

Bayberry Tannin-modified SiO₂ used for ⁶⁸Ge/⁶⁸Ga Generator

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Abstract: A synthetic method of modified SiO₂ grafted with bayberry tannin (SiO₂-BT) was reported. When the prepared SiO₂-BT was used for the treatment of the mixed solution of Ge and Ga, it could achieve a 99.99% Ge adsorption performance with hardly Ga adsorb. In addition, this SiO₂-BT also exhibited excellent acid resistance, in 0.1-0.5 M HCl solutions, it maintaining over 99.8% Ge adsorption efficiency. The results of radioactive experiments showed that with 10 μCi ⁶⁸Ge loaded, this SiO₂-BT could achieve an elution efficiency of ⁶⁸Ga of 75% while the breakthrough of ⁶⁸Ge maintained below 5×10⁻⁶. Overall, this SiO₂-BT has excellent acid resistance, highly efficient ⁶⁸Ga elution, and the characteristic of long-term low ⁶⁸Ge breakthrough, making it a potential adsorbent for ⁶⁸Ge/⁶⁸Ga generators.

Keywords: ⁶⁸Ge/⁶⁸Ga Generator; Adsorbent; PET; SiO₂.

1. Introduction

PET (positron computed tomography) is a high-resolution, highly sensitive and non-invasive imaging technology, plays an important role in the field of medical image diagnosis. Positrons emitted by radionuclides such as ¹⁸F^[1], ⁸⁹Zr^[2], ¹²⁴I^[3], ¹¹C^[4], ⁶⁸Ga^[5], etc., annihilated with electrons around tissues to emit two γ-photons with energy of 511 keV. And the γ-photons were detected by the instrument to obtain high-resolution and high-sensitivity images^[6].

As an important positron radionuclide, ⁶⁸Ga has a short half-life (67.7 minutes), matches the pharmacokinetics of many peptides and other small molecules, and emits maximum β⁺ emission energy of 1899.1 keV (87.7%). It maintains long-term radioactive equilibrium with its long half-life parent nuclide ⁶⁸Ge (half-life 271 days)^[7-9]. The short half-life of ⁶⁸Ga allows healthcare professionals to perform PET scans with a suitable ⁶⁸Ga radiotracer label while keeping the radiation doses received by patients within acceptable limits. The generator-accessible properties of ⁶⁸Ga makes it an excellent source of ready-to-use positron nuclides, enabling PET imaging in hospitals without on-site cyclotrons. In addition, Ga³⁺, as a Lewis hard acid, is easy to form thermodynamically stable complexes with Lewis hard base ligands containing N and O (such as DOTA and NOTA). Therefore, ⁶⁸Ga has a high labeling efficiency^[10]. As a diagnostic radionuclide, ⁶⁸Ga can pair with therapeutic isotopes such as ¹⁷⁷Lu or ²²⁵Ac which realizing the integration of diagnosis and treatment^[11]. Due to the excellent properties of ⁶⁸Ga, researchers have been developing and researching ⁶⁸Ge/⁶⁸Ga generators for many years.

At present, a large number of studies have reported the use of metal oxides SnO₂, TiO₂, Al₂O₃, Ta₂O₅, CeO₂, ZrO₂, etc., and non-metallic oxides modified SiO₂ as adsorbents^[12-13]. And there are numbers of ⁶⁸Ge/⁶⁸Ga generators such as SnO₂ of iThemba Labs (South Africa), TiO₂ of Cyclotron corporation (Russia), and modified SiO₂ of ITG (Germany) has entered the market. However, these adsorbents still have some defects, such as high ⁶⁸Ge breakthrough in the eluent, high content of metal impurities, large eluent volume (4-10 mL), high concentration of HCl (>0.5mol/L), and short service life. In addition, repeated elution will significantly

reduce the elution efficiency of ⁶⁸Ga, increase the ⁶⁸Ge breakthrough, and shorten the service life of generator. Some generator eluents need to be pre-purified to meet the labeling requirements, which makes the labeling process complicated. Therefore, it is urgent to develop a ⁶⁸Ge/⁶⁸Ga generator adsorbents which can achieve low concentration of hydrochloric acid elution, high elution rate of ⁶⁸Ga, low leakage of ⁶⁸Ge and long service life.

