Middle-East Journal of Scientific Research 12 (3): 392-396, 2012
ISSN 1990-9233

DOI: 10.5829/idosi.mejsr.2012.12.3.1062

Antibiotic Release Process from Hydrogel Nano Zeolite Composites

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Abstract: In this study, a composite made of nano zeolite and hydrogel with some biodegradable polymers (polyethylene glycol, poly acrylic acid and polyacrylamid) was prepared and its controlled drug release was tested in phosphate buffer solution (with pH =7.8) and at temperature of 37°C which is similar to the human blood situation. The drug release rate over time was measured with UV spectrophotometer. Various percentages of nano zeolite were used and their effects on the controlled drug release were considered. A sample containing 3 wt.% zeolite had lowest rate of drug release. Distribution of particles in the polymer matrixes was studied by scanning electron microscopy (SEM) and their characteristics were identified by X-ray diffraction. The temperature and pH effects on the controlled drug release from hydrogel nano zeolite were investigated.

Key words: Controlled release · Antibiotics · Hydrogel · Nano zeolite · Tissue

INTRODUCTION

There are several researches on the drug release process since 1930 [1, 2]. For the first time, estrogen was compressed into a tablet, placed under the skin and its release was studied. The release of loaded hormones was studied in 1950 [3].

Figure 1 is according to the drug conventional usage. As shown in this figure, drug concentration firstly increases and then suddenly decreases in plasma [1] while a uniform drug concentration is observed for the controlled release.

It can also be demonstrated that the drug uniform concentration is obtained drug patient recovery when the drug delivery system is applied. Another benefit for patients is this they no need to remember that they should take their drugs over time [4-7].

This paper aims to develop biodegradable polymer nano zeolite polymer composite systems for controlled release drug delivery [8]. Care and maintenance of bone tissue or body after exposure is important. It is necessary to have good body cells to stick to it and influence its growth [9-12]. For this purpose, the biodegradable polymeric hydrogel nano zeolite composite with the antibiotics release can be coated on bone to protect it [13]. The biodegradable polymeric hydrogel nano zeolite composite is prepared by combining the various components with specific release profiles [14]. Antibiotics are directly loaded into the system and the controlled release is applied over time. It maintains bone tissue from inflammation [15-17].

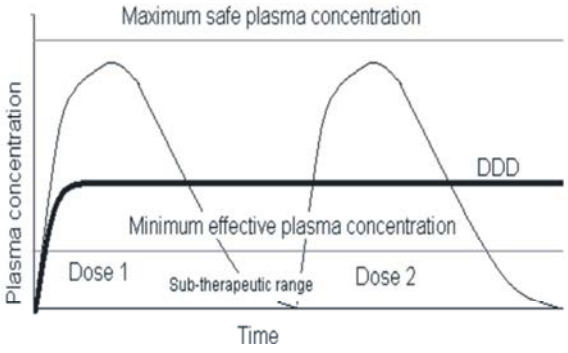

Fig. 1: Drug concentration in plasma for the drug conventional usage and for the drug controlled release (DDD) [1]

The controlled drug release system in body supplies medicine cycle without a serious harm to the liver. Further, lower amounts of drug will be required in this method [18]. Since some medicines affect the special locations of body, local drug delivery system is preferred while medicine gulp will affect the whole of body [19].

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Harrison *et al.* studied the controlled drug release in some patients who had cancer [20].

MATERIALS AND METHODS

Materials: Polyethylene glycol [(PEG), HO (C_2H_4O) NH, M_w=1000 g.gmol^{-1}], Acrylamide ($C_2H_3CONH_2$), Acrylic acid (CH_2CHCO_2H), Ammonium persulphate [(APS) as the initiator, *N*,*N*,*N*,*N*-tetra-methylethylendiamin [(TEMED) as the accelerator] were purchased from Merck company. N,N'-methylene bisacryamide as the cross-linker was supplied by Sigma Aldrich. Nano zeolite A as the dispersed phase in the polymer matrix was used. Phosphate buffer saline [(PBS) with pH=7.8 containing NaCl 0.138 M, KCl 0.0027 M and phosphate buffer saline 0.01 M)] was purchased from Merck company and used in vitro release study.

