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In vitro hemocompatibility of PVA-alginate ester as a candidate for hemodialysis membrane

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ABSTRACT

Alginate based biopolymer with improved physical and chemical properties after esterification using polyvinyl alcohol (PVA) has been studied for possible application as a hemodialysis membrane. The alginic acid to vinyl alcohol molar ratio was predetermined at 0, 0.1, 0.5 and 1. Mechanical strength, hydrophilicity and Ca^{2+} adsorption of the membrane before and after modification were evaluated. The obtained PVA-alginate (PVA-Alg) ester membrane was also confirmed using FTIR and SEM. It shows that the PVA-Alg membrane tensile strength is higher than that of native alginate. The water contact angle of the membrane was found to be around 33–50°. The Ca^{2+} adsorption capacity tends to decrease with the increase in molar ratio. Furthermore, the modified PVA-Alg ester membrane achieves better protein adsorption and platelet adhesion than the unmodified one. It also exhibits a dialysis performance of 47.1–50.0% for clearance of urea and 42.2–44.6% for clearance of creatinine, respectively. It is expected that this PVA-Alg ester may challenge cellulose acetate for potential application as hemodialysis membranes.

1. Introduction

Hemodialysis is an essential medical treatment to remove toxic compounds in the blood serum of a patient with severe renal disease. The main component of a hemodialysis instrument is a semipermeable membrane that allows selective transport of low molecular weight solutes present in the blood serum i.e. urea and creatinine [1,2]. Cellulose acetate is one of the first generations of natural biocompatible polymers used to prepare hemodialysis membranes [3,4]. Another natural polymer being evaluated as a membrane material and expected to compete with cellulose acetate is alginate. This natural polymer has attracted many researchers in this field due to its high biocompatibility and low toxicity. It also has other reasonable characteristics such as biodegradability, having a rigid molecular chain, flexibility and ability to form film. This polymer can form an insoluble gel in water, which is important for membrane preparation. Alginate also possesses both hydroxyl and carboxyl groups in its structure that can possibly facilitate further structure modification [5–12]. Based on those qualities, alginate can be considered as the future of hemodialysis membrane pending significant improvement of both physical and chemical properties.

A hemodialysis membrane usually has good mechanical strength, permeability for water and solutes as well as hemocompatibility [13]. Since alginate has both hydroxyl and carboxylate groups in the structure, it may be able to form channels for toxic uremic of urea and creatinine through a hydrogen bond. Unfortunately, the alginate membrane is normally found in a wet state because the presence of hydroxyl and carboxyl groups in the structure can attract excessive water molecules that eventually lower its mechanical strength. Therefore, the mechanical strength of alginate membrane must be improved. One way to improve its mechanical strength is by chemical modification with a much stronger polymer backbone without loss of biocompatibility.

In this study, PVA is used as polymer modifier. PVA has excellent mechanical strength and biocompatibility. This polymer is also non-toxic [9–11]. The PVA hydroxyl groups are expected to react with carboxyl groups of alginate to form an ester derivative. The mechanical strength of the produced membrane is thought to improve due to the esterification reaction. The carboxyl groups in the structure of native alginate can interact with the amine groups of protein causing much more protein to be adsorbed. However, the membrane protein adsorption and platelet adhesion are predicted to be low after successful esterification [12]. Therefore, the esterification of alginate by PVA can result in an improvement

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of hemocompatibility as implied by a decrease in surface protein adsorption and platelet adhesion.

2. Experimental

2.1. Preparation and characterization of PVA-alginate ester membranes

Sodium alginate (2% aqueous solution with viscosity of 250 cps at room temperature) was purchased from Sigma and PVA (CAS-No.9002-89-5 with degree of hydrolyzation > 98%) was acquired from Merck. These chemicals were used without further treatment. Alginate was reacted with PVA to form a PVA-Alg ester derivative. The PVA-Alg membrane was prepared after the esterification reaction was completed. An aliquot of 10.0 mL of aqueous sodium alginate (2% w/v) and PVA with predetermined weight (0, 7.7, 38.6 and 77.2 mg) was poured into a 6-cm Petri dish to form a mixture and give vinyl alcohol to alginic acid a molar ratio of 0, 0.1, 0.5, and 1.0. The mixture was stirred for 30 min and was allowed to cool in a refrigerator at 4 °C for 24 h to eliminate air bubbles. The alginate mixture was dried at 80 °C for 8 h before the addition of 10.0 mL HCl 1.0 M. The mixture was incubated further at 40 °C for 1 h. The resulting film was washed with distilled water and dried at 40 °C for 24 h. The FTIR spectra were obtained on a Shimadzu FTIR spectrometer in with a wavenumber range of 400–4000 cm^{-1}.

