Siderophore-Mimetic Hydrogel for Iron Chelation Therapy

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ABSTRACT: Two, three dihydroxybenzoic acid (DHBA), a portion of the metal chelating domain of enterobactin, was immobilized on crosslinked organic polymer polyallylamine (PAAm) and used as a chelating agent for iron removal from aqueous solutions. The swelling behavior of PAAm and PAAm hydrogels conjugated with dihydroxybenzoic acid and the effect of contact time on the swelling and binding capacity of the hydrogel was investigated at several pH values to define the absorption mechanism. Iron uptake kinetics followed the pseudosecond order Ho model and equilibrium was described by either Temkin or Freundlich isotherms. Maximum chelating capacities of the hydrogels were found to be 500–1500 mg Fe^{3+} g^{-1} and 1500–2500 mg Fe^{2+} g^{-1} for PAAm and PAAm/DHBA hydrogels, respectively, depending on the pH of the media. The selectivity of the conjugate hydrogel toward ferric ions was studied at several different pH values. At every pH ranging from 2 to 7.5, the conjugate hydrogel showed relatively high binding affinity for ferric ions. The selective and rapid, high affinity binding of iron by this siderophore-mimetic hydrogel offers potential application as a nonabsorbed chelator for iron in the gastrointestinal tract of patients suffering from iron overload diseases. © 2011 Wiley Periodicals, Inc. J Appl Polym Sci 121: 1384–1392, 2011

Key words: hydrogel; siderophore-mimetic; chelating; selectivity

INTRODUCTION

Chelate-forming hydrogels have found widespread application in the selective extraction of trace heavy metal ions from aqueous solutions.[1–4] More recently, studies have shown that hydrogels have been successfully used as nonabsorbable drugs for sequestrating phosphate and cholesterol.[5–8] Desirable chelating hydrogels have a higher selectivity than ion-exchange resins in sorption processes. Chemical modification of hydrogels is a well-established technique for the fabrication of selective chelate-forming polymers.[9–11] Functional monomer(s) or grafted side groups may be introduced to the hydrogel to form covalent or noncovalently bonds.[11,12] The chelation characteristics of the modified hydrogel is largely dependent on the density and composition of the ligands incorporated into the polymeric matrix as well as the type of linker used for conjugation in the case of grafted polymer.

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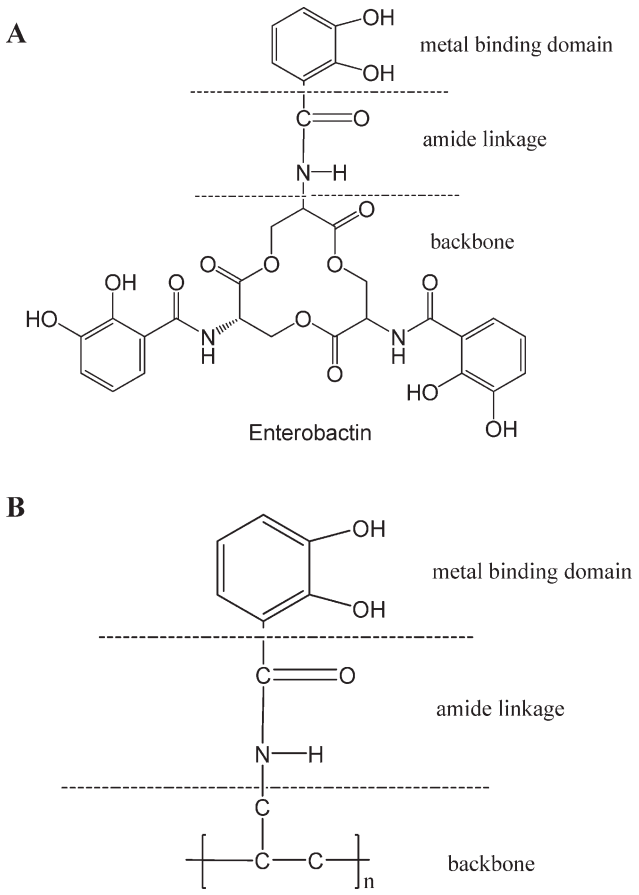
Fe(III) chelators are currently desired because of the toxic effects of iron overload and the biological implications of excess iron in all living organisms.[13–15] As a specific approach for the removal of Fe(III), immobilization of Fe(III) chelators onto Sepharose hydrogels has been investigated. This method was found to be useful in the treatment of Fe(III) overload and wastewater treatment.[16,17] The Fe(III) chelating resins and polymeric Fe(III) chelating agents reported so far are based on immobilized desferrioxamine or hydroxamic acid polymers.[12,16–20] Desferrioxamine (DFO), a naturally occurring Fe(III) chelator, has a strong affinity and selectivity for Fe(III). DFO is one of the drugs approved by FDA in clinical use for the treatment of iron overload in patients.[21,22]

Microorganisms have developed a sophisticated Fe(III) acquisition and transport systems involving siderophores. Siderophores are low molecular weight chelating agents that bind Fe(III) ion with high specificity. These potent and specific chelators usually include either catecholate or hydroxamate functional groups for iron coordination.[23,24] Enterobactin, a naturally occurring triscatechol siderophore, is the most powerful Fe(III) chelator known with an overall stability constant of 10^{49} (Scheme 1). More recently researchers have been trying to mimic the structure of this siderophore to design iron chelators with relatively high affinity and selectivity toward iron.[25,26]

