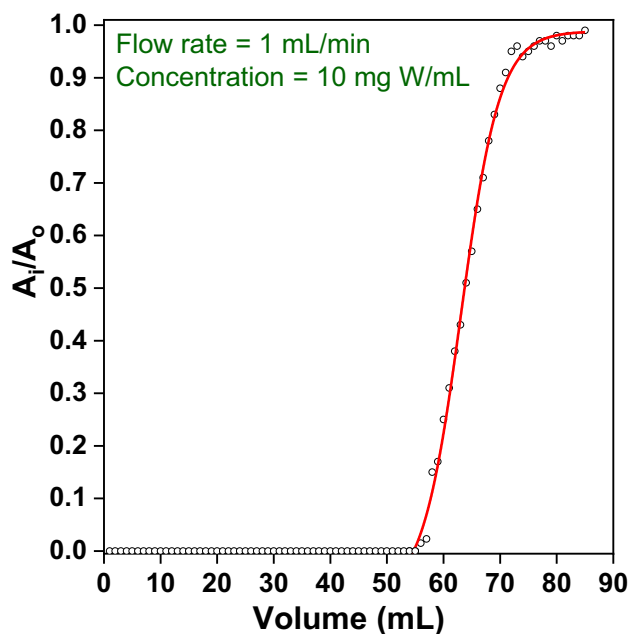


Fig. 3 Breakthrough profile on passing ^{187}W solution (10 mg W/mL, pH~3) through a chromatographic column containing 1 g of mesoporous alumina

is the amount of metal ion adsorbed at equilibrium time (expressed in units of mg/g) and q is the amount of metal ion adsorbed at any time (also expressed in units of mg/g). Integrating Eq. (9) for the boundary conditions of $t=0$, $q=0$ gives the linear equation:

$$t/q = 1/(k_2 \times q_e^2) + (1/q_e)t \tag{10}$$

$$h = k_2 \times q_e^2 \tag{11}$$

From the fittings (Fig. 2b, Figure S5), it could be inferred that the sorption process follows pseudo-second-order kinetics indicating that the process is chemisorption and irreversible [25]. The kinetic parameters k_2 , q_e and h were determined to be $3.07 \times 10^{-4} \text{ g min}^{-1} \text{ mg}^{-1}$, 312.5 mg g^{-1} and $30.1 \text{ mg g}^{-1} \text{ min}$, respectively. It is pertinent to mention here that adsorption mechanisms cannot be accurately assigned based on observing simple kinetic experiments or by fitting kinetic models [26, 27]. They can only be established by using several analytical techniques [27]. However, such studies have not been pursued as they were outside the scope of the present work.

Under dynamic conditions, the breakthrough capacity of the sorbent was determined to be $550 \pm 12 \text{ mg W/g}$ (Fig. 3), which is ~ 10 times higher than the conventionally used bulk alumina [28]. A comparative evaluation of the breakthrough capacity of mesoporous alumina

Table 2 Comparison of the breakthrough capacity of mesoporous alumina with that of other sorbent materials reported in the literature

Sorbent	Breakthrough capacity (mg/g)	References
Polymeric zirconium compound	#	[14]
Polymeric titanium oxychloride	#	[16]
Synthetic alumina	180	[13]
Polymer embedded nanocrystalline titania	102	[18]
Nanocrystalline zirconia	120	[19]
Nanocrystalline -alumina	300	[15]
Mesoporous alumina	550	This work

#Owing to the slow sorption kinetics, the sorption capacity under dynamic conditions was not determined

determined under dynamic conditions with that of other high capacity sorbents reported for the preparation of $^{188}\text{W}/^{188}\text{Re}$ generator is provided in Table 2. It can be seen from the table that the breakthrough capacity of mesoporous alumina is much higher than that of other reported materials, which demonstrates its suitability for preparation of clinical-scale $^{188}\text{W}/^{188}\text{Re}$ generator.

