

# Studies of the Water Permeability and Mechanical Properties of a Film Made of an Ethyl Cellulose–Ethanol–Water Ternary Mixture

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**ABSTRACT:** A water permeability study of ethyl cellulose (EC) film made from an EC–ethanol–water ternary mixture is presented. EC films were prepared by pouring the solution onto a polycarbonate plate and by spraying. The results reveal that the permeability of water, estimated by diffusion experiments, increases as the amount of the nonsolvent increases in the liquid–liquid demixing process. In addition, a relative decrease in the evaporation rate of ethanol compared to that of water following an increase in casting temperature or a higher EC concentration produces a membrane with lower permeability. A mechanical evaluation of the films is also presented. Addition of water to the solvent leads to decreases in the modulus of elasticity, stress, and elongation, due to changes in the morphology of the film. The surface of the film was visualized by SEM photomicrography. © 1999 John Wiley & Sons, Inc. *J Appl Polym Sci* 74: 2056–2062, 1999

**Key words:** ethyl cellulose; phase separation; water permeability; mechanical testing

## INTRODUCTION

Polymeric membranes have been used in a number of industrial areas for many years. One specific field of application involves their use as delayed- or sustained-release film in tablets. The release characteristics of film-coated formulations are strongly dependent on the properties of the film, such as water permeability and modulus of elasticity.<sup>1</sup> The porosity and pore size distribution of the film coat determine the permeability. Pores in a coating membrane can be produced in several ways. One method is to mix a water-soluble polymer, such as polyethylene glycol, with a water-insoluble polymer like ethyl cellulose (EC)<sup>2</sup> or to

use micronized sucrose as a pore-creating substance.<sup>3</sup> The most common method (although not used in the pharmaceutical industry) is to prepare a membrane using phase separation. Four main techniques are involved: thermally induced phase separation,<sup>4</sup> air-casting of a polymer solution,<sup>5</sup> precipitation from the vapor phase, and immersion precipitation.<sup>6</sup> Narisawa et al.<sup>7</sup> studied a coating layer prepared using an EC–ethanol–water ternary system. They studied how the density of the film was affected by changes in the composition of solvent (ethanol) and nonsolvent (water). The resulting pores were noncircular and tortuous.

As mentioned, the modulus of elasticity, and thereby the strength of a coating layer, is a very important factor. Increasing the porosity of a film by phase separation can affect the modulus of elasticity. An evaluation of mechanical behavior

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can be valuable in determining whether a film is capable of being used as a coating material, by coping with compression in the tablet manufacturing process, for example.

The mechanical and physical properties of EC films prepared using a pseudolatex coating system<sup>8</sup> or cast from ethanol solutions have been evaluated.<sup>9</sup> Arwidsson et al.<sup>10</sup> studied the mechanical properties on free EC films cast from organic solvents. They noted that if water was involved in the film-formation process, the film became porous and spongy, thereby reducing its mechanical strength. An understanding of the film process is very important to facilitate the development and production of controlled-release formulations. The main purpose of this work is to describe how water permeability and mechanical properties are affected by the use of different ethanol-water mixture solvents

## EXPERIMENTAL

### Materials

The viscosity grade of EC N10 (Ethocel® standard premium, ethoxy content 46–48%, viscosity 10 cP; Dow Chemical Co., U.S.) was used as received. Ethanol 99.5% v/v (AB Svensk Sprit, Sweden) and deionized water, purified by reverse osmosis (MAXIMA Ultra Pure Water; ELGA, U.K.), were used. Tritium-labelled water was purchased from Amersham, U.K.

### Preparation of Free Films

EC was dissolved in an ethanol-water solvent and stirred for 3 h. Ethanol acted as the solvent; water, as the nonsolvent. The free films were then prepared in one of two ways, either by spraying polymer solution on a rotating cylinder, as described previously by Allen,<sup>11</sup> at room temperature and 20% relative humidity, or using a casting method. In the casting procedure, the polymer solutions were poured onto a round polycarbonate plate, and the mold was placed in an incubator for at least 24 h. This method was chosen to produce pieces of film under varying temperature conditions.

The amounts of water and ethanol in the free film were then analyzed. The former was detected using the Karl-Fisher method; the latter was measured by gas chromatography (GC: HP 5890

with a Perkin-Elmer HS 40), with a detection limit of less than 0.1%.

