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A Review of Synthetic Polymers in Hemodialysis Membranes: Impact on Biocompatibility and Performance

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ABSTRACT

A wide range of synthetic polymers is employed in hemodialysis (HD) applications, each offering unique advantages and potential limitations that can impact patient outcomes. These polymers are primarily chosen for their excellent permeability to uremic solutes and superior biocompatibility, which are critical for efficient blood purification. However, challenges such as membrane fouling, protein adsorption and long-term blood compatibility remain concerns that can affect the overall efficacy and safety of the treatment. In recent years, advances in polymer engineering have led to the development of new membrane materials with improved selectivity, durability, and reduced inflammatory response. Polysulfone (PS), polyurethane (PU), polyethersulfone (PES) and polyacrylonitrile (PAN) are among the most widely used polymers in commercial dialyzers, each with specific performance characteristics tailored to patient needs. In the current review, we overviewed various types of polymers used as hemodialyzer material and their contribution to enhance patient life span.

Keywords: Hemodialysis, synthetic polymers, biocompatibility

1.0 INTRODUCTION

Hemodialysis remains a life-saving procedure for over 2.6 million individuals suffering from end-stage renal disease (ESRD), with projections indicating a 30% increase in dialysis patients by 2030 [1]. The efficiency of this treatment is largely dependent on the performance of the hemodialyzer membrane, which serves as an artificial kidney. Hemodialysis membranes are vital components of dialysis setups used for end-stage renal disease patients. The membrane extracts waste substances and unnecessary fluids from the bloodstream of renal patients. Although numerous synthetic polymers are employed in dialyzer fabrication, challenges like thrombogenicity, protein fouling, and immunogenicity persist. With emerging trends in nanotechnology and surface engineering, it becomes critical to evaluate and compare how these materials fare in real-world applications.

The success of dialysis therapy depends mainly on the preferred synthetic polymer materials used to construct dialyzer membranes [2]. There are several biocompatibility concerns when selecting a synthetic polymer-based dialyzer for renal patients. Platelet adhesion, aggregation, and coagulation occur when proteins bind to membrane

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surfaces, thus requiring dialysis patients to use anticoagulants, and complications can occur [3]. Synthetic polymers tend to be hydrophobic, which causes membrane fouling and reduces efficiency. Patients can develop severe allergic reactions when they use an incompatible dialyzer. The treatment demands regular examination and dialysis control throughout each dialysis procedure [4]. Figure 1 represents the graphical illustration of dialyzer used for HD patients' treatment.

Despite the availability of various synthetic polymers, challenges like thrombogenicity, protein fouling, and complement activation continue to reduce dialysis efficiency and patient comfort. Emerging technologies such as zwitterionic coatings, surface PEGylation, and nanocomposites offer promising solutions but lack consolidated evaluation [5-7]. This mini review aims to bridge material science with clinical outcomes by systematically evaluating synthetic polymers used in HD membranes focusing on their biocompatibility and performance.

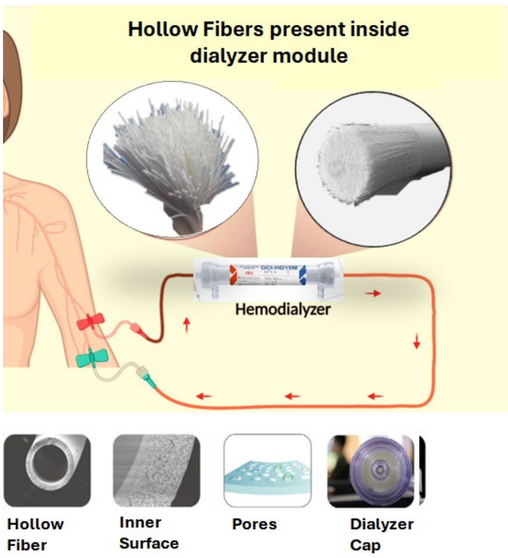

Figure 1 Graphical illustration of hemodialyzer, containing different parts with hollow fibers membrane

2.0 SYNTHETIC POLYMERS IN HEMODIALYSIS MEMBRANES

2.1 Polyurethane

Polyurethane (PU) is a versatile synthetic polymer, chemically formed by the reaction of the Isocyanate group with the hydroxyl group by the urethane linkage. The most used isocyanate sources are Methylene diphenyl diisocyanate or Toluene diisocyanate, whereas Polyols (ethylene oxide or propylene oxide) provide the hydroxyl component (Fig. 2). PU has good biocompatibility, mechanical strength, flexibility, and wear resistance [8].

