Asymmetric Cellulose Acetate Dialysis Membranes: Synthesis, Characterization, and Performance

Ehsan Saljoughi, Mohammad Amirilargani, Toraj Mohammadi

Research Centre for Membrane Separation Processes, Department of Chemical Engineering, Iran University of Science and Technology, Narmak, Tehran, Iran

Received 20 September 2008; accepted 17 October 2009
DOI 10.1002/app.31645
Published online 14 January 2010 in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: Cellulose acetate (CA) is highly comparable to other synthetic polymer materials and is effective in the hemodialysis process. In this work, asymmetric CA membranes were synthesized with the phase-inversion method. CA with a molecular weight of 52,000, poly(ethylene glycol) (PEG) with a molecular weight of 400, and 1-methyl-2-pyrrolidone (NMP) were used as the polymer, additive, and solvent, respectively. The effects of the CA and PEG concentrations and coagulation bath temperature (CBT) on the morphology, pure water permeability (PWP), insulin/human serum albumin (HSA) transmission, and finally thermal and chemical stability of the prepared membranes were determined and investigated. In general, increasing the PEG concentration and CBT and reducing the CA concentration resulted in increased PWP and insulin/HSA transmission. Also, these variations facilitated the formation of macrovoids in the membrane sublayer. On the other hand, increasing the PEG and CA concentrations and reducing CBT resulted in increased thermal and chemical stability of the prepared membranes. Also, ratios of 15.5/10/74.5 and 17.5/10/72.5 (w/w) for the CA/PEG/NMP casting solutions and their immersion into coagulation baths with CBTs of 0 and 25°C, respectively, resulted in the preparation of membranes that had not only optimum sieving properties and higher PWP but also thermal and chemical stability better than that of conventional CA hemodialysis membranes. © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 116: 2251–2259, 2010

Key words: membranes; phase separation; dialysis

INTRODUCTION

With the advent of membrane technology, separation, concentration, and purification have become industrially viable unit operations because of the high separation efficiency, low energy use of the operation, spatial requirements, simplicity of the operation with modern compact modules, and so forth.[1] During the past century, medical applications of membranes have been developed along with industrial applications. W. J. Kolf demonstrated the first successful artificial kidney in the Netherlands in 1945. It took almost 20 years to refine the technology for use on a large scale, but these developments were completed by the early 1960s. Since then, the use of membranes in artificial organs has become a major life-saving procedure. Nowadays, more than 800,000 people are sustained by artificial kidneys.[2,3] The total world sales of dialysis membranes in 1994 have been estimated at $1400 million (US dollars), and they account for about 40% of the total predicted membrane sales (worth $4000 million). Until the year 2000, hemodialysis treatment cost around $140, and this promised about $20,000 of profit per year per patient.[4]

Various polymers have been used for the preparation of hemodialysis membranes. Basically, these polymeric materials should have the following:

1. Excellent biocompatibility, which is equivalent to low platelet adhesion,[5] low clot formation, which results in a reduction of the dosage of the anticoagulant required during hemodialysis,[7,8] low activation of leukocytes,[2,5,6] more protection for patients against oxidative stress,[8] and a high blocking efficiency versus harmful substances contained in the dialysate.[9,10]
2. Low cost.
3. Fiber-spinning ability.
4. Appropriate morphology.[4,11]

Also, the membranes should have appropriate sieving properties. In other words, hemodialysis membranes should facilitate the passage of uremic toxins of low and moderate molecular weights (MWs) such as urea [weight-average molecular weight (M_w) = 60 g/mol], uric acid, creatinine (M_w = 130 g/mol), insulin (M_w = 5700 g/mol), and β_2-microglobulin (M_w = 11,800 g/mol) and simultaneously reject proteins such as human serum albumin (HSA; M_w = 66,000 g/mol) and bigger particles.[12,13]

Correspondence to: T. Mohammadi (torajmohammadi@iust.ac.ir).

In recent years, various polymers have been used for the preparation of hemodialysis membranes, such as cellulose acetate (CA), polyacrylonitrile, poly (methyl methacrylate), ethylene vinyl alcohol copolymer, polysulfone, poly(ether sulfone), and polyamide.[4,11,14,15] Some researchers have concluded that the survival rates of dialysis patients are very much dependent on the type of membrane material used. Others have found that there are no significant differences in the survival rate of patients and have indicated that the type of membrane material does not affect the survival rate. In short, the issue of dialysis membranes as a significant cause of hemodialysis outcomes still remains unclear.[4]

Among the aforementioned polymeric materials, CA has always been used as the basic material for dialysis membranes because of its maximum uniformity and permselectivity, relatively low cost, and optimum physical properties such as flexibility. Many studies have proven that CA is highly comparable to other synthetic polymer materials and effective in the hemodialysis process.[4] For example, Sevillano et al.[16] reported that CA membranes improve some aspects of red blood cell function in hemodialysis patients.

However, despite these advantages, CA membranes show low thermal/chemical resistance, which makes them impossible to reuse[1,17] because the reuse of membranes applied in medical applications depends on steam or γ sterilization and cleaning with aggressive solutions.[1,3,18] The low thermal/chemical resistance of CA membranes results in damage to these membranes during sterilization/cleaning processes. Thus, the application of CA membranes to blood purification has been limited in comparison with that of expensive and more stable membranes such as polysulfone and poly(ether sulfone). Thus, improvements in the thermal/chemical stability of CA membranes along with no undesirable changes in their sieving properties and hemocompatibility are important events in the development of hemodialysis membranes.