### SEM Observation

A Jeol JSM-5400 scanning electron microscope was used to visualize the roughness and the morphology of the surface of the cast film. The polymer samples were coated with a thin layer of gold in a JFC-1100E (JEOL Ltd., Japan) ion sputtering device before observation.

### DSC Analysis

Small pieces of the cast film were cut out and put in an aluminum pot. The glass transition temperatures ( $T_g$ 's) were measured on a Mettler-Toledo TA 8000 differential scanning calorimeter by heating the film sample at a rate of 10°C/min. The temperature range evaluated was 25–200°C, and samples were tested at least twice to ensure reproducibility.

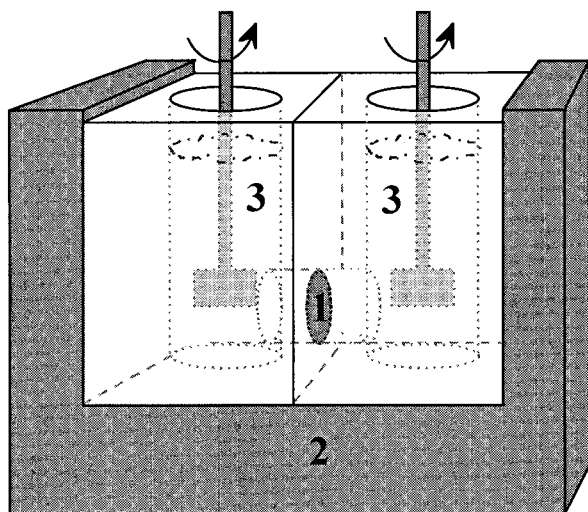
### Vapor Sorption Measurements

The evaporation rate was measured gravimetrically in SMS Ltd. dynamic vapor sorption equipment. The evaporation rate was determined at 25°C and at 50°C. Due to limitations in the apparatus, the maximum permissible temperature was 50°C.

### Permeation Measurements

The permeation experiment was performed using an Ussing chamber, depicted schematically in Figure 1. A circular film segment was cut out of the cast film, and the thickness was measured with a micrometer. The piece of film was then placed between the two cell compartments. At the beginning of each experiment, 15 mL of deionized water was added to both cell compartments simultaneously, to avoid any pressure on the membrane. After 15 min, a small amount of tritiated water (10  $\mu$ L, 400 kBq) was added to the donor compartment, and two paddles were used to stir the water at a speed of 200 rpm. A water jacket containing 37°C water maintained the temperature throughout the experiment.

Samples of 500  $\mu$ L were taken from the receiver compartment at specified time intervals and replaced by the same amount of pure distilled water. The water was weighed and analyzed in a Wallac Win Spectral model 1414 liquid scintillator counter.



**Figure 1** Ussing chamber: (1) free film, (2) water jacket (37°C), (3) donor and receiver compartments.

The increase in tritium activity in the receiver compartment was divided by the tritium activity per unit volume in the donor cell. As the tritium activity in the donor compartment is much higher than in the receiver, the counterdiffusion of tritium was not taken into account.

The effects of sprayed and cast films on permeation were also compared. Sprayed films are, naturally, more realistic in comparison with the coating conditions in pharmaceutical applications, but, when fundamental properties are studied, it is often more convenient to cast the polymer solution. According to Aulton,<sup>12</sup> casting is a better means of obtaining accurate data on polymer properties.

### Designed Evaluation

To obtain a better understanding of the change in the permeability properties of the film due to changes in solvent mixture and evaporation temperatures, a designed experiment was carried out. The factors studied and the levels chosen are shown in Table I. The levels were chosen to reflect realistic ranges for industrial applications. If the polymer content is too high, the resulting viscosity will lead to problems with the coating process. Increasing the amount of water results in a membrane with mechanical properties of no interest. The relative air humidity was kept constant at approximately 25%. A simplex-centroid design augmented with three interior points was used, as shown in Figure 2. Nine experiments at an evaporation temperature of 22°C were performed,

