# Polyacrylonitrile-Reinforced Poly(vinyl alcohol) Membranes: Mechanical and Dialysis Performance

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**SYNOPSIS**

Membranes used for hemodialysis should have good mechanical strength to withstand the maximum transmembrane pressure. Although crosslinked poly(vinyl alcohol) membrane has superior permeability to solutes, its wet breaking strength is low. Mechanical strength, dry and wet, of membranes made from crosslinked blendmers of poly(vinyl alcohol) and polyacrylonitrile was investigated. The possibilities of these membranes for the application as dialysis membranes were evaluated by estimating its solute permeabilities. The optimum membrane selected shows permeability and mechanical properties comparable with the commercial regenerated cellulose membrane. Polyelectrolyte grafting made the membrane more blood-compatible. © 1995 John Wiley & Sons, Inc.

## INTRODUCTION

The vital part of the extracorporeal hemodialyzer is the semipermeable membrane that removes certain toxic substances from blood by diffusion. The important characteristics of dialysis membranes are the permeability properties, material biocompatibility, and mechanical integrity.[1] Regenerated cellulose membranes, currently being used on the largest scale in hemodialysis,[2] because of their good mechanical strength and solute permeability, are known to activate most strongly the complement system,[3] which results in transient leucopenia.[4] Complement activation can be reduced by modification of the cellulose surface with poly(ethylene glycol) (PEG), having terminal carboxyl groups.[5,6] Since permeability is directly related to the molecular weight of the solute, there is little selectivity in the filtering of closely related molecules through cellulosic membranes.[2,7] Therefore, novel membranes need to be developed with high selectivity.

Poly(vinyl alcohol) (PVA) is used as a basic material for a variety of biomedical applications, including contact lens material, skin-replacement material, reconstruction of vocal cords, and articular cartilage replacement. But its main disadvantage is its weak mechanical strength.[8] Efforts have also been made to use PVA membranes for artificial kidney applications,[9-11] as they have superior permeability characteristics and blood compatibility. Still, its application is limited due to lack of adequate wet breaking strength. With the proper composition of hydrophobic and hydrophilic regions, membranes with ample strength and permeability can be developed. Many studies have been carried out in this direction.[12,13] Inclusion of the hydrophilic group in the hydrophobic membrane structure by blending, copolymerization, or crosslinking induced by chemical reactions is reported for high selectivity toward water.[14-16]

We attempted to develop membranes based on PVA having wet breaking strength comparable to commercial regenerated cellulose membrane. In the present work, crosslinked blendmers of PVA and polyacrylonitrile (PAN) were prepared in various ratios and the membranes obtained were studied for their mechanical and permeability properties. Membranes containing PAN cause less activation of the complement during dialysis and were found to cause a reduction in dialysis-related symptoms.[17] The membrane with an optimum blend ratio is further modified by grafting syn-

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thetic polyelectrolyte and evaluated by its antithrombotic and permeability properties. Polyelectrolyte-grafted PVA–PAN membranes exhibit permeability, mechanical properties, and antithrombogenicity comparable with the commercial cellulose membrane.

## MATERIALS

Polyelectrolyte was synthesized in our laboratory from poly(*cis*-1,4-isoprene) (natural rubber) as per the standard procedure.[11,18] PVA (MW 125,000, 88% mol hydrolyzed, viscosity of 40 g/L aqueous sol. at 20°C, 35–50 cP, BDH Chemicals, No. 29791) and PAN (MW 150,000, cat. #3914, Polysciences Inc.) was used as obtained. Standard cellulose membrane (0.1 mm thickness, MW cutoff 6000) from Thomas Scientific, Swedesboro, USA, was used as the control. All other chemicals used were of AR grade.

## EXPERIMENTAL

### Preparation of Membranes

PVA (100 g/L) was dissolved in dimethyl sulfoxide. The desired amount of the PAN solution (30 g/L) was added and mixed well to obtain blends of different ratios. A sufficient amount of paraformaldehyde was added (for 1 g PVA, 1 g paraformaldehyde) and mixed well. Solutions were spread over a leveled glass plate and heated in a vacuum oven at 60°C for 48 h. Membranes were peeled off from the glass plate and soaked in NaOH solution (20 g/L) for 1 h and cleaned with distilled water. These membranes were of 0.1 mm thickness.

