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Nano-titania: a novel purification and concentration adsorbent for ^{125}I production for medical uses

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Abstract The presented work describes the efficient use of nano-crystalline titania (TiO$_2$) to remove trace levels of cesium radio-contaminants (^{134}Cs and ^{137}Cs) in iodine-125 (^{125}I) solution produced via neutron activation of natural ^{124}Xe target. The adsorption parameters of TiO$_2$ were investigated to attain the optimum purification and concentration conditions of ^{125}I solution. The maximum sorption capacity of Cs and ^{125}I were approximately 56 and 67 mg/g TiO$_2$, respectively. The final ^{125}I solution was of high radiochemical, radionuclidic and chemical purities, besides, it showed high radioactive concentration that confirming its suitability for nuclear medicine applications and ^{125}I brachytherapy sources preparation.
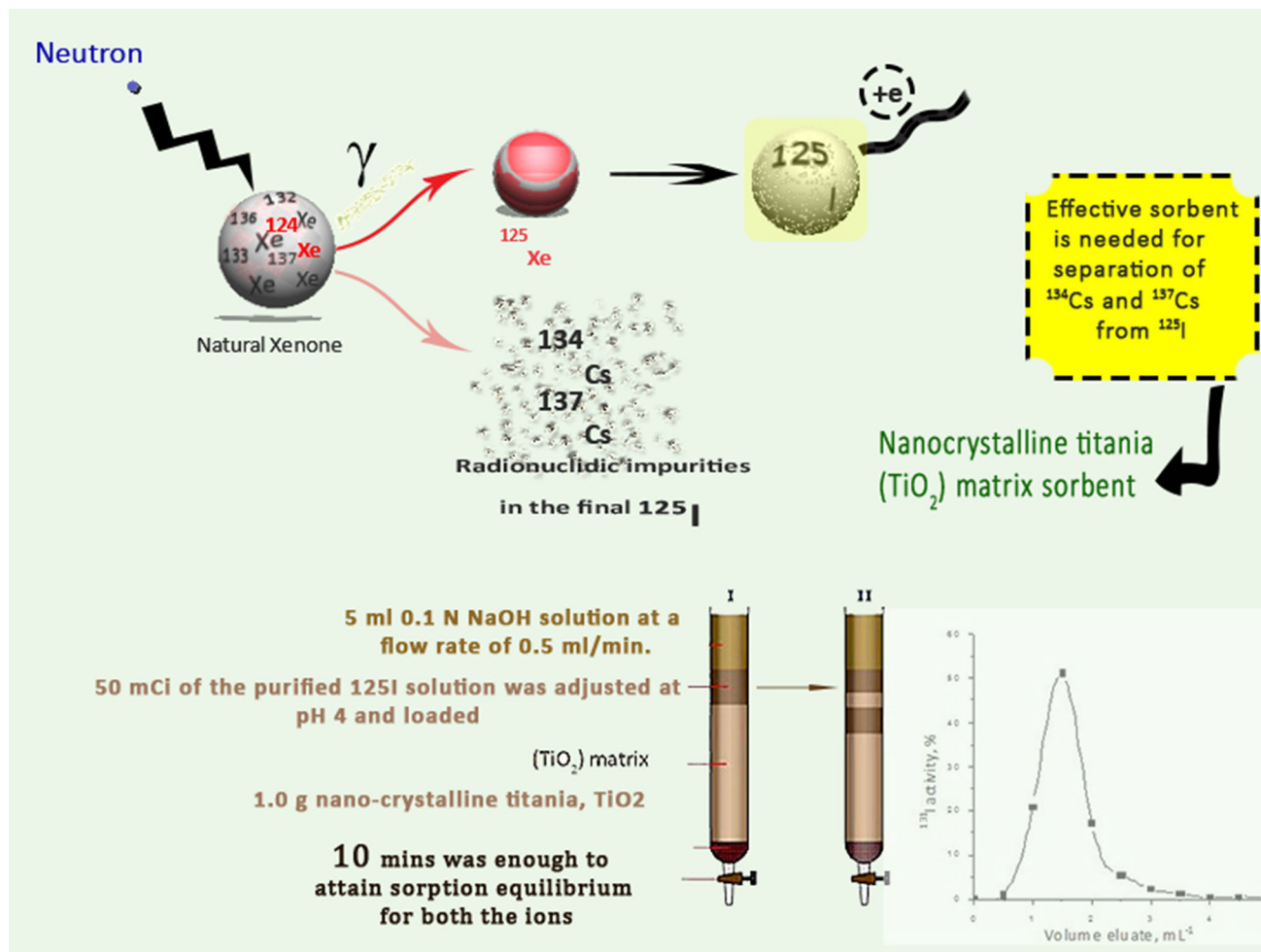
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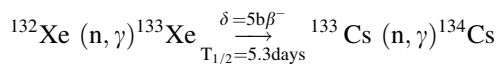
Graphical abstract

