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Preparation of Poly Acrylic Acid Acrylamide Nanometer Material and its Drug Delivery Control Potential in Alkaline Condition

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Abstract. In order to explore a smart carrier which can control drug delivery in special pH environment, a type of nanometer material, namely, poly acrylic acid acrylamide (P(AA-AM)) was synthesized with acrylic acid and acrylamide as monomers. Its structure was determined using Fourier transform infrared spectroscopy (FTIR) and its swelling properties were tested by measuring its weight evolution. The drug delivery control potential was estimated by monitoring its swelling performances in the solutions of different pH values. The cycle characteristics were also investigated to determine its degradation properties in the environment. The results indicate that the synthesized material is sensitive to pH and is suitable for controlling drug delivery at the pH range from 10 to11 and below 7. Furthermore, this material can be automatic decomposition in the environment so that it is a degradable green material without causing burden to the environment.

Introduction

With the development of science and technology, various kinds of biological and chemical agents have been explored, such as medicine, pesticide, chemical fertilizer. These materials play an important role in the development of modern industry which greatly improved the life quality of people. Meantime, the use of chemical materials also brings many environmental problems, such as drug residue and water pollution, which poses a threat to the stability of the human health and ecological environment. At the same time, it is reported that chemical products lost or waste is very common in their usage process. Therefore, it is necessary to develop drug delivery control techniques. The concept of drug delivery has greatly evolved over the years from immediate-release oral dosage forms to targeted-release drug delivery systems and nowadays conventional fabrication methods used to produce immediate-release systems progressively evolved towards multi-step manufacturing technologies, including granulation, extrusion or coating processes, to allow the development of controlled-release systems [1].Among which, the development of new smart carriers seems to be mandatory to reach the goal of control the drug delivery in special condition [2-4]. In many cases, only when the drug releases in a certain pH environment, it can work. For example, medication used for small intestine can exert the best effect only if it is in the condition with the pH higher than 7.In concrete, the corrosion rate of steel rebar is very low due to the existence of rebar passive film, and the effect of corrosion inhibitor is very limited at pH values greater than 11, however, if the corrosion inhibitor is applied just when the corrosion of steel rebar corrosion start at pH lower than 11, the damage of the passivation membrane can be maximally repaired and the corrosion of steel rebar can be significantly reduced [5].This can be achieved by using a pH sensitive material as the carrier of corrosion inhibitor. Among the smart control materials, nanometer particle produced by hydrogel is an excellent choice. Investigations by our team have indicated that hydrogel of poly acrylic acid derivate has pH sensitivity and are potential inhibitor carriers[6]. However, their large volume limits the application in concrete. In the work described in this paper, a polymer using acrylic acid and acrylamide as monomers was synthesized and milled to nanometer size. FTIR was conducted to determine the structure of these nanometer particles, their swelling kinetics as well as pH sensitivity were studied to evaluate their potential to be the smart carrier of drugs delivery in alkaline environment, such as corrosion inhibitor for rebar in concrete.

Experimental

Preparation of nanometer poly acrylic acid and acrylamide (P(AA-AM)) particles. The acrylic acid and acrylamide monomers with the mole ratio of 2:3 were dissolved in anhydrous ethanol. Then distilled water, crosslinking agent, namely, N, N '- methylene bisacrylamide and the initiator $NaHSO_3$and $(NH_4)_2S_2O_8$ were added into the reactor, mixed uniformly and sealed in the reactor for 24h in an water bath with the temperature of 25 ℃.The prepared polymer was taken out of the reactor and washed 3 times with distilled water to remove un-reacted, crosslinking agent and initiator, then it was placed in a drying oven with the temperature of 50 ℃to constant weight. Finally, the polymer was milled to particles of nanometer size using high speed lapping machine.

Solution preparation

The buffer solutions with the pH values from 3 to 8 were prepared by 0.2mol/L dipotassium hydrogen phosphate solution and 0.1 mol/L sodium citrate solution, and the one with the pH value from 9 to 11 were prepared using0.1mol/L sodium bicarbonate and 0.1mol/L sodium carbonate. Saturated calcium hydroxide solution was used to be the solution of pH 12.6.The solution with the pH value of 1 was prepared by diluting concentrated hydrochloric acid while the solution with the pH value of 13 was prepared using 0.1mol/L sodium hydroxide. All the pH values of the solutions were determined using PHS-25 digital pH meter accurately and all the agents used are AR degree.

Equilibrium swelling ratio determination. The equilibrium swelling properties could be determined by weight method. After immersion in the buffer solutions of different pH for a certain time, P(AA-AM) samples were taken out of the solutions and the moisture on their surfaces were removed with filter paper. In this case, the wet weight could be obtained by weighing the sample and noted M1.Then the sample was put into the drying oven to constant weight at 50 ℃,and the dry weight could obtained, namely, M2. Then according to the equation ESR= (M1-M2) /M2×100(%), the equilibrium swelling properties could be measured.

