On the Restriction of the Release of Water-Soluble Component from Polyvinyl Alcohol Film by Blending β-Cyclodextrin

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Received 22 March 1995; accepted 12 February 1997

ABSTRACT: The effect of adding β-Cyclodextrin with poly(vinyl alcohol)(PVA) hydrogel on the release of a water-soluble component has been investigated. It is found that the release of a model drug, salicyclic acid, from PVA matrix in the presence of β-cyclodextrin prolonged considerably the release of the profile of the drug from the PVA gel. The profound influence of β-cyclodextrin on the drug release has been assigned to the ability of β-cyclodextrin to form an inclusion complex with salicyclic acid. © 1997 John Wiley & Sons, Inc. J Appl Polym Sci **65:** 1829–1832, 1997

INTRODUCTION

Because of several desirable properties, such as nontoxicity and noncarcinogenicity, polyvinyl alcohol (PVA) in different physical forms finds extensive application as a biomaterial.[1–4] The material has been used in artificial kidneys.[5] Recent reports have shown that PVA is a good candidate for contact lens application.[6] The most interesting uses of PVA are perhaps in the controlled release of pharmaceutical components. Several researchers have shown that PVA hydrogels could be used for the sustained release of drugs.[7–9] Another application in which PVA could be used effectively is in wound management.[10,11]

An ideal wound dressing should have antibacterial and wound-healing properties in addition to having the essential swelling capability to absorb exudates and the necessary oxygen permeability. The normal practice when adding antibacterial properties to wound-dressing film is to incorporate a suitable drug. It is often a problem to get effective drug concentration at the site, in a controlled fashion, for a suitable period of time.

β-Cyclodextrin (β-CD) is well known for its ability to form inclusion complexes with various class of compounds.[12–14] Due to this inherent property, β-CD has been used widely in pharmaceutical and allied fields. To the best of our knowledge, however, β-CD has not been used in PVA hydrogel to modify the sustained release of drugs. This report describes our effort in this direction.

EXPERIMENTAL

PVA, with a number-average molecular weight of 125,000, and β-CD were from Sigma Chemical Co. (St. Louis, MO) and were used as received. The model drug used in this study was salicyclic acid (BDH, Bombay, India).

PVA (1 g) and β-CD (0.4 g) were dissolved in deionized distilled water. Sixty milligrams of the drug was added to this solution. The solution was stirred magnetically for about 1 h at 60°C to get a clear solution. After the solution was cooled to room temperature, 1 mL of 0.1*N* hydrochloric acid and 1 mL of 0.1% glutaraldehyde (Sigma Chemical Co.) prepared in water were added. The resulting solution was stirred briefly and poured

into a Petri dish to get an air-dried film. In a similar fashion, PVA film with the same amount of drug was prepared without adding β-CD. Both films were prepared by evaporating water at room temperature by keeping in an vacuum oven for about 24 h.

Films having an area of 2 cm^2 and a thickness of 2 mm were placed in 5 mL of deionized distilled water at room temperature (30 $\pm$ 1°C) with occasional stirring. At regular intervals, the samples were taken out and kept in other bottles containing 5 mL of water. The amount of drug released was estimated by a chromatographic procedure.

A Waters Assoc. Inc. high-performance liquid chromatographic system consisting of a model 6000A solvent delivery pump, a model U6K injector, and a model 486 tunable absorbance detector was used for the analysis. A μ-Bondapak phenyl column (Waters Assoc. Inc.) in conjunction with deionized distilled water as mobile phase at a flow rate of 1 mL/min was used for the analysis at room temperature. The column effluents were monitored at 236 nm, and the chromatograms were obtained on an Ominiscribe strip chart recorder (Houston Instruments, Houston, TX).

For preparing the pure inclusion complex of β-CD and salicyclic acid, the following procedure was used. β-CD and salicyclic acid in a 1 : 1 ratio were placed in 250 mL of deionized distilled water and kept at elevated temperature (45°C) under stirring for about 2 h to get a clear solution. The solution was allowed to cool to room temperature, stirred for a further period of 4 h, and then kept at room temperature overnight. The precipitate that settled to the bottom was collected by filtration, vacuum dried, and subjected to infrared spectroscopic studies.

A Perkin-Elmer model 597 infrared spectrophotometer was used for obtaining the specttra of the samples. The sample, dispersed in potassium bromide in the form of a pellet, was scanned from 4,000 to 400 cm^{-1}.

RESULTS AND DISCUSSION

Figure 1 shows the release of the profile of salicyclic acid from PVA gel (panel A) and PVA–β-CD gel (panel B). Within 20 h, nearly 90% of the drug is released from the PVA gel. On the other hand, the drug release from the PVA–β-CD gel is much less, indicating the considerable influence of the added β-CD.

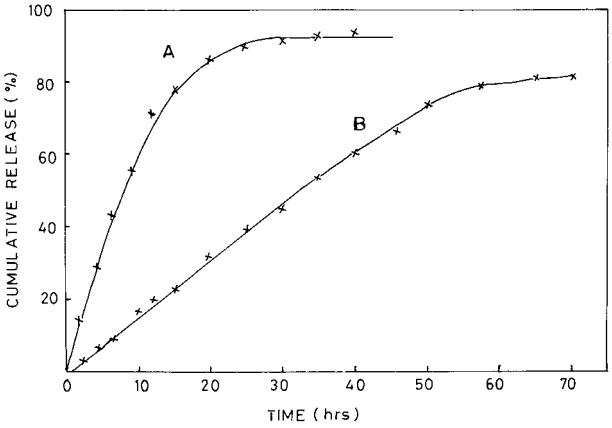

Figure 1 Release profile of salicyclic acid from (A) PVA gel and (B) PVA–β-CD gel.