Introduction

^{125}I demand is increasing worldwide due to its suitability for research, therapeutic and diagnostic purposes [1–3]. It is used for all these purposes due to its unique physico-chemical parameters such as: long physical half-life (59.4 days), 35 keV γ-rays, 27 keV X-rays and its high specific activity (No Carrier Added form) [4–9]. Moreover, It is one of the most interested radioisotopes suitable for brachytherapy applications for prostate cancer, breast cancer and brain tumor, beside its use in radioimmunoassay (RIA) procedures for the quantification of biomolecules concentrations (nanomole) such as hormones, drugs, etc. [1–3, 9, 10].

^{125}I is produced by the (n,γ) irradiation of natural or enriched ^{124}Xe target in nuclear reactor as show in Fig. 1. [11, 12]. The produced ^{125}I will undergo electron capture and decays to the stable ^{125}Te completing its radioactive decay process.

In case of enriched ^{124}Xe gas production route, it is most favored due to the absence of any secondary nuclear reactions resulted in superior radionuclidic purity. But its main drawback is that enriched ^{124}Xe is a highly expensive target material. While in case of natural xenon gas production route, natural xenon is much cheaper than enriched ^{124}Xe, but natural xenon is containing a mixture of nine stable isotopes with percentages: ^{124}Xe (0.096%); ^{126}Xe (0.090%); ^{128}Xe (1.92%); ^{129}Xe (26.44%); ^{130}Xe (4.08%); ^{131}Xe (21.18%); ^{132}Xe (26.89%); ^{134}Xe (10.44%); and ^{136}Xe (8.87%) [11, 13], which after neutron activation raises the level of radio-contaminants such as ^{134}Cs and ^{137}Cs contributing to the radionuclidic impurities of the produced ^{125}I as follows:
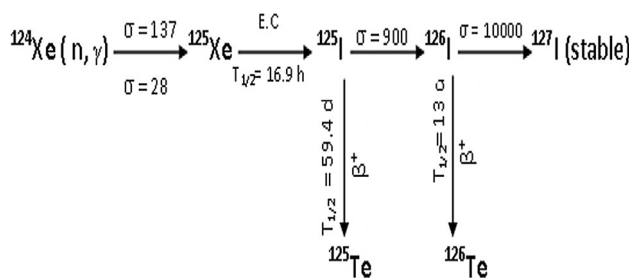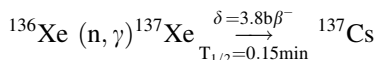
$$^{132}\text{Xe } (n, \gamma)^{133}\text{Xe} \xrightarrow[T_{1/2}=5.3\text{days}]{\delta=5b\beta^-} {}^{133}\text{Cs } (n, \gamma)^{134}\text{Cs}$$

Fig. 1 Schematic diagram of ^{125}I production from ^{124}Xe target

$$^{136}Xe \ (n, \gamma)^{137}Xe \xrightarrow[T_{1/2}=0.15min]{\delta=3.8b\beta^-} \ ^{137}Cs$$

All of this necessitates the removal of ^{134}Cs and ^{137}Cs for the ^{125}I product when it is produced for the natural xeno gas, which is mainly accomplished via distillation [14]. Although the distillation is an effective technique, the need for high temperature operations (hundreds of degrees centigrade) is its main disadvantage.

For seeking an efficient sorbent to attain the efficient separation of ^{134}Cs and ^{137}Cs from ^{125}I, our attention was directed towards the use of nano-sorbents. Many scientific fields started to explore the effectiveness of nano-sorbents as novel replacements to the commonly used sorbents that are mainly as bulk materials [15]. As nano-sorbents interact with numerous ways with different ions in an aqueous solution based upon their nano-scale features such as size, shape, surface area and particle charge, this raises up the potentiality to achieve the required efficient separations capacity [16].

