PREPARATION OF FLAT SHEET CELLULOSE ACETATE DIALYSIS MEMBRANE, SUITABLE FOR CLEARANCE OF UREA SOLUTION

A. Idris*, K. Y. Lee

Department of Bioprocess Engineering, Faculty of Chemical and Natural Resources Engineering, Universiti Teknologi Malaysia, 81300 UTM, Skudai, Johor, Malaysia.
*Corresponding author. Phone: 607-5535603, Fax: +607-5581463
Email: ani@fkkksa.um.my

ABSTRACT

Flat sheet cellulose acetate dialysis membranes were prepared using phase inversion method using acetic acid as the solvent. Effect of modifying agent (polyethylene glycol 400 - PEG 400) and non solvent (distillated water) were investigated. Six different formulations were used, and the performances of the obtained membranes were tested for protein separation using a 1 mg/mL urea solution. It was found that the membrane obtained from the formulation consisting of 20 %wt cellulose acetate, 60 %wt acetic acid, 15 %wt PEG 400 and 5 %wt distillated water gives the best clearance performance for urea solutions. In addition, it was found that the presence of modifying agents in the casting solutions enhanced the clearance performance. Different amount of different modifying agents presence in the casting solutions will gives a totally different trend of results achieved. However, the amount of modifying agents is restricted in the range of 20 %wt to avoid weakness in solutes clearance efficiency.

Key words: Dialysis Membrane, Cellulose Acetate, Modifying Agent, Clearance, Urea

1 INTRODUCTION

Dialysis membranes are fast gaining importance due to the increase in the number of patients having kidney failure. It has been estimated than between 28,000 and 50,000 people died each year in the United States from kidney diseases of one kind or another. In addition, some three million residents of the United States are though to have undiagnosed kidney diseases (King, 1971). In Malaysia, over 1000 people with kidney problems died in year 2001 (News Straits Time, 31/12/2001) and the latest statistic showed that the number of kidney patients in Malaysia increase by some 2,200 to 2,300 each year (The Stars, 1/6/2004). Therefore, developments in the field of dialysis become significantly important to reduce the mortality number shown.

Various materials have been used for dialysis membranes. Amongst them are cellulose acetate, poly-acrylonitrile (PAN), poly-methyl methacrylate (PMMA), ethylene vinyl alcohol (EVAL) copolymer, polysulfone (PS) and polyamide (Sakai, 1994). Off all, cellulose acetate is the commonly used material for making dialysis membranes. Cellulose acetate dialysis membrane had been known for almost five decades since World War II, reported by Kolf (Kolf, 1965). Till now, cellulose membranes are still widely used for hemodialysis due to its excellent properties such as biocompatibility, good desalting, high flux and relatively low cost (Hokhorst et al., 1981).

In recent years, the development of this field had been focused mostly on the characteristics and the properties of commercially available dialysis membranes. Studies had been carried out such as the sieving properties, flow maldistribution, mechanical properties, diffusive permeability and pores distribution, to understand more about dialysis membranes (Wendt et al., 1979; Noda et al., 1979; Klein et al., 1977, 1976; Broek et al., 1992). Since 1980s, the emphasis on adsorption, biocompatibility, large molecule flux and convective transport of the dialysis membranes has been studied and reported (Koda et al., 2001). The studies to improve the clearance on "middle large molecules" (> 500 Dalton)

of dialysis membranes were carried out intensively (Boure, 2004; Masaki et al., 1999; Kreiter et al., 2003; David et al., 1998). Even so, the large number of papers on the differences in dialysis membranes biocompatibility, flux as well as the technology implied, the true effect has long been controversial in the clinical setting (Koda et al., 2001). Although much work has been aimed at highlighting the different results achieved in development of the field of dialysis membranes, the conclusions reached by these various studies were far from unanimous and were often markedly discordant (Stefoni et al., 2000).