Here, we report the synthesis and characterization of a highly effective iron chelator that mimics the



Scheme 1 A structural diagram of enterobactin with one arm of the ligand emphasized (A). Structure of the hydrogel synthesized in this study (B).

enterobactin structure (Scheme 1). Polyallylamine (PAAm) is a polycation hydrogel consisting of reactive primary amine side groups which can be conjugated to 2,3 dihydroxybenzoic acid (2,3 DHBA), the iron chelating domain of the enterobactin.[27,28] PAAm hydrogel was synthesized by crosslinking the precursor PAAm chains. Conjugation of 2,3 dihydroxybenzoic acid dramatically improved the iron binding affinity and iron selectivity of the final hydrogel. The selective and rapid, high affinity binding of iron by this siderophore-mimetic hydrogel offers potential for applications in iron chelation therapy in patients suffering from iron overload diseases.

EXPERIMENTAL SECTION

Materials

Poly(allylamine hydrochloride) (PAAm) with an average molecular weight of 56 kDa and analytical grade reagent *N,N′*-methylenebisacrylamide (MBA) were obtained from SigmaAldrich and used without further modification. The 2,3 dihydroxybenzoic acid, *N,N,N*-triethylamine, dimethylformamide (DMF), citric acid, potassium phosphate, and all metal chlorides were purchased from Fisher Scientific and used as received. Dicyclohexylcarbodiimide (DCC) and *N*-hydroxysuccinimide (NHS) were purchased from Thermo Scientific and used without further modification. Deionized water (DI) was obtained from a Barnstead EasyPure water purifier.

Preparation of PAAm hydrogel

PAAm was crosslinked with MBA by a Michael-type addition reaction. This crosslinking procedure was developed by Oliveira et al. to synthesize PAAm and poly(α-L-lysine hydrobromide) hydrogels.[29] Briefly, a 20% w/v polymer solution containing a predetermined amount of MBA was prepared. The crosslinker was dissolved in deionized water (flushed with nitrogen for 5 min) and then added to the polyallylamine polymer. Several different molar ratios of crosslinking agent to PAAm were investigated. TEA, the crosslinking catalyst (300 μL), was then added to the solutions and mixed thoroughly. Next, the precursors were transferred by micropipette into small plastic cuvettes and subsequently covered with parafilm. The cuvettes were held at ambient temperature for 1 h and then cooled to ~ 3°C and held there for an additional 24 h. After this time, hydrogels were removed from the cuvettes and washed with 0.05*M* sodium chloride for several days. Multiple synthesis conditions were employed to prepare the hydrogel investigated in this study (Table I). Synthesis at various crosslinker : polymer ratios facilitated identification of an acceptable range of swelling indices for biomedical applications while maintaining an acceptable reaction yield. These values are known to provide sufficient mechanical integrity and chemical stability after oral administration, based upon research reports and on data for the FDA-approved product, Renagel®.[5–8]

Swelling studies

The swelling behavior of hydrogels was studied using buffered solutions (sodium hydroxide as a buffering agent) with fixed ionic strength (0.5*M*). An historic protocol by Elving et al. was used for making buffer

TABLE I
Reaction Conditions and Swelling Behavior of Hydrogel at pH = 6

PAAm (mg)	Cross-linker (mg)	A/B[a]	Swelling index[b]	Yield (%)
123.6	21.2	0.1	8.0	79.6
124.3	33.9	0.2	7.1	75.7
126.4	45.8	0.3	5.0	76.8
124.9	58.9	0.4	4.6	68.0

[a] Mole ratio of crosslinker double bonds to polymer amines.
[b] Swelling index of PAAm/DHBA hydrogel.

solution with a known ionic strength.[30] Dried samples with known weights were placed in a solution of defined pH at room temperature. Samples were taken from the solution after reaching equilibrium. The swelling indices (SI) were calculated using the eq. (1):

$$\mathrm{SI} = \frac{w_s - w_d}{w_d} \quad (1)$$

where w_s is the weight of the swollen hydrogel at an equilibrium state and w_d is the weight of the dried hydrogel.

2,3-Dihydroxybenzoic acid modification of hydrogel

A solution of 2,3 DHBA (100 mg, 0.65 mmol) and NHS (74 mg, 0.65 mmol) in 5 mL of DMF was mixed with a solution of DCC (67 mg, 0.325 mmol) in 5 mL of DMF. The mixture was stirred at low temperature for 6 h to give a white precipitate. The precipitate was filtered, and the filtrate was added directly to a dry gel with known weight (25 mg). The reaction mixture was held at room temperature for 3 days. PAAm conjugate hydrogel was then washed with water for several days.

Quantification of amine functional groups

Primary amine groups were quantified by potentiometric titration. After grinding to a powder, 40 mg of PAAm and PAAm/DHBA polymer were suspended in 35 mL of 0.2*M* aqueous KCl solution. Next, 140 μL of 8*M* KOH aqueous solution was added to polymer suspensions to raise the pH to $\sim$ 12. Standard 0.1*M* HCl was used to titrate the suspension. HCl was added until the pH was about 2.5 in both polymer suspensions. Free amine groups were quantified from potentiometric data.

