POLYSULFONE/IRON OXIDE NANOPARTICLES MIXED MATRIX MEMBRANES FOR HEMODIALYSIS APPLICATION

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Dedicated to my love,
(Muhammad Nidzhom Bin Zainol Abidin)
my beloved parents,
(Said Bin Md Hassan and Che Tom Binti Jafri)
my in laws,
(Zainol Abidin Bin Anas, Azizah Binti Senawi and Sharuwiah Binti Jaafar)
family and friends who gave me inspiration, encouragement and endless support
throughout the success of my study.
May this thesis be an inspiration and guidance in the future.

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ABSTRACT

Hemodialysis is a process of purifying the blood of a person whose kidneys are not working normally. The design of a hemodialysis membrane with superior uremic toxin separation and sufficient biocompatibility is of great demand. Hence, the objective of this study is to fabricate a high performance and biocompatible polysulfone/iron oxide nanoparticles (PSf/IONPs) mixed matrix membrane (MMM) for hemodialysis application. In the first phase of the study, the poor dispersion of IONPs in the polymer solution was addressed by a chemical modification using citric acid (CA) at the weight ratio of 1:5-1:25 (IONPs:CA). The dispersion of the IONPs was studied by observing the particle stability in water. PSf/IONPs MMMs comprised of 18 wt% PSf, 4.8 wt% polyvinylpyrrolidone and 0.1 wt% IONPs at various IONPs:CA weight ratios were then prepared by dry-wet spinning process. The results revealed that the optimum IONPs:CA weight ratio was 1:20, in which 49% of the IONPs was recovered after 3 days in water. As a result of the improved IONPs dispersion, the MMM exhibited good water transport features. In the second phase of the study, the effect of dope extrusion rate (DER) from 1.0 to 2.5 mL/min, and air gap from 10 to 60 cm, on the MMM morphology and liquid separation characteristics was investigated. The higher DER increased the MMM wall thickness, while the increase of air gap reduced the MMM diameter. The ideal morphology for hemodialysis membrane was obtained at the DER of 1.0 mL/min and the air gap of 50 cm. At those membrane spinning conditions, the MMM achieved pure water permeability (PWP) of 70.84 $Lm^{-2}h^{-1}bar^{-1}$, bovine serum albumin (BSA) rejection of 98.2% and high sieving coefficient of urea (1.0) and lysozyme (0.7). In the next phase, the effect of IONPs loading (0-0.1 wt%) on the MMM physicochemical properties and separation performance were studied. The PSf/IONPs MMM possessed an improved thermal stability at higher IONPs loading. Besides, the MMM porosity and surface hydrophilicity were enhanced by increasing the IONPs loading. It was found that the MMM fabricated at 0.05 wt% IONPs loading recorded the highest PWP and BSA rejection (P= 110.47 $Lm^{-2}h^{-1}bar^{-1}$; R= 99.9 %). Moreover, the MMM displayed the best separation performance by removing 82% urea and 46.7% lysozyme. In the final phase of the study, the membrane surface morphology was studied and the biocompatibility of the MMMs was evaluated in terms of protein adsorption, platelet adhesion, blood coagulation time and compliment activation. The PSf/IONPs MMMs possessed a smoother surface and smaller surface pore size compared to the common PSf membrane. Furthermore, the PSf/IONPs MMM demonstrated lesser protein adsorption and platelet adhesion at higher IONPs loading while keeping a normal blood coagulation time and satisfactory complement activation. The PSf/IONPs MMM showed an excellent separation performance and good biocompatibility for hemodialysis application.

