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Full Length Research Article

Starch Based Hydrogel with Potential Biomedical Application as Artificial Skin

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ABSTRACT

Hydrogel wound dressing can protect injured skin and keep the wound surface appropriately moist to speed the healing process by absorbing exudates while maintaining the products of tissue repair, including growth factor and lysosomes, in contact with the wound. The design and development of novel membrane of hydrogel prepared by crosslinking of polyvinyl alcohol with starch suspension using glutaraldehyde as a crosslinking agent was attempted. The membrane was characterized by FTIR spectroscopy. The mechanical property of the hydrogel membrane was characterized by tensile tests. The diffusion coefficient of salicylic acid through the membrane was also evaluated using diaphragm cell technique. FTIR spectra of the membrane indicated the absence of free aldehydic groups of glutaraldehyde. The membrane had sufficient strength to be used as artificial skin. At 30 °C, the measured value of the diffusion coefficient of salicylic acid was approximately 4.11×10^{-6} cm^2/s.
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INTRODUCTION

Hydrogels are hydrophilic natured three-dimensional networks, held together by chemical or physical bonds. Water absorbed by hydrogel is not released under ordinary conditions. Hydrophilic groups absorb and store water. If interstitial space exists within the network, water molecules can become trapped and immobilized, filling the available free volume [LaPorte, 1997; Mark et al, 1966]. The water holding property brings about the specific benefit of hydrogels in wound treatment. They immediately function as moist wound dressings and do not need further wound secretions to attain a gelatinous consistency. At the same time they are capable of absorbing the surplus contaminated exudates and safely retaining them within the gel structure. The absorption of secretions causes an expansion of the cross-links in the polymer chains, making room for the inclusion of foreign bodies such as bacteria, detritus, and odor molecules that are irreversibly taken up along with the liquid. The basic physical features of hydrogel dressings can be specifically modified, according to the properties of the polymers used.

Hydrogels save the wound from fluid loss and are capable for providing the lesion with additional moisture, and securely protect it against external noxae [Krasner, 2001; Falanga, 2000; Mulder and Vande Berg, 2002]. Under the dressing a microclimate is developed, that stimulates and regulates all cellular activities and nutritional processes during the individual phases of wound healing. The high moisture content and the soft-elastic, cushioning properties of the hydrogel almost act like a "second skin". The dressing adapts perfectly to the wound and has a light cooling effect, which is agreeable to the patient and helps to ease pain. This feature is of special significance in the treatment of superficial epithelial wounds such as donor sites for split skin grafts, which can often be extremely painful, due to the concomitant exposure of free nerve endings lying underneath the epidermis [Hartmann International, 2005].

The hydrogel dressing removal is almost painless because hydrogel does not adhere to the wound surface. Hydrogel stays permanently moist and can be easily removed after prolonged application without pain and risk of wound irritation [Krasner, 1997; Gruen, 1996; MacLellan, 1994]. Treatment with hydrogels may bring about great relief for both the patient and the nursing staff. Due to the above reasons the hydrogel wound dressings are highly accepted by the patient.

Hydrogels of natural polymers, especially polysaccharides, have been used recently because of their unique advantages. Polysaccharides are, in general, non-toxic, biocompatible, biodegradable, and abundant [Cascone et al, 2001]. However, as polysaccharides dissolve easily in water, cannot form stable hydrogel, an effective method is to make them into a synthesized polymer gel networks to form natural and synthesized polymer blend hydrogels, which is becoming a subject of academic as well as of industrial interest. Hydrogels can be applied as an interface between bone and an implant [Netti et al, 1993], as artificial skin [Young and Wu, 1998], as contact lenses [Brinkman et al, 1991], as blood contact materials [Taguchi et al, 1998] and in-controlled release applications for delivery of enzymes, hormones, contraceptives, anticoagulant, etc. [Abusafieh et al, 1997].