In dialysis membrane making, several variables can be adjusted to control membrane properties and performance such as the composition of the polymer, type and concentration of modifying agents used. Although there have been research on the effect of the mentioned variables on membrane properties, most of the work involved reverse osmosis, ultrafiltration, microfiltration and gas membranes. Besides the work of Henne (1986), Diamantoglou et al. (1992, 1995) and Dunwerg et al. (1995), not much has been reported regarding the effect of the modifying agents or additives and nonsolvents on performance of dialysis membranes. Most of the mentioned works regarding dialysis membranes are patents and the parameters affecting the membrane performance and properties such as modifying agent and non solvent concentration in the dope had not been systematically investigated.

In view of this, the main objective of this study is to investigate the effect of non-solvent and modifying agent such as water and PEG 400 respectively on urea clearance. In this experiment, the dialysis membranes produced were prepared from six different dope formulations with 2 different non-solvent compositions and various ratios of acetic acid/PEG 400.

2 EXPERIMENTAL

2.1 MATERIALS

Cellulose acetate with the average molecular weight of 30,000 Dalton (Sigma-Aldrich) was used as the membrane-forming polymer. The solvent used was acetic acid (Acc) with analytical purity of 99% and distilled water was used as non-solvent agent. Polyethylene glycol 400 (PEG 400) was used as a modifying agent. Experiments were performed using urea (60.02 MW) obtained from Sigma-Aldrich.

2.2 PREPARATION PROCESS

The polymer dope was prepared in a reaction vessel, where acetic acid was added in first, followed by cellulose acetate. The polymer dope was heated to approximately 70°C and a high stirrer speed was used to assist in the dissolution of polymers. The cellulose acetate was added in slowly, to ensure a complete dissolution. Finally, the PEG 400 and distilled water were added slowly to avoid any agglomeration in the polymer dope. When the entire polymer is completely dissolved, as indicated by the clear solution obtained, it was cooled and poured into a storage bottle. Subsequently, the solution was degassed in an ultrasonic bath for about two hours to remove any air bubbles present and kept away from direct sunlight to slow down its aging process. The six dope formulations prepared in this work are shown in TABLE 1.

2.3 MEMBRANE CASTING

The membranes were prepared using a casting knife on a glass plate. The flat sheet membrane formed with thickness of 200 μm was sprayed with nitrogen gas for a few seconds. This is to allow the solidification and pre-orientation of the membrane skin by partial evaporation. Next, the membrane was immersed in a water bath to complete the phase separation, where exchange of phases occurs between the solvent and water. Then, the membrane was transferred to another container containing glycerol for post-treatment to remove the excess acetic acid from the membrane. Eventually, the membrane was transferred to another container containing distillated water ready to be tested in the dialyser.

2.4 SCANNING ELECTRON MICROSCOPY (SEM)

The membranes were snapped under liquid nitrogen to give a generally consistent and clean break. The membrane is then sputter coated with thin film of gold. The membrane was mounted on a brass plate using double side adhesion tape in a lateral position. Images of cross sections of the membranes were obtained using Phillip SEM Model XL-40 microscope.

2.5 MEMBRANCE TESTING USING UREA

The performance of the dialysis membrane in terms of clearance using 1 mg/mL urea was evaluated using the testing system shown in FIGURE 1. The flow rate of the testing solution on the reservoir side is 100 mL/min whilst that on the pure water reservoir side is 300 mL/min. The temperature was maintained at 37 ± 2 °C using a Digi-sense temperature controller. Samples were collected at both reservoirs at 30 minutes intervals for a period of 210 minutes. The concentration of urea was evaluated using a commercial diacetyl method obtained from Eagle-Diagnostics. A 0.02 mL sample was added to 1.5 mL color reagent and 3.0 mL acid reagent and allowed to react. The urea concentration was determined from the difference in absorbance reading at 520 nm using UV spectrophotometer (UV-Spec Shidmazu UV-160).

