SUPPORTING INFORMATION

Mechanochemical Synthesis of Mesoporous Tin Oxide: A New Generation Nanosorbent for $^{68}Ge/^{68}Ga$ Generator Technology

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Optimization of Conditions for Synthesis of MTO Nanoparticles

With an objective to achieve high ^{68}Ge-sorption capacity, the mechanochemical synthesis protocol was optimized by variation in molar ratios of stannous chloride, ammonium carbonate and glucose. After the mechanochemical reaction, calcination of the precursor was carried out at 600 °C for 3 h. The practical ^{68}Ge-sorption capacity of the nanomaterial synthesized under each condition was determined adopting the procedure described in the section on 'Determination of Sorption Capacity of MTO nanoparticles' below and the results are summarized in **Tables S1** and **S2**. The data reveal that maximum ^{68}Ge-sorption capacity could be achieved for MTO nanoparticles, when the molar ratio of stannous chloride : ammonium carbonate : glucose in the reaction mixture was 1 : 1.25: 1.5. Further, the calcination temperature and time required for calcination was varied after carrying out the mechanochemical reaction using optimal molar ratios of reactants (**Figure S1**). It can be seen from the figures that maximum sorption capacity (86 ± 5 mg Ge/g) could be attained when calcination was carried out at 600 °C for 3 h. At lower calcination temperature or shorter calcination time, the carbonaceous material could not be completely removed which was evident from the black particles observed in the resultant material. The presence of the carbonaceous material probably leads to lower sorption capacity. Calcination at higher temperature or for a longer period of time also led to lower sorption capacity, probably, due to sintering in pore structure of the material.

Structural Characterization of MTO Nanoparticles

XRD data were collected on the powder sample for the phase identification and crystallite size estimation, using monochromatized Cu-K_α radiation on a PANalytical X-ray diffractometer (X'pert PRO). The instrument was operated at 40 kV and 30 mA. Silicon was used as an external standard for the correction due to instrumental line broadening. The MTO

powder was ground and loaded in the groove of the Perspex sample holder. XRD pattern was recorded in the 2θ range of 10-90° for 1 h with a scan step size of 0.02°.

Scanning electron microscope (JEOL JSM-7600F FEG-SEM) was used for scanning electron microscopy (SEM) analysis. The chemical composition was obtained by energy dispersive X-ray spectroscopy (EDS) analysis (Oxford, model INCA E350). TEM data were recorded using a JEOL FX microscope (Jeol Ltd., Tokyo, Japan), on the powder sample. The preparation of samples for TEM analysis involved sonication in ethanol for 5 min and deposition on a carbon-coated copper grid. The accelerating voltage of the electron beam was 200 kV.

The small-angle X-ray scattering (SAXS) experiment on powder sample has been performed using a lab-based SAXS facility with Cu-K_α x-ray radiation. The scattering intensity of X-rays from the sample is recorded as a function of scattering angle θ. The magnitude of the wave vector transfer q is defined as $q=4\pi\sin\theta/\lambda$ where λ is the wavelength of the X-rays (λ=1.54 Å). The wave vector transfer in present experiment was 0.1-2.5 nm^{-1}. The surface area analysis were carried out by nitrogen adsorption (BET) technique (21) at 77 K using Quantachrome, Autosorb-1 analyzer (Quantachrome Instruments, FL 33426 USA).

Small-angle neutron scattering (SANS) measurements have been carried out using a SANS instrument at the Dhruva reactor, India.[1] The mean incident neutron beam wavelength (λ) was 5.2 Å with a wavelength resolution (Δλ/λ) of ~ 15%. The scattered neutrons were collected in an angular range of 0.5–15° using a linear position-sensitive detector (PSD). The samples were kept in a quartz sample holder having a thickness of 2 mm. The scattered neutrons were measured for wave-vector transfer, Q ($Q = 4\pi\sin(\theta)/\lambda$, where 2θ is the scattering angle) in the range of 0.15-3.0 nm^{-1}. The measured SANS data were corrected for the background, the empty cell contribution, and the transmission.

Determination of Zeta-Potential of MTO Nanoparticles

The zeta potential of MTO nanoparticles was studied at different pH environments. The samples were prepared by adding 5 mg of MTO nanoparticles to 50 mL of de-ionized water and the pH of the suspension was adjusted using HCl and NH_4OH solution. Zeta-potential of the suspensions was measured at different pH using a zeta potential analyzer (Zetasizer Nano ZS/ZEN3600, Malvern Instruments Ltd., UK).

