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Electrically controlled Aloin from poly(p-phenylene vinylene)/polyacrylamide hydrogel system

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Abstract *— The apparent diffusion coefficients, D_{app}, and the release mechanisms of Aloin-doped poly(phenylene vinylene)/polyacrylamide hydrogels, Aloin-doped PPV/PAAM, were investigated. In the absence of an electric field (passive release), the diffusion of Aloin from the SA-doped PPV/PAAM hydrogel is delayed in the first 3- 6 hr due to the ionic interaction between the anionic drug and PPV. Beyond this period, Aloin can diffuse continuously into the buffer solution through the PAAM matrix. D_{app} of Aloin-doped PPV/PAAM is higher than that of the Aloin-loaded PAAM, and the former increases with increasing electric field strength due to the combined mechanisms: the expansion of PPV chains inside the hydrogel; the reduction reaction under a negative potential driving the Aloin through the PAAM matrix, or iontophoresis; and the electroporation of the matrix pore. Thus, the presence of the conductive polymer and the applied electric field can be combined to control the drug release rate at an optimal desired level.*

Keywords— polyacrylamide hydrogels, Aloin-doped poly(phenylene vinlene), diffusion coefficients, electrically controlled drug release

1. INTRODUCTION

Conductive polymer is composed of conjugated polymer chain with π-electrons delocalized along the backbone contributing to electrical conductivity. Because of the special properties, it is used in a controlled drug delivery system [1]. Hydrogels, consisting of tri-dimensional structures formed by crosslinking hydrophilic polymeric chains, possess the ability to swell in solution in response to the chemical nature of the media, the pH, the ionic strength, the electric field, and temperature

Both, hydrogels and conductive polymers are suitable candidates in controlled drug release applications. Conductive polymer can fulfill two important requisites of the ideal drug release device: the possibility of switching on/off and the precise control of the release rate as functions of the applied potential. In typical drug delivery systems, hydrogels have played a importance role than the conducting polymers; but they often have slow responses, which limits the ability to deliver the stimuli efficiently throughout the gel.

Thus Poly (p-phenylene vinylene), or PPV, is selected as the conductive polymer because of its unique properties: non-linear optical properties, electroluminescence, and high electrical conductivity upon doping [1]. These characteristics are desirable properties for a new class of controlled release devices when subjecting them to an electric field.

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In this work, a combined conductive/hydrogel system was prepared as a controlled drug release devices. The physiochemical phenomena which are involved in the electrical controlled release of a drug-doped poly(p-phynylene vinylene)/polyacrylamide hydrogel system were studied.

2. METHODOLOGY

Materials

Aloin (AR grade, Fluka), was used as the model drug. Acrylamide, AAM (AR grade, Fluka, China), N,N′ methylenebisacrylamide, (N,N'-MBA) (AR grade, Fluka), tetramethylenediamine, TEMED (AR grade, Fisher Scientific), and ammonium peroxodisulfate (AR grade, Fluka) were used as the monomer, the crosslinker, the catalyst, and the initiator, respectively. Sodium acetate (AR grade, Ajax Chemicals) and glacial acetic acid (AR grade, Mallinckrodt Chemicals) were used without further purification. α,α'-dichloro-p-xylene and tetrahydrothiophene, THT (AR grade, Aldrich,), were used to synthesize poly(p-phenylene vinylene). Acetone and methanol (AR grade, Merck) were used as received.

Synthesis of Poly(p-phenylene vinylene)

The PPV was synthesized via a polyelectrolyte precursor according to the method of Burn et al. (1992) [2]. To a suspension of 10 g of α,α'-dichloro-p-xylene in 150 mL of methanol, added 15 mL of tetrahydrothiophene, THT. The resulting mixture was heated in a 50 °C oil bath overnight, and 250 mL of acetone was added in to precipitate the salt p-phenylene dimethylene bis tetramethylene sulfonium chloride. The mixture was stirred in an ice bath for 0.5 hr before filtration. The white solid salt obtained was washed with acetone and dried under vacuum at room temperature until two sequential weighings were the same. The yield was 85% [2]. Then 1.0 g of the washed and dried salt was dissolved in 7.5 cm^3 of methanol and then cooled to 0 °C, and was added to 6.3 cm^3 of aqueous sodium hydroxide (0.4M). After

duration of 120 min, 1 cm^3 of hydrochloric acid (0.4 M) was added to stop the reaction. The solution of 14.8 cm^3 was then dialyzed against a water-ethanol mixture (1:1, 3 x 1000 cm^3) for a period of three days. After cooling, the aqueous solution of poly [(p-phenylene) bis(tetrahydrothiophenechloride)] was poured onto a glass dish and allowed to evaporate at room temperature in a free air stream. After 24 hours, the yellowish-green precursor films were heated at 200 °C for 16 hr in a vacuum oven to yield PPV film. The obtained PPV film was ground by a jar mill for 2 days.

