Hemodialysis Membranes Prepared from Poly(vinyl alcohol): Effects of the Preparation Conditions on the Morphology and Performance

J. Barzin,[1] S. S. Madaeni,[2] S. Pourmoghadasi[3]

[1]*Biomaterials Department, Iran Polymer and Petrochemical Institute, Tehran, Iran*
[2]*Chemical Engineering Department, Razi University, Kermanshah, Iran*
[3]*Chemical Engineering Department, Tarbiat Modaress University, Tehran, Iran*

Received 25 July 2006; accepted 28 September 2006
DOI 10.1002/app.25627
Published online in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: Poly(vinyl alcohol) was employed for the preparation of hemodialysis membranes with and without the addition of acetic acid and poly(ethylene glycol) with the phase-inversion process. Aqueous solutions of sodium sulfate and sodium hydroxide were chosen as coagulant baths. The performances of the membranes were estimated by the measurement of the removal of uremic toxins (urea, uric acid, and creatinine) from human blood serum. The morphologies of the membranes were investigated and correlated to the membrane performance. Increasing the poly(ethylene glycol) concentration in the polymer solutions resulted in porous, spongelike structures because of the higher polarity of the polymer solutions and the enhancement of the diffusion rate of the nonsolvent (sodium sulfate and sodium hydroxide) into the polymer solutions. The porous structures of the membranes enhanced the removal of uremic toxins. The presence of acetic acid, with greater ionization strength, resulted in higher electrostatic interactions between positive and negative ions in the coagulation baths and polymer solutions. © 2007 Wiley Periodicals, Inc. J Appl Polym Sci 104: 2490–2497, 2007

Key words: electron microscopy; membranes; morphology

INTRODUCTION

Synthetic polymeric membranes are used for a wide variety of applications, such as the purification of liquids, desalination of saline water, food and diary applications, and medical applications, including blood hemodialysis.[1–7] Semipermeable membranes are the most important part of hemodialysis devices for removing certain uremic toxin substances from the blood of kidney patients.[8,9] Several polymeric materials such as polyamide, polysulfone, cellulose acetate, poly(ether sulfone), and regenerated cellulose[10–15] are widely employed for the preparation of hemodialysis membranes. Because of its superior permeability and blood compatibility, poly(vinyl alcohol) (PVA) is used as a basic material for a variety of biomedical applications. These include skin-replacement materials, contact lens materials, articular cartilage replacement, and reconstruction of vocal cords, and in recent years, different attempts have been made to use PVA for hemodialysis membranes.[16–20]

Phase inversion is a common procedure for the fabrication of flat and hollow-fiber PVA membranes with symmetric and asymmetric structures. For flat membranes, wet phase inversion is carried out by the immersion of a thin layer of PVA dissolved in an appropriate solvent into a concentrated coagulation bath, in which an exchange of the solvent and nonsolvent takes place.[21–23] Because of the weak mechanical strength of PVA, coagulation processes are normally followed by the chemical crosslinking and/or heat treatment of the membranes. Furthermore, special properties can be obtained by the dissolution of additional additives into the casting solution.[24–26]

In this study, PVA was employed as the main polymer for the preparation of hemodialysis flat membranes. Polymer solutions were prepared from PVA in double-distilled water as a solvent with and without acetic acid (AcOH) and poly(ethylene glycol) (PEG) as additives. An aqueous solution of sodium sulfate (Na_2SO_4) and sodium hydroxide (NaOH) was chosen as a coagulant bath solution. The fixation of the membranes was carried out in an aqueous solution of sulfuric acid (H_2SO_4), Na_2SO_4, and glutaraldehyde [$HCO(CH_3)CHO$]. Hemodialysis membranes were fabricated with different components with wet phase inversion. The performance of the membranes was estimated by the measurement of the removal

Correspondence to: S. S. Madaeni (smadaeni@yahoo.com).
Contract grant sponsor: National Scientific Research Council of Iran.

TABLE I
Compositions of the Casting Solutions for the Preparation of the PVA Hemodialysis Membranes

Membrane	Membrane solution composition (wt %)				
	PVA	PEG600	PEG400	AcOH	H_2O
8.5 wt % PVA	8.5	0	0	0	91.5
8.5 wt % PVA, 8.5 wt % PEG600	8.5	8.5	0	0	83
8.5 wt % PVA, 12.75 wt % PEG600	8.5	12.75	0	0	78.75
8.5 wt % PVA, 8.5 wt % PEG400	8.5	0	8.5	0	83
10.5 wt % PVA	10.5	0	0	0	89.5
10.5 wt % PVA, 10.5 wt %, PEG600	10.5	10.5	0	0	79
10.5 wt % PVA, 10.5 wt % PEG400	10.5	0	10.5	0	79
12 wt % PVA	12	0	0	0	88
12 wt % PVA, 12 wt % PEG600	12	12	0	0	76
12 wt % PVA, 12 wt % PEG400	12	0	12	0	76
10.5 wt % PVA, 10.5 wt % AcOH	10.5	0	0	10.5	79
10.5 wt % PVA, 21 wt % AcOH	10.5	0	0	21	68.5
10.5 wt % PVA, 42 wt % AcOH	10.5	0	0	42	47.5

of uremic toxins (urea, uric acid, and creatinine) from human blood serum.[27,28] The morphology and performance of the membranes were investigated, and their relationships were correlated.