3.3 Production of ^{188}W and development of $^{188}\text{W}/^{188}\text{Re}$ generator

The theoretical specific activity of ^{188}W calculated using simplified Bateman equation under different neutron flux conditions is shown in Figure S6. The specific activity of ^{188}W increased with increase in flux and an irradiation period of ~6 months was required to get appreciable specific activity. On irradiation of 1.25 g of enriched (99.9% in ^{186}W) tungsten oxide target at a flux of 1.5×10^{14} n.cm⁻².s⁻¹ for 6 months, 15.1 ± 0.4 GBq of ^{188}W could be produced with a specific activity of 15.0 ± 0.3 GBq/g which is comparable to that obtained by theoretical calculation.

A 14.0 GBq $^{188}\text{W}/^{188}\text{Re}$ generator (Figure S7) was developed and its performance was evaluated over a period of 6 months. The elution profile of the generator was recorded at the beginning of every month and shown in Fig. 4a. The elution profiles are reasonably sharp and they gradually broadened with passage of time. The gradual broadening in elution profiles is not unexpected and is due to decay loss of ^{188}W and repeated elution of ^{188}Re from the same generator column over a prolonged period of time. Nevertheless, it can be seen from the elution profiles that ^{188}Re could be quantitatively eluted in 8 mL of saline solution. In the conventional bulk alumina based $^{188}\text{W}/^{188}\text{Re}$ generators, a much larger volume of saline solution (> 15–20 mL) is required for elution of ^{188}Re [29].

As evident from the elution profiles (Fig. 4a), the radioactive concentration of ^{188}Re could be further increased by adopting fractionated elution approach. The elution yield of ^{188}Re was initially ~90% and it marginally decreased over the period of 6 months of study (Fig. 4b). A typical γ -spectrum of ^{188}Re eluted from the generator is shown in Figure S8. From the analyses of the decayed samples of ^{188}Re , the level of ^{188}W impurity could be quantified as < 10⁻⁴% over the 6 months of elution (Fig. 4c). The radiochemical purity of ^{188}Re in the form of ReO_4^- was > 98%, as determined by the paper chromatographic study (Figure S9). Inductively coupled plasma—atomic emission spectroscopy (ICP-AES) analysis of the decayed samples revealed that the level of tungsten impurity was below detectable limit (<0.01 ppm) and the level of Al ions was 0.11 ± 0.02 ppm. No other trace metal impurity could be detected in the ^{188}Re samples indicating high chemical purity for preparation of radiopharmaceuticals. This performance remained consistent even after 6 months of usage of the $^{188}\text{W}/^{188}\text{Re}$ generator, indicating high stability of the mesoporous alumina sorbent even in intense radiation environment. If mesoporous alumina sorbent did not retain its stability over a prolonged period of time, deteriorating performance of the $^{188}\text{W}/^{188}\text{Re}$ generator in terms of increased ^{188}W breakthrough and significant amounts of Al ions impurity would have been observed in the ^{188}Re eluate.

In all the batches, the ^{188}Re eluate was found to be sterile and the level of bacterial endotoxins was < 25 EU, which is within acceptable limit as per Indian Pharmacopoeia [30]. Overall, it could be inferred from these quality control studies that ^{188}Re obtained from this generator was amenable for use in clinical context.

4 Conclusions

In summary, solid state mechanochemistry has been found to be a viable method for synthesis of mesoporous alumina sorbent for preparation of chromatographic $^{188}\text{W}/^{188}\text{Re}$ generator using ^{188}W produced in a medium flux research reactor. The sorbent exhibits high sorption capacity (~550 mg W/g), which is adequate for preparation of clinical-scale generator. The ^{188}Re obtained from this chromatographic generator met all the requirements for clinical use. Adoption of this strategy would aid towards wider availability of $^{188}\text{W}/^{188}\text{Re}$ generators for clinical use at more affordable cost, since ^{188}W produced in medium flux research reactors could be effectively utilized. This would be especially beneficial for developing countries which do not have access to high flux research reactors for radioisotope production.