Preparation of Aloin-Doped Poly(p-phenylene vinylene)/Polyacrylamide Hydrogel (Aloin-doped PPV-loaded PAAM Hydrogel)

The Aloin-doped PPV/PAAM hydrogels were prepared by the free-radical polymerization of 2.32 g of acrylamide in an aqueous solution with 7.5 mg of Aloin-doped PPV, N, N′ MBA, and ammonium persulfate and TEMED, then was cast in a mold as previously described in the preparation of Aloin-loaded PAAM hydrogels.

Drug Release Studies

The diffusion through a pig skin was carried out in order to study the release characteristics of the drug from a Aloin-doped PPV/PAAM hydrogel. A pig skin was placed on top of the acetate buffer solution on a custom built modified Franz diffusion cell. The pig skin was allowed to come into equilibrium and in contact with the acetate buffer (pH 5.5) in the receptor chamber; the buffer was magnetically stirred throughout the experiment period (48 h) at a thermostatically maintained temperature (37 ± 2 °C). The Aloin-doped PPV/PAAM hydrogel with particular crosslinking ratios (mol $_{MBA}$: mol $_{AAM}$ = 0.002, 0.005, 0.016, or 0.024) were placed between the copper cathode and the net, which was mounted onto the receptor compartment. To study the effect of electric field strength on the release of the Aloin from the Aloin-doped PPV/PAAM hydrogels, the cathode electrode (copper electrode) was connected to a power supply, which provided various electrical voltages across the hydrogel, the nylon net, and the buffer solution. The anode electrode pin was positioned in the buffer solution. The amount of the drug in the withdrawn solution sample was determined using a UV spectrophotometer. The experiments were carried out in triplicate and the data were reported as average values.

3. RESULTS AND DISCUSSION

Aloin-Doped Poly(p-phenylene vinylene)/Polyacrylamide Hydrogel (Aloin-doped PPV-loaded PAAM Hydrogel)

Figure 1 shows FT-IR spectra of synthesized PPV, Aloin, and Aloin doped PPV. The synthesized PPV FTIR spectrum indicate distinct adsorption peaks at 3022, 550, 830 and 1511 cm^{-1}. They represent the trans vinylene C-H stretching mode, the phenylene out of plane ring bending, the p- phenylene ring C-H out of plane bending, and the C-C ring stretching, respectively [2]. The FTIR spectrum of salicylic acid doped PPV shows new bands at 1485, 1315and 1150 cm^{-1}. The emergence of these new bands in the spectra is due to the formation of the quinoid structures. The quinoid structure is a result of a symmetry breaking of the polymeric chain. Although the formation of the quinoid structure occurs for the doping agent used, certain FTIR peak (3022, 550, 830 and 1511 cm^{-1}) still remain after the doping process which can be associated with the benzoid structure (undoped PPV). Therefore, even after the extensive oxidation process, only a partial oxidation of the polymer takes place and the two structures coexist.

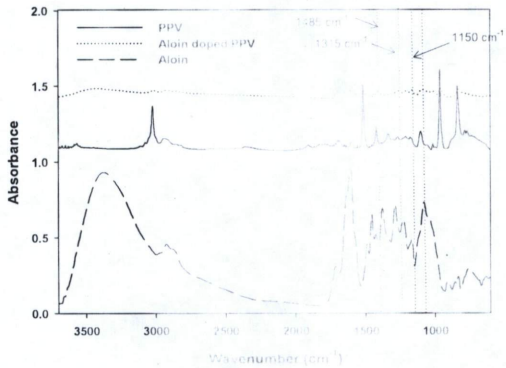

Figure 1 Absorption infrared spectra of: poly(phenylene vinylene), PPV, Aloin; and Aloin doped poly(phenylene vinylene), Aloin-doped PPV.

