EFFECT OF PEG ADDITIVES ON PERFORMANCE OF HEMODIALYSIS MEMBRANE

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Dedicated to my beloved father, mother, sisters and all loved ones, for their support and encouragement.

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ABSTRACT

Dialysis membranes are fast gaining importance nowadays in membrane separation industries, mainly used in medical industry to remove uremic toxic, excess water and undesirable protein out of the human blood. Unfortunately, the current trend of dialysis technology in Malaysia still depends on foreign countries and the development of dialysis industries are far behind the world latest era. Therefore, the main objective of this study is to develop flat sheet membranes, suitable for dialysis of biomolecules such as urea and determine the optimum formulation for the dialysis membrane produced. The performance of the cellulose acetate membranes produced using various dope solution formulations were studied by varying the acetic acid (Acc)/polyethylene glycol (PEG) ratio and the amount of water as well as the different molecular weight PEG used. Three different additives were used namely PEG 200, PEG 400 and PEG 600 in the membrane formulations. The membranes were tested using a single layer continuous dialysis system. The molecular weight cut off clearance efficiency range, the permeability and sieving properties of the dialysis membranes were determined. The response surface method, central composite design was applied to construct the experimental trials for this study. Cross section image of each membrane produced were obtained by scanning electron microscopy (SEM) to explain the results obtained. The results revealed that the ratio of acetic acid/PEG is the significant factor that affects urea clearance performance. The amount of the distilled water was an insignificant factor to urea clearance performance, but its presence is vital in the membrane formulation. Dialysis membranes consist of acetic acid/PEG ratio of 16.5 gives the best urea clearance performance of 40.37 %. Among the additives used, PEG 200 shows the highest clearance rate of urea. When a triple layer continuous dialysis system was used to test the membranes and it was found that the performance was increase by 25 – 50 %. Dialysis membranes consisting of lower molecular additives gives higher molecular clearance cut off efficiency. Final stage experiments using human blood revealed that dialysis membranes produced were comparable to the commercialized membranes with urea clearance of 60 – 70 %.

ABSTRAK

Dewasa ini, membran dialisis semakin penting dalam industri membran, terutamanya dalam industri perubatan untuk penyinggiran toksik urik, air berlebihan dan protin yang tidak diperlukan daripada darah manusia. Malangnya, teknologi dialisis dalam Malaysia masih bergantung kepada luar negara dan pembangunan industri dialisis dalam negara adalah jauh di belakang era dunia kini. Oleh itu, objektif utama dalam penyelidikan ini adalah untuk menghasilkan membran kepingan nipis yang sesuai untuk proses dialysis bagi biomolekul seperti urea dan formulasi optimum membran dialisis ditentukan. Membran selulosa asetat dengan formulasi berbeza dihasilkan dan penampilan dikaji dari segi perubahan nisbah asid asetik/PEG dan kandungan air serta additif yang berbeza digunakan.Tiga additif yang berbeza, PEG 200, PEG 400 dan PEG 600 digunakan dalam formulasi membran. Membran yang dihasilkan dikaji dengan menggunakan sistem dialisis berterusan satu lapisan. Julat *molecular weight cut off clearance efficiency,* ciri-ciri kebolehtelapan serta keupayaan permisahan bagi membran bagi membran dialisis yang dihasilkan juga ditentukan. Metodologi permukaan respons, rekaan pusat komposit digunakan untuk membentuk eksperimen bagi penyelidikan ini. Imej rajah silangan bagi setiap membran yang dihasilkan diambil dengan menggunakan mikroskop imbasan electron bagi menjelaskan keputusan diperolehii. Keputusan menunjukkan bahawa kuantiti air adalah tidak penting bagi penyingkiran urea tetapi kewujudannya adalah penting dalam membran formulasi. Nisbah asid asetik/PEG merupakan faktor utama yang mempengaruhi keputusan penyingkiran urea. Membran dialisis dengan nisbah asid asetik/PEG 16.5 menunjukkan perfomasi yang terbagus dengan 40.37 % kadar penyingkiran urea. Antara additif digunakan, PEG 200 menunjukkan kebolehannya dengan kadar penyingkiran urea yang tertinggi. Sistem dialisis berterusan tiga lapisan membran digunakan untuk kajian penampilan membran dihasilkan dan didapati keputusan penyingkiran urea telah naik sebanyak 25 – 50 %. Membran dialisis dengan additif bermolekul rendah akan menghasilkan *molecular cut off clearance efficiency* yang lebih tinggi. Eksperimen pada tahap terakhir yang menggunakan darah manusia menunjukkan bahawa membran dialisis yang dihasilkan dalam penyelidikan ini adalah setanding dengan membran dialisis komersial yang berupaya menyinkirkan 60 – 70 % urea.

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LIST OF SYMBOLS

Symbol		Units
k_M	- Diffusive permeability	m s^{-1}
D_W	- Diffusion coefficient	m^2 s^{-1}
S_D	- Diffusion pore inlet steric hindrance factor	-
A_k	- Membrane surface porosity	m^2
ΔX	- Membrane thickness	m
L_P	- Hydraulic permeability	ml m^{-2} s^{-1} atm
r_P	- Membrane pore radius	m
σ	- Staverman reflection	-
S_F	- Filtration pore inlet steric hindrance factor	-
q	- Solute radius to pore radius factor	-
f (q)	- Diffusion friction coefficient	-
g (q)	- Filtration friction coefficient	-
J_B	- Water flux	ml s^{-1}
Δp	- Pressure difference	atm
$\Delta \pi$	- Osmotic pressure difference	atm
J_S	- Solute flux	ml s^{-1}
C_t	- Solute concentration at time t	mg ml^{-1}
C_o	- Solute concentration at time 0	mg ml^{-1}

A	- Membrane area	m^2
V	- Reservoir volume	m^3
α	- Slope of the plot of $\ln(C_t/C_o)$ versus time	min^{-1}
K	- Clearance efficiency coefficient	ml min^{-1}

LIST OF ABBREVIATIONS

%wt	- Weight percentage
%v/v	- Volume per volume percentage
NaCl	- Sodium chloride
KCl	- Potassium chloride
Na acetate. $3H_2O$	- Sodium acetate trihydrate
$MgCl_2 . 6H_2O$	- Magnesium chloride hexahydrate
$CaCl_2 . 2H_2O$	- Calcium chloride diahydrate
$BaCl_2$	- Barium chloride
KI	- Potassium iodide
PEG	- Polyethylene glycol
BSA	- Bovine serum albumin
CA	- Cellulose acetate
RBC	- Red blood cell
WBC	- White blood cell

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CHAPTER 1

INTRODUCTION

1.1 Overview

Dialysis first was reported in 1861 by Graham, who used parchment paper as a membrane, based on the observations that animal membranes were less permeable to colloids than to sugar or salt. Over the next 100 years, dialysis became widely used as a laboratory technique for the purification of small quantities of solutes. Yet, it was realized that there is no large-scale industrial applications for dialysis process. In the last 20 years, development of dialysis for the treatment of kidney failure has brought about a resurgence of interest in dialysis for a wide range of separations (Klein, 1987).