2.1.1 Biocompatibility of Polyurethane

Polyurethane illustrates lesser hemolysis (destruction of red blood cells) and platelet activation when exposed to blood [9]. PU membranes are associated with relatively lower inflammatory responses than other synthetic materials, exhibit favorable interactions with endothelial cells, which line the blood vessels, help maintain vascular integrity, and maintain good compatibility with albumin and other essential plasma proteins [10]. This is largely used in patients due to its favorable interaction with endothelial cells, which helps maintain vascular integrity and reduces the likelihood of clot formation. Furthermore, PU has biocompatible advantages, needs to be considered in applications involving immune-sensitive patients [10, 11].

2.2 Polymethylmethacrylate

Polymethylmethacrylate (PMMA) is a synthetic polymer, consisting of *vinyl* group (CH_2=), methyl group, and an ester group ($COOCH_3$), and chemically prepared by the polymerization of monomer methyl methacrylate (Figure 2). The membranes demonstrate exceptional features such as both high absorption ability of urea and protein-bound toxins and good compatibility which results in better clinical results. PMMA membranes function as a vital equipment for managing the complex health needs of dialysis patients. [12].

2.2.1 Biocompatibility of Polymethylmethacrylate

In the immune system, the presence of a signaling protein, Interleukin-6 (IL-6), promotes immune response and inflammation against any foreign particle. During the dialysis process, the PMMA-based dialysis membrane adsorbs cytokines (e.g., IL-6 and CD40), which can prevent immunoglobulin production; thus, hypothetically, immune balance is maintained and does not activate against PMMA HD membranes [12, 13]. PMMA membranes reduced total cholesterol and triglycerides and cardiovascular events, CD40-Ligand, which improved the cardiovascular health with decreased endothelial cell dysfunction and vascular smooth muscle cell calcification [13, 14]. PMMA based dialyzers are suitable for patients with chronic inflammation or those suffering from inflammatory diseases, because PMMA can reduce the inflammatory burden during dialysis and particularly beneficial for individuals whose immune system responses are heightened during dialysis [15].

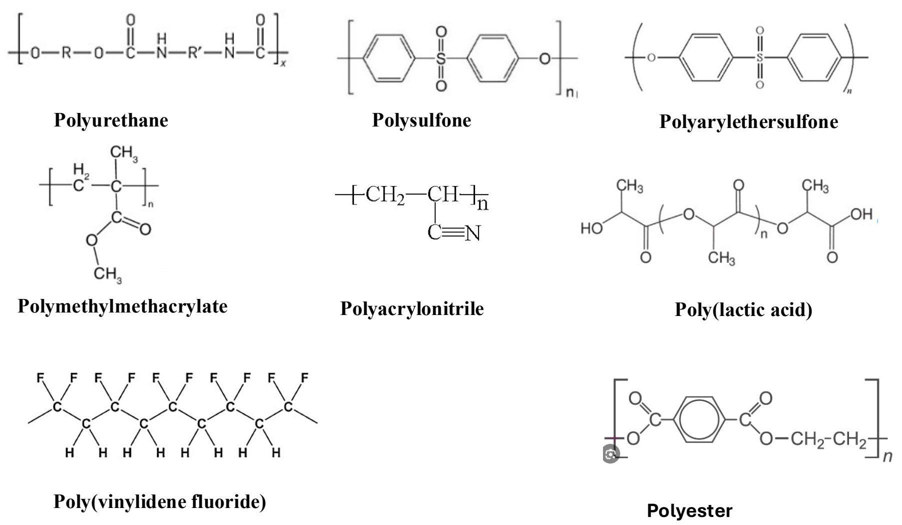

Figure 2 The chemical composition of different polymers used as hemodialysis membranes

2.3 Polysulfone and Polyethersulfone

Polysulfone (PS) and polyethersulfone (PES) are high-performance thermoplastic polymers that belong to synthetic polymers and are widely used in hemodialysis membranes. PS and PES-based HD membranes showed excellent chemical resistance, thermal stability, and mechanical strength. PES is synthesized from Bisphenol S and dichlorodiphenyl sulfone groups, whereas PS uses Bisphenol A and dichlorodiphenyl sulfone by nucleophilic aromatic substitution reaction. PS consists of aromatic rings which attach through $–SO_2–$ and –O–

group linkages, whereas PES has an aromatic ring and an ether between them (Figure 2) [16, 17].

