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Cellophane For Kidney Dialysis*

D. W. MONK and E. WELLISCH, *Olin Corporation, Film Division, Pisgah Forest, North Carolina*

Synposis

A new cellophane has been developed for use as a membrane in artificial kidney dialysis. Modification of the standard viscose casting and regeneration conditions produced films having permeabilities highly competitive with the cellulosic membranes presently employed in kidney dialysis. These modified cellophanes have permeabilities superior to the European cuprammonium films for all molecular species investigated. The greater permeabilities were found to be due to a much increased swelling of these films resulting in a very small amount of cellulose which forms the barrier to molecular diffusion. These new cellophane structures also exhibit reasonable wet strength characteristics. The cellophane membranes offer the potential for obtaining a domestic membrane supply. This study indicates that although additional development work is required to produce a highly competitive membrane, these early results look extremely promising.

INTRODUCTION

Commercial cellophanes have been investigated previously as potential kidney dialysis membranes; and, in general, the permeability of cellophane has been found to be significantly lower than that of the cellulosic membranes presently used in kidney dialysis.[1–3] The regenerated cellulose membranes now in general use in artificial kidney treatments are produced in Europe using the cuprammonium process and are very permeable to the waste species removed from blood during dialysis. Cellophane films are produced by the viscose process and are designed as packaging films which are intended to serve as barriers to diffusion by moisture, gases, grease, etc. Consequently, cellophanes are produced with minimum rather than maximum porosity. Films produced by the cuprammonium process are inherently less ordered and much more permeable than commercial viscose cellophanes.[1,2]

A modified viscose cellophane having increased permeability could conceivably be produced; but the kidney membrane market is not sufficiently large to justify such a film's development and production.[4] The use of commercial cellophane as a kidney membrane material offers several significant advantages over cuprammonium films in that (a) cellophane membranes could be obtained from a domestic rather than European sup-

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plier, (b) a more-than-adequate supply would be available, and (c) viscose cellophane membranes could be produced at costs significantly less than the cuprammonium films. Evaluation of the available commerical cellophanes, as well as an investigation of the affect of some processing changes, should be useful information in considering cellophane as a competitor in the kidney dialysis market.

EXPERIMENTAL

To evaluate cellophane films as potential membranes, the dialysis permeabilities were determined for a single molecular species, NaCl. The permeabilities of the cellophane films were compared to the permeabilities of cuprammonium control films to determine the relative significance of the results. The more promising candidates were further evaluated for permeability to other materials, i.e., urea, uric acid, vitamin B_{12}, and albumin, and were again compared to cuprammonium film controls.

Dialysis Permeability Measurements

The dialysis permeability measurements were performed using 10 cm^3 continuous flow dialysis cells (Cole Palmer Cat. No. 6782-3). The effective membrane area of these cells was determined to be 10.1 cm^2. The retentate solution was pumped continuously using a Ministatic Pump (Manostat Corporation Cat. No. 72-894-21) at a flow rate of 70 cm^3/min. The sample side, although not circulated, was stirred using a 1 cm × 2 mm glass stirring bar and a magnetic stirrer.

Samples of the dialyzed solution were taken at 15-min intervals for 1 hr and the concentrations analyzed. Care was taken not to distend the membrane during sample addition and removal. Duplicate runs were made simultaneously using two matched dialysis cells; these results agreed to ±5%.

The permeabilities of various membranes were determined for NaCl, urea, uric acid, vitamin B_{12}, and albumin. The NaCl was dialyzed using a 0.2 wt-% solution and the concentrations analyzed by titrations with 0.01*N* $AgNO_3$. A 0.2 wt-% urea solution was employed for the urea permeability measurements and the concentrations analyzed colorimetrically. Uric acid solutions were analyzed spectrophotometrically (286 mμ), and a 0.25 mg-% solution was dialyzed. Vitamin B_{12} solutions were analyzed at 545 mμ, and 5 mg-% solutions were employed; bovine albumin solutions (0.1%) were analyzed at 297 mμ.