Clinical evidence has shown that in the absence of normal renal function, the artificial kidney is a good substitute with regard to electrolyte, solute and water balance. In fact, approximately 28,000 to 50,000 people died each year due to kidney disease of one kind or another in the United States and over 300,000 people worldwide rely on the artificial kidney for chronic support (King, 1971). Of these, perhaps 6000 to 10,000 would be suited either to an artificial kidney or to transplantation as a form of long-term support. In addition, some three million residents of the United States are thought to have undiagnosed kidney diseases. In Germany, the total number of dialysis patients is increasing by about 8 % per year and the latest figure of 48,000 patients, being reported. From year 1993 to 1995, the number of patient receiving renal replacement therapy (RRT) including hemodialysis and transplantation increased about 20 % in United Kingdom. Moreover, the total number of chronic dialysis patients in Spain is up to 17,800, representing around 454 per million population (pmp) (Locatelli *et al*., 2000). Latest statistic shows that in Malaysia, intake of new dialysis patients increased from 43 in 1980 to 2223 in 2002 and prevalent dialysis patients increased from 59 in 1980 to almost 10,000 at year-end 2003 (Lim and Lim, 2003). Furthermore, over 1000 Malaysian with kidney problems died in year 2001 (Lim, 2001) and these figure are expected to soar.

From the economy prospect, membranes have made many inroads into the market, especially in the 1970s and 80s (Edward, 2003). Today, there are many refinements and more drastic growth. The total world sales of dialysis membrane in 1994 have been estimated at US$ 1400 million, accounting for about 40 % of the total predicted membranes of US$ 4000 million (Setford, 1995). Till year 2000, a treatment of hemodialysis cost around US$ 140, which promised about US$ 20,000 per year of profit margin per patient (Locatelli *et al*., 2000). The world demand of dialysis treatment increased rapidly and entailed its fast gaining importance due to the increase in the number of patients having kidney failure. Therefore, dialysis membrane industries are a far more profitable and encouraging field to be emphasized.

The early hemodialysis used membranes are highly permeable to small solutes up to 200 Dalton. Clearance of small solutes is governed by membrane permeability and diffusion resistances in the blood and the dialysate phases. In the early 1970s, most of the researches on dialysis membranes were focused on producing membranes with better solute diffusion and water removal properties. Interests in removal of relatively small solutes from blood by convective transport have become more intensive. Lack of permeability of the early membranes for some middle molecular weight solutes in the range of vitamin B_{12}, which in the range of 1355 Dalton, was held responsible for the appearance of uremic polyneuritis (Shettigar, 1989).

Research has been done by Colton *et al.* (1975) to study the solute rejection characteristics of a hollow-fiber blood ultrafilter. The following year, Green *et al.* (1976) measured the solute rejection for two flat sheet hemodialysis membranes, which provided data that guided the design of hemofiltration devices. Mechanical properties of dialysis membranes have also being reported by Klein and co-workers (1976). Further investigation on the diffusive and hydraulic permeability of commercially available dialysis membrane was carried out by Klein *et al.* (1977) to measure the mass transport properties and to compare amongst manufacturing variability of those dialysis membrane. Noda *et al.* (1979) have shown the feasibility of fractionating solutes, the permeabilities of which are relatively close, by using a highly selective multi-stage dialysis process.

Nevertheless, since the late 1980s to recent times, the emphasis had been on adsorption, biocompatibility, large molecule flux and convective transport (Koda *et al.*, 2001). Biocompatibility describes materials, which cause only minor biochemical and biological effects. Research had been carried out to compare the biocompatibility of market available dialysis membrane (Boure and Vanhoulder, 2004). Complement activation occurs almost universally during clinical hemodialysis with the consequential generation of several complement activation products (Hakim *et al.*, 1984). Products such as anaphylatoxin C3a, anaphylatoxin C5a and beta-2-microglobulin increases in chronic renal failure and need to be removed during hemodialysis process. Amongst the activation products generated, the plasma levels of C3a during hemodialysis commonly are used as an index of dialysis membrane biocompatibility (Deppisch *et al.*, 1990). Adsorption refers to a characteristic of synthetic membranes, which contributes to the removal of noxious compounds such as interleukin-1, tumour necrosis factor, peptides, interleukin-6 and β_2-microglobulin (β_2-M) (Bouman *et al.*, 1998). However, adsorption capacity will rapidly be saturated due to the restricted surface area of dialysers (Boure and Vanhoulder, 2004). This process will lower the diffusive permeability and need to be reduced in order to enhance dialysis adequacy of the patients.

Several investigators dealt with the problem of inadequate clearance of β_2 – microglobulin, 11,800 Dalton molecular weight, a middle large molecule that need to be removed that is associated with dialysis-amyloidosis to patient. Lornoy *et al.* (2000) reported that treatment with on-line hemodialfiltration with highly permeable and biocompatible membrane has proven to be an efficient, well-tolerated and safe technique that leads to a low prevalence of dialysis amyloidosis. The influence of the type of dialysis membrane has also been reported (Strihou *et al.*, 1991; Chanard *et al.*, 1989). Gerhard and Karl (2002) also reported the effect of ultra pure dialysate and the type dialyzer membrane to the beta-2-microglobulin amlyloidosis. It was found that synthetic dialyzer membranes were able to reduce the complications of β_2 – microglobulin.

Dialysis membranes are often classified as either high flux or low flux based on their ultrafiltration coefficient (Cheung and Leypoldt, 1997). Considerable struggle has been made to improve the clearance of middle large molecules greater than 500 Dalton. This led to development of high-flux and super-flux synthetic membrane. High flux membranes have larger pores and tend to clear middle molecules more efficiently, compared with low flux membranes (Leypoldt *et al.*, 1997). The middle large molecules concentration significantly decreases during dialysis with super-flux membranes. In contrast, the only controlled mortality study, the hemodialysis (HEMO) study, failed to document the superiority of high-flux compared with low-flux membranes (Eknoyan *et al.*, 2002). Therefore, although there might be a trend for superiority of high-flux membranes regarding mortality, this finding must be confirmed by further studies, before definite conclusions can be drawn (Boure and Vanhoulder, 2004).

1.2 Background of the Problem

The dialysis membrane is no longer seen as a simple semi-permeable barrier for solutes and water, but is considered an important interface with the patients blood and subsequently, as an outcome predictor (Koda *et al.*, 2001). 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.* (2004) investigated on the biocompatibility of polysulfone dialysis membranes containing polyvinylpyrrolidone and found that its biocompatibility is very much dependent on the amount of PVP and also its surface structure. Sang *et al.* (2005) modified cellulose acetate hollow fiber membranes with phospholipids polymer to improve its biocompatibility.