In this study, the phase-inversion method[19–25] was used for the preparation of flat-sheet membranes. CA (MW = 52,000) was used as the polymer, and poly(ethylene glycol) (PEG; MW = 400) as the plasticizer and pore-forming agent and distilled water as the nonsolvent were selected. Various membranes with different combinations of CA and PEG concentrations and coagulation bath temperatures (CBTs) were prepared. The morphology, pure water permeability (PWP) or pure water permeation flux, sieving properties, and thermal/chemical stability of the prepared membranes were determined and discussed. In fact, in this study, we tried to investigate simultaneous effects of the PEG concentration and CBT on the permeability and thermal/chemical stability as important characteristics of CA hemodialysis membranes.

EXPERIMENTAL

Materials

CA with an average MW of 52,000 g/mol (Fluka, Buchs, Switzerland) was used as the membrane-forming polymer. The solvent was NMP with an analytical purity of 99.5% (Merck, Darmstadt, Germany), and distilled water was used as the nonsolvent. PEG with an average MW of 400 g/mol (Lobachemie Co., Murud, India) was used as an additive. Experiments were performed with 20% HSA with an average MW of 66,000 g/mol (Biotest AG, Germany) and regular insulin solutions (Exir Co., Tehran, Iran).

Preparation of the casting solution

CA/PEG/NMP solutions of various ratios were prepared. Their compositions are shown in Table I. The

TABLE I
Levels of the Synthesis Parameters and Viscosities of the Casting Solutions

		Solution properties			
		Solution composition			
Membrane code	CBT (°C)	CA (wt %)	NMP (wt %)	PEG (wt %)	Viscosity (cp)
M1	0	15.5	84.5	0	37,660
M2				5	43,366
M3				10	51,110
M4	25	15.5	84.5	0	37,660
M5				5	43,366
M6				10	51,110
M7	0	17.5	82.5	0	65,049
M8				5	81,776
M9				10	110,083
M10	25	17.5	82.5	0	65,049
M11				5	81,776
M12				10	110,083

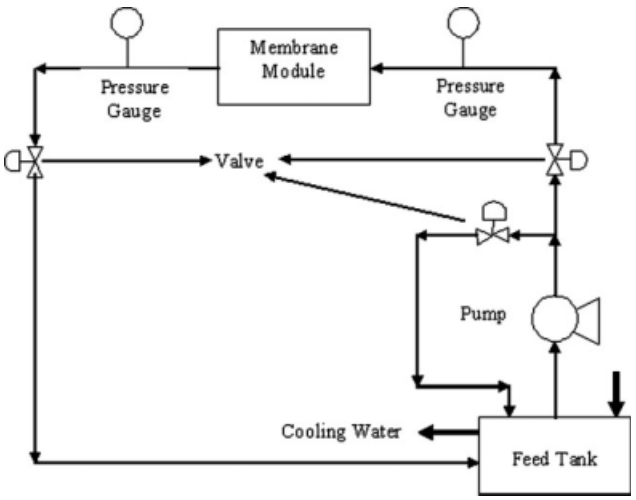

Figure 1 Schematic diagram of the experimental setup.

solutions were stirred continuously to ensure that the polymers were completely dissolved. When the entire polymers were completely dissolved, as indicated by the clear solution obtained, the solutions were subsequently degassed in an ultrasonic bath for about 2 h to remove any air bubbles present and kept away from direct sunlight to slow down the aging process.

Membrane casting

The CA casting solution was cast onto a glass plate with a casting knife with a thickness of 180 μm. The casting solution film was then immersed in a distilled water bath to complete the phase separation, and there the exchange between the solvent and nonsolvent was induced. Then (after gelation), the membranes were heat-treated in a 50°C deionized water bath for at least 30 min to remove the excess NMP and PEG from the membranes. Eventually, the membranes were transferred to another container containing deionized water and were ready to be tested.

PWP and protein permeation experiments

Flux and protein permeation experiments were carried out in a batch mode. A schematic representation of the setup is shown in Figure 1. At first, the membranes were subjected to a pure water experiment. PWP was calculated with eq. (1):[11,26]

$$\mathrm{PWP} = V/S \tag{1}$$

where V is the water permeation rate (mL/h) and S is the effective area of the membrane (m^2). Furthermore, PWP was normalized by pressure:[11]

$$\mathrm{PWP} = V/SP \tag{2}$$

where P is the operating pressure (mmHg).

HSA and insulin solutions were prepared at a concentration of 0.01 wt % in a phosphate buffer (0.5 M, pH 7.2) with distilled water and were used as standard feed solutions. Then, the HSA and insulin solutions were filtered through each membrane individually. The permeate HSA/insulin concentration, collected over measured time intervals, was estimated with a UV–vis spectrophotometer (Shimadzu, model UV2550, Tokyo, Japan) at a wavelength of 280 nm. The sieve coefficient was defined as follows:[13]

$$\text{Sieve coefficient} = C_P/C_F \tag{3}$$

where C_P and C_F are the concentrations of the permeate and feed solutions, respectively.