The permeability results were calculated according to the following relationship:

$$\ln C_0/C_t = \frac{PAt}{V}$$

where C_0 is the initial concentration of dialyzate, C_t is the concentration of dialyzate at time t, P is the dialysis permeability constant, A is the membrane area, and V is the volume inside of the dialysis cell. In practice, the logarithm (natural) of the concentration ratio is plotted against time and the slope determined. The permeability constant is obtained by

$$P = \frac{V}{A}\,(\text{slope})$$

for the cells used in this work $V = 10\ \text{cm}^3$ and $A = 10.1\ \text{cm}^2$.

Ultrafiltration Permeability Measurements

The ultrafiltration permeabilities were determined using a Gelman stainless-steel pressure filtration funnel (Gelman Instrument Company Cat. No. 4280). Pressures from 5 to 20 psi were employed, and a No. 1 Whatman filter paper disk was used to protect the membrane from the rough wire support screen. Readings were taken initially at a low pressure, then at a higher pressure, then once again at the lower pressure to ensure against leaks and pinholes. The ultrafiltration permeability was determined from the amount of water which permeates 1 cm^2 of membrane in 60 min at 100 mm of mercury pressure.

Gel Swelling Index Measurements

The gel swelling indexes were determined from the ratio of the weight of water-swollen film to the weight of dry cellophane as given below:

$$\text{gel swelling Index} = \text{GSI} = \frac{\text{weight of water wet film}}{\text{weight of dry film}} \times 100.$$

The gel swelling index was determined on both primary (never-dried) gel film and on secondary (previously dried and reswollen) gel film.

RESULTS

The sodium chloride dialysis permeability was determined for several commercial cellophanes having a thickness of 0.9×10^{-3} in. (32 g/m^2 unit weight) and compared to the permeability of a cuprammonium control film having the same thickness. These permeability results are given in Table I for both primary and secondary gel cellophanes. The data show, as anticipated, that cellophanes have permeability to sodium chloride that is well below that of the cuprammonium control film. Even the never-dried, primary gel cellophanes have permeabilities lower than the previously dried and reswollen cuprammonium kidney membrane.

The permeability of the cellophanes is seen in Table I as increasing with increasing gel swelling index. This relationship is given in Figure 1 and is not unexpected, since gel swelling index is a measure of base sheet accessibility, and it seems reasonable that a correlation be obtained between gel swelling index and dialysis permeability. The cuprammonium film shows a significantly higher permeability and a significantly lower gel swell-

TABLE I
Sodium Chloride Permeability of Various Commercial Cellophanes Compared to a Cuprammonium Control Film[a]

Sample	Membrane description	Gel swelling index		NaCl permeability $\times 10^3$, cm/min
		Primary	Secondary	
L12553A	cast cellophane	—	249	12.5
L12872A	cast cellophane	—	275	14.9
L28772B	cast cellophane	—	304	18.2
L12556	primary (never-dried) cellophane	404	—	16.5
L12553B	primary (never-dried) cellophane	433	—	19.2
L13810	cuprammonium control film	—	215	25.2

[a] Film thickness, 0.9×10^{-3} in.

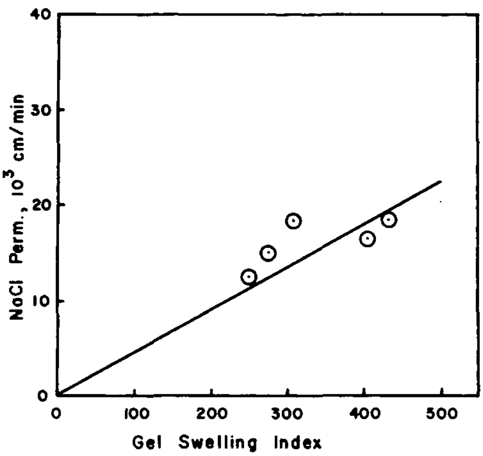

Fig. 1. Effect of gel swelling index of conventional cellophane films on sodium chloride permeability.

ing index, which point out the differences in film structure between viscose and cuprammonium-produced regenerated cellulose film. The cuprammonium film is less ordered and obviously more porous than films produced by the viscose process.[1,2]

The dialysis rates of several cellophanes were measured as a function of film thickness. The sodium chloride permeabilities of various gauge films are given in Table II and related to film thickness in Figure 2. These data imply that permeability increases and levels off as the film thickness decreases; even the thinnest film (0.6×10^{-3} in.) did not have a permeability comparable to the cuprammonium control. Considering the gel swelling data of Table II, which were not identical, the importance of film structure, which relates to the casting process, is indicated. Only at the same gauge