Several prospective trials have provided some evidence that membrane choice is important in recovery of acute renal failure. Research done by several investigators revealed that biocompatible dialysis membranes yielded better efficiency of hemodialysis process and showed higher patients survival rate as compared to cellulosic cuprophane dialysis membranes (Schiftfl *et al*., 1994; Parker *et al*., 1996; Kuchle *et al*., 1996; Himmerlfarb and Hakim, 1997; Hartmann *et al*., 1997 and Neveu *et al*., 1996).

However, the results presented in several other reports are completely different from those reported by the defenders of biocompatible membranes mentioned previously. The non-biocompatible dialysis membranes (cellulosic cuprophane) and the so-called biocompatible dialysis membranes (polysulfone, PAN and PMMA) give similar patients mortality rate as well as the survival rate. The rate and degree of recovery of renal function were similar in all groups and the membrane type had no impact on the outcome findings (Hakim *et al*., 1994; Kurtal *et al*., 1994; Cosentino *et al*., 1994; Liano *et al*., 1996 and Valeri *et al*., 1994). The brief overview of these studies mentioned will be discussed more detail during literature review in the next chapter.

There is no doubt that much research has been carried out in improving the chronic dialysis process and also in studying the relationships between technologies and the patients' biological and clinical profile. Much work has also been focused in highlighting the different results achieved with different type of dialysis membrane and methodologies. The conclusions reached by the various studies are far from unanimous and were often markedly discordant (Stefoni *et al*., 2000). However, most of the studies mentioned above had focused solely on well-developed dialysis membranes and rarely pin point the self-produced dialysis membranes. Further studies are urgently needed to help define the role of the dialysis membranes (biocompatible or incompatible) as well as defining optimal intensity of dialysis in chronic renal failure (Himmelfarb *et al*., 1997). Investigation regarding the making of dialysis membranes is essential as it is the heart of the any dialysis process or hemodialysis devices. Factors such as biocompatibility, flux rate, solute separation properties that effecting renal failure recovery can be taken into account when fabrication dialysis membranes.

Indeed, numerous parameters can be investigated in order to improve the efficiency of membrane separation process such as membrane composition, membrane properties and the membrane fabrication process. Nevertheless, most of these investigations mentioned involved reverse osmosis, ultrafiltration and gas membranes. The effect of additives and non-solvent on the performance of the dialysis membrane had not been systematically investigated. Consequently, the investigations on the effect of dialysis membrane composition to the membrane performance are urgently important**.**

In 1986, Henne and Dunweg proposed a single or multilayer dialysis membrane made of regenerated cuprammonium cellulose. The new membrane was prepared by the known cupraamonium process but with the addition of a finely ground CuO with a maximum particle size of 20 microns to the standard cupraamonium solution. The membrane produced provides significantly higher pore volume content. Diamantoglou *et al*. (1992, 1995) invented a dialysis membrane made of polysaccharide ethers, which improve the biocompatibility of the membranes. The parameters of biocompatibility in Diamantoglou case are blood coagulation, leucopenia and compliment activation. Dunweg *et al* (1995) reported dialysis membrane in the form of hollow fiber with a continuous internal cavity made of cellulose acetate or cellulose acetate derivative. The dialysis membrane proposed by Dunweg consist of an organic carboxylic as the solvent with at least one modifying agent added. The invention provided a membrane that exhibited low albumin loss over a wide range of ultrafiltration rates while exhibit high permeability to beta-2-microglobulin in all ranges. The membrane produced was claimed to achieve an ultrafiltration rate of 2 to 200 ml/m^2 h mm Hg and a maximum sieving coefficient of 0.1 for albumin with a molecular weight of 68,000.

Besides the work of Henne and Dunweg (1986), Diamantoglou *et al.* (1992, 1995, 2000), Dunweg *et al.* (1995) not much has been reported regarding the effect of the polymer composition in dialysis membranes. Most of the above mentioned works are patents. The parameters affecting the membrane preparation such as polymer concentration in the dope had not been systematically investigated. Although much research have been carried out on the effect of composition of polymer on membrane properties, most of the work involved reverse osmosis, ultrafiltration, microfiltration and gas membranes. In recent years, technological innovations in dialysis equipment and new modalities have improved the quality of dialysis treatment but there are still many acute complications or symptoms that is associated with the dialysate composition, type of diffusive treatments and the type of dialysis membrane used (Locatelli and Manzoni, 2000). Thus, in this study, dialysis membranes were prepared with several variables adjusted to control membrane properties. Amongst these variables are the composition of the polymer such as the type and concentration of additives used to investigate the factor that influenced the quality of dialysis membranes mentioned above.

1.2 Objectives And Scope

Despite the many technical advances in dialysis membrane, its composition has always been a trade secret. Locally used membranes must be developed so as to gain more insight into its fabrication process and reduce its cost. Unfortunately, the current trend of dialysis technology in Malaysia still solely depends on foreign countries. The developments in the field of dialysis for renal failure patients are far behind compared to the world latest era. Synthetic membranes are known to be highly permeable, have larger pores that provide better convective transport and the removal of mid-sized and large molecules. Therefore, the main objective of the study is to study the influence of additives particularly PEG and water on the performance of dialysis membranes in separating biomolecules such as urea subsequently determine the optimum formulation for the dialysis membrane. The performance of the hemodialysis membranes were then investigated by determining the molecular weight cut off clearance efficiency, permeability and sieving properties. Finally, the performance of the membrane produced is evaluated using human blood.

In order to achieve the objectives mentioned above, response surface method (RSM), central composite design (CCD) is used to design a set of experimental trials that covers the scope of this study. The scope of this study includes the fabrication of flat sheet dialysis membranes using cellulose acetate as the polymer together with acetic acid as solvent, water and polyethylene glycol as the non-solvent. The formulations were varied based on the solvent/non-solvent ratio, water content and the different types of additives used. The performances of the dialysis membrane produced were evaluated using different molecular weight substances such as urea, bovine serum albumin (BSA) and polyethylene glycol (PEG).

Upon identifying the influence of the PEG and water based on the design of experiments, further experiments were carried out using different types of PEG, namely PEG 200, 400 and 600 as the additives. The testing of the dialysis was performed on the single and triple membrane dialysis system. The final stage involved testing of the best-selected membrane on the single and multi dialysis system using human blood. The final structure details of the dialysis membranes were correlated with the performance of the membranes produced. The properties of the membranes produced such as the diffusive permeability and the solute clearance coefficient were also determined using close-loop single-pass flow model (Klein *et* *al*., 1976) and mass balance equations approached by Morti and Zydney (1998). Figure 1.1 showed an overall view of the summarized experimental methodology.