Determination of Distribution Coefficients (K_d) of Ge and Ga Ions

The K_d values of Ge and Ga ions in MTO nanoparticles were determined by batch equilibration method. A stoppered conical flask containing 200 mg of MTO nanoparticles, immersed in 20 mL of HCl solution spiked with 37 kBq of the $^{68}Ge/^{68}Ga$ radiotracer, was shaken for 1 h at room temperature (25°C). Subsequently, the supernatant solution was filtered through a Whatman filter paper (No. 542). For determination of the activity of ^{68}Ge, the filtrate was allowed to decay for 24 h, whereas in the case of ^{68}Ga the measurement was done immediately after filtration. The activities of the solution before and after equilibration were measured in a well-type NaI (Tl) counter using the appropriate window setting (400–600 keV). The K_d values were calculated by using the following expression:

$$K_d = \frac{(A_i - A_{eq})V}{A_{eq}\, m} \ \mathrm{L\ g^{-1}}$$

where, A_i is the initial total radioactivity of 1 mL the solution, A_{eq} is the unadsorbed activity in 1 mL of the solution at equilibrium, V is the solution volume (mL) and m is the mass (g) of the sorbent. All equilibration experiments were carried out in triplicate.

Determination of Time Required to Attain Sorption Equilibrium

In order to study the time dependence of the sorption of ^{68}Ge onto MTO nanoparticles, the K_d of ^{68}Ge ions in 0.01 M HCl medium was determined at different time

intervals. The attainment of equilibrium was indicated by the constant K_d value after a certain period of time (**Figure S2**).

Determination of ^{68}Ge-Sorption Capacity of MTO Nanoparticles

The sorption capacity of MTO nanoparticles was evaluated under both static and dynamic conditions. The solution of non-radioactive Ge(IV) was prepared by dissolving GeO_2 in 0.1 N NaOH solution. The concentration and the initial pH of the Ge solution were adjusted with 0.1 N HCl. A HPGe detector coupled with a multichannel analyzer (Canberra Eurisys, France) with a 1.5 keV resolution at 1333 keV and range from 1.8 - 2 MeV was used for analysis of ^{68}Ga and ^{68}Ge and also for their quantitative determination.

Static sorption capacity

The static sorption capacity of MTO nanoparticles for Ge was determined by batch equilibration method. An accurately weighed amount of sorbent (~200 mg) was taken in a stoppered glass conical flask and equilibrated with 20 ml of the Ge solution (5 mg of Ge per mL) spiked with ~370 kBq (10 μCi) of ^{68}Ge for 1 h at pH 2. Subsequently, the contents were filtered and the filtrate was allowed to decay for 24 h. The activity of the decayed ^{68}Ge solution was compared with the standard solution taken from the equilibrium mixture before equilibration with MTO nanoparticles. The capacity was calculated using the following expression:

$$\text{Capacity} = \frac{(A_o - A_e)V.C_o}{A_o\, m},$$

where, A_o and A_e represented the radioactivity of ^{68}Ge in 1 mL of supernatant solution before and after sorption, respectively, C_o was the total Ge content (5 mg) in 1 mL of solution before sorption, V was the volume of solution and m was the mass (g) of the sorbent.

Breakthrough pattern under dynamic conditions

In order to evaluate the Ge sorption capacity under dynamic conditions, a borosilicate glass column of dimension 8×0.6 cm (i.d.) with a sintered disc (G_0) at the bottom was packed

with 0.5 g of the sorbent. After the column was conditioned with 0.01 M HCl, Ge solution (5 mg Ge ml^{-1}), spiked with the $^{68}Ge/^{68}Ga$ radiotracer, was allowed to pass through the column at a flow rate of ~ 0.25 mL min^{-1}. One millilitre of this solution was kept as reference (Co). The effluent was collected in fractions of 1 mL aliquots (C) and allowed to decay for 1 day. The ^{68}Ge activity in the reference (Co) and effluent fractions was determined by measuring the 511 keV γ-ray peak in a HPGe detector. The ratio of the count rate C of each 1 mL effluent to the count rate Co of 1 mL of the original feed Ge solution was taken as the parameter to follow the sorption pattern.

Practical sorption capacity

In order to determine the maximum achievable (practical) sorption capacity under column-flow conditions, a borosilicate glass column of dimension 8 cm × 0.6 cm (i.d.) with sintered disc (G_0) at the bottom was packed with 1 g of MTO nanoparticles. After the column was conditioned with 0.01 M HCl, 20 mL of Ge solution (5 mg Ge mL^{-1}, pH 2-3), spiked with ^{68}Ge tracer (18.5 MBq) was allowed to pass through the column at a flow rate of 0.25 mL min^{-1}. The column was washed with 100 mL of 0.25 M HCl solution. The effluents were pooled together and the sorption capacity was determined by comparing the ^{68}Ge activity in the effluent with that added into the column.

The practical sorption capacity of MTO nanoparticles was compared with that of bulk SnO_2. Bulk SnO_2 was synthesized by oxidation of metallic Sn with hot concentrated nitric acid, as per the method reported by Das et al. [2] The practical sorption capacity of bulk SnO_2 was found to be 11 ± 2 mg Ge/g of sorbent, which is significantly lower than that of MTO nanoparticles (85 ± 5 mg Ge/g).

