

Chitosan-Magnetite Nanocomposites for Effective Removal of Urea in "Magnetic Hemodialysis Therapy": A Novel Concept

Abhishek Pathak, Sunil K. Bajpai

Polymer Research Laboratory, Department of Chemistry, Govt. Model Science College (Auton.), Jabalpur, Madhya Pradesh 482001, India

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ABSTRACT: The present study explores the possibilities of using chitosan-magnetite (CM) nanocomposites for removal of urea in blood serum. The CM nanocomposites, with an average diameter in the range of 12–33 nm, were characterized by transmission electron microscopic and selected area electron diffraction analysis. The particles demonstrate fair ability to remove urea in human blood serum. The maximum removal efficiency

was nearly 26%, when 200 mg of CM nanocomposites were allowed to agitate with 25 mL of urea solution of concentration 100 mg/dL. The CM nanocomposites could be easily removed by applying moderate magnetic field. © 2009 Wiley Periodicals, Inc. *J Appl Polym Sci* 114: 3106–3109, 2009

Key words: chitosan; urea; magnetite; hemodialysis

INTRODUCTION

The goal of dialysis for patients with chronic renal failure is to remove nitrogenous end-products of catabolism and to restore the composition of the body's fluid environment toward normal.¹ With renal failure of any cause, toxic end products of nitrogen metabolism (urea, uric acid, creatinine etc.) begin to accumulate in blood and tissues. Finally, the kidneys are no longer able to function as endocrine organs,² and the patient has to undergo hemodialysis treatment. The central element of a hemodialysis instrument is a semipermeable membrane which allows for the selective transport of low-molecular weight biological metabolites. The membrane removes excess blood urea and other solutes by diffusional/convective flux. On an average, it takes nearly 4–5 h for a hemodialysis dose.³ To reduce this treatment time, various materials have been proposed as urea adsorbents. These include activated carbon,⁴ polyethylenepolyamine/Cu(II) complex,⁵ tolylene di-isocyanate crosslinked β -cyclodextrin,⁶ etc. However, due to low adsorption capacity and poor biocompatibility, they could not be used. There have been continuous attempts made

to reduce this duration of time by developing membranes with more effective urea removal rate.

We hereby propose a novel and unique approach which consists of injecting magnetic chitosan-magnetite (CM) nanocomposites into blood stream where they shall bind to urea. These particles may later on be removed by electromagnetic poles of a magnetic field generator attached in series across "conventional dialyser". In this way, the urea shall not only be removed by filtration across the membranes, but also by adsorption onto CM nanocomposites.

EXPERIMENTAL

Materials

Ferric chloride, ferrous chloride and urea were obtained from Hi Media Laboratories, Mumbai. Chitosan, obtained by deacetylation of chitin in 50 wt % NaOH, had degree of deacetylation of 96% and molar mass 1.42×10^6 as determined by using Mark-Houwink equation.⁷

Preparation of CM nanocomposites

CM nanocomposites were prepared by chemical coprecipitation of Fe^{3+} and Fe^{2+} ions by NaOH in the presence of chitosan followed by hydrothermal treatments.⁸ In brief, to a 2% (w/v) solution of chitosan, Fe(III) and Fe(II) were added in 2 : 1 molar ratio and kept for 2 h at 30°C. The above solution was added dropwise into 2 M NaOH solution under

Correspondence to: S. K. Bajpai (mnlbpi@rediffmail.com).

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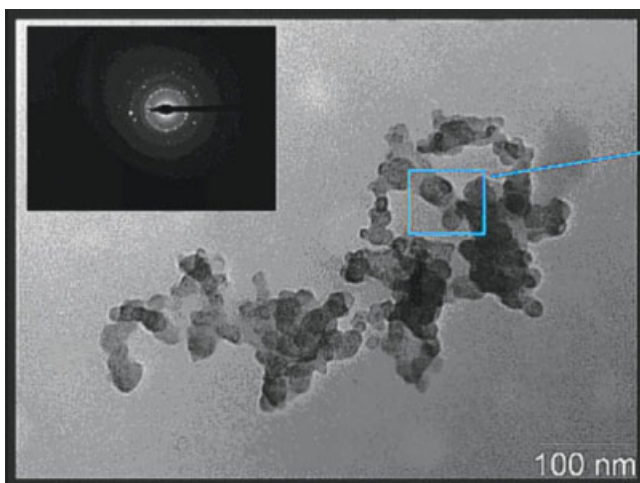


Figure 1 Photograph showing TEM image of CM nanocomposites with selected area electron diffraction image in inset. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

constant stirring. After the complete addition of chitosan solution, the resulting precipitated mass was heated at 80°C for a period of 2 h. The nanocomposites were centrifuged at 200 rpm and washed several times with water and ethanol, dried at electric oven (Tempstar, India).

