Bulgarian Chemical Communications, Volume 54, Issue 3 (pp. 242-246) 2022 *DOI: 10.34049/bcc.54.3.F004*

Preparation of modified polyethersulfone membranes for hemodialysis

Ö. Ş. Kahraman[1], M. T. Phoo[1], İ. Küçük[1], A. Hasanoğlu[1,2]*

[1]*Yıldız Technical University, Chemical Engineering Department, Esenler, Istanbul, Turkiye*
[2]*Bursa Technical University, Food Engineering Department, Yıldırım, Bursa, Turkiye*

Accepted: July 14, 2022

Polyether sulfone (PES) is one of the common materials used as a membrane in hemodialysis. However, its use in pristine form is limited since its contact with blood can cause various interactions between the membrane and blood cells. Therefore, PES should be modified to reduce these reactions before its use in hemodialysis applications. In this study, tissue and blood-compatible PES based dialysis membranes were prepared by phase inversion method. To improve the biocompatibility and hemo-compatibility of the membrane, the PES polymer was blended with two polymers; polyvinylpyrrolidone (PVP) and polyethyleneglycol (PEG). PES polymer (15% (wt)) in N-methylpyrrolidone was used to prepare the pristine PES membranes while a polymer blend of 5% (wt) PVP or PEG additives and 10% (wt) of PES in the same solvent was used to prepare the modified PES membranes. Biocompatibility and hemo-compatibility of the prepared membranes were defined by water sorption, BSA protein and creatinine adsorption values. The sorption and BSA adsorption experiments indicated that the addition of PVP and PEG in the membrane matrix increased the hydrophilicity of the membrane and decreased the protein adsorption rate. In the light of these results, it was seen that the biocompatibility of the membranes can be increased using PVP and PEG additives in the PES membrane by reducing the amount of protein adsorption, and the modified membranes can prevent complications from contact with blood.

Keywords: Hemodialysis, biocompatible membranes, polyether sulfone, polyvinlypyrrolidone, polyethylene glycol

INTRODUCTION

Hemodialysis is a clinical process used for kidney patients, which aims to remove toxic biological substances from blood such as urea and creatinine. Acute kidney diseases can be mortal for the patients and the number of kidney patients is growing by 6-7% annually worldwide [1]. The core element of the hemodialysis process is the membrane which provides the separation of the toxic materials. The most important requirement for a hemodialysis membrane is the biocompatibility and hemo-compatibility of the membrane material, as well as the high rejection to toxic substances. The membrane should eliminate the toxic metabolites and excess water from blood by means of its preferential selectivity and should prevent clotting and platelet adhesion owing to its biocompatibility and hemo-compatibility. When polymeric membranes are in contact with blood, blood proteins tend to adsorb on the membrane surface and this phenomenon may have several adverse effects such as coagulation of blood cells and thrombosis. Thus in hemodialysis, the most crucial issue is the development of highly biocompatible membranes with high separation performance. In order to increase the biocompatibility of the membrane material several techniques such as surface modification, blending, grafting, nanoparticle adding have been applied [2-4].

Several polymeric materials have been applied for hemodialysis membranes including polysulfone [5], PAN and PAN/PVP [1, 6], chitosan [7], cellulose acetate [8] and polyethersulfone (PES) [1, 9-11]. Among the polymers used in medical applications, PES is one of the most applicable membranes thanks to its high performance properties such as high thermal and mechanic stability and easy handling for film preparation. Over the last four decades, PES membranes have been used commonly in microfiltration and ultrafiltration applications. Furthermore, it has been used in several medical applications such as artificial organs, hemodialysis, hemofiltration, plasma collection [12]. However, PES should be modified for its use in medical applications since it has poor hydrophilic properties which can cause protein adsorption and other problems such as aggregation and coagulation. Several methods have been reported in the literature to enhance the biocompatibility of PES membranes [12-14]. Fang *et al.* (2009) blended PES with acrylonitrile and acrylic acid followed by BSA grafting on the surface. They reported that the water contact angle and protein adsorption significantly decreased after the modification [12]. Zhu *et al.* (2007) blended PES with styrene-maleic anhydride to increase the hydrophilicity [13]. Irfan *et al.* (2014) used nanoparticles for surface modification of PES. First, they functionalized multi-wall carbon nanotubes, mixed the nanoparticles with polyvinyl-