Development of $^{68}Ge/^{68}Ga$ Generator

A borosilicate glass column of dimension 8 × 0.6 cm (i.d.) with a sintered disc (G_0) at the bottom was packed with 0.5 g of MTO nanoparticles and kept in a lead-shielded

container. It was preconditioned with 0.01 M HCl solution. A schematic diagram of the $^{68}Ge/^{68Ga}$ generator system is shown in **Figure 1B**. All the operations were carried out in a closed cyclic system using connecting tubes. Input/output connections were made with standard Teflon tubings of 1 mm inner diameter and connectors. The generator column, connectors and connection tubings were integrated within a small portable lead-shielded unit throughout experimental use for radioprotection purposes. Only the elution vial and output vial were accessible externally. A disposable 0.22-μm membrane filter was attached to the generator column output by Teflon tubing. The $^{68}Ge/^{68}Ga$ solution containing 740 MBq (20 mCi) of ^{68}Ge at pH ~ 2 was percolated into the column maintaining a flow rate of 0.25 mL min^{-1}. The ^{68}Ge-loaded column was dried under vacuum for 1 min.

In order to optimize the concentration of HCl solution required for elution of ^{68}Ga with maximal elution yield, 5 mL of HCl solutions of different concentrations (0.01 -1.0 M) were passed through the generator column after allowing sufficient time for in-growth of ^{68}Ga (***Table S3***). It was found that the ^{68}Ga-elution yield was maximal when 0.25 M HCl solution was used. Subsequently, the generator column was washed with 100 mL of 0.25 M HCl solution.

Gallium-68 was regularly eluted from the loaded column with 0.25 M HCl solution. Generally, for the commercially available bulk SnO_2-based $^{68}Ge/^{68}Ga$ generator, 0.6-1 M HCl is used as eluent,[3] which is higher than the concentration of HCl used in our study.

The performance of the generator was evaluated for 1 year, by periodic elutions at 24 h intervals. The activity of ^{68}Ga was measured using a pre-calibrated HPGe detector coupled with an MCA. The measured activity of ^{68}Ga after allowing time 't' for its growth, is denoted by $A_s(t)$, and the elution yield is calculated by using the following equation:

$$\text{Elution yield (\%)} = \frac{A_s(t)}{A_{10}(1 - e - \lambda_2 t)}$$

where A_{10} is the activity of ^{68}Ge and λ_2 is the decay constant of ^{68}Ga.

Elution Profile of the $^{68}Ge/^{68}Ga$ Generator

The generator elution profile was studied by collecting the eluate as 0.5 mL aliquots, and the activity of each fraction was determined by measuring the 511 keV γ-ray peak in a HPGe detector.

Quality Control of ^{68}Ga

Radionuclidic purity

Radionuclidic purity of the samples was assessed using a calibrated HPGe detector coupled to a multichannel analyzer. A typical γ-spectra of ^{68}Ga eluate from MTO-based $^{68}Ge/^{68}Ga$ generator is shown in **Figure S3**. The ^{68}Ge contamination level in ^{68}Ga was quantified by allowing the separated ^{68}Ga samples to decay for 2 days and then measuring the 511 keV γ-peak of ^{68}Ga daughter. This in turn corresponds to the level of ^{68}Ge contaminant.

Radiochemical Purity

The radiochemical purity of ^{68}Ga in the form of Ga^{3+} ions was determined by paper chromatographic (PC) technique. For this purpose, 5 µL of radioactive solution was spotted on a PC paper at 1.5 cm from the bottom. The chromatogram was developed in saline as well 0.05 M sodium citrate medium. Subsequently, the paper was dried and cut into 1 cm pieces and activity of each piece was determined using a NaI (Tl) counter. The radiochemical purity of nanoparticles was expressed as the percentage of the total activity which remained at the point of application (R_f = 0 - 0.1) in the chromatogram developed. When the chromatogram was developed in saline medium, $^{68}Ga^{3+}$ ions remained at R_f = 0-0.1, while it moved to the solvent front when developed in 0.05 M citrate medium (***Figure S4***).

Chemical Purity

In order to determine the presence of chemical impurities (in the form of other metal ions) in the ^{68}Ga eluate, the samples were allowed to decay for 7 days. The trace levels of the metal ion contamination in the decayed samples were determined by ICP-AES analysis

(***Table S4***). The calibration curves for these ions were obtained by using standard solutions having known concentration of these ions.

Biological Purity

Sterility of ^{68}Ga solution obtained from the ^{68}Ge/^{68}Ga generator was tested using tryptic soya broth medium (Himedia). Pyrogenicity of the preparation was checked by PTS (point-of-use test system, Charles River, USA).

Preparation of Clinically Relevant Dose of ^{68}Ga-DOTA-RGD$_2$

In order to demonstrate the suitability of ^{68}Ga obtained for preparation of radiopharmaceuticals, 1.0 mL of 0.25 M sodium acetate containing 20 μg of peptide conjugate was taken in a sterile vial and set aside for 10 min at room temperature after mixing 3 mL of generator eluate (370-600 MBq of ^{68}Ga) with the peptide solution.