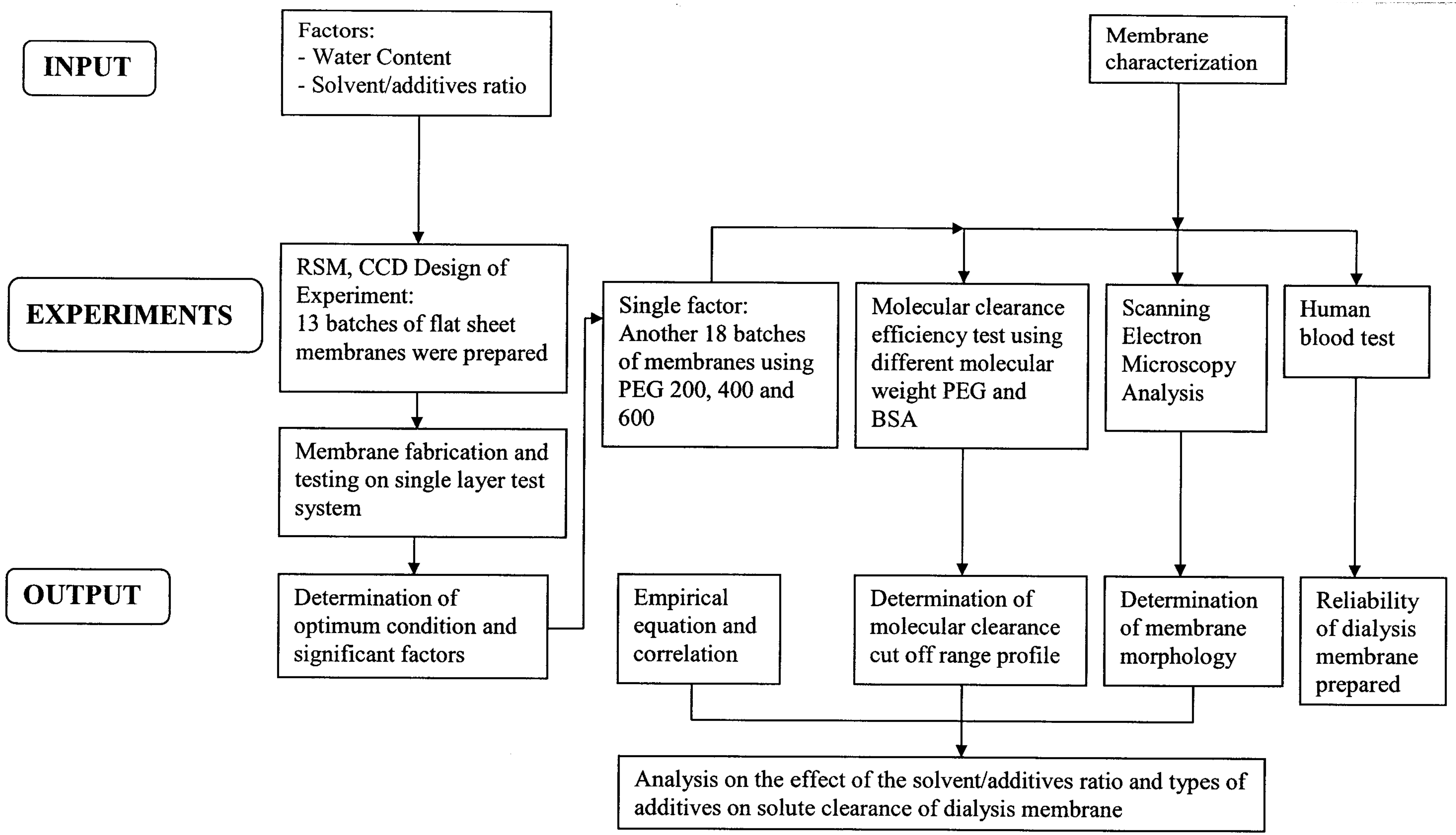

Figure 1.1 Schematic diagram summarizing the experimental methodology

REFERENCES

Anderson, V. L. and McLean, R. A. (1974). *Design of Experiments, a realistic approach*. New York: Marcel Dekker Inc.

Ani, I. (2001). *Fabrication and optimization of asymmetric hollow fiber membranes for reverse osmosis*. Universiti Teknologi Malaysia: Ph.D. Thesis.

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. *J. Teknologi* 34: 39-50.

Aoyagi, S., Hayama, M., Hasegawa, U., Sakai, K., Tozu, M., Hoshi, T. and Kudo, M. (2004). Estimation of protein adsorptioin on dialysis membrane by means of TOF-SIMS imaging. *J. Membr. Sci*. 236: 91-99.

Artanareeswaran, G., Thanikaivelan, P., Srinivasn, K., Mohan, D. and Rajendran, M. (2004). Synthesis, characterization and thermal studies on cellulose acetate membranes with additives. *Eur. Polymer J.* 40: 2153-2159.

Avram, M. M., Slater, P. A., Gan, A., Iancu, M., Pahilan, A. N., Okanyua, D., Rajpa, K., Paik, S. K., Zouabi, M. and Fein, P. A. (1985). Predialysis BUN and creatinine do not predict adequate dialysis, clinical rehabilitation, or longevity. *Kidney Int*. 28: S-100.

Barzin, J., Feng, C., Khulbe, K. C., Matsuura, T., Madaeni, S. S. and Mirzadeh, H. (2004). Characterization of polyethersulfone hemodialysis membrane by ultrafiltration and atomic force microscopy. *J. Membr. Sci*. 237: 77-85.

Bergstrom, J., Asaba, H., Furst, P. and Oules, R. (1976). Dialysis ultrafilatraion and blood pressure. *Proc. Eur. Dial. Trans. Assoc.* 13: 293.

Bloembergen, W. E., Hakim, R. M. and Stannard, D. C. (1999). Realationship of dialysis membrane and cause-specific mortality. *Am. J. Kidney Dis*. 33: 1-10.

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

Boure, T. and Vanholder, R. (2004). Which dialyser membrane to choose?. *Nephrol. Dial. Trans.* 19: 293-296.

Bouman, C. S., van Olden, R. W. and Stoutenbeck, C. P. (1998). Cytokine filtration and adsorption during pre- and postdilution hemofiltration in four different membranes. *Blood Purif*. 16: 261-268.

Box, G. E. P. and Draper, N. R. (1987). *Empirical model-building and response surfaces*. New York: John Wiley and Sons, Inc.

Box, G. E. P. and Wilson, K. G. (1951). On the experimental attainment of optimum conditions. *J. of the Royal Statistical Society* B13: 1-45.

Brogniart, Pelouze and Dumas. (1839). En effet, il y a dans les bois le tissu primitif, isomere avec amidon, que nous applerons cellulose, et de plux une matiere qui en remplit les cellules, et qui constitue la matiere ligneiuse veritable. *C. R. Acad. Sci. Paris* VIII: 51.