EXPERIMENTAL

Materials

The following materials were employed for the preparation of the membranes: PVA (weight-average molecular weight = 72,000 g/mol, hydrolysis degree = 98%) provided by Aldrich Chemical Co. (St. Louis, MO) as the membrane matrix, PEG [$H(OCH_2CH_2)_nOH$; weight-average molecular weight = 600 g/mol] supplied by Merck Co. (Darmstadt, Germany) AcOH (i.e., CH_3COOH; purity = 99%) provided by Merck as an additive, and double-distilled water as a solvent. Na_2SO_4 and NaOH aqueous solutions were used as nonsolvent baths. A Na_2SO_4, H_2SO_4, and $HCO(CH_3)CHO$ solution was used as a crosslinking medium for the final fixation of the membrane structure; all were provided by Merck.

Membrane preparation

Homogeneous casting solutions of PVA with and without PEG and AcOH (additives) dissolved in distilled water were prepared via refluxing in a round flask connected to a condenser at 85°C for 12 h. The different compositions of the membrane casting solutions were obtained through changes in the percentages of PVA, PEG, and AcOH, as listed in Table I.

The polymer solutions were kept for 6 h at room temperature for the removal of air bubbles. The resulting homogeneous solutions of the membranes were cast onto a smooth glass plate by a film applicator at room temperature with a uniform speed. The glass plates were immediately immersed into a coagulation bath containing an aqueous solution of Na_2SO_4 (300 g/L) and NaOH (60 g/L) for 30 min at 25°C. After coagulation, the membranes were stored in an aqueous solution of H_2SO_4 (1.5 g/L), Na_2SO_4 (300 g/L), and $HCO(CH_3)CHO$ (2.5 g/L) for final membrane fixation.

Scanning electron microscopy (SEM)

The cross sections and bottom sides of the prepared membranes were inspected with a Philips XL30 (Eindhoven, The Netherlands) scanning electron microscope. For cross-section studies, the samples of the membranes were frozen in liquid nitrogen and fractured. The bottom sides and cross sections of the membranes were transferred into the microscope with a sample holder after sputtering with gold.

Membrane performance

The hemodialysis capability of the membranes was investigated on the basis of the removal of uremic toxins, that is, urea, uric acid, and creatinine, from human blood. The details of the dialysis instrument and the calculation of the membrane performance have been illustrated elsewhere.[7] The batch dialyzer consisted of two horizontal chambers and stirrers. The feed chamber was filled with human blood serum, and the strip chamber was filled with distilled water. The hemodialysis flat membrane was clamped between the two chambers. The uremic toxin concentration gradient at the two sides of the hemodialysis membranes was the driving force. The toxin concentrations in human blood serum before and after the trials were measured by sampling and testing according to the standard methods in a medical laboratory. The membrane performance,

