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Temperature responsive hydrogel magnetic nanocomposites for hyperthermia and metal extraction applications

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ABSTRACT

The present work deals with the development of temperature and magnetic responsive hydrogel networks based on poly (N-isopropylacrylamide)/acrylamido propane sulfonic acid. The hydrogel matrices are synthesized by polymerizing N-isopropylacrylamide (NIPAM) monomer in the presence of acrylamido propane sulphonicacid (AMPS) using a cross-linker (*N*,*N*-methylenebisacrylamide, MBA) and redox initiating system [ammonium persulphate (APS)/tetramethylethylenediamine (TMEDA)]. The magnetic nanoparticles are generated throughout the hydrogel networks using in situ method by incorporating iron ions and subsequent treatment with ammonia. A series of hydrogel-magnetic nanocomposites (HGMNC) are developed by varying AMPS composition. The synthesized hydrogel magnetic nanocomposites (HGMNC) are characterized by using Fourier Transform Infrared (FTIR) Spectroscopy, X-ray diffraction (XRD), Thermal Analyses and Electron Microscopy analysis (Scanning and Transmission Electron Microscope). The metal extraction capacities of the prepared hydrogel (HG) and hydrogel magnetic nanocomposites (HGMNC) were studied at different temperatures. The results suggest that HGMNCs have higher extraction capacity compared to HG and HG loaded iron ions. This data also reveals that the extraction of metals by hydrogel magnetic nanocomposites (HGMNCs) is higher at higher temperatures than room temperature. The prepared HGMNCs are also subjected to hyperthermia (cancer therapy) studies.

1. Introduction

Temperature sensitive hydrogels can absorb huge amount of water below their lower critical solution temperature (LCST) but hold less amount of water above their LCST [1]. These temperature-sensitive hydrogels have large potential applications in biomedical field such as controlled drug delivery systems, immobilized-enzyme reactors [2,3] and for other biological applications [4,5].

Poly (N-Isopropylacrylamide) (PNIPAM) is one of the most popular well known temperature-responsive hydrogel [6,7]. Unfortunately, normal PNIPAM-based hydrogels, prepared by free radical polymerization of NIPAM monomers using small-molecular chemical cross linkers such as N,N^1-methylene-bis-acrylamide (MBA) exhibit very slow responding property towards external stimuli. Therefore, intensive efforts have been made to improve the response rate of PNIPAM-based hydrogels. Up to now, three main kinds of strategies have been developed to improve the response rate of PNIPAM-based hydrogels, i.e., (1) reducing the dimension of hydrogels, (2) generating porous structures in the NIPAM hydrogel network, and (3) chemically modifying the polymeric networks of NIPAM hydrogels. Among these three methods, chemical modification of the hydrogel networks plays an important role in the improvement of the response rate. Generally these method involve the introduction of hydrophilic groups in the hydrogel network.

Incorporation of magnetic nanoparticles into these temperature responsive hydrogel produces hydrogel magnetic nanocomposites. These magnetic sensitive hydrogels have been explored for the hyperthermia treatment of cancer, which consists of raising the temperature of tumor-loaded tissue to 40–43 °C by means of an alternating magnetic field. For hyperthermia, super paramagnetic and ferromagnetic iron oxides have been explored

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extensively [8]. The encapsulation of these particles in a polymer matrix protects the biological tissue from contact with the inorganic particles, and the resulting ferrogel presents the properties of both the polymeric matrix and the magnetic nanoparticles [9–11].

2-Acrylamido-2-methyl-1-propanesulfonic acid [AMPS] can be used as a reactor to produce magnetic iron oxide nanoparticles. AMPS have received attention in recent years due to its strongly ionizable sulfonic acid group [12–14]. Increasing the number of ionic groups in the hydrogels causes increase in the swelling capacity of the corresponding hydrogel. AMPS dissociate completely in all pH range, and therefore, the hydrogels derived from AMPS also exhibit pH-independent swelling behavior.

The object of the work described in the present paper was to synthesize poly[NIPAM–AMPS] based magnetic superabsorbent hydrogels (smart hydrogels) for hyperthermia applications as well as for removing toxic metals from industrial waste water. From technological viewpoint, the smart hydrogels developed in this work could also replace the conventional hydrogels due to the simplicity of their synthesis. Further, these samples have fast response to external stimuli such as magnetic field and temperature. The smart hydrogel nanocomposites were characterized by Fourier-Transform Infrared (FT-IR) Spectrophotometry, X-ray diffraction (XRD), Scanning Electronic Microscopy (SEM), and Transmission Electron Microscopy (TEM). The amount of magnetic nanoparticles incorporated into the gel network was determined by Thermo Gravimetric Analysis (TGA). The magnetic properties of these nanocomposites were evaluated by Vibrating Sample Magnetometer. Finally the prepared nanocomposites were subjected to swelling, metal absorption and hyperthermia studies.

