Preparation and Solvents Effect Study of Asymmetric Cellulose Acetated/Polyethyleneimine Blended Membranes for Dialysis Application

Hizba Waheed
School of Chemical and Materials Engineering (SCME)
National university of Science and Technology (NUST)
H-12, 44000, Islamabad, Pakistan.
hizbawaheed@scme.nust.edu.pk

Arshad Hussain
School of Chemical and Materials Engineering (SCME)
National University of Science and Technology
H-12, 44000, Islamabad, Pakistan.
Arshad.hussain@scme.nust.edu.pk

***Abstract*- The aim of this research is to study the effect of various solvents on membrane morphology and performance of cellulose acetate (CA) based polymeric membranes having Polyetyleneimine (PEI) additive. The CA/PEI blended membranes are to be used for dialysis operation. For this purpose, acetic acid, formic acid, 1-Methyl-2-pyrolidone (NMP) and N, N-Dimethylacetamide (DMAC) are used. The best performing membrane is selected and is modified using various solvents to choose the best solvent that can enhance the membrane performance efficiently. Afterwards contact angle measurement, pure water flux and water up take of modified membranes are determined to check the change in dialysis performance. Surface morphology of membrane is studied using SEM and AFM. All these results displayed blending of polymer, solvents and additive in different ways. All prepared membranes were also tested for bovine serum albumin (BSA) rejection and urea clearance. From all the solvents used, formic acid gave the best results. The blending is homogeneous and macro void formation is appropriate for dialysis application. The replacement of acetic acid with formic acid (C.A+ F.A+PEI) showed hydrophilic nature and increased the BSA rejection percentage. Urea clearance was augmented as well to an appreciable value. The results revealed that from all the mentioned above solvents, formic acid is most suitable one for dialysis operation.**

***Key Words*: Cellulose acetate, Variable solvents, Dialysis, BSA rejection, Urea clearance.**

I. INTRODUCTION

Kidney is a important organ of body that keeps the water and salt balance trough osmoregulation and control waste disposal. Kidney dialysis is a life-support treatment for renal patient that uses a special machine to filter uremic wastes, salt, and excess fluid from patient's blood. Major role played within kidney dialysis is by semipermeable membrane which allows the removal of materials through it. This removal takes place primarily by selective and passive diffusion of the concentration gradient across the membranes [1].

Dialysis membranes are normally composed of regenerated cellulose as the basic polymer. Pore size is variable, molecules larger than pores are engaged on the surface, while the smaller ones can easily pass through the membrane pores and get separated. The first dialyzer, using a flat cellophane tube, was introduced by Kolf and Berk [2]. Advancement of membranes has been observed in both industrial and biomedical separation processes [3,4]. The use of membranes in artificial organs has become a major life-saving technique. Successful use of dialysis membranes has led to the urgency of large-scale production of synthetic membranes.

Cellulose acetate has gained much consideration in dialysis membrane due to its maximum uniformity, permselectivity, and physical properties, such as strength and flexibility [5]. CA polymers are considerable, with characteristics like good toughness, biocompatibility, high flux, and relatively low cost. Many studies have proven that CA is highly comparable to other synthetic polymer materials, being effective in the hemodialysis process [6].

In our previous work we have used CA as basic polymer and added variable additives like Polyethylene glycol (PEG), glycerin, sericin, polyvinyl pyrolidone (PVP) and polyethylene imine (PEI) to impart desired characteristic to the fabricated membrane that include favorite pore size, biocompatibility and mechanical behavior [7,8,9]. This work is focused on testing the effect of different solvents on the characteristics and performance of CA based membranes doped with PEI. For this purpose, we tested Acetic acid (A.A), Formic acid (F.A), N-Methyl-2-pyrrolidone (NMP) and Dimethylacetamide (DMAC). Scanning electron microcopy (SEM) was used to investigate the morphology and pore size of the membranes. Atomic force microscopy (AFM) was used to study the surface roughness. The performance of the fabricated membranes was tested on a dead-end filtration cell and laboratory-scale experimental setup.

