Jurnal Teknologi, 51(F) Dis. 2009: 67–76

PREPARATION OF CELLULOSE ACETATE DIALYSIS MEMBRANE USING D-GLUCOSE MONOHYDRATE AS ADDITIVE

ANI IDRIS[1*], HEW KA YEE[2] & CHAN MIEOW KEE[3]

Abstract. Dialysis membrane containing cellulose acetate (CA) as polymer, formic acid (FA) as solvent and D-glucose monohydrate as additive was prepared by phase inversion method. The main objective of this study is to investigate the influence of D-glucose monohydrate as an additive on the performance of dialysis membrane in terms of urea and creatinine clearance. The concentration of D-glucose is varied from 2 to 10 wt%. Microwave heating which is capable of reducing dissolution time was used to dissolve the CA polymer in the formic acid solvent. Results revealed that the membrane produced from the 20 wt% cellulose acetate, 70 wt% formic acid and 10 wt% D-glucose monohydrate gives the best performance with urea and creatinine clearance of 49.77% and 19.54% respectively. When testing the same membranes with BSA solutions, it gives a BSA rejection rate as high as 96.78%, which seems to be comparable with the commercial cellulose acetate dialysis membranes. Membrane morphology was observed by using a scanning electron microscopy (SEM). The SEM images illustrated that the increment of D-glucose monohydrate in casting solution tends to promote macrovoid formation.

Keywords: Dialysis membrane; cellulose acetate; SEM images; urea clearance; creatine clearance; BSA rejection rate

Abstrak. Dialisis membran yang mengandungi sellulosa asetat (CA) sebagai polimer, asid formik (FA) sebagai pelarut dan glukosa-D monohidrat sebagai bahan tambah telah disediakan melalui proses fasa balikan. Objektif utama bagi penyelidikan ini adalah untuk menyelidik pengaruh bahan tambah glukosa-D terhadap prestasi membran dialisis dari segi pemisahan urea dan kreatinina. Kepekatan glukosa-D diubah daripada 2 hingga 10 wt%. Pemanasan menggunakan ketuhar mikrogelombang yang dapat memendekkan masa pelarutan digunakan untuk melarutkan CA polimer dalam pelarut asid formik. Keputusan menunjukkan bahawa membran yang dihasilkan daripada 20 wt% selulosa asetat, 70 wt% asid formik dan 10 wt% glukosa-D monohidrat memberi prestasi yang terbaik bagi penyingkiran urea and kreatinina sebanyak masing-masimg 49.77% dan 19.54%. Apabila membran yang sama dikaji bagi penahanan BSA, ia memberikan peratus penyingkiran larutan BSA sebanyak 96.78%. Berbanding dengan membran dialisis selulosa asetat komersial, didapati bahawa keputusan adalah memuaskan. Gambar SEM menunjukkan bahawa penambahan glukosa-D monohidrat dalam larutan memberi pembentukan struktur jejari.

Kata kunci: Membran dialisis; selulosa asetat; penyingkiran urea; penyingkiran kreatinina; peratus penahanan BSA

[1,2&3]Faculty of Chemical and Natural Resources Engineering, Universiti Teknologi Malaysia, 81310 Johor, Malaysia

* Corresponding author: Tel.: +607-5535603, Fax.: +607-5581463. Email: ani@fkkksa.utm.my

1.0 INTRODUCTION

The number of new kidney failure cases diagnosed annually in Malaysia is increasing at an alarming rate. According to the National Kidney Foundation of Malaysia, the number of patients stands at about 15,000 with 2,500 new patients requiring treatment every year. Currently, more than 16,000 Malaysians are on dialysis and this is expected to reach 20,000 by the 2010 [1]. Worldwide, the increase in dialysis patients is estimated to grow at 7% per annum [1]. It shows that the demand for dialysis membranes in Malaysia is increasing in the future.