* To whom all correspondence should be sent:
E-mail: ayca.hasanoglu@btu.edu.tr

pyrrolidone (PVP), and blended them with PES. They reported that the resulting membranes were more hydrophilic than the pristine PES [14]. In general, the modification techniques include bulk modification, surface modification and blending [12]. Blending the PES polymer with other polymers to improve its properties is a practical method in terms of short preparation procedures and easy film casting. Blending method allows to optimize the properties without complicated synthesis processes. Polyethylene glycol (PEG) and PVP are known as good hydrophilic agents in the polymeric blends and are usually used as additives to change the properties of polymers [15, 16]. In this study, PES polymer was modified by the blending method using PVP and PEG with different molecular weights to increase the biocompatibility. Biocompatibility of the membranes was evaluated by water sorption and BSA adsorption. Also creatinine adsorption tests were done for evaluation of the membranes for creatinine removal. This way it was aimed to develop high performance membranes with good biocompatibility and selectivity for hemodialysis.

MATERIALS AND METHOD

Materials

Polyether sulfone (PES, Ultrason E3010) was purchased from BASF, Germany. N-methyl-2-pyrrolidone (NMP) used as solvent was supplied by VWR International. Isopropanol used as solvent was purchased from Isolab GmbH. Polyvinylpyrrolidone (PVP, MW: 58000) was purchased from Acros Organics, New Jersey, US. BSA, creatinine and Folin Ciocalteu's phenol reagent used in protein adsorption determination were purchased from Sigma Aldrich. Polyethylene glycol (PEG, MW:1000 and 10000) used as additive, copper sulfate and sodium carbonate used as analytical reagents for Lowry method were purchased from Merck, Germany.

Membrane preparation

Before membrane preparation, the PES polymer was placed in an oven for 1 hour at 70°C for moisture removal. The dried PES was weighed in the desired amount and then a solution of PES in NMP was prepared by 15% w/w. The solution was stirred for 24 hours at 500 rpm at room temperature. Then the solution was cast onto glass plates with a blade at room temperature and the thickness of the wet films were about 254 μm. Afterwards, the membrane layers were immersed in a coagulation bath containing 77.5% of pure water, 20% of IPA and 2.5% of NMP. The membranes were kept in the bath for 24 hours. Membranes removed from the bath process were taken between Teflon plates and kept there for 24 hours to avoid shrinking while drying. This was aimed to prevent contraction and superficial deformation by ensuring that the moisture removal is slow. Then the membranes were dried in an oven under vacuum at 50°C for 1 hour and at 70 °C for another 1 hour and the process was terminated. For PEG- and PVP-blended membranes the polymer solution was prepared by 10% of PES and 5% of PVP or PEG. All the remaining steps were the same as pristine PES membrane preparation.

Sorption experiments

Membranes with known weights were immersed into closed vessels containing water and kept at room temperature. Every 24 hours, the swollen membranes were wiped off and weighed. When no change was observed in weight, the sorption percentage was calculated using the equation below where m_{wet} and m_{dry} represent the weight of the wet and dry membrane, respectively:

$$Sorption\% = \frac{m_{wet} - m_{dry}}{m_{dry}} \times 100 \quad (1)$$

Adsorption experiments

The membrane samples were cut into small pieces (2 cm × 2 cm) and inserted into closed vessels containing 1 mg/mL of BSA. The vessels were shaken for 8 hours using a shaker at the desired temperature. For the first 4 hours, a sample was taken from the vessels every hour and the concentration of BSA in the solution was measured using UV spectrophotometry (Analytic Jena Specord 200). Later, the samples were taken at the 6^{th} and 8^{th} hour. Then the adsorption amount of the membranes was calculated using the equation below where c represents BSA concentration. BSA concentrations were determined by the Lowry method:

$$Adsorption\% = \frac{c_0 - c_t}{c_0} \times 100 \quad (2)$$

The creatinine adsorption tests were done likewise. In this case the concentration of creatinine was measured directly by UV spectrophotometry at 200 nm without using an analytical reagent.