In this context, t-ZrO$_2$ use seemed to show new hypothesis as it provide the capability to control the adsorptive activity besides, its selectivity by changing the external solution pH [13]. The potential of t-ZrO$_2$ as an adsorbent for column chromatography separation, it was fully exploited its use fullness in a many of radiochemical separation and concentration procedures [15, 17, 18]. Also, nano-composite TiO$_2$/Poly(acrylamide-styrene sodium sulfonate) [TiO$_2$/P (AAm–SSS)] was used for Cs ions separation from its solution at pH 8, [19].

From all of that, the presented study discuss the effective use of nano-titania as a new adsorbent capable of purifying and concentrating ^{125}I that is produced via neutron irradiation of natural xenon gas.

Experimental

Materials

No-carrier-added sodium iodide (NCA Na ^{125}I, 3.7 GBq/mL in 0.1 N NaOH) was purchased from Institute of Isotopes, Budapest, Hungary. Radioactive ^{137}Cs was supplied by Eckert & Ziegler Company. Radioactive ^{134}Cs was produced via irradiation of CsCl target in Egyptian Second Thermal Research Reactor (ETRR-2).

Synthesis of nano-crystalline titania (TiO$_2$)

Nano-crystalline titania (TiO$_2$) was prepared as reported in [20, 21]. In brief, with ratio of 2:1 (v/v), titanium tetra-chloride was added drop by drop to isopropyl alcohol. The formed mass, as semisolid, was left for 5 days. After that, it was IR dried using an infrared lamp at 80 °C for 2 days. The obtained solid material was heated for 2 h at 200 °C in a furnace. After drying, the obtained solid mass was grounded in a porcelain mortar then sieved to get particles size suitable for use in a chromatographic column. TiO$_2$ nanoparticles was formed with BET surface area and average pore diameter (Dp) 320 m^2 g^{-1} and $\sim 0.00,478$ nm, respectively. The particles size was found to be ~ 40 nm [20, 21].

Batch sorption study

Determination of distribution coefficients of I$^-$ and Cs$^+$ ions on nano-crystalline (TiO$_2$)

Cs$^+$ and I$^-$ ions distribution coefficients (K_d) on TiO$_2$ matrix were determined at different pH values, using radioactive I$^-$ and Cs$^+$ tracers. In 50 mL stoppered glass vials, 20 mL solution containing radioactive I$^-$ and Cs$^+$ tracers was placed followed by suspending 200 mg of nano-titania sorbent, in each experimental. The mechanical shaker was used to shake these vials for 30 min at room temperature. The radioactivity of the solution was determined before and after equilibrium using Multichannel spectrometry coupled with a high purity germanium coaxial detector (USA) that was calibrated with: ^{155}Eu (86.5 and 105.3 keV), ^{57}Co (122.1 and 136.5 keV), ^{137}Cs (661.6 keV), ^{54}Mn(834.8 keV), and ^{65}Zn(1115.5 keV) as mixed source.

The distribution coefficients (K_d) were calculated using the following equation:

$$K_d = \frac{(A_i - A_r)V}{A_r m} Lg^{-1}$$

where A_i and A_r are the initial total radioactivity of 1 mL the solution and the un-adsorbed activity in 1 mL of the solution at equilibrium, respectively. V is the solution volume (mL) and m is the mass (g) of the sorbent. The standard deviation of K_d values was the mean of three experiments.

Determination of equilibrium time for the sorption of I⁻ and Cs⁺ onto nano-crystalline (TiO₂)

To study nano-TiO₂ kinetic performance, time dependence of sorption of I⁻ and Cs⁺ onto nano-TiO₂ was done by the determination of these ions distribution coefficient (K_d) at different intervals (5–30 min). The K_d of I⁻ was studied at pH 3, while that for Cs⁺ was studied at pH 12. The K_d values were evaluated as the mean of three consecutive experiments. The time that shows unchanged K_d represented the equilibrium indication.

Determination of zeta potential

Zeta potential was determined using PSS-NICOMP Zeta Potential/Particle Sizer 380ZLS (PSS-NICOMP, Santa Barbara, CA, USA). Zeta potential at different pH were measured, as a mean of 3 values, by mixing about 5 mg of the sorbent with 50 mL of deionized water and adjusting the pH of the solution using HClO₄ and NH₄OH.