TABLE II
Sodium Chloride Permeability and Gel Swelling Index for Films of Different Gauges

Sample	Cast (dry) film thickness, mils	Secondary GSI	NaCl permeability $\times 10^3$, cm/min
L11333	1.4	275	10.5
L11335	1.4	277	12.2
L13835	1.2	291	16.6
L13834	1.0	264	18.8
L13830	1.0	299	19.7
M12887	0.9	284	19.9
N10889	0.6	263	19.0

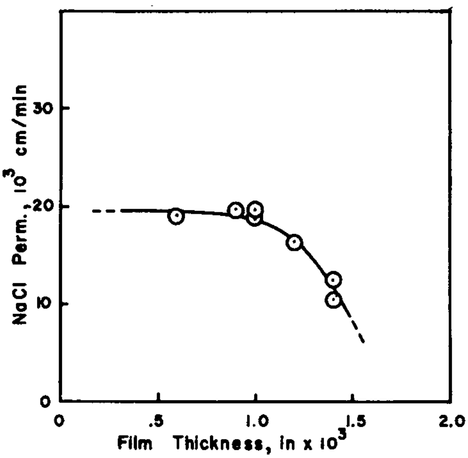

Fig. 2. Effect of film thickness on sodium chloride permeability for various cellophanes.

can gel swell variations be related to permeabilities since such variations again imply structural and processing differences.

Again, the permeability of commercial cellophanes, even very thin films, is considerably less than that of cuprammonium membranes; and, consequently, commercial cellophanes as they are currently produced are not adequately permeable to compete with the cuprammonium films as kidney membranes.

Influence of Increasing the Gel Swelling Index

Decreasing film thickness does not appear to be a reasonable approach to improving film permeability. However, the results of Table I suggest that increasing gel swelling index will lead to increased membrane porosity. The gel swelling index can be increased by several methods[5], however, modifying the regenerating conditions of the viscose was considered to be the least difficult and most effective.

Films were machine cast under various regenerating conditions and were evaluated for NaCl permeability. The permeability and gel swelling index

TABLE III
Gel Swelling Index and NaCl Permeability for Various Modified Cellophanes

Roll no.	Secondary GSI	NaCl permeability $\times 10^3$, cm/min
B834	339	15.7
32400	346	18.7
32403	381	20.3
B927	418	27.5
B932	433	29.4

data are given in Table III, and it is seen that the permeability increases with increasing gel swelling index. The films having the highest gel swelling indexes give NaCl permeabilities above that of the cuprammonium control film.

Permeability to Urea, Uric Acid, Vitamin B_{12}, and Albumin

The modified cellophanes which gave the highest permeability to NaCl were evaluated along with cuprammonium control films for permeability to other solute species. Table IV shows the permeability results, and the data indicate that several of these films have permeabilities comparable or superior to the cuprammonium control. The dialysis permeability of the best modified film to several molecular species is given in Table V compared to the cuprammonium film. The relationship between the permeability and solute molecular weight is given in Figure 3. These data show that this film has superior permeability to all molecular species investigated.

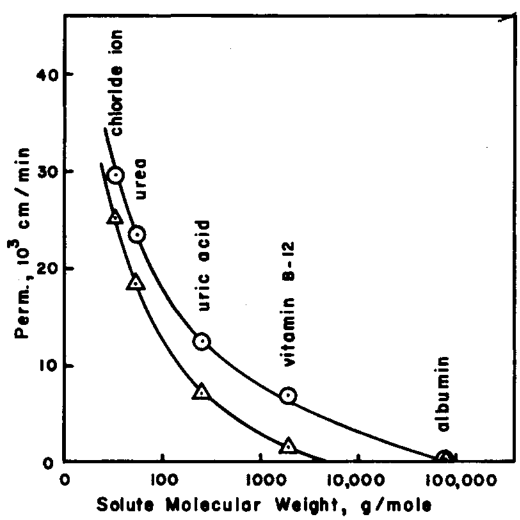

Fig. 3. Permeability of modified cellophane B-932 (⊙) and permeability of the cuprammonium control (△) for various solute species having increasing molecular weight.

