Drug Transport Across Nylon 610 Films: Influence of Synthesis Variables

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Nylon 610 is a hydrophilic polymer with considerable potential as a membrane for drug microencapsulation. To better understand drug transport through such membranes, the influence of the solvents and monomers used in the synthesis of nylon films were examined using a full factorial study. Nylon 610 films were synthesized by an interfacial polycondensation reaction using hexamethylenediamine (HD) in the water phase and sebacoyl chloride (SC) in the organic phase, which was a solvent blend of chloroform and trichlorotrifluoroethane at ratios of 1:1, 1:4, and 4:1. Monomer concentrations studied were 0.2, 0.4, and 0.6 M with respect to their appropriate phase, while the monomer ratios were 1:1, 3:1, and 1:3. The molecular weight, porosity, thickness, and crystallinity of the films were characterized. The transport of potassium chloride, hydrocortisone, and *m*-cresol was studied at 25°C as a function of the syntheses variables. Potassium chloride was selected to measure the porosity of the membrane. Hydrocortisone and *m*-cresol, a known solvent for nylon 610, were used to study pore and solution-diffusion transport, respectively. The molecular weight of the films was proportional to the chloroform concentration. As the molecular weight increased, film thickness, porosity, and hydrocortisone permeability increased. As the molecular weight decreased, film thickness and porosity decreased, while *m*-cresol permeability increased. These results can be explained on the basis of HD ability to readily partition into a good solvent such as chloroform permitting high molecular weight polymer to form before precipitation.

KEY WORDS: Nylon 610; Film; Interfacial polycondensation; Polymer; Permeability.

A. INTRODUCTION

The development of microencapsulated products as a viable means of drug delivery has received much attention over the years (1). Products of this type that can release controlled quantities of drug to their external environment over a period of time require thorough investigation of the structure and morphology of the rate-controlling membrane. One way to produce such membranes is by interfacial polycondensation, whereby a polymer membrane precipitates at a water/organic interface. The polymer membrane's physical property affect release of the encapsulated solute. The procedure of preparing microcapsules containing water requires two steps in the interfacial polycondensation method. First, an aqueous solution of hexamethylenediamine (water soluble monomer) is emulsified in a cyclohexane-chloroform mixture to form a water-in-oil emulsion, and, second, a sebacoyl chloride (oil soluble monomer) solution is added to initiate polymer formation at the interface of the water droplets.

Several factors are known to influence the polymer membrane's molecular weight, thickness, and morphology (2). These factors include (i) organic solvent, (ii) monomer concentration, (iii) monomer ratio, and (iv) polymerization time. Also, these factors may influence the transport properties or permeability of the membrane. Because the polycondensation reaction occurs on the organic side of the interface, the physical-chemical properties of the organic solvent will affect the characteristics of the polymer produced. Organic solvents that readily extract the diamine permit the formation of high molecular weight polymer. The presence of water dissolved in the organic solvent tends to hydrolyze the acid chloride, reducing its reactivity in the polycondensation reaction. The organic solvent also influences partitioning of the diamine, and the resultant shift in monomer ratios may affect the point at which polymer precipitates. Typically, studies reporting water-filled nylon microcapsules use an organic solvent of chloroform and cyclohexane in a 1:4 ratio, respectively. This solvent blend has a density similar to water, and the microcapsules remain dispersed homogeneously in the organic phase. Because of the similar phase densities, the microcapsules are prevented from creaming or settling and aggregation is minimized (3).

To date, there have been few systematic studies examining the influence of synthesis variables on the permeability of the polymer membranes used in microencapsulation. Many of the studies have simply reported on the release rates of solutes diffusing from microcapsules. Emphasis has centered on microcapsule characteristics such as size, polydispersity, and method of formation rather than on membrane properties. In the work reported here, polyamide membranes were produced by an interfacial polycondensation reaction between a diacid chloride in an organic solvent and a diamine in an aqueous solvent. Specifically, the reaction between sebacoyl chloride (SC) and hexamethylenediamine (HD) produces nylon 610 according to the following scheme:

$$\mathrm{NH_2(CH_2)_6NH_2 + ClOC(CH_2)_8COCl} \rightarrow$$
$$\mathrm{(-NHOC(CH_2)_8CONH(CH_2)_6NH-)_n + HCl}$$

It was the intention of this work to study permeability characteristics across nylon 610 films prepared by interfacial polycondensation, and test the hypothesis that membrane permeability is influenced by the above mentioned synthesis variables.

Therefore, the objectives of this research were to:

1. Measure permeability coefficients across polymer films rather than microcapsules;
2. Identify polymer synthesis variables that influence the permeability of nylon 610 films; and
3. Identify the transport mechanisms of a number of solutes across nylon 610 films.

A full factorial study design was conducted to examine the influence of three synthesis variables: organic solvent,

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monomer concentrations, and monomer ratio, on the transport properties of nylon films. Nylon 610 films were synthesized by an interfacial polycondensation reaction using HD in the water phase and SC in the organic phase. Because diamine partitioning between the water and organic phase can influence the polymer, a solvent blend was used to vary the partition coefficient without chemically changing the organic solvent. The organic phase selected was a solvent blend of chloroform and trichloro-trifluoroethane (Freon® TF) at ratios of 1:1, 1:4, and 4:1. HD partitions favorably into chloroform with a reported partition coefficient of 1.4; partitioning into Freon TF is less favorable (2). The monomer concentrations studied were 0.2, 0.4, and 0.6 M with respect to their appropriate phase. The monomer ratios resulting from this experimental design were 1:1, 3:1, and 1:3, even though a report (3) in the literature suggests that the monomer ratio is not significant if the diamine concentration is greater than the acid chloride concentration. These workers suggest that a 1:1 balance occurs at the interface and the precipitating power of the organic solvent is more important than the diamine partition coefficient.

The transport parameters of potassium chloride, hydrocortisone, and *m*-cresol were measured across the films as a function of the synthesis variables. KCl was selected because of its inability to partition into nylon 610, leaving porous diffusion as the only means of transport. *m*-Cresol was studied because of its ability to partition into, and diffuse through nylon 610. Because the polarity of hydrocortisone was intermediate between potassium chloride and *m*-cresol, its transport across the films was anticipated to occur by porous diffusion as well as partitioning into the polymer membrane.