Nano Composite Hydrogel Preparation: 2 g PEG, 1.42 g Acrylamide and 0.23 g N,N'-methylene bisacryamide were dissolved in 20 cm^3 of twice distilled water and mixed for 1 h at ambient temperature. 6 cm^3 Acrylic acid was then added to the solution and mixed again for 1 h. 0.013 g of Amoxicillin as a drug was loaded to the solution and was stirred. Then nano zeolite was added and mixed again for 2 h. The slurry solution was poured into a 250 cm^3 flask equipped with a stirrer and a nitrogen line to purge atmospheric oxygen (for preventing APS oxidation). The initiator APS and TEMED as the accelerator were added. The obtained hydrogel must be kept about 24 h to complete the polymerization reaction [19]. Then the products were removed from the flask and cut to small pieces and dried to reach a constant weight.

Drug Release Process: Dry gel was allowed to swell in the Phosphate buffer saline solution (with pH=7.8 which is very similar to the blood pH). The amounts of the drug release were measured by a UV-spectrophotometer (Perkin Elmer, Model: Lambda15, USA) at various temperatures.

RESULTS AND DISCUSSION

Figure 2 shows the effect of nano zeolite percentage enhancement in the composite on antibiotic release. As shown in this figure, the drug release is in the lowest amounts when nano zeolite percentage is 3 wt.%. The drug release slightly increases when nano zeolite percentage is 4 wt.%.

Table 1: Percentages of drug release from hydrogel nano composites for various amounts of nano zeolite

Wt% of nano zeolite	1	2	3	4
Drug release%	27	26	25	27

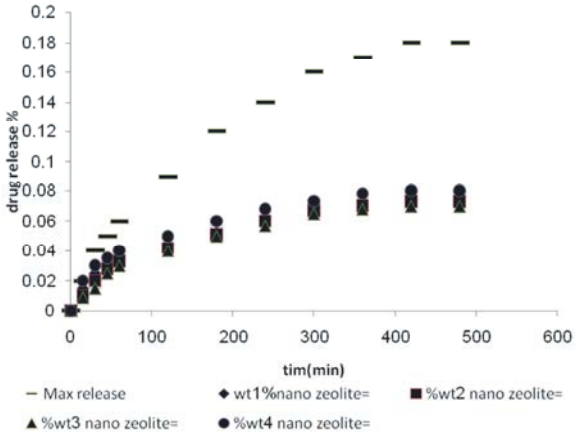

Fig. 2: Effect of nano zeolite enhancement on the controlled drug release from nano composite hydrogel

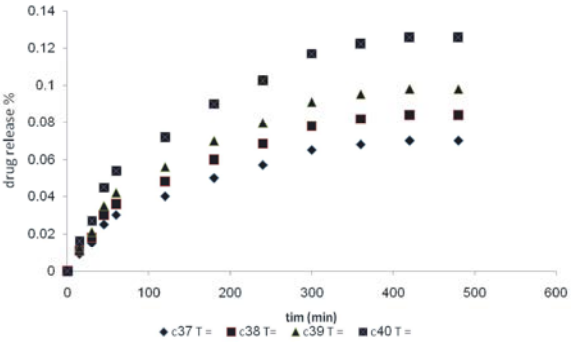

Fig. 3: Effect of temperature on drug release from hydrogel nano zeolite composite

This is due to aggregation of nano zeolite particles. Nano zeolite percentage enhancement increases the nano composite strength and it reduces the drug release. Table 1 also illustrates that the minimum drug release (25%) is in nano zeolite of 3 wt.%.

Figure 3 shows the drug release from the network versus time at various temperatures. A sample with 3 wt.% nano zeolite which had more controlled release was chosen. As shown in this figure, the drug release increased with increasing temperature. Its reason is due existing poly AAm and poly AAc which are heat sensitive polymers [19-20].