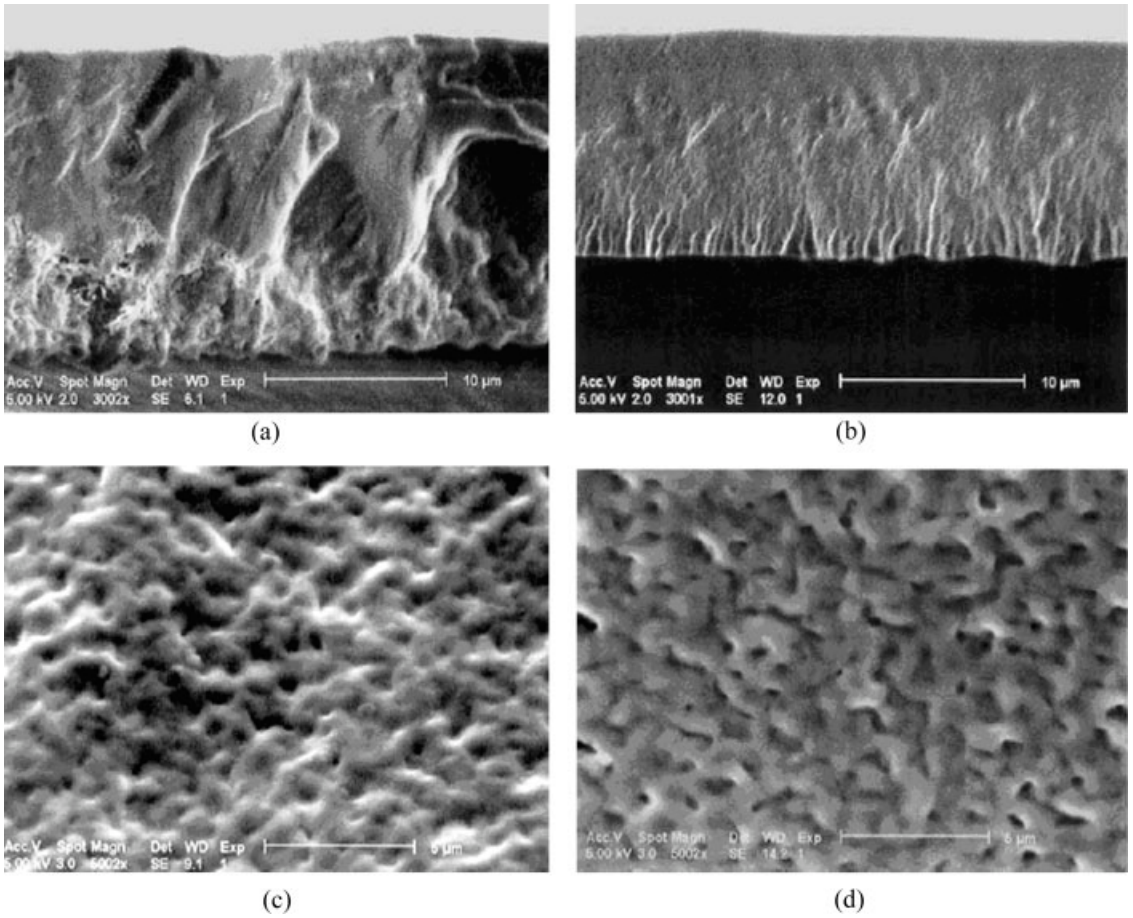

Figure 1 SEM micrographs of the cross sections and bottom sides of hemodialysis membranes as functions of the PVA percentage: (a) 8.5 wt % PVA cross section, (b) 10.5 wt % PVA cross section, (c) 8.5 wt % PVA bottom side, and (d) 10.5 wt % PVA bottom side.

that is, the concentration reduction (CR) of the uremic toxins, was calculated as follows:

$$\mathrm{CR} = 100 \times (C_1 - C_2)/C_1 \quad (1)$$

where C_1 and C_2 are the uremic toxin concentrations in blood before and after the trials, respectively.

RESULTS AND DISCUSSION

Membrane morphology

Micrographs of the cross sections and bottom sides of the membranes prepared from PVA/water/$NaOH/Na_2SO_4$ systems are presented in Figure 1. The SEM micrograph of the membrane prepared from 8.5 wt % PVA [Fig. 1(a)] indicates an asymmetric structure with a thick layer on top of the membrane and a thinner, porous-sponge structure underneath. In the case of the membrane prepared with a 10.5 wt % PVA concentration [Fig. 1(b)], a dense structure and a very thin, porous layer can be observed from the top to the bottom of the membrane and underneath, respectively. A comparison of the membranes with 8.5 wt % PVA [Fig. 1(a)] and 10.5 wt % PVA [Fig. 1(b)] indicates that the porous-sponge structure area in the membranes decreases and turns into a dense structure when the PVA concentration increases in the polymer solution. Figures 1(c,d) indicates that, with an increase in the PVA concentration, the pores of the membrane in the bottom side decrease in size and number. Similar observations of structure compaction with increasing polymer concentration have been reported by Stropnik et al.,[29] Barth et al.,[30] Kaiser and Stropnik,[31] Barzin and coworkers,[7,14,15] and Kim et al.[23] for polyamide, poly(methyl methacrylate), polysulfone, poly (ether sulfone), and PVA flat-sheet membranes.

Membrane performance

The membrane performance, that is, the removal of uremic toxins from blood, in different PVA concentrations is presented in Figure 2. A normal hemodialysis process currently takes 5 h for patients with kidney failure.[32] Therefore, data collection was carried out for 0, 1, 2, 4, and 5 h. A comparison of the

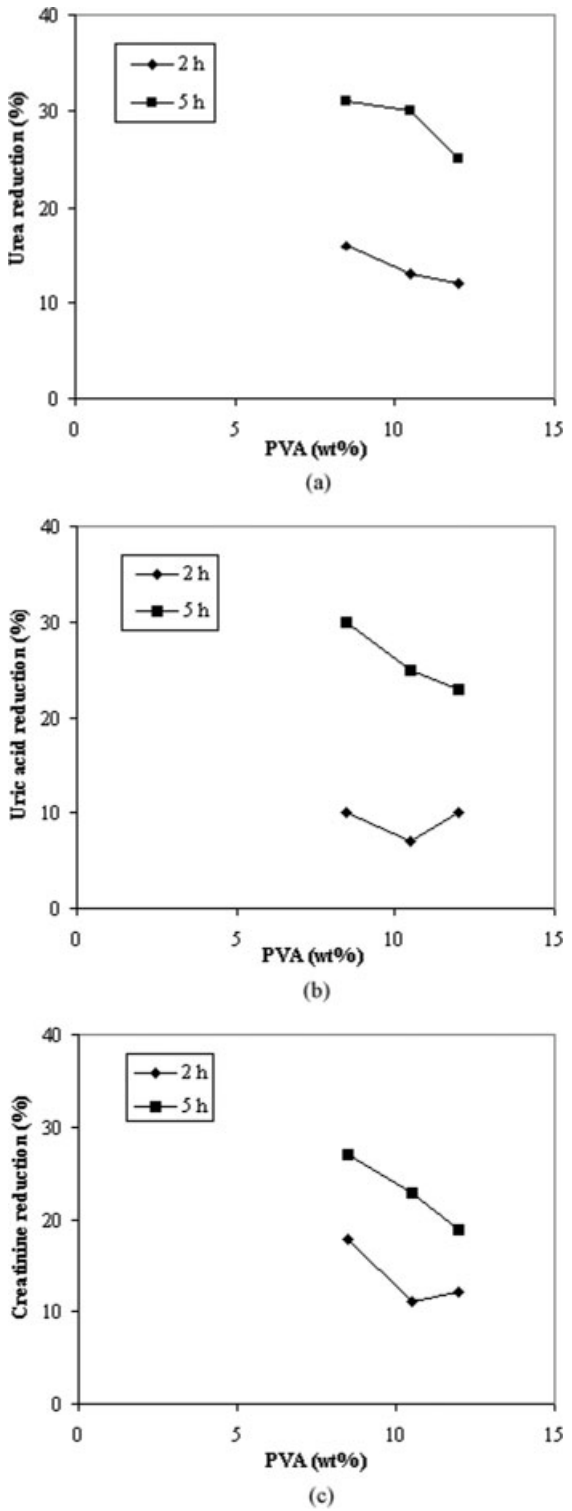

Figure 2 Reduction of uremic toxins as a function of the PVA percentage with the hemodialysis membrane after 2 and 5 h (without additives): (a) urea, (b) uric acid, and (c) creatinine.