C. MATERIALS

Hydrocortisone 98%, *m*-cresol 99%, sebacoyl chloride 99%, 1, 6 hexamethylenediamine 98%, and nylon 610 pellets were purchased from Aldrich (Milwaukee, WI). Chloroform HPLC grade was purchased from Fisher Scientific (Norcross, GA). The solvent 1,1,2-trichloro-1,2,2-trifluoroethane (Freon® 113) was a gift from Glaxo Research Institute, Research Triangle Park, NC. All chemicals were used as received.

D. METHODS

1. Film Synthesis

Forty five milliliters of water was pipetted gently onto 45 ml of the organic solvent contained in a square glass container, 6 × 6 × 4 cm. Care was taken to avoid emulsification of the two liquids. The HD was initially weighed and dissolved in water to make a 5 ml solution, whereas SC was weighed immediately before polymerization and made up to 5 ml with organic solvent. The HD and SC solutions were slowly injected simultaneously into the aqueous and organic phases, respectively, at a rate of about 20 ml/min. The initial film that formed at the interface between the aqueous and organic layers was discarded. Subsequent films were removed at intervals of 30 seconds from the interface and placed on the back of a petri dish which was submerged immediately in water. The films were then washed three times in ethanol, followed by three washings in double-distilled water. The films were stored in double-distilled water at 4°C until characterized with respect to molecular weight, porosity, thickness, residual organic solvent, and permeability to hydrocortisone and *m*-cresol.

2. Molecular Weight

Polymer molecular weight was determined by drying the films at 35°C under a vacuum of 23 cm Hg for 48 hours. The dried films were then dissolved in *m*-cresol by stirring at 300 RPM for five days to break up polymer aggregates. During this process, the polymer solution was protected from light by wrapping the container in aluminum foil. After five days, the solution was filtered through coarse-grade sintered glass to remove dust particles. Fifteen milliliters of solution were pipetted into a capillary viscometer, and the absolute viscosity of five dilutions measured. These values were compared to the absolute viscosity of the solvent (*m*-cresol) to determine the relative viscosity for each concentration at 25°C. The reduced viscosity, i.e., the relative viscosity divided by the polymer concentration, was plotted against polymer concentration, and the intrinsic viscosity determined by extrapolating to zero concentration. The viscosity average molecular weight of the polymer was determined from the intrinsic viscosity using the Mark-Houwink constants reported by Brandup and Immergut (1989), $a = 0.96$ and $K' = 1.35 \times 10^{-4}$ cm^3/g (4).

3. Available Porous Area for Transport

Film porosity was estimated by measuring the diffusion of potassium chloride across the films. Each hydrated film was secured by membrane clamps and placed between two diffusion cells thermostatted at 25°C. Solutions of 0.1 M and 0.001 M KCl were placed initially in the donor and receiver chambers, respectively, and a chloride ion-selective electrode was used to monitor the appearance of chloride ion in the receiver chamber. The available area for porous transport across the film, A_0, was estimated according to the following equation:

$$\ln\left(1 - \frac{2C_r}{C_o}\right) = \frac{-2DAKt}{Vh}\left(\frac{\epsilon}{\tau}\right) \tag{1}$$

where C_r is the concentration in the receiver chamber, C_o is the initial concentration in the donor chamber, D is the diffusion coefficient of KCl at 25°C (1.994×10^{-5} cm^2/s), V is the volume of each compartment, ϵ is the porosity, τ is the tortuosity, A is the exposed area, and h is the thickness of the membrane (5). All parameters in Equation 1 were known except ϵ and τ, which, taken together, is a dimensionless measure of membrane microstructure. Therefore, the available area for porous transport A_0 is equal to the total area, A, multiplied by this dimensionless factor (ϵ/τ).

4. Film Thickness

Film thickness was measured by scanning electron microscopy. A piece, approximately 1-cm^2 in area was cut from each film and dehydrated by soaking twice in 95% ethanol and twice in absolute ethanol. Complete dehydration with carbon dioxide as a transition fluid was achieved with a Samdri® pvt-3 critical point dryer (Rockville, MD). The films were placed in chambers containing liquid carbon dioxide, and the temperature and pressure were adjusted to achieve the critical point for carbon dioxide (temperature = −57°C, pressure = 5.2 bar). At the critical point, the pressure and temperature were reduced. After critical point drying, each film was mounted on a metal stub and the specimen stage was cooled to 0°C. The samples were sputter-coated with gold-palladium under argon gas with a Polaron Sputter Coater (Hatfield, PA) for 45 seconds at a voltage of 2.2 kV and a current of 18 mA. After coating, the samples were allowed to warm up to room temperature under a steam of argon gas to avoid water condensation. The resulting coat was estimated to be about 200 Å thick. The film thickness was measured with an Etec Autoscan (Hayward, CA) at a magnification of 2,000×. In subsequent experiments, sections of the films were cut and dehydrated in a graded series of ethanol-water solutions, followed by acetone. Dehydrated sections were embedded in Spurr's ultra-low viscosity resin. After curing, they were microtomed and mounted on grid plates. Film thickness and morphology was measured and observed with a Philips (Eindhoven, Netherlands) CM12 transmission electron microscope (TEM).

5. Residual Organic Solvent

The absence of residual organic solvent on the films was verified using a Perkin-Elmer Model 7 (Norwalk, CT) differential scanning calorimeter (DSC). Film samples (generally about 2 mg) were weighed on a Cahn Microbalance (Cerritos, CA) and sealed in aluminum pans. The temperature scans ranged from 25 to 250°C at a heating rate of 10°C/min. All runs were made in a flowing, dry nitrogen atmosphere. The sample heat of fusion was calculated from the area under the curve of the endotherm.