2.3.1 Biocompatibility of Polysulfone and Polyethersulfone

PS and PES HD membranes remove a broad spectrum of uremic toxins, exhibit low tendency for complement system and activating blood cells. PS and PES are known for their low platelet activation compared to other materials, such as PU. PS and PES illustrate minimal cytokine release properties; thus, such membranes are good for patients who have allergies problems. Although PS and PES membranes demonstrate low platelet activation but exhibit a rough surface that enables more protein to bind subsequent activation of biochemical sequences which may cause tissue inflammation [18, 19]. These hemodialyzer are ideal for patients who have clotting disorders, allergic reactions to synthetic materials and an excellent choice for patients with a high uremic toxin burden [17, 20].

2.4 Polyacrylonitrile

PAN is a thermoplastic polymer prepared from the monomer acrylonitrile (CH_2=CH–CN). It is well known for its usage in carbon fiber pioneers, textile fibers, and membrane materials. Each repeat unit of acrylonitrile contains a methylene group (–CH_2–), methine group (–CH–) and nitrile group (–CN) (Figure 2). PAN membranes are known for their high permeability and ability to remove a wide range of uremic toxins, including protein-bound molecules [21]. PAN-based membranes are widely used in medical applications due to their biocompatibility, particularly in hemodialysis [22].

2.4.1 Biocompatibility of Polyacrylonitrile

PAN-based membranes are widely used in medical applications due to their biocompatibility, particularly in hemodialysis and are also known for their high permeability and ability to remove a wide range of uremic toxins, including protein-bound molecules, and caused less inflammatory responses and complement activation [4, 22]. PAN membrane has potential risk of biofouling and blending of hyperbranched polyesters with PAN polymer minimized biofouling, enhanced antifouling and biocompatibility by reduction in platelet adhesion [23]. Due to their minimal inflammatory response and low cytokine release, PAN membranes are ideal for patients who have pre-existing inflammation, prone to allergic reactions or immune responses triggered by other dialyzer materials. Patients who require effective removal of both small and middle-sized uremic toxins and need minimized biofouling, PAN membranes are an ideal choice for them [24].

2.5 Poly(lactic acid)

The condensation process of lactide monomer produced Poly(lactic acid) (PLA) which is a bio-based and biodegradable polymer. Generally, cellular interactions and biocompatibility of PLA are upgraded by its surface modification, which enhanced cell attachment and compatibility with biological tissues [25].

2.5.1 Biocompatibility of Poly(lactic acid)

The osteoblast-like cell compatibility is prompted by integrating chitosan and its derivatives onto PLA surfaces. UV-initiated crosslinking and PEGylation via micro-swelling enhanced the hemocompatibility and reduced protein adsorption [6, 25]. Osteoblast-like cells showing a 2.4-fold increase in cell viability and antioxidant properties when coating PLA membranes with heat-denatured human serum albumin [26]. PLA-based dialyzers could be a better choice for patients who are prone to allergic reactions or immune system sensitivity and cardiovascular issues with other dialyzers. Furthermore, PLA help minimize complement activation and platelet aggregation and due to its biodegradable nature does have leave any impact on environment [27].

2.6 Poly(vinylidene fluoride)

Vinylidene fluoride is the monomer used for fabrication of Polyvinylidene fluoride (PVDF) by free radical polymerization, solution polymerization, or suspension polymerization, followed by purification steps, resulting in white powder or granular form of PVDF. It is widely used for membranes fabrication, and it is considered as emerging material for HD applications. PVDF based HD membranes are generally prepared by dry-jet wet-spinning or non-solvent induced phase separation processes [28]. The PVDF is an elastic membrane that after proper modification showed 11.3 MPa tensile stress at break and 395% tensile elongation considerably higher than those of the F60S membrane [29, 30].