The transmission percentage was calculated with eq. (4):

$$\text{Transmission}(\%) = \text{Sieve coefficient} \times 100 \tag{4}$$

Scanning electron microscopy

The membranes were snapped under liquid nitrogen to produce a generally consistent and clean break. The membranes were then sputter-coated with a thin film of gold. The membranes were mounted on a brass plate with double-sided adhesion tape in a lateral position. Cross-sectional images of the membranes were obtained with a CamScan model MV2300 (Cambridgeshire, England) scanning electron microscope.

Thermal studies: Dynamic mechanical thermal analysis (DMTA)

DMTA of the prepared membranes was performed with a Triton (London, England) DMTA Tritic instrument operating at the frequency of 1 Hz. DMTA scans were performed between 20 and 160°C at the heating rate of 3°C/min.

RESULTS AND DISCUSSION

Membrane formation mechanism

Figures 2–5 show that increasing the PEG concentration and CBT results in increased membrane porosity and PWP. Also, these changes generally (but not absolutely) increase the HSA/insulin transmission. An explanation for these observations requires an understanding of the membrane formation mechanism explained in our previous articles.[27,28] In brief, when the cast film is immersed into the distilled water bath, precipitation starts because of the low miscibility between the polymer (CA) and nonsolvent (water). Simultaneously, the miscibility between the solvent (NMP) and the nonsolvent (water) causes diffusional flow of the solvent and the nonsolvent

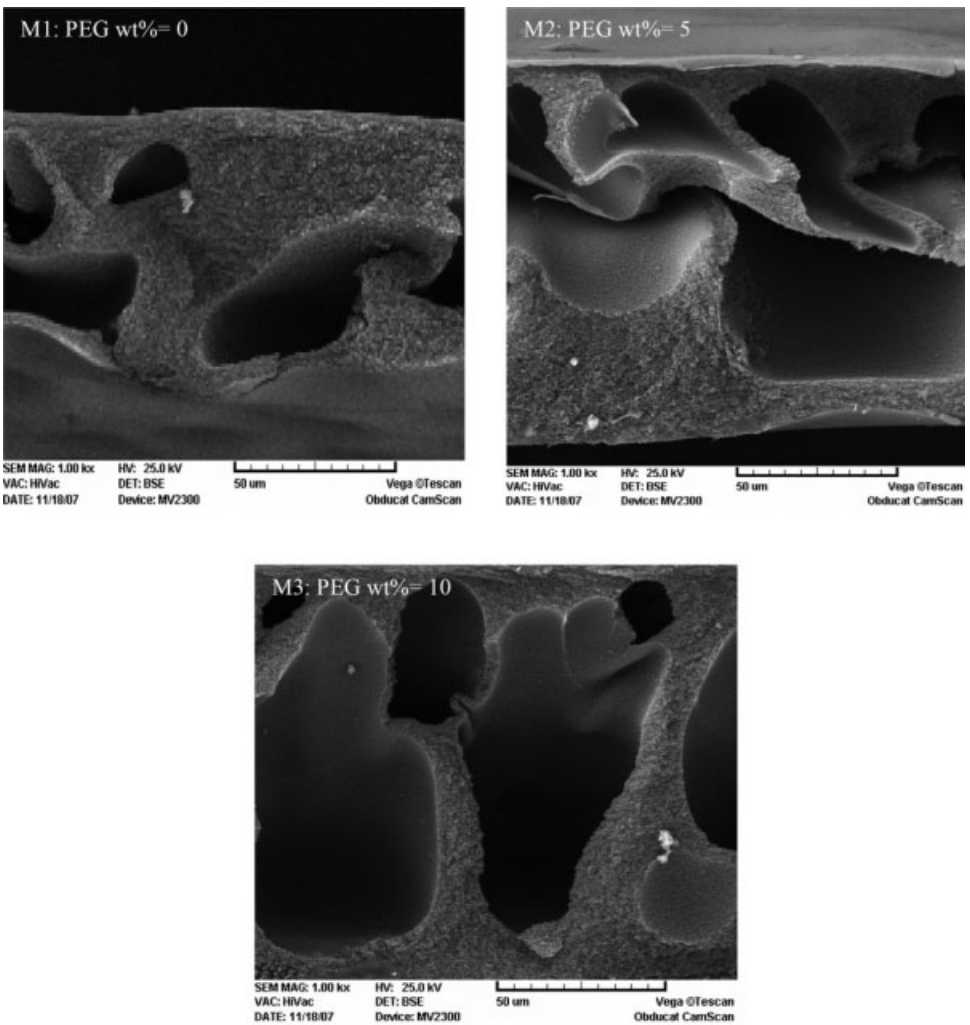

Figure 2 Effect of the PEG concentration on the morphology of the synthesized membranes (CBT = 25°C and CA concentration = 15.5 wt %).