The yield and radiochemical purity of ^{68}Ga-DOTA-RGD$_2$ complex were determined by PC and HPLC techniques.

***PC*:** Aliquots of reaction mixtures (~5 μL) were applied at 1.5 cm from the lower end of chromatography strips. The strips were developed in 50 % acetonitrile in water (v/v) solution, dried, cut into segments of 1 cm each and the radioactivity associated with each segment was measured using NaI(Tl) detector. In PC, the activity corresponding to ^{68}Ga-DOTA-(RGD)$_2$ complex moved to the solvent front (R_f = 0.8 – 1.0), while uncomplexed ^{68}Ga moved remained at the point of applications (R_f = 0 – 0.1), as shown in **Figure S5**.

***HPLC*:** HPLC of the ^{68}Ga-DOTA-(RGD)$_2$ was carried out using a dual pump HPLC unit with a C-18 reversed phase HiQ-Sil (5 μM, 25 cm × 0.46 cm) column. The elution was monitored both by detecting UV signals at 270 nm as well as radioactivity signal using NaI(Tl) detector. Water (A) and acetonitrile (B) mixtures with 0.1% trifluoroacetic acid were used as the mobile phase and the following gradient elution technique was adopted for the separation (0-

4 min 95% A, 4-15 min 95% A to 5% A, 15-20 min 5% A, 20-25 min 5% A to 95% A, 25-30 min 95% A). Flow rate was maintained at 1 mL/min.

In radio-HPLC studies, the radiolabeled conjugate exhibited a retention time of 14.7 min, while the uncomplexed $^{68}GaCl_3$ was eluted in the void volume (**Figure S6**).

The same procedure was used for radiolabeling other targeting ligands such as, [1, 4, 7, 10-tetraazacyclododecane-1, 4, 7, 10-tetraacetic acid]-d-Phe(1)-Tyr(3)-octreotide (DOTA-TOC), [1, 4, 7, 10-tetraazacyclododecane-1, 4, 7, 10-tetraacetic acid]-1-NaI(3)-octreotide (DOTA-NOC), [1,4,7-triazacyclononane,1-gluteric acid-4,7-acetic acid]-E[c(RGDfK)]$_2$, (NODAGA-RGD$_2$, E = glutamic acid, R = arginine, G =glycine, D = aspartic acid), Glu-NH-CO-NH-Lys-(Ahx)-HBED-CC (DKFZ-PSMA-11). The radiolabeling yields of all these ^{68}Ga-labeled agents were > 95 %, indicating the suitability of ^{68}Ga-obtained from the generator for radiopharmaceutical preparation (**Table S5**).

Biodistribution Studies with ^{68}Ga-DOTA-(RGD)$_2$ in Melanoma Tumor Bearing Mice

All animal studies were conducted following the protocol approved by the institutional Animal Ethics Committee. Biological efficacy the ^{68}Ga-DOTA-RGD$_2$ was evaluated in female C57BL/6 mice (6-8 weeks age) bearing melanoma tumors. Melanoma cell line (ATCC-CRL-6475^{TM}), used for raising the tumors, was purchased from National Center for Cell Sciences (India). The animals were bred and reared in the laboratory animal facility of our Institute under standard management practice. Melanoma tumors were developed by injecting ~ 1×10^6 melanoma cells suspended in 200 µL of PBS subcutaneously into the right thigh of each C57BL/6 mice weighing 20-25 g. The animals were observed for visibility of tumors and allowed to grow for about 2 weeks. Animals having tumors with a mean diameter of ~ 8 mm (range, 6-9 mm) were used in the biodistribution experiments. The radiotracer [~100 µL, 3.7-5.5 MBq] was injected into each animal through a lateral tail vein. The animals were sacrificed by cardiac puncture post-anaesthesia at 10 min, 30 min and 60

min post-injection (p.i.). Four animals were used in each time point. Various organs, tissue and tumors were excised following sacrifice, washed with normal saline, dried and the radioactivity associated with each organ and tissue was determined using a flat type NaI(Tl) counter (Electronics Corporation of India Limited, India) by keeping the baseline and windows at 450 keV and 100 keV, respectively. The weight of each organ and tumor were determined by using an analytical balance. The percent injected dose (%ID) in various organs, tissues and tumor were calculated from the above data and expressed as percentage injected dose per gram (%ID/g) of organ/tissue. The activity excreted was indirectly determined from the difference between total injected activity (dose) and the %ID accounted for in all the organs.

Blocking studies were performed to ascertain whether the uptake of ^{68}Ga-DOTA-RGD_2 in melanoma tumor is receptor mediated. For this, four C57BL/6 mice bearing melanoma tumors were used and each animal was administered with ~3.7 MBq (100 μCi) of the radiotracer along with 500 μg (20-25 mg/kg of body weight) of E[c(RGDfK)]$_2$ (RGD_2). Such a high dose of peptide was used to ensure that all the integrin $\alpha_v\beta_3$ receptors are blocked. The animals were sacrificed at 30 min p.i. %ID/g of organ/tissue was determined following the procedure mentioned above (**Figure S7**). The uptakes in different organs/tissue and tumor were compared to that obtained in the absence of excess RGD_2.

