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Report

Structure and Permeability of Composite Films of Two Analogous Acrylate Methacrylate Copolymers

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Two analogous acrylate methacrylate copolymers, A and B, which form films with compact surface zones (skins) have been layered into composite films AB and BA. Electron micrographs of the composite film internal structure revealed a porous asymmetry; the mean pore size in layer A was 2.4 ± 0.3 μm, and that in layer B 0.71 ± 0.06 μm. The actual surface pores were considerably smaller than the internal pores, below the limit of resolution of the electron microscope. AB (layer A accepting the permeant first) was 17 times more permeable to the solute, urea, than BA. Exposure of the film surfaces to solvent vapor before layering caused dissolution of the "skin" in component layers; resulting composite films were therefore more permeable than theoretical expectation.

KEY WORDS: composite films; asymmetric permeability; composite film pore structure.

INTRODUCTION

Mass transport through polymer films has important biomedical applications including controlled release of drugs and hemodialysis. Film permeability may be modified and controlled by a layered structure on the basis that the total resistance, R_t, against permeation in the layered structure would be a sum of the individual resistance of component layers (1), i.e.,

$$R_t = r_1 + r_2 + \ldots r_n \qquad (1)$$

where r_1 and r_n are the resistances of the first and nth layers. Resistance may be defined as the reciprocal of the film permeability, P, multiplied by the film thickness, L, i.e., $R = L/P$; for a two-layer film AB (thickness of A = that of B), the total resistance to permeation would be.

$$L/P = \tfrac{1}{2}L/P_A + \tfrac{1}{2}L/P_B \qquad (2)$$

or

$$1/P = \tfrac{1}{2}\frac{(P_B + P_A)}{P_A P_B} \qquad (3)$$

Permeability should be independent of layer permutation, however, in situations where the permeant interacts with one of the layers to promote its swelling, asymmetric permeability is diplayed (2); permeability the now depends on the order of layering. This feature can also be associated with porous asymmetry, where there is surface difference in film pore structure (3). In a preliminary study (4) a composite film comprising two analogous acrylate methacrylate copolymers (designated A and B) displayed permeability asymmetry; this report presents the basis of that observation.

MATERIALS AND METHODS

Two acrylate methacrylate copolymers, designated A and B, were received from Rhom Pharma, Darmstadt. A and B differ only in their content of quaternary ammonium (polar) groups at a ratio 2:1 (A:B). A is therefore more hydrophilic than B. Urea (analar, BDH) was used as solute permeant. Ethanol (absolute alcohol, BDH), acetone (analar, BDH), and glycerol triacetate (reagent alcohol, BDH) were used as solvents and plasticizer, respectively, in film casting. Films of polymer A cast from ethanol were designated A_1.

Film Preparation

Films (mean thickness, 19.8 ± 0.3 and 39.4 ± 0.7 μm) were prepared by casting on a PTFE mold from an acetone solution containing the polymer (2.5%, w/w) and plasticizer (0.5%, w/w) using a method described earlier (3). Single films of polymers A and B (each 19.8 μm thick) were layered to composite films AB or BA (mean thickness 39.0 ± 0.2 μm) after exposure of the film surfaces to acetone vapor for 2 hr at 22°C (5). Layering was in the order L–U–L–U, where L is the film lower surface (in contact with the mold during casting) and U is its upper (air-dried) surface.

Permeation Experiments

Solute permeation through the films (exposed area, 23 cm^2) was conducted at 30°C using the double (donor and acceptor)-compartment cell and technique described earlier (3). The donor fluid [135 ml, 10% (w/v) urea, aq.] and the acceptor fluid (135 ml water) were stirred at 300 rpm using magnetic stirrers. The film lower surface was upstream in all permeation experiments. Samples were withdrawn from the acceptor fluid at 1-hr intervals for 5 hr. Urea was determined using the spectrophotometric technique of Watt and Chrisp

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(6). The experiments were carried out in four replicates; results were reproducible to ±7.5% of the mean.

Film Swellability

The volume fraction of fluid in the films or changes in their dimensions, length, and breath were determined after their equilibriation in water or permeant solutions (30°C, 3hr) and taken as an index of swellability. Single films of 39.4-μm thickness were used.

Determination of Film Pore Structure

Cross sections and surfaces of the composite films were vaccum coated with carbon followed by a gold shadow using a Nanotech Mini 250 vacuum coating machine. Specimens were examined at various magnifications up to 10,000 using a scanning electron microscope (SEM; Phillips 500).