TABLE IV
Permeability of Several Modified Cellophane Films

Roll no.	Film description	Permeability × 10^3, cm/min		
		NaCl	Urea	Uric acid
32400	modified cellophane	18.7	18.2	—
32403	modified cellophane	20.3	22.0	9.3
B927	modified cellophane	27.5	—	9.4
B932	modified cellophane	29.4	23.6	12.3
	cuprammonium control	25.2	18.7	7.3

TABLE V
Permeability of Cellophane Film B932 Compared to a Cuprammonium Control Film for Various Molecular Species

Solute	Solute molecular weight, g/mole	Permeability × 10^3, cm/min	
		B932	Cuprammonium film
Cl^-	35	29.4	25.2
Urea	60	23.6	18.7
Uric acid	168	12.3	7.3
Vitamin B_{12}	1355	7.3	1.5
Albumin	69000	0	0

Ultrafiltration Permeability

The ultrafiltration permeability was determined for several modified cellophanes and for the cuprammonium control film at several pressures; these results are given in Table VI. It is obvious from the results that the ultrafiltration permeability of the modified cellophanes is significantly greater than that measured for the cuprammonium film. The ultrafiltration permeability data also appear to relate to the processing conditions which affect the gel swelling index. These results indicate that by changing the processing conditions, both dialysis and ultrafiltration permeability can be controlled over a significant range.

TABLE VI
Ultrafiltration Permeability, Sodium Chloride Permeability, and Gel Swelling Index for.Several Modified Cellophanes and a Cuprammonium Control Film

Sample	Description	Ultrafiltration permeability, ml/cm²/hr/ 100 mm Hg	NaCl permeability 10^3, cm/min	Secondary GSI
B932	modified cellophane	0.232	29.4	433
B927	modified cellophane	0.078	27.5	418
34746	modified cellophane	0.043	19.7	339
	cuprammonium control	0.0097	25.2	—

DISCUSSION

The dialysis permeability of commercially produced cellophanes has been evaluated to determine if these films could compete with the permeabilities of the cuprammonium film presently used in kidney dialysis. No commercial cellophanes were found which had permeabilities comparable with the cuprammonium films. By modifying the casting process, films were produced having permeabilities highly competitive with cuprammonium membranes. The dialysis permeability to sodium chloride, urea, uric acid, and vitamin B_{12} was superior, and the ultrafiltration permeability was significantly higher for the modified cellophane compared to cuprammonium films.

The gel swelling index and dialysis permeability of these modified cellophanes were significantly higher than those of conventional cellophanes, and it was of interest to determine the factors which were most responsible for the increase in membrane permeability. Since the dialysis cells measure permeability through a given area of film surface, the quantity of cellulose which forms the membrane barrier should significantly influence the dialysis permeability From the plasticizer and moisture levels and film unit weight, the amount of cellulose in a given area of film can be determined; these results are given in Table VII and are shown plotted against the NaCl permeability in Figure 4.

The linear relationship given in Figure 4 indicates the importance of reducing the amount of cellulose per unit area of the film which forms the dialysis membrane. Other workers have evidently reached a similar conclusion since attempts have been made to achieve increased dialysis permeability by producing ultrathin cellulosic membranes.[6,7]

Since dialysis occurs through water-swollen membranes, the extent to which a film swells becomes important, and the relationship given in Figure 4 is not sufficient. Previously, workers have been concerned with limiting the swelling of films to reduce the wet thickness of membranes and achieve a thinner barrier and, consequently, improved permeability.[8] The important factor, however, appears to be the swelling in the plane of the film rather than in the thickness direction. Membranes which show maximum swelling or expansion in the plane of the film will contribute most to reducing the amount of cellulose per area of membrane surface.