This study reports the surface modification method of SiO₂ employed as an adsorbent for the ⁶⁸Ge/⁶⁸Ga generator. The synthesized SiO₂ adsorbent (SiO₂-BT) fabricated via this approach exhibits high acid resistance and enables rapid and efficient separation of Ge and Ga. When applied to the ⁶⁸Ge/⁶⁸Ga generator, the SiO₂-BT adsorbent can achieve an ⁶⁸Ga elution efficiency of 75% with 10 μCi of ⁶⁸Ge loaded, while limited the ⁶⁸Ge breakthrough 5×10⁻⁶. In summary, the prepared SiO₂-BT is a potential ⁶⁸Ge/⁶⁸Ga generator adsorbent, which provides a new way for the selection of ⁶⁸Ge/⁶⁸Ga generator adsorbent.

2. Experiment

2.1. Chemicals and materials

Bayberry tannin (Guangxi Baise Forest Chemical Plant), C₆H₁₂ (Cyclohexane, AR, content ≥99.7%, Chengdu Jinshan Chemical Reagent Co., LTD.), CH₃(CH₂)₅OH (N-hexyl alcohol, AR, Chengdu Jinshan Chemical Reagent Co., LTD.), APTES (≥98%, Sigma), SiO₂ (AR, 99.5%, 8 μm, Aladdin), C₅H₈O₂ (Glutaraldehyde, AR, Content ≥50%, Chengdu Jinshan Chemical Reagent Co., LTD.)

2.2. The Synthesis of SiO₂-BT

20 ml cyclohexane and 5 ml N-hexanol were added to 200-ml deionized water, and a emulsified solution was formed after magnetic stirring for 5-10 min. Then, 15 ml of APTES and 10 g SiO₂ were added into the emulsion and stirred for 24 h. The amino functionalized SiO₂ was obtained after washing, filtering, and dried in 80 °C oven overnight. Dissolve 10 g of bayberry tannin (BT) in 200 ml of water. Subsequently, add 10 g of amino-functionalized SiO₂ and stir for 12 hours. After that, introduce 40 ml of Glutaraldehyde solution and continue to stir at 30 °C for 24 hours. The resultant product is then

washed with deionized water, filtered, and dried in an oven at 80 °C, thus BT modified SiO₂ was obtained and marked as SiO₂-BT.

2.3. Characterizations

The crystal structure of SiO₂-BT was detected by X-ray diffractometer (XRD, X'Pert pro, PANalytical) at a velocity of 2° min⁻¹ in the range of 3°-80° and the surface functional groups were identified by Fourier infrared spectroscopy (FT-IR, Nicolet iS 50). The morphology of SiO₂-BT was studied by scanning electron microscopy (SEM Ultra55, Carl zeissNTS GmbH). And Inductively coupled plasma mass spectrometer (ICP-MS, PerkinElmer NexION 300X; iCAP6300) was used to measure the concentration of Ge and Ga ions in the supernatant. The breakthrough efficiency of ⁶⁸Ge was measured with a scaler (FH463A), and the radioactivity of ⁶⁸Ga was measured with an activity meter (CRC-15R, Capintec).

2.4. Non-radioactive Ge/Ga adsorption separation experiment

In this study, SiO₂ (SiO₂-BT) modified with myriceberry tannin was used as the adsorbent. Firstly, 1 g SiO₂-BT was weighed and added into 25 mL glass bottle, and 20 mL 0.1/0.2/0.3/0.4/0.5 M HCl solution containing 1 ppm Ge and Ga was added. Placed the glass bottles on the magnetic stirrer for stirring. After absorbing, 1 mL of supernatant was filtered by 0.22 μm membrane every 5 min, absorbing 0.5 mL of supernatant and diluting it to 5 mL for ICP-MS measurement. The adsorption efficiency was calculated by measuring the concentration of Ge and Ga, and the adsorption efficiency of Ge and Ga was calculated as:

$$\text{Ge/Ga adsorption efficiency (\%)} = \left(1 - \frac{10 \times C_t}{C_0}\right) \times 100\%$$

Among them, C_t is the concentration of Ge or Ga in solution after absorption by SiO₂-BT, and C₀ is the initial concentration of Ge and Ga in solution, that is, 1ppm.