II. EXPERIMENTAL

Materials

In this study, asymmetric polymeric membranes were synthesized for dialysis application. For this objective Cellulose acetate (CA) polymer with average molecular weight of 30,000 was obtained from EASTMAN, Polyetyleneimine/ polyaziridine (PEI) branched with average molecular weight of 25,000 was purchased from Aldrich, Acetic acid (ACS reagent ≥ 99.7%), Formic acid with purity ≥98% provided by EMD, 1-Methyl-2-pyrolidone (NMP) was provided by Fisher scientific, N,N-Dimethylacetamide with 99+% purity was provided by Acros organics were used as solvents.

This is an open access article under the CC BY-SA 4.0 license (https://creativecommons.org/licenses/by-sa/4.0/)

For application testing, Urea (MW 60.06) were provided by Sigma Aldrich and Bovine Serum Albumin BSA (MW 66,000 Da) was provided by Sigma Aldrich.

III. CASTING SOLUTION PREPARATION:

CA (15.5%) solutions were made with different solvents with addition of 1% PE1 dissolved in 1% distilled water. For complete dissolution, continuous stirring was ensured to get a clear solution. To remove trapped air bubbles the casting solution was sonicated for two hours. Later, the solution was poured on a flat glass sheet and spread with the help of a casting knife to a uniform thickness. The glass plate was then immersed into a water bath controlled at 25°C to get the phase separation between the solvent and non-solvent phase. Distilled water was used as the non-solvent phase. Prepared membranes were washed several times to remove any traces of solvents. Washed membranes were then placed in distilled water for 24 h before testing. Schematic presentation of membrane casting method is shown in Fig 1.

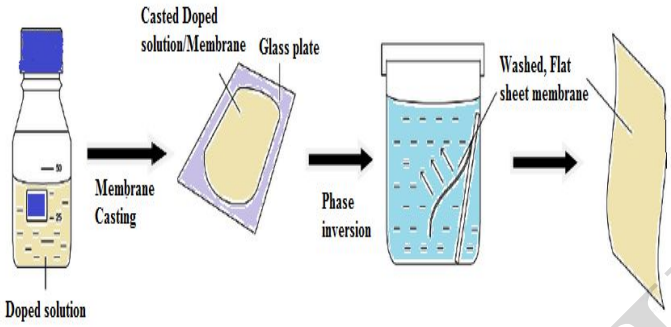


Fig. 1: Process Diagram For Membrane Fabrication

Various CA/solvent/PEI polymer blends were prepared. Process scheme used for membrane synthesis is given in Table 1 showing the compositions and coagulation bath temperature for different synthesized membranes.

Table I. Different types of membranes, their compositions, and coagulation bath temperature

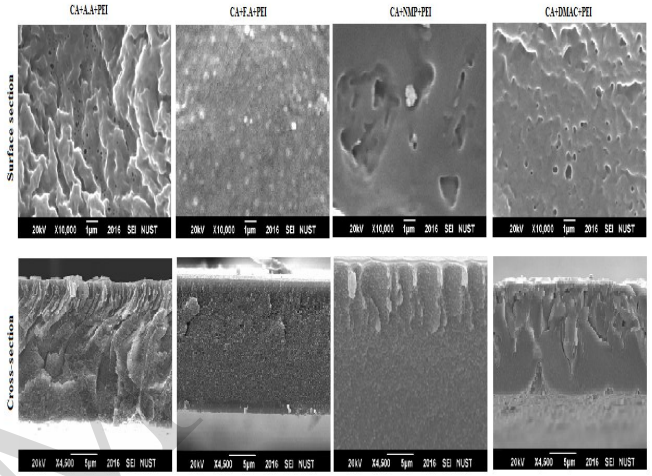
Membrane type	Solution Composition (wt. %)				CBT (°C)
	CA	Solvent	PEI	D.Distl H_2O	
CA+A.A+PEI	15.5	82.5 (A.A)	1.0	1.0	25°
CA+F.A+PEI	15.5	82.5 (F.A)	1.0	1.0	25°
CA+NMP+PEI	15.5	82.5 (NMP)	1.0	1.0	25°
CA+DMAC+PEI	15.5	82.5 (DMAC)	1.0	1.0	25°

IV. MEMBRANE CHARACTERIZATION, RESULTS AND DISCUSSIONS

1. Scanning Electron Microscopy (SEM)

SEM (JSM 6490LA, Jeol, Japan) was used to study the surface morphology of fabricated membranes i.e gives information about morphology and pore-size distribution on the membrane surface. Micrographs of all prepared membranes are presented in Fig 2. Upper row presents the surface micrographs while lower row is presenting cross section of fabricated membranes.