### Mechanical Properties

The tensile strength and elongation under dry and wet conditions were evaluated according to the method of ASTM D-882 by use of a universal test machine (Chatillon, UTSE-2) at a crosshead speed of 25 mm/min. Samples were cut into strips of 5 mm and a grip length of 25 mm was used. For testing the wet tensile strength, membranes were preswelled in distilled water (D.W.). Wet dimensions were used for the calculations.

### Degree of Swelling

The weight of completely dried samples of equal area were taken, and these samples were dipped in D.W. for equilibrium swelling. The degree of swelling was calculated from the relation

$$QW(\%) = [(X2 - X1)/X1] \times 100$$

where $X1$ is the weight of the dried samples, and $X2$, the weight of the swollen samples.

### Permeability Studies

An equilibrium-type dialysis cell (3784-D30, Arthur H. Thomas Co., USA) was used for determining the permeability properties of various molecules through the membrane at room temperature. The membrane was clamped between two compartments using a suitable supporting and sealing device. The volume of each chamber was 12 $cm^3$ and the effective membrane area was 12 $cm^2$. The upper compartment was filled with a mixture of solutes containing urea (1 g/L, MW 60), creatinine (0.1 g/L, MW 113), uric acid (0.1 g/L, MW 168), inulin (0.25 g/L, MW 5000), and albumin (1 g/L, MW 69,000) in 0.1*M* phosphate buffer, pH 7.4, or calf blood having urea (0.58 g/L) creatinine (0.0096 g/L) and albumin (32.7 g/L) and the lower compartment with phosphate buffer, pH 7.4. Dialysis was performed for 4 h, dialysates collected, and the permeability of solutes analyzed by noting the optical density, colorimetrically, employing a diacetyl monoxime reagent for urea,[19] an alkalic medium with picric acid for creatinine,[20] and a bromcresol green reagent for albumin.[21] The optical density (O.D.) is directly proportional to the concentration of the solute. The permeability percentages were calculated from triplicate experiments as

$$\text{Permeability}\ (\%) = \frac{\text{O.D. of solute in dialysate}}{\text{O.D. of solute in mixture or blood}} \times 100$$

### Octane Contact Angle

Here, the octane/water method was selected as a probe for investigating the polar interactions across the polymer/water interface.[22] Briefly, the preswelled substrates were completely immersed in triple-distilled water in a glass container. The goniometer (Kernco Instruments, El Paso, Texas, USA) was aligned and focused on the polymer–water interface and a drop of 0.1–0.2 $\mu$L of 99.99% pure *n*-octane was allowed to adhere to the interface. The apparent octane–polymer contact angle was measured immediately. At least 30 angles were measured

**Table I Characteristics of PVA–PAN Membranes**

| Sample | Degree of Swelling (%) | Tensile Strength ($MN/m^2$) | | Elongation (%) | |
|---|---|---|---|---|---|
| | | Dry | Wet | Dry | Wet |
| PVA | 95 | 40.22 ± 2.5 | 21.68 ± 2.1 | 255 ± 16 | 847 ± 31 |
| PVA–PAN (90 : 10) | 91 | 41.69 ± 2.9 | 34.72 ± 1.2 | 202 ± 15 | 404 ± 18 |
| PVA–PAN (87 : 13) | 91 | 41.79 ± 2.6 | 38.84 ± 2.1 | 142 ± 12 | 592 ± 21 |
| PVA–PAN (85 : 15) | 72 | 42.67 ± 1.9 | 37.37 ± 1.4 | 120 ± 10 | 474 ± 20 |
| PVA–PAN (83 : 17) | 74 | 44.24 ± 2.5 | 24.52 ± 1.5 | 112 ± 13 | 352 ± 18 |
| Cellulose | 49 | 42.86 ± 2.8 | 38.65 ± 1.1 | 61 ± 5 | 82 ± 4 |

on each surface, averaged, and expressed by their standard deviation.

### Polyelectrolyte Grafting

Polyelectrolyte (PE) was grafted onto the PVA–PAN membrane (87 : 13) by exposing it to 5 g/L aqueous solution of PE overnight, and the membranes were vacuum-dried and $Co^{60}$ $\gamma$-irradiated with a dosage of 0.275 Mrads in a nitrogen atmosphere.[23]

### Platelet Adhesion Studies

Calf platelets were isolated by centrifugation within 2 h after collection from citrated blood as described elsewhere[24] and washed with tyrode solution for the platelet-adhesion studies.[25] The number of platelets adhered onto the membranes were counted under an optical microscope in randomly selected fields. A total of 30 fields from triplicate experiments were counted, averaged, and expressed as the mean number of platelets adhered per square millimeter with standard deviation.