2.5. Radioactive elution experiment

⁶⁸Ge loading: Dilute ⁶⁸Ge with an activity of 3.7×10⁵ Bq (10 μCi) into 5 mL solution (mother liquor) with a concentration of 0.1 M HCl, connect the peristaltic pump system, and set the pump speed to 0.1mL /min, until the solution is fully collected into a 10 ml centrifuge tube. After loaded, 50 mL 0.1 M HCl solution was used to quickly wash the adsorption column at 1 mL/min pump rate. Collecting the washing liquid and after loading liquid for the ⁶⁸Ge upload efficiency measurement after 24 h. The calculation formula of ⁶⁸Ge column ratio is as follows:

$${}^{68}\text{Ge upload efficiency (\%)} = 1 - \frac{\text{Activity after loading and washing for 24h}}{\text{Activity of mother liquid}}$$

The elution process of ⁶⁸Ga is as follows: Put 5 ml of HCl with a certain concentration into the elution container and adjust the pump speed to 1 ml/min until 5 ml solution is completely collected. To calculate the elution efficiency of ⁶⁸Ga, the collected eluent is immediately measured with an activity meter. The formula for calculating ⁶⁸Ga elution efficiency is as follows:

$${}^{68}\text{Ga elution efficiency (\%)} = \frac{{}^{68}\text{Ga activity of eluate}}{{}^{68}\text{Ga activity of column}}$$

The activity of ⁶⁸Ge is measured with a scaler, and the ⁶⁸Ge breakthrough is calculated as follows:

$${}^{68}\text{Ge breakthrough (\%)} = \frac{{}^{68}\text{Ga activity of eluate after 24 h}}{{}^{68}\text{Ga activity of column}}$$

3. Results and Discussion

3.1. Synthesis and characterization

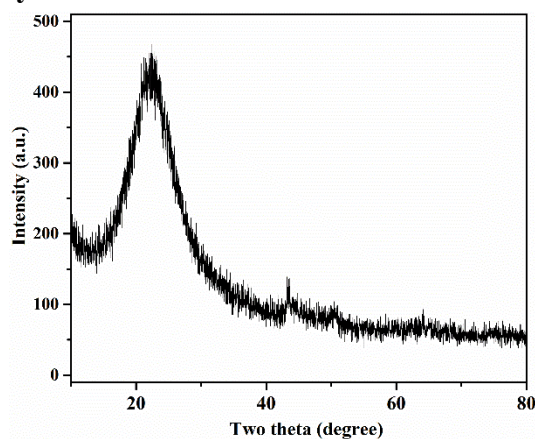


Figure 1. XRD pattern of SiO₂-BT material

Firstly, the amino functionalized SiO₂ was obtained by condensation of the silica hydroxyl group produced by the hydrolysis of APTES with the hydroxyl group on the surface of SiO₂, and then the BT was crosslinked with the amino functionalized SiO₂ by glutaraldehyde to obtain SiO₂-BT. Subsequently, the phase of SiO₂-BT was characterized by XRD. As shown in Figure 1, the Broad peak of SiO₂ at 20 degree of 24.4° indicates that the oxides of SiO₂-BT prepared are amorphous^[14].