Release Characteristic

Figure 2 shows the amounts of Aloin released from Aloin-doped PPV/PAAM versus time at electric field strength 0 V. From Figure 2, in the absence of an electric field, the Aloin molecules are not released from the Aloin-doped PPV/PAAM during the first 3, 10, 14, 8 and 8 hr for PAAM_01, PAAM_02, PAAM_03, PAAM_04 and PAAM_06, respectively. Beyond that period, the amount released gradually increases until reaching equilibrium. From Figure 3, it is evident that the amount of Aloin released from Aloin doped PPV/PAAM is greater at a higher electric field strength due to the stronger reduction reaction of Aloin doped PPV. As PPV is reduced, PPV chains expand and create a larger free volume in the hydrogel, which facilitates the diffusion of Aloin through the PAAM matrix [3]. The second driving force comes from the electrostatic force between the negative charge and the cathode electrode [4,5]. The third driving force originates from the direct expansion of the PAAM hydrogel pore size due to the electric field.

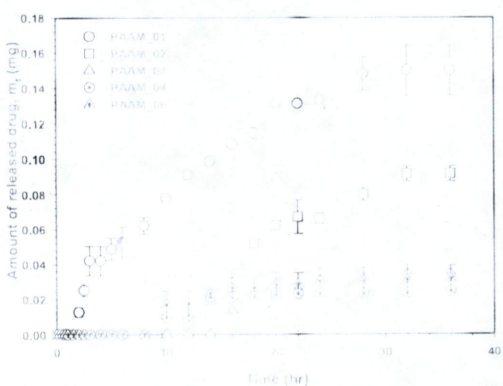

Figure 2 Amounts of Aloin released from Aloin-loaded PAAM hydrogels at time t (hr) at various crosslinking ratios, E = 0 V, pH 5.5, and at 37 °C.

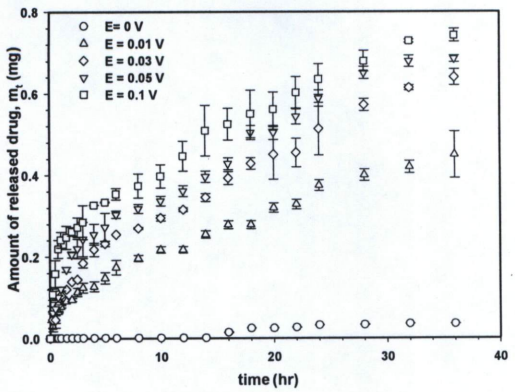

Figure 3 Amounts of Aloin released from Aloin-loaded PAAM hydrogels at time t (hr) at various electric field strength, pH 5.5, and at 37 C

4. CONCLUSIONS

The Aloin doped PPV-loaded PAAM hydrogels were prepared by varying the crosslinking ratio to study the release mechanisms and the apparent diffusion coefficient, D_{app}, of the model drug from drug doped conductive polymer-loaded PAAM with and without an electric field. With the absence of electric field, Aloin cannot be released from Aloin doped PPV-loaded PAAM hydrogel in first period and then it is released until reaching an equilibrium value. The zero amount of release drug in the first period becomes from the ionic interaction between the conductive polymer and its counter ion (PPV/aloin ion) and after this period drug anion can diffuse out through PAAM matrix. It is possible to conclude that by varying crosslinking density, the electric field strength, the drug size and the hydrogel matrix pore size, the drug-matrix interaction, and the presence of a conductive polymer, the drug release rate can be precisely controlled towards an optimal desired level.

ACKNOWLEDGMENT

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ELECTRICALLY CONTROLLED ALOIN FROM POLY (P-PHENYLENE VINYLENE)/POLYACRYLAMIDE HYDROGEL SYSTEM

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Abstract

Aloein which is the active compounds that decrease pain and inflammation and stimulate skin growth and repair are selected as the model drug in this work. From the low content of active compound (<5 %v/v) in Aloe-vera, the development of controlled Aloe-vera extraction system is required to increase the efficiency of drug therapeutic. The development of control-released Aloe-vera extraction, aloein from polyacrylamide hydrogel system as transdermal drug delivery patch was studied. The apparent diffusion coefficients, D_{app}, hydrogel pore size and the release mechanisms of aloein from aloein/polyacrylamide hydrogels (aloein/PAAM) were investigated in the effect of crosslinking ratio of hydrogel. The pore size of crosslinked polyacrylamide hydrogel increases with decreasing amount of crosslinker. The amount of aloin release and D_{app} increase with increasing hydrogel pore size. For larger pore size of hydrogel system, aloein can easily diffuse out than smller pore size hydrogel system. Thus, the amount of aloin released and D_{app} can be controlled by controlling the hydrogel pore size.

Keywords —Aloein / Hydrogel /Paper Aloe-vera Extraction, Transdermal drug delivery patch, Diffusion coefficient