

Effect of ligand denticity on the removal of ^{238}Pu from dilute aqueous solutions by hydroxamate-based chelating gels

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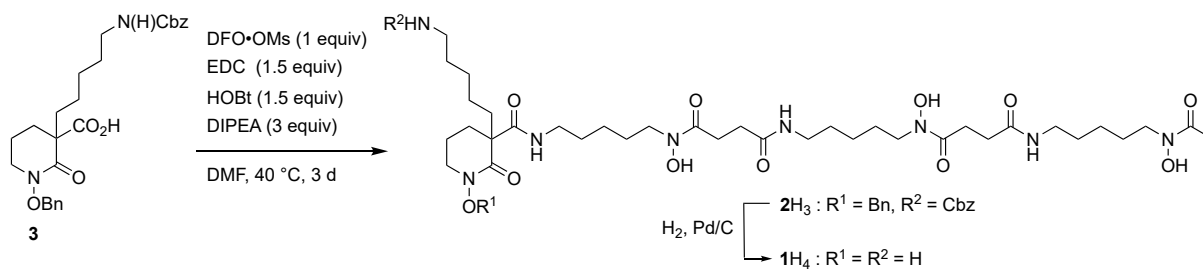
Supplementary Information

Supplementary experimental section

General. 10% Palladium on charcoal was activated by heating at 100 °C under vacuum for 1 h. *N,N*-dimethylformamide was dried by soaking with anhydrous magnesium sulfate, followed by distillation under vacuum and stored over anhydrous magnesium sulfate under argon. Diisopropylethylamine was dried by refluxing over sodium followed by distillation and collection under argon over pellets of potassium hydroxide. Compound **3** was prepared as reported in the literature.¹

Instrumentation. ¹H NMR spectra were recorded with a Bruker Avance III spectrometer operating at 400 MHz. FT-MIR spectra were obtained with a VERTEX 70v FT-IR spectrometer equipped with a RockSolid interferometer and a DLaTGS MIR detector. C, H, and N elemental analyses were carried out with a CHNS/O Thermo Electron Flash EA 1112 Series instrument or a CHNS/O ThermoFisher Scientific Flash 2000 instrument. Inductively coupled plasma optical emission spectrometry (ICP-OES) analyses were performed with an iCAP 7400 (Thermo Scientific) instrument with axial and radial viewing. Beforehand, all resin samples were mineralized in nitric acid using an ultraWAVE (Milestone) digestion system. Visible absorption spectrophotometric measurements were performed on a Cary 60 (Agilent) spectrophotometer using quartz Suprasil-300® cuvette (Hellma) of 1 cm optical-path length. Scanning Electron Microscopy (SEM) images were taken on a JEOL JSM 7600F microscope equipped with a Schottky thermo-assisted cathode, available at the ARCEN platform belonging to the "Laboratoire Interdisciplinaire Carnot de Bourgogne" (ICB, UMR 6303, CNRS, Université Bourgogne Europe, Dijon). Thermogravimetric (TGA) analyses were conducted on a Netzsch STA 409 PC thermal analyzer. Samples were heated in alumina crucibles from 25 to 1000 °C with a heating rate of 5 °C min⁻¹ (25 ≤ θ ≤ 600 °C) or 10 °C min⁻¹ (600 ≤ θ ≤ 1000 °C) under a N₂ (30 mL min⁻¹)/O₂ (10 mL min⁻¹) gas flow. Data were corrected for buoyancy effects. Onset temperatures (T_{onset}) were calculated according to the norm ISO 11357-3 as the intersection between the tangent in the inflection point and the selected baseline. Acid-base titrations of pristine CM Sephadex C-25® were carried out in triplicate according to a previously published procedure.²