ABSTRAK

Hemodialisis ialah proses membersihkan darah seseorang yang buah pinggangnya tidak berfungsi seperti biasa. Reka bentuk membran hemodialisis dengan pemisahan toksin uremik yang unggul dan biokeserasian yang mencukupi mendapat permintaan yang tinggi. Justeru, objektif kajian ini adalah untuk menghasilkan membran bermatriks campuran (MMM) polisulfon/partikel nano besi oksida (PSf/IONPs) yang berprestasi tinggi dan bioserasi untuk aplikasi hemodialisis. Pada fasa pertama kajian, penyerakan IONP yang rendah dalam larutan polimer ditangani oleh pengubahsuaian kimia menggunakan asid sitrik (CA) pada nisbah berat 1:5-1:25 (IONPs:CA). Penyerakan IONPs dikaji dengan memerhatikan kestabilan partikel tersebut di dalam air. PSf/IONPs MMMs terdiri daripada 18 % berat PSf, 4.8 % berat polivinilpirrolidon dan 0.1 % berat IONPs pada pelbagai nisbah berat IONPs:CA kemudiannya dihasilkan melalui proses putaran kering-basah. Dapatan kajian menunjukkan bahawa nisbah berat IONPs:CA yang optimum adalah 1:20, di mana 49% daripada IONPs telah diperoleh setelah 3 hari di dalam air. Hasil daripada penyerakan IONP yang lebih baik, MMM mempamerkan ciri-ciri pengangkutan air yang baik. Pada fasa kedua kajian, kesan kadar penyemperitan larutan polimer (DER) daripada 1.0 hingga 2.5 mL/min, dan sela udara daripada 10 hingga 60 cm, terhadap morfologi dan ciri-ciri pemisahan cecair MMM telah dikaji. DER yang lebih tinggi meningkatkan ketebalan dinding MMM, manakala peningkatan sela udara mengurangkan diameter MMM. Morfologi yang sempurna untuk membran hemodialisis diperolehi pada DER 1.0 mL/min dan sela udara 50 cm. Pada keadaan putaran membran tersebut, MMM mencapai kebolehtelapan air tulen (PWP) sebanyak 70.84 $Lm^{-2}h^{-1}bar^{-1}$, penyingkiran serum albumin bovin (BSA) sebanyak 98.2% dan faktor pengayakan urea (1.0) dan lisozim (0.7) yang tinggi. Pada fasa seterusnya, kesan muatan IONPs (0-0.1 % berat) terhadap sifat fizikokimia dan prestasi pemisahan MMM dikaji. PSf/IONPs MMM mempunyai kestabilan haba yang lebih baik pada muatan IONPs yang lebih tinggi. Selain itu, keliangan dan sifat hidrofilik permukaan MMM telah dipertingkatkan dengan meningkatkan muatan IONPs. Telah didapati bahawa MMM yang dihasilkan pada 0.05 % berat muatan IONPs merekodkan PWP dan penyingkiran BSA (P = 110.47 $Lm^{-2}h^{-1}bar^{-1}$; R = 99.9%) tertinggi. Selain itu, MMM tersebut mempamerkan prestasi pemisahan terbaik dengan menyingkirkan 82% urea dan 46.7% lisozim. Pada fasa terakhir kajian, morfologi permukaan membran dikaji dan biokeserasian MMM dinilai dari segi penjerapan protein, pelekatan platelet, masa pembekuan darah dan pengaktifan pelengkap. PSf/IONPs MMMs mempunyai permukaan yang lebih rata dan saiz liang permukaan yang lebih kecil berbanding membran PSf yang biasa. Tambahan pula, PSf/IONPs MMM menunjukkan penjerapan protein dan pelekatan platelet yang berkurang pada muatan IONPs yang lebih tinggi sambil mengekalkan masa pembekuan darah yang normal dan pengaktifan pelengkap yang memuaskan. PSf/IONPs MMM menunjukkan prestasi pemisahan yang cemerlang dan biokeserasian yang baik untuk aplikasi hemodialisis.

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LIST OF ABBREVIATIONS

AFM - Atomic force microscope
APTT - Activated partial thromboplastin time
BSA - Bovine serum albumin
CA - Citric acid
CNTs - Carbon nanotubes
DER - Dope extrusion rate
EDX - Energy-dispersive X-ray
ESRD - End-stage renal disease
FTIR - Fourier transform infrared
HAP - Hydroxyapatite
HGG - Human gamma globulin
HSA - Human serum albumin
ID - Inner diameter
IONPs - Iron oxide nanoparticles
IUPAC - International union of pure and applied chemistry
LER - Linear extrusion rate
MF - Microfiltration
MMMs - Mixed matrix membranes
MWCNTs - Multi walled carbon nanotubes
N_2 - Nitrogen gas
NF - Nanofiltration
NKF - National Kidney Foundation
NMP - N-methyl-2-pyrrolidone
OD - Outer diameter
PAN - Polyacrylonitrile
PBS - Phosphate buffer saline
PES - Polyethersulfone