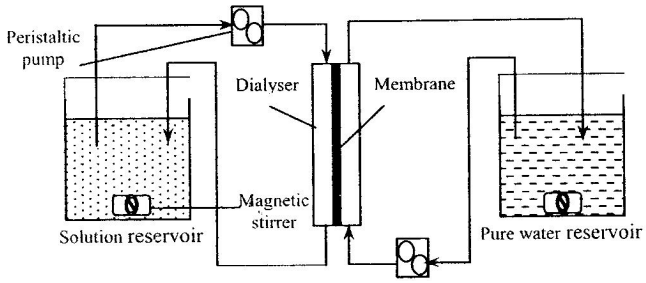

FIGURE 1. Schematic diagram of single membrane dialysis system

3 RESULTS AND DISCUSSION

TABLE 1 shows the clearance percentage of urea solutes and the urea removal rates of the various dialysis membranes casted. In order to ensure reproducibility of the results, each of the membranes was tested three times and the average results were tabulated in TABLE 1. From TABLE 1, membrane 1, 2 and 3 can be grouped into one category while membrane 4, 5 and 6 form another due to the different amounts of distilled water content. The dialysis membranes in both categories have the same amount of cellulose acetate but different amount of distilled water. According to TABLE 1, a high ratio value of Acc/PEG indicates a high content of the acetic acid and a low PEG.

TABLE 1. Formulation of six different dope solutions

Cate -gory	For -mula -tions	CA %wt	Water, %wt	Ratio of Acc / PEG	Acetic acid, (Acc) %wt	PEG 400, %wt	Clearance Percentage, -%	Rate of Urea Removal, mg/mL.min
1	1	20	5	4	60.00	15.00	45.25	0.0020
	2	20	5	9	67.50	7.50	9.27	0.0004
	3	20	5	14	70.00	5.00	36.68	0.0017
2	4	20	15	4	52.00	13.00	26.03	0.0014
	5	20	15	9	58.50	6.50	23.99	0.0012
	6	20	15	14	60.67	4.33	34.12	0.0017

The typical experimental results for the clearance of urea solutes versus time for the various membranes are shown in FIGURE 2. In the first category, it is observed that membrane 1 has the highest urea clearance percentage of 45.25 %. Membrane 1 contains 20 %wt cellulose acetate, 60 %wt of acetic acid, 15 %wt PEG 400 and 5 %wt distillated water. After 210 minutes, 42.25 % of urea has been removed. It can also be observed that the rate of removal of urea for membrane 1 is the highest compared to the other membranes indicated by the steep gradient in FIGURE 2. This is probably due to the high PEG content in membrane 1 formulation indicated by the low ratio of Acc/PEG.