2.6.1 Biocompatibility of Poly(vinylidene fluoride)

PVDF in pristine form showed poor biocompatibility and surface modification are needed to improve its biocompatibility. These modifications enhance hydrophilicity and reduce protein adsorption, leading to lower hemolytic ratios and better anticoagulation performance [31]. Incorporating various additives like polyvinyl alcohol and chitosan improve anticoagulation performance by reducing the protein adsorption leading to lower hemolytic ratios. Modified membranes show increased prothrombin time and activated partial thromboplastin time. Further, the PVDF membranes exhibit superior clearance rates and UF coefficients for stripping middle molecules during dialysis sessions [31, 32]. PVDF dialyzers are ideal for patients with hemophilia or those at high risk of thrombosis (rheumatoid arthritis) and beneficial because they minimize blood cell destruction. Further, patients who need a high flux dialyzer that can remove beta-2 microglobulin with selectivity with efficient removal of a wide range of uremic toxins select PVDF based dialyzers [28, 29].

2.7 Polyester Polymer Alloy

Polyethylene terephthalate (PET) or polybutylene terephthalate (PBT) are the based polymers used to prepare the Polyester Polymer Alloy (PEPA). Condensation reaction of terephthalic acid (PTA) and ethylene glycol used to form PET that's by polymerization process produced PEPA. In case of PBT fabrication and further polymerization, terephthalic acid and butanediol are the initial reactants [33]. The chemical make-up of PEPA based HD membranes in combination with others polymer and chemicals directly shapes their capacity to be compatible with patient biology along with healthcare results [34].

2.7.1 Biocompatibility of Polyester Polymer Alloy

The blood compatibility of PEPA membranes stands out because they reduce persistent inflammation and complement systems activation in addition to showing small variations in platelet and leukocyte count [35]. PVP addition to PEPA based membranes improves their hydrophilic nature which decreases protein binding and enhances blood compatibility by stopping platelet and leukocyte activation processes [34]. PEPA-based hemodialyzers are ideal for patients who require frequent dialysis and experience inflammation and high rates of protein in blood because complications arising that led to nephrotic syndrome or high protein concentrations in patients' blood. These hemodialyzers are also designed to reduce vascular smooth muscle cell calcification and endothelial dysfunction [36, 37].

Table 1 summarizes the properties of different polymers used as hemodialysis material which provides a brief description of each polymer properties, whereas Table 2 provides a summary of the main advantages and disadvantages of each polymer in the context of their use in hemodialyzer manufacturing, along with references for further study.

Table 1 Concise comparison of key synthetic polymer uses as hemodialysis membranes, highlighting their biocompatibility characteristics, uremic toxin removal capabilities, and relevant citations

Polymer	Modifications	Properties	References
Polyurethane	N-3-(triethoxysilyl) propylamine grafted MCM41, Sulfonated dihydroxypropyl chitosan	Reduced protein adsorption, enhanced thrombin time, prothrombin time and plasma recalcification time, acceptable 2–4% red blood cell destruction. The clearance rates of 57.6% and 55.2% for creatinine and urea, respectively	[9, 16]
Polyacrylonitrile	Poly(ethylene glycol) (PEG) Immobilization.	High permeability, less complement activation, Removes protein-bound molecules, reduces inflammation, used in AN69 membranes, hydrophilic, high permeability, and specific adsorptive properties	[5, 38]
Polymethylmethacrylate (PMMA)	poly (vinyl pyrrolidone)-block-poly (acrylate-graft-poly (methyl methacrylate))-block-poly-(vinyl pyrrolidone)	Modulating the immune system and reducing inflammation, positively impact cardiovascular health, significant reductions in total cholesterol and triglycerides, better peripheral circulation and fewer dialysis-related side effects.	[39]
Polysulfone (PSu)	Blended with polyvinylpyrrolidone (PVP) and polyethylene glycol (PEG)	Minimal platelet activation, Efficient removal of broad spectrum of uremic toxins, low cytotoxicity, effective endotoxin retention, low cytotoxicity and high flux	[40, 41]
Polyethersulfone (PES)	Blended with PVP and PEG, modified with heparin-mimicking polymer brush functionalized carbon nanotubes (f-CNTs)	Enhanced biocompatibility, reduced protein adsorption, enhanced toxin removal, and antifouling properties, Efficient removal of small and middle molecules	[16, 19]