Nano-TiO₂ column dynamic sorption studies

Determination of breakthrough profile of Cs⁺ ion and I⁻ from nano-TiO₂ column

In order to determine the Cs and I sorption capacity under dynamic conditions, two glass columns [8 cm (l) × 0.5 cm (i.d.)] having a glass wool piece in the bottom were packed with 0.5 g of TiO₂. On first nano-TiO₂ column, 50 mL CsCl solution (2.5 mg Cs mL⁻¹) at pH 12 (the pH adjusted using HClO₄ and NH₄OH) tagged with ¹³⁴Cs tracer (∼36 MBq) was loaded with a flow rate of 0.5 mL min⁻¹. On second nano-TiO₂ column, 50 mL NaI solution (5 mg I/mL) at pH 4 and tagged with ¹²⁵I (∼180 MBq) tracer was loaded with a flow rate of 0.5 mL min⁻¹.

Standard samples of feeding the ¹³⁴Cs and ¹²⁵I solutions, 2.0 mL, were kept as reference (C₀). The effluents, in fractions equal in volume to the reference (2.0 mL each), were collected. The ¹³⁴Cs and ¹²⁵I radioactivity in the reference (C₀) and effluent fractions (C) were evaluating by counting the 605 and 35 keV γ-ray energy peaks of ¹³⁴Cs and ¹²⁵I, respectively, using a HPGe detector. The ratio of count rate C of the effluent after equilibrium to the original feed ¹³⁴Cs solution was taken as the parameter to follow the sorption pattern.

The dynamic sorption capacity, Q, was calculated by the equation:

$$Q = \frac{(V_{50\%} \times C_o)}{W} \text{ M mole Cs or I/gm TiO}_2$$

where, $V_{50\%}$ is the effluent volume (mL) at $C/C_o = 0.5$ (as indicated by measuring the counting rate of the initial solution and different effluent fractions), C_o is the initial concentration M⁻¹ of ¹³⁴Cs or ¹²⁵I and W is the column matrix weight.

Purification and concentration of ¹²⁵I solution from ¹³⁴Cs and ¹³⁷Cs radio-impurities

A 8 cm (l) × 0.5 cm (i.d.) chromatographic column with a glass wool piece in the bottom was packed with 1 g of nano-TiO₂ and conditioned at pH 12 using HClO₄ and NH₄OH. Simulation solution, as that produced from neutron irradiated of natural ¹²⁴Xe, was prepared by mixing 20 mL from ¹²⁵I (180 MBq) with radio-impurities ¹³⁴Cs (36 MBq) and ¹³⁷Cs (18 MBq). This simulation solution was adjusted at pH 12 and was loaded on the nano-TiO₂ column with flow rate of 0.5 mL min⁻¹. The effluent was collected and its activity was measured in an ionization chamber. The pH of purified ¹²⁵I was adjusted to 4 and it was concentrated by passing through 0.5 g of nano-TiO₂ [8 cm (l) × 0.5 cm (i.d.)] chromatographic column conditioned at pH 4 and with flow rate of 0.5 mL min⁻¹. The adsorbed ¹²⁵I was milked from the column using 0.5 M NaOH solution at flow rate of 0.5 mL min⁻¹. In order to estimate the elution profile, the eluate was collected as 0.5 mL and the each fraction activity was measured.

Quality control parameters of ¹²⁵I product solution

Elution efficiency

Passing 5 mL 0.5 M NaOH solution carried out elution of ¹²⁵I from chromatographic column. Fractions of eluted solution were collected in equal volume to the reference (0.5 mL each) with a flow rate of 0.5 mL/min. The elution efficiency was calculated by

$$E_{\text{eff}}, \% = \frac{I_E}{I_L} \times 100$$

where, I_E is the activity of eluted ¹²⁵I as summations of collected elution fractions and I_L is the activity of ¹²⁵I loaded in column.

Radionuclidic purity

¹²⁵I eluate radionuclidic purity represents the proportion of ¹²⁵I radionuclide to the total eluate radioactivity that was evaluated using a γ-ray spectroscopy multichannel analyzer [22].

Radiochemical purity

^{125}I eluate radiochemical purity was determined using the ascending paper chromatography method by developing a Whatman No.1 paper strip by a mixture solution [75% methanol and 25% water (v/v)].