PEG - Polyethylene glycol
PLA - Poly(lactic acid)
PMMA - Polymethylmethacrylate
POC - 1,8-octanediol citrate
PPP - Platelet poor plasma
PRP - Platelet rich plasma
PSf - Polysulfone
PT - Prothrombin time
PU - Polyurethane
PVA - Polyvinyl alcohol
PVDF - Polyvinylidenefluoride
PVP - Polyvinylpyrrolidone
PWP - Pure water permeability
RO - Reverse osmosis
SDS - Sodium dodecyl sulfate
SEM - Scanning electron microscope
STEM - Scanning transmission electron microscope
TGA - Thermal stability analysis
TMP - Transmembrane pressure
TPGS - D-a-tocopheryl polyethylene glycol 1000 succinate
UF - Ultrafiltration
UV - Ultraviolet
VIS - Visible light

LIST OF SYMBOLS

A	-	Membrane surface area (m^2)
Ad	-	Adsorbed proteins (μg/cm^2)
C	-	Solute clearance (%)
C_f	-	Concentration of solute in feed (mol.m^{-3})
C_{f1}	-	Finial concentration of solute feed (mg/L)
C_i	-	Initial concentration of solute in feed (mg/L)
C_p	-	Concentration of solute in permeate (mol.m^{-3})
cP	-	Centipoint
C_1	-	Concentration of IONPs recovered in solution (mg/L)
C_2	-	Concentration of IONPs originally in solution (mg/L)
K	-	Dialyzer urea clearance (mL/min)
K_d	-	Toxin clearance (mL/min)
K_oA	-	Mass transfer area coefficient (mL/min)
l	-	Membrane effective length (m)
p	-	Operating pressure (bar)
ΔP	-	Trans-membrane pressure (Pa)
P_f	-	Feed pressure (bar)
P_{pw}	-	Pure water permeability (Lm^{-2}h^{-1}bar^{-1})
Q	-	Volume of the permeate water per unit time (m^3/s)
Q_b	-	Blood flow rate (mL/min)
Q_d	-	Dialysate flow rate (mL/min)
Q_f	-	Feed flow rate (mL/min)
r_m	-	Mean pore radius (nm)
R	-	Solute rejection (%)
r	-	Average pore radius (m)
R_a	-	Mean surface roughness
SC	-	Sieving coefficient

T - Temperature (°C)

T - Duration of dialysis (h)

Δt - Permeation time (h)

V - Volume (L)

W_{wet} - Weight of wet membrane (g)

W_{dry} - Weight of dry membrane (g)

λ_{max} - Maximum wavelength (nm)

ε - Porosity (%)

ρw - Density of water (g/cm^3)

η - Water viscosity

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CHAPTER 1

INTRODUCTION

1.1 Research Background

One of the most dangerous diseases faced nationwide is kidney disease. Over the past ten to fifteen years, the number of chronic kidney diseases patients has increased terrifically where these patients suffer from the incapability of filtering and removing body waste. The latest statistics issued by National Kidney Foundation (NKF) in March 2016 revealed the total number of 38,157 Malaysians on dialysis and that number was expected to rise to 49,000 by the end of 2018 (Hammim, 2017). The further detail of the number of registered hemodialysis patients in Malaysia from year 2005 to 2016 is shown in Figure 1.1.