2.2. Mechanical strength measurement

The film was cut to 2-cm × 11-cm size. The mechanical properties of the membrane were measured using a universal testing machine. The stress applied is measured in MPa while the rate is in mm/min.

2.3. Hydrophilicity test

Film hydrophilicity was estimated based on the data of water contact angle measurement [14]. A dried film with flat surface was placed on a glass slide. A drop of water (10.0 μL) was laid on the top of the film from 1-cm above. The water contact angle was recorded every minute for the first 10 min and every 5 min after that. The water contact angle was determined based on the image produced.

2.4. Measurement of Ca^{2+} adsorption

A portion of 100-mg of the film was soaked in 10.0 mL solution of 0.025 M $CaCl_2$. The membrane Ca^{2+} adsorption was calculated based on the Ca^{2+} concentration in the solution after 15, 30, 60, 120, and 180 min of soaking.

2.5. Hemocompatibility test

Hemocompatibility of the membrane was examined by conducting a test for hemolysis ratio, protein adsorption, and platelet adhesion. Human whole blood (WB) with an anticoagulant of sodium citrate was used for hemolysis testing. Samples of platelet rich plasma (PRP) were obtained by separation of WB with spinning rate of 1000 rpm for 10 min using a centrifuge. Samples of platelet poor plasma (PPP) were obtained by separation of WB with spinning rate of 3000 rpm for 15 min using a centrifuge.

For the hemolysis ratio test, a 1 × 1 cm^2 cut membrane was prepared and washed three times with doubly distilled water and 0.90% NaCl solution. The membrane was soaked in 0.9% NaCl solution for 30 min at 37 °C, then soaked in the WB mixture (5 mL solution of 0.9% NaCl and 20 μL WB) at 37 °C for 1 h. The soaking time varied from 30, 45, and 60 min. The WB mixtures were separated using a centrifuge with spinning rate of 1500 rpm for 10 min. The UV–Vis absorbance of the solution was measured at 546 nm. The hemolysis ratio (HR) was later calculated using Eq. (1) [15].

$$HR = \frac{(A_S - A_N)}{(A_P - A_N)} \quad (1)$$

where A_S is the absorbance of samples, A_N is the absorbance of negative control, and A_P is the absorbance of positive control.

For protein adsorption test, a 2 × 2 cm^2 cut membrane was immersed in 1 mL PPP and incubated at 37 °C for 1 h. It was subsequently rinsed with PBS solution and double distilled water. The membrane was washed with 2% sodium dodecyl sulfate (SDS) to remove the adsorbed protein. The protein concentration in the washing solution was determined by the biuret spectrophotometric method.

For platelet adhesion test, a 2 × 2 cm^2 cut membrane was used. After washing with PBS buffer solution (pH 7.4), the membrane was immersed in 1 mL PRP at 37 °C for 1 h. The platelet concentration before and after immersion was determined using a hemocytometer (Neubauer, Germany). The membrane was rinsed three times using PBS to remove lightly adsorbed platelets. An aqueous solution of 2.5% glutaraldehyde was added (1.0 mL) into the solution and it was allowed to settle for one night to fix the adsorbed platelets. The samples were dehydrated stepwise using ethanol/water solution of 25%, 50%, 75%, 100% (v/v) for 10 min each. The platelet adhesion on the membrane surface was observed by SEM after freeze drying.