Binding kinetics study

Ferric chloride solution (2 mg mL^{-1}) was adjusted to pH 6.5 using NaOH while purging with N_2. The solution was kept at room temperature for kinetic studies. Samples were taken from the media at different time intervals to determine the rate of iron binding by PAAm/DHBA.

Binding experiments

Known concentrations of ferric chloride and ferrous chloride solutions (0.25, 0.5, 1, 2, 2.5) mg mL^{-1} were prepared. Binding experiments were carried out by taking 20 mL of metal solutions in 125 mL volumetric flasks, solutions were adjusted to the desired pH while maintaining iron concentration. Next, a known mass of PAAm/DHBA hydrogel was added to the mixture and was held at room temperature for 2 h or until equilibrium was reached. The solutions were then filtered and the filtrates were analyzed for metal concentration.

Selectivity study

The selectivity for Fe by PAAm/DHBA in the presence of several heavy metals such as copper, zinc, manganese, calcium, and potassium was studied. Metal solutions (10 mL) containing a 1 : 1 (wt) mixture of iron and heavy metals were prepared (2 mg mL^{-1}). The solution mixtures were then adjusted to pH 2.5, 4, 5, and 7 and held at room temperature for 2 h after adding a known mass of PAAm/DHBA dry gel.

Metal analysis

Mono- and multi-elemental analysis of samples was quantified by Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES) (Optima 2000 DV, PerkinElmer, USA) fitted with an AS 93plus autosampler (PerkinElmer, USA). A Cross-Flow nebulizer and a Scott spray chamber were used. The RF Power was 1300 W and nebulizer and auxiliary flows were 0.8 and 0.2 L min^{-1}, respectively. Sample flow was set at 1.5 mL min^{-1}. ICP-OES data was processed using Winlab 32 (Ver. 3.0, PerkinElmer, USA). The analytical curves used for samples analysis had coefficients of correlation >0.999.

Adsorption isotherms

Different isotherm models were employed to determine how the metal molecules distributed between the liquid phase and the solid hydrogel phase when the adsorption process reached equilibrium state. Langmuir, Freundlich, and Temkin isotherm models were applied to the data. Adsorption parameters of ferric and ferrous ions were calculated at different pHs. The accuracy of the isotherm models was evaluated by linear correlation coefficient (R^2) values.

Langmuir isotherm

Langmuir isotherms assume monolayer adsorption onto a surface containing a finite number of adsorption sites. The linear form of the Langmuir isotherm equation is given as:

$$\frac{C_e}{q_e} = \frac{1}{q_{\max} K_L} + \frac{C_e}{q_{\max}} \quad (2)$$

where C_e is the equilibrium concentration of the metal ion (mg L^{-1}), q_e is the amount of metal ion adsorbed per unit mass of hydrogel (mg g^{-1}), K_L and $q_{\max}$ are Langmuir constants related to the

TABLE II
Isotherm Parameters for Ferric and Ferrous Binding by PAAm/DHBA

Isotherm model	Ferric			Ferrous		
pH	2.2	5.4	7.4	2.2	5.4	7.4
Freundlich						
K_F	$77.53 \times 10^{+1}$	$34.55 \times 10^{+2}$		$31.33 \times 10^{+2}$	$22.29 \times 10^{+2}$	$43.84 \times 10^{+2}$
n	3.680	1.510		2.770	1.580	2.150
R^2	0.9884	0.9902		0.9927	0.9233	0.9895
sen	1.826×10^{-2}	3.289×10^{-2}		1.545×10^{-2}	9.546×10^{-2}	2.395×10^{-2}
sey	1.610×10^{-2}	2.821×10^{-2}		1.504×10^{-2}	2.928×10^{-2}	2.573×10^{-2}
Langmuir						
q_{max}	$52.63 \times 10^{+1}$	$14.28 \times 10^{+2}$		$20.00 \times 10^{+2}$	$25.00 \times 10^{+2}$	$14.28 \times 10^{+2}$
K_L	63.33	17.50		25.00	2.000	87.50
R^2	0.9998	0.9823		0.9581	0.8216	0.9840
sen	3.100×10^{-7}	4.431×10^{-6}		1.901×10^{-6}	2.135×10^{-5}	5.699×10^{-7}
sey	1.126×10^{-5}	1.713×10^{-4}		6.645×10^{-5}	6.150×1010^{-5}	1.253×1010^{-4}
Temkin						
A	331.70	1.000		199.3	19.20	635.7
B	21.06	6.190		5.130	4.080	7.770
R^2	0.9637	0.9646		0.9639	0.9380	0.9612
sen	4.691	37.78		4.669×10^{-2}	7.805×10^{-2}	3.054×10^{-2}
sey	9.522	74.62		0.1046	5.512×10^{-2}	7.556×10^{-2}

Gels were equilibrated in 2 mg/mL iron solutions.

adsorption/desorption energy and adsorption capacity, respectively. When C_e/q_e was plotted against C_e, a straight line with slope of $1/q_{max}$ was obtained. The R^2 values are summarized in Table II. The Langmuir constants K_L and q_{max} were calculated from eq. (2) and their values are shown in Table II.