**Table I** Levels of Factors Used in the Designed Evaluation

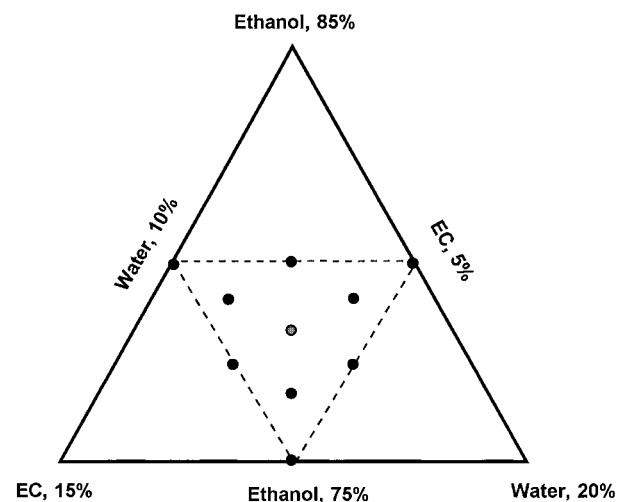
Factor	Level		
	-1	0	1
Ethanol (w%)	0.75	0.775	0.80
Ethyl cellulose (w%)	0.05	0.075	0.10
Water (w%)	0.10	0.0125	0.15

at all points apart from the center point. To obtain an estimation of the pure error, three experiments were repeated at the center point. A total of 12 experiments were conducted. The response measured was the water permeability.

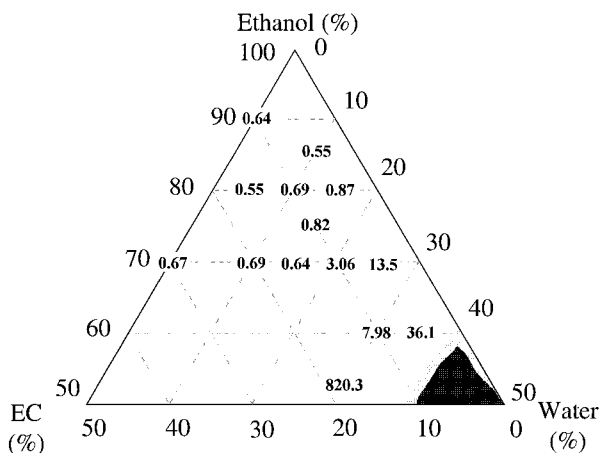
To evaluate the importance of temperature in the casting process, a study was conducted at an evaporation temperature of 54°C. The solvent mixture chosen comprises the three points shown in Figure 2 at the corners of the triangle. Two or more experiments were carried out at each point.

### Mechanical Evaluation

The mechanical characterization of the films was performed on a Hounsfield H2000 tensile apparatus using a 200 N load cell. Samples 80 mm long and 10 mm wide were cut from the free film produced by spraying. A sharp knife was used to avoid any jagged edges, and the films were examined visually. Film thickness was measured at various points using a micrometer, and the mean thickness was used for the computation of me-



**Figure 2** A simplex-centroid design augmented with three interior points and one center point.



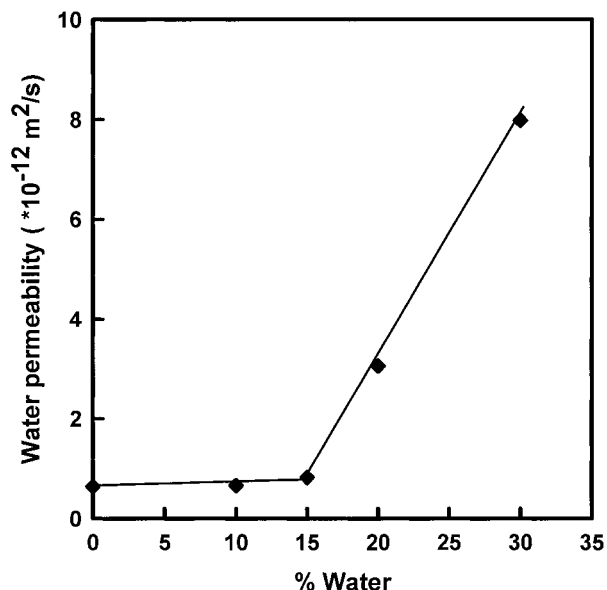
**Figure 3** Triangular phase diagram at 22°C. The bold figures represent water permeability ( $\times 10^{-12}$  m<sup>2</sup>/s).

chanical properties. The initial gauge length was 40 mm, and the measuring speed was 4 mm/min (i.e., 10% per min). Eight or more parallel measurements were made on each film. The load and the extension were recorded during the test. Stress at break was then calculated as the maximum load divided by the cross-sectional area of the sample, and the elongation at break was determined as the change in length at failure divided by the original length. Finally, the modulus of elasticity was computed from the slope of the linear elastic deformation on the load-time profile.