(exchange of the solvent and nonsolvent) at several points of the film's top layer and the sublayer, which subsequently leads to the formation of nuclei of a polymer-poor phase. In fact, the low affinity between the CA chains and water molecules at points at which water molecules diffuse results in the repulsion of CA chains and consequently the formation of nuclei of a polymer-poor phase. Because of the continuation of the diffusional flow of the solvent and nonsolvent, the aforementioned nuclei continue to grow until the polymer concentration at their boundaries becomes too high and solidification occurs (the demixing process is completed).[27,28]

The rate of the demixing process affects the morphology of the membranes. Instantaneous demixing often leads to the formation of macrovoids in the membrane structure, whereas slow demixing results in a denser structure. In the case of slow demixing, nucleation occurs after a certain period of time, and the polymer concentration increases in the top layer. Then, nucleation starts in the inferior layer at short time intervals successively. Hence, the size and composition of the nuclei in the former layer are such that new nuclei are gradually formed in their neighborhood.[19,28] In other words, in slow demixing, free growth of limited nuclei (on the top layer) is prevented, and a large number of small nuclei are created and distributed throughout the polymer film. Consequently, contrary to instantaneous demixing, the formation of macrovoids is suppressed, and denser membranes are synthesized.

Effect of CBT

Decreasing CBT reduces mutual diffusivity between the solvent and nonsolvent during solidification of the casting solution. This causes slow growth of nuclei that are poor in terms of CA and consequently the formation of more nuclei in front of them.[3,28] The formation of too many nuclei that

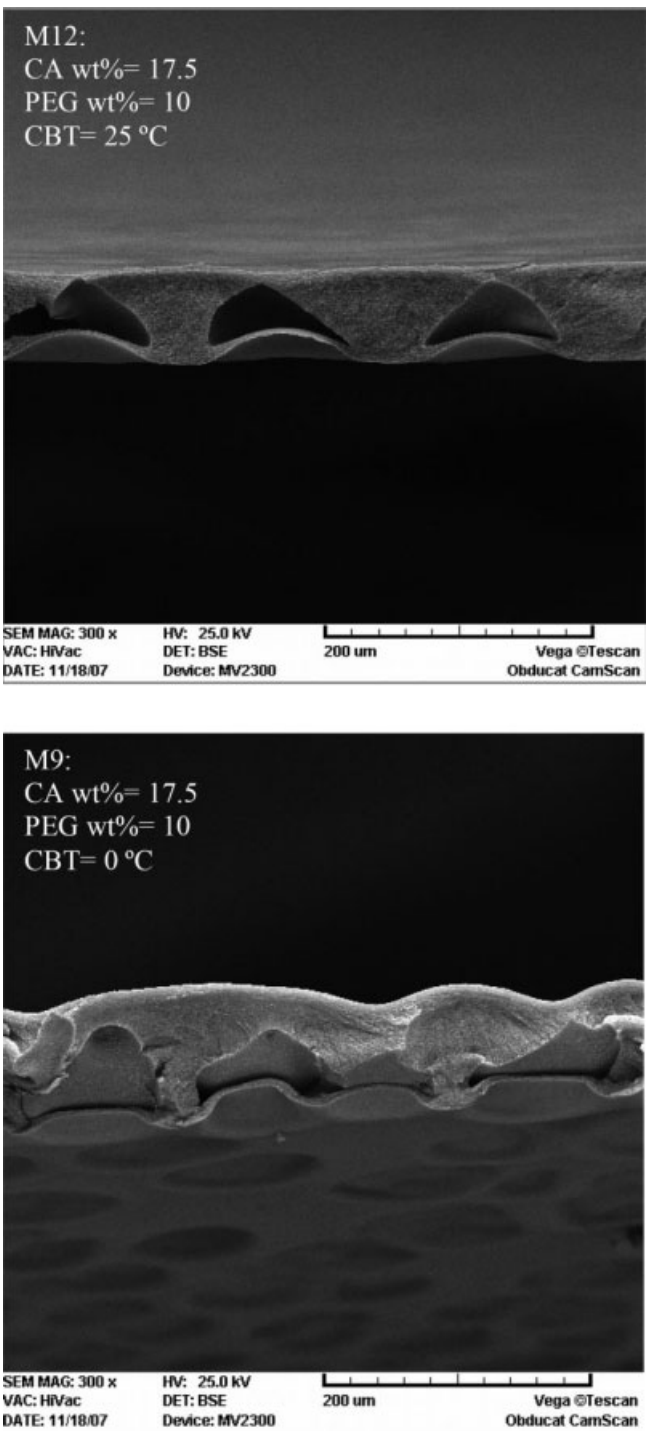

Figure 3 Effect of CBT on the morphology of the synthesized membranes (PEG concentration = 10 wt % and CA concentration = 17.5 wt %).

grow slowly results in the formation of a denser structure (Fig. 3) and consequently the reduction of PWP and the HSA/insulin transmission (Figs. 4 and 5). The aforementioned observations are in agreement with the literature.[29] In general, it can be said that the formation of macrovoids occurs under quick precipitation conditions, and the precipitation is faster at higher temperatures.

Effect of PEG

In this study, the presence of PEG as a hydrophilic additive with nonsolvent properties [an additive that, similar to a nonsolvent, has high and low affinity to the solvent (NMP) and the polymer (CA), respectively][24] increases the thermodynamic instability of the cast film and consequently can lead to instantaneous demixing in the coagulation bath and thus the formation of macrovoids in the membrane structure.[27]

From another point of view, the presence of PEG increases the viscosity of the cast film (as shown in Table I). Increasing the viscosity of the cast film slows the diffusional exchange rate of the solvent (NMP) and nonsolvent (water) during the solidification process and consequently hinders instantaneous demixing. This can lead to delayed demixing and consequently the suppression of macrovoids and formation of a denser structure.