Freundlich isotherm

Freundlich isotherms assume heterogeneous surface energies, in which the energy term in the Langmuir equation varies as a function of the surface coverage. The linear form of the Freundlich isotherm is given by the following equation:

$$\ln q_e = \ln K_F + \frac{1}{n} \ln C_e \tag{3}$$

where C_e is the equilibrium concentration of the metal ion (mg L^{-1}), q_e is the amount of metal ion adsorbed per unit mass of hydrogel (mg g^{-1}), K_F (mg g^{-1} (L mg^{-1})$1/n$) and n are Freundlich constants with n giving an indication of how favorable the absorption process is. The plot of $\ln q_e$ versus $\ln C_e$ gave a straight line with slope of $1/n$. Freundlich constants K_F and n were also calculated and are listed in Table II.

Temkin isotherm

Temkin and Pyzhev considered the effects of indirect adsorbate/adsorbent interactions on adsorption isotherms.[31] The heat of adsorption of all the molecules in the layer would decrease linearly with coverage due to adsorbate/adsorbent interactions. The Temkin isotherm has been used in the form as follows:

$$q_e = \left(\frac{RT}{b}\right) \ln(AC_e) \tag{4}$$

A plot of q_e versus $\ln C_e$ yielded a straight line. The constants A and b together with the R^2 values are shown in Table II.

RESULTS AND DISCUSSION

Synthesis and characterization

Poly(allylamine hydrochloride) was crosslinked with *N*,*N*-methylenebisacrylamide (MBA) by a Michael-type addition reaction.[32] The reaction was performed in water using several monomer to crosslinker ratios. An acceptable hydrogel yield was obtained for various reaction conditions (Table I). Although crosslinking was done by linking the primary amine groups, there were still a considerable number of reactive amino sites available for further modification of the PAAm hydrogel. The 2,3 DHBA was covalently linked to the PAAm hydrogel via DCC/NHC conjugation chemistry.

Swelling studies

The swelling kinetics of PAAm and PAAm/DHBA were studied to determine the time to reach equilibrium. Hydrogel swelling increased with time; however, it eventually plateaued, thus, allowing calculation of the equilibrium swelling percentage. PAAm hydrogel reached equilibrium in 10 h whereas PAAm/DBHA reached equilibrium in less than 1 h [Fig. 1(A,B)].

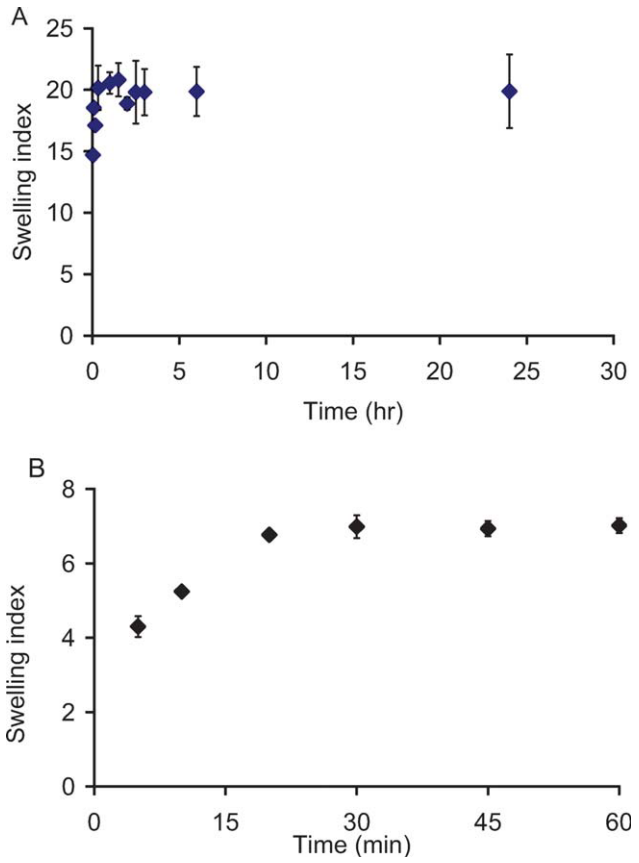


Figure 1 Kinetic swelling data for PAAm (A) and PAAm/DHBA (B) hydrogels at pH = 6, PAAm : DHBA = 5.68. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

The crosslinker concentration was varied and the swelling behavior of the final PAAm hydrogels were determined. Table I includes swelling indices of PAAm hydrogels with different PAAm: crosslinker ratios. A 2.7 ratio was selected because the swelling index for this ratio is within an acceptable range for either chemical or biomedical applications.[33] Next, The swelling behaviors of the hydrogels were further investigated as a function of pH by immersing the gels in buffered solutions at pH 1, 2, 4, 5, and 7.4 at room temperature (~25°C). The swelling behavior of PAAm was determined after equilibrating at different pHs [Fig. 2(A)]. The swelling of the PAAm hydrogel is higher at low pH values, with the maximum swelling observed at a pH of 2.2. This could be attributed to the complete protonation of the amine groups of PAAm at low pH. The pK_a of primary amines in PAAm is ~ 9.67; therefore, the behavior observed resulted from the ionized amines of the polymer as expected. Osmotic pressure results from counterions to the protonated primary amines and is a probable cause of swelling. When immersed in electrolyte solutions, ion exchange takes place in these types of hydrogels during the swelling process and can exert a considerable effect on the water absorption.