The release of drugs from hydrogels seems to be influenced by several factors, such as polymer composition, water uptake, degree of crystallinity, association of the drug with the polymer, and structure of the drug.[15] In particular, the degree of swelling could have a higher influence on the drug release.

The drug release from the PVA gel is nonlinear with time, which is expected due to the substantial swelling of the PVA matrix. However, even though the PVA–β-CD gel also swells, similar to the PVA gel, the drug release is nearly proportional to time, which may be traced to the effect of added β-CD.

The ability of β-CD to form inclusion complexes is well known. Figures 2 and 3 depict the infrared spectra of β-CD and salicyclic acid, respectively. Figure 4 illustrates the infrared spectrum of the precipitate collected from the β-CD–salicyclic acid solution. The spectrum of Figure 4 shows the characteristic peaks of β-CD centered at 3,400 and 1,050 cm^{-1} and severable features of salicyclic acid such as a —CO— stretching band around 1,660 cm^{-1}. The only visible difference of this spectrum compared with the spectra of β-CD and salicyclic acid (Figs. 2 and 3) is the slight downward shift of the —CO— stretching frequency, which could be due to the H-bonding interaction between the —CO— group and the —OH groups of the β-CD.

Certainly, it is difficult to visualize the formation of a complex between the drug and β-CD in

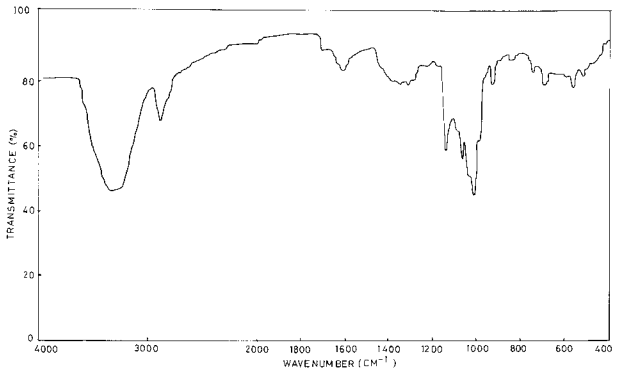

Figure 2 Infrared spectrum of β-CD.

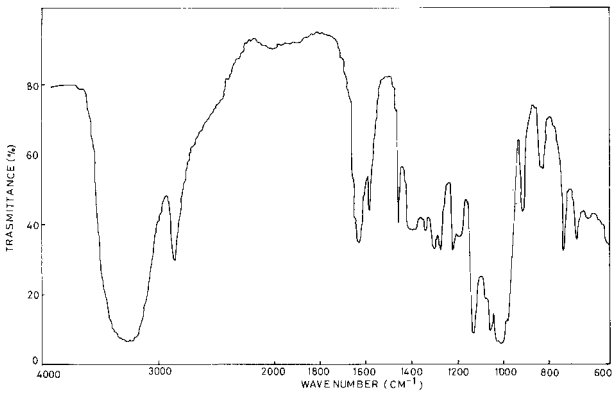

Figure 4 Infrared spectrum of β-CD–salicyclic acid complex.

the PVA matrix, even though the complexation is possible, as evidenced by Figure 4. The drug, during its migration through the PVA gel, could be included inside a suitably oriented β-CD cavity. Additionally, the drug could form a complex during the initial mixing process. The primary factor responsible for the variation in the release profile of the drug in the presence of β-CD, we feel, is due to the complex formation between β-CD and salicyclic acid.

The swellability of PVA–β-CD is marginally higher than the swellability of the PVA gel, indicating that the crosslink density is higher in the PVA–β-CD system than in the PVA gel. The higher crosslink density may be an additional factor in retarding the migration of the drug in the presence of β-CD. However, it seems that the complexing ability of β-CD is the major factor influencing the drug release. The local variation in swelling in the PVA–β-CD matrix presumably results in considerable variation in the conformation of β-CD molecules. These conformational alterations could accelerate the dissolution of the drug to aqueous medium.

In the PVA gel, the drug is randomly dispersed. As mentioned earlier, the degree of crosslinking is the major factor governing the migration of the drug. The water solubility of the drug may further accelerate the dissolution process. These aspects could be responsible for an almost total transport of the drug within a rather short period of time.

PVA–β-CD gel without the drug also kept in water in a similar fashion. We could not detect any β-CD in the water, indicating the lack of β-CD migration into water.

Our preliminary results show that the release of drug, particularly water-soluble drugs, from hydrogels could be controlled effectively by the addition of β-CD. Although untested, the method may be useful in the preparation of wound-dressing materials based on hydrogels.

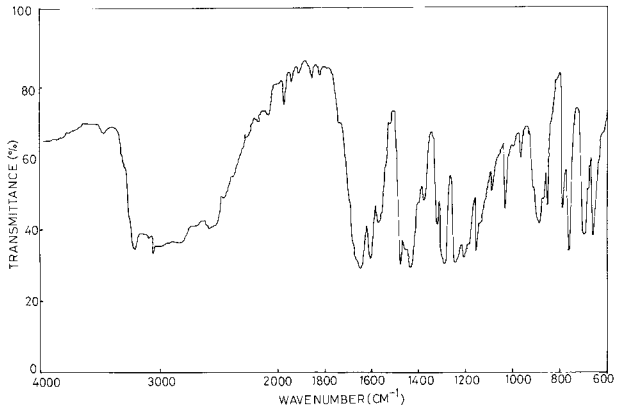

Figure 3 Infrared spectrum of salicyclic acid.

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