References

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2. S.S Das, S. Chattopadhyay, Md. N. Alam, Madhusmita, L. Barua, M.K. Das. *Appl. Radiat. Isot.*, 2013, **79**, 42-7.
3. E. de Blois, C.H Sze, C. Naidoo, D. Prince, E.P. Krenning, W.A. Breeman. *Appl. Radiat. Isot.*, 2011, **69**, 308-15.

Table S1: Variation in molar ratio of $(NH_4)_2CO_3$ while keeping $SnCl_2$ and glucose fixed for synthesis of MTO nanoparticles to achieve maximal sorption capacity

$SnCl_2$: $(NH_4)_2CO_3$: Glucose	Practical Sorption Capacity (mg Ge / g)
1 : 1 : 1.5	77 ± 4
1 : 1.25 : 1.5	86 ± 5
1 : 1.5 : 1.5	86 ± 8
1 : 2 : 1.5	87 ± 6

N = 5

Table S2: Variation in molar ratios of glucose while keeping $SnCl_2$ and $(NH_4)_2CO_3$ fixed for synthesis of MTO nanoparticles to achieve maximal sorption capacity

$SnCl_2$: $(NH_4)_2CO_3$: Glucose	Practical Sorption Capacity (mg Ge / g)
1 : 1.25 : 1	70 ± 3
1 : 1.25 : 1.25	82 ± 5
1 : 1.25 : 1.5	86 ± 5
1 : 1.25 : 1.75	86 ± 7
1 : 1.25: 2	86 ± 3

N = 5

Figure S3: Elution yield of ^{68}Ga from MTO based $^{68}Ge/^{68}Ga$ generators using HCl solution of different concentrations

Concentration of HCl solution (M)	Elution yield (%)
0.01	13 ± 4
0.05	38 ± 4
0.1	62 ± 6
0.25	83 ± 2
0.5	85 ± 4
0.75	88 ± 5
1.0	89 ± 4

N = 5

Table S4: Level of chemical impurities in ^{68}Ga eluate obtained from the $^{68}Ge/^{68}Ga$ generator. The generator was eluted daily over a period of 1 year and randomly selected samples from each month were used for analyses.

Month	Concentration (µg / mL)						
	Sn	Fe	Co	Cu	Mn	Ni	Zn
1	0.7 ± 0.1	0.07 ± 0.03	0.004 ± 0.002	0.02 ± 0.01	0.002 ± 0.001	0.003 ± 0.002	1.6 ± 0.3
2	0.8 ± 0.2	0.12 ± 0.07	0.006 ± 0.002	0.05 ± 0.02	0.002 ± 0.001	0.005 ± 0.003	2.2 ± 0.4
3	0.5 ± 0.3	0.14 ± 0.08	0.005 ± 0.003	0.06 ± 0.03	0.004 ± 0.002	0.007 ± 0.002	1.7 ± 0.5
4	0.7 ± 0.3	0.09 ± 0.03	0.004 ± 0.002	0.05 ± 0.04	0.003 ± 0.001	0.004 ± 0.002	1.2 ± 0.4
5	0.5 ± 0.1	0.14 ± 0.02	0.003 ± 0.001	0.07 ± 0.03	0.004 ± 0.003	0.006 ± 0.002	1.1 ± 0.5
6	0.7 ± 0.2	0.11 ± 0.03	0.005 ± 0.002	0.05 ± 0.04	0.005 ± 0.002	0.004 ± 0.001	1.2 ± 0.3
7	0.6 ± 0.3	0.12 ± 0.04	0.006 ± 0.002	0.05 ± 0.01	0.004 ± 0.002	0.003 ± 0.001	1.8 ± 0.7
8	0.3 ± 0.1	0.15 ± 0.07	0.003 ± 0.001	0.08 ± 0.02	0.003 ± 0.001	0.004 ± 0.002	1.9 ± 0.3
9	0.5 ± 0.3	0.09 ± 0.05	0.008 ± 0.003	0.03 ± 0.01	0.004 ± 0.002	0.005 ± 0.002	1.2 ± 0.5
10	0.3 ± 0.1	0.13 ± 0.06	0.004 ± 0.002	0.04 ± 0.02	0.005 ± 0.001	0.007 ± 0.004	1.4 ± 0.6
11	0.7 ± 0.1	0.12 ± 0.02	0.005 ± 0.002	0.06 ± 0.04	0.003 ± 0.002	0.008 ± 0.005	1.3 ± 0.3
12	0.6 ± 0.2	0.11 ± 0.05	0.004 ± 0.001	0.05 ± 0.03	0.004 ± 0.003	0.006 ± 0.002	1.6 ± 0.4

N = 3

Table S5: Radiolabeling yields of ^{68}Ga-labeled DOTA-TOC, DOTA-NOC, NODAGA-RGD$_2$, DKFZ-PSMA-11

Targeting ligand	Radiolabeling yield (%)
DOTA-TOC	98.2 ± 0.7
DOTA-NOC	97.6 ± 0.4
NODAGA-RGD$_2$	99.1 ± 0.3
DKFZ-PSMA-11	98.8 ± 0.4

N=5; For each study, 20 µg of respective peptide conjugate was used.

