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Synthesis and Characterization of a Melamine-modified Hydrogel: The Study of Doxorubicin Slow Release

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Abstract: In the present study, a melamine-modified hydrogel was synthesized for use as Doxorubicin delivery carrier. In the first step, poly (acrylic acid-*co*-maleic anhydride) was synthesized via free radical polymerization. Then the prepared copolymer was crosslinked by melamine to obtain the final carrier. The swelling behavior of the carrier was carried out afterwards. Moreover, different analyses such as FT-IR, techniques was used to characterize the final polymer. In the final step, the Doxorubicin drug was loaded on the polymer and the slow-release study of the drug was investigated.

Keywords: Doxorubicin, Hydrogel, Copolymer, Drag delivery

Introduction

New drugs derived from cell mechanism deferent illness in other to purposive this drugs, modern drug delivery systems.it is derived that medical sciences will be extended by using drug delivery systems, this technology effect on drug sciences, increase efficiency of drug, in some instances new drug species have been created controlled release purposive are to effective categories in drug sciences which led to decrease beside effect of drugs and increase the biologic effect[1-4].

Targeting Drug Delivery Systems: the drug will be transferred into a desirable tissue in different ways in this systems. In general, tissues are desirable in pharm dynamic point of view, then the drug will affect the desirable site[5-8] .

Hydrogels, especially those kinds which are used for drug delivery and bio-medical purposes, must have acceptable biocompatibility and biodegradability[9] . 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[10] .

In this study, a melamine-modified hydrogel was synthesized for use as Doxorubicin delivery carrier. Poly (acrylic acid-co-maleic anhydride) was synthesized via free radical polymerization. Then the prepared copolymer was cross-linked by melamine to obtain the final carrier. The swelling behavior of the carrier was carried out afterwards. A template drug was used in order to study the drug release ability of the prepared carrier. Doxorubicin drug was loaded on the polymer and the slow-release study of the drug was investigated.

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.

Synthesis of melamine-modified poly (vinyl acetate –co- maleic anhydride) (PVA-MAa) hydrogel

In a 100 ml two-necked round-bottom flask equipped with magnetic stirrer ,reflux condenser and gas inert and autlet maleic anhydride(1 g,10 m mol) and dry THF(40 ml) were added followed by adding newly distilled acrylic acid(0/735 g,10 mmol).

The contents were degassed with argon using capillary for twenty minutes after that, AIBN (0/007, 0/04 mmol) was added to the flask and the contents were stirred for 8 hours at 70^0 C under inner atmosphere to complete the polymerization, reaction. After the mentioned time a solution of melamine (1/286) in hot water (40 ml) was added to the flask and let to be stirred for additional for 24 hours. The final product was filtered, washed several times with hot water and dried at 60^0 c.

Results and discussion

First, PVA-MAa was prepared as described in the materials and method section. To study the characterization of PVA-MAa, Fourier-transform infrared spectroscopy (FT-IR) was used (Fig. 1). In the spectrum of FT-IR, the broad stretching band at 2400-3400 $cm^{-1}$is related to hydroxyl group. Peaks at 3100 and 3500 cm^{-1} correspond to the stretching vibration of N–H of the primary amino group, The absorption peak at 1700-1730cm^{-1} is attributed to the stretching vibration of carbonyl group of carboxylic acid and the peak appeared at 1640-1670 cm^{-1} belong to the stretching vibration the carbonyl group of amide unit. The absorption peak at 1550-1640 cm^{-1} is assigned to the bending vibration of amide group and the peak appeared at 1210-1320 cm^{-1} correspond to the stretching vibration of C–O.