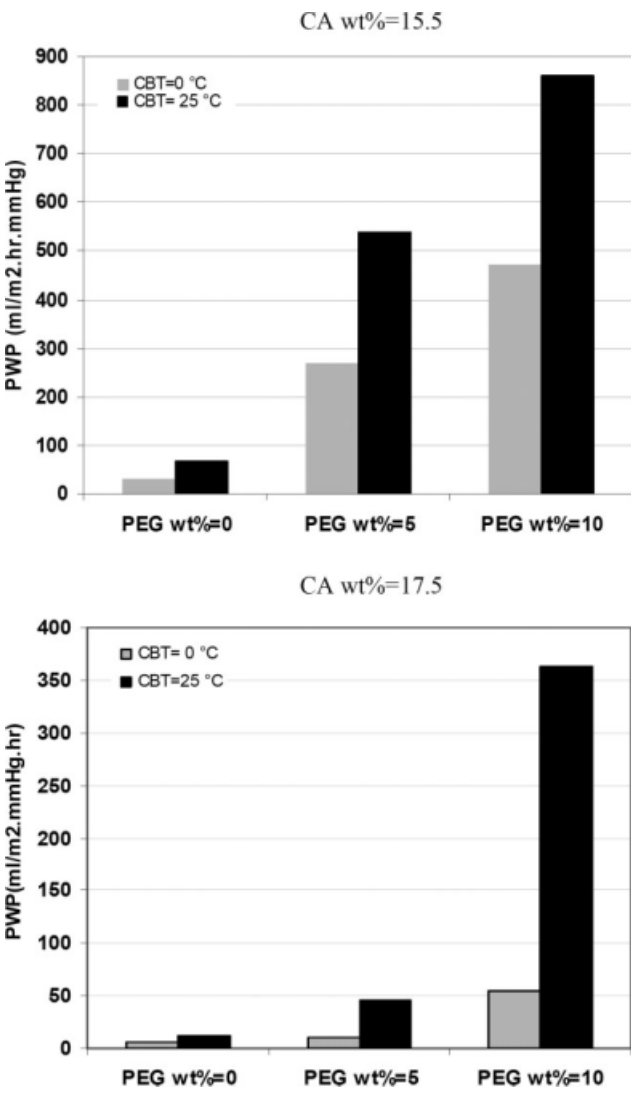

Figure 4 Effect of the synthesis parameters on PWP of the prepared membranes.

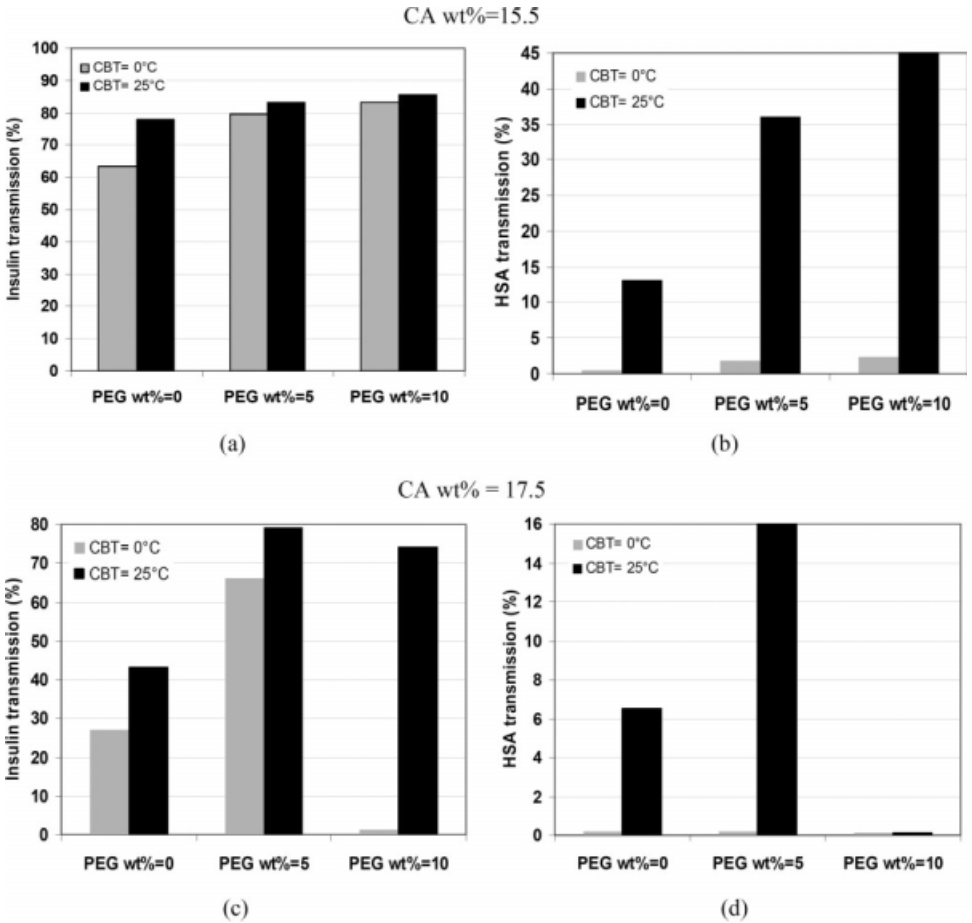

Figure 5 Effect of the synthesis parameters on the HSA/insulin transmission through the prepared membranes.