All the images show formation of folds and large pores with large diameter except membranes prepared with CA as basic polymer, formic acid (F.A) as solvent and PEI as additive. Membrane CA+F.A+PEI showed the uniform distribution of pores all over the surface and the average pore diameter was recorded to be 70.3nm which is less as compared to membranes prepared using NMP and DMAC as solvents. Whereas membranes prepared using acetic acid (A.A) was with lower pore diameter (49.46nm) but it was having non-uniform pore distribution because of formation of scaffolds.



2. Effect of solvent on membrane morphology

From the SEM images given in Fig 2 it is obvious that solvent played an important role in defining the morphology, pore size and pore size uniformity in membrane. In case of Acetic acid (A.A) the pore forms are smaller and form efficient macrovoids and scaffolds in membrane structure but uniformity of pore is not much visible.

However, in case of formic acid (F.A) the pores generated are with appropriate size and their distribution on membrane surface is also uniform that impart good and efficient characteristics to the dialysis membrane formed [10, 11]. In case of DMAC and NMP the SEM image shows that the blending was not homogeneous which resulted in the formation of irregular pores with variable pore sizes. The cross-section also showed dense and porous patchy membrane image.

3. Atomic force microscopy (AFM)

The surface roughness of pure and blend membranes was examined using AFM (JSPM-5200, Japan). It is shown in the Fig 3. that membrane prepared using formic acid and acetic acid as solvent shows less roughness. Membrane prepared with formic acid is much smooth thus is more suitable for hemodialysis application as lower is the surface roughness higher is the biocompatibility of fabricated membrane.

IJHM

This is an open access article under the CC BY-SA 4.0 license (https://creativecommons.org/licenses/by-sa/4.0/)

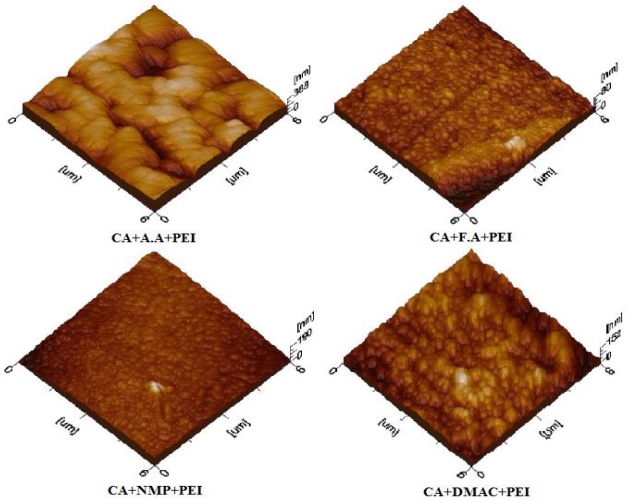


Fig. 2: AFM micrographs of fabricated membranes.

V. MEMBRANE PERFORMANCE TESTING

1. *Wettability Properties*

The hydrophilicity of prepared membranes was measured using contact angle (Tantec Contact Angle Meter). A sessile drop method was used to measure the contact angle [12, 13]. A drop of distilled water was allowed to stay on the membrane surface (2 x 2 cm) and the contact meter was aligned and focused on the membrane water interface. Each contact angle of the membrane was measured for at least 8 times to get the average value. Contact angle measured for all prepared membrane is shown in Fig 4.