membrane performance data for 2- and 5-h tests indicates that urea, uric acid, and creatinine removal from blood increases with time. Furthermore, Figure 2 indicates that the removal of all uremic toxins is higher for lower PVA concentrations. In other words, the dialysis performance or passing of uremic toxins through the membranes decreases with increasing polymer concentration. This behavior indicates that the permeability of urea, uric acid, and creatinine through the membranes with a porous-sponge, asymmetric structure (8.5 wt % PVA) is higher than that of membranes with a thick, dense morphology (10.5 and 12 wt % PVA). However, there is a limitation for the preparation of membranes with very low or very high polymer concentrations. Membrane preparation with a PVA concentration less than 7.5 wt % is not a favorable procedure. This is due to the poor mechanical properties of the manufactured membrane. Moreover, membrane handling is not an easy task. The preparation of membranes with PVA concentrations higher than 20 wt % is not suggested because of the high solution viscosity and difficulty of the polymer processing.

Effect of PEG on the membrane morphology

Figure 3 shows the results of SEM studies of cross sections and bottom sides of membranes prepared from a quaternary system containing PVA, water, PEG, and a nonsolvent. The micrographs indicate that when PEG is added to the polymer casting solution, the structures of the membrane cross section and bottom side are changed. For membranes prepared from 8.5 wt % PVA with the addition of 8.5 wt % PEG [Fig. 3(a)], the porous, spongelike area increases compared with that of the membrane without PEG [Fig. 1(a)]. Similarly, for n 8.5 wt % PVA membrane with 12.75 wt % PEG [Fig. 3(b)], the porous, spongelike structure area increases compared with that of the PVA membranes with 8.5 wt % PEG [Fig. 3(a)] and the PVA membranes without PEG [Fig. 1(a)].

In summary, increasing the PEG concentration in a polymer solution results in a porous, spongelike structure. The addition of a water-soluble, pore-former polymer such as PEG to the PVA solution results in an increment in the nonsolvent flow rate into the polymer solution. This increases with increasing the PEG concentration in the casting solution. The presence of hydroxyl groups in PEG changes this polymer to a polar polymer, resulting in a higher polarity for the PVA solution. The polarity of the casting solution enhances the diffusion rate of the nonsolvent (Na_2SO_4 and NaOH) into the polymer solution because of the higher interaction between the polar solution and cations in the coagulation bath. Increasing the exchange rate between the solvent and nonsolvent results in a porous, spongelike structure.

The effect of PEG addition on the membrane morphology can be confirmed by the investigation of the