### Plasma Recalcification Time (PRT)

PRT was determined using the standard techniques of Austen and Rhymes.[26] Platelet-rich plasma was separated from citrated calf blood and tested for recalcification time under controlled pH (7.4) and temperature (37°C). Clean glass tubes were coated with PVA, PAN, and a PVA–PAN blend from their respective solutions, dried in a vacuum oven, rinsed with D.W., and vacuum-dried at 60°C for 4 h. Calf plasma 0.1 mL, was pipetted into these tubes containing 0.1 mL of 0.9% saline and thermostated at 37°C. After incubation of exactly 2 min, 0.1 mL of 0.25*M* $CaCl_2$ was added and the clotting time was registered. The test was repeated at least five times and the recalcification time expressed in seconds with the standard deviation.

### IR Spectra and Microscopy

The IR spectra of PVA, PAN, and PVA–PAN film (87 : 13) were recorded using an IR spectrophotometer (Perkin-Elmer, 597). The surface morphology of the PVA–PAN (87 : 13) membrane was observed using a scanning electron microscope (SEM, Hitachi, S-2400).

### Sterilization of the Membranes

Sterilization of the membranes were done by $Co^{60}$ $\gamma$-irradiation at a total dose of 2.5 Mrads or by autoclaving at a temperature of 121°C under 138 $kN/m^2$ pressure for 10 min.

## RESULTS AND DISCUSSION

The characteristics of membrane samples are shown in Table I. The degree of swelling is decreased with the increasing concentration of PAN. The swelling of hydrogel membranes is mainly due to its amorphous region.[27] Blending causes a decrease in the noncrystalline region, which decreases the swelling property of the membranes. In the dry state, tensile strength is only marginally increased, whereas elongation has decreased significantly with an increasing concentration of PAN. It is interesting to note that in the wet state the tensile strength increased when the concentration of PAN increased to 13% (PVA–PAN, 87 : 13), whereas a further increase in PAN content decreased the mechanical strength. As PAN content increases beyond 13%, segregation of PAN may take place, and in the swollen condition, this may hinder chain orientation along the stress direction and cause a decrease in wet mechanical strength. Hydrogel membranes which swell in an

**Table II Permeability[a] of Solutes Through PVA–PAN Membranes**

| Sample | Urea | Creatinine | Uric Acid | Insulin | Albumin |
|---|---|---|---|---|---|
| PVA | 61.8 ± 2.6 | 36.9 ± 1.0 | 24.9 ± 1.0 | 7.3 ± 0.5 | 1.5 ± 0.5 |
| PVA–PAN (90 : 10) | 61.7 ± 1.5 | 37.6 ± 1.5 | 22.1 ± 1.0 | 8.3 ± 0.5 | 2.9 ± 0.5 |
| PVA–PAN (87 : 13) | 56.6 ± 1.5 | 34.1 ± 2.0 | 19.2 ± 1.5 | 7.3 ± 1.0 | 1.8 ± 0.5 |
| PVA–PAN (85 : 15) | 56.6 ± 1.5 | 31.4 ± 1.5 | 17.5 ± 1.5 | 7.5 ± 0.5 | 1.5 ± 0.5 |
| PVA–PAN (83 : 17) | 51.2 ± 1.0 | 25.4 ± 1.5 | 14.6 ± 1.0 | 5.0 ± 0.5 | 0.8 ± 0.5 |
| Cellulose | 60.4 ± 1.0 | 35.9 ± 1.0 | 21.6 ± 1.5 | 8.8 ± 0.5 | 1.4 ± 0.5 |

[a] Permeability expressed as percentage passed.

aquous media would show poor mechanical strength in the swollen state. From the viewpoint of mechanical properties, hydrophobic polymers are preferable, being tough and tear-resistant.[28] It has been reported that inclusion of the hydrophilic group in the membrane structure decreases the mechanical strength[28]; conversely, inclusion of the hydrophobic group increases the mechanical strength.