2.6. Dialysis simulation

The membrane was fixed into the dialysis apparatus between two compartments with effective diffusion area 3.14 cm^2. The source compartment was filled with 30 mL of PBS solution containing urea and creatinine. The urea and creatinine concentration in the solution is 200 mg/dL and 5 mg/dL respectively. The dialysate compartment was filled with 30 mL of blank PBS (pH 7.4). The concentration of urea in both compartments after 0, 1, 2, 3, and 4 h of dialysis test was determined by phenol blue enzymatic method and creatinine was determined by picric alkali method. The urea and creatinine clearance during dialysis test was calculated using Eq. (2) [16].

$$SC(\%) = \left[\frac{C_0 - C_t}{C_0}\right] \times 100 \quad (2)$$

where SC is the solute clearance; C_0 and C_t are the solute concentrations in the testing reservoir solution at the prescribed time, respectively. The flux of urea and creatinine was determined using Eq. (3) [17].

$$J = \frac{W}{At} \quad (3)$$

where J is the flux of the solute (mg cm^{-2} h^{-1}); W is the mass of the diffuse solute (mg); A is the diffusion area (cm^2), and t is the diffusion time (hour).

3. Results and discussions

3.1. Characterization of membrane surface

The FTIR spectra of the PVA-Alg membranes are shown in Fig. 1. The peaks at 1735 and 1250 cm^{-1} are observed. These are attributed to the C=O stretching and C–O stretching, respectively. This is consistent with the FTIR spectra of an ester. The native alginate itself has a peak at 1620 cm^{-1} due to the C=O stretching of COOH group. The success of the esterification reaction is clear for the membrane with vinyl alcohol to alginic acid molar ratio of 0.5 or higher. The peak seen at 3433 cm^{-1} is due to O–H stretching, with sharper peaks at molar ratio of 1. PVA itself has hydroxyl groups that show

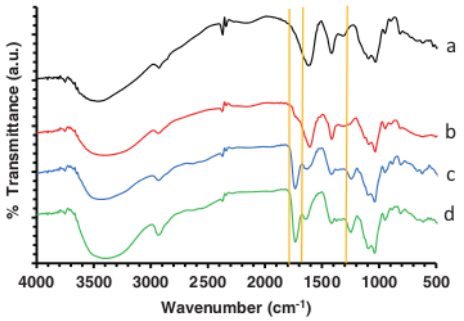

Fig. 1. FTIR spectra of prepared PVA-Alg membranes; native alginate (a), PVA-Alg with molar ratio of 0.1 (b), 0.5 (c), and 1.0 (d).

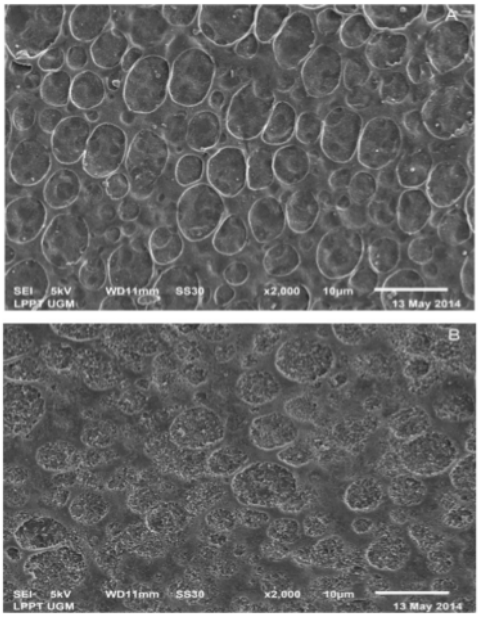

Fig. 2. SEM images of PVA-Alg membranes in state of dry (A), and in state of wet after diffusion use (B).

its sharp peak at about 3400 cm^{-1}. The FTIR data are needed to ascertain the formation of cross-link polymer product of PVA-Alg ester. The remaining hydroxyl groups and carboxyl groups from respected polymers could help transport urea and creatinine across the membrane. The FTIR spectra suggest that hydroxyl groups in PVA and carboxyl groups in alginate do not entirely form esters.