Large scale preparation of compound 1H₄



Compound 2H₃. [(DFO)H₄]CH₃SO₃ (5.957 g, 9.064 mmol), EDC·HCl (2.607 g, 13.6 mmol), HOBT·H₂O (2.090 g, 13.6 mmol) were charged into a flask. The system was degassed and suspended into DMF (25 mL). A solution of compound 3 (4.247 g, 9.064 mmol) in DMF (75 mL) was then injected via canula into the reaction mixture, followed by diisopropylethylamine (8.5 mL, 48.8 mmol), and DMF (25 mL). The reaction mixture was heated to 42 °C, temperature at which it became a clear solution. Heating was stopped after 24 h. The solvent was removed by distillation under vacuum. The orange viscous residue was dissolved into methanol (125 mL), transferred into a round-bottom flask, and the solvent evaporated to dryness. The residue was further dried under vacuum at 35 °C. It was dissolved into methanol (28 mL) at 55 °C, followed by hot acetone (280 mL). The solution was left to cool down to room temperature, then stored in the freezer overnight, which produced the apparition of the product as a very fine precipitate. The supernatant solution was carefully removed with a Pasteur pipette and the precipitate was transferred into two centrifugation tubes with the help of acetone. The tubes were centrifuged for 6 min at 2050 rpm, the supernatant solution was removed, the precipitate was rinsed with acetone (20 mL), and a second centrifugation run in the same conditions. After removing the supernatant solution, the product was washed with cold acetone (15 mL), and a third centrifugation was run. The procedure was repeated using acetone (20 mL). After removal of the supernatant, the precipitate was transferred into a 100 mL flask and dried under vacuum, which afforded compound 2H₃ (3.772 g). The solvents of the combined supernatant solutions were evaporated and the residue was dissolved in methanol (7 mL) at 55 °C. Acetone at this temperature (120 mL) was then added, and the solution stored in the freezer for two days after cooling down to room temperature. The precipitate was collected by centrifugation and washed as reported above. This purification procedure was repeated until no more precipitate formed in the methanol/acetone solvent mixture. The different fractions and their conditions of obtention are collected in Table S1. A stacked plot of their ¹H NMR spectra is given in Figure

S1, p. S5. After the sixth precipitation, it was no longer possible to obtain a precipitate. The total amount of compound **2H₃** obtained by controlled precipitation was 6.483 g, which corresponds to a yield of 71%.

Table S1. Purification of compound **2H₃** by fractional precipitation.

Fraction n°	Volume of methanol (mL)	Volume of acetone (mL)	Mass (g)
1	28	280	3.772
2	7	120	0.841
3	5	80	0.208
4	2	100	0.235
5	2	100	0.598
6	1.5	100	0.829
Total mass of pure product			6.483

Compound 1H₄. Compound **2H₃** (1.289 g, 1.275 mmol) and 10% palladium on charcoal (0.816 g, 0.765 of Pd) were placed in a round-bottom flask equipped with a septum and two gas inlets (for argon and dihydrogen). The solids were conditioned under argon, then methanol (60 mL) was introduced via syringe and the reaction mixture conditioned under dihydrogen. The mixture was stirred for 3 h under dihydrogen. The catalyst was decanted, the supernatant solution was collected and filtered over a Chromafil PET 45/25 disk. The catalyst was rinsed with methanol (2 × 20 mL) and the solvent evaporated to dryness by rotary evaporation. Further drying under vacuum at 38 °C afforded compound **1H₄** (0.938 g) in 94% yield. Its ¹H NMR spectrum was in conformity with the one of an authentic sample.

Conditioning of CM Sephadex C25[®] in the acidic form. The resin CM Sephadex C25[®] is supplied as its sodium salt. Its capacity is 4–5 mmol g⁻¹ of carboxylate functions. We used the following two-step procedure to convert the sodium carboxylate-functionalized resin into the corresponding carboxylic acid-functionalized resin. Typically, 6 g of resin were soaked in a beaker containing water (90 mL). The resin was collected on a sintered glass filter, then this procedure was renewed once. Next, the resin was soaked in a 0.5 M sodium chloride solution (120 mL). At this stage, the pH of the filtrate is neutral. The resin was finally soaked twice in water (120 mL) and collected by filtration. In the second step, the resin was transferred into a glass column and eluted with a 0.5 M hydrochloric acid solution (120 mL). It was then washed

with water (240 mL) until the pH of the eluate was neutral. Finally, the resin was dried under vacuum until constant weight (4.293 g).

Calculation of the grafting ratio (GR). In order to calculate the grafting ratio (GR) of modified CM Sephadex C25[®], it is necessary first to precisely determine the millimolar ratio of pendant carboxylic acid groups per gram of resin (between 4 and 5 mmol g⁻¹, according to the supplier). This ratio was determined as 4.27 mmol g⁻¹ by potentiometric titration. Given that the pristine resin contains only C, H, and O atoms, the grafting ratio can be determined from the nitrogen content according to equation (1).

$$GR(\%) = \frac{10 \times N\%}{14 \times n_N \times n_{CO_2H}} = \frac{n_{Chelator}}{n_{CO_2H}} \quad (1)$$