The R_f value was calculated using the following formula:

$$R_{\mathrm{f}} = \frac{\text{The distance (cm) travelled by the I}^-\text{radionuclide from the starting line to the peak position}}{\text{The distance (cm) travelled by the solvent from the starting line to the solvent front}}$$

Radiochemical purity, R_c, is the contribution of a specific isotope chemical species counts, n, to the total counts of the spot. It was calculated from the following equation:

$$R_c = \frac{I_n}{I_t} \times 100$$

where, I_n is counts of the specified radioisotope chemical form (cpm), determined by area under the corresponding R_f peak and I_t is the total counts in the spot applied to the start line of the chromatographic paper (cpm), under similar counting conditions.

Results and discussion

Production of ^{125}I

^{125}I is produced by neutron activation of natural or enriched ^{124}Xe gas as reported [9]. In this work, a simulation of producing ^{125}I from natural Xe gas was done by dissolving 300 mg NaI in 50 mL 0.1 N NaOH solution (5.0 mg I/mL) then adding 125 mg CsCl with stirring (2.5 mg Cs/mL) followed by tagging the whole mixture with 5.0 mCi ^{125}I, 1.0 mCi ^{134}Cs and 0.5 mCi ^{137}Cs radiotracers. The radioactivity of ^{125}I was measured in ionization chamber while ^{134}Cs and ^{137}Cs radiotracers were evaluated by γ-ray spectroscopy using multichannel analyzer, HPGe detector by monitoring the 605 and 661 keV peaks for ^{134}Cs and ^{137}Cs, respectively, Fig. 2.

Batch sorption study

The K_d values of I$^-$ and Cs$^+$ ions at different time intervals are very efficient approach to evaluate the optimum nano-TiO$_2$ sorption contact time.

The plot of K_d versus time is demonstrated in Fig. 3. It is clear that by increasing the contact period of I$^-$ and Cs$^+$ ions with the sorbent, the K_d values increase and that a contact period of 10 min was enough to obtain the sorption equilibrium for I$^-$ and Cs$^+$ ions.

The adsorbed ions kinetics are controlled by many independent processes that can affect in series or in parallel, such as chemical reaction (chemisorption), external mass transfer (film diffusion), bulk diffusion and intraparticle diffusion. Due to the availability of reactive surface area of nano-TiO$_2$, it showed an extraordinarily fast

Fig. 2 Typical gamma-ray spectra of ^{125}I solution containing ^{134}Cs and ^{137}Cs impurities
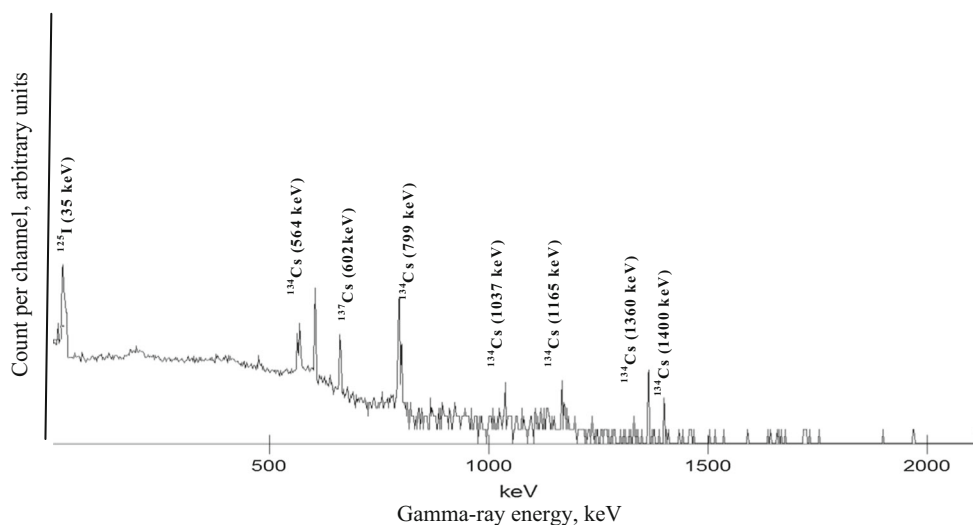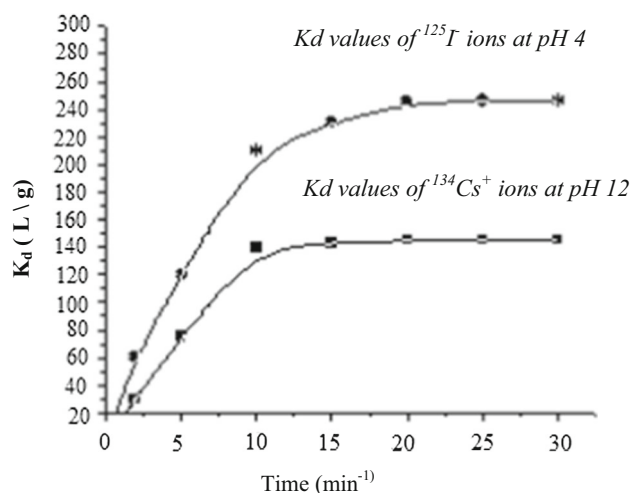
Fig. 3 Determination of the sorption equilibration time of I^- and Cs^+ ions on TiO_2: K_d values for I^- and Cs^+ ions were determined at pH 4 and 12, respectively