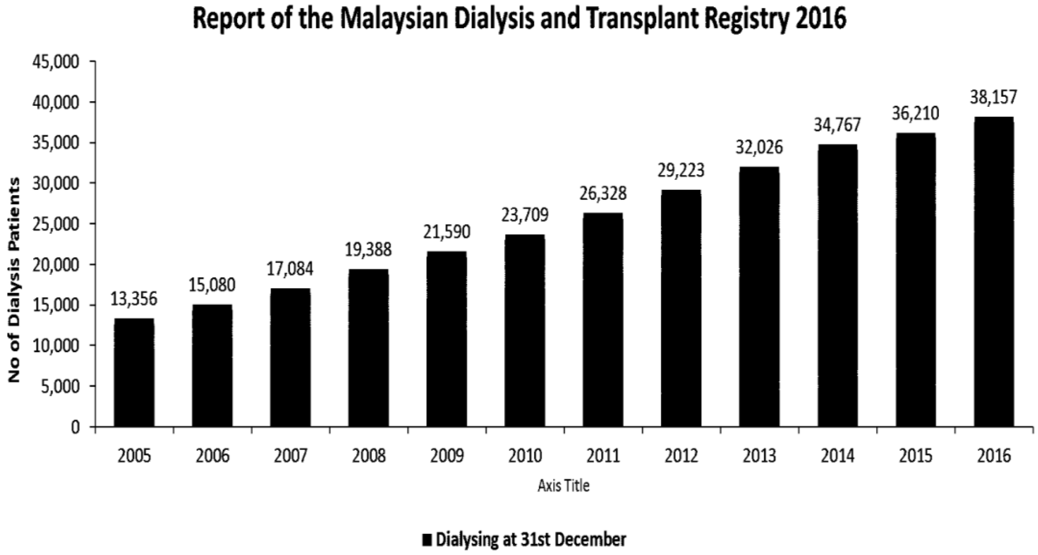

Figure 1.1 Statistics of the number of registered hemodialysis patients in Malaysia from year 2005 to 2016 (Goh and Ong, 2015)

Hemodialysis is considered as a highly successful therapy that provides the second chance to live. Since the beginning of the first semipermeable membranes for hemodialysis, the membrane technology keeps developing until it has been successfully used for hemodialysis treatment for patients who suffer from acute renal disease and end-stage renal disease (ESRD). In general, the main component of hemodialysis machine is dialyzer, where semipermeable membrane is situated. The membrane is arranged in the middle, serves as membrane contactor to form separate adjacent paths for blood and dialysis fluid (dialysate). It filters waste products (i.e. urea, creatinine, β_2-microglobulin), removes excess water and balances electrolytes such as sodium, potassium, and bicarbonate.

Various materials ranging from cellulose-based polymers to synthetic polymers have been used as the main material for the development of hemodialysis membrane. Cellulose and its derivatives are known as the first-generation polymers used in hemodialysis. However, due to their weak hydraulic permeability and low molecular cut-off, synthetic polymer such as polysulfone (PSf) and polyethersulfone (PES) which are also known as the second-generation polymers have been employed for hemodialysis. PSf, an amorphous polymer having a sulfone group in its structure, is the most commonly used polymeric material in producing hemodialysis membrane. It is due to its excellent thermal, chemical and mechanical stability. In addition, PSf-based membranes are one of those having the best biocompatibility. The initial development of PSf membrane coincided with the scientific reports regarding leukopenia and complement cascade caused by cellulosic hemodialysis membranes (Carpi, Donadio, and Tramonti, 2011).

An efficient hemodialysis membrane correlates to achieving excellent membrane separation performance with minimal adverse effects. Since 2014, the incorporation of inorganic nanomaterials in membrane matrices has become an emerging trend in membrane technology to enhance the permeability, selectivity and physicochemical properties of the membranes (Souza and Quadri, 2013; Cao *et al*., 2006). The nanomaterials have been promisingly used as nanofiller of polymer matrix (Favvas *et al*., 2014; Ng *et al*., 2013; Japip *et al*., 2014), forming a new class of membrane known as mixed matrix membrane (MMM).

The recent progress in the development of MMM for hemodialysis application involved mainly on the use of carbon nanoparticles. Previous studies on the hemodialysis membranes incorporated with carbon nanotubes (CNTs) for examples showed a substantial increase in water transport properties and toxin removal as compared to the neat polymeric membrane (Irfan *et al*., 2014; Yu *et al*., 2017). However, MMMs were seldom prepared in hollow fiber configuration which is more suitable for hemodialysis application. In addition, the use of other classes of nanomaterials like metal and metal oxide in hemodialysis membrane has never been studied before and their capability to improve the membrane dialysis performance has never been reported elsewhere.