$N\%$ is the analytical content of nitrogen by weight of grafted resin, n_N is the number of nitrogen atoms in a molecule of chelator, $n_{Chelator}$ is the content of chelator in the resin in mmol g⁻¹ of the grafted resin, and n_{CO_2H} is the content of carboxylic acid functions in mmol g⁻¹ of the pristine resin. For the iron-complexed resins, GR was calculated using the analytical content of Fe by weight of grafted resin ($Fe\%$), according to equation (2):

$$GR(\%) = \frac{10 \times Fe\%}{55.85 \times n_{CO_2H}} = \frac{n_{Chelator}}{n_{CO_2H}} \quad (2)$$

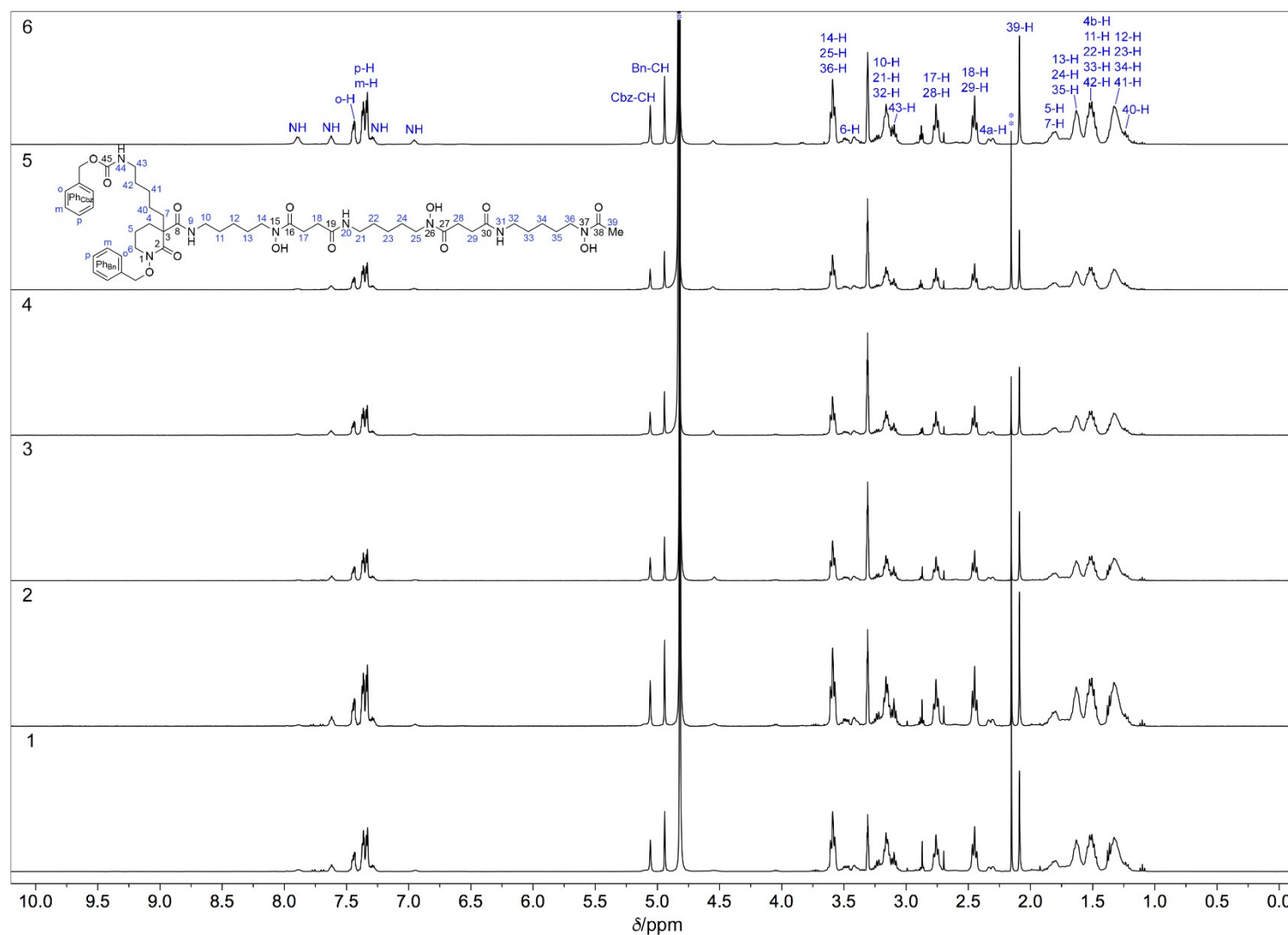


Figure S1. Stacked plot of the ^1H NMR spectra obtained in the course of the fractional precipitation of compound 2H_3 (400 MHz, CD_3OD). The numbers on the left side of the spectra are those of the batches of Table S1, p. S3.