Table 1 Distribution coefficient (K_d) values of I^- and Cs^+ TiO_2 ions at different pH and the zeta potential values of TiO_2 at the corresponding pH

pH value	K_d (L/g)		Zeta potential (mV)
	$^{137}Cs^+$	$^{125}I^-$	
1	No uptake	21 ± 2	36 ± 2
2		50 ± 4	45 ± 3
3		237 ± 6	53 ± 3
4		246 ± 6	25 ± 2
5		180 ± 5	−20 ± 3
6	0.5 ± 0.1	132 ± 5	−44 ± 5
7	8 ± 2	98 ± 2	−51 ± 3
8	32 ± 2	71 ± 2	−56 ± 5
9	49 ± 3	9 ± 2	−59 ± 3
10	112 ± 4	0.1 ± 0.1	−61 ± 4
11	132 ± 5	No uptake	−63 ± 3
12	145 ± 5		−66 ± 4
13	143 ± 5		−68 ± 5
14	138 ± 5		−70 ± 3

$n = \pm 3$ indicates standard deviation. The isoelectric point of TiO_2 occurs between pH 4 and 5

rate of sorption. The nano-sorbent zeta potential is its surface charge and its determination clarifies the understanding the electrostatic interactions between the adsorbed ions and TiO_2. The two main parameters that intensively affect the zeta potential, and in turn the interactions between the adsorbed ions and adsorbent are pH and the ionic conditions [13, 14]. Besides, the pH change doesn't only affect the adsorbed ions charges but also the adsorbent surface properties, showing a mutual effect that sharply needs to be considered for understanding their interactions.
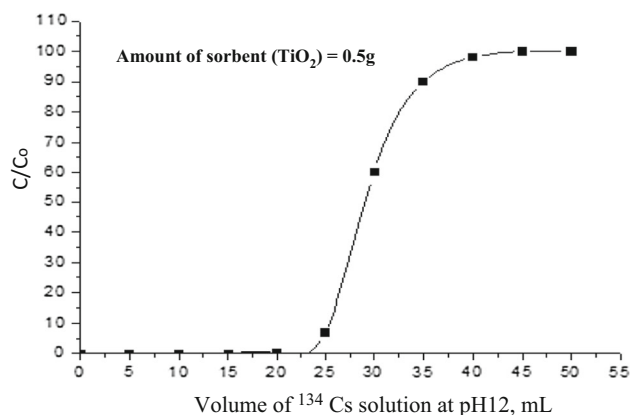

Fig. 4 Breakthrough profile of ^{134}Cs on passing ^{134}Cs (2.0 mg Cs ml^{-1}) solution at pH 12 through a 0.5 g TiO_2 chromatographic column at a flow rate of 0.5 ml min^{-1}

The results summarized in Table 1 show the zeta potential of TiO_2 at different pH values.

In the pH range 1–4, the values of zeta potential value are positive. By increasing pH, the values of zeta potential pass through zero (isoelectric point at which the zeta potential is zero) then it goes to the negative increasing values up to pH 10. At pH 1–4, the sorbent zeta potential is a positive value showing no affinity for the positively charged Cs^+ ion and adsorbs the negatively charged I^- ion. Also, at pH 3–4, the maximum I^- ion uptake was observed.