Figure 4 shows the effect of pH enhancement on the drug release from the nano zeolite. In fact, electrostatic repulsion and osmotic pressure differences

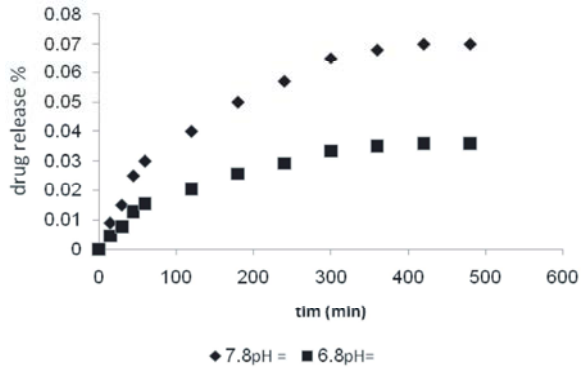

Fig. 4: Effect of pH on drug release from hydrogel nano zeolite

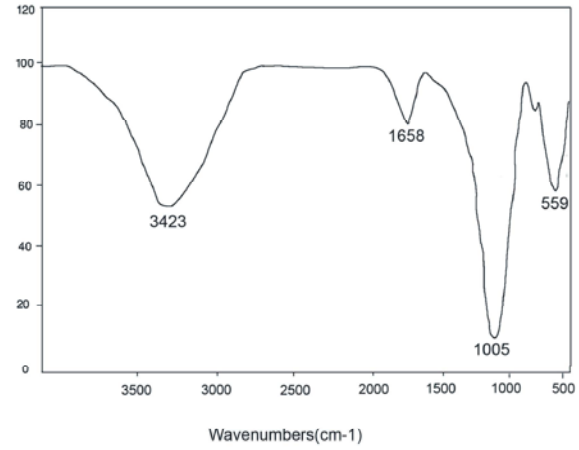

Fig. 5: FTIR for nano zeolite A

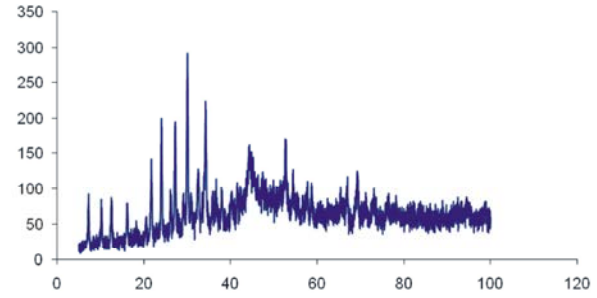

Fig. 6: XRD spectra for pure nano zeolite A

caused the swelling of the nano composite and water infiltration into it. The environment pH enhancement increases its basic property. Therefore, carboxylic ions accumulation inside the network increases water discharge from it (due to weakening hydrogen bonds between water molecules and carboxylic groups) and the nano composite shrinks.

Figure 5 shows FTIR spectra zeolite A. As shown in this figure, there are three peaks at wavelengths of 467, 667 and 1005 cm^{-1} which belong to *Si*, *Al* and O_4 bendy vibrations, symmetric tensile vibrations of tetragonal external connections and asymmetric tensile vibrations of tetragonal internal connections, respectively. There are two peaks at wavelengths of 1658 and 3423 cm^{-1} which belong to water molecules inside the zeolite pores.