Dialyser contains a membrane, which is used for dialysis. In the treatment of patients with renal failure, hemodialysis membrane is important in removing accumulated uremic toxins, excess ions and water from the patient and supplying insufficient ions via the dialysate [2]. Polymeric membranes have been widely used in blood purification therapies such as hemodialysis, hemofiltration, and hemodiafiltration for renal failure patients. For dialysis membrane, the polymer material should have: (a) excellent biocompatibility; (b) low cost; (c) fiber spinning ability; (d) appropriate morphology [3]. The cellulose acetate (CA) membrane was the first high performance asymmetric membrane. CA membrane has excellent hydrophilicity, which is very important in minimizing fouling, good resistance to chlorine and solvent [4–5]. A regenerated CA membrane that was hydrolyzed from cellulose acetate has significantly improved solvent-resistance and thermostability properties [6].

Cellulose acetate (CA) membranes with asymmetric structures were developed by Loeb and Sourirajan [7] and since then CA membranes have been successfully applied in bioseparation systems for ultrafiltration, nanofiltration, and reverse osmosis [8]. Many researchers have proved that the structural permeable performance of CA membranes could be modified by optimizing the hydrophilic/hydrophobic balance of the membrane materials and controlling the conditions during the preparation procedures [9].

There were many attempts to improve the efficiency of dialysis process, not only to the dialysis system but also to the properties of the dialysis membrane itself. Recently, Hayama *et al.* [10] investigated on the biocompatibility of polysulfone dialysis membranes containing polyvinylpyrrolidone and found that its biocompatibility is very much dependent on the amount of polyvinylpyrrolidone and also its surface structure. Ye *et al.* [11] modified cellulose acetate hollow fiber membranes with phospholipids polymer to improve its biocompatibility.

In hemodialysis separation, low and middle molecular weight uremic toxins such as urea, uric acid, creatinine and, β_2-microglobulin (β_2-MG, 11,800 Da) have to be removed from blood. However, proteins such as albumin (66,000 Da) should be retained. Generally uremic toxins are subdivided into three groups: free water soluble low molecular weight (MW) solutes like urea, uric acid or creatinine; protein bound solutes like *p*-cresol or indoxyl sulfate (high MW) and middle MW molecules like peptides [12]. Lesaffer *et al.* [13] found that removal is only 29% for *p*-cresol versus 75%

for urea and 66% for creatinine. This is generally explained by the strong protein binding of *p*-cresol. *p*-cresol is a model of the protein bound uremic toxins which are not efficiently removed by filtration across hemodialysis membranes [3].

The addition of organic or inorganic components as a third component to a casting solution has been one of the important techniques used in membrane preparation. However, the role of organic and inorganic additives, such as poly(vinylpyrrolidone) (PVP), polyethylene glycol (PEG), water, LiCl, and $ZnCl_2$, has been reported as a pore-forming agent to enhance the permeation properties. This behavior was explained in terms of their water-soluble characteristics [14]. Merrill *et al*. [15] reported that the presence of PEG additive in the polymer solution or grafted PEG on the polymer surface would improve anticoagulation.

In order to suppress macrovoids in the hollow fiber membranes, Li *et al*. [16] added high concentration of PEG400 to the dope of polyethersulfone (PES) and using PEG400 aqueous solution as the coagulant to control the morphology of the resulting hollow fiber. Li *et al*. [16] employed a co-extrusion spinneret to prepare dual-layer Matrimid/PES hollow fibers. In another study, Chou *et al*. [14] added high concentration (66%) of PEG (MW 100 kDa) to the spinning dope in order to suppress the macrovoids of the PES layer.

Recently Idris *et al*. [17] studied the effect of different molecular weight PEG additives on cellulose acetate asymmetric dialysis membrane performance and the results revealed that low concentration of PEG, less than 5 wt% in the dope solution, enhanced the urea clearance. However when the concentration of PEG was further increased to greater than 10 wt%, the membrane performance deteriorated. In this study, only PEG was used as additives. PVP as an additive is often blended into the dope solution to increase hydrophilicity and flux of membranes. However, the addition of high MW PVP results in a low flux membrane due to swelling of the residual PVP at the surface of pore walls when water passes through the membrane pores [18].