Under alkaline conditions, the negative zeta potentials indicated that the surface of nano-TiO_2 has a negative charge that adsorb efficiently the positively charged Cs^+ ions onto negatively charged sites of nano-TiO_2 and confirming no affinity for the negatively charged I^- ions. The
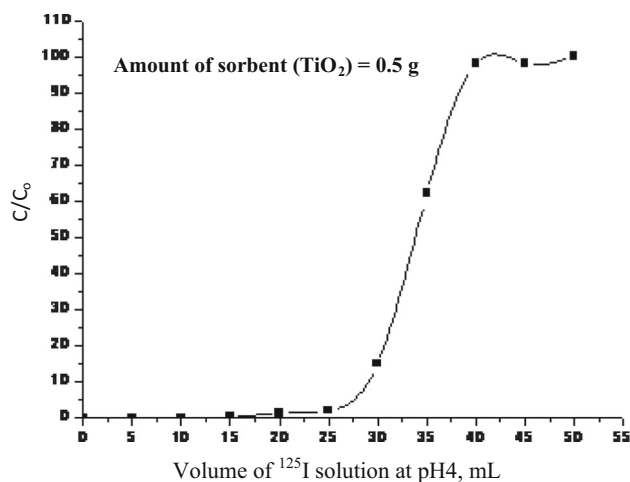

Fig. 5 Breakthrough profile of ^{125}I- iodide on passing ^{125}I (2.0 mg Cs ml^{-1}) solution at pH 4 through a 0.5 g TiO_2 chromatographic column at a flow rate of 0.5 ml min^{-1}

change in sorbent zeta potential with changing pH is confirming with the K_d values.

Nano-TiO$_2$ column dynamic sorption studies

Determination of breakthrough profile of Cs$^+$ ion and I$^-$ from nano-TiO$_2$ column

Figure 4 shows that the dynamic breakthrough profile of Cs at pH $\sim$12 loaded on 0.5 g of prepared nano-TiO$_2$ matrix in glass column was found to be $\sim$56 $\pm$ 2 mg Cs/g TiO$_2$. Ram et al. [13] showed that the breakthrough point was reached after 50 $\pm$ 2 mg of Cs was quantitatively retained by 1.0 g of t-ZrO$_2$ at pH 13.

Also, Fig. 5 shows that the dynamic breakthrough profile of ^{125}I at pH $\sim$4 loaded on 0.5 g of prepared TiO$_2$ matrix in glass column was found to be $\sim$67 $\pm$ 2 mg I/g TiO$_2$. It was reported that breakthrough capacity of t-ZrO2 for I$^-$ ions is 30 $\pm$ 2 mg of I$^-$ per gram of sorbent [23].

Purification and concentration of ^{125}I solution from ^{134}Cs and ^{137}Cs radio-impurities

In light of the ^{125}I radionuclide purity after the passage of ^{125}I solution containing ^{134}Cs and ^{137}Cs radio-contaminants, γ-ray spectrometric analysis of the separated ^{125}I samples was done. From Fig. 6, the absence of photo peaks pertaining to ^{134}Cs and ^{137}Cs confirms the success of the purification step by the quantitative removal of ^{134}Cs and ^{137}Cs. From the radioactivity data of ^{125}I measured before and after the purification step, it was observed that the radioactive yield of ^{125}I was $\geq$95%.

Concentration of ^{125}I solution using nano-TiO$_2$ as adsorbent for the purified ^{125}I solution was done to improve
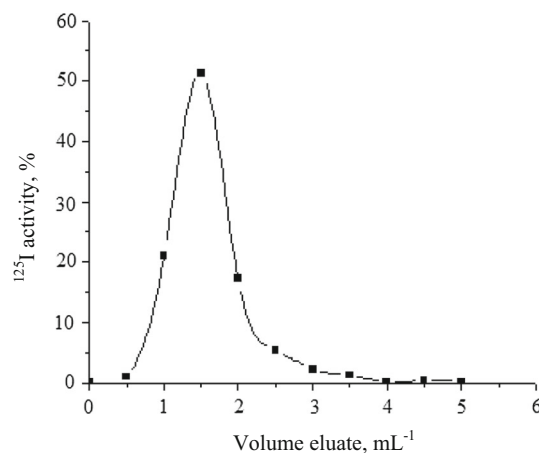

Fig. 7 Elution profile of ^{125}I adsorbed on a column chromatography of nano-TiO$_2$ on passing 0.5 M NaOH solution at a flow rate of 0.5 ml/min

the radionuclidic purity of ^{125}I solution. The breakthrough capacity of nano-TiO$_2$ for I$^-$ ions was 67 $\pm$ 2 mg of I$^-$ per gram of sorbent. The specific activity of ^{125}I was (1.3 $\times$ 10^{7}Ci) per 1.0 g of iodine.