To understand the morphology of the membrane surface, SEM images were recorded. The SEM images of PVA-Alg films are shown in Fig. 2. It is observed that the surface of the membrane is flat and has no visible cracks. However, the inner structure of the membrane is less uniform. The estimated pore size is around 1 µm. After being used in the transport experiment, it does not show fouling, although in general it shows swelling and erosion.

3.2. Mechanical strength of membranes

Mechanical strength of the membrane is a critical factor to consider for dialysis applications. For a membrane, tensile strength is expressed in MPa whereas elongation is expressed in percent [18]. The results of tensile strength and elongation measurements are

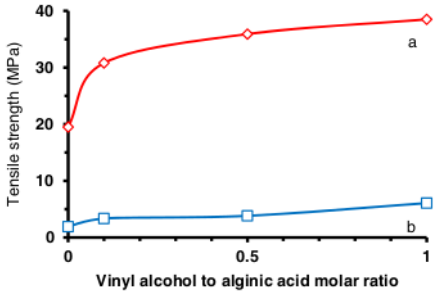

Fig. 3. Tensile strength of PVA-Alg membranes in state of dry (a), and wet (b).

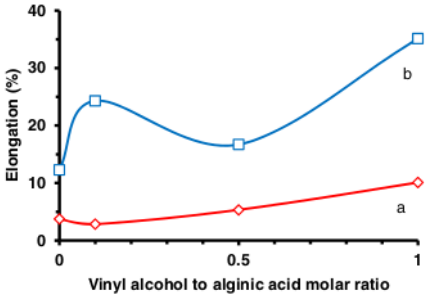

Fig. 4. Elongation of PVA-Alg membranes in state of dry (a), and wet (b).

shown in Figs. 3 and 4, respectively. The membrane of unmodified alginate has a tensile strength of only 19.5 MPa. On the other hand, the PVA-Alg membrane at a molar ratio of 0.1, 0.5, and 1.0 each gives tensile strength of 30.8, 35.9 and 38.5 MPa, respectively. The presence of PVA in the alginate film appears to improve its tensile strength significantly. The maximum tensile strength was obtained from PVA-Alg film at molar ratio of 1.0.

The addition of PVA to alginate seems to improve the membrane elongation, indicating that PVA has a chemical interaction with alginate. The explanation for this behavior is that alginate reacts with PVA to form an ester derivative, as suggested by FTIR data. In a dry state, the interaction between alginate and PVA causes an increase in both membranes' tensile strength and elongation. The wet PVA-Alg membrane has a low tensile strength but high elongation, which could be due to the membrane's plasticizing effect. Wang et al. observed a decrease in tensile strength of the membrane prepared using chitosan-cellulose blends from 55 MPa for wet film to 35 MPa for dry film. Meanwhile, the elongation increases from 9% for wet film to 15% for dry film [15].

3.3. Hydrophilicity of membrane

Hydrophilicity of the membrane surface can be evaluated from the results of water contact angle measurement. The low water contact angle indicates high hydrophilicity of the membrane surface and vice versa [19]. The data of membrane water contact angle measurements are shown in Fig. 5. After 30 min of drop age, the native alginate gives water contact angle of 14°, which is low. The PVA-Alg membranes with vinyl alcohol to alginic acid molar ratio of 0.1, 0.5, and 1 yields water contact angle of 45, 50, and 30, respectively. The addition of PVA to alginate causes the membrane water contact angle to decrease. It means that PVA is able to reduce hydrophilicity of alginate films.

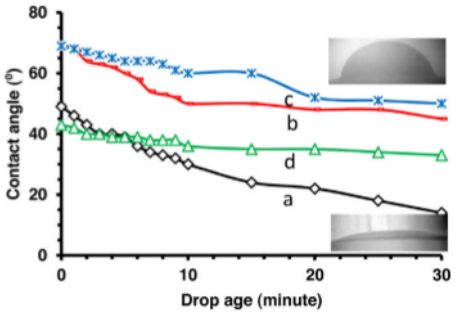

Fig. 5. Hydrophilicity of PVA-Alg membranes; native alginate (a), PVA-Alg in the mole ratio 0.1 (b), 0.5 (c), and 1 (d).