Polymer	Modifications	Properties	References
Poly(vinylidene fluoride) (PVDF)	Surface modification with polydopamine and cysteine	Excellent hydrophilicity, stable mechanical properties, good hemocompatibility, high water flux, and selectivity	[42]
Polyester Polymer Alloy (PEPA)	Inclusion of PVP	Improved blood compatibility, variable sieving coefficients for albumin based on PVP content	[43]
Poly(lactic acid) (PLA)	Grafted with zwitterionic polymer (PSBMA)	Upgraded hydrophilicity, anti-fouling, and hemocompatibility, good dialysis performance	[7]

Table 2 A summary of the main advantages and disadvantages of hemodialysis polymers

Polymers	Advantages	Disadvantages	Ref.
Polyurethane	Biocompatible, Durable and flexible, Good chemical resistance, High mechanical strength	Can be prone to oxidation, Limited hydrophilicity, More expensive compared to other materials	[11, 44]
Polymethylmethacrylate	High clarity and transparency, Chemically inert, Well-established as a dialyzer membrane material	Poor mechanical strength, Susceptible to fracture under stress, Limited durability in long-term use	[45]
Polysulfone and Polyethersulfone	High thermal stability, Biocompatibility, Excellent mechanical strength, Hydrophilic properties	May require additional modification for some uses	[46, 47]
Polyacrylonitrile	High chemical resistance, Good biocompatibility, High tensile strength, Can be used in ultrafiltration	Poor hydrophilicity, Prone to fouling, May require modifications to improve performance	[48]
Poly(lactic acid)	Biodegradable, Environmentally friendly, Good tensile strength, Non-toxic	Low chemical stability, High tendency to degrade in physiological environments, Limited long-term durability	[49]
Poly(vinylidene fluoride)	Excellent chemical resistance, High mechanical strength, Good thermal stability, Hydrophobicity	High cost, Not biodegradable, Poor hydrophilicity in its native form	[50]
Polyester Polymer Alloy	Enhanced mechanical properties, High biocompatibility, Improved durability and stability over time	Expensive production, Poor hydrophilicity, Not ideal for ultrafiltration use	[36]

3.0 CONCLUSIONS

Hemodialysis membranes with specific material compositions demonstrate direct effects on treatment results for patients. Highly biocompatible membranes that efficiently remove uremic toxins from patient blood have proven to decrease inflammatory responses and enhance immune function thus leading to better HD results. The biocompatibility of hemodialysis membranes directly corresponds to their capacity to control inflammatory reactions and prevent complement activation. Membranes with high biocompatibility minimize the release of inflammatory cytokines TNF-α and interleukins and block complement components C3a and C5a activation. Patients with higher inflammation problems, PMMA based membrane are best for HD treatments as they absorbed most of the inflammatory cytokines. PS membranes demonstrate lower cardiovascular complication rates and better survival results whereas, PU-based dialyzer achieved reduced clotting and inflammatory response. PAES membranes along with PS types eliminate a wide range of uremic toxins through their ability to interact with proteins while maintaining hydrophilic characteristics which leads to reduced complement activation and inflammation. PLA supports cell compatibility of osteoblasts and strengthens antioxidant effects while PVDF reduces blood cell destruction and improves anticoagulation properties. Currently, death caused by kidney disease is ranked 10th, and the number of patients is increasing day by day [1]. In such a case, continued innovation in membrane development is essential to enhance biocompatibility further and improve the quality of life for hemodialysis patients.

The future of hemodialysis lies in the development of multifunctional membranes that not only improve toxin removal but also enhance patient outcomes by minimizing inflammation. With advancements in nanotechnology, and smart materials, the next generation of hemodialysis membranes could feature adaptive filtration properties, and better compatibility with biological systems. Furthermore, the integration of wearable dialysis devices and personalized medicine is set to revolutionize treatment, offering patients greater autonomy and improved quality of life. Continued innovation in membrane materials and modification techniques will be crucial to addressing the challenges of fouling, biocompatibility, and efficiency in hemodialysis therapies.

CONFLICTS OF INTEREST

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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