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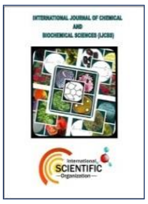

Biocomposites as Candidates for Hollow Fiber Dialysis

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Abstract

Hemodialysis is a common therapy for patients with kidney failure which the main element is a semi-permeable membrane. Dialyzer membrane with pure PES material has low hydrophilicity and hemocompatibility properties causing fouling. This study aims to determine the characteristics of PES hollow fiber membrane with the addition of PVP. The making of PES-PVP hollow fiber membrane was using phase inversion method with spinning technique. The PVP concentration was varied and they were characterized on their morphology, hydrophilicity, tensile strength, hemolysis behavior and performance. The morphology characteristics showed that sample with the highest PVP was suitable for hemodialysis membrane, which has pore diameter of 0.067-0.095 μm. The membrane was more hydrophilic as the PVP concentration increases. An increase of tensile value was obtained from 8.902 N/mm2 to 20.148 N/mm^2 although not yet compatible with the standard of hollow fiber tensile strength. The increase in PVP concentration decreased the percentage of hemolysis by 1,88%. The best result of flux value to urea was 148,705 mL/m^2 minutes while rejection value was 54.57%. The PES-PVP hollow fiber membrane has potential as a dialyzer membrane candidate based on its characteristics.

Keywords: Hollow Fiber, Dialysis Membrane, Polyethersulfone, Polyvinylpyrrolidone.

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1. Introduction

Like other parts of the world, Indonesia equally suffers from a high burden of chronic kidney disease (CKD). Nevertheless, data regarding the epidemiology of CKD in Indonesia is scarce and inconsistent. The National Basic Health Research (Riset Kesehatan Dasar, Riskesdas), reported that the CKD (eGFR<60ml/min/1.73m^2) prevalence was 3.8 permil (‰) in 2018, increased from 2.0 permil (‰) in 2013 [1]. In-center hemodialysis (HD) is the most common dialysis, and over 98% of Indonesian patients with end-stage renal disease (ESRD) receive in-center HD [2]. Hemodialysis therapy aims to remove toxic residue, excess water, and fluid, as well as to improve electrolyte balance using external dialysis system with filtration, osmosis, and diffusion principles. Hemodialysis can be defined as an artificial kidney machine, consisting of a semi-permeable membrane with blood on one side and a dialysis fluid on another [3]. The balance between hydrophilicity and hydrophobicity on the membrane's surface has a major effect on the character and function of the membrane [4]. Synthetic polymers which are potentially developed as the basic material of hemodialysis membrane are polyethersulfone (PES). Using hemodialysis membranes made from Polyethersulfone has been widely practiced since 1980 due to its stable sterilization and minimal degradation toward a long-term membrane performance [5]. Polyethersulfone is one of the most popular polymers types used as a membrane material, because of its good mechanical character and easy-to-shape modules in various configurations [6]. Synthetic polyethersulfone polymers is hydrophobic. Its hydrophobic nature of dialysis membrane causes fouling formulation due to the protein absorbed on the membrane surface. The fouling causes the hollow fiber of the hollow fiber membrane to clot and affects the process of blood purification [7]. The fouling also makes the membrane short-lived and requires a high maintenance cost [8]. There are 3 modification methods to make PES more hydrophilic, namely: 1. bulk modification; 2. surface modification; and 3. blending [9].

Modification by blending the hydrophobic polymer with hydrophilic additives and so on. Polyvinylpyrrolidone (PVP) is an additive serving as a hydrophilizing agent. This research focuses on the formation of polyethersulfone using blending method with variation of additive concentration of polyvinylpyrrolidone as a hollow fibre's membrane dialyzer candidate. Membrane formation is conducted through a phase of inversion technique which is a process of material change from fluid to solid. Hollow fibre membrane's printing is done by spinneret in a spinning process.

2. Materials and Methods

2.1. Synthesis dope solution

PES-PVP-DMF dope solution was prepared using PVP's concentration variation which consists of 5 samples with PES/PVP/DMF compositions: Sample A (control) 18/0/82, Sample B 18/3/79, Sample C 18/6/76, Sample D 18/9/73, and Sample E 18/12/70. Then, the solutions were mixed by stirring for 9 hours at room temperature. The dope solution is allowed to stand for 20 minutes to remove the bubbles formed. After all the bubbles are lost then in print using spinneret tool. PES-PVP's hollow fiber membrane was printed using phase inversion method, spinning technique, and spinneret.

