Absorption Characteristics of a Novel Semi-IPN Membrane Based on β-Cyclodextrin Toward Testosterone and Progesterone

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Received 8 June 1996; accepted 19 November 1996

ABSTRACT: β-Cyclodextrin was coupled to the —OH group of 2-hydroxyethyl methacrylate using hexamethylene diisocyanate. Segmented polyurethane and the modified monomer were dissolved in dimethylacetamide and subsequently heated to about 80°C in the presence of AIBN to polymerize the modified monomer to form a semi-interpenetrating network. The potential of the new polymer as a membrane was evaluated by studying the sorption of testosterone and progesterone. The preliminary data showed that the polymer could differentiate structurally close molecules with some degree of selectivity, indicating the possibility of exploring further the polymer, particularly as a membrane. © 1997 John Wiley & Sons, Inc. J Appl Polym Sci **64:** 1811–1814, 1997

INTRODUCTION

Cyclodextrins (CDs), the oligomers of glucose, are well known for their ability to form inclusion complexes with a variety of components.[1–4] Over recent years, extensive studies basically on the complexing ability of CDs have been reported.[1–5] The potential of CDs have been explored widely in varied fields like the pharmaceutical and food industry and analytical chemistry.[6,7] The hydrophobic cavity enables CDs to recognize isomers and this property has been further explored in chiral separation in chromatography.[8,9]

Efforts to synthesize polymeric systems based on CDs with a view to develop membranes capable of imparting selectivity toward the separation of components have been made.[10–14] The inferior mechanical properties of CD-based polymers is one of the serious drawbacks toward the realization of CD-based mechanically stable polymeric membranes. Recently, we synthesized an acrylate monomer coupled with β-cyclodextrin (BCD).[14] The CD-containing monomer can be grafted easily onto mechanically stable polymers like polyurethanes and poly(vinyl chloride), which may be studied as membranes. Additionally, the CD-containing monomer can be mixed with polymers like polyurethane and, subsequently, can be polymerized to form semi-interpenetrating networks (semi-IPN) which would be highly stable and have a high CD content throughout the polymer matrix. This article reports the preparation of a semi-IPN based on BCD coupled to 2-hydroxyethyl methacrylate and polyurethane and its preliminary evaluation as a novel membrane.

EXPERIMENTAL

2-Hydroxyethyl methacrylate (HEMA), β-cyclodextrin (BCD), progesterone, and testosterone were obtained from Sigma Chemicals, St. Louis, MO. Hexamethylene diisocyanate and azobisisobutyronitrile (AIBN) and ethylene glycol dimethacrylate (EGDA) were obtained from Fluka, Germany. The polyurethane used in this study was based on poly(tetramethylene glycol) (MW 1000), methylene bis(*p*-cyclohexyl isocyanate),

and 1,4-butanediol. The weight-average molecular weight of the polyurethane was 98,000 and wt % hard segment content was 30%. All other reagents (chromatographic or analytical grade) were obtained from E-Merck, Bombay, India.

SYNTHESIS

The synthesis and characterization of the modified BCD by coupling HEMA to one of the —OH groups of BCD using diisocyanate was reported elsewhere.[14] Briefly, 0.012 mol of hexamethylene diisocyanate was allowed to react with 0.01 mol of HEMA at 45°C for 35 min in the presence of dibutyltin dilaurate (catalyst) in 15 mL of dimethylacetamide. Dried BCD, 0.01 mol, was dissolved in 25 mL dimethylacetamide and added to the above solution. The temperature was increased to 50°C and stirred magnetically for nearly 2 h.

Excess dimethylacetamide was evaporated by heating at 45°C in a vacuum oven. Ten grams of the syrupy liquid was mixed with 20 mg AIBN and 0.001 mol EGDA. Five grams of polyurethane was dissolved in 15 mL dimethylacetamide. These two solutions were mixed and placed in a Petri dish and kept at 70–80°C overnight. The film formed was taken out and washed extensively with methanol and dried.

Solutions of progesterone and testosterone were prepared by dissolving these components separately in methanol. The concentration of the components in the solutions were 1 mg/mL. From the differences in the absorption intensities, the amount of progesterone and testosterone absorbed by BCD were estimated.