Membrane characterization

SEM pictures of the membranes were taken using a Zeiss EVO LS 10 model and brand scanning electron microscopy equipment.

RESULTS AND DISCUSSION

Membrane morphologies

The cross-section SEM pictures of the membranes are given in Figure 1.

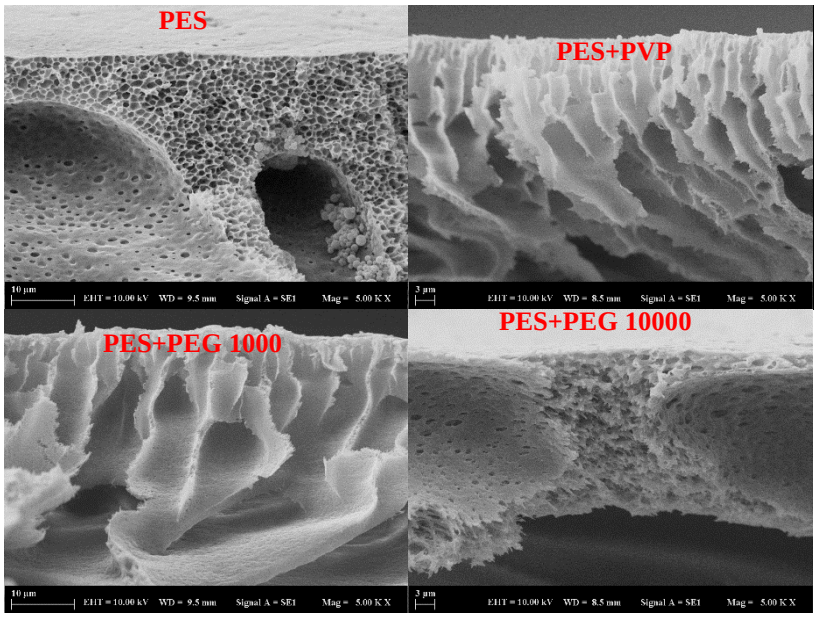

Figure 1. The cross section SEM pictures of the membranes

As can be seen in Figure 1, the structure of the membranes is modified by including the additives in the PES matrix. Furthermore, it can be seen that the porosity is increased for the modified membranes, especially for PVP and PEG 1000 additives. The pristine PES has sponge-like pores while the structures of the pores are converted to finger-like with the addition of PVP and PEG 1000. When the structures of all the membranes are compared, it can be seen that PVP has the highest porosity. On the other hand, the addition of PEG 10000 did not affect the porosity significantly.

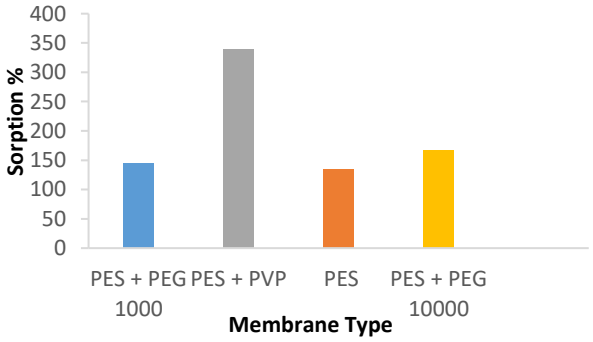

Figure 2. Sorption percentages of the membranes in water

Sorption results

In medical and biotechnological applications membrane hydrophilicity is favored since it prevents the biofouling. The hydrophilicity of the membrane leads to formation of a thin aqueous layer on the surface impeding the deposition of the proteins on the surface [1, 7]. Thus, the water sorption values of the membranes were determined to obtain the hydrophilicity of the membrane materials.