Biodegradable polymers such as for instance poly (lactic acid) (PLA), poly (glycolic acid) (PGA) and their respective copolymers are already applied in several drug delivery systems [Zhu et al, 1990; Youxin et al, 1993]. However, only a few attempts [Heller et al, 1990; Pereira et al, 1998] have been reported in trying to use starch-based polymers in these type of applications; despite being well known that they are biodegradable materials [Bastioli, 1995] they have been proposed in several works to be used as biomaterials [Reis et al, 1996; 1997]. Starch is one of the most abundant and cheap polysaccharides. Usually starch includes about 30% amylose (a linear α-(1,4) glucan) and 70% amylopectin (dendritically branched version). Chemically modified starches with improved properties are becoming more and more important in industry application not only because they are low in cost, but mainly because the polysaccharide portion of the product is biodegradable. Chemical modification of starch via graft copolymerization of vinyl monomers onto it has been studied widely in recent years [Athawale and Vidyagauri, 1998; Kiatkamjornwong et al, 2000]. But only a few studies on starch polymer blend hydrogels have been reported [Hashim et al, 2000]. In this work PVA/starch blend hydrogels will be prepared by chemical crosslinking technique and efforts will be maid to characterize the hydrogel.

MATERIALS AND METHODS

Materials

Corn starch (CS), salicylic acid (SA), ethanol and glutaraldehyde (GA) were obtained from Loba-Chemie Indoaustranal Co., Mumbai, India. Polyvinyl alcohol (PVA), mol. wt. 125000, was obtained from s.d. fine-chem. limited, Mumbai, India. Hydrochloric acid 35% pure was obtained from Merck Limited, Mumbai, India. Double distilled water was used throughout the study.

GA reagent was prepared by mixing 0.5ml of GA in a solution mixture of 10ml ethanol and 0.05ml Hydrochloric acid.

Preparation of hydrogel

Fifty ml of 10% PVA solution was taken in a beaker. To the PVA solution 50ml of 5% starch suspension in water was added with constant stirring to get a homogeneous mixture. To this mixture GA reagent (10.55ml) was added with constant stirring. Care was taken to eliminate entrapment of air bubbles during mixing and the mixture was used to obtain a membrane by the conventional solution casting method at room temperature. The membrane so obtained was named as RT. RT was washed thoroughly with distilled water to wash off the hydrochloric acid and GA, if any. Then the membrane was dried at room temperature.

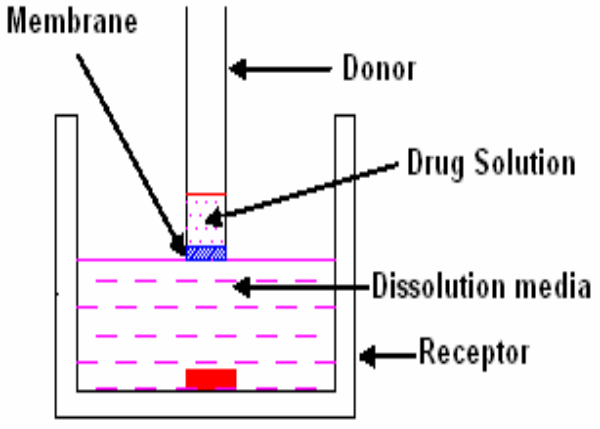

Fig. 1
Diaphragm cell used to measure diffusion coefficient

Characterization

Corn starch (CS) and PVA were subjected to FTIR spectroscopy in the range of 4000-400cm^{-1} as KBr pellets and the membrane was subjected to Attenuated Total Reflectance FTIR (ATR) spectroscopy in the range of 4000-400cm^{-1}. FTIR spectrophotometer (NEXUS –870, Thermo Nicolet Corporation) was used for the study.

The raw materials and the patch were subjected to X-ray diffraction (XRD-PW 1700, Philips, USA) using CuKα radiation generated at 40KV and 40 mA; the range of diffraction angle was 10.00-70.00^{o} 2θ.