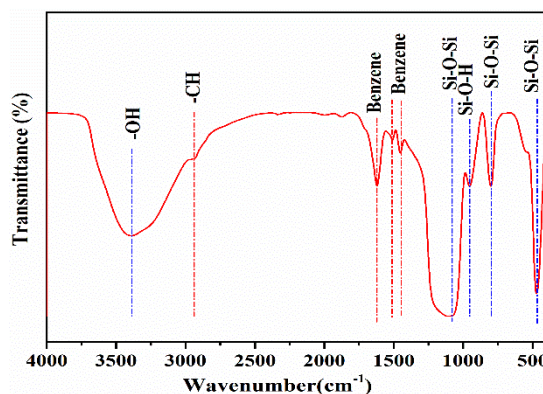


Figure 2. FT-IR spectrum of SiO₂-BT material

In order to verify the successful grafting of myricetannin (BT) on SiO₂, FT-IR was further used to characterize SiO₂-BT adsorbent. As shown in Figure 2, the peak around 3400 cm⁻¹ was attributed to the -OH group of Bayberry tannin and the stretching vibration peak of -OH group on carrier SiO₂. Peaks in the range of 1620 to 1450 cm⁻¹ (1620 cm⁻¹, 1543 cm⁻¹ and 1450 cm⁻¹) indicate the presence of tannin aromatic rings. The peak at 1356 cm⁻¹ belongs to the in-plane flexural vibration of the tannin hydroxyl group^[15]. The infrared spectrum analysis of SiO₂-BT material showed that Bayberry tannin had been successfully grafted onto amino functionalized silica material, which confirmed the successful preparation of SiO₂-BT material.

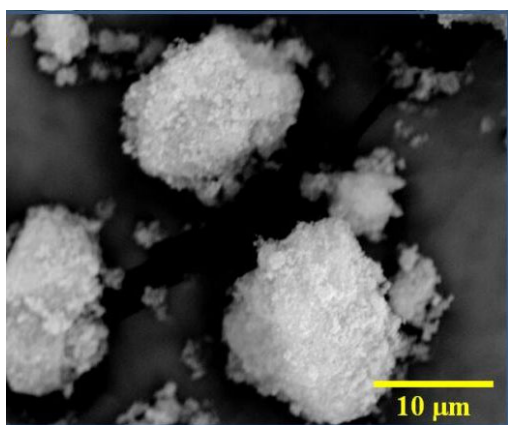


Figure 3. SEM image of SiO₂-BT

The microstructure of SiO₂-BT was analyzed by SEM. As shown in Figure 3, SiO₂-BT material is granular, with loose particles and rough surface. The loose and rough surface characteristics of the SiO₂-BT particles are conducive to enhancing its Ge adsorption performance.

3.2. Adsorption experiment

In order to study the Ge and Ga adsorption properties of SiO₂-BT, 1g SiO₂-BT was placed in 20 mL of 1 ppm Ge and Ga solution containing HCl with a concentration of 0.1/0.2/0.3/0.4./05 M and stirred on a magnetic stirrer. Every 5 minutes, the supernatant was taken for concentration ICP-MS test to calculate the adsorption efficiency of Ge and Ga. In this case, the time-efficiency curves of adsorption of Ge and Ga by SiO₂-BT are obtained.

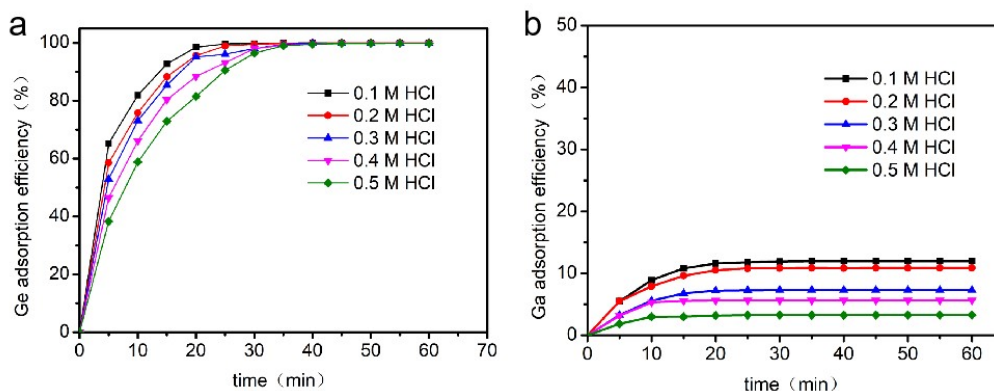


Figure 4. Time-adsorption efficiency curves of SiO₂-BT adsorption of (a) Ge and (b) Ga