Figure S1: Variation in ^{68}Ge-sorption capacity of MTO nanoparticles with change in (A) calcination temperature, and (B) calcination time. Practical sorption capacity is considered here.

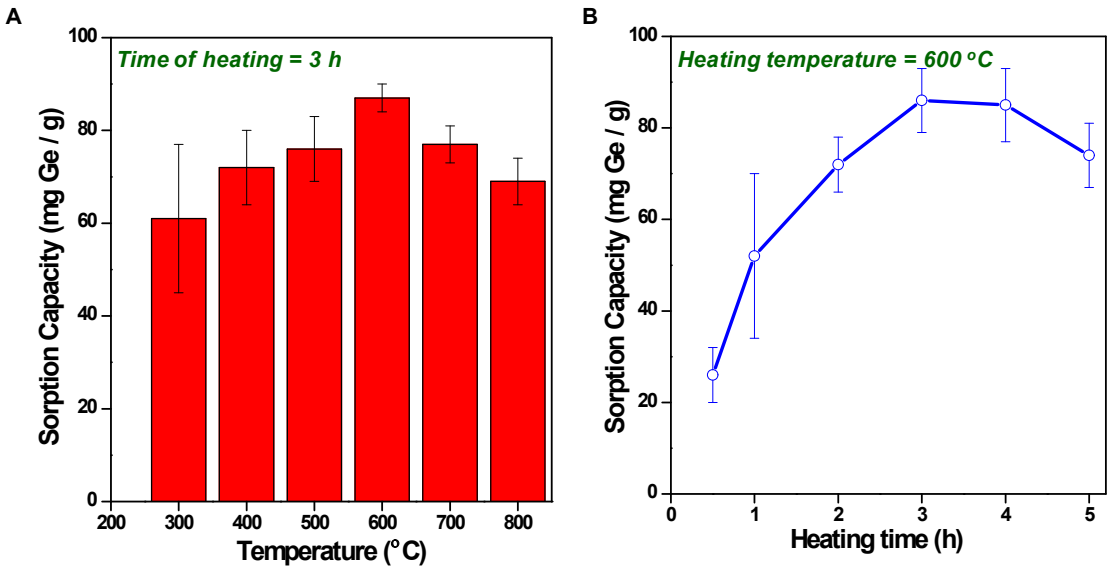

Figure S2: Variation in K_d value of ^{68}Ge ion with time using MTO nanoparticles as sorbent