The same experiment was carried out for PAAm conjugate hydrogels and the swelling behavior of the 2,3 DHBA modified gels was studied at different pH values [Fig. 2(B)]. Because many of the amine groups were occupied via amide linkage, the ionizable groups within the hydrogel were diminished. Almost no significant changes in the swelling behavior were observed for PAAm/DHBA at different pHs.

Images of equal weights of the different hydrogels also illustrated the vast difference in swelling. PAAm hydrogels showed a significant reduction in swelling after modification by 2,3 DHBA [Fig. 3(A,B)]. The occupation of ionizable amine groups after conjugation of DHBA greatly reduced water uptake and presumably reduced the uptake of counterions. Moreover, PAAm/DHBA hydrogel further collapsed after immersion in a 2 mg mL^{-1} solution of ferric chloride [Fig. 3(C)]. Hydroxyl groups along with oxygen molecules bearing a negative charge (due to the partial double bond characteristic of the amide linkage) provided probable coordination sites for Fe. Moreover, as evident from potentiometric data, some protonated amine groups may also contribute to the coordination of Fe. The potentiometric

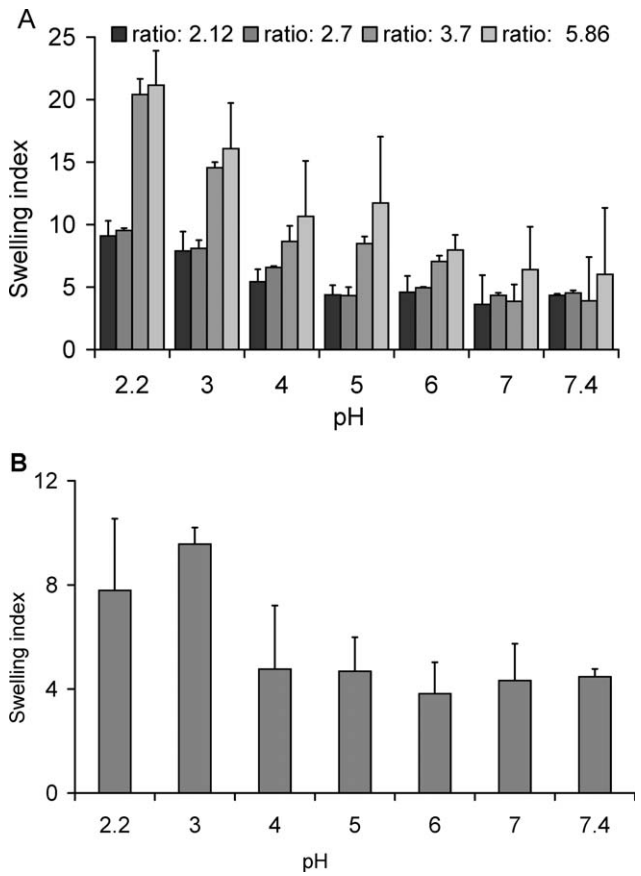


Figure 2 Swelling index of PAAm hydrogels with different cross-linker : polymer ratios at different pH values (A), swelling index of PAAm/DHBA with a 2.7 cross-linker : polymer at different pH values (B) (ionic strength = 0.5*M*).

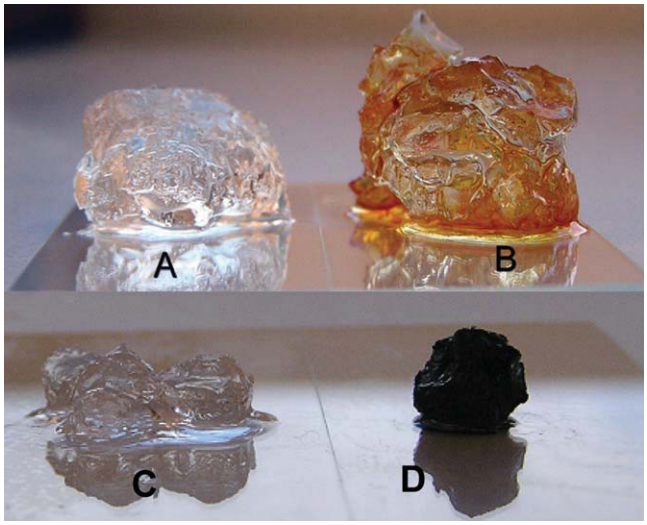


Figure 3 PAAm equilibrated in DI water (A), PAAm equilibrated in 2 mg mL^{-1} ferric solution (B), PAA/DHBA equilibrated in DI water (C) and PAAm/DHBA equilibrated in 2 mg mL^{-1} ferric solution (D). All hydrogels had equal masses. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

data obtained for PAAm and PAAm/DHBA indicated that about 23% of amine groups was occupied after conjugation reaction. Further collapse of PAAm/DHBA hydrogel in the ferric solution may be explained by multiple DHBA coordination of Fe.

