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Preparation of a New Magnetic Drug Carrier Based on Poly(vinyl alcohol): Synthesis, Characterization, and Drug Release Studies

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Abstract: In this study, poly (vinyl alcohol) (PVA) as a biodegradable and biocompatible polymer was modified for use as drug delivery carrier. In the first step, PVA was modified by APTES and then underwent crosslinking using 1,2-dichloroethane. On the other hand, Fe_3O_4 magnetic nanoparticles (MNPs) were reacted with TEOS and modified with hexamethylene diisocyanate. The modified MNPs were reacted with the free hydroxyl groups of the crosslinked PVA to obtain the final magnetic carrier. A template drug was used in order to study the drug release ability of the prepared carrier. The carrier was also characterized using different analyses such as FT-IR, and VSM techniques.

Keywords: Polyvinyl alcohol-Magnetite nanoparticles-Controlled drug delivery system -Doxorubicin

Introduction

Hydrogels are three-dimensional networks of polymer configurations that canable absorb large amounts of water or biological fluids are. These compounds tend to absorb water due to the presence of hydrophilic groups such as -OH, -CONH‹, -COOH and -SO3H and ... the polymers that make up the structure of the hydrogel [1].

Hydrogels, especially those kinds which are used for drug delivery and bio-medical purposes, must have acceptable biocompatibility and biodegradability[2,3]. Drug delivery systems based on nanotechnology have led to reach significant improvements due to changing the drug pharmacokinetics, increasing the durability of the drug in bloodstream, reducing toxicity, and increasing the half-life of the drug. These outstanding properties are achieved from the targeted delivery of the drug; in which the magnetic nanoparticles as drug carriers play efficient role in this field of research due to their exclusive characteristics[4]. It should also be noted that the performance of magnetic nanoparticles varies with different coatings. Generally, the toxicity of coated nanoparticles are lower than that of uncoated ones; but the type of the coating layer is also determinative on the rate of the toxicity [5].

At the first,polyvinylalcohol(PVA) functionalized in reaction with 3-aminopropyltriethoxysilane (APTES)And then reacted with 1 and 2 dicholoroethane and crosslinked.in the next step, Magnetite nanoparticles (MNPs)in reaction with tetraethyl orthosilicate (TEOS) it has silane And then in reaction with hexamethylene diisocyanate it has modificated.Unreacted hydroxyl groups on the polyvinylalcohol(PVA) crosslinked,in the final step ,reaction with modified nanoparticles, The final carrier is then prepared for loading and releasing Doxorubicin. The following studies have been done loading and drug release.

Experimental

General

All the solvents, chemicals and reagents were purchased from Merck, Fluka and Aldrich. Concentration of the dye solutions were estimated using absorbance recorded on UV/VIS spectrophotometer model Agilent 8453 Diode Array, USA.

Modification of poly (vinyl alcohol) (PVA)

In the first step, PVA (0.5 g, full hydrolyzed) and 3-aminopropyltriethoxysilane (APTES) with the molar ratio of 1:1 toward hydroxyl groups were added into a 100 mL round-bottom flask equipped with magnetic stirrer and reflux condenser followed by adding NMP (40 mL). The contents were stirred for 48 hours at 120oC and the final product was precipitated in diethyl ether. After complete drying, the modified PVA underwent crosslinking in the presence of excess 1,2-dichloroethane in DMF at 100oC.

Synthesis of magnetite (Fe_3O_4) nanoparticles

In a 250 mL three-necked round-bottom flask equipped with magnetic stirrer, reflux condenser and a dropping funnel, $FeCl_3.6H_2O$ (5.838 g) and $FeCl_2.4H_2O$ (2.147 g) were added followed by adding 100 mL degassed distilled water. Then ammonia solution (25%, 10 mL) was added to the dropping funnel and the hotplate temperature rose up to 80^o C under inert atmosphere. After reaching to the mentioned temperature, the ammonia solution was added to the flask at once. The contents were stirred for more 45 minutes with vigorous stirring. The final product was separated with external magnet, washed with distilled water successively and dried at 50^o C. The nanoparticles were then coated with TEOS.