Fourier transforms infrared (FTIR) spectra analysis. After prepared the ample with the dry nanometer particles produced according to 2.1 and potassium bromide, FTIR spectra (Nicolet 560) were collected between 400 and 4000 cm^{-1}.

Results and discussion

FTIR analysis

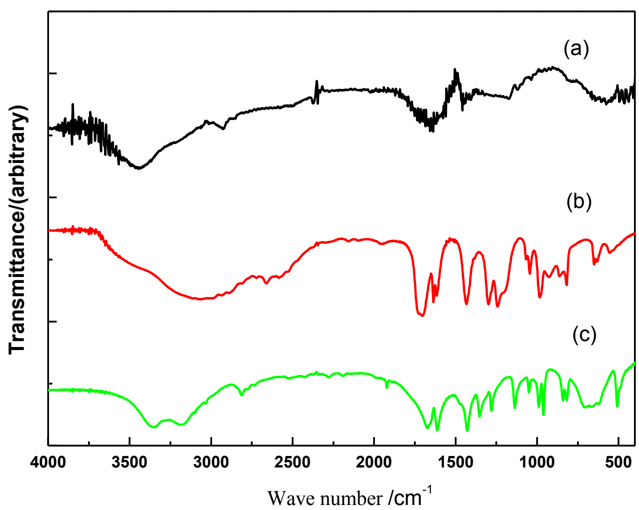

Fig. 1 FTIR spectra of P(AA-AM)nanometer particles(a), acrylic acid(b)and acrylamide(c).

In order to characterizethe strcuture of the nanometer materials, FTIR was conducted using potassium bromide method. For comparison purpose, the FTIR performances of the monomers were also included.Fig.1 displays the FTIRspectra of P(AA-AM) particles as well as acrylic acid and acrylamide.It is noteble that significant differrences can be observed between the polymer and the moners.Compared to the FTIR spectra of the monors, some peaks have disappered in the spectrum of the poly nanometer material. In the band of acrylic acidand acrylamide, the peak assigned to the vibrations of H in C=C–H at about 980cm^{-1}is very clear,but it disappered in the spectrum of the poly nano material;meanwhile, the peak indicated theC–C (1170 cm^{-1})become obvious in the band of nanometer material,which suggested polymerization reaction has occured to the monors and a polyer has obtained[7].Similarly, the peak assined to the vibrations of H in CH_2=CH–COOR at 3030 cm^{-1} disapperared but the dsorption peak of C–H in methylene group is visible in 2930cm^{-1}[8]. It is also notebale that a large blunt peak appeared In the band of the polymer in the rang between 1480 and 1850 cm^{-1} which should be peaks induced by C=O(1710 cm^{-1}), N–H(1650cm^{-1}), C–O(1680cm^{-1}),C–C(1620cm^{-1}),O=C–O(1560 cm^{-1})overlapped in the polyer, with significant signs of the monor structure,which indicate the aim material had been synthesized[7,8].

pH sensitivity tests.

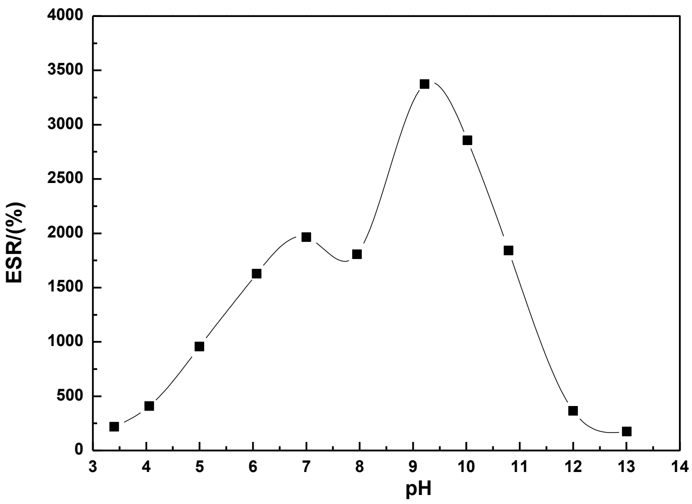

Fig.2 ESR of P(AA-AM) in solutions with different pH values

Fig.2 shows the ESR evolution of P(AA-AM) with pH. It is clear that P(AA-AM) is sensitive to pH variation in alkaline environment. At pH range from 8 to 10, the ESR of P(AA-AM) increases with the increasing pH value which is ascribed to that the dissociation degree of –COOH groups are increased with increasing pH value, and cause the negative charges increasing in the polymer chain, thus, its volume increases due to the electrostatic repulsion[9]. However, when the pH value is higher than 10, all the–COOH groups have been dissociated, meanwhile, the cations gathered in the negative polymer chain increase due to the Coulomb effect and the electrostatic repulsion of the polymer chain is weakened, leading to the decrease of ESR. Similar effect also occurs in the acid solution, however, in this case, the ESR evolution is related to the dissociation degree of $–NH_2$ groups. The pH sensitive properties of P(AA-AM) entitle it to be an excellent carrier material for inhibitor delivery control. If it is used as rebar inhibitor carrier, the rebar inhibitors can be released just when the pH value of the concrete decreases to 11 and the inhibition effect of rebar inhibitor can be maximized. It should be noticed that this material can also be used to control drug delivery at the pH range lower than 7 where the pH value of the environment is much lower 7 before the drug is released.