Binding kinetics

Determination of the kinetics of metal absorption is critical in elucidating the reactivity of PAAm/DHBA and evaluating its potential for chemical and biomedical applications. The kinetics of metal binding was monitored using a known initial concentration of metal solution (2 mg mL^{-1}, $FeCl_3$) in the presence of a known mass of dry hydrogels. The equilibrium binding was found to be 1180 and 810 mg Fe g^{-1} Gel for PAAm/DHBA and PAAm, respectively, (Fig. 4). About 80% of the total iron absorption was attained in less than 5 min for the PAAm/DHBA hydrogel. This rapid absorption behavior is important in biomedical application especially for treatment of acute metal poisoning. To derive the rate constant and binding capacity, the kinetic data were modeled with pseudofirst-order (Lagergren model) and pseudosecond-order (Ho model) kinetic models which are expressed in their linear forms as:

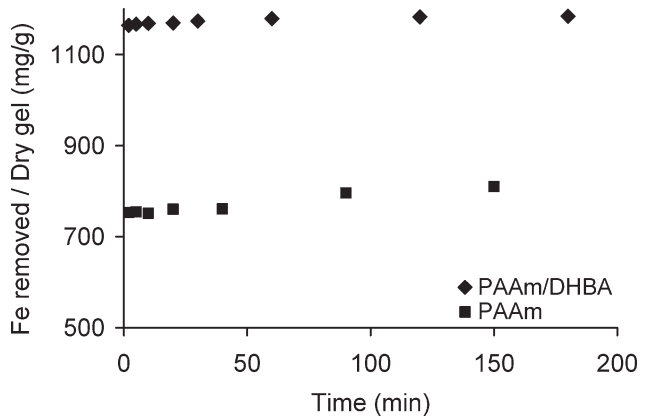


Figure 4 Ion binding by PAAm/DHBA hydrogels. Gels were equilibrated in 2 mg mL^{-1} ferric solution (pH = 2, ionic strength = 0.5*M*).

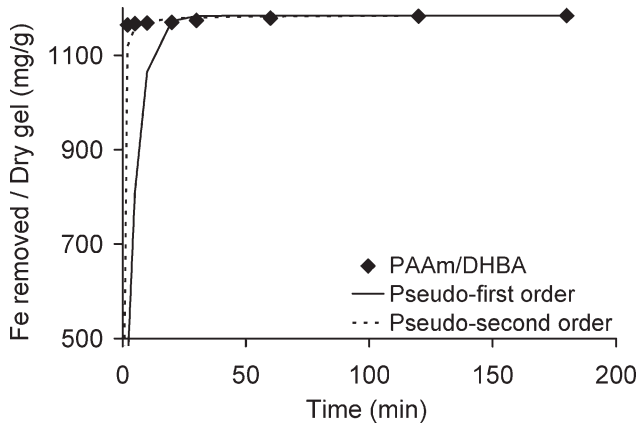


Figure 5 Kinetic models fitted for PAAm/DHBA hydrogel. Gel was equilibrated in 2 mg mL^{-1} ferric solution (pH = 2, ionic strength = 0.5*M*).

$$\log(q_e - q_t) = \log(q_e) - \frac{k_1}{2.303}t \quad (5)$$

$$\frac{t}{q_t} = \frac{1}{q_e^2 k_2} + \frac{t}{q_e} \quad (6)$$

where k_1 (L min^{-1}) and k_2 (g mg^{-1} min^{-1}) are pseudo-first-order and pseudosecond-order rate constants, respectively. Fitted kinetic models are shown (Fig. 5), and the model variables obtained by linear regression were compared (Table III). The pseudosecond order reaction model showed the best fit for ferric ions because its R^2 was ~ 1.

Binding isotherms

The metal ion binding capacity was determined at different pH values and different isotherm models were used to fit the data. At low pH, the metal ion uptake was relatively high. This could be due to the presence of protonated primary amine groups along with iron coordination sites, which together may improve the binding capacity of the hydrogel for

TABLE III
Kinetic Parameters for Ferric Binding by PAAm/DHBA at pH = 2

Kinetic model	Rate constant	Ion	R^2
Pseudo-first order	0.24	Ferric	0.9988
Pseudo-second order	0.23	Ferric	1

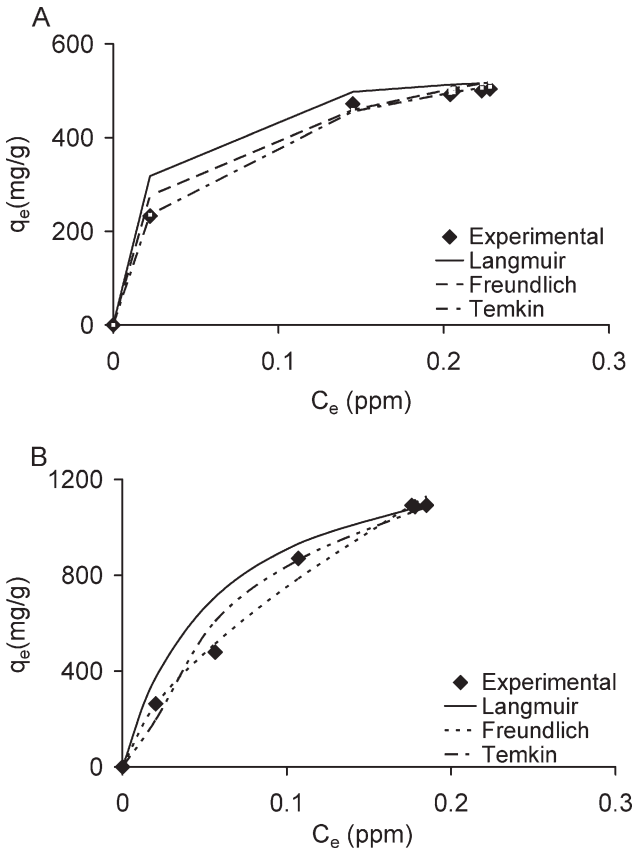


Figure 6 Binding isotherms for ferric ions at pH 2–3 (A) and 5–6 (B).

iron. Increasing the pH decreased the ionization of the remaining primary amine groups, and in turn lower values for the metal ion uptake were observed. The respective isotherm curves of ferric and ferrous solutions were obtained at different pH values (Figs. 6 and 7).