RESULTS AND DISCUSSION

The structure of the single films A and B is characterized by a porous asymmetry (3,7); compact surface zones (skins) bound a porous core. The film upper surface is, in turn, more compact than its lower surface (3). A composite film AB or BA should therefore have an additional skin zone at the interface comprising the upper surface skin (U_1) of the first layer and the lower surface skin (L_2) of the second layer (Fig. 1a). A micrograph of the composite film internal structure (Fig. 1b) reveals the skins (L_1 and U_2) on the outer surface zones only, evidenced by the intense gold shadow in these zones; in contrast, the film porous core generally displayed a dark (carbon) background. The absence of a zone displaying gold shadow at the interface between the two films could be taken as evidence that the skins on the contacting film surfaces dissolved during layering to allow fusion of the two components.

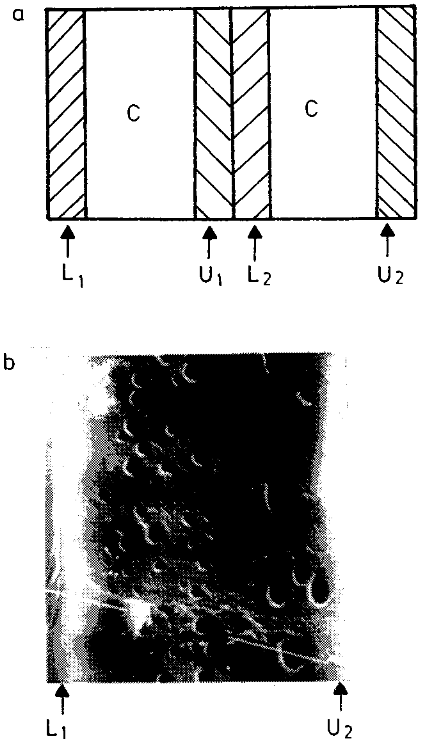

Fig. 1 (a) A diagrammatic representation of a cross section of a composite film showing the skins (L and U) and the loose spongy core (C) of each component layer. L_1 and U_1 are the lower and upper skins, respectively, of the first layer, while L_2 and U_2 are for the second layer. (b) An electron micrograph of a cross section of an actual composite film, BA. Note the presence of skins L_1 and U_2; U:$_1$ and L_2 had dissolved during layering. ×2500; reduced XX% for reproduction.

Amounts of urea permeating the single (component) films (thickness, 19.8 μm) and the composite films (thickness, 39.4 μm) as a function of time are presented in Fig. 2. Permeation rates obtained from the slopes of these plots were 480 (A), 1.0 (B), 46 (AB), and 2.7 mg hr^{-1} (BA). The higher permeability of A compared with B relates to the higher porosity of A (3), AB (layer A accepting the permeant first) was 16 times more permeable than BA (B accepting the permeant before A). The film permeability thus depended on the order of layering, a phenomenon termed permeability asymmetry. Solute transport through the films studied involves entry and diffusion through aqueous-filled pores (3–5). According to the theory of permeation through such systems (8), the resistance to flux includes (a) the steric hindrance against the penetration of solute molecules from the external liquid phase into the film pores and (b) the viscous drug of solute molecules along the pore wall in the film internal structure, i.e., resistance to flux = $a + b$ where b is the total resistances within the barrier and a is an external factor determining entry into the barrier. Furthermore, the theory (8) says that the probability of a solute (radius r_s) penetrating into a pore (radius r_p) is given by

$$A_{P/A_o} = (1 - r_s/r_p)^2 \qquad (5)$$

where $A_p = (r_p - r_s)^2$ is the actual area available for penetration and $A_o = r_p^2$ is the pore area. Hindrance becomes

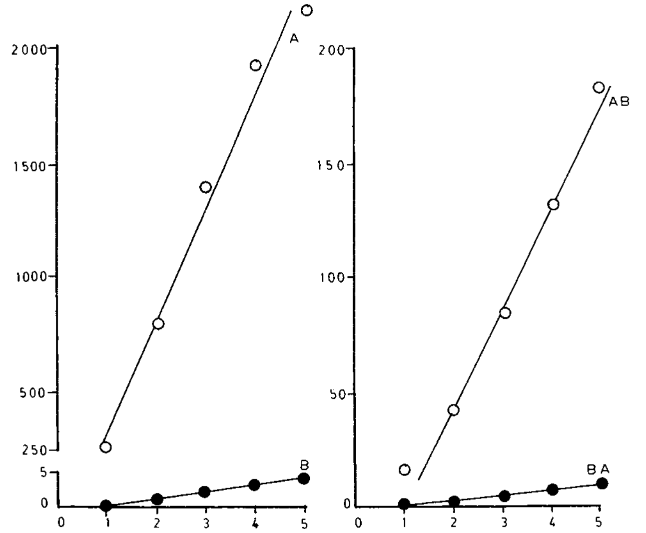

Fig. 2. Differences in the urea permeability of single films of polymers A and B (thickness, 19.8 μm) and composite films AB and BA (thickness, 39.4 μm); note the asymmetry AB > BA. Ordinate, solute transferred (mg); abscissa, time (hr).

significant when r_s approximates to r_p and insignificant when $r_p \gg r_s$.