Urea uptake studies

A known quantity of urea was dissolved in blood serum to give a final concentration of 100 mg dL⁻¹. A preweighed amount of CM nanocomposites were agitated in urea solution under constant stirring. An aliquot of solution was taken out at different time intervals and analyzed for urea.⁹ The percent uptake was given as

$$\% \text{ Urea uptake} = \frac{C_o - C_e}{C_o} \times 100$$

where C_o and C_e are concentrations of urea solutions, initially and at different time intervals respectively. Finally, the particles were removed by applying moderate magnetic field.

Characterization of CM nanocomposites

Transmission electron microscopic (TEM), selected area electron diffraction (SAED) analysis

Transmission electron microscopic (TEM) measurements were performed with a JEOL JEM-2000 operating at 200 kV. The sample was prepared by dispersing 2–3 drops of gel-magnetite solution, obtained by sonication, on 3 mm copper grid and removing excess solution using a filter paper and drying the grid for a day.

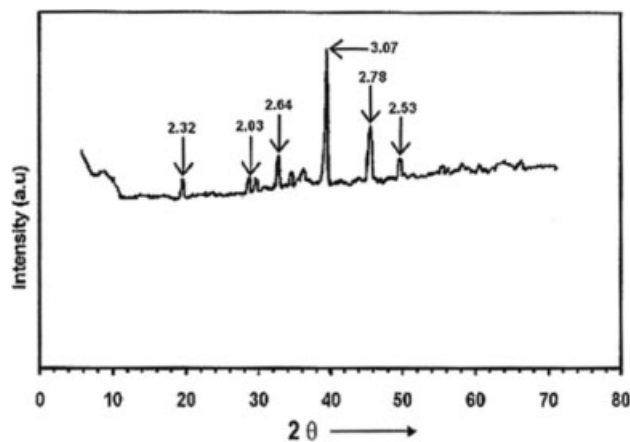


Figure 2 XRD pattern of CM nanocomposites.

XRD analysis

XRD analysis was performed with a Rigaku diffractometer (Cu radiation, $\lambda = 0.1546$ nm) running at 40 kV and 40 mA.

B-H analysis

The magnetic property of the magnetic polymer was determined by using vibrating sample magnetometer. A hysteresis curve (M-H curve) was measured and plotted for the sample to determine saturation (M_s), coercivity (H_{ci}) and magnetic retentivity (M_r).

EXPERIMENTAL RESULTS

TEM, SAED analysis

Figure 1 shows the TEM image of the CM nanocomposites. It can be clearly seen that magnetite nanoparticles are almost uniform in size. The SAED, shown in the inset, also confirms the formation of magnetite. The particle size distribution was obtained by measuring the diameters of 20 particles selected from an arbitrarily chosen area of TEM image. Nearly 40% particles have an average

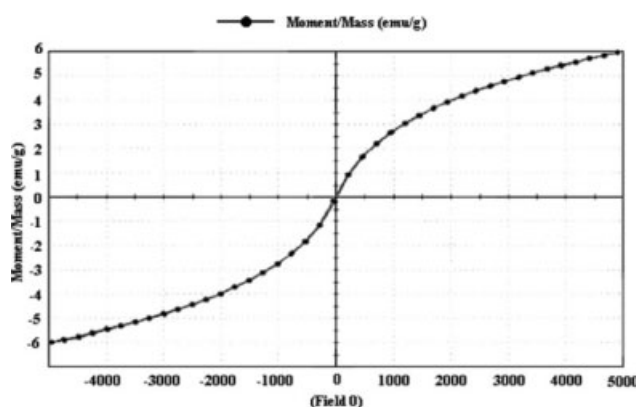


Figure 3 Curve between magnetization and applied field.

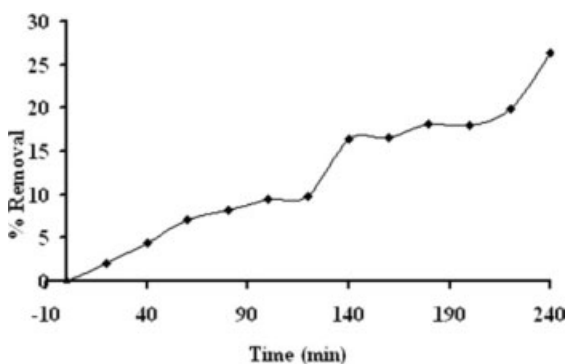


Figure 4 Dynamic uptake of urea into CM nanocomposite particles.

diameter of 27 nm and the distribution appears to be more or less symmetrical with all nanoparticles falling within the range 12–33 nm.