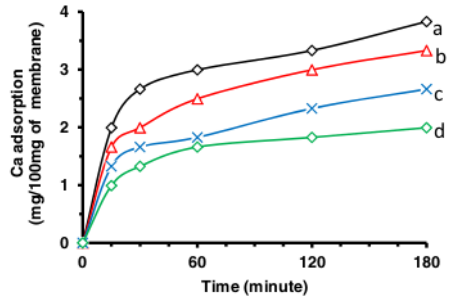

Fig. 6. Ca^{2+} adsorption by PVA-Alg membranes; native alginate (a), PVA-Alg with mole ratio of 0.1 (b), 0.5 (c), and 1.0 (d).

3.4. Ca^{2+} adsorption

The results of Ca^{2+} adsorption by the membranes are shown in Fig. 6. The membrane Ca^{2+} adsorption is expressed in mg Ca^{2+}/100-mg of membrane. It shows that the Ca^{2+} adsorption decreases from 3.83-mg/100-mg for the PVA-Alg membrane at molar ratio of 0.1–2.66-mg/100-mg at molar ratio of 0.5, and to 1.9-mg/100-mg at molar ratio of 1.0. These results reveal that the increase in the molar ratio causes a decrease in the Ca^{2+} adsorption. The membranes with high molar ratios demonstrate smaller Ca^{2+} adsorption than that of membranes with low molar ratios. The Ca^{2+} ions form strong electrostatic bonds with carboxyl groups in the original alginate structure. As expected, the native alginate membrane has more carboxyl groups than that of the PVA-Alg membrane. Successful esterification reaction is able to reduce the membrane Ca^{2+} adsorption. Li et al. reported that a polyethersulfone modified membrane has high Ca^{2+} adsorption [20].

3.5. Hemocompatibility of membrane

Hemolysis ratio (HR) is an important feature of hemocompatibility. It is used to detect the erythrocyte damage caused by membrane materials. Fig. 7 shows the HR value of different membranes. It demonstrates that after 30 min of contact the PVA-Alg membranes at molar ratio of 0.1, 0.5 and 1 have considerably low HR values of 0.043, 0.049 and 0.058, respectively.

Protein adsorption on the membranes is one important factor to evaluate the hemocompatibility of the membranes [21,22]. Hydrophobic interaction between the membrane surface and protein can have great effect on the surface protein adsorption [20]. In the present work, the membrane adsorption of plasma protein was studied in vitro. The data are presented in Fig. 8. The PVA-Alg ester membranes exhibit low protein adsorption. The lowest

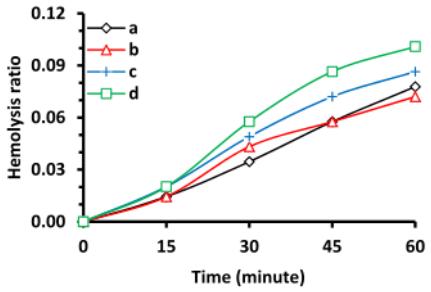

Fig. 7. The hemolysis ratio of the membranes; native alginate (a), PVA-Alg with molar ratio of 0.1 (b), 0.5 (c), and 1.0 (d).

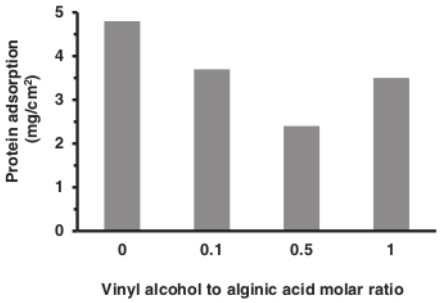

Fig. 8. Plasma protein adsorption on PVA-Alg membranes with various molar ratios.

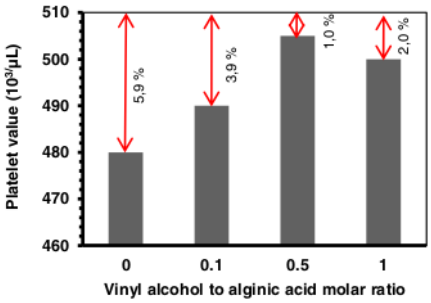

Fig. 9. Percent degradation of platelet in PRP after interacting with $2 \times 2\,cm^2$ of PVA-Alg membranes for 1 h. Initial amount of the platelet in PRP is 510,000 cells/μL.

protein adsorption was observed for the film with vinyl alcohol to alginic acid molar ratio of 0.5. Factors that affect the interaction between membrane surface and protein include hydrophilicity, roughness, surface charge, surface free energy, topological structure, solution environment, and protein type [1]. The low protein adsorption means less protein loss during hemodialysis trial.