Thus, the aim of this study is to gain insight into the role of non solvent additive like D-glucose monohydrate on membrane formation and performance. D-glucose monohydrate is a new additive and the effect of D-glucose has not been studied in membrane performance. In this experiment, the dialysis membranes produced were prepared using six different dope formulations by varying the ratio of formic acid/D-glucose monohydrate.

2.0 EXPERIMENTAL

2.1 Materials

In this study, cellulose acetate with average molecular weight of 100,000 Dalton (Acros), formic acid with analytical purity of 85% and D-glucose monohydrate are the main materials. Dope solution was prepared in a polymer reaction vessel by dissolving a

polymer (cellulose acetate) in food grade formic acid. D-glucose monohydrate which was used as the additive was added into the solvent during the experiment.

2.2 Polymer Dissolution

The formulated dope solution listed in Table 1 was prepared. Microwave method was used in preparing the formulated dope solution. The formulated dope solution was prepared in a polymer reaction vessel which is placed in the microwave [19]. Formic acid solvent was poured into the reaction vessel followed by polymer cellulose acetate and additive D-glucose monohydrate. The mixture was then heated up at low pulse in the microwave oven for 8 minutes and then stirred at 500 rpm in the vessel for one hour continuously so as to ensure homogeneity.

Table 1 Composition of dope solutions

Material	Cellulose Acetate(wt%)	Formic Acid (wt%)	D-Glucose Monohydrate(wt%)
1	20	80	0
2	20	78	2
3	20	76	4
4	20	74	6
5	20	72	8
6	20	70	10

2.3 Membrane Casting

Membrane was casted by using a casting knife of 200 μm thickness. The cast polymer solution film was immersed into a distilled water bath to complete the phase separation. After that, the membrane was post treated in distilled water in a beaker. It is then heated in the microwave oven for 10 minutes at medium mode followed by immersion in methanol to remove excess formic acid.

2.4 Membrane Testing

The performance of dialysis membrane is measured in terms of urea and creatinine clearance and also BSA rejection. The testing system is shown in Figure 1. The total effective area of membrane is 30 cm^2. The flow rate of the testing solution on the reservoir side is 50 mL/min whilst that on the pure water reservoir side is 100 mL/min. The temperature was maintained at 37 ± 2 °C using a Digi-sense temperature controller. Samples were collected at both reservoirs at 30 min intervals for a period of 210 min. In order to ensure reproducibility, the experiments were repeated at least three times. Urea Nitrogen (Diacetyl) Reagent Set and Creatinine (Direct) Reagent Set (Eagle

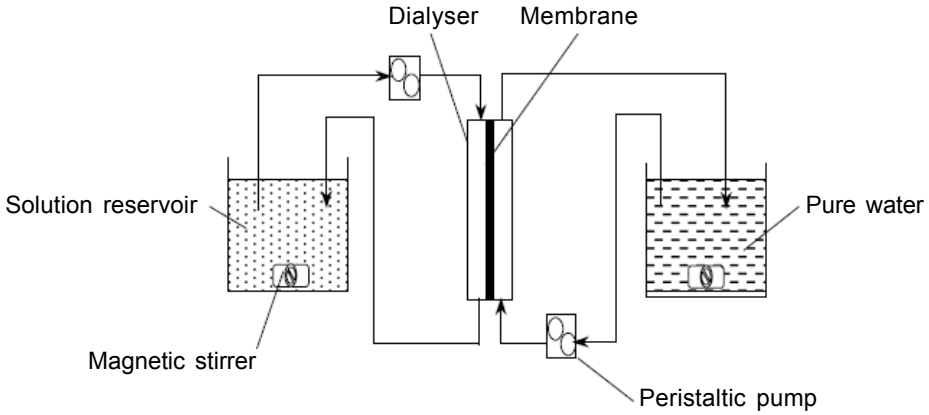

Figure 1 Schematic diagram of single membrane dialysis system [15]

Diagnostics) were used to analyze the urea and creatinine concentration of samples [20] while BSA concentration was tested using Biuret reagent [21].