The tensile strength of the membrane was determined in the Hounsfield H10KS tensile testing machine. The following test conditions were maintained:

a) Cross-Head Speed: *50mm/min*
b) Temperature: *18^{o}C and*
c) Relative Humidity: *60%.*

Measurement of diffusion coefficient

A diaphragm cell shown in *Figure 1* was used to measure the diffusion coefficient. The cell consisted of two chambers separated by the hydrogel (~0.2-mm thick). The first chamber, donor, contained 5ml of SA solution in water (1.6mg/ml). The other chamber consisted of distilled water (receptor). The system was placed in a constant-temperature water bath. A pipette was used to draw 0.1ml sample from donor and 1.0ml sample from the receptor compartment periodically. The samples withdrawn were replaced by same amount of distilled water. The samples were analyzed by acidic ferric chloride solution to determine the concentration of SA in each chamber as a function of time. The diffusion coefficient, *D*, of the drug through the hydrogel was calculated from these results. The experimentation was conducted at 30^{o}C.

RESULTS AND DISCUSSIONS

Distinct peaks of hydroxyl groups can be observed at around 3300 cm^{-1} from the FTIR spectra of CS and PVA (*Figure 2a and 2b*). FTIR spectra of RT (*Figure 2c*) indicated the presence of free hydroxyl group in the hydrogel membrane. Also there were no free carbonyl group peaks at 1740-1720 cm^{-1} in the membrane which indicated that all the carbonyl groups of GA have been used up for crosslinking.