## RESULTS AND DISCUSSION

The amount of water in the free film studied using the Karl-Fisher method was less than 1–2% by weight, and no significant differences were observed between films produced from different solvents. No ethanol could be detected by GC headspace.

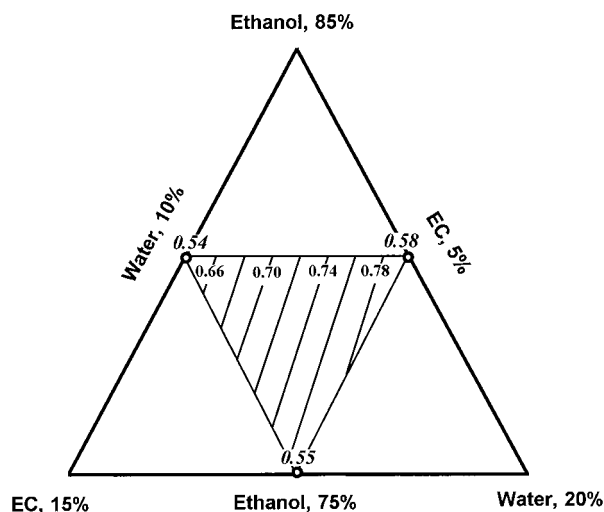
Measuring the  $T_g$  of EC is difficult. The signal is weak and broad, due to the nature of the polymer chains. The distribution of ethyl groups is probably not heterogeneous, and the molecular weight distribution is far larger than that of many synthetic polymers. This results in a polymer with a broad transition interval. The results give a  $T_g$  of  $124 \pm 1^\circ\text{C}$ . Entwisle and Rowe<sup>13</sup> reported the  $T_g$  of pure EC as  $129^\circ\text{C}$ . The discrepancy between these results can be explained by such factors as heat transmission, humidity, and



**Figure 4** Effect of water content in the solution on film permeability.

sample size. The important result of this study was the observation that there was no discrepancy between the  $T_g$ 's of films obtained from different solvent mixtures. Using DSC, the crystallinity of the films can also be investigated, but no crystallinity was determined in these films.

All of these measurements indicate that the free film consists of pure EC, with perhaps a small amount of bonded water.



**Figure 5** Response surface showing the water permeability ( $\times 10^{-12}$  m<sup>2</sup>/s) at 22°C. The corners (○) show the water permeability at 54°C.

**Table II Rate of Evaporation**

Solution	Evaporation Rate (mg/min)	
	25°C	50°C
Water	0.25	0.63
Water, 10% EC	0.24	0.63
Ethanol	0.74	1.80
Ethanol, 10% EC	0.66	1.72

### Water Permeability

Figure 3 is a phase diagram for the EC–ethanol–water system at room temperature (22°C). The bold figures in the triangle represent the water permeability of a free film made from the solvent mixture represented by the position of the numbers. As can be seen, water permeability increases as the amount of water in the mixture increases. The film-forming process is naturally the main reason for this result. The evaporation rate of water is far lower than that of ethanol, and the mixture goes through a gel phase prior to the formation of a film. This gel phase occurs just before the two-phase area, shown in Figure 3 as a gray scale. This gel phase probably determines the geometrical formation (e.g., pore size and pore structure) of the film and thereby the water permeability. Figure 4 reveals that a drastic increase in water permeability occurs when the amount of water in the solvent is greater than 15% by weight.