The platelet adhesion on the membrane surface is closely related to the protein adsorption [1]. Fig. 9 showed the number of adhering platelets on the PVA-Alg membranes. After 1 h of contact, the maximum number of adhering platelets to the membrane is 3.9% and 1.0% of the initial for the membrane with molar ratios of 0.1 and 0.5, respectively. The initial platelet concentration is 510,000-cells/μL. In this experiment, a $2 \times 2\,cm^2$ cut membrane was applied. Even with a low molar ratio, the modified membranes still have lower platelet adhesion than that of the unmodified ones.

Blood plasma platelet adhesion on the membrane surface and morphology of the adhering platelet are used to evaluate the hemocompatibility of a hemodialysis membrane. The SEM images of platelet adhesion for representative zones are shown in Fig. 10.

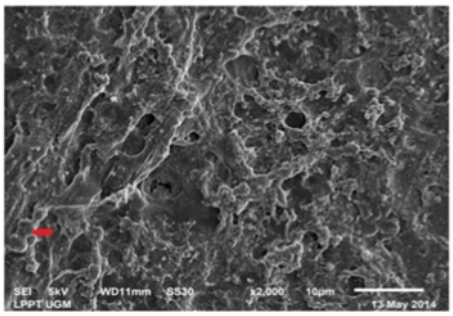

Fig. 10. SEM image of platelet adhesion on the surface of a PVA-Alg membrane.

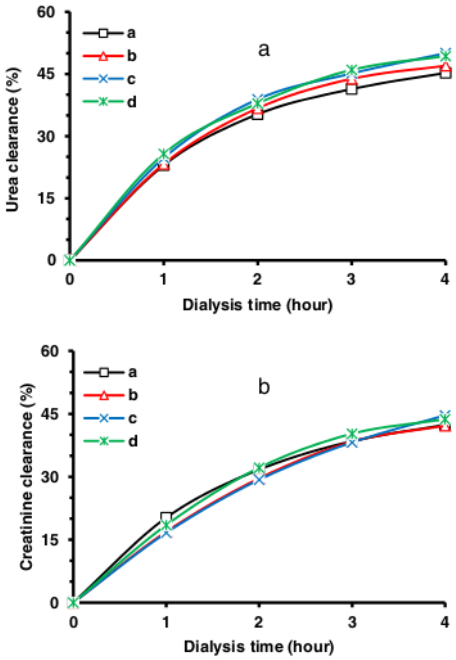

Fig. 11. Performance of urea clearance (a) and creatinine clearance (b) of the PVA-Alg membranes with molar ratio of 0 (a), 0.1 (b), 0.5 (c), and 1 (d) in the dialysis simulation experiment for 1, 2, 3 and 4 h.

Thrombocyte adhesion on the membrane surface takes place along with protein adsorption. Therefore, the thrombocytes seem to be covered by the plasma protein, especially fibrinogen.

3.6. *Dialysis performance of PVA-Alg membrane*

Clearance of urea and creatinine was determined to evaluate the dialysis performance of the proposed membranes. The clearance of urea and creatinine by the PVA-Alg membranes are shown in Fig. 11. The membrane clearance efficiency is evaluated based on the clearance of uremic compounds i.e. urea and creatinine from the source compartment. A comparison is made between the data taken after 1 h and after 4 h of dialysis trial. It indicates that the clearance of urea and creatinine increases with time. Hemodialysis for patients with renal failure is usually performed for about 4 h. The PVA-Alg membranes with molar ratio of 0, 0.1, 0.5 and 1.0 show the urea clearance of 45.3, 47.0, 50.0, and 49.3% after 4 h of dialysis test whereas the creatinine clearance is 42.4, 42.2, 44.6 and 43.7%, respectively. In general, the PVA-Alg ester membrane with vinyl alcohol to alginic acid molar ratio of 0.5 shows the highest clearance of urea and creatinine. However, the clearance of urea and creatinine with other molar ratios was not significantly different. The flux of urea and creatinine across the PVA-Alg membrane in the dialysis experiment was also examined. The flux of urea and creatinine is shown in Table 1.