Figure 4a shows the time-adsorption efficiency curve of SiO₂-BT at different HCl concentrations. The Ge adsorption efficiency of SiO₂-BT improves with the increase of adsorption time, and the adsorption equilibrium is basically reached at 35 minutes. Among them, SiO₂-BT can achieve the highest Ge adsorption efficiency of 99.99% at 0.1 M HCl concentration, and The stable Ge adsorption efficiency decreases to 99.98%, 99.92%, 99.87% and 99.85% with the increase of hydrochloric acid concentration. The results showed that SiO₂ grafted with bayberry tannin could achieve high Ge adsorption efficiency in a wide acidity range. Figure 4b shows the Ga time-adsorption efficiency of SiO₂-BT. As

shown in the figure, the saturation Ga adsorption efficiency of SiO₂-BT decreases continuously with the increase of HCl concentration. With the increase of HCl concentration, the values decreased to 10.88%, 7.3%, 5.65% and 3.25%. The above results show that the synthesized SiO₂-BT can achieve the selective adsorption of Ge in the mixed solution of Ge and Ga under non-radioactive experimental conditions.

Based on the experimental results, the Ge and Ga distribution coefficients (K_d) of SiO₂-BT material were calculated by the saturation Ge and Ga adsorption efficiency at various HCl concentrations, as shown in Table 1.

Table 1. Distribution coefficients of Ge and Ga of the synthesized SiO₂-BT adsorbent

absorbent	HCl concentration (M)	K_d	
		Ge	Ga
SiO ₂ -BT	0.1	9999	0.136
	0.2	4999	0.122
	0.3	1249	0.079
	0.4	768	0.060
	0.5	665	0.034

It can be seen from Table 1 that the distribution coefficient of Ge on SiO₂-BT is extremely high, reaching 9999 and 4999 respectively at 0.1 and 0.2 M HCl solution. And the distribution coefficient of Ge decreases with the increase of acidity of the solution. On the contrary, in the range of HCl concentration, the distribution coefficient of Ga on SiO₂-BT decreases continuously, indicating that high acidity is conducive to the elution of Ga. However, due to the increase of ⁶⁸Ge breakthrough in the ⁶⁸Ge/⁶⁸Ga generator eluate decreases the PET image quality, the optimal upper column leaching condition is 0.1 M HCl.

For evaluating the ⁶⁸Ga elution efficiency and ⁶⁸Ge breakthrough of SiO₂-BT on the radioactive ⁶⁸Ge column, radioactive elution experiments were carried out. The HCl concentration of ⁶⁸Ge with an activity of 3.7×10⁵ Bq (10 μCi) was adjusted to 0.1 M, and then the mother liquid was pumped into the ⁶⁸Ge/⁶⁸Ga generator by peristaltic pump for ⁶⁸Ge loading. After loading, the adsorption column was quickly washed and removed with 50 mL of 0.1 M HCl solution at 1 mL/min pump rate. After 24 hours, the activity of mother liquor and the washing solution were tested for calculating the ⁶⁸Ge upload efficiency.

After the column loading completed, the SiO₂-BT generator was placed in the hot chamber for 24 hours until radioactive equilibrium was reached. Then, 5 mL 0.1 M HCl was used to elute the generator at the speed of 1 mL/min. The solution was collected immediately after the elution for activity test to calculate the ⁶⁸Ga elution efficiency, and then the solution was placed for 24 hours for ⁶⁸Ge breakthrough test. The test results show that the ⁶⁸Ge upload efficiency is as high as 99.99% with the absorbent of SiO₂-BT. In addition, the elution efficiency of ⁶⁸Ga in the eluate reaches 75% while the ⁶⁸Ge breakthrough is only 5×10⁻⁶.

4. Conclusion

In summary, this experiment successfully synthesized the surface modified SiO₂ grafted with Bayberry tannin. The static adsorption experiment confirmed that the synthesized SiO₂-BT could achieve highly Ge selective adsorption efficiency in the mixed solution of Ge and Ga in 0.1-0.5 M HCl (the adsorption efficiency of Ge was greater than 99.8%) while only less than 12% of the Ga in the solution is adsorbed. Subsequent radioactive elution experiments show that SiO₂-BT can achieve 99.99% ⁶⁸Ge upload efficiency, and ensure 75% of ⁶⁸Ga elution efficiency while limited ⁶⁸Ge breakthrough below 5×10⁻⁶. The above results show that SiO₂-BT has high research value and provides a new choice for commercial ⁶⁸Ge/⁶⁸Ga generator column absorbent.

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