Nevertheless, metal and metal oxide nanoparticles have been utilized in other separation processes due to their hydrophilic nature and high surface area, thus producing membranes with good interconnectivity and porosity (Ng *et al.*, 2013). Moreover, some metal oxide like iron oxide nanoparticles (IONPs) are biocompatible, chemically stable and have relatively low toxicity. The useful attributes offer great potential for IONPs to be employed as membrane nano-filler for hemodialysis application.

In this study, IONPs were incorporated in PSf hollow fiber membranes for hemodialysis application. To enhance the distribution of IONPs throughout the membrane, a naturally ubiquitous organic compound, namely citric acid (CA) was added into the dope solution as a stabilizer. The effect of different IONPs-CA weight ratios was extensively studied for the development of hollow fiber membrane. Next, the optimum spinning condition and IONPs loading were determined. The MMMs were evaluated in terms of their morphology, physicochemical properties, separation performance and biocompatibility. In brief, this study would be beneficial to those interested in the design of metal oxide nanocomposite and the strategized development of a safe and high-performance membrane for efficient liquid separation especially in ultrafiltration (UF) and hemodialysis treatment. Besides, the employment of metal oxide nanoparticles in hemodialysis membrane would provide the insight on membrane’s potential commercialization.

1.2 Problem Statement

The major problem associated with current hemodialysis treatment is the membrane incapability to remove the middle molecules, i.e. lysozyme and β_2-microglobulin. Normally, the removal of toxin by membrane is based on the concentration differences rather than the convective separation of solutes, which only works on small molecules such as urea and creatinine. Besides that, the current commercial membranes could not remove these ‘middle’ size molecules efficiently due to inadequate membrane pore size and thick skin layer. Some membranes that possess large pores ended up losing essential proteins. Either way, this makes the treatment less efficient.

On the other hand, the hydrophobic property of hemodialysis membranes makes them difficult to achieve high UF capacity since they attract the naturally existing hydrophobic proteins such as albumin and poorly interact with water molecules in blood. Furthermore, hydrophobicity is related to a rough surface of membrane, thus increases the possibility of proteins to get stuck on the surface. The effect on the membrane biocompatibility includes platelet adhesion and subsequently activating blood coagulation process. A series of hydrophobic protein and other components of blood that are activated can block the opening of membrane pores and subsequently cause performance drop, i.e. reduction in water permeability of the membrane. Besides, the rougher membrane surface can induce immunological responses such as complement activation when in contact with blood.

To tackle the stated problems, a high flux membrane with porous structure is needed. Thus, surface modification is usually done on the membrane. Previous efforts include the blending of hydrophilic polymer, for example polyethylene glycol and polyvinylpyrrolidone (PVP) together with PSf to increase the surface hydrophilicity of the membrane. Nevertheless, the tendency of PVP to swell in water and elude during dialysis (Irfan *et al.*, 2014) makes it less stable, despite becoming a good pore forming agent. Moreover, this approach did not improve the UF capacity of the membrane, thus made no difference on the separation of middle molecules. The efforts then have been shifted to the development of MMMs by incorporating nanoparticles to overcome the limitation of polymeric membranes.

IONPs are among the metal oxide nanoparticles that received most attention due to their nanoscale dimension, chemically inertness, good hydrophilicity and remarkable total surface area (Krishnamoorthy and Sagadevan, 2015). On the other hand, IONPs have been used for a long time in the biomedical such as tissue repair, drug delivery, magnetic resonance imaging and treating hyperthermia (Kumar and Gupta, 2005), which justified their biocompatibility with human body. The IONPs nano-structure behaves as a good liquid transport medium, thus producing membranes with good interconnectivity and porosity which could facilitate water movement across the membrane at minimal operating pressure. The presence of the hydrophilic IONPs at the membrane surface can reduce the membrane surface roughness, hence minimizing the protein adsorbed on the membrane. Certainly, MMM is a viable option to address the existing issues in hemodialysis.