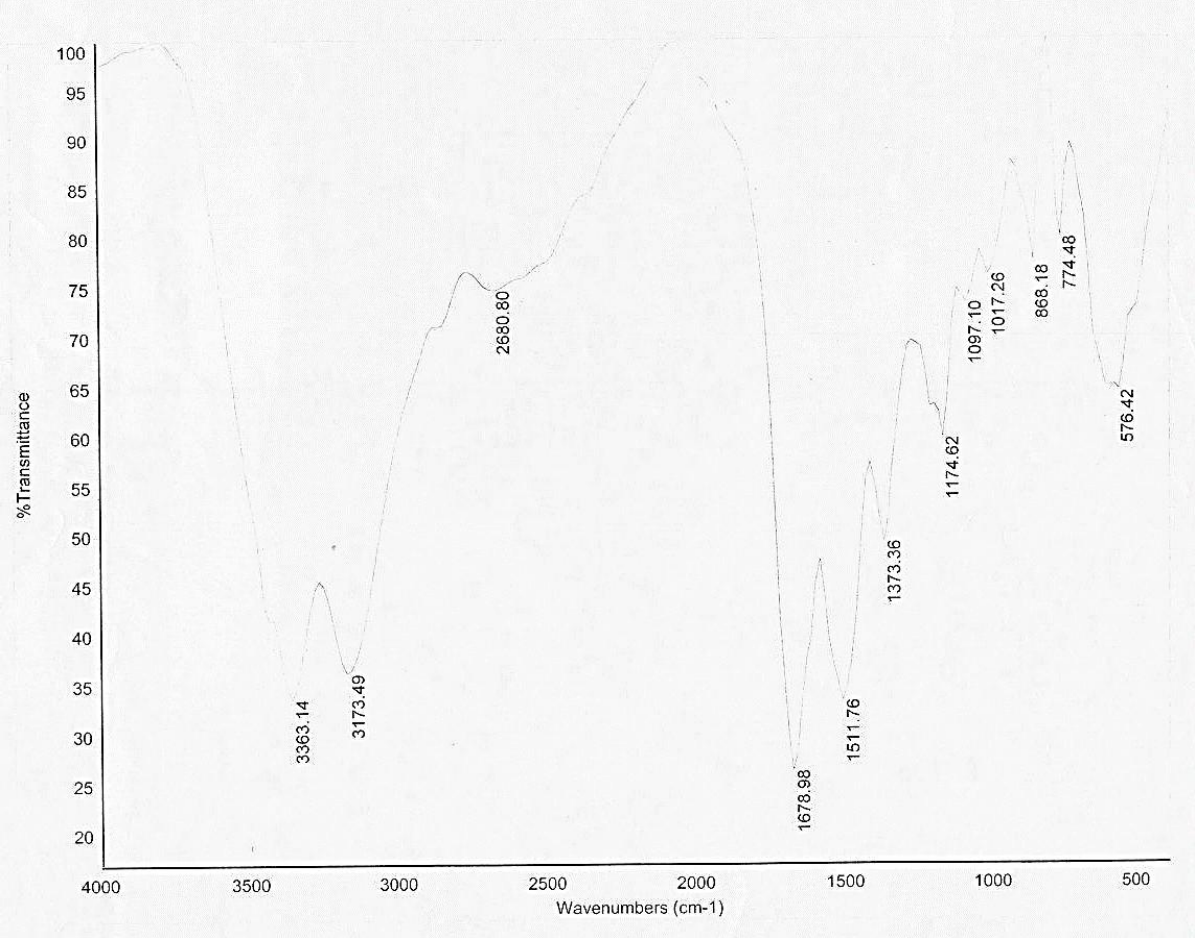

Fig. 1. FT-IR spectra of PVA-MAa

To study the Doxorubicin in vitro release process, 20 mg of the loaded PVA-MAa 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 analysed with UV-Vis. spectrophotometer at 480 nm until reaching to a constant absorption value (Fig.2).

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 120 hours. Moreover, as shown in the profiles, the hydrogel, has a more controlled release, which is attributed to its more suitable interactions and more compatible cavities toward the drug.

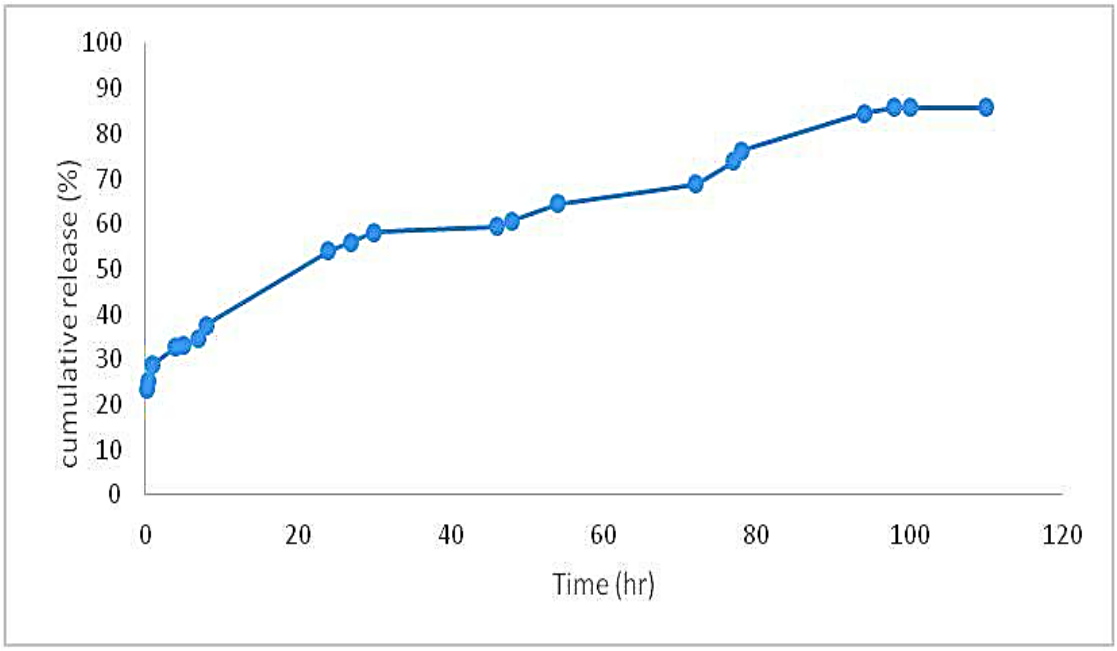

Fig. 2. Releasing the drug from the surface of the hydrogel

4. Conclusions

Finally, in the present study, the researcher synthesized and modified poly (acrylic acid-*co*-maleic anhydride), then, synthesized Synthesis of melamine-modified PAA-MAa and modified them was successful. In conclusion, by changing the structural parameters of this hydrogel, a rate-controlled drug release may be achieved. 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.

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