Solute clearance (%) was calculated as follows:

$$\text{Solute clearance } (\%) = \left(\frac{C_t - C_0}{C_0} \right) \times 100 \quad (1)$$

where

C_0 = Sample concentration at time $t = 0$
C_t = Sample concentration at time t

2.5 Scanning Electron Microscope (SEM)

Cross section images of the flat sheet dialysis membranes were obtained using SEM Model SUPRA 35VP. The membrane was snapped under liquid nitrogen to produce a consistent and clean cut. The membrane was then sputter coated with thin film of gold before mounted on a brass plate using a double sided adhesion tape in a lateral position.

3.0 RESULTS AND DISCUSSION

3.1 Membrane Performance in Terms of Urea and Creatinine Clearance

The results in terms of urea and creatinine clearance for the membranes produced are shown in Figure 2. Membranes that contain 10 wt% of D-glucose monohydrate gave highest urea clearance percentage of 49.77% and creatinine clearance of 19.54% while membranes without any additive gave urea clearance of 16.25% and creatinine clearance

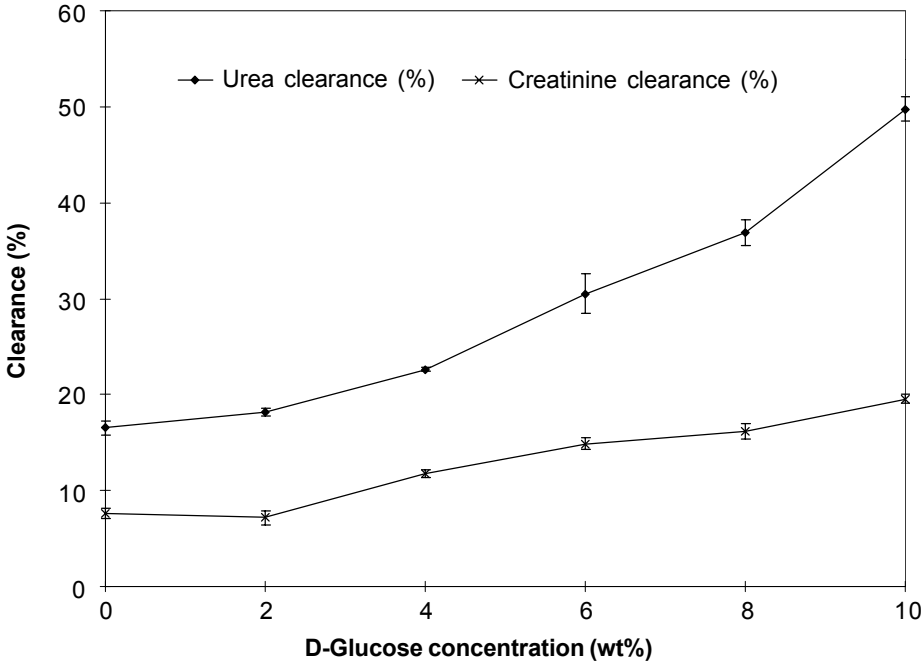

Figure 2 Clearance percentage of urea and creatinine versus D-glucose concentration

of 7.84%. It is believed that the hydrophilic D-glucose additive has enhanced the membrane performance.