2.2. Morphology test

Phenom Prox Scanning Electron Microscopy is used for morphlogy test. Samples were observed in the form of cross section (to measure inside and outside diameter) and inner layer (to observe pore size of membrane).

2.3. Hydrophilic and Hydrophobic Test

PES-PVP membranes are prepared in a flat shape to facilitate the testing process. The membrane surface was distilled with aquadest of 10μl, observed, captured and determined by contact angle. The hydrophilic properties can be determined by the low contact angle generated and when the resulting contact angle is large it is hydrophobic.

2.4. Mechanical Testing

Autograph was used for tensile testing of the hollow fiber membrane which were prepared using a paper. Each end of the membrane is attached to the authograph and the pulling load is mounted on Newton's load unit. Samples are withdrawn at certain speeds until broken. The stress or tensile strength (σ) is defined as the magnitude of force (F) divided by the cross-section area (A) : σ = F / A. Strain or elongation (ε) due to attraction to the material is defined as the ratio of the length increase (ΔL) to the initial length (Lo), can be mathematically written:

$$\varepsilon = \Delta L / Lo$$

2.5. Hemolysis Assay

Human blood samples were given anti coagulant Ethylene Diamine Tetraacetic Acid Dipotasium Salt (EDTA). Blood and EDTA then dissolve with saline and placed on a microtube. The sample was inserted into a microtube containing blood with saline and then incubated for 2 hours using a waterbath temperature of 37°C. Samples were taken and blood was centrifuged for supernatant removal. The supernatant measured its wavelength uptake using UV-Vis spectrophotometry.

The value of the test results obtained then processed using the following formula [10]:

$$\text{\% Hemolysis} = \frac{A_{Sample} - A_{Negative\ Control}}{A_{Positive\ Control}} \times 100\%$$

2.6. Filtration Test

The membrane performance test was initiated by preparing a feed solution using a urea solution of 25mg/dl (urea concentration in patients with renal failure). The feed solution is fed through a hollow fiber membrane that has been arranged into a module. The feed solution is separated into permeate solution (filtration result) and random (unfiltered). The result of filtration test of urea solution can be used to know the value of clearance of the dialiser membrane from the calculation [11] :

$$\text{Flux : } J = V / (A.t)$$

$$\text{Sample : } C = \frac{As \times Cb}{A_b}$$

Concentration
C = Sample Concentration (permeat solution)
Cb = Standart Concentration (feed solution)
As = Sample Absorbance
Ab = Feed Absorbance

$$\text{Rejection : } R = 1 - \frac{C_p}{C_f} \times 100\%$$

Coefficient
R = Rejection Coefficient (%)
Cp = Soluble concentration in permeate
Cf = Concentration dissolved in the feed

Characterization is needed to determine the ability of the dialyzer membrane. The Water Contact Angle (WTA) test is to determine the wettability of materials, if WCA is smaller than 90°, the material is hydrophilic, if WCA is larger than or equal to 90°, the material is hydrophobic [12]. Tensile test is to determine the tensile strength of the material. Scanning Electron Microscopy (SEM) test is to determine morphology of membrane surface. Haemolysis test to determine the blood compatibility of the membrane, and performance test to determine the coefficient of rejection on the membrane.

3. Results and Discussions

In this research has successfully made membrane of hollow fiber polyethersulfone (PES)- polyvinylpyrrolidone (PVP) dialiser. Variation of PVP concentration was done with the aim to know the result of composite hollow fiber PES-PVP and get optimum composition of variation based on physical characterization and biological hollow fiber. The results of the hollow fiber membrane morphology test are presented in Table 1. Based on the measurement results in Figure 1, the higher PVP concentration will form the smaller pore size. This is because the high polymer concentration causes polymer bonding in PES and PVP which makes the molecule so tightly that the smaller pore structure is formed. In addition, the viscosity of the dope solution is a factor that may affect pore formation. The concentration in dope solution will affect the viscosity level where during the PVP molding process can form membrane pores by diffusing into water.