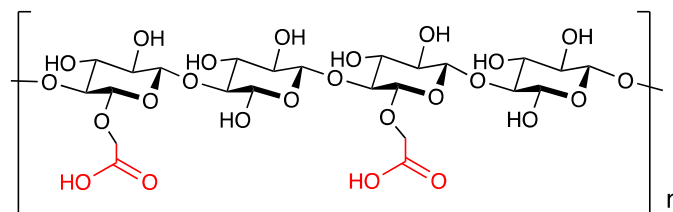


Figure S2. Simplified chemical structure of the resin CM Sephadex C-25[®].

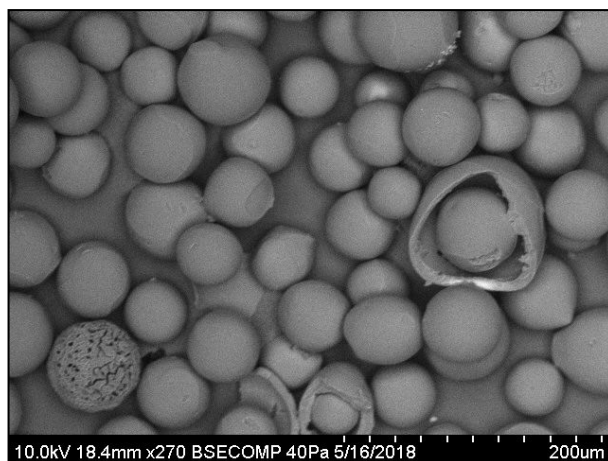


Figure S3. SEM picture in back scattering electron (BSE) mode of pristine CM Sephadex C-25[®] resin beads. Magnification: $\times 270$, working distance: 18.4 mm, acceleration voltage: 10.0 kV, vacuum: 40 Pa.

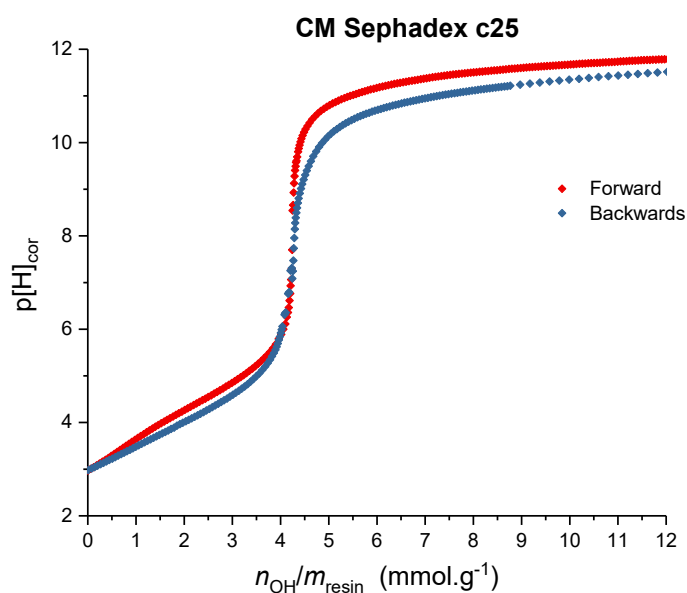


Figure S4. Plot of the potentiometric titration of the CM Sephadex C-25[®] resin with a 0.1 M aqueous solution of sodium hydroxide.