Table 1
Flux of urea and creatinine across the PVA-Alg membranes.

Vinyl alcohol to alginic acid molar ratio	Flux (mg cm^{-2} h^{-1})	
	Urea	Creatinine
0	2.541	0.059
0.1	2.621	0.057
0.5	2.791	0.059
1	2.782	0.060

The cellulose acetate based membrane is able to reduce urea and creatinine contents by 17.2 and 10.8%, respectively. Using membranes prepared using cellulose acetate modified with urease, the urea clearance improved from 45.8 to 53.2% with the creatinine clearance of 31.2% [2]. This figure is much lower than of the alginate-based membrane prepared in this study. The functional groups present in the alginate-modified-PVA membranes could provide molecular channels for uremic compounds. The molecular channels formed across the membrane could be beneficial in the dialysis process. In the dialysis tests, the PVA-Alg membranes show clearance of uremic compounds and flux comparable with that of cellulose acetate membranes.

4. Conclusions

In search of a better biocompatible hemodialysis membrane, alginate has been cross-linked with PVA to form a corresponding ester. The PVA-Alg ester based membranes show higher tensile strength than that of the native alginate membranes. When the alginic acid to vinyl alcohol molar ratio was set to 1, the resulting PVA-Alg membranes show the highest tensile strength of 38.5 MPa. The membrane hydrophilicity also improves after modification using PVA as indicated by an increase in the water contact angle. The membrane Ca^{2+} adsorption tends to decrease with the increase in molar ratio. Conversely, the hemolysis ratio tends to increase with the increase in the molar ratio. The PVA-Alg membranes exhibit hemocompatibility better than that of native alginate membrane as suggested by low protein adsorption and platelet adhesion. The highest hemocompatibility characteristic of PVA-Alg membrane was observed at molar ratio of 0.5 with urea and creatinine clearance of 50.0% and 44.6%, respectively. Meanwhile, the flux of urea and creatinine across the membrane was found to be 2.791 and 0.059 mg cm^{-2} h^{-1}, respectively. In conclusion, this PVA-Alg ester may be considered as a possible substitute for cellulose acetate as a material for hemodialysis membranes.

References

[1] W.C. Lin, T.Y. Liu, M.C. Yang, Hemocompatibility of polyacrylonitrile dialysis membrane immobilized with chitosan and heparin conjugate, Biomaterials 25 (2004) 1947–1957.
[2] J.T. Daugirdas, P.G. Blake, T.S. Ing, Handbook of Dialysis, 4th ed., Lippincott Williams & Wilkins, Philadelphia, USA, 2007.
[3] D.F. Stamatialis, B.J. Papenburg, M. Girones, S. Saiful, S.N.M. Bettahalli, S. Schmitmeier, M. Wessling, Medical applications of membranes: drug delivery, artificial organs and tissue engineering, J. Membr. Sci. 308 (2008) 1–34.
[4] A. Gao, F. Liu, L. Xue, Preparation and evaluation of heparin-immobilized poly (lactic acid) (PLA) membrane for hemodialysis, J. Membr. Sci. 452 (2014) 390–399.
[5] M. Davidovich, H. Bianco, A quantitative analysis of alginate swelling, Carbohydr. Polym. 79 (2010) 1020–1027.