XRD Characterization

(a) CS

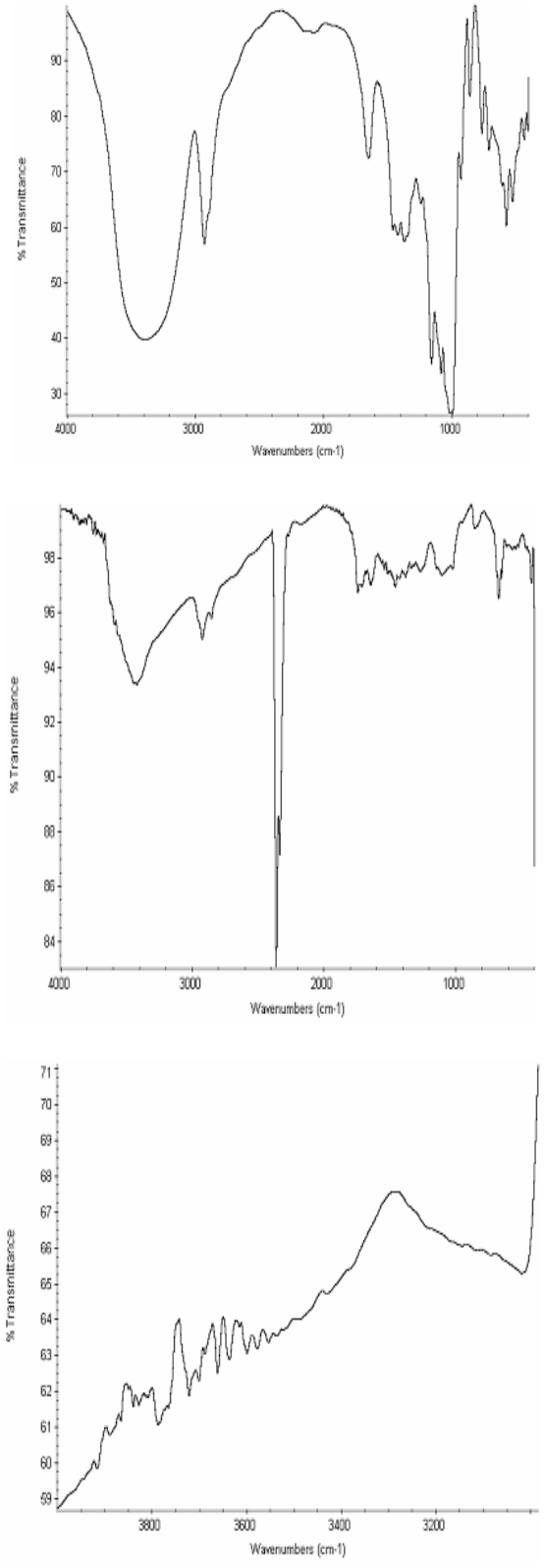

Figure 2.
FTIR spectra of raw materials and hydrogel membranes

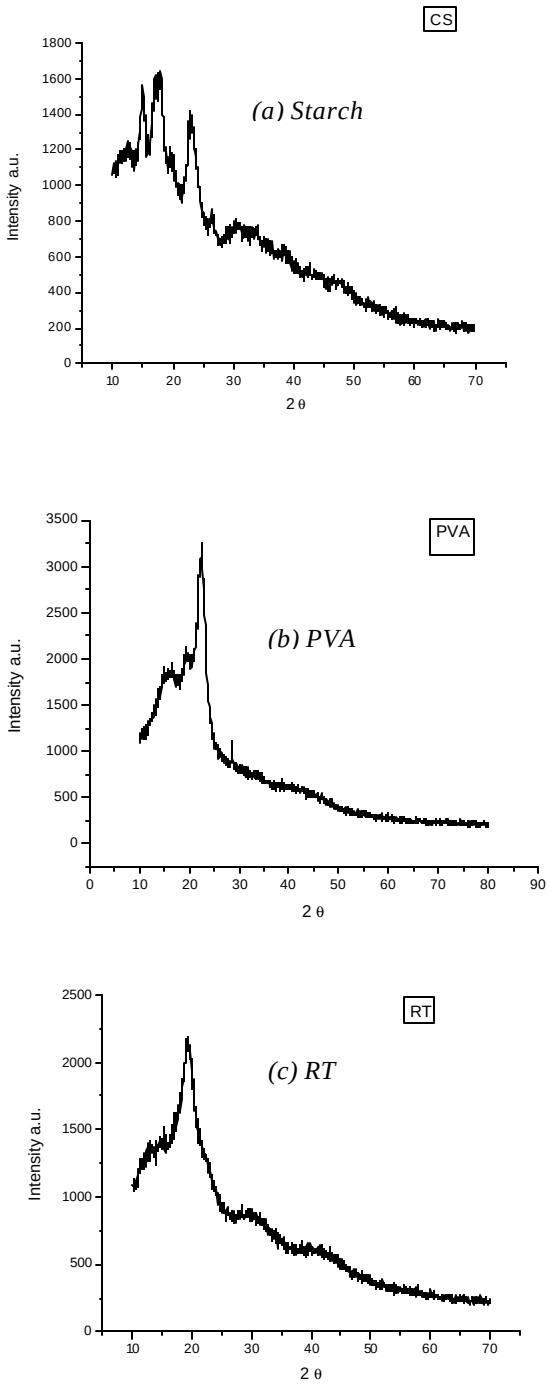

Figure 3.
XRD patterns of raw materials and hydrogel membranes

XRD patterns of raw materials and membranes are shown in *Figure 3*. It can be observed that CS *(Figure 3a)* had peaks at 15°, 17°, 18°, 23° and 26.5° 2θ where the peak at 18° 2θ was most intense while PVA

(Figure 3b) had peaks at 19.5°, 22.5°, and 28.6° 2θ and the peak at 22.5° 2θ was most intense. In the case of RT *(Figure 3c)* there was only one peak at 19.25° 2θ indicating that the crystallinity of the membrane is mainly due to PVA.

Tensile strength of the membrane

In order to evaluate the mechanical property of the hydrogel membrane, the tensile strength of the membrane was measured. The tensile strength of the hydrogel membrane was found to be 35.92±1.87 MPa which is comparable to the failure strength of skin (34 MPa) [Bhat, 2002]. So, the membrane developed could be tried as artificial skin that can give a cushioning effect to the wound.

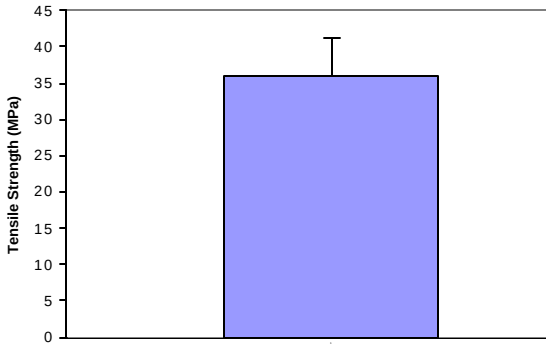

Figure 4.
Tensile strength of the hydrogel membrane

Diffusion coefficient

The desired hydrogels can be produced consistently with the technique outlined above. Typical variations of the concentration of SA in the two chambers during a single experiment are shown in *Figure 5*. As can be expected, the concentration of SA in donor decreases over time, while there is a corresponding increase in the concentration of SA in receptor. At any time, *t*, the concentration values in the two chambers can be used to calculate the diffusion coefficient, *D*, of the drug in the hydrogel from the following equation:

$$D = \frac{1}{bt} x \ln \frac{C_R(t) - C_D(t)}{C_R(0) - C_D(0)} \qquad (1)$$

with

$$b = \frac{A_H}{W_H} x \left[\frac{1}{V_1} + \frac{1}{V_2} \right] \qquad (2)$$

where: $C_D(0)$ =initial concentration of SA in donor; $C_R(0)$=initial concentration of SA in receptor; $C_D(t)$=concentration of SA in donor after time t; $C_R(t)$=concentration of SA in receptor after time t; A_H=effective cross-sectional area of diffusion in the hydrogel sample; W_H=width of the hydrogel sample; V_R=Volume of SA solution in receptor; and V_R=Volume of dissolution media in receptor.

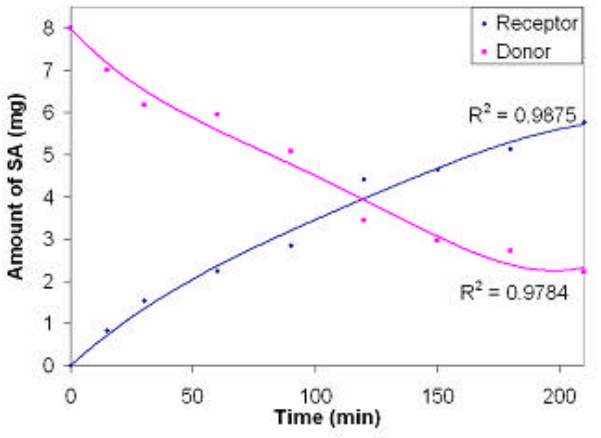

Figure 5.
Diffusion of SA through RT

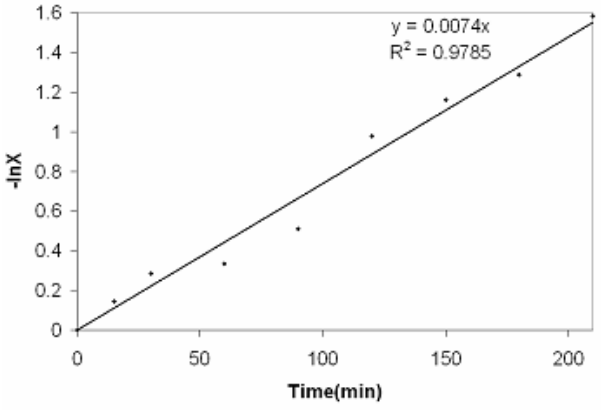

Figure 6.
lnX Vs Time plot, whose slope was used for determining Diffusion coefficient (D)

A plot of $-\ln \frac{C_D(t) - C_R(t)}{C_D(0) - C_R(0)}$ (denoted by –lnX)

with time yielded a straight line as shown in *Figure 6*. The slope of this line was used to calculate the diffusion coefficient, *D* as indicated in Eq. 1. The diffusion coefficient, *D*, of the SA through the RT hydrogel membrane was found to be 4.11×10^{-6} cm^2/s. The membrane could be tried as artificial skin and various nutrients/healing factors and medicaments can be delivered directly to the site of action (wound surface) by putting a swab/hydrophilic matrix containing the nutrients/healing factors and medicaments over the artificial skin.

Conclusion

Membrane obtained by crosslinking of corn starch and PVA with GA showed sufficient strength. FTIR spectra of the membrane indicated the absence of free aldehydic groups of GA thus substantially reducing the chance of toxicity. The XRD studies suggested that the crystallinity imparted in the crosslinked product of CS and PVA was mainly due to PVA. The diffusion coefficient, *D*, of the SA through the cross linked CS and PVA membrane was found to be 4.11×10^{-6} cm^2/s. The prepared hydrogel membrane could be tried as artificial skin and at the same time various nutrients/healing factors and medicaments can be delivered directly to the site of action.

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