Hence, the addition of hydrophilic additives such as PEG to the casting solution has a dual effect on the membrane morphology. In fact, the final structure depends on the superiority of instantaneous or delayed demixing, both of which, as mentioned before, come from the presence of PEG in the cast film. In this study, it seems that instantaneous demixing was preferred over delayed demixing because, according to Figures 2–5, an increase in the PEG concentration generally resulted in increased membrane porosity, PWP, and HSA/insulin transmission. However, some exceptions were observed in the membranes with 17.5 wt % CA in their cast film composition [Fig. 5(c,d)]. According to this figure, increasing the PEG concentration initially (from 0 to 5 wt %) resulted in increased HSA/insulin transmission. However, a greater increase in the PEG concentration from 5 to 10 wt % resulted in a reduction of the HSA/insulin transmission. This reduction was more noticeable in the membranes formed at a CBT of 0°C, so M9 showed approximately no HSA/insulin protein transmission [Fig. 5(c,d)]. The aforementioned reduction of the HSA/insulin transmission that was observed after the PEG concentration was increased from 5 to 10 wt % can be interpreted with the viscosity values from Table I. According to this table, for solutions containing 17.5 wt % CA in their composition, increasing the PEG concentration from 5 to 10 wt % resulted in noticeable increases in the viscosity value (110,083 cp was the highest viscosity value among the prepared solutions), which intensively slowed the growth of limited nuclei formed after the immersion of the cast film into the coagulation bath. This slow growth of primary nuclei, intensified at lower CBTs, resulted in the formation of numerous nuclei in the cast film structure. However, as mentioned previously, increases in the number of nuclei and consequently the number of pores/voids in the synthesized membrane structure occurred along with a significant reduction of the rate of growth of nuclei and consequently the pore/void size in the synthesized membrane structure. Thus, under these conditions and during membrane testing, the following is true:

1. Because of the increasing number of pores, the transmission of tiny particles similar to water molecules can be facilitated. In fact, the transmission of these tiny particles is more related to the number of pores than the membrane

pore size. Water molecules are so tiny that only dense structures can prevent their transmission. Thus, the aforementioned increase in the number of pores, despite a decrease in the membrane pore size, can facilitate the transmission of tiny water molecules. Figure 4 confirms the correctness of this claim: according to this figure, increasing the PEG concentration always resulted in increased PWP.

2. Because of the decreasing membrane pore size, the transmission of bigger particles similar to HSA/insulin molecules can be restricted. Basically, there is a competition between the water molecules and the HSA/insulin molecules for transmission through the membrane. The passage of particles similar to the HSA/insulin molecules, which are very large in comparison with the water molecules, is significantly related to the membrane pore size. Thus, it is evident that a decrease in the membrane pore size, despite an increase in the number of pores, restricts the HSA/insulin transmission in competition with the water molecule transmission. This can be observed in Figure 5(c,d).

Selection of suitable membranes

As mentioned before, hemodialysis membranes should have appropriate sieving properties so that they can facilitate the transmission of low- and middle-MW uremic toxins such as urea, uric acid, creatinine, insulin, and β_2-microglobulin and simultaneously completely reject proteins such as HSA and greater blood materials.[12,13] Sieving coefficients for insulin and HSA during transmission through conventional high-flux hemodialysis membranes are 85–90% and 0–3%, respectively.[13] The insulin and HSA sieving coefficients of M2, M3, and M12 membranes meet this standard of conventional high-flux hemodialysis membranes. However, according to Figure 4, the aforementioned prepared membranes have higher PWP (270–470 L/m^2 h mmHg) in comparison with conventional hemodialysis membranes (their PWP is restricted to 250–300 L/m^2 h mmHg).[11] Thus, the noticeable presence of PEG as a pore former (5 wt % in M2 and 10 wt % in M3 and M12) along with a cold coagulation bath (M2 and M3) or a viscous casting solution film (M12) can lead to the preparation of membranes with appropriate sieving coefficients and higher PWP.

Thermal/chemical stability of the prepared membranes

We also investigated whether the presence of PEG along with a cold coagulation bath or a viscous casting solution film could lead to improvements in the thermal/chemical stability of the prepared membranes.