Sorption results of the membranes in water are shown in Figure 2. As can be seen, the water sorption values of the blended membranes increased compared to the neat PES membrane. The addition of PEG and PVP additives increased the hydrophilicity of the membrane. When the membranes with the two additives of PEG and PVP are compared, it can be seen that PVP is more effective to increase the hydrophilicity. This can be a result of increased porosity of the PVP-blended membranes.

Adsorption results

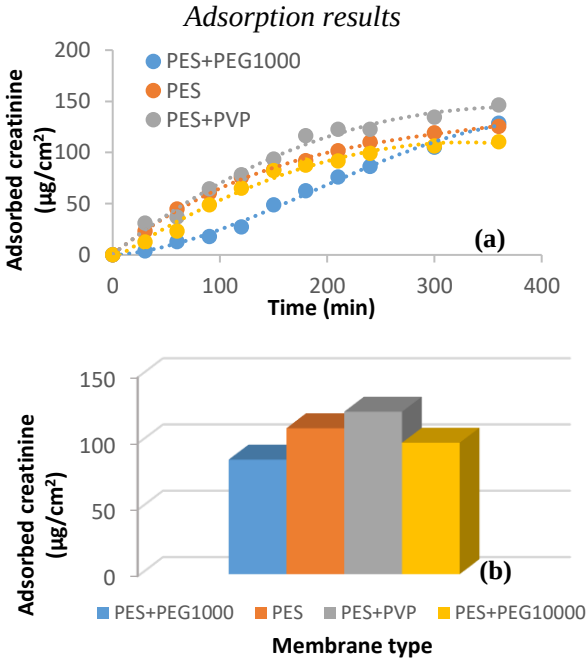

Figure 3. Adsorbed amounts of creatinine onto the membranes a) as a function of time b) in 4 hours

BSA and creatinine adsorption experiments were carried out to evaluate the biocompatibility of the membranes and the affinity of the membranes with creatinine. BSA adsorption onto the membrane is undesired since the adsorption of blood proteins onto the membrane material can cause complex problems. On the other hand, creatinine adsorption is desired since it should be removed from the blood using the membrane. Figure 3 shows the adsorbed creatinine amount onto the membranes.

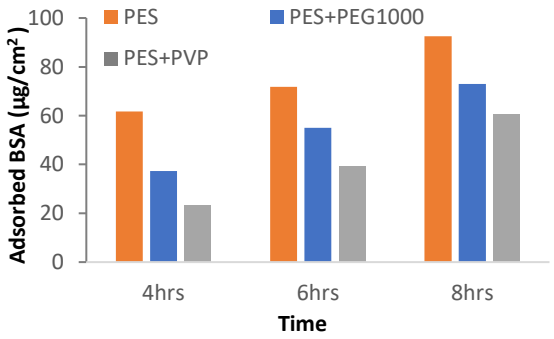

Figure 4. Adsorbed BSA amounts onto the membranes

As can be seen from Figure 3, PVP blended membranes adsorbed more creatinine than the neat PES membrane and the PEG-blended membranes. With the addition of PEG into the membrane, a slight decrease in creatinine adsorption was observed. PVP showed better surface affinity towards creatinine. Thus, PVP-blended membranes are expected to permeate the creatinine molecules better than the neat membranes since the surface interactions with creatinine increased by the addition of PVP in the PES matrix. PVP-blended membranes have a potential to remove the creatinine not only by diffusion, but also by surface adsorption. Tijink *et al*. (2013) studied PES/PVP-based mixed matrix membranes containing activated carbon and reported that after 4 hours of simulated hemodialysis operation, both diffusion and adsorption equally contributed to the total creatinine removal [9]. The membranes were evaluated also in terms of their protein adsorption. Since PEG showed lower adsorption towards creatinine, only PEG1000-blended membrane was evaluated among the PEG blended membranes since it was easier to handle because of its lower viscosity. Figure 4 shows BSA adsorption of the membranes.