XRD analysis

The x-ray diffraction pattern of magnetite-loaded chitosan sample is shown in the Figure 2. It is clear from the Figure 2 that the peaks corresponding to magnetite, appear at $d = 3.07, 2.78, 2.64, 2.53, 2.32,$ and 2.03 which resemble closely with the theoretical values of $2.97, 2.78, 2.64, 2.51, 2.33,$ and 2.10 respectively.^{10,11} This confirms the formation of magnetite within the polymer matrix.

B-H analysis

The magnetite behavior of the representative sample has been documented by the hysteresis curve measured at 300 K as shown in Figure 3 with magnetic parameters in inset. The lower saturation magnetization value of 6.9 obtained for the nanocomposites

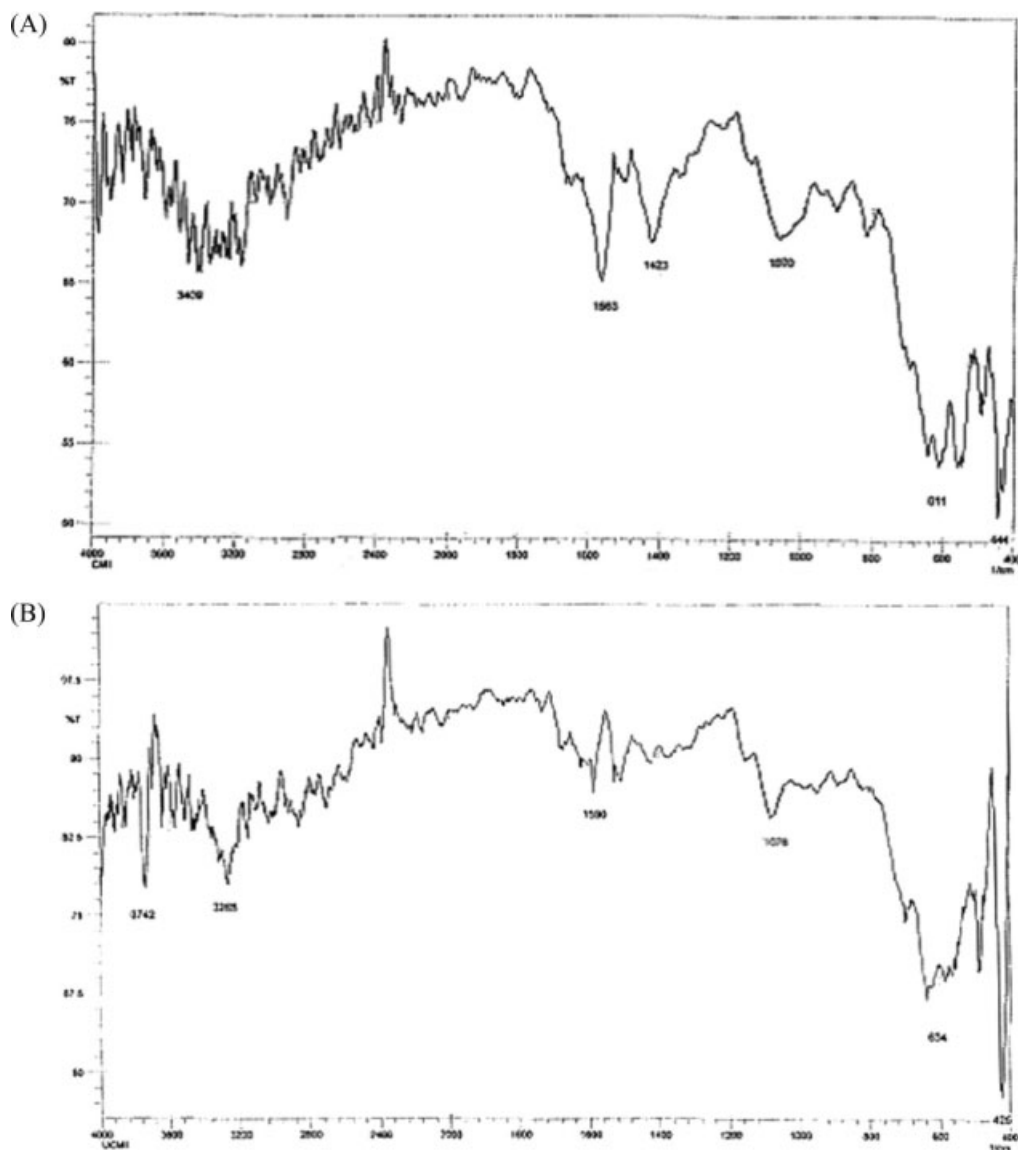


Figure 5 FTIR analysis (A) CM and (B) urea bound CM.