Figure 2 also exhibits that the increase in concentration of D-glucose monohydrate in dope solution has improved the dialysis membrane performance in terms of urea and creatinine clearance. As the concentration of D-glucose in the casting solution increases, the clearance percentage for both urea and creatinine increases with the highest clearance percentage at 10 wt% concentration. However increasing the D-glucose concentration beyond 10 wt% is not practical because of the high solution viscosity and also its bubbly characteristics which make casting process difficult resulting in many imperfections in the final membrane.

3.2 Membrane Performance in Terms of BSA Rejection

The results in terms of BSA rejection for the various membranes are tabulated and shown in Table 2. The results indicate that D-glucose monohydrate based membrane can retain most of the BSA successfully and with the highest rate of only 96.78% at 10 wt% concentration. Although the membrane without any additive has a BSA rejection rate of 98.64% which means that it can retain higher percentage of BSA compared to D-glucose based membrane, the difference is not too significant as compared to the improvement in the urea and creatinine performance.

Table 2 Membrane performance in terms of BSA rejection

Material	Cellulose Acetate (wt%)	Formic Acid (wt%)	D-glucose Monohydrate (wt%)	BSA Rejection (%)
1	20	80	0	98.64
2	20	78	2	92.40
3	20	76	4	92.12
4	20	74	6	93.14
5	20	72	8	93.68
6	20	70	10	96.78

3.3 Scanning Electron Microscope (SEM)

The membrane morphology was observed using a scanning electron microscopy (SEM). The cross section structures of the membranes produced from the various dope solutions are shown in Figure 3.

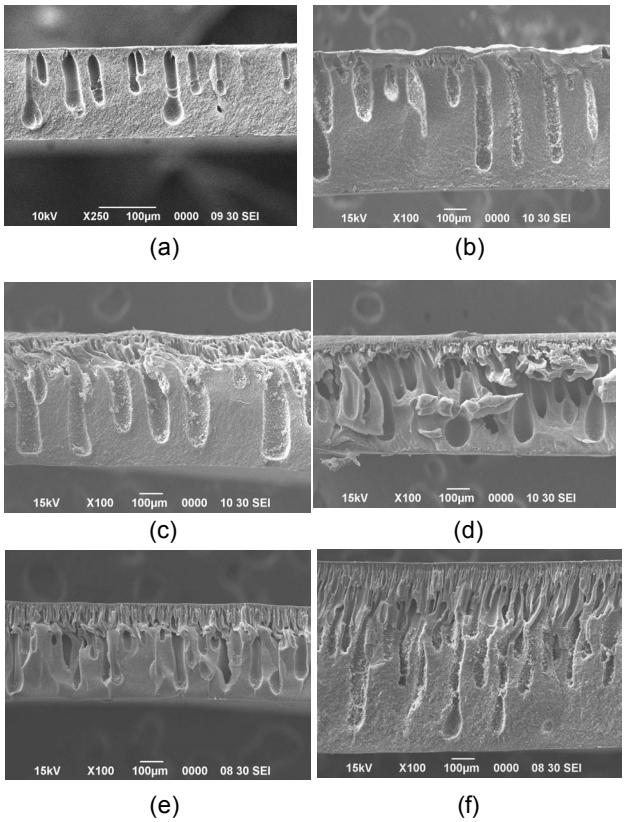

Figure 3 SEM cross-section images of dialysis membrane produced: (a) without D-glucose, (b) 2 wt% D-glucose, (c) 4 wt% D-glucose, (d) 6 wt% D-glucose, (e) 8 wt% D-glucose and (f) 10 wt% D-glucose

Figure 3(a) depicts the SEM cross section images of the dialysis membranes produced without any additives. A dense spongy structure with some macrovoids is observed. The addition of 2 and 4 wt% D-glucose apparently promotes the formation of macrovoids within the support layer as depicted in Figure 3(b) and (c). When the concentration of D-glucose increases from 6 wt% to 10 wt% consecutively, the macrovoids structure disappears and formation of finger like structure seems to occur as depicted in Figure 3(d), (e) and (f) respectively.