Modeling of isotherm data is vital for deriving meaningful information of binding characteristics, such as maximum binding capacity and binding constant. Therefore, several theoretical isotherm equations, including those of Freundlich, Langmuir, and Temkin, were employed to evaluate which could best describe the experimental data. Generally, the Freundlich and Temkin models are applicable to heterogeneous systems, while the Langmuir model is based on a homogeneous monolayer adsorption. Among the three models, both Freundlich and Temkin models provided accurate ferric and ferrous isotherms at low implying the heterogeneous nature of adsorption (Figs. 6 and 7). R^2 values obtained for these models were close to unity compared to the Langmuir model (Table II). The data may allow speculation that more than one type of binding site with different affinities may be involved in iron binding by PAAm/DHBA. This hypothesis will require further studies to confirm or refute.

Feng et al. reported the removal of iron from different systems using Sepharose-desferrioxamine B gels.[12] They also studied the effect of the immobilization of other iron chelators like l-(fl-aminoethyl)-3-hydroxy-2-methyl-4^2-pyridinone (HP) and L-mimosine onto Sepharose.[34] However, the effectiveness of the immobilized DFO was low. Even though gels had a high affinity for Fe(III) and were used for removing iron from milk, wine, whey, and lactoferrin, they were not very stable mainly due to hydrolysis of their isourea bonds.[12,34] In another study, Polomoscanik et al. studied the iron binding

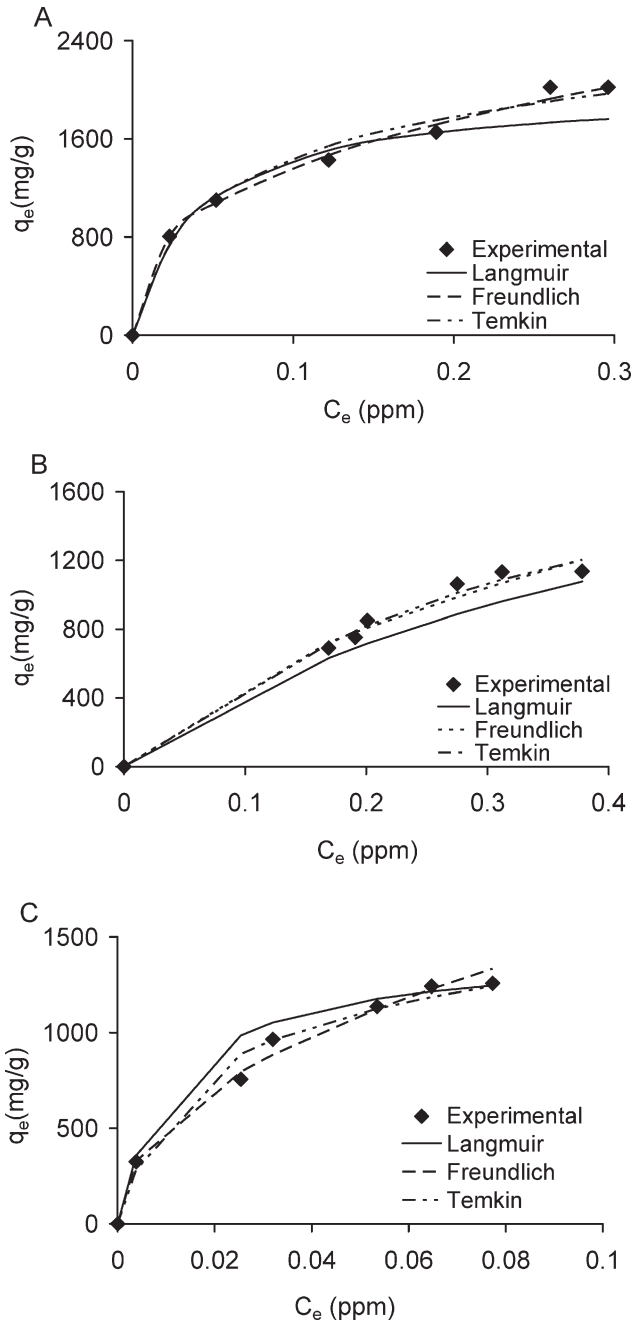


Figure 7 Binding isotherms for ferrous ions at pH 2–3 (A), 5–6 (B), and 7.4 (C).