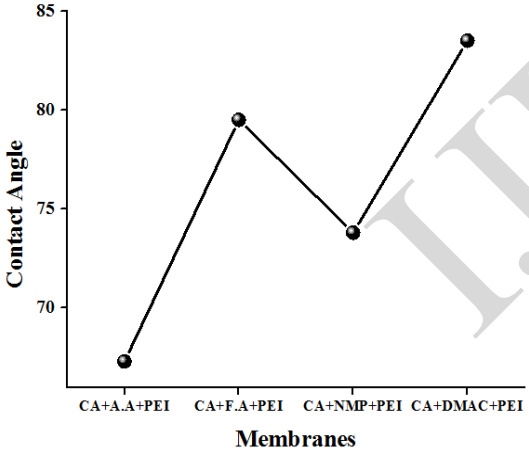


Fig. 3: Contact angle measurements of fabricated membranes.

2. *Pure Water Flux*

Pure water flux or water permeation was measured using dead-end filtration setup. N_2 gas was used to adjust the pressure and membranes were tested on pressure ranging from 2-3 atm. Water flux was calculated using equation (1) below

$$Flux\ (J) - \frac{Q}{\Delta t \times A}$$

Where J represents the permeation flux ($Lm^{-2}h^{-1}$) for pure water, Q is the volume of permeate solution (L), Δt is the permeation time (h) and A represents the active area of testing membrane.

Fig 5. shows that testing various membranes it was found that the membrane prepared using formic acid gave optimum flux value (80Lit/hr.m^2) that is suitable for dialysis operation. However, the flux value of acetic acid membrane was also closed to formic acid i.e 70Lit/hr.m^2. Water flux values of membrane casted using NMP and DMAC are too high which make them inappropriate for dialysis application as they will result in loss of water soluble useful contents of patient's blood.

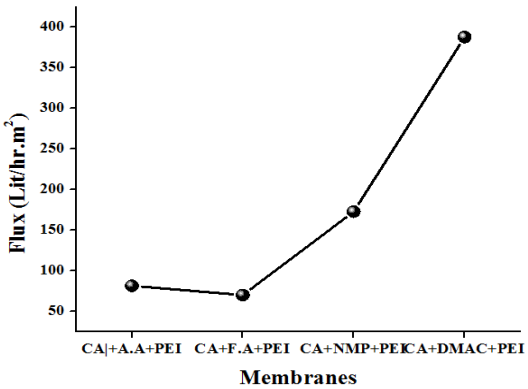


Fig. 4: Dead-End Filtration setup and pure water flux fabricated membranes.

3. *BSA Rejection Measurements*

Dialysis patients would experience albumin loss associated syndrome if albumin (≈67 kDa) was lost during the dialysis treatment [14]. Thus, an ideal dialysis should avoid albumin loss during dialysis. Fig 6 represents the % rejection of all fabricated membranes using variable solvents.

All the membranes have above 90% rejection of BSA while membrane C.A+F.A+PEI has 99% rejection, which was compulsory for all dialysis membranes to prevent albumin loss [15]. The rejection of BSA by the fabricated membrane was calculated by equation (2) below.

$$\%\ rejection = \left(1 - \frac{C_p}{C_r}\right) \times 100$$

Where C_p and C_r are concentrations of permeate and retentate respectively.

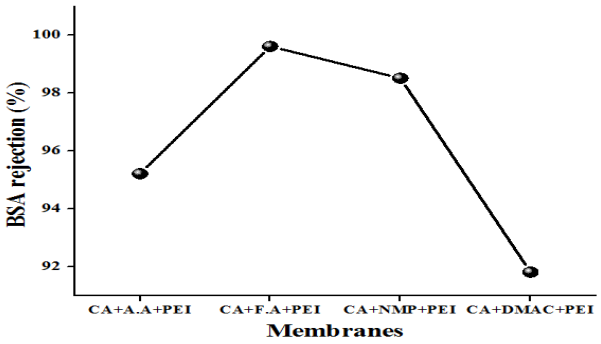


Fig. 5: BSA rejection measurements of fabricated membranes

IJHM

This is an open access article under the CC BY-SA 4.0 license (https://creativecommons.org/licenses/by-sa/4.0/)

4. Urea Clearance Measurements

Uremic toxics are the collection of complexes in the human body, which are present in urine under normal conditions [16]. When the concentration of uremic toxic increased beyond the standard range, undesirable effects will arise and this was named as a uremic syndrome. Urea is the main component of uremic toxins and is generally used to quantify the quality of hemodialysis membranes [17, 18].