Modification of the magnetite nanoparticles

In a 50 mL round-bottom flask, magnetite nanoparticles (0.2 g) were added followed by adding dry DMF (20 mL) and hexamethylenediisocyanate (4 mL). Then one drop of diluted DBTDL catalyst was added to the flask and the contents were stirred at 80^{o} C for 4 hours under inert atmosphere. The final product was separated with external magnet, washed with dry ether and dried under inert atmosphere.

Synthesis of the modified PVA/Fe_3O_4

In a 100 mL round-bottom flask equipped with magnetic stirrer and reflux condenser, the coated nanoparticles (0.2 g) and the modified PVA (0.5 g) were added followed by adding DMF (40 mL). The contents were stirred for 72 hours at 80^{o} C under inert atmosphere. The product was separated with external magnet, washed with methanol and dried at room temperature.

Results and discussion

Finally, in the present study, the researcher synthesized and modified poly-vinyl alcohol (PVA), then, synthesized nanoparticles of iron oxide and modified them. The new compound is a biodegradable hydrogel which would be applicable to make convenience in drug delivery process, it would be used as a new drug carrier in cancer treatment.

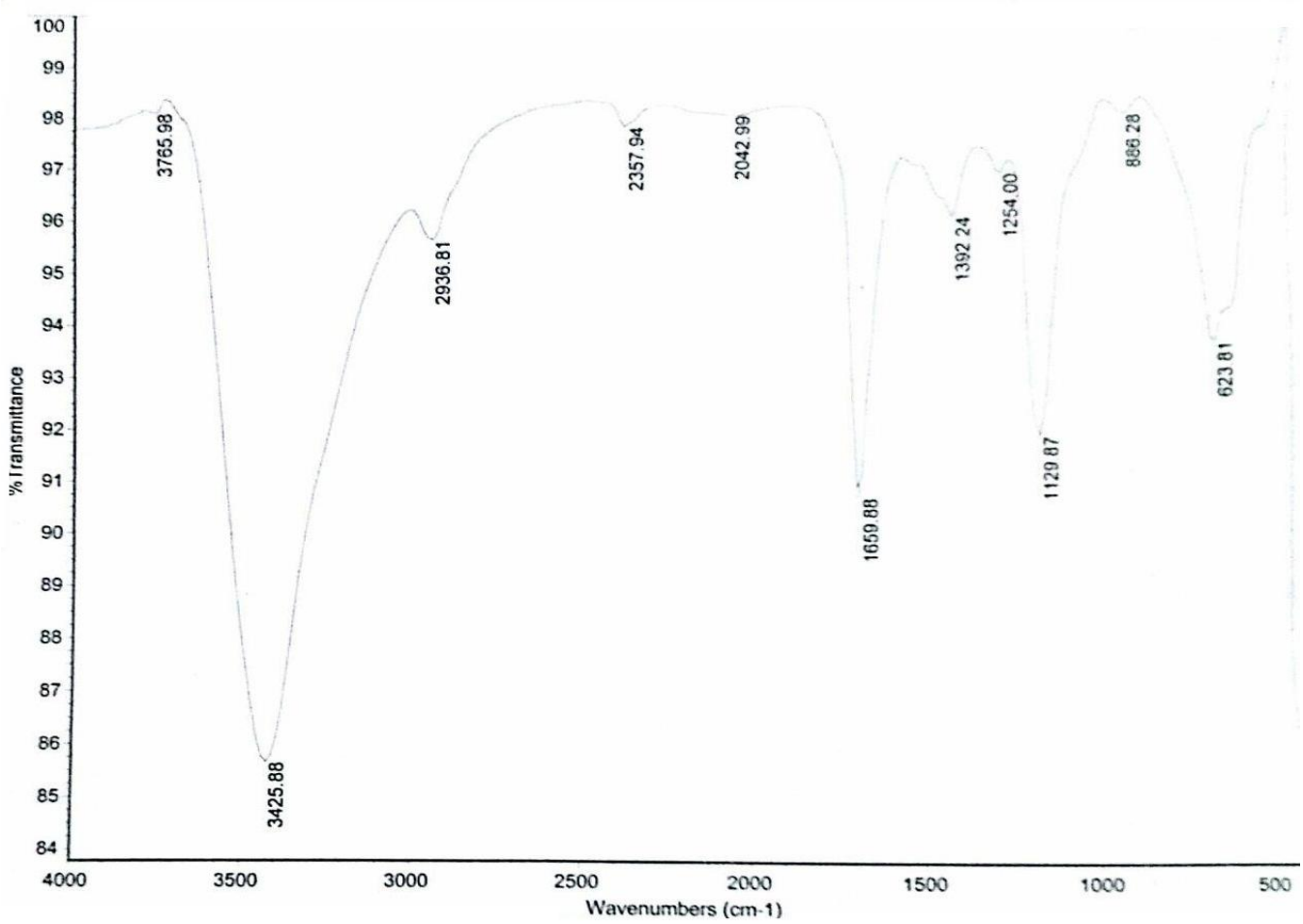