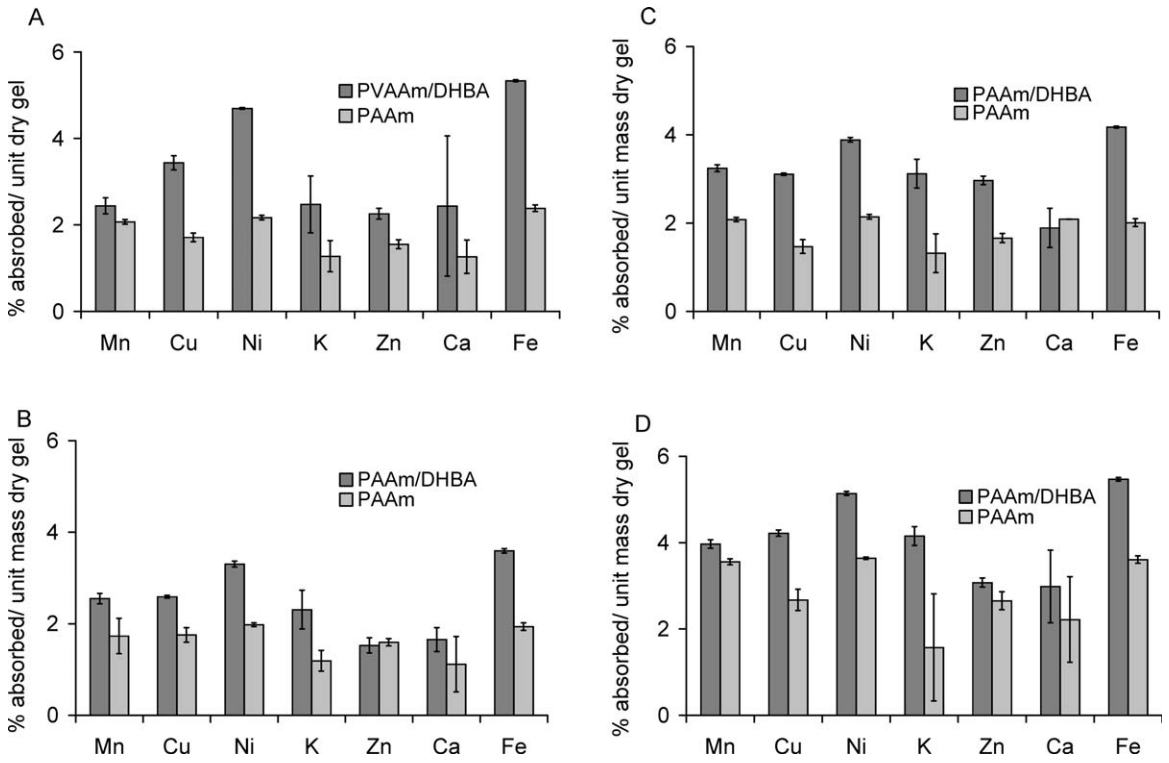


Figure 8 Selectivity study for PAAm/DHBA and PAAm hydrogels toward ferric ion in the presence of Mn^{2+}, Cu^{2+}, Ni^{2+}, K^{+}, and Ca^{2+} at different pH ranges. A: pH = 2.5, B: pH = 4, C: pH = 5, and D: pH = 7.

parameters of hydroxamic acid-containing hydrogels derived from derived from crosslinked polymeric acid chloride precursor and polymeric hydroxyethyl ester precursor. The maximum iron(III) binding capacities of these hydrogels were 0.81 and 0.45 mmol g^{-1}, respectively.[35] The maximum iron(III) binding capacity of PAAm/DHBA hydrogel varies between 9.3 and 25.5 mmol g^{-1} depending on the pH of the solution.

Selectivity studies effect of essential metals

One of the important features of metal chelating hydrogels is their ability to specifically target the metal of interest and remove it from the media. Selectivity is especially important if the desired application of the hydrogel is in the treatment of metal poisoning. The hydrogel selectivity may affect the bioavailability of some other essential metal ions such as Cu^{2+}, Zn^{2+}, Ca^{2+}, Mn^{2+}, Ni^{2+}, or K^{+}. Selective absorption of essential metals could cause serious damage to vital organs. The influence of essential metals on the binding of ferric ions was investigated using a multi-solute system to evaluate the metal selectivity of PAAm/DHBA at different pHs. At an equal concentration of all metals (2 mg mL^{-1}), PAAm/DHBA absorbed almost 80% of the iron present in the media while typically the absorption for essential metals (e.g., Ca, Zn) was less than 50% (Fig. 8). The ratio was similar across a wide range of pHs. Zhou et al. has studied the selectivity of 3-hydroxypyridin-4-one hexadentate ligand-containing copolymers (DMAA) for iron in the presence of some essential metals. Even though the DMAA hydrogel showed high affinity for iron it still bound Cu^{2+} efficiently (more than 53%). Comparatively, PAAm/DHBA showed a higher selectivity toward Fe in the presence of other metals, implying the greater stability of the Fe-PAAm/DHBA complex.

CONCLUSIONS

The 2,3 dihydroxybenzoic acid was immobilized on polyallylamine hydrogel to mimic the structure of the enterobactin, a potent, naturally occurring Fe(III) chelator. The final hydrogel was able to remove and accumulate ferric and ferrous ions from aqueous solutions at relatively low concentrations. PAAm/DHBA demonstrated an rapid iron absorbance when equilibrated in ferric solution. The pseudosecond order Ho kinetic model was found to be an excellent fit with the experimental results. These siderophore-mimetic hydrogels also exhibited a high affinity and selectivity for iron at different pH values. Freundlich and Temkin adsorption models adequately described the relationship between metal concentration in solution and the amount retained by the hydrogel. The high

affinity and selectivity of PAAm/DHBA hydrogel for iron provides important features for this hydrogel in biomedical and chemical applications.

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