A measurable permeability is an indication that pores are present in the film structure, although their presence on the film surface could not be demonstrated by scanning electon microscopy, perhaps because their sizes were below the limit for clear resolution of the microscope used; magnifications > 10,000 produced blurred pictures. Nevertheless, the extremely low permeation rate observed in B (Fig. 2) is evidence that the pore size was extremely small; similarly the high permeability observed in A could be taken as evidence of the presence of pores considerably greater in size than the solute molecular size. Therefore in the order BA hindrance against penetration was significant and the resistance amounted to $a + b$, whereas in the order AB the hindrance was insignificant and the resistance reduced to b only, thus giving the asymmetry AB > BA.

Further evidence for this mechanism of asymmetry was obtained by substituting a more porous film, A_1, for B in the composite barriers to obtain AA_1 and A_1A instead of AB and BA. A_1 was considerably more permeable than A (Fig. 3), which was in turn more permeable than B (Fig. 2), indicating that of the films, A_1 had the largest pore size although this could not be directly quantified by electron microscopy for reasons mentioned above. Permeation rates of AA_1 and A_1A were 1005 and 1000 mg hr^{-1}, respectively, indicating the absence of asymmetry. In these systems the barrier was freely penetrable irrespective of the layer that was upstream during permeation experiments.

Table I. Differences in the Swellability (i.e., Volume Fraction of Fluid) in Single Films of Polymers A and B Equilibrated (30°C, 3 hr) in Permeant Solutions

	Swellability in urea solutions of concentrations (%, w/v)				
Film type	0	2.5	5	7.5	10
A	0.39	0.40	0.43	0.44	0.44
B	0.33	0.32	0.30	0.30	0.30

Permeant–polymer interactions to promote film swelling could be a basis for permeability asymmetry (2) but as can be seen in Table 1, film swelling was hardly dependent on permeant concentration. BA was more permeable than B (Fig. 2). The presence of the more hydrophilic film A increased the aqueous swellability (i.e., percentage increase in film area) of B while in the composite structure; for instance, the swellability of A, B, and AB or BA was 20.6, 4.7, and 13.8%, respectively. Dissolution of the upper surface skin of B during layering could have also lowered the internal resistance of BA; hence also the observed permeability of BA (2.7 mg hr^{-1}) was higher than that (2.0 mg hr^{-1}) expected from theory [Eq. (3)]

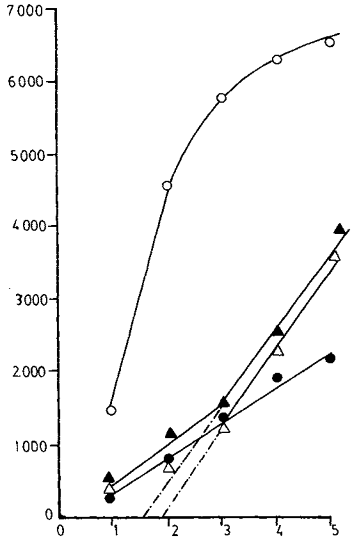

Fig. 3. Differences in the urea permeability of single films A (●) and A_1 (○), each of thickness 19.8 μm, and composite films AA_1 (▲) and A_1A (▲). A_1, film of polymer A cast from ethanol instead of acetone. Ordinate, solute transferred (mg); abscissa, time (hr).

CONCLUSION

Certain composite films of the types AB and BA displayed permeability asymmetry, AB > BA; the mechanism is based on hindrance to penetration of permeant molecules into the barrier when the less porous layer B was upstream in permeation experiments. Such hindrance is manifested only when the pore size approximates the permeant molecular size; hence the asymmetry could not be reproduced in types AA_1 and A_1A composite films, both layers being sufficiently porous and freely penetrable to permeant molecules.

A, being more hydrophilic than B, promoted swelling and permeability of B in the resulting composite film. Thus layered structures of the polymer films studied may be used to control film performance in the design of drug delivery systems.

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