Supporting Information

Porous Hydroxyapatite Microparticles Loaded with ^{169}Er for Treatment of Inflamed Small Joints: Harnessing Mechanochemistry for Synthesis of an Advanced Biomaterial

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Ex vivo biodistribution study: For ex vivo biodistribution study, twenty-one healthy Wistar rats (~300 g) were euthanized by CO_2 asphyxiation. Then, 25 µL of 9.25 MBq (~ 0.25 mCi) of [^{169}Er]Er-HA MPs was administrated intra-articularly into one of the ankle joint of each rats and they were randomly divided into seven group of three each. Subsequently, the Wistar rats were euthanized at four different time points by CO_2 asphyxiation. After that, different organs and ankle joint were carefully removed and the weight associated to them were measured using a pre-calibrated balance. Then the activity of different organs and ankle joint were measured using NaI(Tl) detector and the dose associated with each organ and ankle joint was expressed in terms of percentage of injected radioactivity dose per gram (%ID/g) of organ/tissue.

The results of the biodistribution study showed excellent retention of injected radiolabeled agent inside the ankle joint cavity. It was observed that the ankle joint uptake of [^{169}Er]Er-HA MPs was 94.5 ± 4.8 % at 6 h post injection (p.i.) and significant retention of the radiolabeled formulation was observed even at 120 h p.i., which is desirable for a RSV agent. As expected, a small quantity of radioactive MPs cleared through the hepatobiliary route, with liver uptake of 0.42 ± 0.02 %ID/g at 6 h p.i., which changed to 0.02 ± 0.001 %ID/g at 120 h p.i. time point. The uptake of [^{169}Er]Er-HA MPs in any other organ/tissue was also negligible, as evident from the biodistribution pattern.

Table S1: Determination of sorption capacity of nanoporous HA MPs for ^{169}Er at different temperatures

Batch No	Temperature (°C)	Capacity (mg/g)
1	300	110 ± 5
2	500	187 ± 3
3	700	285 ± 8
4	900	282 ± 5

Table S2: Production yield of ^{169}Er from thermal neutron irradiation of 98.2 % enriched [^{168}Er]Er_2O_3 at 24 h of EOB. The target was irradiated for 21 d at flux of 1×10^{14} n cm^{-2} s^{-1}

Batch No	Specific activity (mCi/mg)	Radionuclidic impurity (%)	Radiochemical purity (%)
1	10.1 ± 1.1	> 99.99	> 99.9
2	10.2 ± 0.9	> 99.99	> 99.9
3	10.0 ± 1.1	> 99.99	> 99.9
4	9.9 ± 0.9	> 99.99	> 99.9
5	9.8 ± 1.2	> 99.99	> 99.9

Table S3: Determination of sorption capacity of nanoporous HA MPs and its comparison with commercially available bulk HA MPs for the sorption of ^{169}Er

Batch No.	Capacity (mg/g)	
	Nanoporous HA MPs	Bulk HA MPs
1	275 ± 6	85 ± 5
2	272 ± 5	92 ± 3
3	285 ± 8	99 ± 4
4	280 ± 5	95 ± 5

Table S4: Theoretical calculations comparing the requirement for nanoporous HA MPs and commercially available bulk HA MPs for preparation of clinically relevant dose (1 mCi) using ^{169}Er produced under different irradiation conditions

Flux of the reactor (n cm^{-2} s^{-1})	Time of irradiation (d)	Specific activity of ^{169}Er (mCi/mg)	Requirement of bulk HA (mg)	Requirement of nanoporous HA (mg)
5.0×10^{13}	3	0.50	21.3	7.4
	5	0.78	13.7	4.8
	7	1.02	10.5	3.6
	14	1.64	6.5	2.3
	21	2.00	5.3	1.8
1.0×10^{14}	3	1.01	10.6	3.7
	5	1.57	6.8	2.4
	7	2.05	5.2	1.8
	14	3.28	3.2	1.1
	21	4.01	2.6	0.9
1.2×10^{14}	3	1.21	8.8	3.1
	5	1.88	5.7	2.0
	7	2.46	4.3	1.5
	14	3.94	2.7	0.9
	21	4.82	2.2	0.7

Table S5: Comparison of the requirement of bulk HA MPs and nanoporous HA MPs for formulation of ~1 mCi dose of [^{169}Er]Er-HA using [^{169}Er]$ErCl_3$ of specific activity ~ 10 mCi/mg. This activity was produced by thermal neutron irradiation in 98.2 % enriched [^{168}Er]Er_2O_3 at a flux 1 × 10^{14} n cm^{-2} s^{-1} for 21 d and 24 h of EOB

Batch No.	Amount of bulk HA MPs required (mg)	Amount of nanoporous HA MPs required (µg)
1	1.88	370
2	1.90	372
3	1.87	371
4	1.89	374