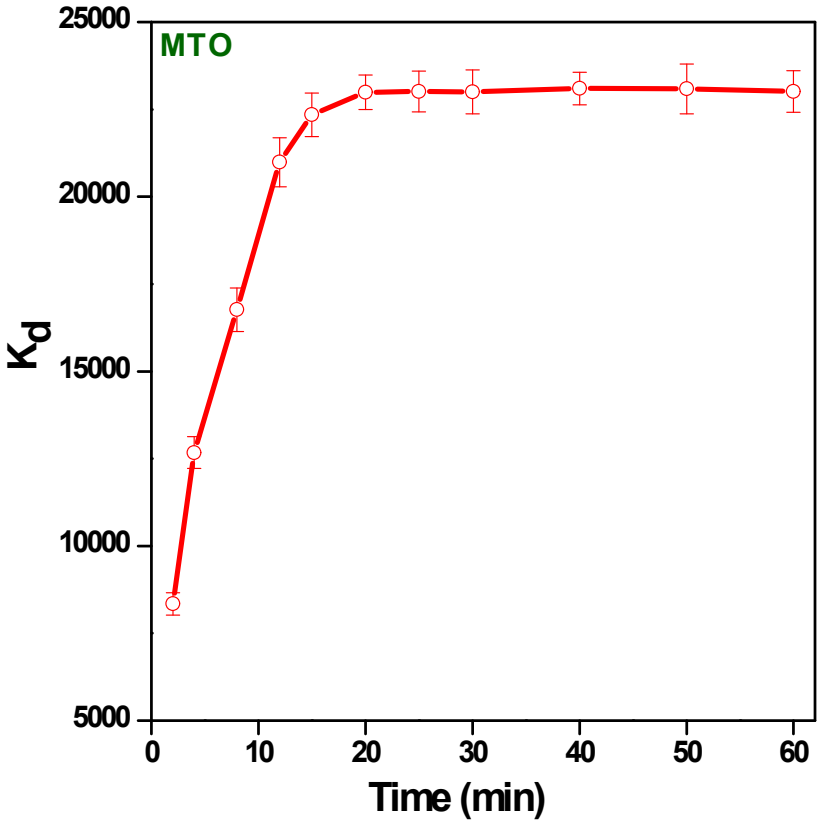

Figure S3: Typical γ-spectra of ^{68}Ga taken in HPGe detector coupled with MCA

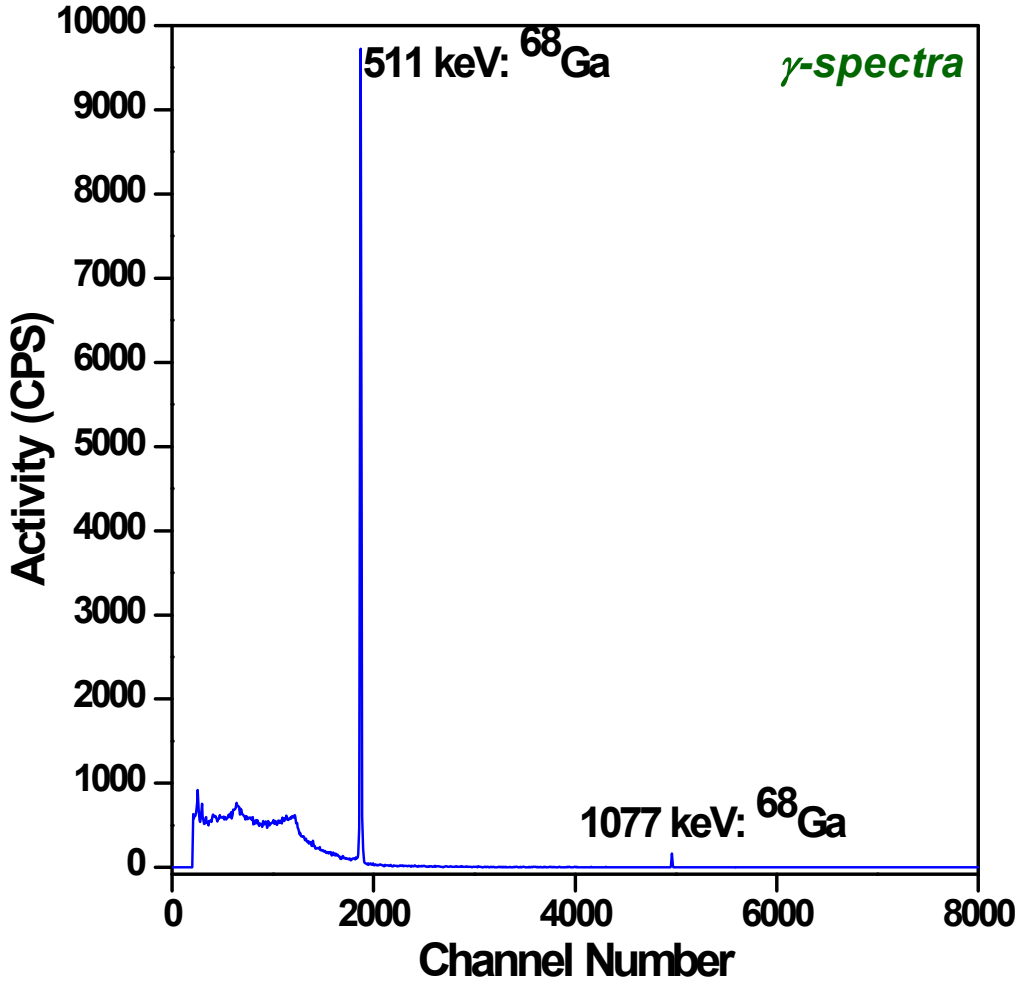

Figure 4: Paper chromatographic pattern of ^{68}Ga eluate when developed in (A) saline and (B) 0.05 M citrate media