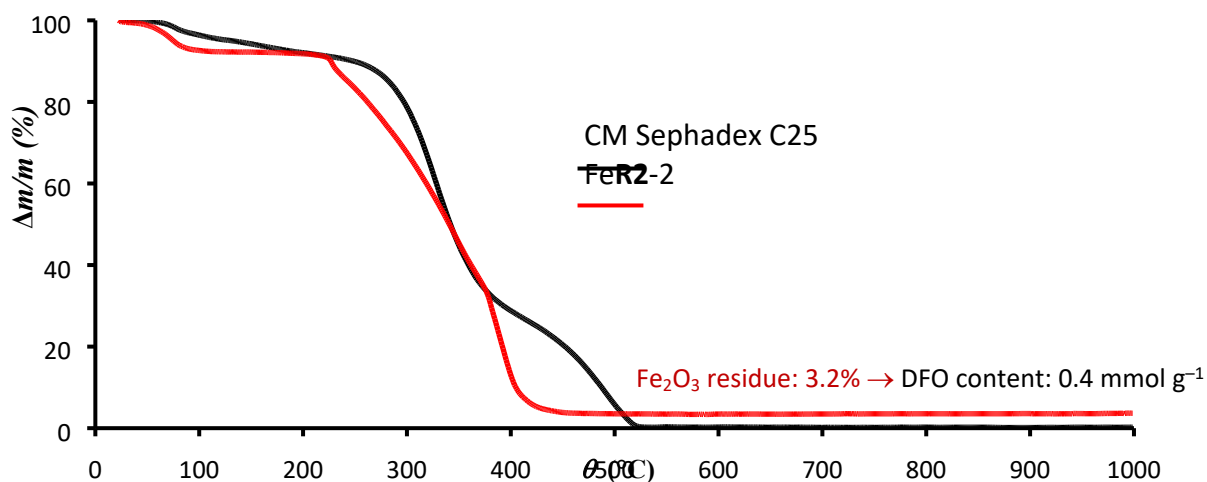


Figure S5. Comparison of the TGA thermograms of CM Sephadex C-25[®] and of FeR2-2.

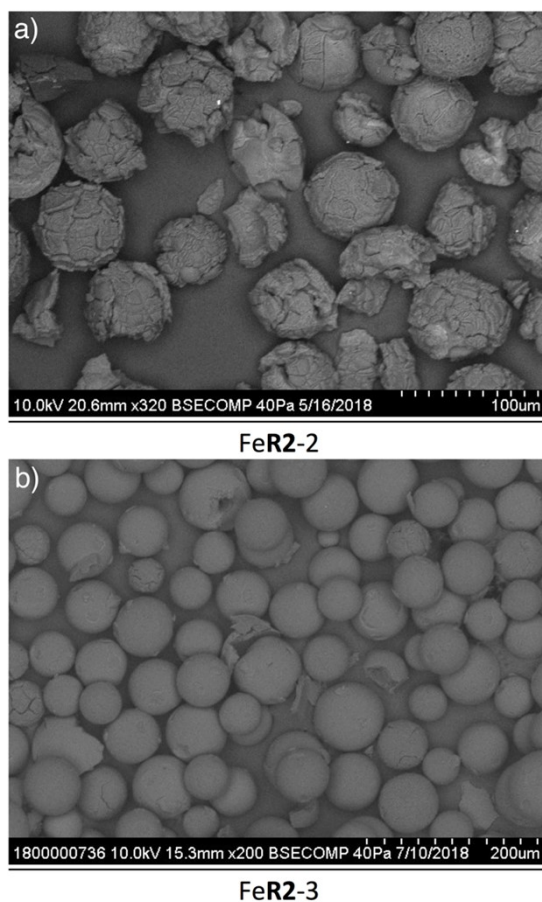


Figure S6. SEM pictures in back scattering electron (BSE) mode of FeR2 resins obtained in different stirring conditions. (a) Magnetic stirring for FeR2-2. Magnification: $\times 320$, working distance: 20.6 mm, acceleration voltage: 10.0 kV, vacuum: 40 Pa. (b) Orbital stirring for FeR2-3. Magnification: $\times 200$, working distance: 15.3 mm, acceleration voltage: 10.0 kV, vacuum: 40 Pa.

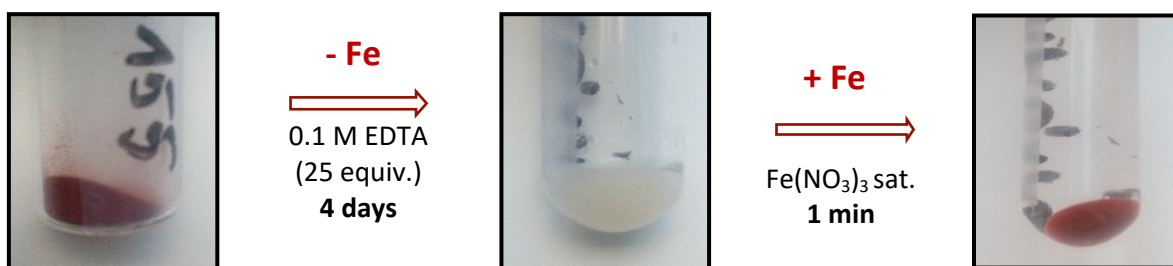


Figure S7. Iron removal from a sample of FeR2-2 by treatment with a 0.1 M aqueous solution of $\text{Na}_2\text{H}_2(\text{EDTA})$. Conditions and pictures of the samples.