Nevertheless, the aggregation of IONPs due to Van de Waals forces becomes the main issue since it is quite impossible to fabricate a uniform hollow fiber membrane, especially in small dimension. IONPs have a large surface to volume ratio and therefore possess high surface tension. Consequently, they tend to aggregate to reduce the surface energies. Some strategies to keep the stability of IONPs include grafting or coating with organic compounds such acids, polymer and biomolecules (Wu *et al.*, 2008). CA, which is a stabilizer from the class of organic acid was used in this study to improve the dispersion stability of IONPs.

In addition, there is a commitment to tailor the membrane morphology by manipulating the spinning parameter, since membrane morphology also plays a huge role in determining the sieving properties of a membrane. Throughout this study, attempts were made to fabricate PSf/IONPs MMMs at the optimum spinning parameter and IONPs loading to heighten the separation performance of the membranes, with the focus to remove both small and middle molecular weight molecules.

1.3 Objectives

The overall aim of this study is to develop a high performance and biocompatible PSf/IONPs MMM for hemodialysis application. The specific objectives of this study are:

i) To perform non-covalent modification of IONPs using CA at various IONPs-CA weight ratios and investigate the dispersion stability of IONPs and its impact on the MMMs water transport properties.

ii) To study the effects of various dope extrusion rates (DERs) and air gaps on the MMMs morphology and liquid separation characteristics.

iii) To investigate the effects of various IONPs loadings on the MMMs physicochemical properties and the removal of urea and lysozyme.

iv) To examine the surface morphology and biocompatibility of the fabricated MMMs for hemodialysis application.

1.4 Scopes of the Study

To fulfil the above objectives, the following scopes of work are outlined:

1) Modifying the surface of IONPs through the direct addition of CA at the weight ratio of 1:5-1:25 (IONPs:CA) and determining the dispersion stability of the blends by measuring the percent of IONPs recovered in water at designated time intervals for 3 days using UV-vis spectrophotometer.

2) Investigating the influence of CA towards the dispersion of IONPs using Fourier transform infrared (FTIR) spectrometry and scanning transmission electron microscopy (STEM). The pH and viscosity changes of PSf/IONPs dope solution after the addition of CA were also studied.

3) Fabricating the PSf/IONPs MMMs with different IONPs-CA weight ratios (1:5, 1:10, 1:15, 1:20, and 1:25) via dry-wet spinning process at 40 cm air gap. The MMMs hydrophilicity was determined using contact angle goniometer, before examining the morphology of the fabricated MMMs using scanning electron microscopy (SEM) and measuring their porosity and pore size. The water transport properties of the MMMs were also determined.

4) Studying the impact of spinning parameters by fabricating the PSf/IONPs MMMs at different DERs (1.0-2.5 mL/min). The MMMs were evaluated in terms of their morphology using SEM.

5) Fabricating the PSf/IONPs MMMs at various air gaps (10-60 cm). The morphological properties of the MMMs were examined using SEM. The liquid separation characteristics of the MMMs were evaluated based on the pure water permeability (PWP), bovine serum albumin (BSA) rejection and sieving properties, performed at the pressure of 0.7 bar.

6) Preparing PSf/IONPs dope solutions at different IONPs loadings (0-0.1 wt%). The viscosity of dope solutions was measured using a viscometer, before fabricating the MMMs at the optimum air gap and DER. The MMMs were characterized in terms of morphology using SEM, thermal stability using TGA, hydrophilicity using contact angle goniometer and porosity. Next, the PWP and BSA rejection tests were performed at the pressure of 0.7 bar.

7) Selecting the optimum feed and dialysate flow rates to be used in dialysis performance test based on the efficiency of the membrane module by calculating the mass transfer area coefficient of urea and lysozyme.

8) Determining the percent clearance of urea and lysozyme achieved by the MMMs of different IONPs loadings at the pre-optimized feed and dialysate flow rates.

9) Studying the leaching phenomenon of IONPs from MMMs by determining IONPs content in water permeate using UV-vis spectrophotometer.

10) Casting PSf/IONPs MMMs in the form of flat sheets via dry-wet phase inversion process with evaporation time of 6 seconds using water as the coagulation bath. The surface morphology of PSf/IONPs flat sheets was studied using atomic force microscope (AFM).