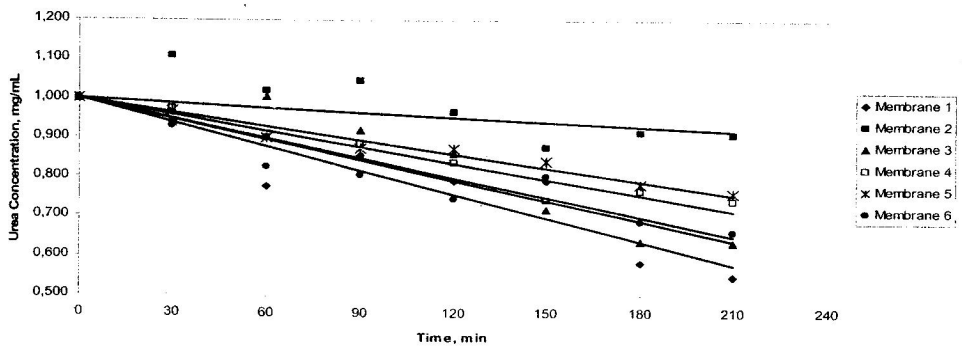

FIGURE 2. Urea solutes concentration as a function of time during experiments

The effect of PEG 400 for the category 1 membranes is clearly depicted by the trendline shown in FIGURE 3. For the category 1 membranes, where the water content is only 5 %wt, it can be found that increase in PEG content results in higher urea clearance. Higher amount of PEG in membrane 1 reduced or readjusts the dissolving power of the solvent for the polymer and induces the formation of numerous porous polymer network entities with a finite size (Kessler et al., 1992). Membrane 1, which contains the highest amount of PEG, exhibits highest urea clearance. The presence of modifying agents, PEG in this case reduce the rate of precipitation and favor a more dense sponge structure as can be seen in FIGURE 4 (a). This result seems to be in agreement with that obtained by Frommer et al., (1973). However, it should be noted that the water content in this category of membrane is only 5%, which is considered as insignificant compared to the amount of PEG 400. Thus it is the presence of PEG that controls the rate of precipitation of the membrane.

SEM images of Category 1 membranes revealed that macrovoids were formed with decreasing of PEG content and this can be observed by the SEM images taken in FIGURE 4 (a), (b) and (c). Macrovoids are often observed on the asymmetric membranes made by the phase inversion technique. It is known that macrovoids are suitable for ultrafiltration process and can be employed as support layers for composite membrane (Smolders et.al., 1992). However, the presence of macrovoids create weak points leading to membranes compactions and collapse (Seong et.al., 2004). In our case for dialysis membranes, the presence of macrovoids does not seem to be favorable as it leads to a low urea removal.

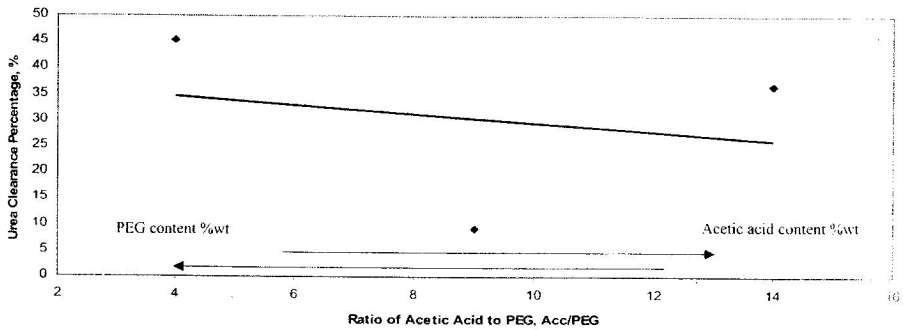

FIGURE 3. Urea clearance percentage as a function of acetic acid/PEG ratio for category 1 membranes

(a) (b) (c)

FIGURE 4. SEM image of category 1 dialysis membranes produced (a) membrane 1 (b) membrane 2 (c) membrane 3

However, an opposite phenomena occurred for the category 2 membranes. Membrane 6 has the highest urea clearance of 34.12 %. Upon analyzing its composition, it is observed that membrane 6 has the least amount of PEG (4.33 %wt) amongst all the category 2 membranes. The presence of increased amounts of PEG 400 reduces the urea clearance as depicted in FIGURE 5. In these category 2 membranes, the presence of high amounts of non solvents, which is water (15 %wt) seems to have a significant effect compared to those membranes in category 1. Upon analyzing the membranes' compositions, they are found to contain very little solvent but high amounts of total non solvents (PEG 400 and water). This result appears to be in agreement with several studies. According to Reuvers et al. (1987) and Smolders et al. (1992), appropriate amount of non-solvent additives enhanced the formation of macrovoids while too much non-solvent suppressed their formation due to the delayed demixing in the growth stage is inhibited.