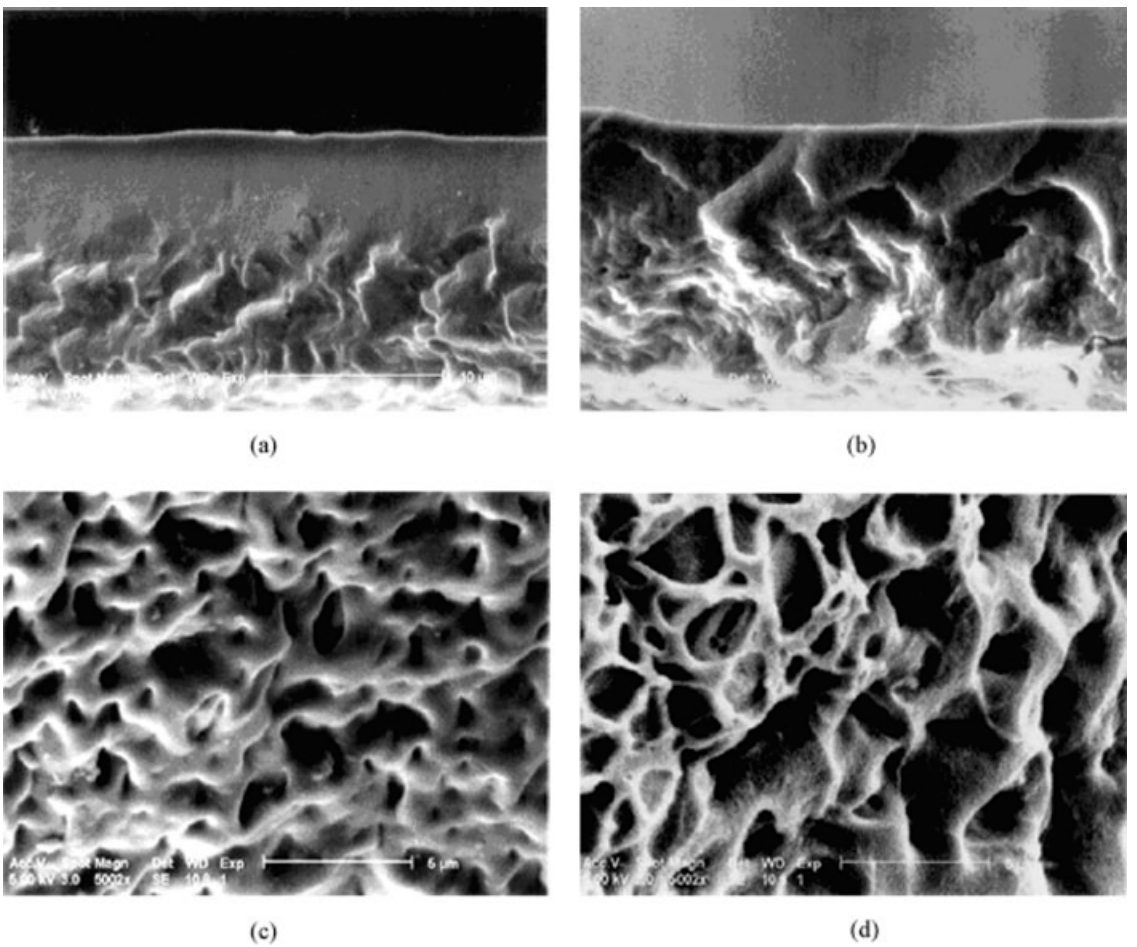

Figure 3 SEM micrographs of the cross sections and bottom sides of hemodialysis membranes as functions of the PEG percentage (8.5 wt % PVA): (a) 8.5 wt % PEG cross section, (b) 12.75 wt % PEG cross section, (c) 8.5 wt % PEG bottom side, and (d) 12.75 wt % PEG bottom side.

pore sizes in the bottom sides of the membranes. The SEM micrographs, that is, Figure 1(c) (without PEG) versus Figure 3(c) (8.5% PEG) and Figure 3(d) (12.75% PEG), indicate that the pore sizes are improved at higher PEG concentrations.

Effect of PEG on the membrane performance

The hemodialysis performances of PVA membranes with different PEG concentrations are presented in Figure 4. For membranes without PEG, the removal of urea, uric acid, and creatinine was 31, 30, and 27% after 5 h. For a membrane with an equal ratio of PEG and PVA, the removal of the toxins was increased to 40% for urea, 36% for uric acid, and 29% for creatinine after 5 h. Furthermore, when the PEG/PVA percentage increased up to 1.5%, a better membrane performance was observed. The removal of urea was 44%, the removal of uric acid was 38%, and the removal of creatinine was around 30% for 5-h experiments.

In summary, the membrane performance or removal of uremic toxins is improved by the introduction of PEG or an increase in the PEG concentration in a polymer solution because of the larger porous structure of the membrane, which results in a higher capability of the uremic toxins for passing through the membrane.

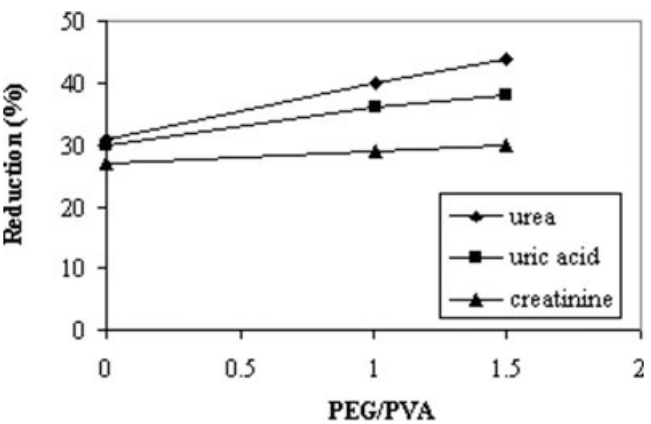

Figure 4 Reduction of uremic toxins as a function of the PEG/PVA ratio after 5 h (8.5% PVA).