6. Partition Coefficient

Partition coefficients of hydrocortisone and *m*-cresol were measured between nylon 610 and water. A stirred aqueous solution of the solute, thermostatted at 25°C, was connected to a UV detector at the λmax for each solute. The volume of nylon 610 pellets was measured by displacement in methanol, following which the pellets were placed in a known concentration of solvent. Solute disappearance from the aqueous phase was monitored as a function of time. Subsequently, the nylon pellets were separated, rinsed with double distilled water, and placed in a known volume of double distilled water. Desorption was determined by monitoring the appearance of the solute in water. The initial rate constants for the sorption and desorption data were obtained with a nonlinear least-squares regression estimation program (MINSQ®). The partition coefficient was estimated from the ratio of these initial rate constants. The rationale behind this pulse-chase experiment for partition measurement is that an equilibrium constant is a ratio of rate constants for forward and reverse physical or chemical processes.

7. Membrane Permeability

The permeability of the films to hydrocortisone and *m*-cresol was measured independently. The hydrated films were mounted in membrane clamps. A hydrocortisone solution of known concentration and double-distilled water were poured initially into the donor and receiver chambers, respectively. One-ml samples were withdrawn at appropriate intervals and replaced with fresh medium. Hydrocortisone concentrations were measured with a reverse-phase HPLC assay. The mobile phase consisted of 45:55 (v/v) acetronitrile:water mixture. A Spectra Physics IsoChrom LC pump controlled the mobile phase flow rate at 1.5 ml/min. The analytical column was an Alltech (Deerfield, IL) octadecylsilane 10-μm particle size column. Hydrocortisone was detected with a Kratos (Ramsey, NJ) Spectroflow 773 UV variable wavelength absorbance detector set at 242 nm. The chromatograms were integrated with PE Nelson software. The transport experiments for *m*-cresol were the same except a dilute aqueous solution (0.2 mg/ml) of *m*-cresol and double-distilled water were poured initially in the donor and receiver chambers, respectively, and *m*-cresol concentrations were monitored in the receiver chamber by a Shimadzu 2101PC UV spectrophotometer at a wavelength of 271 nm.

Amounts (Q) of solute appearing in the receiver chamber were recorded as a function of time and permeability coefficients were calculated according to Fick's first law:

$$Q = \frac{D_{app}AKD_{dt}}{h} \tag{2}$$

where D_{app} is the apparent diffusion coefficient, which contains information on the porosity and tortuosity of the membrane.

E. RESULTS

Three synthesis variables, namely (i) organic solvent, (ii) HD concentration, and (iii) SC concentration, were studied for their influence on four film parameters, namely polymer molecular weight, apparent area for transport, thickness, and permeability. A high and low value was selected for each variable, thereby limiting the number of polymer formulations studied to eight (2^3). This full factorial study design decreased the number of experiments required to identify the synthesis variables that influence polymer permeability.

Before the permeability experiments were conducted, the absence of residual organic solvent within the polymer films was verified. The presence of organic solvent residue remaining on the films from the synthesis reaction would alter the permeability data. Differential scanning calorimetry (DSC) was used to detect the endothermic peak of any residual organic solvent associated within the films. Figure 1 is a typical thermogram of a film synthesized with 20% Freon in the organic solvent. Immediately before the DSC run, the film was spiked with about 10-μl of chloroform. As shown in Figure 1, an endotherm appeared at about 30°C due to the associated chloroform, and an endotherm appeared at about 221°C corresponding to the melting temperature of nylon 610 (6). Therefore, a sample of film from each experiment was scanned from 0 to 50°C to verify the absence of the chloroform peak. These experiments confirmed that the washing

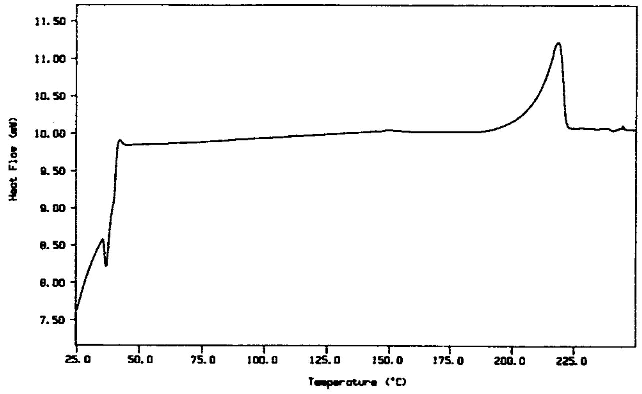

Fig. 1. DSC scan of nylon 610 film spiked with chloroform. The temperature ranged from 25 to 250°C at a heating rate of 10°C/minute. An endotherm appears at about 30°C and 221°C, which correspond to chloroform and nylon, respectively.

procedure was sufficient to eliminate residual organic solvent remaining on the films after film synthesis.

In order to inspect the data visually, separate three dimensional plots were constructed for each parameter. The parameter considered in Figure 2a is molecular weight. The x, y, and z axes are labeled SC, Freon, and HD, respectively for the three dimensional graphs considered. A significant molecular weight shift can be seen between the high and low Freon concentrations; a lesser shift is seen between the high and low concentrations of SC and HD. A similar analysis was seen with film thickness as the parameter considered (data not shown). As measured by SEM, the polymer films were thicker at low Freon concentrations.

The film porosity or apparent area available for porous diffusion was estimated from potassium chloride transport experiments. Potassium chloride was chosen because it will not partition into the membrane due to its ionic character. Ions of neutral salts can diffuse at different rates, but the potential between the two ions cause them to move at the same velocity (diffusion potential) and preserves electroneutrality (5). In order to minimize this potential, a 1:1 neutral salt with ions of similar mobilities, such as KCl, was chosen. A distinct difference in apparent area was observed, depending on the organic solvent used for film synthesis. As seen in Figure 2b, a greater area available for porous diffusion consistently resulted at low, compared to high, Freon concentrations for the organic solvent. This trend was not as significant in comparing the low and high concentrations of the monomers.

The three probe solutes to assess membrane permeability were potassium chloride and hydrocortisone, which diffuse through porous pathways in the membrane, and *m*-cresol, which both partitions into the membrane and diffuses through porous pathways. The permeability data for hydrocortisone and *m*-cresol exhibited similar variations as the porosity data with respect to Freon concentrations in the organic solvent.