D-glucose monohydrate seems to encourage the mechanism of phase inversion transit from delayed demixing to instantaneous demixing, consequently promotes the formation of macrovoids and finger like structures. The addition of D-glucose does not only affect the performance of membranes but also has an influence on the membranes' morphology. A very dense spongy structure is observed when no D-glucose is used as depicted in Figure 3(a). However, increasing amounts of D-glucose (2 wt% to 10 wt%) added seem to promote instantaneous demixing forming finger like structure which seems to be favorable in dialysis membranes.

Based on SEM images as illustrated in Figure 3, membrane became more porous as the amount of D-glucose increased. Porous supporting layer of membrane is desired as porous structure allows solutes to pass through the membrane easier compared to dense structure. Flux will increase with an increase in membrane porosity [22]. In addition, it is also observed that the skin layer thickness decreased when the concentration of D-glucose monohydrate reached to 10 wt%. Since the surface layer governs the membrane transport [22], thin selective layer always exhibits high flux [23] and high permeability properties [24]. Thus reduced in skin layer of membrane and porous structure caused increased in urea (49.77%) and creatinine clearance (19.54%). It is believed that the presence of the hydroxyl groups in D-glucose have improved the hydrophilic structure of the membranes thus influenced the permeation properties of membrane performance.

4.0 CONCLUSION

The effect of D-glucose monohydrate as an additive on the performance of flat sheet dialysis membrane has been studied and investigated. The results illustrated that membrane performance in terms of urea and creatinine clearance improved remarkably when the percentage of D-glucose monohydrate is increased. The membrane containing 10 wt% D-glucose monohydrate exhibits urea clearance of 49.77%, creatinine clearance of 19.54% and BSA rejection rate of 96.78%. When compared to the membrane without any D-glucose monohydrate a lower urea clearance of 16.25% and creatinine clearance of 7.84% is obtained. Thus, D-glucose monohydrate can be considered as a suitable additive for dialysis membrane.

ACKNOWLEDGEMENTS

Financial support from the Ministry of Science, Technology and Environment through IRPA funding vote no. 79037 and 79186 is gratefully acknowledged.

REFERENCES

[1] Marry C. G. 2007. Number of Kidney Cases Soars. Press release from National Kidney Foundation Malaysia (NKF).

[2] Sakai, K. 1994. Determination of Pore Size Distribution 2. Dialysis Membranes. *Journal of Membrane Science*. 96: 91–130.

[3] Barzin, J., C. Feng, K. C. Khulbe, T. Matsurra, S. S. Madaeni and H. Mirzadeh. 2004. Characterization of Polyethersulfone Hemodialysis Membrane by Ultrafiltration and Atomic Force Microscopy. *Journal of Membrane Science*. 237: 77–85.

[4] Chaudry, M. A. 2002. Water and Ions Transport Mechanism in Hyperfiltration with Symmetric Cellulose Acetate Membranes. *Journal of Membrane Science.* 206: 319–332

[5] Combe, C., E. Molis, P. Lucas, R. Riley and M. M. Clark. 1999. The Effect of CA Membrane Properties on Adsorptive Fouling by Humic Acid. *Journal of Membrane Science.* 154: 73–87.

[6] Chen, Y., X. P. Xiong, G. A. Yang, L. N. Zhang, S. L. Lei and H. Liang. 2002. Characterization of Regenerated Cellulose Acetate. *Chinese Journal of Polymer Science*. 20: 369–375.

[7] Loeb, S. and S. Sourirajan. 1963. Sea Water Demineralization by Means of an Osmotic Membrane. *Adv. Chem. Ser*. 38: 117.

[8] Kesting, R. E. 1985. *Synthetic Polymeric Membranes–A Structure Perspective*. 2nd ed. New York: Wiley.

[9] Ye, S. H., W. Junji, I. Yasuhiko and K. Ishihara. 2002. Novel Cellulose Acetate Membrane Blended With Phospholipid Polymer for Hemocompatible Filtration System. *Journal of Membrane Science*. 210: 411–421.