Quality control parameters of ^{125}I product solution

Elution efficiency

The elution yield was high and up to $\sim$95%. Figure 7 shows elution profile of ^{125}I adsorbed on a column chromatography of nano-TiO$_2$ on passing 0.5 M NaOH solution at a flow rate of 0.5 mL/min.
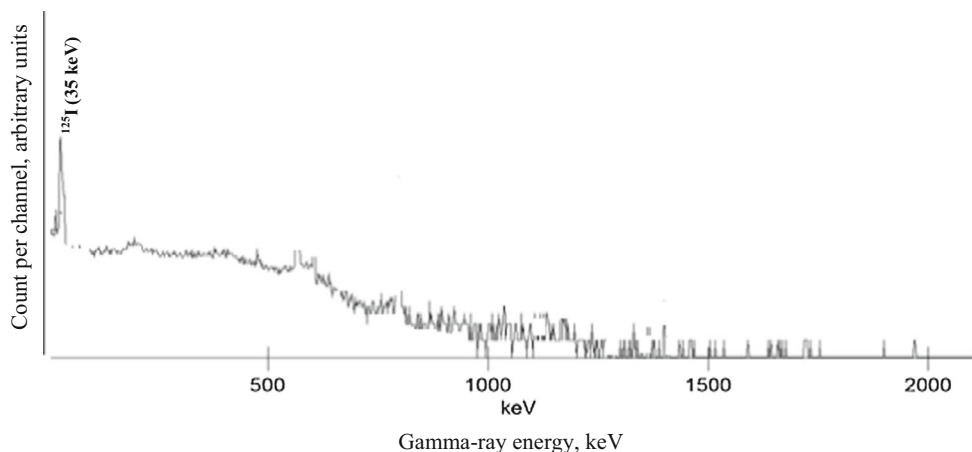

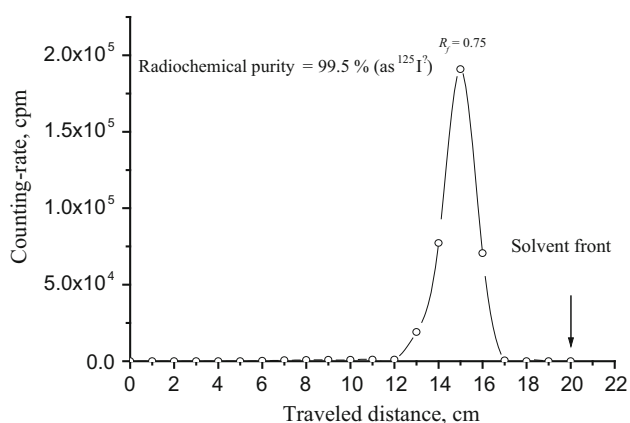**Fig. 6** Typical gamma-ray spectra of final ^{125}I product solution

Fig. 8 Radiochromatogram of ^{125}I eluted from TiO$_2$ chromatographic column

Radionuclidic purity

Radionuclidic purity of ^{125}I was found to be $\sim 99.99\%$, Fig. 6, as no any other gamma-ray radio-contaminant energy peaks were detected in the ^{125}I eluate γ-ray spectra measured immediately after elution for 200 s [11, 13].

Radiochemical purity

Radiochemical purity expressed as % I$^-$ anions in the ^{125}I elutes was evaluated by the paper chromatography method [11, 13]. Figure 8 shows that only one peak zone was detected on the radio-chromatogram of ^{125}I elutes at R_f value of 0.75 corresponding to I$^-$ anions confirming radiochemical purity of $\sim 98\%$ I$^-$.

Statistical analysis

In this work, data were expressed as a mean $\pm$ SD. Statistical analysis was done using Minitab 16 where one-way analysis of variance (ANOVA). Differences were considered to be significant for values of $P < 0.05$.

Conclusion

Nano-crystalline titania (TiO$_2$) can be considered as a potential sorbent material for the separation of Cs radio-contaminants from ^{125}I solution that can be used for ^{125}I production form irradiated natural Xe gas, ^{124}Xe(n,γ)^{125}I. Nano- TiO$_2$ showed maximum sorption capacity of Cs and I $\sim 56 \pm 2$ and 67 ± 2 mg/g TiO$_2$, respectively. The purified ^{125}I was easily concentrated also using TiO$_2$ column. The Purified ^{125}I showed high ^{125}I elution yield $\sim 95\%$ with high radionuclidic and radiochemical confirming its suitability for use in medical radio-diagnosis and radiotherapy.

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