Factorial design becomes a powerful technique when allied to analysis of variance (ANOVA), because an objective assessment of the relative importance of the factors and interactions can then be obtained. The molecular weight, porosity, and permeability data were analyzed according to the Yates algorithm for a full factorial study. From the algorithm, an ANOVA table was constructed, and an F statistic was calculated for each factor or interaction. A factor is significant at $p < 0.05$ if the F statistic is greater than 18.5. The factor that was significant consistently was the Freon concentration in the organic solvent during synthesis (Table I).

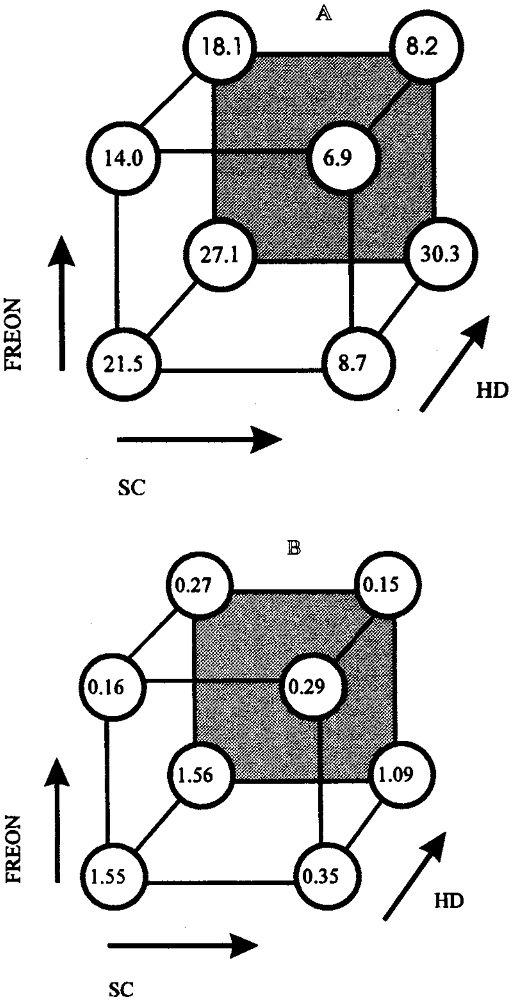

Fig. 2. Three dimensional plot of the synthesis variables influence on (A) viscosity average molecular weight × 10^{-3}, and (B) apparent area available for porous transport of the polymer films.

From the above analysis, a series of experiments was designed to maintain the HD to SC concentrations constant at 0.6 to 0.2 M, respectively, while varying the Freon concentrations in the organic solvent at 20, 35, 50, 65, and 80%.

Table I. Calculated F Statistic for Freon Concentration of Each Factor Considered

Factor	F-statistic
Apparent area for diffusion	59.6
Molecular weight	29.5
Film thickness	18.5
Hydrocortisone permeability	201
m-cresol permeability	10.1

In order to eliminate polymerization time as a variable, the films in these experiments were removed from the interface at exactly 15-second intervals in contrast to the previous experiments where the films were removed within 30-second intervals. Polymer morphology was observed with transmission electron microscopy (TEM) using cross sections of the films embedded in resin.

In Figure 3, the polymer molecular weight is plotted as a function of percent Freon used in the organic phase during film synthesis. An inverse relationship existed between Freon concentration and molecular weight, suggesting that the polymer molecular weight was influenced by the organic solvent used for interfacial polycondensation. An inverse relationship also was noted between film thickness and percent Freon in the organic phase (Figure 4). The focus of this research was to determine if the permeability of the films was influenced by the synthesis variables. Therefore, the permeability data for potassium chloride, hydrocortisone, and *m*-cresol are plotted in Figure 5 as a function of Freon concentration in the organic solvent for film synthesis, and several mathematical models were fit to the apparent diffusion coefficient. A logarithmic relationship was found to best fit the data. The coefficients fall in the expected molecular weight order of KCl > *m*-cresol > hydrocortisone. However, of primary interest is the mechanism of transport across these films for each solute.

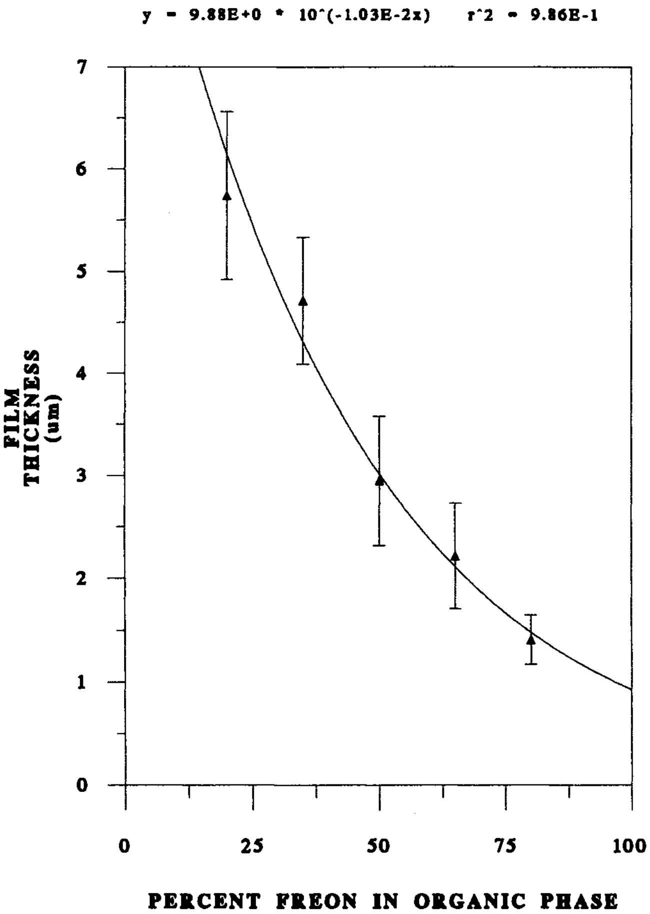

Fig. 4. Film thickness as measured by SEM as a function of percent Freon in the organic solvent and maintaining the monomer ratio constant for polymer synthesis.