Swelling kinetics investigation. Fig.3 depicted the swelling evolution performance of the nanometer material with time in the buffer solution of pH = 10.It is visible that the nanometer material can reach equilibrium in about 24hour and the value of ESR is very high. This should be ascribed to that the material has large network-like cross linking structure with many hydrophilic groups, which is conducive to water molecules and enable them to diffusion to the internal network, resulting in the fast swelling response of the polymer. The short time before equilibrium and high value of ESR indicates the material can be used as an excellent drug delivery carrier, which can load quite a lot of medicines in a short time by just simple immersion method.

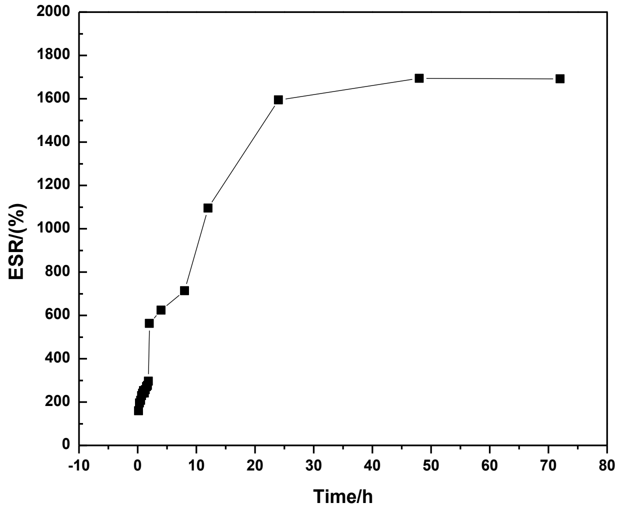

Fig.3 Swelling kinetics curve of the nanometer material with time in the buffer solution of pH = 10

Cycle performance determination.

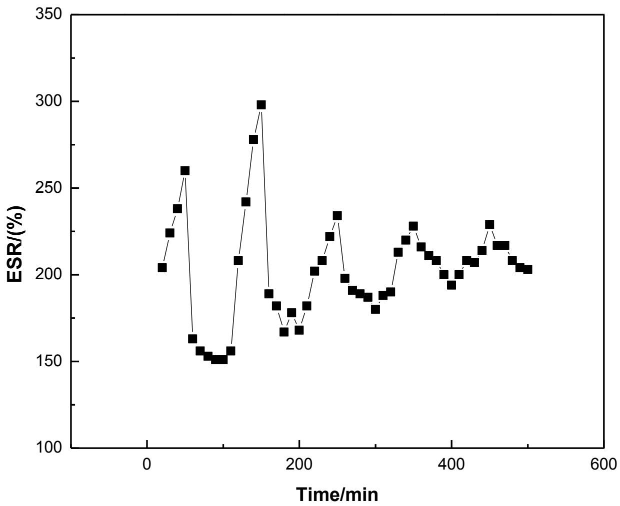

Fig.4 Dynamical change of P(AA-AM) in solutions of pH=1 and pH=13.

In order to test the degradable properties of P(AA-AM), cycle performance determination were conducted by measuring the weight of P(AA-AM) in the solutions of pH=1 and pH=13alternately. Firstly, P(AA-AM) was put in the 0.1 mol /L NaOH solution with the pH value of pH= 13and the weights of P(AA-AM) were measured each 10 min. 1hourlater, it was transferred to the hydrochloric acid solution of pH=1. These processes were repeated for 10 hour. Then the swelling dynamical evolution properties of P(AA-AM) could be obtained, as shown in Fig.4. It can be seen from Fig.4 that P(AA-AM) is shrinking in acidic medium and is swelling in alkaline environment. As analyzed previously, it is related to ionization of–COOH groups[9,10]. These results suggested that the pH response properties of the material prepared exhibit good reproducibility and its pH response activities can be reversible. However, it should be noticed that the floating degree become smaller as the immersion time increases, which is ascribed to that frequently dissociation of –COOH and $–NH_2$ groups leads to much water adsorbed on the material and reduces its bond strength. As a result, the material become easy to decomposition and can be degradable in the environment. Thus, the utility of such material will not cause additional burden to the environment and it is a green material.

Summary

A pH sensitive smart material was prepared using acrylic acid and acrylate as monomers. The synthesized material is suitable for controlling drug release in the systems that dug delivery is in the range from10 to11or below 7. The material is potential to be an intelligent drug delivery controller which can carry a large amount of drugs in a short time and can control release them in the designed condition identified by pH. This material is degradable in its service environment which indicate it is totally a green material.

Acknowledegments

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