Fig. 1. FT-IR of modified PVA/Fe_3O_4

To study the characterization of modified PVA, Fourier-transform infrared spectroscopy (FT-IR) was used. Fig. 2.show the FT-IR spectra of modified PVA. The spectrum of modified PVA has a peak at 1658 cm−1 showed the Si-O banding. The N-H vibration showed a peak at 3425 cm^{-1}.

The magnetic property of the modified PVA/Fe_3O_4 was characterized using a vibrating sample magnetometer (VSM) at room temperature (Fig. 2). The magnetic property of the Fe3O4 is 50 emu g_1. The magnetic property of is modified PVA/Fe_3O_4 about 13 emu g_1. This dropping in the magnetic potential is due to the addition of modified PVA to the Fe_3O_4. The obtained modified PVA/Fe3O4 has a good magnetic potential and can be separated from the reaction medium easily by a magnet.

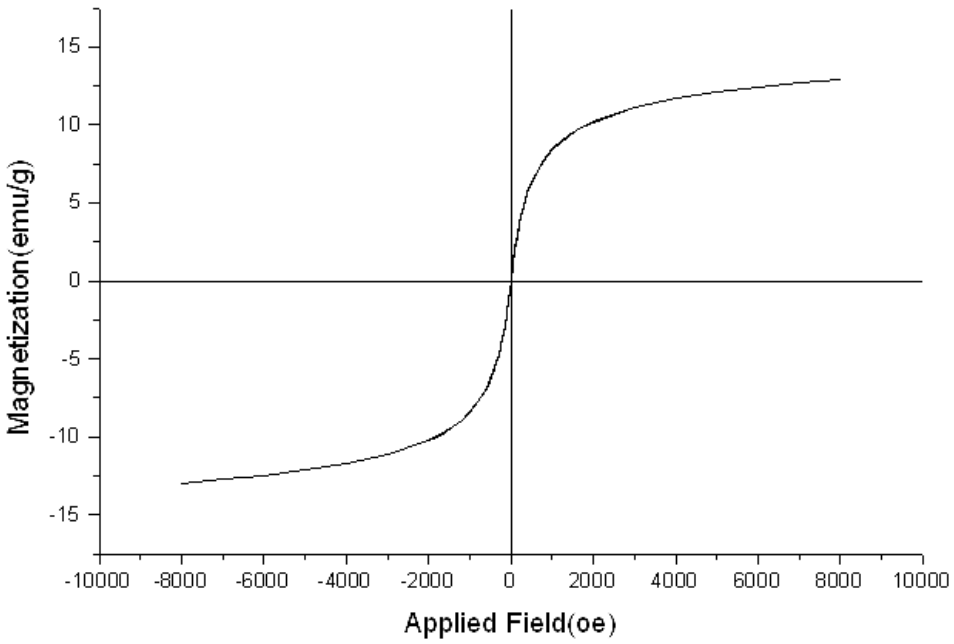

Fig. 2. VSM curve of modified PVA/Fe_3O_4

To study the Doxorubicin in vitro release process, 20 mg of the loaded polymer was introduced into a dialysis tube and immersed in a vial containing 50 ml of pH=7.41 PBS solution at room temperature without stirring. At specific time intervals, the supernatant was analyzed with UV-Vis. spectrophotometer at 480 nm until reaching to a constant absorption value (Fig.3).