The divergence in the water permeability between sprayed and cast film was no more than 5% for films obtained from a polymer solution with a water content of up to 15% w/w. The discrepancy increased somewhat as the amount of water in-

**Table III Composition of the Polymer Solutions Prepared for Mechanical Properties<sup>a</sup>**

Film	EC 10 cps	Ethanol (99.5%)	Water
E0	1.87	16.8	—
E1	1.87	15.0	1.87
E2	1.87	14.1	2.81
E3	1.87	13.1	3.75
E4	1.87	12.2	4.68
E5	1.87	11.2	5.61
E6	1.87	10.3	6.54

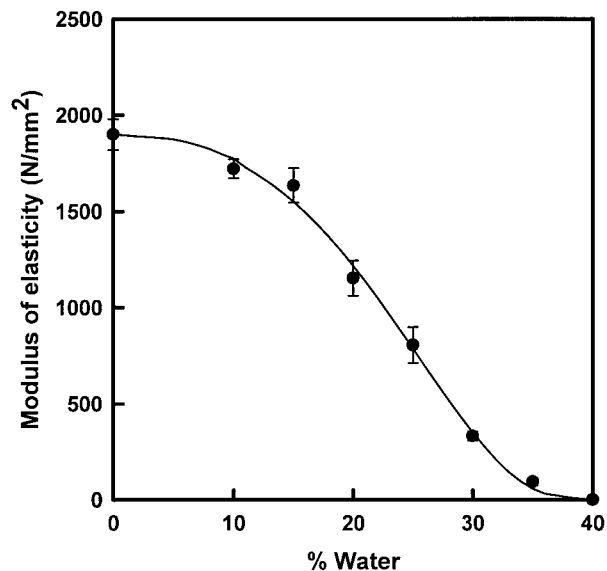
<sup>a</sup> Values expressed in g for each component.**Table IV Mechanical Properties of the Free Films**

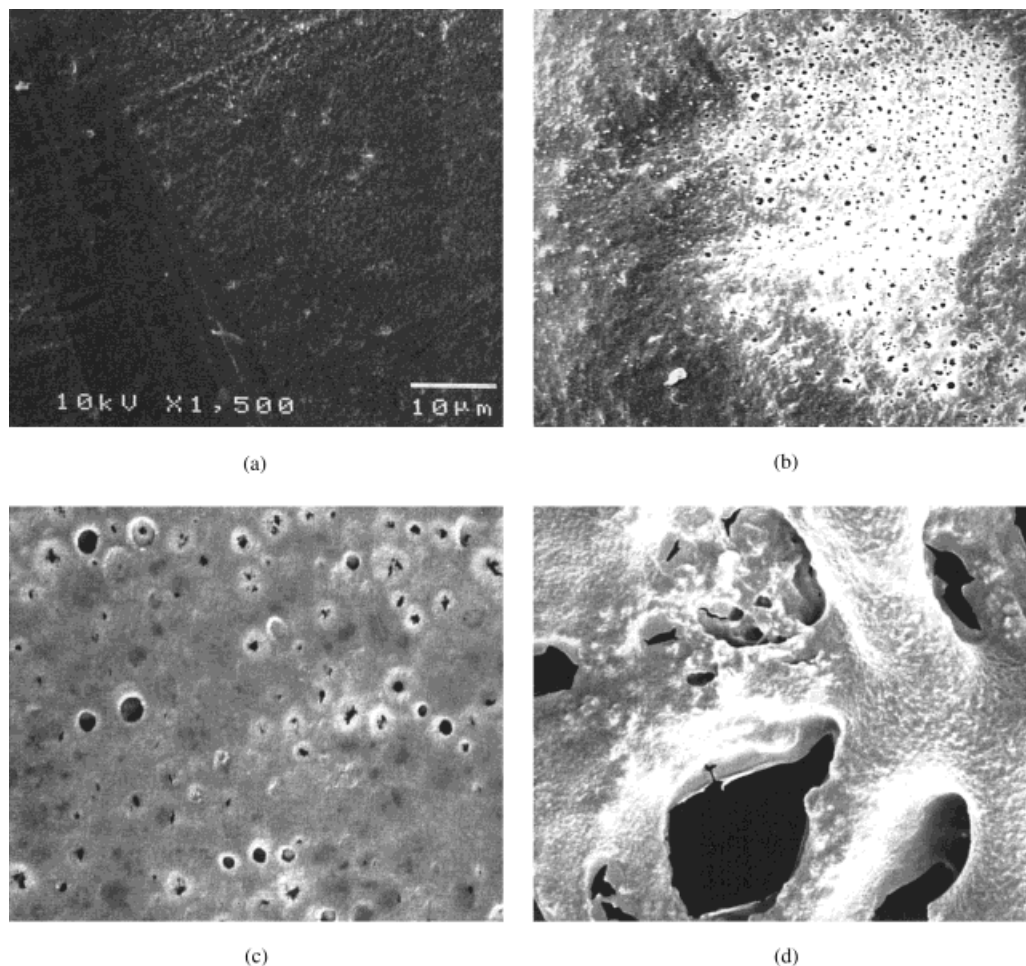
Film Composition	Stress at Break ± SD (N/mm <sup>2</sup> )	Elongation at Break ± SD (%)
E0	40.1 ± 1.2	1.69 ± 0.41
E1	39.6 ± 4.2	4.15 ± 1.81
E2	31.9 ± 3.8	0.97 ± 0.19
E3	27.1 ± 2.1	1.41 ± 0.20
E4	13.4 ± 1.2	0.88 ± 0.14
E5	3.9 ± 0.7	0.61 ± 0.14
E6	0.7 ± 0.2	0.10 ± 0.02