[6] S.D. Bhat, B.V.K. Naidu, G.V. Shanbhag, S.B. Halligudi, M. Sairam, T.M. Aminabhavi, Mesoporous molecular sieve (MCM-41)-filled sodium alginate hybrid nanocomposite membranes for pervaporation separation of water–isopropanol mixtures, Sep. Purif. Technol. 49 (2006) 56–63.
[7] S. Sakai, K. Kawakami, Synthesis and characterization of both ionically and enzymatically cross-linkable alginate, Acta Biomater. 3 (2007) 495–501.
[8] S. Kalyani, B. Smitha, S. Sridhar, A. Krshnaiah, Pervaporation separation of ethanol–water mixtures through sodium alginate membranes, Desalination 229 (2008) 68–81.
[9] S.H.S. Saniour, A.M.A. El-Ghaffar, F.I.I. El-Bab, S.A. Saba, Effect of composition of alginate impression material on "recovery from deformation", J. Am. Sci. 7 (9) (2011) 443–448.
[10] S. Zhang, J. Luo, Preparation and properties of bacterial cellulose/alginate blend bio-fibers, J. Eng. Fiber Fabr. 6 (3) (2011) 69–72.
[11] E. Tolba, B.M. Abdelhady, B. Elkholy, H. Elkady, M. Eltonsi, Biomimetic synthesis of guided-tissue regeneration hydroxyapatite/polyvinyl alcohol nanocomposite scaffolds: influence of alginate on mechanical and biological properties, J. Am. Sci. 6 (7) (2010) 239–249.
[12] H.T. Spijker, R. Graaff, P.W. Boonstra, H.J. Busscher, W.V. Oeveren, Review: on the influence of flow conditions and wettability on blood material interactions, Biomaterials 24 (2003) 4717–4727.
[13] T. Caykara, S. Demirci, Preparation and characterization of blend films of poly(vinyl alcohol) and sodium alginate, J. Macromol. Sci. Part A: Pure Appl. Chem. 43 (2006) 1113–1121.
[14] G. Lamour, A. Hamraoui, A. Buvailo, Y. Xing, S. Keuleyan, V. Prakash, A. Eftekhari-Bafrooei, E. Borguet, Contact angle measurements using a simplified experimental setup, J. Chem. Educ. 87 (12) (2010) 1403–1407.
[15] X. Wang, P.R. Chang, Z. Li, H. Wang, H. Liang, X. Cao, Y. Chen, Chitosan-coated cellulose/soy protein membranes with improved physical properties and hemocompatibility, BioResources 6 (2) (2011) 1392–1413.
[16] A. Idris, H.K. Yee, C.M. Kee, Preparation of cellulose acetate dialysis membrane using D-glukosamonohidrate as additive, J. Teknol. 51(F) (2009) 67–76.
[17] B.G. Lokesh, K.S.V. Krishna Rao, K. Mallikarjuna Reddy, K. Chodoji Rao, P. Srinivasa Rao, Novel nanocomposite membranes of sodium alginate filled with polyaniline-coated titanium dioxide for dehydration of 1,4-dioxane/water mixtures, Desalination 233 (2008) 166–172.
[18] D. Braun, H. Cherdron, M. Rehahn, H. Ritter, B. Voit, Polymer Synthesis: Theory and Practice Fundamentals, Methods Experiments, 4th ed., Springer-Verlag, Berlin, Heidelberg, Germany, 2005.
[19] W. Haitao, Y. Liu, Z. Xuehui, D. Qiyun, Improvement of hydrophilicity and blood compatibility on polyethersulfone membrane by blending sulfonated polyethersulfone, Chin. J. Chem. Eng. 17 (2) (2009) 324–329.
[20] L. Li, C. Cheng, T. Xiang, M. Tang, W. Zhao, S. Sun, C. Zhao, Modification of polyethersulfone hemodialysis membrane by blending citric acid grafted polyurethane and its anticoagulant activity, J. Membr. Sci. 405–406 (2012) 261–274.
[21] H. Wang, L. Yang, X. Zhao, X. Hao, T. Yu, Q. Du, Improvement of hydrophilicity and blood compatibility on polyethersulfone membrane by blending sulfonated polyethersulfone, Chin. J. Chem. Eng. 17 (2) (2009) 324–329.
[22] L.R. Wang, H. Qin, S.Q. Nie, S.D. Sun, F. Ran, C.S. Zhao, Direct synthesis of heparin-like poly (ether sulfone) polymer and its blood compatibility, Acta Biomater. 9 (2013) 8851–8863.

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