For a good hemodialysis membrane, urea clearance should be at least 60% [19]. Fig 7. illustrates the urea reduction of different membranes prepared. The concentration of urea was determined by the equation (3) where C_i and C_f are initial and final concentration at time t respectively

$$\text{Urea clearance } \% = \frac{C_i - C_f}{C_i} \times 100$$

C.A+A.A+PEI was with 67.2% urea reduction. Membrane C.A+F.A+PEI shows the highest urea reduction of 69.6% in contrast to all other membrane prepared which is higher than commercial parameters of good dialysis membrane as described by Eknoyan [20].

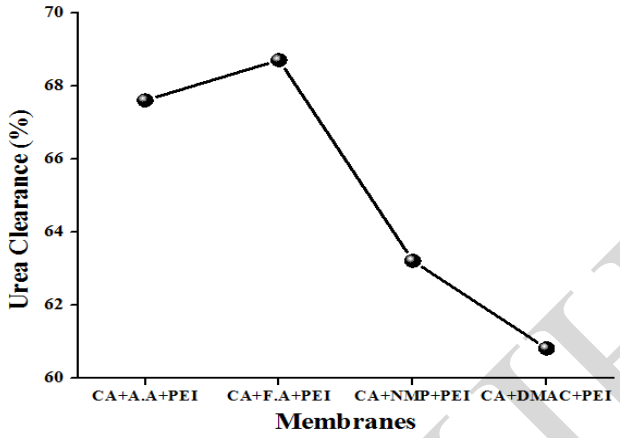


Fig. 6: Urea Reduction measurements of fabricated membranes

VI. CONCLUSION

In this work, PEI was used as filler for the fabrication of PEI/CA mixed matrix flat sheet membranes prepared through the diffusion induced phase separation process. Various solvents are used to check their effect on membrane morphology nad dialysis performance. Acetic acid (A.A), formic acid (F.A), 1-Methyl-2-pyrolidone (NMP) and N, N-Dimethylacetamide (DMAC) were used. The results showed that using formic acid as solvent showed compact structure with porous skin layer and macro-voids in cross section. SEM and AFM images of C.A+ A.A+PEI and C.A+ F.A+PEI membranes depicted homogenous spread of micropores that results in smooth surface.

From all the solvents used, formic acid gave the best results. The blending is homogeneous and macro void formation is appropriate for dialysis application. The replacement of acetic acid with formic acid (C.A+ F.A+PEI) showed hydrophilic nature and increased the BSA rejection percentage from 95% to 100% . Urea clearance was augmented to 69% as compared to 67%, 63% and 61% in case of C.A +A.A +PEI, C.A +NMP +PEI and C.A +DMAC +PEI respectively. The results revealed that from all the mentioned above solvents, formic acid is most suitable one for dialysis operation.

ACKNOWLEDGEMENTS

This work was supported by School of Chemical and Materials Engineering, National University of Sciences and Technology, Islamabad, Pakistan.

REFERENCES

[1] U.S. Renal Data System, USRDS, (2009) Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD.

[2] http://cjasn.asnjournals.org/content/4/Supplement_1/S5.full

[3] L.C Smeby, Wideroe, T.E, Balstad T, Jorstad S, "Biocompatibility aspects of cellophane, cellulose acetate, polyacrylonitrile, polysulfone and polycarbonate hemodialyzers", Blood Purificat, 1986, 4:93–101.

[4] K. Hartmann, B. M. Henz, S. Kruger-Krasagakes, J. Kohl, R. Burger, S. Guhl, I. Haase, U. Lippert, T. Zuberbier, "C3a and c5a stimulate chemotaxis of human mast cells", Blood, 1997, 89:2853–2870.

[5] F.Fushimi, M. Nakayama, K. Nishimura, T. Hiyoshi, "Platelets adhesion, contact phase coagulation activation, and c5a generation of polyethylene glycol acid-grafted high flux cellulosic membrane with varieties of grafting amounts", Artif Organs, 1998, 22:821–826.