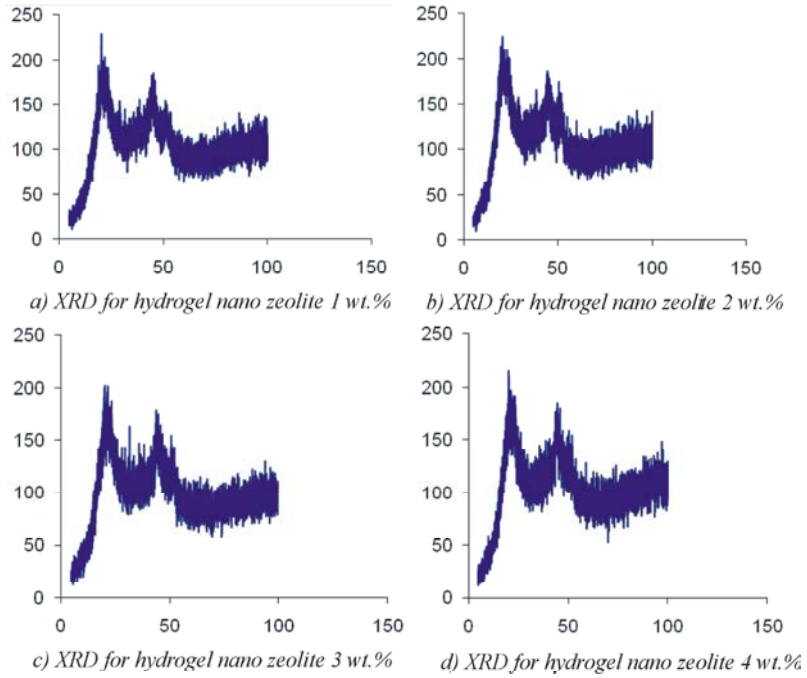

Fig. 7 (a-d): XRD for hydrogel and nano zeolite 1-4 wt.%

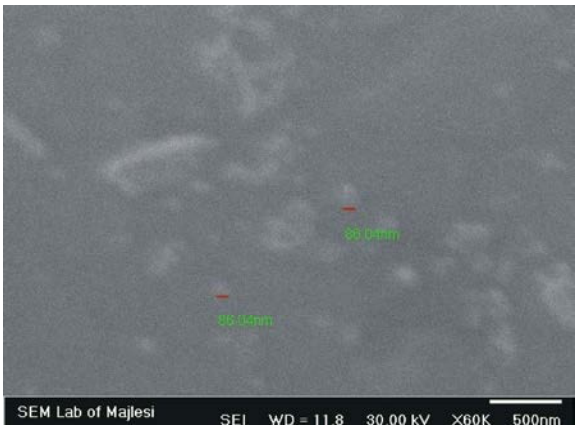

Fig. 8: SEM for hydrogel nano zeolite 1 wt.%

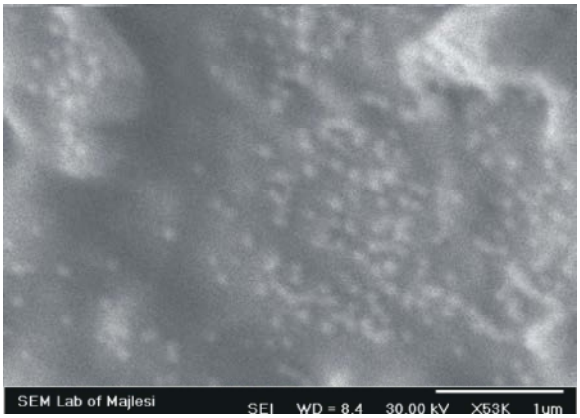

Fig. 9: SEM for hydrogel nano zeolite 3 wt.%

XRD analysis shows the sample crystalline structure. Figure 6 shows XRD spectra for pure nano zeolite A. The sharpest peak represents the nano zeolite crystalline structure, clearly.

Figures 7 (a-d) show XRD spectra for nano zeolite 1 to 4 wt.%. As shown in these figures, XRD spectra were quite different for the nano composite samples in comparison with the pure nano zeolite. This difference is due to interacting polymer with the zeolite matrix. The samples (a-d) have nano zeolite however their intensities are a bit different. These figures show that interactions between polymer and zeolite matrix do not change with increasing the zeolite percentage. Furthermore, XRD spectra indicate that the polymer chains penetrate the empty spaces of nano zeolite and fill them. Therefore, an appropriate and expected interaction is obtained.

Figure 8 shows Scanning Electron Microscopy (SEM) for hydrogel nano zeolite 1 wt.% which had the highest drug release (the worst sample). The bright points show the nano zeolite particles marked with their sizes. The dark area shows the polymer matrix, as well.

Figure 9 shows SEM for hydrogel nano zeolite 3 wt.% which had the lowest drug release (the best sample which has controlled drug release). The bright points indicate nano zeolites dispersed in the polymer matrix.

CONCLUSIONS

In this study, biodegradable polymeric hydrogels based on PEG, poly acrylamide and poly acrylic acid were prepared and studied. The controlled release was considered on antibiotics loaded in nano zeolites. It was concluded that 3 wt.% nano zeolite had the minimum and more controlled drug release in admissible ranges of pH and temperature of body.

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