Solute permeability of blended membranes from a mixture of different solutes are given in Table II. Solute permeability is reported as the percentage passed in 4 h as the comparative data. Cellulose membrane was used as a control. As the concentration of PAN increases, the permeability of all solutes decreased. Even though the blending significantly increased the mechanical properties, the decrease in the degree of hydration had a negative impact on the permeability. It is observed that the modification that increases the strength usually decreases the permeability and methods that improve the permeability degrade the mechanical property.[28] PAN is known to be a glassy polymer, and, in general, glassy polymers show low permeability. Based on the free-volume theory of diffusion, Yasuda et al. indicated that the diffusive permeability of solutes through hydrogel membranes is explained by the water content.[29,30] The permeation of water or water-soluble solutes is reported to be dependent on the degree of swelling of PVA films[31] and it is assumed that it diffuses only through the water phases in the water-swollen membranes. Here, also, it seems that permeability of solutes is directly proportional to the equilibrium water content of the blend membranes. However, the permeabilities of cellulose and PVA membranes for different solutes are close, while their degree of swelling varies significantly. Lee et al. reported different states of water in hydrogels, referred to as "bound water," "intermediate water," and "bulk water."[32] Water-soluble solutes are difficult to diffuse through intermediate water and even more difficult to diffuse through bound water.[33] It seems that the amount of bulk water allowing the diffusive permeation may be same in cellulose and PVA membranes. Cellulose membrane is considered to be a porous membrane with a molecular weight cutoff of 6000 and the primary action is that of a sieve.[2] Also, the total permeability may be due to separate contributions from "pore" and "solution–diffusion" mechanisms.[34] The permeability through the PVA membrane may be only through a diffusion mechanism.

Lee and Won reported that inclusion of the hydrophilic group in the PAN membrane structure enhanced its permeation flux to about 10 times that of homogeneous membrane.[35] We selected an optimum blend ratio of 87 : 13 (PVA : PAN) by making a compromise between the wet breaking strength and solute permeability. IR spectra of this membrane is depicted in Figure 1. The blended membrane showed all the characteristic peaks of PVA and PAN (O — H stretching # 3300–3200, C — N stretching # 2300–2200). However, the peaks related to PAN are weak because of their low PAN content. The position of all bands in PVA–PAN are the same as in the components. This is an indication that within the limitations of this technique little interaction

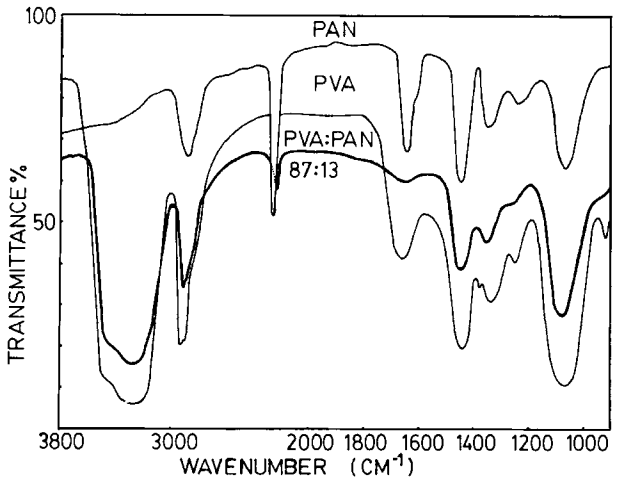


**Figure 1** IR spectra of (1) PVA, (2) PAN, and (3) PVA–PAN membrane (87 : 13).

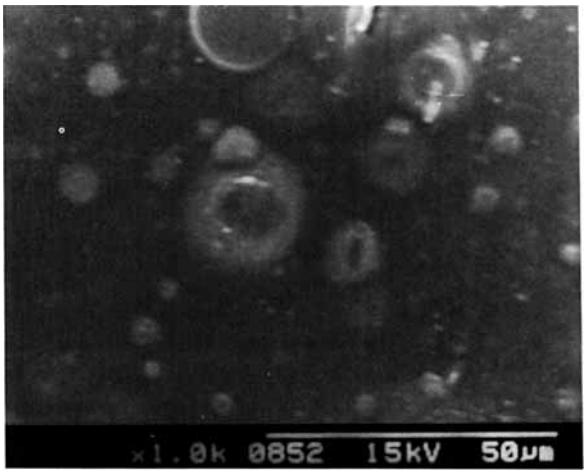


**Figure 2** SEM micrograph of PVA–PAN membrane (87 : 13).

between component polymers have taken place during blending. From the SEM study, it seems that the surface of PVA–PAN (87 : 13) is smooth and the blending is homogeneous. It shows no phase separation and it can be assumed that PAN is a finely dispersed filler which acts as a reinforcement. However, beyond 13% of PAN content, some segregation of PAN may take place. A typical micrograph of the PVA–PAN (87 : 13) membrane surface is shown in Figure 2.