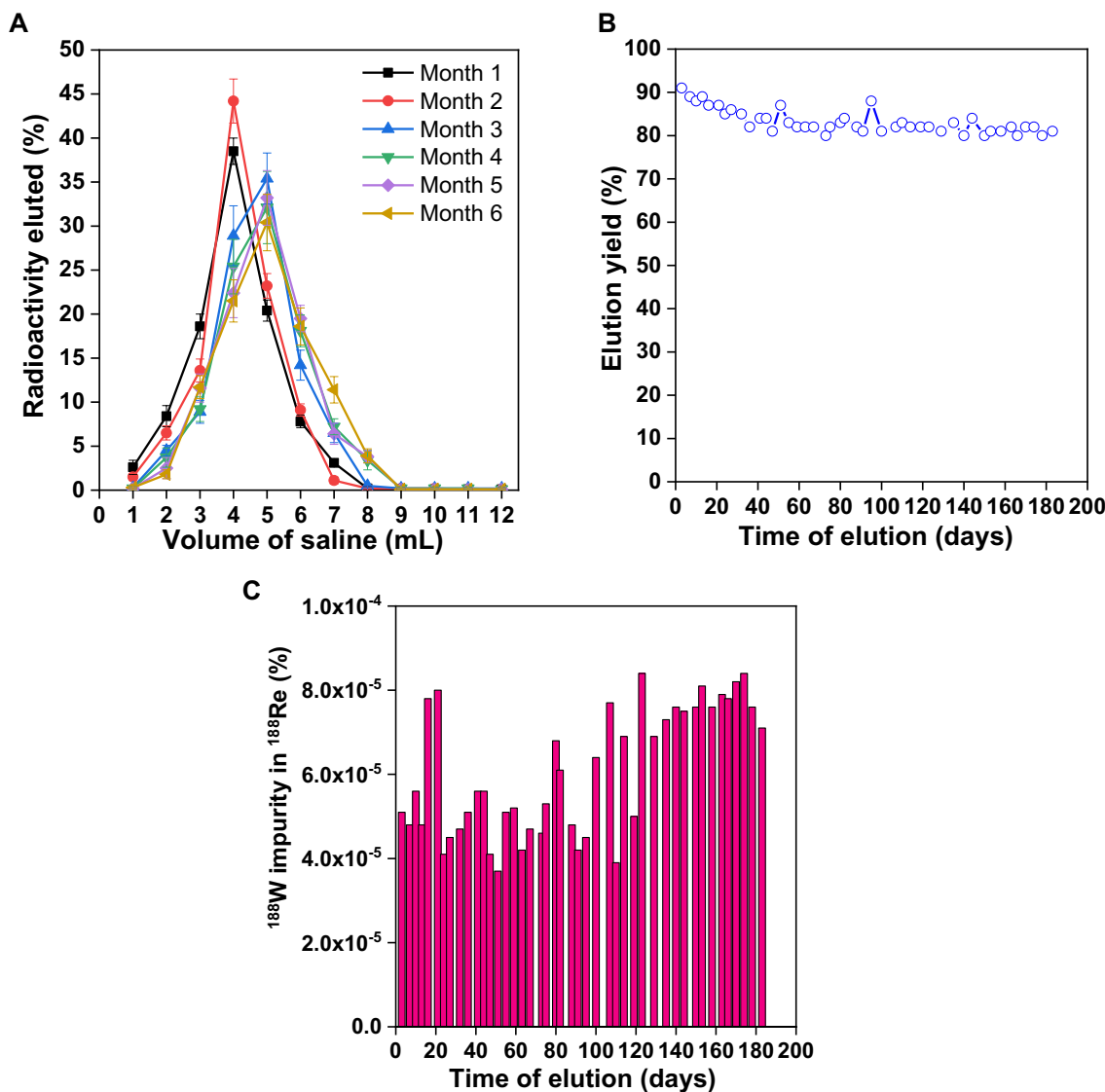


Fig. 4 Performance evaluation of the ¹⁸⁸W/¹⁸⁸Re generator over a period of 6 months (a) Elution profiles at the beginning of each month, (b) Elution yield, (c) Level of ¹⁸⁸W impurity in ¹⁸⁸Re

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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