Bucha, E., Kreml, R. and Nowak, G. (1999). *In vitro* study of r-hirudin permeability through membranes of different haemodialysers. *Nephrol. Dial. Trans.* 14: 2922-2926.

Cabasso, I., Klein, E., Smith J. K. (1977). Polysulfone holow fiber. II. Morphology. *J. Appl. Polymer Sci*. 21: 165.

Chanard, J., Bindi, P., Lavaud, S., Toupance, O., Maheut, H. and Lacour, F. (1989). Carpal tunnel syndrome and type of dialysis membrane. *BMJ* 298: 867-868.

Chanard, J., Lavaud, S., Radoux, C. and Rieu, P. (2003). New insights in dialysis membrane biocompatibility: relevance of adsorption properties and heparin binding. *Nephrol. Dial. Trans.* 18: 252-257.

Cheung, A. K. and Leypoldt, J. K. (1997). Evaluation of hemodialyzer performance. *Semin. Dial.* 11: 131-137.

Chuang, W. Y., Young, T. H., Chiu, W. Y. and Lin, C. Y. (2000). The effect of polymeric additives on the structure and permeability of poly (vinyl alcohol) asymmetric membranes. *Polymer* 41: 5633-5641.

Collins, A., Ilstrup, K., Hansen, G, Berkset, R and Kehaviah, P. (1986). Rapid high-efficiency hemodialysis. *Artif. Org.* 10: 185.

Colton, A. K., Henderson, L. W., Ford, C. A. and Lysaght, M. J. (1975). *J. Lab. Clin. Med.* 85: 355.

Cosentino, F., Chaff, C. and Piedmonte, M. (1994). Risk factors influencing survival in ICU acute renal failre. *Nephrol. Dial. Trans.* 9(Supply 4): 179-182.

Cross, C. F. and Bevan, E. (1910). The cellulose acetates about to be described are of undetermined molecular weight. *Cellulose* III: 162.

Dedrick, R., Gabelnick, H. and Bischoff, B. (1968). Kinetics of urea distribution. *Annu Conf. Eng. Med. Biol.* 10: 36.

Depprisch, R., Schmitt, V., Bommer, J., Hansch, G. M., Ritz, E. and Rauterberg, E. W. (1990). Fluid phase generation of terminal complement complex as a novel index of bioincompatibility. *Kidney Int.* 37: 696-706.

Dharnidharka, S. G., Kirkham, R. and Kolff, W. J. (1973). Toward a wearable artificial kidney using ultrafiltrate as dialysate. *Trans. Am. Soc. Artif. Intern. Org.* 14: 92.

Diamantoglou, M. and Horst-Dieter, L. (1992). *Dialysis membrane made of polysaccharide ether*. (United States Patent 5,171,444).

Diamantoglou, M., Dunweg, G. and Thomas, R. (1995). *Dialysis membrane composed of polysaccharide ether II*. (United States Patent 5,427,684).

Diamantoglou, M., Martin, N. and Winfried, H. (2000). *Method of making cellulosic dialysis membrane*. (United State Patent 6,019,925).

Dorgan, J. R. (1992). Polymer membranes for separations. In: David S. S., *Polymer applications for biotechnology- Macromolecular separation and identification*. New Jersey: Prentice Hall. 64-97.

Dunweg, G., Lother, S. and Wolfgang, A. (1995). *Dialysis membrane made of cellulose acetate*. (United States Patent 5,403,485).

EdREN. (2005). Renal Unit at the Royal Infirmary of Edinburgh. Scotland. Unpublished.

Edward, C. G. (2003). Primer on membrane filtration media. E.C.Gregor and Associates. Unpublished.

Eknoyan, G., Beck, G. J., and Cheung, A. K. (2002). Effect of dialysis dose and membrane flux in maintenance hemodialysis. *N. Eng. J. Med.* 347: 2010-2019.

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.

Funck-Brentano, J. L. (1987). Toward dialysis “a La Carte”. *Artif. Org.* 11: 447.

Gastaldello, K., Melot, C., Kahn, R. J., Vanherweghem, J. L., Vincent, J. L. And Tielemans, C. (2000). Comparison of cellulose diacetate and polysulfone membranes in the outcome of acute renal failure. A prospective randomized study. *Nephrol. Dial. Trans.* 15: 224-230.

Gerhard, L. and Karl M. K. (2002). Beta-2-microglobulin amyloidosis: Effects of ultrapure dialysate and type of dialyzer membrane. *J. Am. Soc. Nephrol.* 13: S72-S77.

Gerrit, L., Rita, D. S., Norbert, L., Annemieke, D., Philippe, D. and Raymond, V. (2000). Intradialytic removal of protein-bound uraemic toxins: role of solute characteristics and of dialyser membrane. *Nephrol. Dial. Trans.* 15: 50-57.

Giordano, C., Esposito, R., Leo, V. A. D., Bello, P. and Quarto, E. (1980). Further studies on the realization of a cold carbon portable artificial kidney. *Artif. Org.* 4 : 44.

Gornall, A. G., Bardawill, C. J. and David, M. M. (1949). Determination of serum proteins by means of the Biuret Reaction. *J. Biol. Chem.* 177: 751.

Graham, T. (1861). Liquid diffusion applied to analysis. *Philos. Trans. R. Soc. London*. 151: 183-224.

Green, D. M., Antwiler, G. D., Moncrief, J. W., Decherd, J. F. and Popovich, R. P. (1976). *Trans. Am. Soc. Artif. Int. Org.* 22: 627.

Grethlein, H. E. (1973). A study on reproducibility of cellulose acetate membranes. *Desalination* 12: 45-60.

Hakim, R. M., Fearon, D. T. and Lazarus, J. M. (1984). Biocompatibility of dialysis membranes: effects of chronic complement activation. *Kidney Int*. 26: 194-200.

Hakim RM, Tolkoff-Rubin N, Himmerlfarb J, Wingard RL and Parker RA. (1994). A multicenter comparison of bioincompatible and biocompatible membranes in the treatment of acute renal failure. *J. Am. Soc. Nephrol.* 5: 394.

Han, M. J. and Nam, S. T. (2002). Thermodynamic and rheological variation in polysulfone solution by PVP and its effect in the preparation of phase inversion membrane. *J. Membr. Sci*. 202: 55-61.

Hartmann, J., Fricke, H., Schiff, H. (1997). Biocompatible membranes preserve residual renal function in patients undergoing regular hemodialysis. *Am. J. Kidney Dis*. 30: 366-373.

Hayama, M., Yamamoto, K., Kohori, F. and Sakai, K. (2004). How polysulfone dialysis membranes containing polyvinylpyrrolidone achieve excellent biocompatibility? *J. Membr. Sci*. 234: 41-49.