In samples D and E have the smallest pore size of 0.037 and 0.067µm which fall within the pore size of the ultrafiltration membrane. The smaller pore size will increase the ability to pass small particles such as urea to have a high clearance value [13]. The morphological analysis of the shape and size of the diameter for the hollow fiber membrane is formed to observe the inside and outside diameters as shown in Table 2 but have been successfully shaped hollow fibers (Figure 2). During the membrane molding process, the water gap distance, the gas pressure, and the magnitude between the diameter of the coagulant needle and the diameter of the spinneret hole used can influence the shape and size of the resulting diameter [14]. Determining hydrophilic and hydrophobic characters of the hollow fiber membrane can be conducted by measuring the contact angle which is generated from the liquid droplets on the membrane surface. In hydrophilic membrane, the water will spontaneously wet the membrane, whereas the wetting does not occur in hydrophobic membrane [12]. Figure 3 illustrates the decrease of water arch during an increase of PVP concentrate. It is because PVP is a hydrophilic additive material [15]. Besides, the solvent used in this was dimethylformamide contained polar hydroxyl (-OH) compound, so that the member can absorb water and decrease water contact angle. The hydrophilicity level of a membrane is divided into 5 categories, namely superhydrophilic (0-0°), hydrophilic (0°<θ<90°), hydrophobic (90°<θ<120°), ultrahydrophobic (120°<θ<150°), and superhydrophobic (θ> 150°) [12]. The mechanical quality of the PES-PVP hollow fiber membrane was determined by observations on elongation, tensile strength, and modulus young. The value of strain or elongation obtained shows the ability of a material where it has been added long before the material is broken or often referred to as elasticity. Based on Table 3 the elongation value to five samples included in hollow fiber membrane range is 3.5 - 13.1%, where the lowest elongation value is in sample E of 3.7%. From elongation data that have been obtained, then made the graph of correlation of PVP concentration to elongation value as presented in Figure 4.

In the graph the strain values obtained by hollow fiber membrane tend to decrease along with the increase of PVP concentration. Increased elongation or strain values indicate an increase in pore size when deformed by pressure [16]. The value of stress or tensile strength indicates if the material has a high strength. In Table 3 the highest value of tensile strength belongs to sample E that is 20.148 N/mm^2. This value is not includes in the standart value of tensile strength of hollow fiber membrane which is in the range of 23.1–33.8 N/mm^2, but with added concentration can increase the value of tensile strength obtained as seen in Figure 5. This can happen because the addition of concentration causes the membrane formation molecules to increase so that the molecular distance becomes more compact. The molecular density of membrane constituents makes the pore size smaller. The highest Young Modulus is in sample E that is 544, 540 MPa as shown in Figure 6. Sample E has the highest stress and the lowest strain among the five samples that make Young Modulus higher. If the Young Modulus is high it can be interpreted that the membrane can retain pore size when it gets pressure but selectively to certain molecules [17].

The results of hemolysis test in Figure 7 show that hemolysis percentage in Sample A was 4.18%; Sample B was 3.34%; Sample C was 2.71%; Sample D was 2.30%; and Sample E was 1.88%. The largest percentage of hemolysis was recorded by Sample A (without the addition of PVP). This shows that the addition of PVP influences PES-PVP hollow fiber positively by reducing the percentage of hemolysis. In a graph shown, the hemolysis percentage from Sample A to Sample E decreases along with an increase of PVP concentration. Hemolysis percentage is deemed safe if it is recorded at less than and similar to 5%, so that all samples are cleared for a contact with blood. According to ASTM 756-17, there was several hemolysis levels based on hemolysis index, such as hemolysis index at 0-2% at non-hemolysis level; 2-5% slight hemolysis; and more than or similar to 5% hemolysis [18].

The quality of membrane performance can be observed from the permeability and selectivity of the membrane. Hollow fiber membrane flux test using E sample formed module that has a working method such as hemodialysis membrane. In this flux value test using cross flow method and urea solution as feed solution with 3 times iteration. The value of each iteration does not have a high difference as shown in Table 4 with an average flux value of 148.705 mL m^2.min. However, the resulting flux value has not corresponded to the flux value in the F60 (Frenesius Polysulfone Membrane) dialyzer membrane product having a value of 163mL/min. This may occur because the membrane module is less in line with the actual membrane dialiser specifications, for example, can be seen from the number of hollow fiber membranes. In each model the actual dialiser membrane as much as 100 more hollow fiber with a length of 25-30 cm while on the test only 70 membranes with a length of 20cm, resulting in a small surface area of 0.343 m^2. The surface area of the hollow fiber dialysis membrane is 1.5m^2. Membrane selectivity is shown in the rejection coefficient in which the membrane capability passes certain species and retains the other species. Rejection measurements for the urea solution were performed after the flux test to obtain urea solution before and after filtration. They were measured for their degree of turbidity using UV-Vis spectrophotometer. Based on the results from Table 5, the rejection coefficient of PES-PVP hollow fiber membrane of sample E was ranging from 52.8 to 57.2%. Smaller percentage of rejection coefficient indicates the ability of hollow fiber membrane to resist or hold the urea less, so that many urea molecules penetrate the membrane.