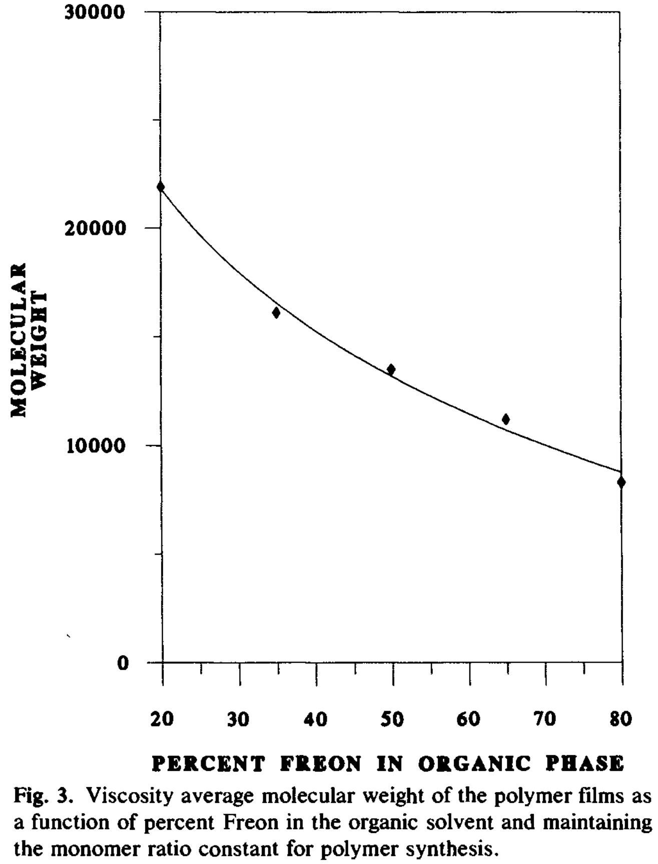

Fig. 3. Viscosity average molecular weight of the polymer films as a function of percent Freon in the organic solvent and maintaining the monomer ratio constant for polymer synthesis.

The data in Figure 5 were normalized by dividing each measured apparent diffusion coefficient by the diffusion coefficient of the solute in free solution. The diffusion coefficients for potassium chloride and hydrocortisone are reported in the literature (7,8), while that for *m*-cresol in water was calculated based on the Wilke-Chang Equation (9). This equation is a modified form of the Stokes-Einstein relationship, and was developed by measuring the diffusion coefficient of 25 organic compounds in water and then determining an expression that best fit the data. Thus:

$$D = \frac{7.4 \times 10^{-8} T \sqrt{\Phi M}}{\eta V^{0.6}} \tag{3}$$

where Φ is a dimensionless association factor for the solvent, M is the molecular mass of the solvent, η is the viscosity of the solvent, and V is the molar volume of the solute at its boiling point. The calculated diffusion coefficient for *m*-cresol in water at 25°C was 1.04×10^{-5} cm^2/s. The normalized data are plotted in Figure 6 as a function of percent Freon in the organic solvent. A best fit line was drawn through each data set along with the resulting equation. As in Figure 5, the apparent diffusion coefficients are in the expected molecular weight order at low Freon concentrations where the films were characterized with a high molecular weight, porosity, and film thickness. However, at higher Freon concentrations, where the molecular weight, porosity, and film thickness is less, *m*-cresol permeability exceeds that of potassium chloride. This suggests that for low porosity membranes, a partitioning pathway within the polymer be-

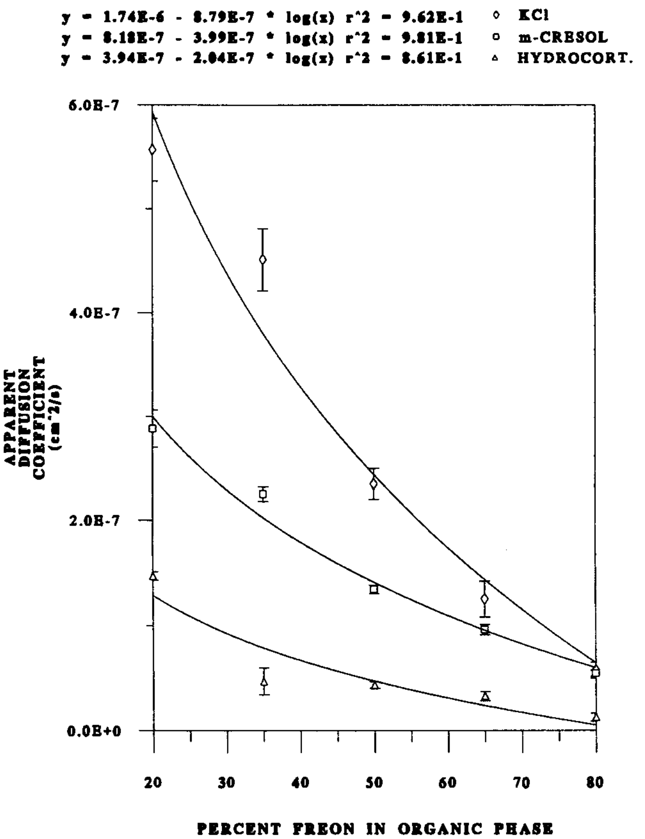

Fig. 5. Apparent diffusion coefficients of potassium chloride, hydrocortisone, and *m*-cresol across polymer films as a function of percent Freon in the organic solvent for film synthesis.