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

Himmerlfarb, J. and Hakim, R. M. (1997). The use of biocompatible dialysis membranes in acute renal failure*. Adv. Ren. Replace Ther.* 4: 72-80.

Himmerlfarb, J., Raymond, M. D. and Hakim, M. (1997). Dialysis membrane biocompatibility and mortality and morbidity in acute renal failure*. J. of Nephrol.* 10(2): 63-64.

Jung, B., Yoon, J. K., Kim, B. and Rhee, H. W. (2004). Effect of molecular weight of polymeric additives on formation, permeation properties and hypochlorite treatment of asymmetric polyacrylonitrile membranes. *J. Membr. Sci*. 243: 45-57.

Kedem, O. and Katchalsky, A. (1958). Thermodynamic analysis of the permeability of biological membranes to non-electrolytes. *Biochem. Biophys. Acta* 27: 229-246.

Kedem, O. and Katchalsky, A. (1961). A physical interpretation of the phenomenological coefficients of membrane permeability. *J. Gen. Phys.* 45: 143-149.

Kedem, O. and Katchalsky, A. (1963). Permeability of composite membranes. Part 3. Series array of composites. *Trans. Faraday Soc*. 59: 1941.

Kesting, R. E. (1964). *Nature of pores in integrally skinned phase inversion membranes*. Ottawa. National Research Council of Canada.

Kesting, R. E. (1985). *Synthetic Polymeric Membranes* 2nd ed. New York. Wiley and Sons Publication.

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

Khayet, M., Feng, C. Y., Khulbe, K. C. and Matsuura, T. (2002). Study on the effect of a non-solvent addtiveis on the morphology and performance of ultrafiltration hollow-fiber membranes. *Desalination* 148: 321-327.

Kim, I. C. and Lee, K. H. (1998). Effect of PEG additives on membrane formation by phase inversion. *J. Membr. Sci*. 138: 153-163.

Kim I. C. and Lee, K. H. (2004). Effect of polyethylene glycol 200 on the formation of a polyetherimide asymmetric membrane and its performance in aqueous solvent mixture permeation. *J. Membr. Sci*. 230: 183-188.

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

Kim, S. W. and Wisniewski, S. (1980). Permeation of water through poly(2-hydroxyethyl methacrylate) and related polymers: temperature effects. *J. Membr. Sci. 6*: 309-318.

Klein, E., Holland, F. F., Angela, D., Albert, L. and Karen, E. (1977). Diffusive and hydraulic permeabilities of commercially available cellulosic hemodialysis films and hollow fibers. *J. Membr. Sci.* 2: 349-364.

Klein, E. (1987). Membrane processes – Dialysis. In: Ronald W. Rousseau. *Handbooks of separation process technology*. USA: John Wiley and Sons, Inc. 954-970.

Klein, E., Holland, F. F., Lebeouf, A., Donnaud, A. and Smith, J. K. (1976). Transport and mechanical properties of hemodialysis hollow fibers. *J. Membr. Sci*. 1: 371-396.

Koda, Y., Nishi, S. I. and Miyazaki, S. (1997). Switch from conventional to high flux membrane reduces the risk of carpal tunnel syndrome and mortality of hemodialysis patients. *Kidney Int*. 52: 1096-1101.

Koda, Y., Suzuki, M. and Hirasawa, Y. (2001). Efficacy of choice of dialysis membrane. *Nephrol. Dial. Trans.* 16: 23-26.

Kolff, W. J. (1956). First clinical experience with the artificial kidney. *Ann.Intern.Med*. 62: 608.

Kolff, W. J. and Berk, H. T. (1944). The artificial kidney: a dialyzer with a great area. *Acta. Med. Scan*. 117: 121-134.

Kranzlin, B., Reuss, A., Gretz, N., Kirschfink, M., Ryan, C. J. and Mujais, S. K. (1996). Recovery from ischemic renal failure: Independence from dialysis membrane type. *Nephron.* 73: 644-651.

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

Kuchle, C., Friske, H. and Held, E. (1996). High-flux hemodialysis postpones clinical manifestation of dialysis-related amyloidosis. *Am. J. Nephrol*. 16: 484-488.

Kuehl, R. O. (2000). *Design of Experiments, Statistical principles of research design and analysis, 2nd edition*. United Stated of America: Brooke/Cole Publishing Company.

Kurtal, H., Von, H. D. and Schefer, K. (1994). Is the choice of membrane important for patients with acute renal failure requiring dialysis? *Int. J. Artif. Org*. 5: 391-394.

Leber, H. W., Wizemann, Y. and Techert, F. (1980). Simultaneous hemofiltration and hemodialysis (HF/HD). *Artif. Organs*. 4: *108.*

Lee, K. Y. (2003). *Production of flat sheet dialysis membrane*. Universiti Teknologi Malaysia: Bachelor Thesis.

Leonard, E. F. and Dedrick, R. L. (1968). *Chem. Eng. Progr. Symp. Ser*. 64 (84): 15.

Leypoldt, J. K., Cheung, A. K. and Deeter, R. B. (1997). Single compartment models for evaluating β_2-microglobulin clearance during hemodialysis. *ASAIO J* 46: 904-909.

Liano, F., Pascual, J. and Madrif ARF Study Group. (1996). Epidemiology of acute renal failure: a prospective, multicenter, community based study. *Kidney Int.* 50: 811-818.

Lim, K. S. (2001). *First 2002 Cabinet meeting should endorse policy that no single Malaysian will die in new year because of inability to afford dialysis treatment to give meaning to Eighth Malaysia Plan health strategy*. New Straits Times, 31/12.

Lim, Y. N. and Lim, T. O. (2003). All Renal Replacement Therapy In Malaysia. *11th Report Of The Malaysian Dial. & Trans. Registry.* 9-12.

Lipps, B. J., Stewart, R. D., Perkins, H. A., Holmes, G. W., Mclain, E. A., Rolfs, M. R. and Oja, P. P. (1967). The hollow fiber artificial kidney. *Trans. Am. Soc. Artif. Intern. Org.* 13: 200-207.

Locatelli, F., Valderrabano, F., Hoenich, N., Bommer, J., Leunissen, K. and Cambi, V. (2000). Progress in dialysis technology: membrane selection and patient outcome. *Nephrol. Dial. Trans.* 15: 1133-1139.

Locatelli, F. and Manzoni, C. (2000). Treatment modalities in comparison: when do clinical differences emerge ?. *Nephrol. Dial. Trans.* 15: 29-35.

Loeb, S. and Sourirajan, S. (1962). Sea water demineralized by means of an osmotic membrane. *Advan. Chem. Ser.* 38: 117.

Lonsdale, H. K., Merten, U. and Riley, R. L. (1965). Transport properties of cellulose acetate osmotic membranes. *J. Appl. Polymer Sci.* 9: 1341-1362.