[6] M. Diamantoglou, M. Nywlt, W. Holz, "Method of making cellulosic dialysis membrane". U.S. Patent, 2000, 6,019,925.

[7] S. H. Ye, J. Watanabe, Y. Iwasaki, K. Ishihara, "In situ modification on cellulose acetate hollow fiber membrane modified with phospholipid polymer for biomedical application", J. Membrane Sci, 2005, 249:133–141.

[8] Idris, C. M. Kee, I. Ahmed, "Effect of monosodium glutamate additive on performance of dialysis membrane", Journal of Engineering Science and Technology, 2008, 2: 172 – 179.

[9] Idris, H. K. Yee, C. M. Kee, "Preparation of cellulose acetate dialysis membrnes using D- glucose monohydrate as additive", *Jurnal Teknologi*, 2009, 51(F) Dis. 2009: 67–76

[10] Idris, L. K. Yet, "The effect of different molecular weight PEG additives on cellulose acetate asymmetric dialysis membrane performance", J Memb **Sci,** 2006,280: 920–927

[11] F. Chiti, C. M. Dobson, "Protein misfolding, functional amyloid and human disease", Annu. Rev. Biochem. 2006, 75:333–366.

[12] Idris, N. M. Zain, M.Y. Noordin, "Synthesis, characterization and performance of a symmetric polyethersulfone (PES) ultrafiltration membranes with poly-ethylene glycol of different molecular weights as additives", Desalination, 2007, 207:324–339.

[13] Idris, K. Y. Hew, M. K. Chan, "Preparation of cellulose acetate dialysis membrane usingd-glucosemonohydrate as additive", J.Teknol.(Kejuruteraan), 2009, 51:67–76.

[14] S. Farrukh, F. T. Minhas, A. Hussain, S. Memon, M. I. Bhanger, M. Mujahid, "Preparation, Characterization, and Applicability of Novel Calix[4]arene-Based Cellulose

IJHM

This is an open access article under the CC BY-SA 4.0 license (https://creativecommons.org/licenses/by-sa/4.0/)

Acetate Membranes in Gas Permeation", J.Appl. Polym. Sci, 2014, 131:.39985
[15] Idris, K. Y. Lee, M. Noordin, M. K. Chan, "Response surface methodology approach to study the influence of PEG and water in cellulose acetate dialysis membranes", J. Teknol. F, 2008, 49:39–49.
[16] Y. Iwasaki, H. Yamato, T. N. Kono, A. Fujieda, M. Uchida, A. Hosokawa, M. Motojima, M. Fukagawa, "Ureamic toxin and bone metabolism". J.Bone Miner. Metab, 2006, 24:172-175.
[17] K. Sakai, "Determination of pore size and pore size distribution 2. Dialysis membranes", J. Membrane. Sci, 1994, 96:91-130.
[18] G. Lesaffer, R. D. Smet, N. Lameire, A. Dhondt, P. Duym, R. Vanholder, "Intra dialytic removal of protein-bound uraemic toxins: role of solute characteristics and of dialyse rmembrane". Nephrol.Dial.Transplant, 2000, 15:50–57.
[19] R. Vanholder, R. V. De Smet, S.M. Ringoir, "Assessment of urea and other uremic markers for quantification of dialysis efficacy", Clin.Chem, 1992, 38:1429–1436.
[20] G. Eknoyan, G. J. Beck, A. K. Cheung, J. T. Daugirdas, T. Greene, J. W. Kusek, M. Allon, J. Bailey, J. A. Delmez, T. A. Depner, "Effect of dialysis dose and membrane flux in maintenance hemodialysis", N Engl. J. Med, 2002, 347:2010–2019.
[21] M. Irfan, A. Idris, N. M. Yusof, N. F. M. Khairuddin, H. Akhmal, "Surface modification and performance enhancement of nano-hybrid f-MWCNT/PVP90/PES hemodialysis membranes", J. Membrane. Sci, 2014, 467:73–84.

IJHM

This is an open access article under the CC BY-SA 4.0 license (https://creativecommons.org/licenses/by-sa/4.0/)