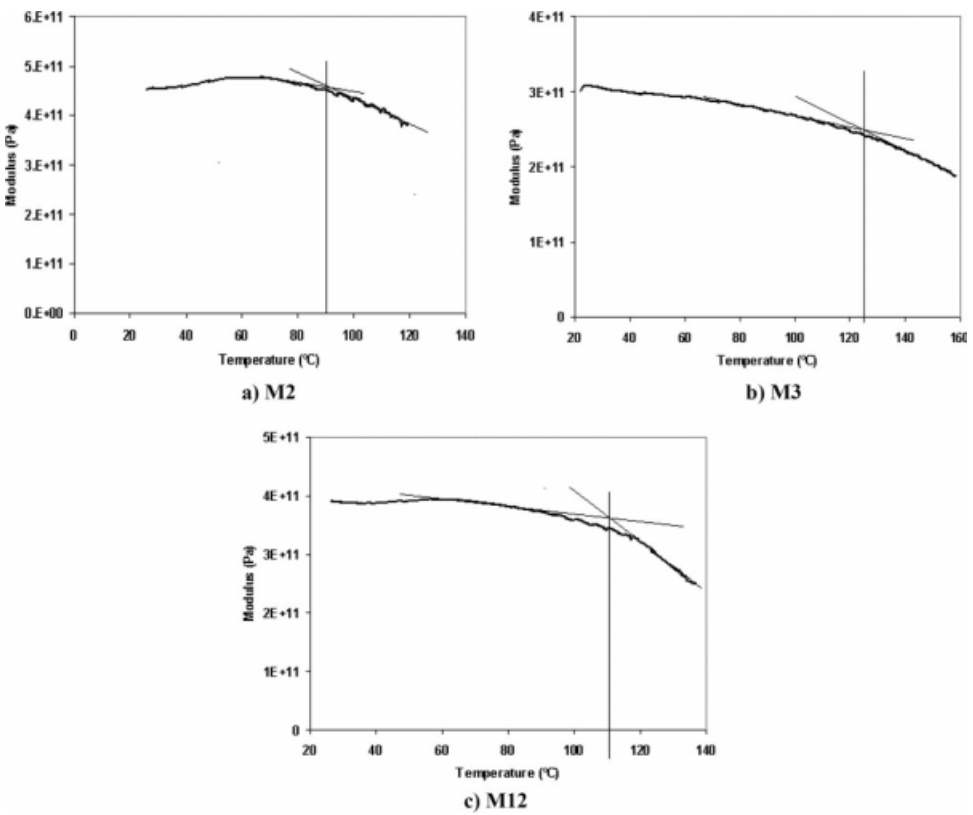

Figure 6 Modulus curves of selected membranes: (a) M2, (b) M3, and (c) M12.

When an amorphous polymer is heated, a temperature exists at which the polymer changes from a glassy state to a rubbery state. This temperature is called the glass-transition temperature (T_g), and it has a significant effect on the thermal and chemical stability of the polymer.[19,28] Up to this temperature, the thermal energy is just sufficient to overcome the restriction of the rotation of segments around the main chain bonds or to overcome the interactions between the chains. For this reason, the important parameters that determine T_g are the chain flexibility and chain interactions.[19]

DMTA is a current technique in thermal studies, and exact values of T_g can be obtained with this technique.[30,31] The DMTA results for the prepared membranes were studied in terms of curves, and T_g values of the prepared membranes are also presented in Figures 6 and 7. According to these figures, a noticeable presence of PEG in the casting solution film (5 wt % in M2 and 10 wt % in M3 and M12) at a lower CBT (M2 and M3) or in the more viscous casting solution film (M12) could lead to the preparation of membranes with higher T_g values and consequently higher thermal/chemical stability in comparison with the conventional CA membranes. This could be due to the following factors:

1. PEG, contrary to NMP, has a relatively low affinity to CA, and consequently, the presence of this additive in the casting solution film results in the aggregation and contraction of the polymer chains during membrane formation in the coagulation bath. This results in a restriction of the rotation of the CA segments around the main-chain bonds and, consequently, higher T_g values of the prepared membranes.
2. A reduction in CBT results in a contraction of the polymer chains after the immersion of the casting film into the coagulation bath and, consequently, a contraction of the prepared membranes. Also, a reduction in CBT results in denser structures (as mentioned previously). It is evident that contraction of the polymer chains, along with denser structures, leads to a restriction in the rotation of the CA segments around the main-chain bonds and thus higher T_g values, and this results in higher thermal and chemical stability.

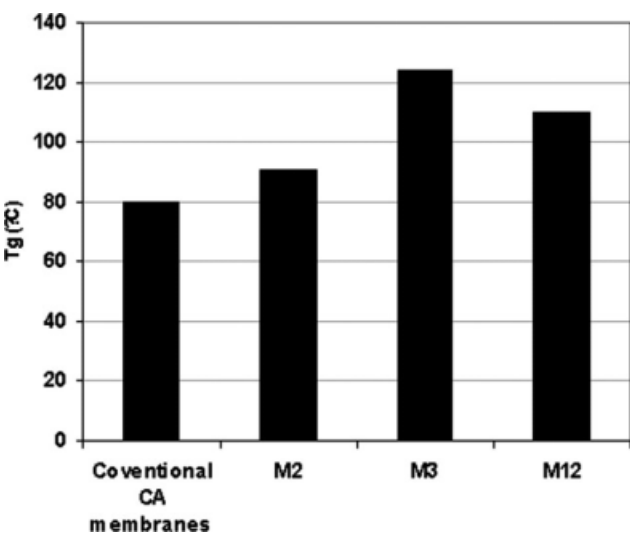

Figure 7 T_g of the selected membranes.