[10] Hayama, M., K. Yamamoto, F. Kohori and K. Sakai. 2004. How Polysulfone Dialysis Membranes Containing Polyvinlpyrrolidone Achieve Excellent Biocompatibility? *Journal of. Membrane Science*. 234: 41–49.

[11] Ye, S. H., J. Watanabe., Y. Iwasaki and K. Ishihara. 2005. In situ Modification on Cellulose Acetate Hollow Fiber Membrane Modified with Phospholipid for Biomedical Application. *Journal of Membrane Science.* 249(1-2): 133–141.

[12] Vanholder, R., R. De Smet, G. Glorieux, A. Argiles, U. Baurmeister, P. Brunet, W. Clark, G. Cohen, G., P. P. De Deyn, R. Deppisch, B. Descamps-Latscha, T. Henle, A. Jorres, H. D. Lemke, Z. A. Massy, J. Passlick-Deetjen, M. Rodriguez, B. Stegmayr, P. Stenvinkel, C. Tetta, C. Wanner and W. Zidek. 2003. *Kidney Int*. 63: 1934.

[13] Lesaffer G. de S., R. Lameire, N. Dhontt. A. Duym P, and R. Vanholder. 2000. Intradialytic Removal of Protein Bound Uremic Toxins: Role of Solute Characteristics and of Dialyser Membrane. *Nephrology, Dialysis, Transplantation.* 15: 50–57.

[14] Chou, W. L., Y. Da-Guang, Y. Ming-Chien and J. Chi-Hsiung. 2007. Effect of Molecular Weight and Concentration of PEG Additives on Morphology and Permeation Performance of Cellulose Acetate Hollow Fibers. *Separation and Purification Technology.* 57: 209–219.

[15] Merrill, E. W., S. Wan and E. W. Salzman. 1986. *Trans. Am. Soc. Artif. Intern. Organs.* 20: 1517.

[16] D. Li, T. S. Chung and R. Wang. 2004. Morphological Aspects and Structure Control of Dual-layer Asymmetric Hollow Fiber Membranes Formed by a Simultaneous Co-extrusion Approach. *J. Membrane Science.* 243: 155–175.

[17] Idris. A. and K. Y, Lee. 2006. The Effect of Different Molecular Eeight PEG Additives on Cellulose Acetate Asymmetric Dialysis Membrane Performance. *Journal of Membrane Science.* 280: 920–927.

[18] Qin, J. J., Y. Li, L. S. and Lee, H. Lee. 2003. Cellulose Acetate Hollow Fiber Ultrafiltration Membranes Made from CA/PVP 360 K/NMP/Water. *Journal of Membrane Science*. 218: 173–183.

[19] Idris, A., A. Iqbal, M. Y. and Noordin. 2008. Microwave Method of Synthesizing Polyethersukfone/Lithium Halide Membranes using Two Solvent Systems. Patent No. 20081128.

[20] Talke, H. and G. E. Schubert. 1965. Enzmatische Harnstoff Bestimmung im Blut and Serum in Optischen Test Hanch Warburg. *Klin Wschr.* 43: 174–175.

[21] Gornall, A. G., C. J. Bardawill and M. M. David. 1949. Determination of Serum Proteins by Means of the Biuret Reaction. *J. Biol. Chem.* 177: 751–766.
[22] Khayet, M. 2008. Membrane Distillation. In: N. N. Li, A. G. Fane, W. S. W. Ho and T. Matsuura. (Ed.). *Advanced Membrane Technology and Applications*. England: John Wiley & Sons, Ltd. 297–360.
[23] Baker, R. W. 2004. *Membrane Technology and Application*. Second Edition. England: John Wiley & Sons, Ltd.
[24] Ulbricht, M. 2006. Advanced Functional Polymer Membranes. *Polymer.* 47: 2217–2262.