creased. However, in this case cast films are an acceptable alternative to sprayed films.

### Designed Evaluation

Figure 5 summarizes the water permeability results from the mixture design. To evaluate the design, the Modde program, version 3.0, was used. The calculation produced an R<sup>2</sup> value of around 0.80, indicating that the empirical model used to describe the result is fairly good. The Q<sup>2</sup> value was only 0.4, indicating that the model cannot be used to predict the water permeability for this region. The statistical basis for this calculation needs more information to increase the Q<sup>2</sup> value. However, the result leads us to conclude that the amount of water is the most important

**Figure 6** Effect of water content in the solution on film modulus of elasticity.



**Figure 7.** SEM micrographs of (A) film E0, (B) film E2, (C) film E3, and (D) film E5.

factor. When the amount of water is increased, the permeability increases.

The effect of casting temperature is illustrated in Figure 5. The circle and numbers in the corners of the triangle in the figure represent the water permeability of a cast film at a temperature of 54°C. As can be seen, the permeability decreased from around  $0.7$  to  $0.55 \times 10^{-12} \text{ m}^2/\text{s}$  when the casting temperature increased. This is due to changes in the rate of evaporation, as given in Table II. This phenomenon is probably due to more effective EC-ethanol interaction at higher temperatures. The ratio of ethanol/water evaporation is decreased by increasing temperature, as reported by Narisawa et al.<sup>14</sup> Because the ratio is decreased (or, in fact, water evaporation is more effective), the volume of the gel phase becomes smaller, thereby lowering the porosity and resulting in decreased permeability.

As shown in Figures 3 and 5, an increased EC concentration in the solution led to decreased water permeability of the film. As shown in Table II, an increase in EC concentration has a greater effect on ethanol evaporation than on water evaporation. The polymer interacts more with ethanol than with water. This causes greater water evaporation during the film-forming process, followed by a smaller volume of water in the gel phase. The reduced gel-phase volume results in a less-porous membrane, and thus decreased permeability. Gelation in the structuring process of a membrane has been a matter of concern in many studies.<sup>15-18</sup>

### Mechanical Properties

The mechanical properties (i.e., stress, elongation, and the modulus of elasticity) are also highly dependent on solvent composition. Table III lists

the polymer solutions used in the mechanical study. Table IV summarizes the results of the tensile testing. As shown, film strength and elongation both decrease as the amount of water in the solvent increases. This is also well illustrated in Figure 6, which shows the modulus of elasticity versus the amount of water. The SEM image in Figure 7 of the structure of E0, E2, E3, and E5 films clearly shows that solvent composition affects the microstructure formation. Note that the pores created are irregular in both shape and distribution. Because the films were prepared following the same procedure, the roughness and structure must be attributed to the nature of the spraying solution. The film becomes more porous as the water content increases. The film prepared from the E0 composition (pure ethanol solution) was transparent. As the amount of water was increased in the solution, the film became more opaque; the E5 film was white.

## CONCLUSIONS

The results of this study reveal that it is possible to modify the water permeability of a membrane using a phase-separation technique. However, changes in water permeability affect a film's mechanical properties. An increase in water, the nonsolvent, in a polymer solution leads to a higher pore content in the free film and also a reduction in the membrane's mechanical strength. SEM images of the surface show that the pores created are noncircular and tortuous. Evaluation of the evaporation rate reveals that when the ratio of ethanol/water evaporation decreases, membrane permeability also decreases.

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