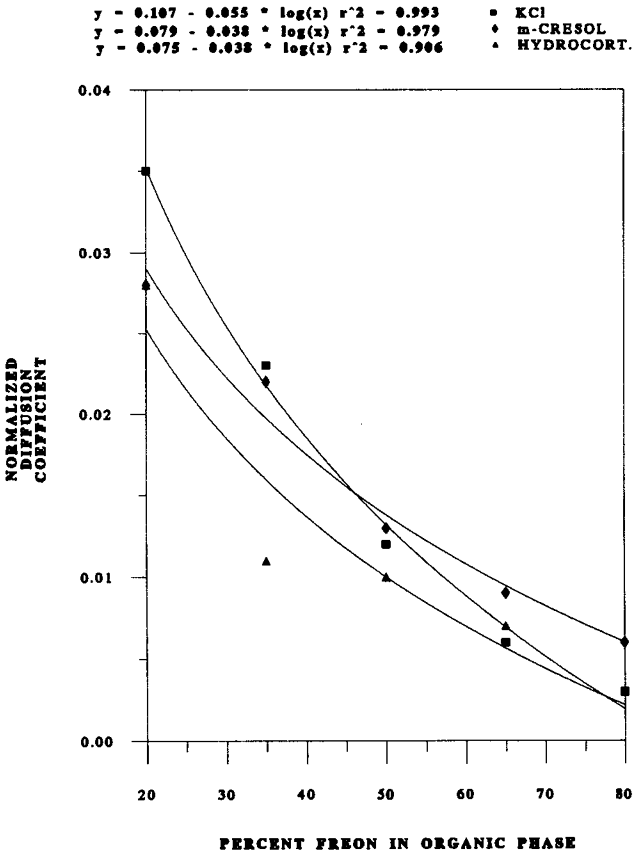

Fig. 6. The data from Figure were normalized by dividing the apparent diffusion coefficient by the diffusion coefficient of the solute in bulk solution. These values were plotted as a function of the percent Freon in the organic solvent for polymer film synthesis.

comes more predominant for *m*-cresol, and further confirms that organic solvents used for synthesis influence the permeability of the polymer films.

To confirm that *m*-cresol is able to partition into nylon 610, the partition coefficient of *m*-cresol between nylon 610 and water was measured. The rate for sorption of *m*-cresol into nylon 610 followed by desorption back into water is shown in Figure 7. The ratio of the initial rates for sorption and desorption was used to calculate an equilibrium partition coefficient between nylon 610 and water of 0.02. This value suggests that *m*-cresol is appreciably sorbed into nylon 610, as might be expected since it is a known solvent for the polymer. The same experimental protocol was followed for hydrocortisone to confirm that it did not partition into the membrane during the permeability experiments. The initial hydrocortisone concentration in water did not decrease even after 24 hours, suggesting that hydrocortisone does not significantly partition into nylon 610. This finding agreed with the permeability data in Figure 6, and strongly suggests that the predominant mode of hydrocortisone transport across nylon 610 films is via porous pathways.

More evidence that polymer structure is influenced by the organic solvent is seen in the DSC thermograms of the polymer films synthesized using a graded series of Freon in chloroform solutions. An unusual endotherm appeared at about 130°C, for the films synthesized at high Freon concentrations in the organic solvent (>50%). Using 50% Freon in the organic solvent, the DSC scans revealed two endotherms at about 130 and 221°C. However, as seen in Figure 8, at 65 and 80% Freon, only one endotherm appeared at the low temperature. This low temperature endotherm coincides with the low molecular weight polymer synthesized at 65 and 80% Freon in the organic solvent (Figure 3). Other investigators (10) have reported a similar endotherm in polyamide membranes. Although its origin was not identified.

Typically, if two endotherms appear on the same scan, this may indicate that the higher temperature endotherm is due to ultimate melting of polymer and reorganization during the experiment (11,12). As the temperature increases during the experiment, the polymer rearranges to a more stable form or crystal giving a high temperature endotherm (13,14). In effect, the polymer is annealed during the DSC experiment, resulting in more stable crystals than then melt at higher temperatures, and therefore recrystallize less readily.

This argument is consistent with the DSC scans showing two endotherms; however, the films synthesized with 65 and 80% Freon only exhibit the low temperature endotherm. Therefore, to verify that only one endotherm appears for the polymers synthesized with the high concentrations of Freon, the samples subjected to DSC were first heated to 150°C, cooled back to 25°C, and run again in the manner of the original samples. Upon reheating the samples, the low temperature endotherm was the only peak that appeared. In contrast, the samples initially with two endotherms that

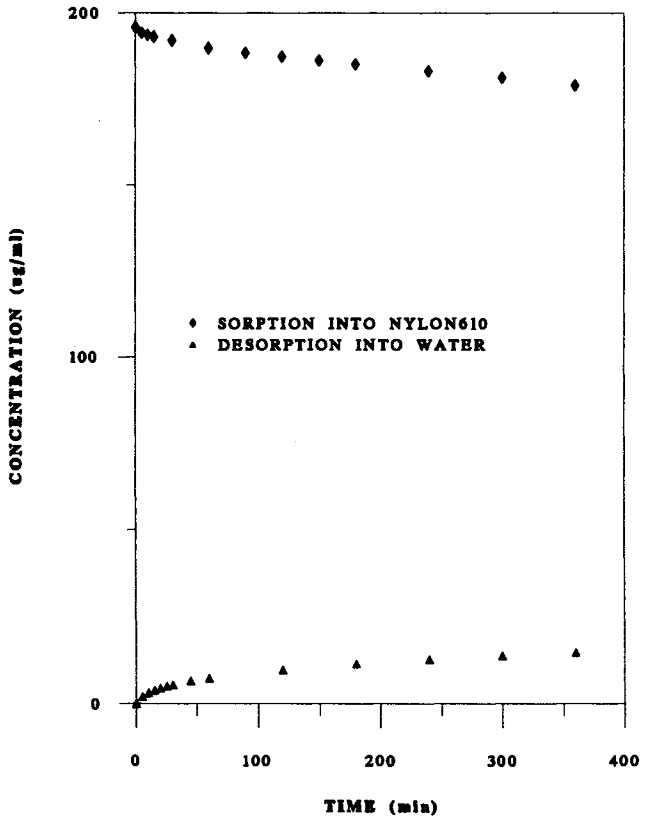

Fig. 7. Sorption of *m*-cresol from water into nylon 610 pellets and desorption from nylon 610 pellets back into water as a function of time. The initial rates for sorption and desorption were calculated from these data, and the ratio of initial rates were used to calculate the partition coefficient.

were reheated, only the high temperature endotherm appeared.