From the octane contact angle data (Table III), it seems that as the concentration of PAN increases the membranes become comparatively hydrophobic. This could be related to the induced hydrophobic moeity of PAN. It is known that cell adhesion is greater on hydrophilic substrates compared to hydrophobic ones.[36] However, it seems that the adhesion of platelets (Table III) onto blended membranes are similar. Further, compared to bare PVA membrane, platelets seen on blended membranes are apparently reduced. The adhesion of blood cells to any substrate differs with the species of blood. Therefore, the results obtained with calf blood platelets cannot be compared with human blood cells in a quantitative way, when studies are directed toward the human hemodialysis problem. However, it can be taken as a relative measure in the pattern of adhesion to the membrane.

From plasma recalcification studies, it seems that there is no difference in the recalcification time for blended membrane surfaces compared to PVA. However, the PE-grafted surface showed a significant inhibition of plasma coagulation. Enhanced biological activity in terms of PRT has been achieved by heparinization of PVA.[37] The outstanding anticoagulant activity of heparin is attributed to the high concentration of sulfamate and carboxylate groups. PE also has sulfamate and caboxylate groups similar to heparin.[38] Compared to cellulose membrane, platelet adhesion onto PE-grafted PVA–PAN membrane is reduced. The increased antiplatelet activity may be due to the electronegetivity of sulfamate and carboxylate groups. Surfaces modified similarly with synthetic PE showed an improved antiplatelet property.[23,39] Adhesion of platelets onto material surfaces plays an important role in the process of thrombus formation,[40] and the clot initiation on any surface may be correlated with its electronegetivity.[41] Vascular walls are anionic mucopolysaccharides possessing a negative net charge associated with the anionic sulfate and carboxylate groups. This negative charge repels platelets and other negatively charged species.[42,43]

Membranes with an optimum blend ratio (87 : 13) selected are further studied along with the PE

**Table III Octane Contact Angle, Plasma Recalcification Time (PRT), and Platelet Adhesion Data of PVA–PAN Substrates**

| Sample | Octane Contact Angle (degree) | PRT (s) | Platelets Adhered/mm$^2$ |
|---|---|---|---|
| PVA | 131 ± 4 | 240 ± 7 | 28 ± 5 |
| PVA–PAN (90 : 10) | 127 ± 2 | 235 ± 13 | 24 ± 5 |
| PVA–PAN (87 : 13) | 121 ± 3 | 239 ± 6 | 24 ± 5 |
| PVA–PAN (85 : 15) | 119 ± 2 | 238 ± 4 | 24 ± 5 |
| PVA–PAN (83 : 17) | 117 ± 4 | 236 ± 7 | 24 ± 5 |
| Cellulose | 130 ± 3 | — | 21 ± 3 |
| PAN | 119 ± 3 | 269 ± 18 | 20 ± 5 |
| (87 : 13) PE | — | 341 ± 10 | 19 ± 4 |
| Glass | — | 140 ± 6 | — |

(87 : 13) PE, polyelectrolyte-grafted PVA–PAN (87 : 13).

**Table IV Permeability[a] of Solutes and No. of Platelets Adhered During Dialysis of Calf Blood Through the PVA–PAN (87 : 13) Membrane Before and After Sterilization**