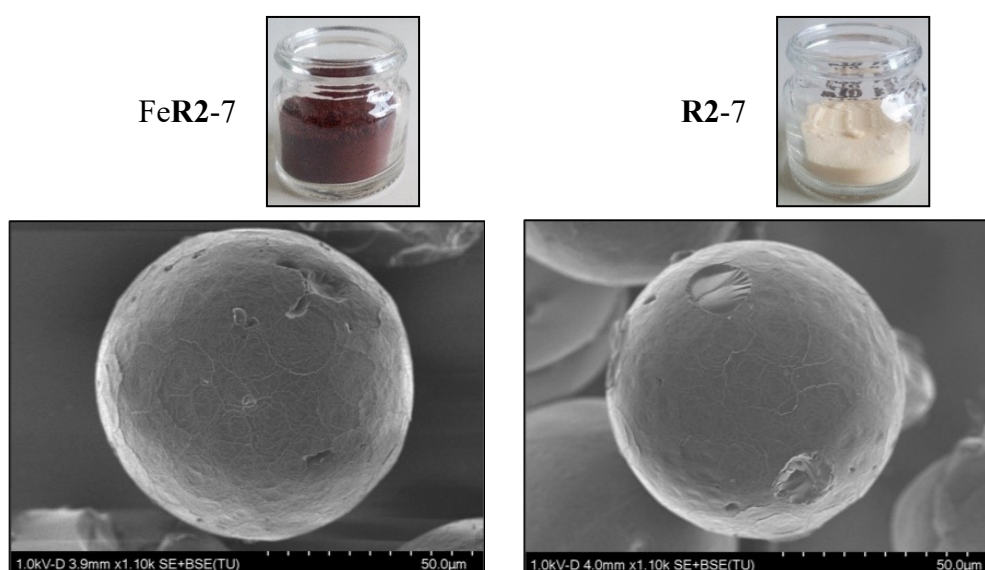


Figure S8. Photographs of the materials and SEM pictures in secondary electron (SE) and back scattering electron (BSE) modes of FeR2-7 (left) and R2-7 (right) obtained after treatment with $\text{Na}_2\text{H}_2(\text{EDTA})$. Magnification: $\times 1100$, working distance: 3.9 (FeR2-7) and 4.0 mm (R2-7), acceleration voltage: 1.0 kV, vacuum: 40 Pa.

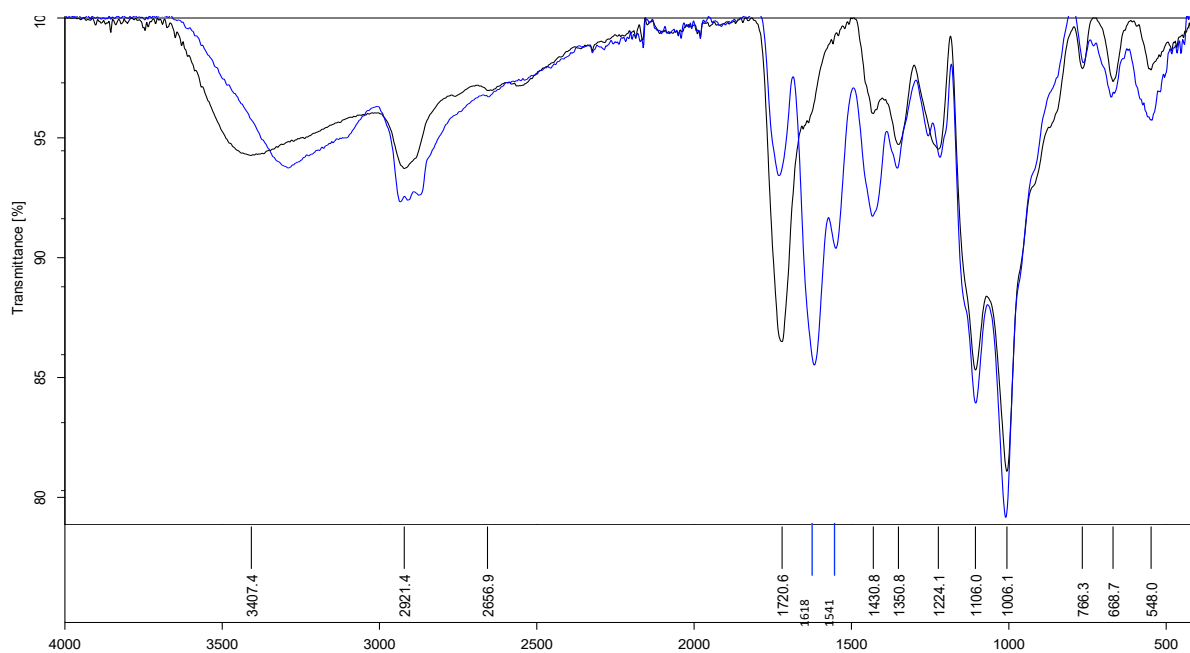


Figure S9. Comparison of the IR (ATR) spectra of CM Sephadex C-25® (black line) and the modified resin **R2-2** (blue line).