2. Experimental

2.1. Materials

N-isopropylacrylamide (NIPAM), N,N-methylenebisacrylamide (MBA), N,N,N^1,N^1-tetramethylethylenediamine (TMEDA), ammonium persulfate (APS) were purchased from Aldrich Chemical Company Inc. (Milwaukee, WI, USA). 2-acrylamido-2-methyl-1-propanesulfonic acid (AMPS), Iron (II) chloride tetrahydrate (99+%) ($FeCl_2 \cdot 4H_2O$) and Iron (III) chloride hexahydrate (99+%) ($FeCl_3 \cdot 6H_2O$) were purchased from Merck (Mumbai, India). Ammonium hydroxide (28% ammonia in water) (99.99%) was purchased from S.D. Fine (Mumbai, India). All the chemicals were used without further purification. Double-distilled water was used for the preparation of all solutions in this study.

2.2. Preparation of gels

Poly (N-isopropylacrylamide)/acrylamido propane sulfonic acid (NIPAM–AMPS) hydrogels were synthesized by employing free radical polymerization using N,N-methylenebisacrylamide (MBA) as a cross-linker and ammonium persulfate/N,N,N^1,N^1-tetramethylethylenediamine (APS/TMEDA) as redox-initiating pair following the usual procedure [15]. In detail, poly[NIPAM–AMPS] hydrogels were prepared by first mixing NIPAM (1 g) with different amounts (0.1, 0.2, 0.3 and 0.4 g) of AMPS in 3 mL of water. In order to finalize an optimized hydrogel for metal and hyperthermia studies, a series of poly[NIPAM–AMPS] hydrogels were synthesized by using NIPAM = 1 g and varying AMPS concentration from 0.2412 to 1.4475 mM. The transparent hydrogels were removed, washed with double distilled water. Table 1 describes the various components used to prepare poly[NIPAM–AMPS] hydrogels.

Table 1
The feed compositions of the hydrogels.

Hydrogel code	Concentration in the feed mixture of the hydrogel net works				
	NIPAM mM	AMPS mM	MBA mM	APS mM	TMEDA mM
NI	8.837	–	0.648	2.191	0.172
NIAM-1	8.837	0.2412	0.648	2.191	0.172
NIAM-2	8.837	0.4825	0.648	2.191	0.172
NIAM-3	8.837	0.9650	0.648	2.191	0.172
NIAM-4	8.837	1.4475	0.648	2.191	0.172

2.3. Preparation of NIPAM–AMPS hydrogel magnetite nanocomposites [HGMNCs]

To prepare hydrogel magnetite nanocomposites, poly[NIPAM–AMPS] hydrogel (Section 2.2) samples were individually placed in 50 mL of double distilled water and allowed to swell completely over a period of 1 day (24 h). The swollen hydrogel was then transferred to another beaker containing 200 mL of aqueous solution consisting of 2.1 g of iron (II) chloride tetrahydrate and 5.8 g of iron (III) chloride hexahydrate and allowed for 24 h to entrap the iron salts throughout the hydrogel networks. Then the hydrogel loaded with iron (II) and iron (III) ions was removed from the iron salt solutions, washed with double distilled water and placed in a 50 mL of 0.5 M ammonium hydroxide (28% NH_3 in water) and left overnight. The resultant black color hydrogel magnetic nanocomposites [HMNC] were removed, washed with double distilled water, and allowed to dry in an oven (GUNA, Chennai, India) at 60 °C.

2.4. Swelling studies

Completely dried poly[NIPAM–AMPS] hydrogels and poly[NIPAM–AMPS] hydrogel magnetic nanocomposites (~50 mg) were equilibrated in distilled water at 30 °C for 3 days. The equilibrium swelling capacity or swelling ratio (Q) of poly[NIPAM–AMPS] hydrogel and poly[NIPAM–AMPS] hydrogel nanocomposites was calculated following the equation:

$$Q = We/Wd \tag{1}$$

where We is the weight of water in the swollen gel at equilibrium and Wd is the dry weight of the dried gel.

2.5. Characterization

2.5.1. FTIR spectroscopy

FTIR spectroscopy was performed for the NI hydrogel, NIAM 4 hydrogel, and NIAM 4-Fe_3O_4 hydrogel. The corresponding spectrums were recorded on a Thermo Nicolet Nexus 670 spectrophotometer (Washington, USA).

2.5.2. X-ray diffraction

The X-ray diffraction studies of the NI hydrogel, NIAM 4, and NIAM 4-Fe_3O_4 were carried out using a Rikagu diffractometer (Rikagu, Tokyo, Japan) employing rotting anode mode Ru-H3R (Cu radiation, k=0.1546 nm) running at 40 kV and 40 mA.

2.5.3. Thermo gravimetric analysis (TGA)

TGA measurements were made to determine the actual iron oxide nanoparticle content in the hydrogel nanocomposites using a SDT Q 600 TGA instrument (T.A. Instruments-water LLC, Newcastle, DE 19720, USA), at a heating rate of 10 °C/min under a constant nitrogen flow (100 mL/min). The samples were run from