Figure S1: Images of HA after heating at (a) 300 ℃ (b) 500 ℃ (C) 700 ℃ and (D) 900 ℃

T= 300 ℃

T= 500 ℃

T= 700 ℃

T= 900 ℃

Figure S2: Thermogravimetric analysis (TGA) analysis of synthesized HA MPs

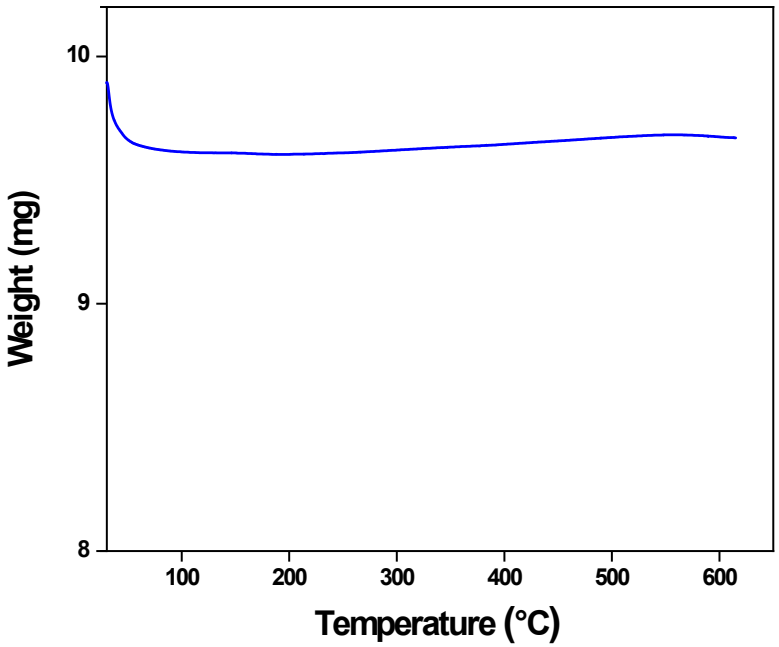


Figure S3: Variation of sorption capacity of synthesized HA MPs with concentration of Er^{3+}