Lornoy, W., Because, I., Billiouw, J. M., Sierens, L., Van, M. P. and Haenes, P. D. (2000). On-line haemodiafiltration. Remarkable removal of beta-2-microglobulin. Long-term clinical observations. *Nephrol. Dialy. Trans.* 15(Suppl 1): 49-54.

Maher, J., Sargent, J. A. and Gotch, F. A. (1989). *Principles and biophysics of dialysis, in (ed):Replacement of renal function by dialysis*, *chap 4.* 3rd ed. Boston, MA. Kluwer Academic Publishers.

Marsh, W. H. (1965). *Clin. Chem. II* : 624.

Matsuura, T. (1994). *Synthetic membranes and membrane separation processes.* United States of America: CRC Press.

Matz, R. (1972). The structure of cellulose acetate membranes. I. The development of porous structure in anisotropic membranes. *Desalination* 10: 1-15.

Montgomery, D. C. (1976). *Design and Analysis of Experiments*. United States of America: John Wiley and Sons, Inc.

Montgomery, D. C. (1997). *Design and analysis of experiments*. 4th ed. New York: John Wiley and Sons, Inc.

Morti, S., Shao, J. H. and Zydney, A. L. (2003). Importance of asymmetric structure in determining mass transport characteristics of hollow fiber hemodialyzers. *J. membr. Sci.* 224: 39-49.

Morti, S. M. and Zydney, A. L. (1998). Protein-membrane interactions during hemodialysis: effects on solute transport. *J. Am. Soc. Artif. Intern. Org*. 44: 319.

Mulder, M. (1996). *Basic principles of membrane technology.* The Netherlands: Kluwer Academic Publishers.

Muller-Steinhardt, M., Kock, N., Hartel, C., Kirchner, H. and Steinhoff, J. (2001). Production of monokines in patients under polysulphone hemodialfiltration is influenced by the ultrafiltration flow rate. *Nephrol. Dial. Trans.* 16: 1830-1837.

Myers, R. H. and Montgomery, D. C. (1995). *Response surface methodology: Process and product optimization using designed experiments*. New York: John Wiley and Sons, Inc.

National Kidney Foundation Homepage. (2004). United State of America. Unpublished.

Neveu, H., Kleinknecht, D., Brivet, F., Loirat, P.H., Landais, P. and French study group on acute renal failure. (1996). Prognostic factors in acute renal failure due to sepsis: results of a prospective multicentre study. *Nephrol. Dial. Trans.* 11: 293-299.

Nicholas, A. H., Celia, W., Susan, S., Sarah, J. R. and Jean, T. (1997). Synthetically modified cellulose: an alternative to synthetic membranes for use in baemodialysis. *Biomaterials* 18: 1299-1303.

Noda, I., Dimabo, G. B., and Carl, C. G. (1979). Effect of flow maldistibution on hollow fiber dialysis-experimental studies. *J. Membr. Sci.* 5: 209-225.

Noordin, M. Y., Venkatesh, V. C., Sharif, S., Elting, S. and Abdullah, A. (2004). Application of response surface methodology in describing the performance of coated carbide tools when turning AISI 1045 steel. *J. Materials Processing Technol.* 145: 46-58.

Oehlert, G. W. (2000). *A first course in design analysis of experiments*. United States of America: W.H. Freeman and Company.

Onsager, L. (1931). Reciprocal relations in irreversible processes I. *Phys. Re*v. 37: 405-426.

Onsager, L. (1931). Reciprocal relations in irreversible processes II. *Phys. Re*v. 38: 2265-2279.

Pappenheimer, J. R., Renkin, E. M. and Borrero, L. M. (1951). Filtration, diffusion and molecular sieving through peripheral capillary membranes – a contribution to the pore theory of capillary permeability. *Am. J. Phys.* 167: 13-46.

Parker, T. F. III., Wingard, R. L., Husni, L., Ikizler, T., Parker, R. A. and Hakim, R. M. (1996). Effect of the membrane biocompatibility on nutritional parameters in chronic hemodialysis patients. *Kidney Int*. 49: 551-556.

Pinnau, I. and William, J. K. (1992). Influence of quench medium on the structures and gas permeation properties of polysulfone membranes made by wet and dry/wet phase inversion. *J. Membr. Sci.* 71: 81-96.

Porter, M. C. (1990). *Handbook of industrial membrane technology.* California. Noyes publications.

Prime, K. L. and Whitesides, G. M. (1991). Self-assembled organic monolayers: model systems for studying adsorption of protein at surfaces. *Sci.* 252: 1164.

Ray, R. J., Kranz, W. B. and Sani, R. L. (1985). Linear stability theory model for finger formation is asymmetric membranes. *J. Membr. Sci*. 23: 155-182.

Reuvers, A. J. (1987). *Membrane Formation: Diffusion Induced Demixing Processes In Ternary Systems*. Twente University of Technology: PhD Thesis.

Ronco, C., Ballestri, M. and Cappelli, G. (2000). Dialysis membranes in convective treatments. *Nephrol. Dial. Trans*. 15: 31-36.

Rotellar, E., Martinez, E., Samso, J. M., Barrios, J., Simo, R., Mulero, J. F., Perez, M. D., Bandres, S. and Pino, J. (1986). Large surface hemodialysis. *Artif. Org.* 10: 387.

Roy, S., Hogg , R. J., Travis, L., Wenzl, J., Reisch, J. S., Fox, W., Green, K., Berry, P. L., Leighton, H. L., Sanjad, S. A., Boineau, F.G., Lewy, J. E., Arnold, W. C., Lum, G. M., Tenney, F., Matson, J. R., Stapleton, B., Arant, B. S., Houser, M.T., Meyer, R. *et al*. (1985). Continuous ambulatory and continuous cycling peritoneal dialysis in children. A report of the Southwest Pediatric Nephrology Study Group. *Kidney Int.* 27: 558-564.

Rutherford, P., Uttley, L., Auer, J., Keogh, A., Soni, R., Jenkins, S., Stein, A., Suchak, P., Said, V. and Mansfield, D. (2004). *Kidney wise Online Community*. United State of America: Baxter Ltd.

Sabde, A. D., Trivedi, M. K., Ramachandran, V., Hanra, M. S. and Misra, B. M. (1997). Casting and characterization of cellulose acetate butyrate based UF membranes. *Desalination* 114: 223-232.

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

Sang, H. Y., Junju, W., Yashuhiko, I. and Kazuhiko, I. (2003). Antifouling blood purification membrane composed of cellulose acetate and phospholipid polymer. *Biomaterials* 24: 4143-4152.

Sang, H. Y., Junju, W., Yashuhiko, I. and Kazuhiko, I. (2005). In situ modification on cellulose acetate hollow fiber membrane modified with phospholipid polymer for biomedical application. *J. Membr. Sci.* 249: 133-141.