11) Evaluating the biocompatibility of the PSf/IONPs flat sheets in terms of protein adsorption, platelet adhesion, blood coagulation time and complement activation.

1.5 Significance of the Study

This study is expected to provide a better understanding on the underlying principle of the fabrication of MMMs for hemodialysis application by considering the changes of the membrane morphology, liquid separation characteristics, surface characteristics and uremic toxin separation due to the addition of inorganic nanofillers. The primary outcome of the research would benefit scientific community in the sense of filling in the knowledge gap in multiple fields which encompass nanotechnology and membrane technology. In addition, the research on hemodialysis membranes in Malaysia is still at early stages. The employment of IONPs in hemodialysis membrane for instance could progressively diversify their potential in this biomedical-device application. The ingenious approach which combined both unique properties of IONPs and versatility of polymer as a host showed great potential to combat the issues commonly faced by polymeric membranes. This novel invention is believed to become a stepping stone which could provide a valuable information for membranologists and lead the way to further study. The aftermath of the research will also benefit the ESRD patients by providing a high performance and biocompatible hemodialysis membrane that is capable and reliable to perform exceptional blood purification with minimal adverse effect. Triggered by the general necessities of serving the social community, the study would attract companies that manufacture or supply medical equipment as a platform to patent and market the product.

1.6 Limitation of Study

With reasonable explanations, these are the limitations the study:

1) The loading range of IONPs in membrane used was from 0 to 0.1 wt%. This range was selected based on the preliminary results obtained during the early stage of the study. At IONPs loading higher than 0.1 wt%, the dope solution became unstable, making it less homogeneous. The resultant membrane shape and dimension became inconsistent. In addition, the set of membranes produced from these IONPs loadings showed more convincing results that can be discussed with logical explanations.

2) Instead of hollow fiber membranes, flat sheet membranes from each membrane composition were utilized for biocompatibility studies. Hollow fiber membrane is hard to handle for the studies, since the active surface is at the inner side where the lumen is very small. The results obtained using flat sheet membrane is comparable reflect the membrane-blood interactions of the hollow fiber membranes.

3) The blood samples used for biocompatibility tests were collected from 3 healthy volunteers of random blood groups. The presented results of each membrane were based on the average value obtained from the 3 blood samples. Hence, the outcomes generated from this part of studies represent the membrane-blood interactions in general, rather than towards human blood of specific types and conditions.

1.7 Organization of Thesis

The thesis consists of 8 chapters altogether. Chapter 1 outlines brief information on the hemodialysis treatment, the use of membrane technology in hemodialysis and current issues that lead us to conduct this research. The objectives, scopes and the significance of this study have also been highlighted in this chapter. In Chapter 2, more detailed descriptions on how membrane works in hemodialysis treatment, the desired properties of a hemodialysis membrane, evolution of the hemodialysis membranes, followed by the specific modifications of the membranes which include chemical modification and fine tuning of the spinning parameters. Chapter 3 focusses on the experimental methods and characterization techniques that were used in this study.

Results and discussion were elaborated in Chapter 4 – Chapter 7. Chapter 4 describes in detail the effects of adding CA on the dispersion stability of IONPs in dope solution, as well as their distribution in membrane, whereby the possible mechanism of the phenomenon was proposed. The IONPs-CA weight ratio was varied from 1:5 to 1:25. The optimum IONPs-CA weight ratio was selected and was used to fabricate the hollow fiber membranes in Chapter 5. Chapter 5 discusses the effect of spinning parameters (DER and air gap) on the morphology and liquid separation characteristics of the hollow fiber membranes. The optimum DER and air gap were applied for the subsequent fabrication of membranes.

Next, the effects of varying the loading of IONPs on the MMMs physicochemical properties and its impact on the uremic toxins removal were addressed in Chapter 6. The same formulation used in Chapter 6 was used in Chapter 7 to fabricate flat sheets for the surface morphological studies and biocompatibility analysis. To conclude this thesis, the general conclusions of this study and some recommendations for future work have been listed in Chapter 8.

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