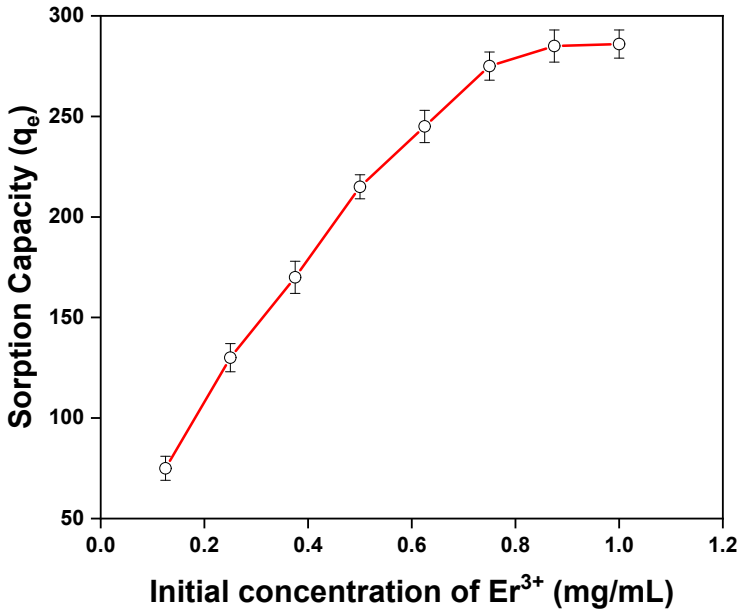


Figure S4: Particle size distribution of commercially procured bulk HA MPs

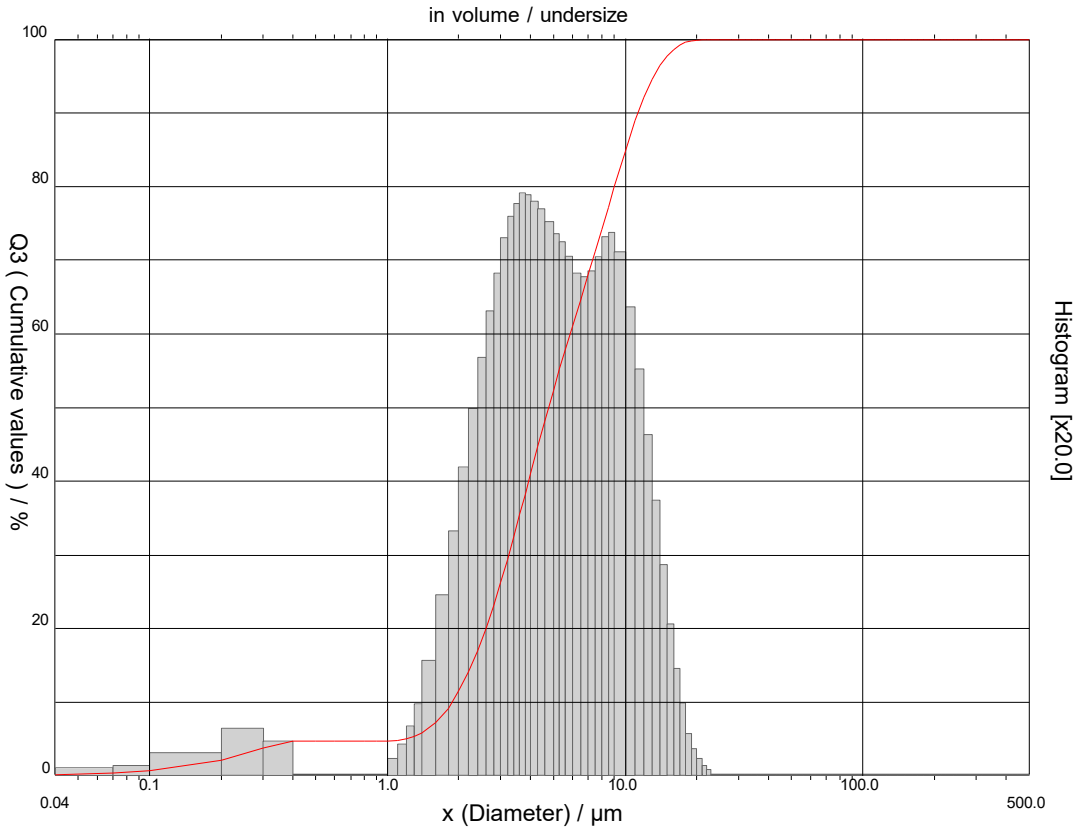


Figure S5: Variation in sorption capacity of nanoporous HA MPs for $Er^{3+}$with change in the incubation time

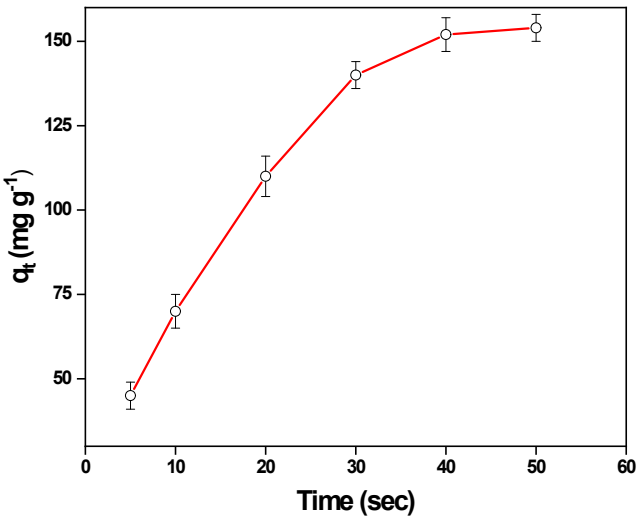
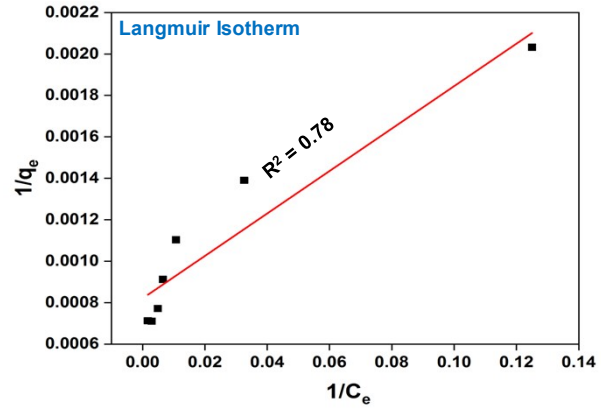


Figure S6: Fitting of the sorption data to the (A) Langmuir isotherm model and (B) Freundlich isotherm model

A



B

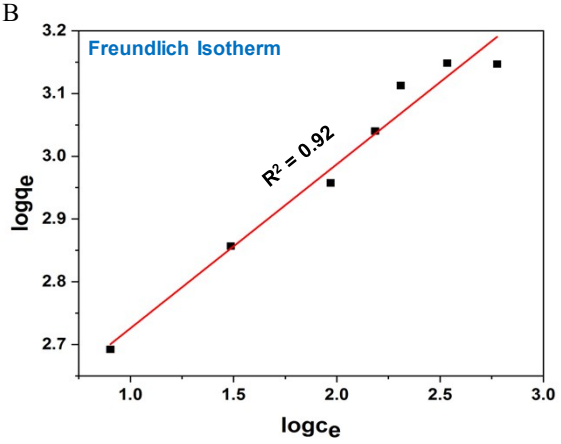


Figure S7: Fitting of the sorption data to the pseudo-first order kinetics model