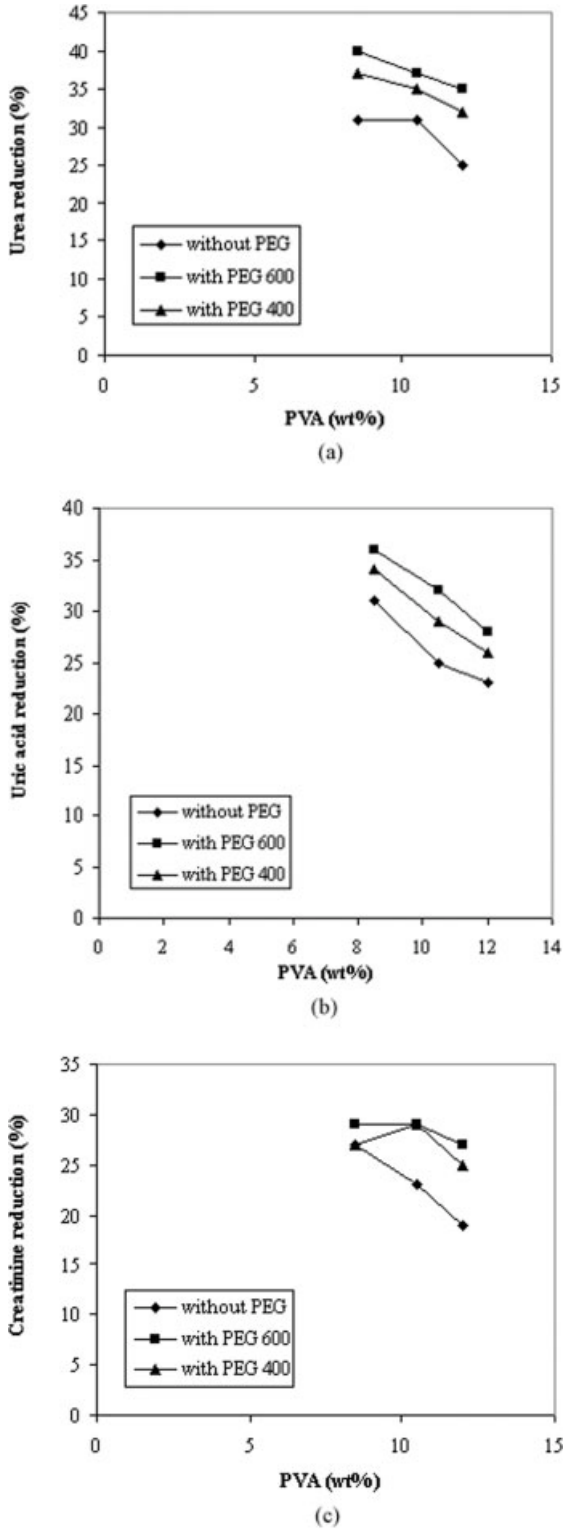

Figure 5 Reduction of uremic toxins with different PEG molecular weights after 5-h trials: (a) urea, (b) uric acid, and (c) creatinine.

Effect of the PEG molecular weight on the membrane performance

Figure 5 represents the effect of the PEG molecular weight on the membrane performance. This figure shows the removal of uremic toxins for PVA/PEG membranes with three different concentrations of PVA with two different molecular weights of PEG (400 and 600) versus PVA membranes without PEG. Figure 5 indicates that the addition of PEG with a larger molecular weight results in an increment in the membrane performance. The membrane containing PEG with a molecular weight of 600 exhibits better performance for the removal of urea, uric acid, and creatinine than the membrane with PEG with a molecular weight of 400 and the membrane without PEG.

The reason for the higher performance in the removal of the toxins by the membranes can be explained as follows: Increasing the molecular weight of PEG in the polymer solution increases the presence of hydroxyl groups, resulting in a higher polarity of the casting solution. A higher polarity means a higher exchange rate between the solvent and nonsolvent and a higher porosity of the membrane.

Effect of AcOH on the membrane morphology

The cross-section morphology of membranes prepared from quaternary systems (PVA/water/AcOH/nonsolvent) is presented in Figure 6. These membranes show a typical asymmetric structure with a very thin and compact layer on the top (skin layer) and a thicker, porous layer on the bottom (support). The cellular structure appears in the membrane cross section with the addition of AcOH. The differences in the morphology can be elucidated by a comparison of these micrographs with membranes without an additive [Fig. 1(a,b)] or membranes with a PEG additive [Fig. 3(a,b)]. Furthermore, Figure 6 signifies that the cellular area increases and the skin-layer thickness decreases with increasing AcOH concentration.

Figure 7 shows the structure of the bottom side of the membranes for different AcOH concentrations. The micrographs indicate that with the addition of AcOH to the polymer solutions, the morphology of the bottom side of the membrane turns to a void structure with large cellular pores.

AcOH shows a higher capability for electrostatic interaction between positive and negative ions in the coagulation bath and polymer solution. This is due to the higher ionization strength of AcOH versus PEG. Moreover, the higher viscosity of the PEG solution versus the AcOH solution results in a reduction in the number of pores in the membrane prepared from PEG.

Effect of the AcOH concentration on the membrane performance

To elucidate the effect of the AcOH concentration, the removal of urea, uric acid, and creatinine from