Schaefer, R. M., Huber, L., Gilge, U., Bausewein, K., Vienken, J. and Heidland, A. (1989). Clinical evaluation of new high-flux cellulose acetate membrane. *Int. J. Artif. Org.* 12(2): 85-90.

Schiffl, H., Lang, S. M., Konig, A., Strasse, T., Haider, M. C., and Held, E. (1994). Biocompatible membranes in acute renal failure: A prospective case controlled study. *Lancet* 344: 570-572.

Schulman, G., Fogo, A., Gung, A., Badr, K. and Hakim, R. M. (1991). Complement activation retards resolution of ischemic renal failure in the rat. *Kidney Int.* 40: 1069-1074.

Scott, K. (1998). *Handbook of industrial membranes*. 2nd ed. United Kingdom: Elsevier Advance Technology.

Seong, H. Y., Jong, H. K., Jae, Y. J., Jongok, W. and Yong, 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.

Setford, S. J. (1995). *A basic introduction to separation science*. United Kingdom: Rapra Rechnology Limited.

Sevillano, G., Rodriguez-Puyol, M., Martos, R., Duque, I., Lamas, S., Diez-marques, M. L., Lucio, J. and Rodriguez-Puyol, D. (1990). Cellulose acetate membrane improves some aspects of red blood cell function in haemodialysis patients. *Nephrol. Dial. Trans*. 5: 497-499.

Sherman, R. A., Swartz, R. D. and Thomas, C. (2004). *Treatment methods for kidney failure: Hemodialysis*. National Institute of Health, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Fact Sheet. USA: 1-19.

Shettigar, U. R. (1989). Innovative extra corporeal membrane systems. *J. Membr. Sci*. 44: 89-114.

Shinazato, T., Sezeki, R., Usada, M., Maeda, K., Ohbayashi, S. and Toyota, T. (1982). Infusion-free hemofiltration. Simultaneous hemofiltration and dialysis with no need for infusion fluid. *Artif. Org.* 6: 453.

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.

So, M. T., Eirich, F. R., Baker, R. W. and Strathmann, H. (1973). *Polymer Letters* 11: 201.

Stat-Ease Inc. (2000). *Design-Expert Software V.6 User's Guide*. Minneapolis. MN.

Staverman, A. J. (1952). Non-equilibrium thermodynamics of membrane processes. *Trans. Faraday Soc.* 48: 176-185.

Stefoni, S., Scolari, M. P., Cianciolo, G., Mosconi, G., De Sanctis, L. B., De Pascalis, A., La Manna, G., Donati, G., Manna, C., Sestigiani, E. and Grammatico, F. (2000). Membranes, technologies and long-term results in chronic haemodialysis. *Nephrol. Dial. Trans.* 15: 12-15.

Stephen, B. K. and Klein, E. (1992). *Dialysis Design, Membrane Handbook*. New York: Van Norstrand Reinhold.

Stepphan, D. D., Werner, J. and Yeater, R. P. (1998). Essential regression and experimental design for chemists and engineers. http://geocities.com/SiliconValley/Netweok/1032/Cgpage1.html.

Stiller, S. and Mann, H. (1987). Utlra-short dialysis and internal physiological resistances. *Trans. Am. Soc. Artif. Intern. Org.* 33: 79.

Strathmann, H., Kock, K., Amar, P. and Baker, R. W. (1975). The formation mechanism of asymmetric membranes. *Desalination* 16: 179-203.

Strathmann, H. and Kock, K. (1977). The formation mechanism of phase inversion membranes. *Desalination* 21: 241-255.

Strihou, C. V. Y., Jadoul, M., Malghem, J., Maldague, B., Jamart, J. and the working party on dialysis amyloidosis. (1991). Effect of dialysis membrane and patient's age on signs of dialysis-related amyloidosis. *Kidney Int*. 39: 1012-1019.

Svartass, T. M., Smeby, L. C., Jorstad, S., Naess, T. B., Wideroe, T. E. and Holtz, M. (1982). Selection and evaluation *in vitro* of the selective dual filtration artificial kidney, SEDURARK. *Artif. Org.* 6: 136.

Teschan, P. E. (1986). Clinical estimates of treatment adequacy. *Artif. Org.* 10: 195.

Torrestiana-Sanchez, B., Ortiz-Basurto, R. I. and Brito-De, L. F. E. (1999). Effect of nonsolvents on properties of spinning solutions and polyethersulfone hollow fiber ultrafiltration membranes. *J. Membr. Sci.* 152: 19-28.

Trafford, A., Ireland, R. and Evans, R. (1979). The use of hemoperfusion as an adjunct to hemodialysis. *Artif. Org.* 3: 249.

US National Kidney And Urologic Diseases Information Clearing House (NKUDIC). (2004). *Treatment methods for kidney failure: Hemodialysis*. USA. Unpublished.

Valeri, A. (1994). Biocompatible membranes in acute renal failure. A study in post cadaveric renal transplant acute tubular nevrosis. *J. Am. Soc. Nephrol.* 5: 481.

Valette, P., Thomas, M. and Dejardin, P. (1999). Adsoprtion of low molecular weight protein to hemodialysis membranes: experimental results and simulations. *Biomaterials* 20: 1621-1634.

Vazquez, M. I. and Benavente, J. (2003). A study of temperature effect on chemical, structural and transport parameters determined for two different regenerated cellulose membranes. *J. Membr. Sci*. 219: 59-67.

Van de Witte, P., Dijkstra, P. J., Van den Berg, J. W. A. and Feijen J. (1996). Phase separation processes in polymer solutions in relation to membrane formation. *J. Membr. Sci*. 117: 1-31.

Verniory, A., Dubois, R., Decoodt, P., Gassee, J. P. and Lambert, P. P. (1973). Measurement of the permeability of biological membranes. Application to the glomerural wall. *J. Gen. Phys.* 62: 489-507.

Ward, R. A., Buscariku, A., Schimidt, B., Stefoni, S., Gurland, H. J. and Klinkmann, H. (1997). A comparison of dialysers with low-flux membranes: significant difference in spite of many similarities. *Nephrol. Dial. Trans*. 12: 965-972.

Yasuda, H., Lamaze, C. E. and Peterlin, A. (1971). Diffusive and hydraulic permeabilities of water in water-swollen polymer membranes. *J. Polymer. Sci* .Part A2 9: 1117-1131.

Young, T. H. and Chen, L. W. (1991). A two step mechanism of diffusion-controlled ethylene vinyl alcohol membrane formation. *J. Membr. Sci*. 57: 69-81.

Yuan, J. H., Shang, P. P. and Wu, H. S. (2001). Effects of polyethylene glycol on morphology, thermomechanical properties and water vapor permeability of cellulose acetate- Free films. *Pharm. Technol. Oct. Press*: 62-73.