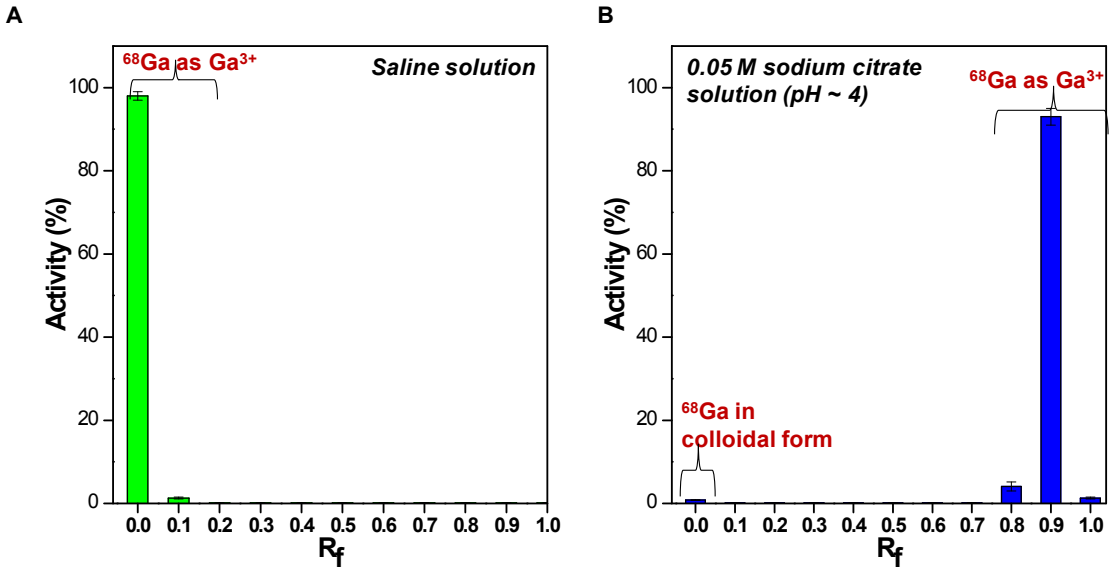

Figure S5: Paper chromatographic pattern of (A) ^{68}Ga-DOTA-RGD$_2$ and (B) uncomplexed ^{68}Ga eluate (control) when developed in 50 % acetonitrile in water (v/v) solution

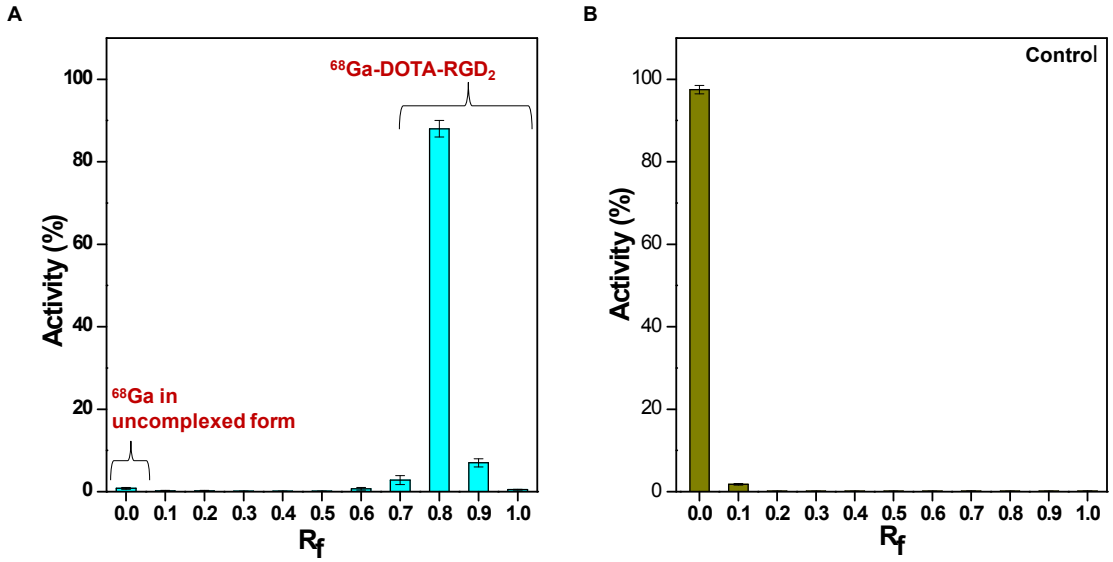

Figure S6: Typical HPLC pattern of ^{68}Ga-DOTA-RGD$_2$

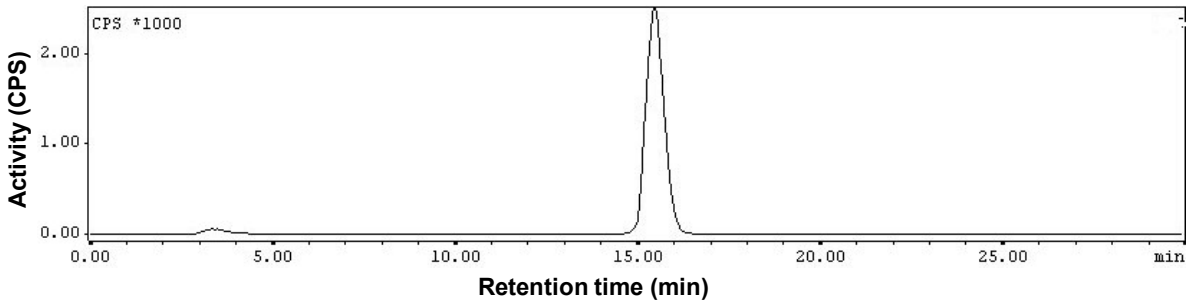

Figure S7: Comparison of biodistribution pattern in C57BL/6 mice bearing melanoma tumors at 30 min p.i. of ^{68}Ga-DOTA-RGD$_2$ with and without blocking dose of 0.5 mg RGD$_2$