| Membranes | Permeability of | | | |
|---|---|---|---|---|
| | Urea | Creatinine | Albumin | Platelets |
| Before sterilization | | | | |
| PVA | 47.7 ± 1.0 | 35.7 ± 3.5 | 1.7 ± 0.5 | 122 ± 10 |
| PVA–PAN (87 : 13) | 45.5 ± 1.5 | 33.3 ± 4.0 | 1.3 ± 0.5 | 112 ± 8 |
| (87 : 13) PE | 50.5 ± 1.5 | 36.6 ± 2.0 | 1.9 ± 0.5 | 82 ± 10 |
| Cellulose | 44.0 ± 1.5 | 32.6 ± 2.5 | 1.5 ± 0.5 | 87 ± 10 |
| After γ-irradiation | | | | |
| PVA | 47.1 ± 1.0 | 34.1 ± 2.5 | 1.4 ± 0.5 | 124 ± 11 |
| PVA–PAN (87 : 13) | 45.5 ± 1.5 | 32.6 ± 1.5 | 1.6 ± 0.5 | 104 ± 11 |
| (87 : 13) PE | 50.9 ± 2.5 | 35.6 ± 3.5 | 1.6 ± 0.5 | 76 ± 9 |
| Cellulose | 45.5 ± 1.5 | 32.3 ± 2.5 | 1.4 ± 0.5 | 86 ± 9 |
| After autoclaving | | | | |
| PVA | 42.9 ± 1.5 | 28.1 ± 3.0 | 0 | 126 ± 13 |
| PVA–PAN (87 : 13) | 40.4 ± 2.0 | 26.1 ± 3.0 | 0 | 110 ± 10 |
| (87 : 13) PE | 44.9 ± 1.5 | 29.2 ± 2.0 | 0 | 80 ± 8 |
| Cellulose | 40.3 ± 1.5 | 26.1 ± 4.5 | 0 | 87 ± 11 |

(87 : 13) PE, polyelectrolyte-grafted PVA–PAN (87 : 13).
[a] Permeability expressed as percentage passed.

grafted for solute permeability from calf blood. The effect of sterilization of these membranes on permeability and mechanical strength are given in Tables IV and V. It seems that the solute permeability through PE-grafted membrane is more than that of nongrafted membrane and is better than that of cellulose membrane. This may be due to the reduction in the deposition of plasma components onto the membrane from blood. It has been reported that a proteinaceous material is continuously deposited on the surface of membranes during dialysis.[44] However, detailed studies are required to evaluate the effect of the adhesion of blood components onto the membrane surface on the efficiency of permeability. There is also a significant reduction in platelet adhesion from blood onto grafted membrane, supporting the antithrombotic activity of PE. Bengeling et al. observed good anticoagulant activity with some PE.[45]

It seems that membranes sterilized by $Co^{60}$ γ-irradiation have no variation in the permeability

**Table V Tensile Strength and Elongation of PVA–PAN (87 : 13) Membrane Before and After Sterilization**

| Membranes | Tensile Strength ($MN/m^2$) | | Elongation (%) | |
|---|---|---|---|---|
| | Dry | Wet | Dry | Wet |
| Before sterilization | | | | |
| PVA | 40.22 ± 2.5 | 21.68 ± 2.1 | 255 ± 16 | 847 ± 31 |
| PVA–PAN (87 : 13) | 41.79 ± 2.6 | 38.84 ± 2.1 | 142 ± 12 | 592 ± 21 |
| Cellulose | 42.86 ± 2.8 | 38.65 ± 1.1 | 61 ± 5 | 82 ± 4 |
| After γ-irradiation | | | | |
| PVA | 39.14 ± 1.3 | 21.58 ± 1.8 | 253 ± 17 | 794 ± 18 |
| PVA–PAN (87 : 13) | 42.86 ± 2.8 | 38.35 ± 2.7 | 117 ± 19 | 543 ± 28 |
| Cellulose | 44.53 ± 4.8 | 38.45 ± 2.7 | 47 ± 5 | 54 ± 6 |
| After autoclaving | | | | |
| PVA | 49.24 ± 1.3 | 42.86 ± 2.3 | 239 ± 26 | 740 ± 36 |
| PVA–PAN (87 : 13) | 52.9 ± 1.9 | 49.83 ± 3.7 | 59 ± 9 | 312 ± 26 |
| Cellulose | 66.41 ± 3.1 | 53.95 ± 8.8 | 62 ± 7 | 69 ± 5 |

property. But autoclaving reduced the solute permeability and increased the overall mechanical strength. Heating makes PVA more crystalline and this may increase significantly its mechanical property. However, $\gamma$-irradiation makes no significant difference in the mechanical property of the PVA–PAN membrane.

## CONCLUSION

It has been shown that the mechanical properties and dialysis performance of PVA membranes are varied by adjusting the blending ratio of PVA and PAN and by grafting synthetic PE. The mechanical strength increased and permeability decreased as the amount of PAN is increased in the blend. A membrane with an optimum ratio of PVA and PAN was selected, compromising the permeability and mechanical properties. Synthetic PE grafted onto this membrane made it more blood compatible, with an increase in permeability of solutes from blood. This PE-grafted membrane showed appropriate wet breaking strength and permeability to solutes, suitable for the possible application as blood-contacting membrane for extracorporeal hemodialysis.

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