As can be seen in the release profiles, the hydrogels show sudden drug release at the early stages, due to the rapid diffusion of the surface-adhered drug. By passing of time, the adsorbed drug from the inner layers of the hydrogels releases with a rather slower rate. Besides, the released drug reached to its maximum amount after about 90 hours. Moreover, as shown in the profiles, the magnetic hydrogel which was crosslinked with 1,2-dichloroethane, has a more controlled release, which is attributed to its more suitable interactions and more compatible cavities toward the drug.

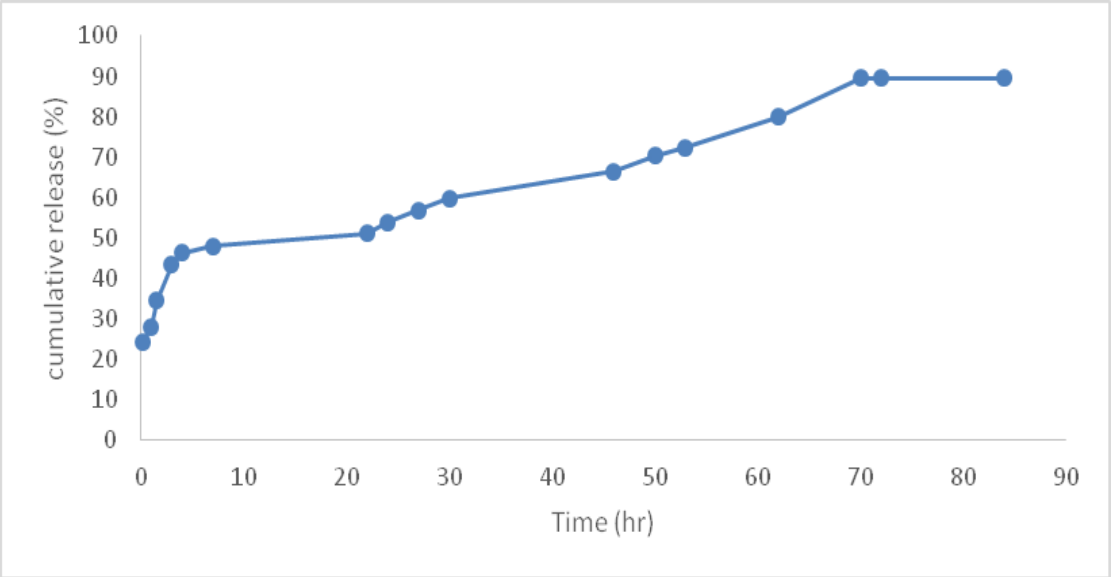

Fig. 3. Releasing the drug from the surface of the hydrogel

Conclusions

The aim of the present study was to investigate the swelling and drug release behaviour of cross-linked New Magnetic Drug Carrier Based on Poly(vinyl alcohol) hydrogel. The structural characterization as well as the kinetics of swelling and drug release were studied as a function of PVA content, cross-linking density, and drug loading percentage. It was found that drug release from swellable PVA hydrogel could be controlled by cross-linking density, PVA content and drug loading percentage. In such networks, drug delivery and also water transport followed mainly a Fackian or diffusion controlled model. In conclusion, by changing the structural parameters of this hydrogel, a rate-controlled drug release may be achieved. Even though most biomolecule- hydrogels still require further research, they are likely to become quite important biomaterials in the near future. Some Sci. of the studies described in this paper will surely lead, not only to a better understanding of the structures and functions of biomolecule-sensitive hydrogels, but also to promising strategies for the development of novel stimuli-sensitive hydrogels.

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