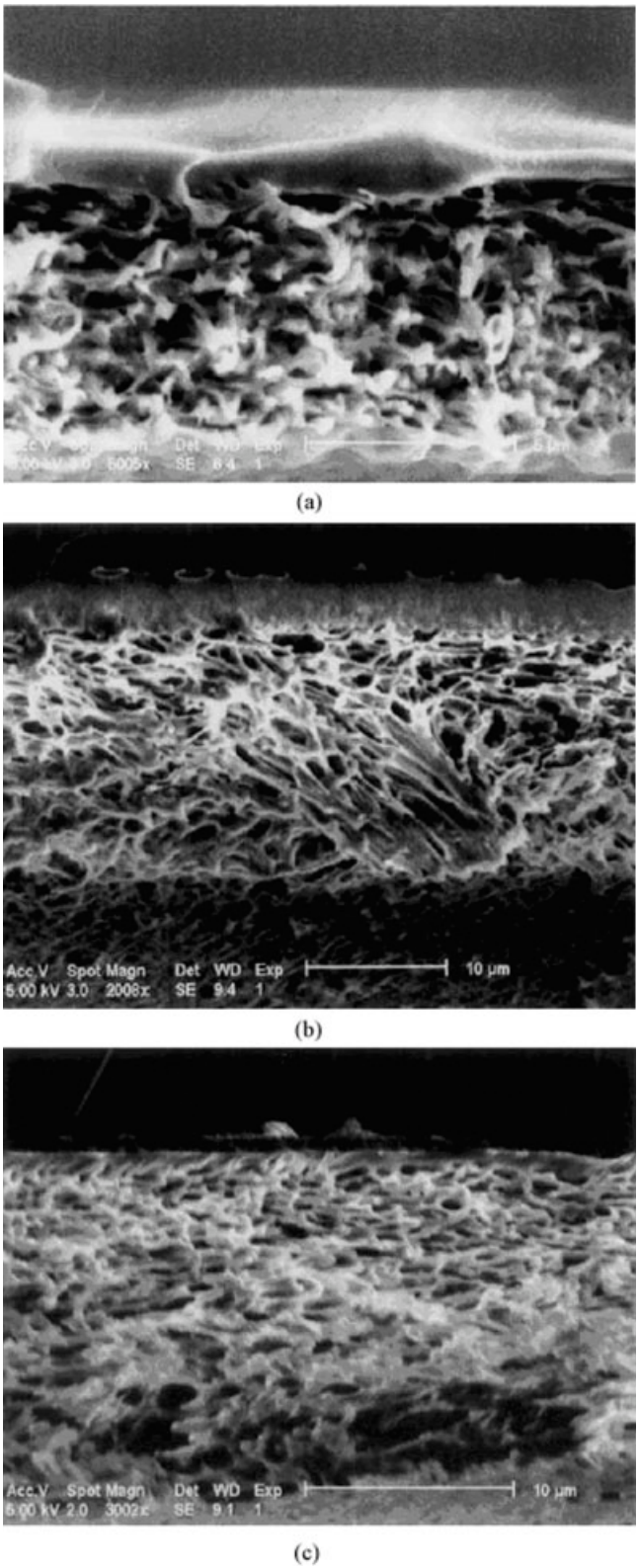

Figure 6 SEM micrographs of the cross sections of hemodialysis membranes as functions of the AcOH concentration (10.5% PVA): (a) 10.5, (b) 21, and (c) 42 wt %.

blood with PVA membranes with various AcOH/PVA compositions was performed (Fig. 8). The removal efficiencies for all uremic toxins increased with the addition of AcOH. The performance was improved with an increase in the AcOH concentration. The addition of AcOH to the polymer solution

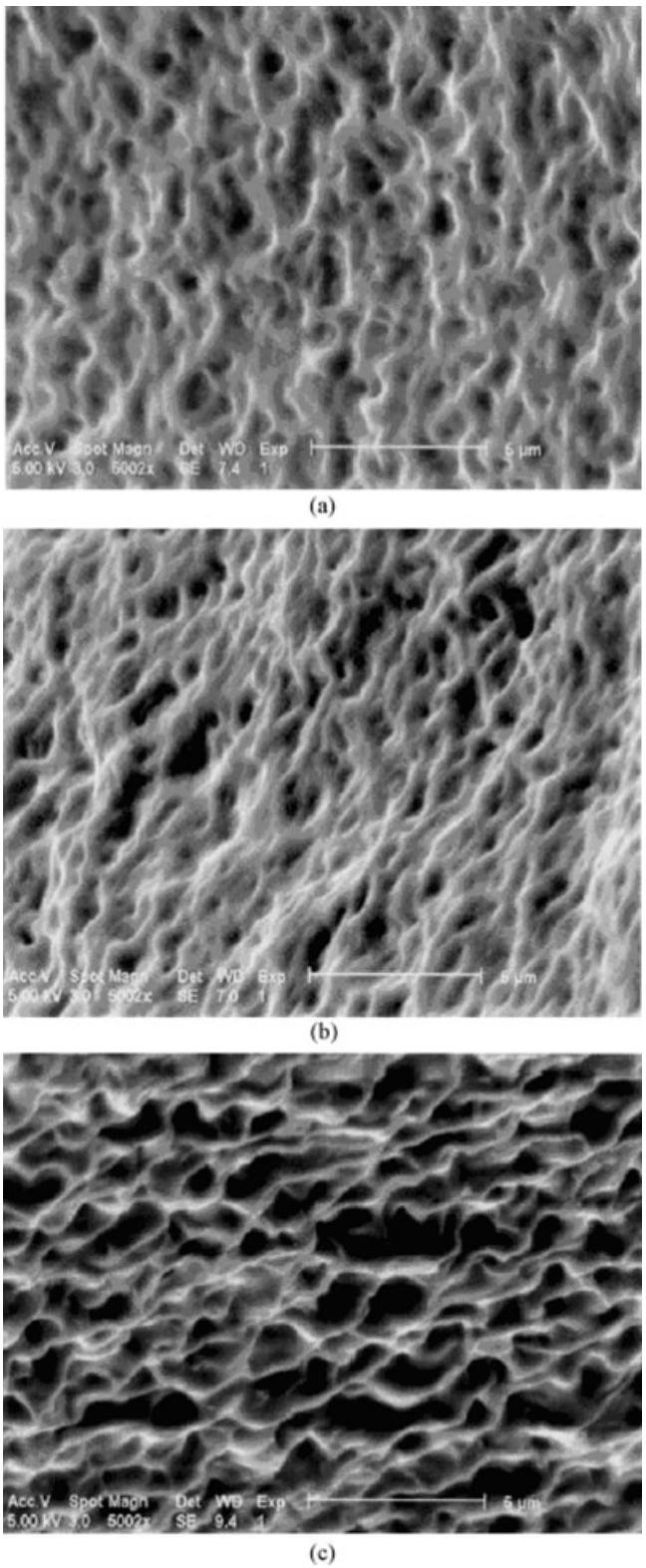

Figure 7 SEM micrographs of the bottom sides of hemodialysis membranes as functions of the AcOH concentration (10.5% PVA) : (a) 10.5, (b) 21, and (c) 42 wt %.

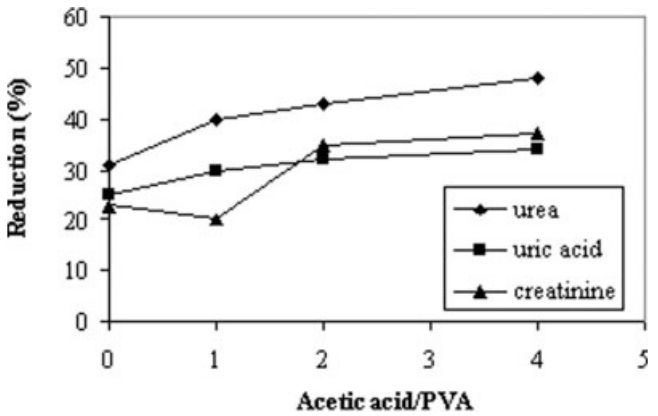

Figure 8 Reduction of uremic toxins as a function of the AcOH/PVA ratio after 5-h trials (10.5% PVA).

for membrane preparation resulted in an increment in the size of the cellular structures and a decline in the thickness of the membrane compact skin layer. This led to higher transport of the uremic toxins through the membranes.