CONCLUSIONS

Asymmetric CA membranes were synthesized with the phase-inversion method. The effects of the CA and PEG concentrations and CBT on the morphology, PWP, insulin/HSA transmission, and finally thermal/chemical stability of the synthesized membranes were investigated. The results showed that increasing the PEG concentration and CBT along with reducing the CA concentration generally resulted in increased PWP and insulin/HSA transmission. Also, these variations facilitated the formation of macrovoids in the membrane sublayer. On the other hand, a noticeable presence of PEG in the casting solution film along with a cold coagulation bath or a viscous casting solution film resulted in not only appropriate sieving coefficients for insulin/HSA during membrane testing but also higher PWP and thermal/chemical stability in comparison with conventional hemodialysis membranes.

References

1. Arthanareeswaran, G.; Thanikaivelan, P.; Srinivasn, K.; Mohan, D.; Rajendran, M. Eur Polym J 2004, 40, 2153.
2. Bhattacharyya, D.; Butterfield, D. A. New Insight into Membrane Science and Technology: Polymeric and Biofunctional Membranes; Elsevier: Amsterdam, 2003.
3. Baker, R. W. Membrane Technology and Application, 2nd ed.; Wiley: Chichester, England, 2004.
4. Idris, A.; Yet, L. K. J Membr Sci 2006, 280, 920.
5. Yuan, J.; Zhang, J.; Zang, X.; Shen, J.; Lin, S. Colloids Surf B 2003, 30, 147.
6. Ward, R. A.; Buscaroli, A.; Schmidt, B.; Stefoni, S.; Gurland, V.; Klinkmann, H. Nephrol Dial Transplant 1997, 12, 965.
7. Kung, F. C.; Yang, M. C. Colloids Surf B 2006, 47, 36.
8. Kung, F. C.; Yang, M. C. Int J Biol Macromol 2006, 38, 157.
9. Hayama, M.; Miyasaka, T.; Mochizuki, S.; Asahara, H.; Yamamoto, K. I.; Kohori, F.; Tsujioka, K.; Sakai, K. J Membr Sci 2003, 219, 15.
10. Yamamoto, K.; Matsuda, M.; Hayama, M.; Asutagawa, J.; Tanaka, S.; Kohori, F.; Sakai, K. J Membr Sci 2006, 272, 211.
11. Barzin, J.; Feng, C.; Khulbe, K. C.; Matsuura, T.; Madaeni, S. S.; Mirzadeh, H. J Membr Sci 2004, 237, 77.
12. Czermak, P.; Walz, M.; Catapano, G. J Membr Sci 2006, 273, 89.
13. Ward, R. A. J Am Soc Nephrol 2005, 16, 2421.
14. Liu, T.-Y.; Lin, W.-C.; Huang, L.-Y.; Chen, S.-Y.; Yang, M.-C. Biomaterials 2005, 26, 1437.

15. Hasegawa, T.; Iwasaki, Y.; Ishihara, K. Biomaterials 2001, 22, 243.
16. Sevillano, G.; Puyol, M. R.; Martos, R.; Duque, I.; Lamas, S.; Diez-Marques, M. L. Nephrol Dial Transplant 1990, 5, 497.
17. Sivakumar, M.; Mohan, D. R.; Rangarajan, R. J Membr Sci 2006, 208.
18. Ronco, C.; Crepaldi, C.; Brendolan, A.; Bragantini, L.; d'Intini, V.; Inguaggiato, P.; Bonello, M.; Krausel, B.; Deppischl, R.; Goehll, H.; Scabard, A. Nephrol Dial Transplant 2003, 18, 10.
19. Mulder, M. Basic Principles of Membrane Technology; Kluwer Academic: Dordrecht, The Netherlands, 1997.
20. Han, M. J.; Nam, S. T. J Membr Sci 2002, 202, 55.
21. Jung, B.; Yoon, J. K.; Kima, B.; Rheeb, H. W. J Membr Sci 2004, 243, 45.
22. Liu, Y.; Koops, G. H.; Strathmann, H. J Membr Sci 2003, 223, 187.
23. Chuang, W. Y.; Young, T. H.; Chiu, W. Y.; Lin, C. Y. Polymer 2000, 41, 5633.
24. Kim, J. H.; Lee, K. H. J Membr Sci 1998, 138, 153.
25. Rahimpour, A.; Madaeni, S. S. J Membr Sci 2007, 305, 299.
26. Fiore, G. B.; Guadagni, G.; Lupi, A.; Ricci, Z.; Ronco, C. Blood Purif 2006, 24, 555.
27. Saljoughi, E.; Sadrzadeh, M.; Mohammadi, T. J Membr Sci 2009, 326, 627.
28. Saljoughi, E.; Amirilargani, M.; Mohammadi, T. J Appl Polym Sci 2009, 111, 2537.
29. Smolders, C. A.; Reuvers, A. J.; Boom, R. M.; Wienk, I. M. J Membr Sci 1992, 73, 259.
30. Sairam, M.; Naidu, B. V. K;,Nataraj, S. K.; Sreedhar, B.; Aminabhavi, T. M. J Membr Sci 2006, 283, 65.
31. Teli, S. B.; Gokavi, G. S.; Sairam, M.; Aminabhavi, T. M. Colloids Surf A 2007, 301, 55.