Polymeric films having a thickness of 0.04 mm and area of 2 cm^2 were placed in the solutions of progesterone and testosterone for 3 h at static conditions. The solutions were subjected to chromatographic analysis before and after placing the films. The extent of the absorption of the molecules by the polymer were estimated from the differences in the absorption intensities of the solutions before and after placing the films. To evaluate the relative affinities of progesterone and testosterone toward BCD, a simple experiment was performed. To a solution of progesterone and testosterone in methanol (1 mg/mL), an excess quantity of BCD (100 mg) was added and kept at 30°C overnight. The solution was subjected to chromatographic analysis before and after placing BCD. Again, from the differences in absorption intensities, the amount of progesterone and testosterone absorbed by BCD was estimated.

Table I Stress–Strain Parameters of the Polymers

Polymer	Stress (kg/cm^2)	Strain (%)
Polyurethane	430 ± 5	452 ± 7
BCD-based semi-IPN	280 ± 6	163 ± 2

A Waters Associates chromatographic system consisting of a Model 6000 A solvent delivery pump, Model U6K injector, and Model 486 tunable absorbance detector was used for the chromatographic analysis. A μ-Bondapak C18 column in conjunction with water : methanol (70 : 30 v/v) as the mobile phase at a flow rate of 1 mL/min was used for the chromatographic separation. The column effluents were at 241 nm (the absorption peak of the steroids studied here) and the chromatograms were obtained on an Ominiscribe strip chart recorder (Texas Instruments, Houston, TX).

RESULTS AND DISCUSSION

The semi-IPN formed appeared to be less transparent. This may be due to the presence of BCD entities which could act as additional crosslinks. The mechanical properties of the polymers are summarized in Table I. The mechanical parameters fall within the range of stiff elastomers which may be due the dispersed hard segments.

The ultimate stress and strain of the polymer are lower than those of the polyurethane. The bulky BCD molecules could interfere with the orientation of polyurethane chains under stress, which, in turn, could affect the ultimate stress–strain parameters. Additionally, BCD molecules could act as interlocks and prevent the stretch-induced chain ordering. The reduced mechanical properties of modified polymers could be attributed to the above-mentioned factors. Although the mechanical properties are less than those of the conventional polyurethane, the modified polymer has a strength typical of a membrane.

Figure 1(A) and (B) shows scanning electron micrographs of polyurethane and the new semi-IPN. Polyurethane has a smooth texture while the semi-IPN shows distinctively altered surface features reflecting the formation of an additional

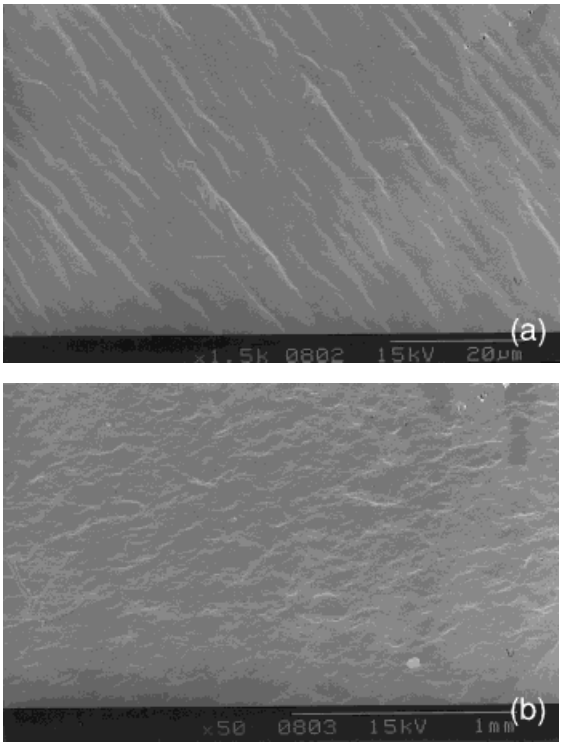

Figure 1 (A) SEM micrograph of polyurethane. (B) SEM micrograph of BCD-based semi-IPN.

phase. However, any phase separation is not evident, which is expected due to the possibility of a hydrogen-bonding interaction between the —OH groups of BCD and the —CO— groups of polyurethane.