F. DISCUSSION

Several variables can influence the molecular weight, permeability, and thickness of polymer films synthesized by interfacial polycondensation. These include: i) hydrolysis of the acid chloride, ii) monomer concentrations, and iii) solubility of the precipitating polymer in the organic solvent. The first variable, hydrolysis of the acid chloride, is due to the ability of water to diffuse through the membrane along with diamine molecules. If the diamine is significantly hydrated, then some water molecules can diffuse through the initial film with the diamine or may even be solubilized in the organic phase. If this occurs, then two competing reactions can take place during polymerization: i) polymerization between the acid chloride and diamine, and ii) a hydrolysis reaction between the acid chloride and water. Hydrolysis of acid chloride would occur according to the following scheme:

$$\text{R-COCl} + \text{H}_2\text{O} \rightarrow \text{RCO}_2\text{H} + \text{HCl} \qquad (3)$$

The hydrolysis product, the free acid, inhibits polymerization because, being less reactive than the acid chloride, it does not react at room temperature to produce a polymer. The hydrolysis reaction, will therefore decrease the average molecular weight, broaden the molecular weight distribution, and decrease film thickness.

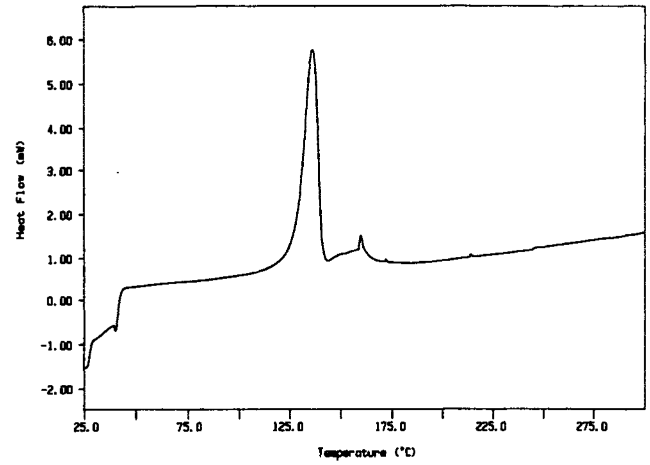

Fig. 8. DSC scan of nylon 610 film that was synthesized with 65% Freon in chloroform. The temperature ranged from 25 to 300°C at a heating rate of 10° C/minute. Only one endotherm appears at about 130°C. The same endotherm appeared for the films synthesized with 80% Freon in chloroform.

The second variable considered above is the monomer concentration. One condition reported to influence polymerization conditions is the ratio of diamine to acid chloride concentrations (2). These investigators determined an optimum reactant ratio by measuring the intrinsic viscosity, molecular weight, of the polymer while keeping the diamine concentration constant and varying the acid chloride concentration. Based on Figure 8 of the reference, the greatest intrinsic viscosity always is achieved when the diamine concentration is greater than the acid chloride concentration. As the acid chloride concentration exceeds the diamine concentration, the intrinsic viscosity gradually decreases. This is reported to result from the fact that diffusion of acid chloride can occur only up to the interface because of the extremely low solubility of sebacoyl chloride in water. The increased acid chloride concentration increases the concentration gradient and restricts the volume of the polycondensation zone (2). As long as the diamine concentration exceeds that of the acid chloride, the intrinsic viscosity does not change appreciably. The diamine is not restricted to the aqueous phase and partitions into the organic phase. However, diamine partitioning is self-limiting, because as diamine partitions into the organic phase, polymerization immediately results in the formation of a polymer membrane. This polymer membrane acts as a barrier for further diamine partitioning, and as film thickness increases, the greater this barrier becomes.

Similarly, an empirical model relating interfacial polycondensation conditions to membrane thickness suggested that the square root of the diamine concentration is proportional to membrane thickness (15). If membrane thickness is proportional to polymer molecular weight as shown in Figures 3 and 4, then the empirical model developed by Poncelet (15) would agree with the data from Morgan and Kwolek (2). As the diamine concentration increased, film thickness would increase but, at some point tend to plateau because of the square root relationship. This reasoning was further justification for using a fixed reactant concentration ratio of 1:3

SC to HD in the latter set of experiments, where a graded series of Freon in chloroform solutions were used as the organic phase.

The third variable considered is the physicochemical properties of the organic solvent; specifically, the solubility of the polymer in the organic solvent because the product of the polymerization reaction precipitates from the organic phase. Solvent blends of chloroform and Freon were chosen because nylon 610 precipitates as high molecular weight polymer films from chloroform, and polymer strands when the organic solvent is Freon.

The morphology of the films can help explain differences in molecular weight, film thickness, and permeability produced by the use of low and high Freon concentrations in the organic solvent during synthesis. Films made with 20% Freon (Figure 9A) reveal distinct bubbles towards the organic side, while the aqueous side is relatively flat and smooth. From the smooth (aqueous) side of the film to the point at which bubble formation begins is thought to be the thickness of the initial film during polymerization, while bubble formation is reported to be due to diamine diffusion across the film, resulting in further polymerization (16). The films made at high Freon concentrations from the aqueous to organic side (Figure 9B) consistently had a greater proportion of bubble formation compared to films made using lower Freon concentrations (Figure 9A). After initial formation, the film thickness increased only if one or both reactants were able to migrate through the initial film. Because sebacoyl chloride is insoluble in water and the diamine is the only migrating monomer, nylon 610 films grow towards the organic phase (10,17). The initial film is the immediate product of precipitation from the organic solvent, and the greater this initial film thickness, the greater the hindrance for diamine diffusion and further polymerization. Therefore, final film thickness is a function of polymer solubility in organic solvent, monomer concentrations, and initial film thickness.