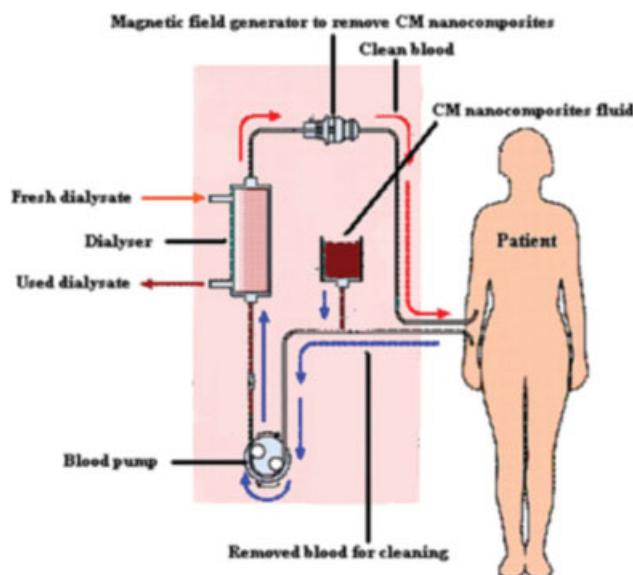


Figure 6 Scheme showing dialysis process through magneto-dialyser. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

may probably be due to higher chitosan content in the nanocomposites. Here, it should be noted that Liu et al.¹² reported saturation magnetization values of nearly 6.0–9.1 for magnetite-loaded gelatin hydrogels. In addition the lower coercivity, H_{ei} (i.e., 8.1 O_e) and complete absence of hysteresis indicates superparamagnetic behavior of synthesized magnetic hydrogels.

Urea uptake studies

The kinetics of urea uptake by CM nanocomposites has been shown in the Figure 4. It is clear that percent urea uptake increases with time and nearly 26% urea is removed from 25 mL of urea solution with initial urea content of 100 mg/dL using 200 mg of CM nanocomposites in nearly 4 h. This indicates that CM nanocomposites have fair capacity to remove urea from the solution. Here we would like to mention that Cu(II)-immobilized chitosan membrane has been reported to adsorb nearly 78.8 mg urea per gram of membrane.¹³ This amount appears to be quite greater than the urea removal in present study. However, the approach adopted in the present study is totally different. We have used magnetite-loaded chitosan nanoparticles as urea adsorbent and proposed them to be used as an attachment in series of conventional dialysis machine.

As we know that Cu(II) has four binding sites out of which two sites are occupied by 'N' atoms of chitosan chain¹⁴ and rest two binding sites are left for the removal of urea through 'O' atom of urea. So, it is expected that Cu(II)-immobilized chitosan

membrane has greater tendency to remove urea as compared to plain chitosan.

Mechanism of urea uptake

To investigate the mechanism of urea uptake by CM nanocomposites, we recorded FTIR spectra of CM and urea bound CM nanocomposites. It is clear from Figure 5(A) that characteristic peak of magnetite appears at 611 cm^{-1} which is due to metal oxygen stretching. Whereas, in Figure 5(B) it has shifted from 611 cm^{-1} to 634 cm^{-1} . This confirms binding of $\text{Fe}^{3+}/^{2+}$ with oxygen of urea owing to 6 co-ordination number of $\text{Fe}^{3+}/^{2+}$. The peak at 1563 cm^{-1} is due to primary amine of chitosan which seems to be shifted in Urea bound CM. The stretching frequency of C=O of urea is expected between 1655 and 1610 cm^{-1} which is almost absent in UCM.

CONCLUSION

From the above study it is obvious that CM nanocomposites have fair capacity for urea removal from blood serum. If these nanoparticles are injected to the impure blood of a kidney patient before it goes to dialysis machine the removal rate of urea can be greatly enhanced. Figure 6 depicts a schematic diagram showing the possible instrumental setup for urea removal using conventional dialyser. It can be seen that if the CM nanoparticles are mixed into blood stream, they shall carry out sorptive removal of urea during the dialysis process and finally will be removed by moderate field generator.

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