CONCLUSIONS

The porous-sponge structure of membranes prepared from PVA/water/NaOH and Na_2SO_4 turns into a dense structure when the PVA concentration increases in the polymer solution, resulting in a lower passage of uremic toxins through the membranes. The addition of a water-soluble, pore-former polymer such as PEG to the PVA solution leads to a porous, spongelike structure and results in an improvement in the removal of uremic toxins. A cellular structure appears in the membrane cross section with the addition of AcOH. This structure is the best for an increment in the removal efficiencies of all uremic toxins.

References

1. Mulder, M. Basic Principles of Membrane Technology; Kluwer: Dordrecht, 1996.
2. Taniguchi, M.; Kimura, S. AIChE J 2000, 46, 1967.
3. Madaeni, S. S.; Rahimpour, A.; Barzin, J. Iranian Polym J 2005, 14, 421.
4. Madaeni, S. S.; Fane, A. G.; Grohmann, G. S. J Membr Sci 1995, 102, 65.
5. Okazaki, M.; Hamada, T.; Fuji, H.; Mizobe, A.; Matsuzawa, S. J Appl Polym Sci 1995, 58, 2235.
6. Krause, B.; Storr, M.; Ertl, T.; Buck, R.; Hildwein, H.; Deppisch, R.; Göhl, H. Chem Ing Tech 2003, 75, 1725.
7. Barzin, J.; Madaeni, S. S.; Mirzadeh, H.; Mehrabzadeh, M. J Appl Polym Sci 2004, 92, 3804.
8. Vicenza, C. R.; Greca, G. L. Hemodialysis Technology; Karger: Basel, Switzerland, 2002.
9. Wenthold, R. M.; Hall, R. T.; Andrus, R. G.; Brinda, P. D.; Cosentino, L. C.; Reggin, R. F.; Pigott, D. T. U.S. Pat. 5,762,798 (1998).
10. Bonomini, V.; Berland, Y. Dialysis Membranes Structure and Predictions; Karger: Basel, Switzerland, 1995.
11. Park, J. B.; Lakes, R. S. Biomaterials; Plenum: New York, 1992.
12. Sakai, K. J Membr Sci 1994, 96, 91.
13. Abe, Y.; Mochizuki, A. J Appl Polym Sci 2002, 84, 2302.
14. Barzin, J.; Feng, C.; Khulbe, K. C.; Matsuura, T.; Madaeni, S. S.; Mirzadeh, H. J Membr Sci 2004, 237, 77.
15. Barzin, J.; Madaeni, S. S.; Mirzadeh, H. Iranian Polym J 2005, 14, 353.
16. Ikada, Y.; Iwata, H.; Horii, F.; Matsunaga, T.; Taniguchi, M.; Suzuki, M.; Taki, W.; Yamagata, S.; Yonekawa, Y.; Handa, H. J Biomed Mater Res 1981, 15, 697.
17. Bray, J. C.; Merrill, E. W. J Biomed Mater Res 1973, 7, 431.
18. Peppas, N. A.; Merrill, E. W. J Biomed Mater Res 1977, 11, 423.
19. Noguchi, T.; Yamamuro, T.; Oka, M.; Kumar, P.; Kotoura, Y.; Hyonyt, S.; Ikadat, Y. J Appl Biomater 1991, 2, 101.
20. Lai, J. Y.; Chen, Y. C.; Hsu, K. Y. J Appl Polym Sci 1991, 43, 1795.
21. Kesting, R. E. Synthetic Polymer Membrane; Wiley: New York, 1985.
22. Baker, R. W. Membrane Technology and Applications; Wiley: New York, 2004.
23. Kim, S.; Kim, Y.; Yun, H.; Lim, G.; Lee, K. J Appl Polym Sci 2003, 88, 2884.
24. Bo, J. J Appl Polym Sci 1992, 46, 783.
25. Muhlebach, A.; Muller, B.; Hofmann, C.; Seiferling, B.; Guerry, D. J Polym Sci Part A: Polym Chem 1997, 35, 3603.
26. Yeom, C. K.; Huang, R. Y. M. Angew Makromol Chem 1991, 184, 27.
27. Ringoir, S.; Vanholder, R.; Massry, S. G. Uremic Toxins; Springer: New York, 1988.
28. Newberry, M. A. Textbook of Hemodialysis for Patient Care Personnel; Thomas: Springfield, IL, 1989.
29. Stropnik, C.; Musil, V.; Brumen, M. Polymer 2000, 41, 9227.
30. Barth, C.; Goncalves, M. C.; Pires, A. T. N.; Roeder, J.; Wolf, B. A. J Membr Sci 2000, 169, 287.
31. Kaiser, V.; Stropnik, C. Acta Chim Slov 2000, 47, 205.
32. Corea, A. L.; Gutch, C. F.; Stoner, M. H. Review of Hemodialysis for Nurses and Dialysis Personnel; Elsevier: Amsterdam, 1999.