Upon comparing category 1 and 2 membranes, the average percentage urea clearance for membranes in category 2 is lower than that those in category 1. This is due to the higher amounts of non-solvent (water) present in the category 2 membranes. The addition of non-solvent into the membrane casting solution will accelerate the coagulation process from solution to gel when the casting solution is immersed in the coagulation bath resulting in very tight and dense skinned membranes (Ani et al., 2001). The SEM images of these membranes are depicted in FIGURE 6 (a), (b) and (c). The uniformity of the membrane will increase the rejection rate of solute removal, in other words result in low urea clearance. In addition, the average solvent content in membrane casting solutions of category 2 is lower than category 1, which cause an increase in viscosity that lower the rates of coagulant penetration in the cast solution during immersion step resulting in delayed demixing occuring (Ani et al., 1999). All these resulted in the lower urea removal.

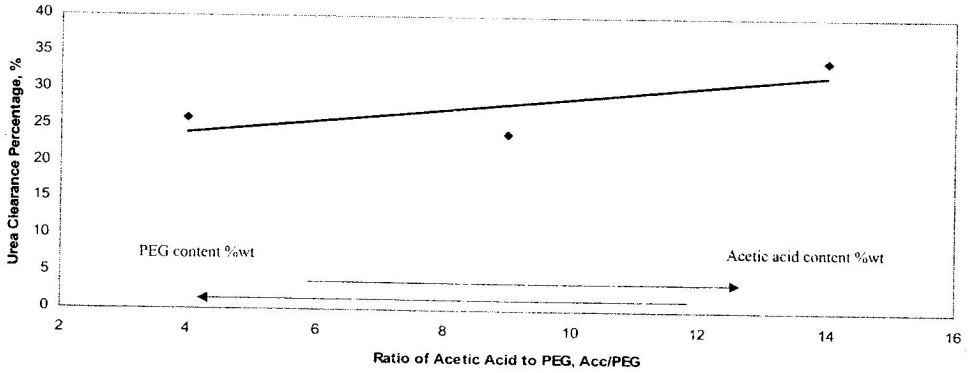

FIGURE 5. Urea clearance percentage as a function of acetic acid/PEG ratio for category 2 membranes

4 CONCLUSION

The cellulose dialysis membrane produced by phase inversion method is an asymmetric membrane with a thin dense like skin layer and spongy structure underneath. Results revealed that membrane 1, which consist of 20 %wt cellulose acetate, 60 %wt of acetic acid, 15 %wt.

(a) (b) (c)

FIGURE 6. SEM images of category 2 dialysis membranes produced (a) membrane 4 (b) membrane 5 (c) membrane 6

PEG 400 and 5 %wt distillated water gives highest urea clearance percentage. The presence of different modifying agents, in different amount will gives a totally different effect to the performance of dialysis membranes. In systems that consist of 5 %wt distillated water, the increase of PEG content will give a better urea solute removal; whilst those that consist of 15 %wt distillated water, the increase of PEG content will result in a lower urea solute removal percentage. However, the total amount of nonsolvents (modifying agent + water) in casting solutions should not be more than 20 %wt, as this will not improve the urea clearance performance in cellulose acetate dialysis membrane.

ACKNOWLEDGEMENTS

Financial support from the Ministry of Science, Technology and Environment, Malaysia through IRPA funding vote no. 74246 is acknowledged with gratitude.

REFERENCES

Ani, I., Ismail, A. F., Iswandi, S. and Shilton, S. J. (2001). "Effect of methanol on the performance of asymmetric cellulose acetate reverse osmosis membranes using dry/wet phase inversion technique." Jurnal Teknologi. 34, 39-50.

Boure, T. and Vanhoulder, R. (2004). "Which dialyzer membrane to choose?" Nephrol Dial. Tranplant, 19, 293-296.

Broek, A.P., Teunis, H. A., Bargeman, D., Sprengers, E. D. and Smolders, C. A. (1992). "Characterization of hollow fiber hemodialysis membranes. pore size distribution and performance." J. Membr. Sci, 73, 143-152.

David, S., Bottalico, D., Taglianvini, D., Mandolfo, S., Scanziani, R. and Cambi, V. (1998). "Behaviour of β_2-microglobulin removal with diefferent dialysis schedules." Nephrol Dial. Transplant, 13, 49-54.