TABLE VII
Amount of Cellulose per Square Meter and Sodium Chloride Permeability for Various Modified Cellophanes

Roll no.	Unit wt., g/m^2	Cellulose, g/m^2	NaCl permeability $\times 10^3$, cm/min
B834	39.6	29.9	15.7
32400	35.0	25.0	18.7
32403	36.0	22.6	20.3
B927	34.2	19.6	27.5
B932	25.4	14.4	29.4

TABLE VIII
Amount of Cellulose per Square Meter for Water-Swollen Modified Films

Roll no.	Cellulose, g/m² cast film	Expansion of film surface area on swelling, %	Cellulose, g/m² water-swollen film	NaCl permeability × 10³, cm/min
B834	28.8	15.8	24.9	15.7
32400	25.0	17.0	21.3	18.7
32403	22.6	16.6	19.3	20.3
B927	19.6	26.2	15.5	27.5
B932	14.4	32.1	10.9	29.4

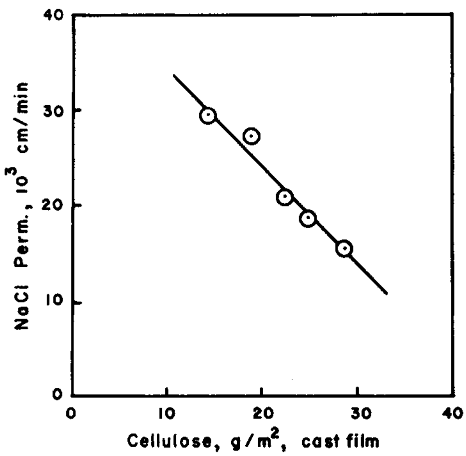

Fig. 4. Relationship between NaCl permeability and amount of cellulose per square meter for several cast, modified cellophanes.

The amount of swelling in surface area in water for each of the modified films was determined, and these data were used to calculate the amount of cellulose per square meter of wet, swollen gel membrane. These results are given in Table VIII, and the correlation between the NaCl permeability and the amount of cellulose in a square meter of water-swollen gel film is shown in Figure 5. The linear relationship again holds, and the significance of the density of the cellulosic barrier in determining dialysis permeability is readily seen. It is interesting to note that the film offering the highest permeability contains only 10.9 g cellulose per square meter of film after swelling, a very small quantity.

These results indicate that the important factor in achieving improved dialysis rates is the quantity of cellulose per unit surface area and not simply film thickness. The approach to achieving increased membrane permeability by producing ultrathin films[6,7] or producing films that swell less in the thickness direction[8] are logical, but they are not completely reasonable for cellulosic materials. Certainly, producing an ultrathin membrane will reduce the thickness or quantity of cellulose forming the membrane barrier;

TABLE IX
Gel Swelling Index and Expansion of Film in Surface Area for Modified Cellophanes and for Conventional Films

Sample	Secondary gel swelling index	Expansion in surface area, %
Modified cellophane	390–430	16–32
Conventional cellophane	260–300	3–14

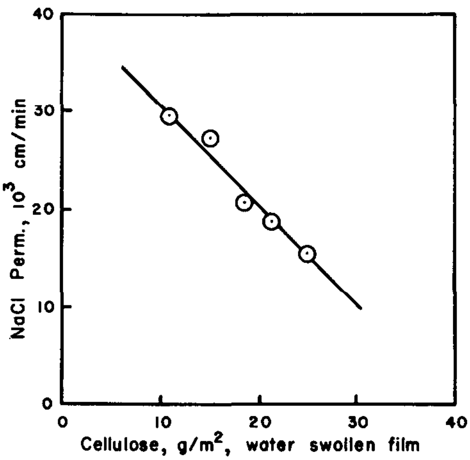

Fig. 5. Relationship between NaCl permeability and amount of cellulose per square meter for water-swollen, modified cellophanes.

however, the casting and general production of ultrathin films[6] is not practical. Also, cellulosic materials swell in water, and hindering this swelling to achieve a thinner water-saturated membrane is not reasonable since preventing swelling in either thickness or lateral direction produces a more dense (and less accessible) membrane. The modified viscose films achieve significant reductions in cellulose per unit surface area, which results in superior membrane permeabilities. A comparison between the gel swelling index and degree of swelling of modified and conventional cellophanes is given in Table IX, and the differences are obvious.

CONCLUSIONS

The films produced by the modified regeneration process appear to be highly competitive with the cuprammonium films imported from Europe. These films have permeabilities superior to the cuprammonium films for all of the molecular species investigated. The greater permeabilities were found to be due to a much increased swelling of these films resulting in a very small amount of cellulose which forms the barrier to molecular diffusion. These new cellophane structures also exhibit reasonable wet strength characteristics.

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