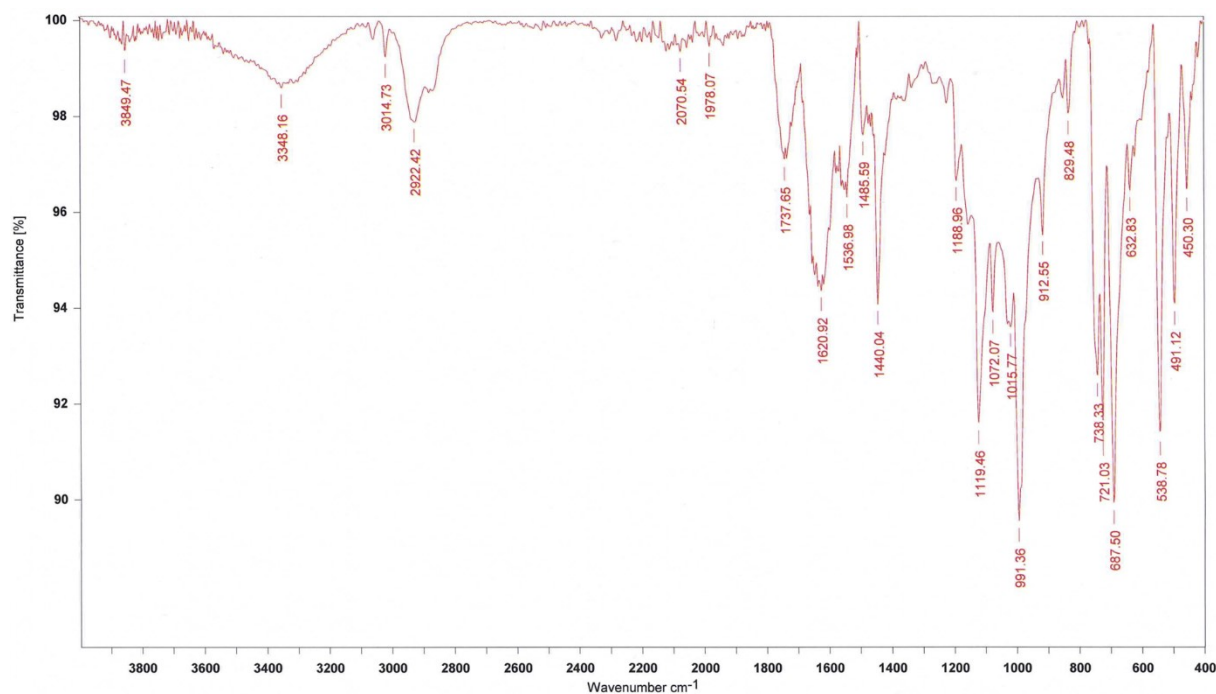


Figure S10. IR (ATR) spectrum of the modified resin **R3-1**.

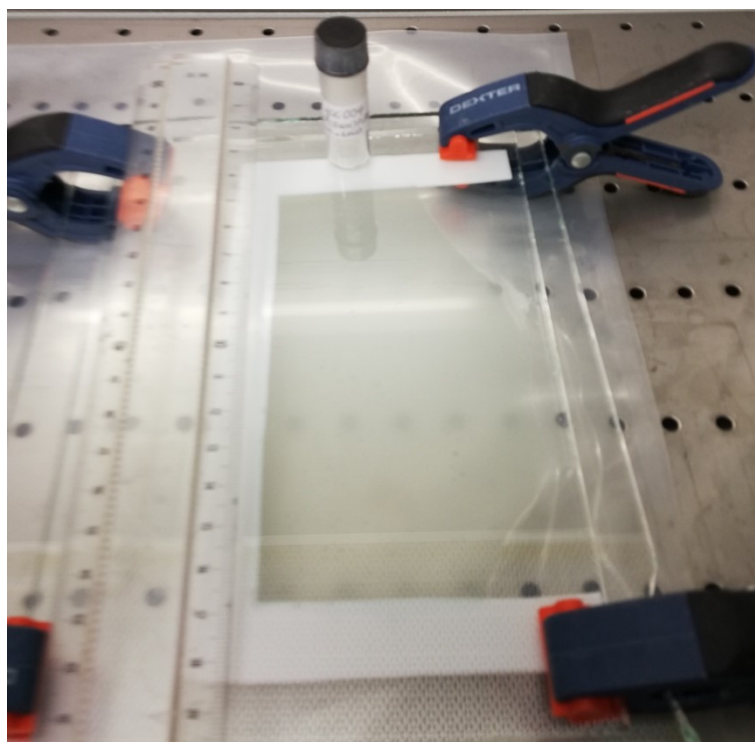


Figure S11. Appearance of the gel **G3-1** immediately after its fabrication.