A recent study by Poncelet (1990) attributed differences in film thickness to the neutral diamine partition constant, which varies with the diamine solubility in the organic solvent. Although this reasoning agrees with the experimental data shown in Figure 10 of the reference, the polymer is precipitating from the organic solvent and the physicochemical properties of the organic solvent influence the precipitation. We hypothesized that the polymer solubility in the organic phase influences the films characteristics during polymerization. The greater the solubility of the polymer in the organic solvent, the greater the molecular weight and film thickness achieved before precipitation. Chloroform is known to solubilize low molecular weight nylon 610 (2). This effect enhances the mobile lifetime of the polymer chains, delaying precipitation and permitting the formation of high molecular weight polymer films. The use of chloroform therefore results in the formation of high molecular weight, thick films. With increasing trichlorotrifluoroethane concentrations, the molecular weight and film thickness decrease implying that nylon 610 is less soluble in Freon. After an initial film precipitates from the organic phase, polymerization does not stop entirely but is decreased greatly in rate because the film is a barrier for diamine diffusion into the organic solvent. When the polymer initially precipitates, it is a relatively thick film of high molecular weight. For further polymerization to occur the diamine must cross this initial film. As a result, polymer forms as bubbles on the organic solvent side.

Studies employing x-ray diffraction have shown that the initial polymer chains synthesized via interfacial polycondensation are oriented perpendicular to the interface, and that, as further polymerization occurs, the polymer chains become disordered (18). This polymer chain disorder, also referred to as secondary polymerization, increases the tortuosity of the pathways a molecule experiences if it were to diffuse across the film. As evidenced from Figure 9, there is more secondary polymer formation, as noted by bubble formation, for the films made with higher Freon concentrations. As noted from Figures 5 and 6, the films synthesized with higher Freon concentrations are relatively less permeable

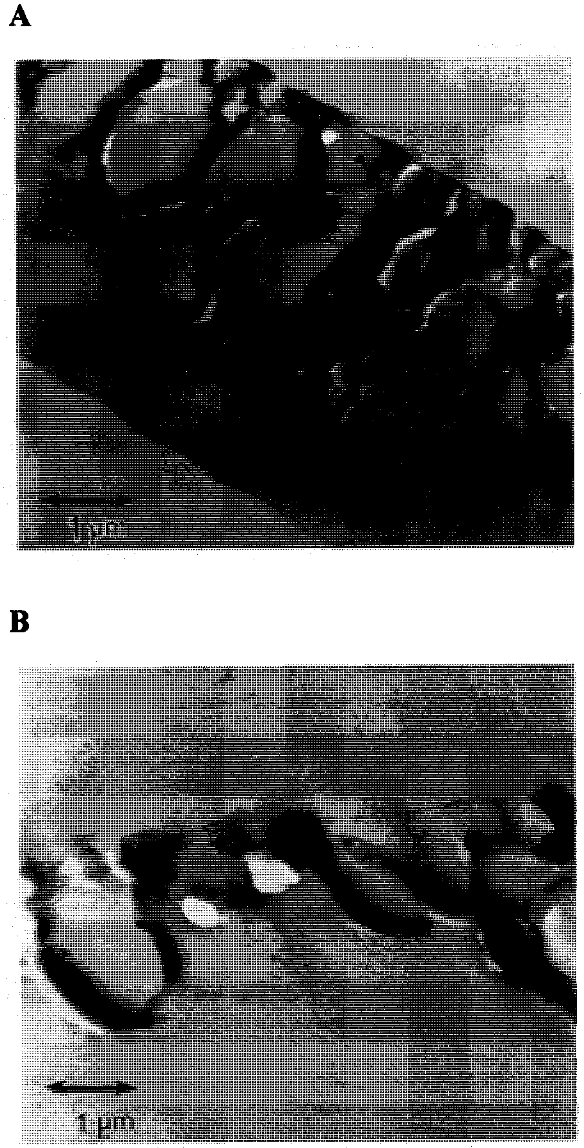

Fig. 9. TEM cross-sectional views of (A) a nylon 610 film polymerized with 20% Freon in the organic phase, and (B) a nylon 610 film polymerized with 80% Freon in the organic phase. The rough and smooth sides correspond to the organic and aqueous sides of the interface, respectively.

because of the added tortuosity from the secondary polymer formation on the organic solvent side of the membrane. In contrast to the films synthesized with 20% Freon in the organic solvent, these were more permeable films. The more permeable films were a thicker and relatively higher molecular weight polymer.

This reasoning agrees with the reported data. At low Freon concentrations the organic phase will hold the polymer in solution until a high molecular weight polymer is achieved. When the polymer precipitates from the organic phase, it is a relatively thick film, which acts as a barrier for diamine diffusion. The initial film thickness dictates the extent of further polymerization. Therefore, Figure 9A, lower Freon concentration, appears to have less secondary polymer formation because of the greater film thickness. This lack of secondary polymer formation leads to less tortuos, more permeable films. If secondary polymerization occurs to a greater degree as in Figure 9B, then bubbles on the organic solvent side of the film begin to appear and add to the tortuosity of the film. This added tortuosity lowers the membrane permeability by increasing the effective distance a molecule must travel to reach the receptor side of the diffusion cell.

G. CONCLUSIONS

This work sought to relate the interfacial polycondensation synthesis variables of nylon 610 to the permeability of the resulting membranes. The synthesis variables considered were monomer concentration, monomer ratio, and organic solvent. The factors used to assess these variables were polymer molecular weight, film thickness, and film permeability. From the full factorial designed experiments, the most significant variable that influenced the film's permeability was the organic solvent, so long as the diamine to acid chloride ratio was greater than one. Nylon 610 is more soluble in chloroform than Freon, and by using more chloroform than Freon in the organic phase during synthesis, the result was a relatively high molecular weight, less tortuos, thick membrane. These polymer characteristics can be controlled by the choice of the organic solvent. For molecules such as potassium chloride and hydrocortisone, which diffuse through porous pathways of nylon 610 films, an organic solvent similar to chloroform would result in greater flux across these films because of less tortuosity. In contrast, molecules such as *m*-cresol, which diffuse by partitioning into the membrane as well as using porous pathways, would exhibit greater flux through nylon 610 films synthesized in an organic solvent similar to Freon. Although interfacial polycondensation is a complex process, the choice of organic solvent plays a vital role in the polymer morphology and hence the transport characteristics.

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