Diamantoglou, M. and Lemke, H. D. (1992). "Dialysis membrane made of polysaccharide ether." United States Patent 5,171,444.

Diamantoglou, M., Dunwerg, .G and Rintelen, T. (1995). "Dialysis membrane composed of polysaccharide ether II." United States Patent 5,427,684.

Dunwerg, G., Steinfeld, L. and Ansorge, W. (1995). "Dialysis membrane made of cellulose acetate." United States Patent 5,403,485.

Frommer, M.A and Massalem, R. M. (1973). "Mechanism of membrane formation, VI, Convenctive flow and large void formation during membrane precipitation." Ind. Eng. Chem. Prod. Res. Develop. 12, 328.

Henne, W. and Dunwerg, G. (1986). "Dialysis membrane and method of making." United States Patent 4,610,791.

Hokhorst, H., Altena, F. W. and Smolders, C. A. (1981). "Formation of asymmetric cellulose acetate membranes." Desalination, 38, 349-360.

Kessler, S. B. and Klein, E. (1992). "Membrane Handbook, Chapter VI, Dialysis Design." Van Nostrand Reinhold, New York.

King, J. C. (1971). "Separation Process." McGraw-Hill Book Company, United States of America.

Klein, R. E., Holland, F. F., Donnaud, A., Lebeouf, A. and Eberle, K. (1977). " Diffusive and hydraulic permeabilities of commercially available cellulosic hemodialysis films and hollow fibers." J. Membr. Sci, 2, 349-364.

Koda, Y., Suzuki, M. and Hirasawa, Y. (2001). "Efficacy of choice of dialysis membranes." Nephrol Dial. Transplant, 16, 23-26.

Kolf, W. J. (1965). "First clinical experience with the artificial kidney." Ann.Intern.Med, 62, 608.

Krieter, D. H. and Canaud, B. (2003). "High permeability of idlyais membranes: what is the limit of albumin loss?" Nephrol Dial. Transplant, 18, 651-654.

Masaki, T., Gilson, J., Leypoldt, J. K. and Cheung, A. K. (1999). "Effect of permeability on indices of hemodialysis membrane biocompatibility." Nephrol Dial. Transplant, 14, 1176-1181.

New Straits Times, 31/12/2001

Noda, I., Brown-west, D. G. and Gryte, C.C. (1979). "Effect of flow maldistibution on hollow fiber dialysis-experimental studies." J. Membr. Sci, 5, 209-225.

Reuvers, A. J. (1987). Membrane formation: Diffusion induced demixing processes in ternary systems, Ph. D Thesis, Twente University of Technology, The Netherlands.

Sakai, K. (1994). "Determination of pore size and pore size distribution 2. Dialysis membranes." J. Membr. Sci., 96, 91-130

Seong, H. Y., Jong; H. K., Jae, Y. J., Won, J. and Yoo, S. K. (2004). "Influence of the addition of PVP on the morphology of asymmetric polyimide phase inversion membranes: effect of PVP molecular weight." J.Membr.Sci. 236, 203-207

Smolders, C. A., Reuvers, A. J., Boom, R. M. and Wienk, I. M. (1992). " Microstuctures in phase-inversion membranes. Part 1: Formation of macrovoids." J. Membr. Sci. 73, 259-275.
Stefoni, S., Csolari, M.P., Cianciolo, G., Mosconi, G., De Sacntis, L. B., De Pascalis, A.,

Manna, L. M., Donati, G., Manna, C., Sestigiani, E. and Grammatico, F. (2000). "Membranes, technologies and long-term results in chronic haemodialysis." Nephrol Dial. Transplant, 15, 12-15.

The Star, 1/6/2004

Wendt, R.P., Klein, E., Bresler,E.H., Holland, F. F., Serino, R. M. and Villa, H. (1979). "Sieving properties of hemodialysis membranes." J. Membr. Sci, 5, 23-49.