Table S2. Optimization of the reaction conditions for the preparation of the grafted resins **R2** and **R3**.^a

Resin	Mass of resin involved (g)	equiv of chelator ^b	Reaction time (h)	Stirring technique	%Fe (ICP)	%N (EA)	Amount of grafted chelator		
							mg g ⁻¹	mmol g ⁻¹	GR
R2-1 ^a	1	0.5	48	Magnetic	-	7.69	513.0	0.915	0.214
Fe R2-1 ^c	1	0.5	48	Magnetic	1.81	-	199.8	0.324	0.076
Fe R2-2	0.1	0.5	48	Magnetic	1.86	3.08	186.7 ^d	0.333 ^d	0.078 ^d
Fe R2-3	0.1	0.5	48	Orbital shaking	-	-	-	-	-
Fe R2-4	0.1	0.2	48	Orbital shaking	1.21	-	133.8 ^d	0.217 ^d	0.051 ^d
Fe R2-5	0.1	0.5	48	Orbital shaking	2.45	-	263.9 ^d	0.428 ^d	0.100 ^d
Fe R2-6	0.1	0.5	130	Orbital shaking	3.06	-	327.4 ^d	0.531 ^d	0.124 ^d
Fe R2-7	6	0.25	130	Mechanical	1.84	-	202.8 ^d	0.329 ^d	0.077 ^d
Fe R2-8	15	0.25	130	Mechanical	1.63	-	180.0 ^d	0.292 ^d	0.068 ^d
Fe R2-9	20	0.25	130	Mechanical	3.13	-	345.3 ^d	0.560 ^d	0.131 ^d
R3-1 ^c	1.32	0.20	120	Shaker agitator	-	4.34	305.3	0.388	0.091
R3-2				Shaker agitator	-	3.42	240.8	0.305	0.072

^a The grafting reactions were run in DMF at 40 °C. ^b (DFO)H₃ for **R2-1**, [Fe(DFO)H]⁺ for Fe**R2**, and 1H₄ for **R3**. ^c Prepared by treatment of **R2-1** with a concentrated aqueous solution of [Fe(NO₃)₃]. ^d Based on Fe content; respectively 205.2 and 0.366 when based on N content. ^e Temperature: 42 °C.

Table S3. Results of the analyses of the material Fe**R2**-2 obtained by grafting of [Fe(DFO)H]⁺ on the resin CM Sephadex C-25®.

Method of analysis	Results	number of mmol of DFO per g of resin (mmol g ⁻¹)	mass of DFO per g of resin (mg g ⁻¹)
ICP-OES ^a	m_{Fe} : 18.6 mg g ⁻¹	0.333	186
Elemental analysis ^a	m_{N} : 30.8 mg g ⁻¹	0.366	205
TGA ^a	Fe ₂ O ₃ : 3.2%	0.400	224
Spectrophotometric measurements ^b	Absorbance at 425 nm: 1.683	0.399	224
ICP-OES ^b	[Fe]: 0.69 mM	0.346	194

^a Analysis of the resin. ^b Analysis of the supernatant solution ($\epsilon = 2460 \text{ M}^{-1} \text{ cm}^{-1}$ at 425 nm).

References

- 1 D. S. Abou, M. Longtine, A. Fears, N. Benabdallah, R. Unnerstall, H. Johnston, K. Shim, A. Hasson, H. Zhang, D. Ulmert, F. Mangin, S. Ozen, L. Raibaut, S. Brandès, M. Meyer, J.-C. Chambron, D. S. Tatum, D. Magda, R. L. Wahl and D. L. J. Thorek, *J. Nucl. Med.* 2023, **64**, 1062-1068.
- 2 A. Sornosa-Ten, P. Jewula, T. Fodor, S. Brandès, V. Sladkov, Y. Rousselin, C. Stern, J.-C. Chambron and M. Meyer, *New J. Chem.*, 2018, **42**, 7765-7779.