As can be seen in Figure 4, the BSA adsorption decreased for the blended membranes compared to the neat PES membrane. As the hydrophilicity of the membranes increased, the protein adsorption decreased. PVP-blended membranes showed the least amount of BSA adsorption because of its highest hydrophilicity. The experiments indicate that the addition of hydrophilic polymer agents into the PES membranes improved the membrane against biofouling.

CONCLUSIONS

In this work the PES membranes were modified with PVP and PEG additives to improve the membrane properties for hemodialysis. The experiments showed that both additives increased the hydrophilicity of the membrane and consequently decreased the protein adsorption onto the membrane. The membranes modified with PVP had the highest hydrophilicity, indicating that it can have a better biocompatibility. Furthermore, the membranes were evaluated in terms of creatinine adsorption. PVP blended membranes showed higher surface affinity towards creatinine. The blended membranes have a potential to be used in hemodialysis applications. Future works will be done to determine the membrane interactions with urea and the membrane permeabilities for each component.

Acknowledgements: *This work has been supported by Yıldız Technical University Scientific Research Projects Coordination Unit under the project number YÜLAP 2019-3711.*

Nomenclature

BSA	bovine serum albumin;
c_0, c_t	concentration initially and at the given time, respectively;
m	weight of the membrane samples;
PAN	polyacrylonitrile;
PEG	polyethyleneglycol;
PES	polyethersulfone;
PVA	polyvinyl alcohol;
PVP	polyvinylpyrrolidone.

REFERENCES

1. X. Yu, L. Shen, Y. Zhu, X. Li, Y. Yang, X. Wang, M. Zhu, B. S. Hsiao, *Journal of Membrane Science*, **523**, 173 (2017).
2. M. Irfan, A. Idris, *Material Science and Engineering C*, **56**, 574 (2015).
3. P. Thevenot, W. Hu, L. Tang, *Curr. Top Med. Chem.*, **8**, 270 (2008).
4. M. Tang, J. Xue, K. Yan, T. Xiang, S. Sun, C. Zhao, *Journal of Colloid and Interface Science*, **386**, 428 (2012).
5. M. Rafat, M. D. De, K. C. Khulbe, T. Nyugen, T. Matsuura, *Journal of Applied Polymer Science*, **101**, 4386 (2005).
6. W. C Lin, T. Y. Liu, M. C. Yang, *Biomaterials*, **25** 1947 (2003).
7. J. Liu, X. Chen, Z. Shao, P. Zhou, *Journal of Applied Polymer Science*, **90**, 1108 (2003).

8. O. Azhar, Z. Jahan, F. Sher, B. K. Niazi, S. J. Kakar, M. Shahid, *Materials Science and Engineering: C*, **126**, 112127 (2021).
9. M. S. L. Tijink, M. Wester, G. Glorieux, K. G. F. Gerritsen, J. Sun, P. C. Swart, Z. Borneman, M. Weeling, R. Vanholder, J. A. Joles, D. Stamatialis, *Biomaterials*, **34**, 7819 (2013).
10. A. Modi, S. K. Verma, J. Bellare, *Journal of Colloid and Interface Science*, **514**, 750 (2018).
11. S. Nie, M. Tang, C. Cheng, Z. Yin, L. Wang, S. Sun, C. Zhao, *Biomaterials Science*, **2**, 98 (2014).
12. B. Fang, Q. Baohong, W. Ling, Zhao, Y. Ma, P. Bai, Q. Wei, H. Li, C. Zhao, *Journal of Membrane Science*, **329,** 46 (2009).
13. L. P. Zhu, X. X. Zhang, L. Xu, C H. Du, B. K. Zhu, Y. Y. Xu, *Colloid Surf. B: Biointerf.*, **57**, 189 (2007).
14. M. Irfan, A. Idris, N. M. Yusof, N. F. M. Khairuddin, *Journal of Membrane Science*, **467**, 73 (2014).
15. J. Huang, J. Xue, K. Xiang, X. Zhang, C. Cheng, S. Sun, C. Zhao, *Colloids Surf. B: Biointerfaces*, **88**, 315 (2011).
16. Q. Yang, T. S. Chung, M. Weber, *Journal of Membrane Science*, **326**, 322 (2009).