Progesterone and testosterone were used for evaluating the semi-IPN membrane in terms of its selectivity in absorption. This pair of molecules was chosen considering their close structural features and molecular weights. Table II summarizes the amount of testosterone and progesterone desorbed from the semi-IPN strips. In spite of the structural similarities of these components, there is a considerable variation in the extent of uptake of testosterone and progesterone by the polymer. The remarkably increased uptake of progesterone by the polymer compared to testosterone could be attributed to the comparatively higher affinity of BCD toward progesterone.

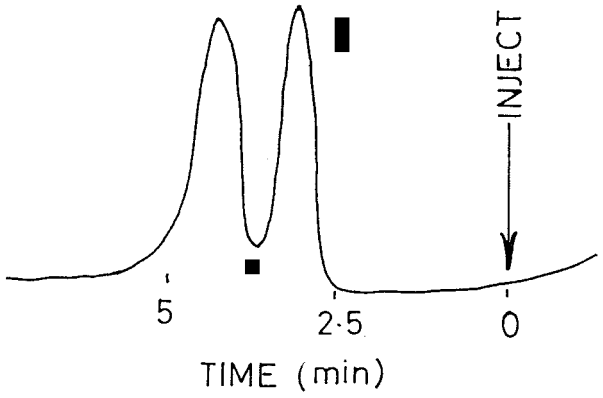

Figure 2 Chromatographic trace of a mixture of testosterone and progesterone.

BCD is known to form complexes with several components including steroids. Extensive efforts have been expended to understand the mechanism as well as the factors governing the complexation of components with BCD.[7] The following factors, namely, hydrophobic interactions between the guest molecules and the cyclodextrin cavity, hydrogen bonding between the polar functional groups of guest molecules and the hydroxyl groups of cyclodextrin, release of high-energy water molecules from the cavity in the complex formation, and the release of the strain energy of the cavity. It has generally been accepted that hydrophobic interaction has a primary role in determining the complexation among the abovementioned factors.

Figure 2 illustrates the chromatographic trace of a mixture of testosterone and progesterone. Under the present chromatographic conditions, testosterone has a retention time of 3.3 min and the retention time of progesterone is 4.1 min. It is well known that in reverse-phase chromatographic separation the polar component elutes first, followed by less polar components. A glance at the chromatogram depicted in Figure 2 points out that testosterone is relatively more polar than is progesterone.

Table II Equilibrium Uptake of the Steriods by the Polymer Membrane

Component	Amount Adsorbed (mg) Wt of the Polymer: 72 mg	% Adsorption (By the Polymer)
Progesterone	5.36 ± 0.2	7.44 ± 0.28
Testosterone	2.64 ± 0.14	3.67 ± 0.2

Table III Extent of Absorption of the Steriods by BCD

Component	% Absorption
Progesterone	18 ± 0.39
Testosterone	10 ± 0.41

Table III summarizes the extent of uptake of progesterone and testosterone by BCD. It is apparent that BCD absorbs more progesterone compared to testosterone. It is reasonable to presume that increased absorption of progesterone can be considered as a measure of the higher affinity of progesterone toward BCD. Indeed, there is variation in the extent of uptake of progesterone and testosterone by the polymer and BCD (see Tables II and III). The BCD could form a complex with the test molecules relatively easily compared to the BCD entity attached to the backbone of the polymer chains in the semi-IPN due to the restricted movement of the BCD entities. The restricted movement may reduce the number of properly oriented BCD entities to form the complexes with the test molecules. This factor could be responsible for the reduced absorption of test molecules by the polymer compared to the free BCD molecules. The increased uptake of progesterone could be due to the higher affinity of progesterone toward BCD (see Table III). The chromatographic results (see Fig. 2) indirectly indicate that progesterone is more hydrophobic than is testosterone, which may be the factor responsible for the increased affinity of progesterone toward BCD.

The ratio of the equilibrium absorption of the test molecules may be considered as a measure of the selectivity factor. Based on the values summarized in Table II, the selectivity factor can be put as 2. Indeed, the selectivity is not high enough to expect an absolute separation of progesterone and testosterone using this membrane. However, it is interesting in the sense that a certain degree of selectivity can be imparted by modifying common polymers like polyurethanes to separate structurally close molecules.

The selectivity of cyclodextrins toward specific molecules can often be enhanced by replacing one of the primary —OH groups by certain entities.[15] Our future efforts will be directed toward the synthesis of chemically modified BCD and the subsequent synthesis of membranes capable of separating structurally similar molecules.

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