Table 1: Test result pore size hollow fiber PES-PVP.

Sample	Variation of PVP Composition (wt%)	Pore Size (μm)
A	0	0,807 – 2,93
B	3	0,523 – 1,69
C	6	0,051 – 1,57
D	9	0,037 – 0,095
E	12	0,067 – 0,095

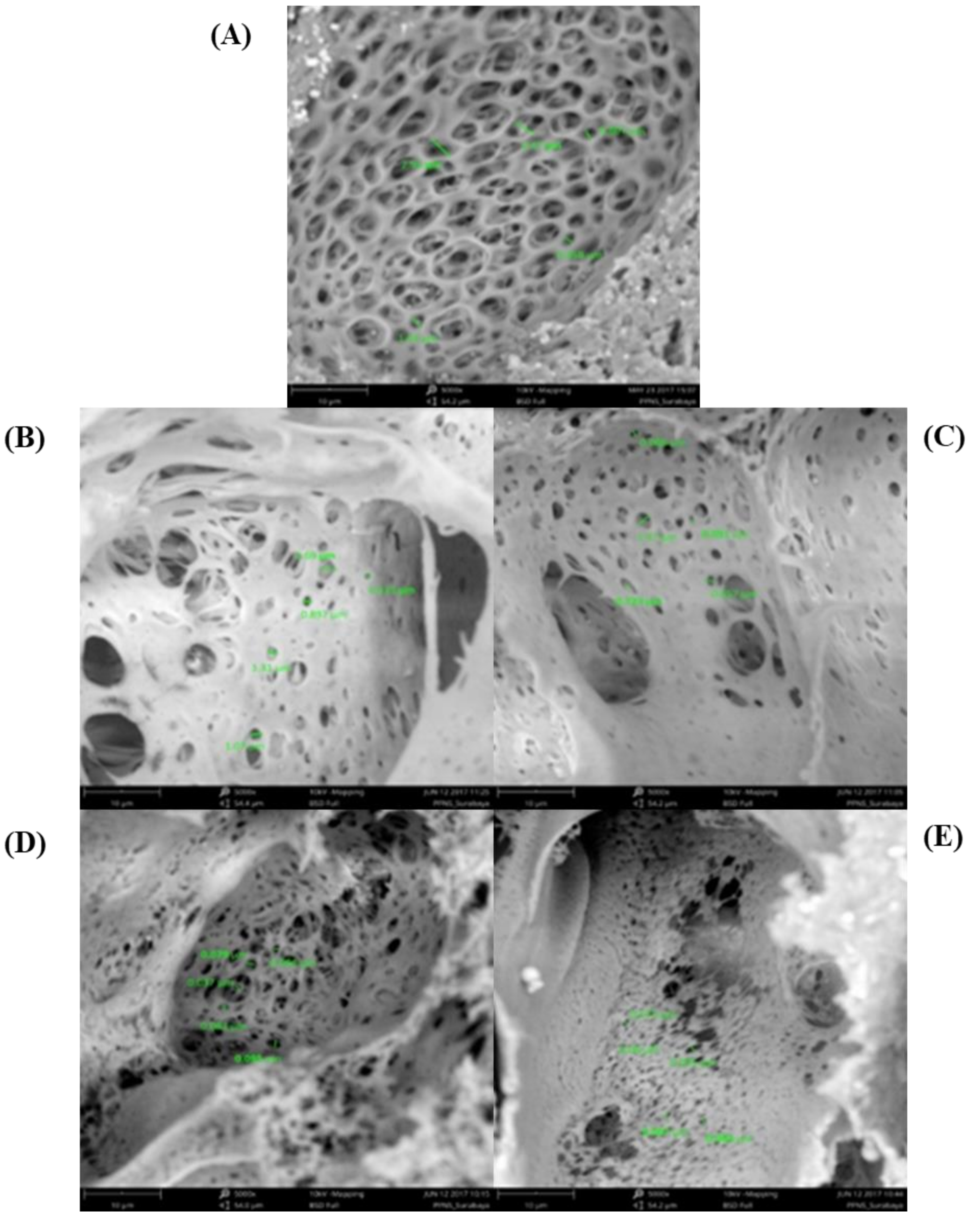

Figure 1: SEM test results Pore Size Hollow Fiber PES-PVP 5000x magnification with PVP variation: (A) 0%; (B) 3%; (C) 6%; (D) 9%; (E) 12%.

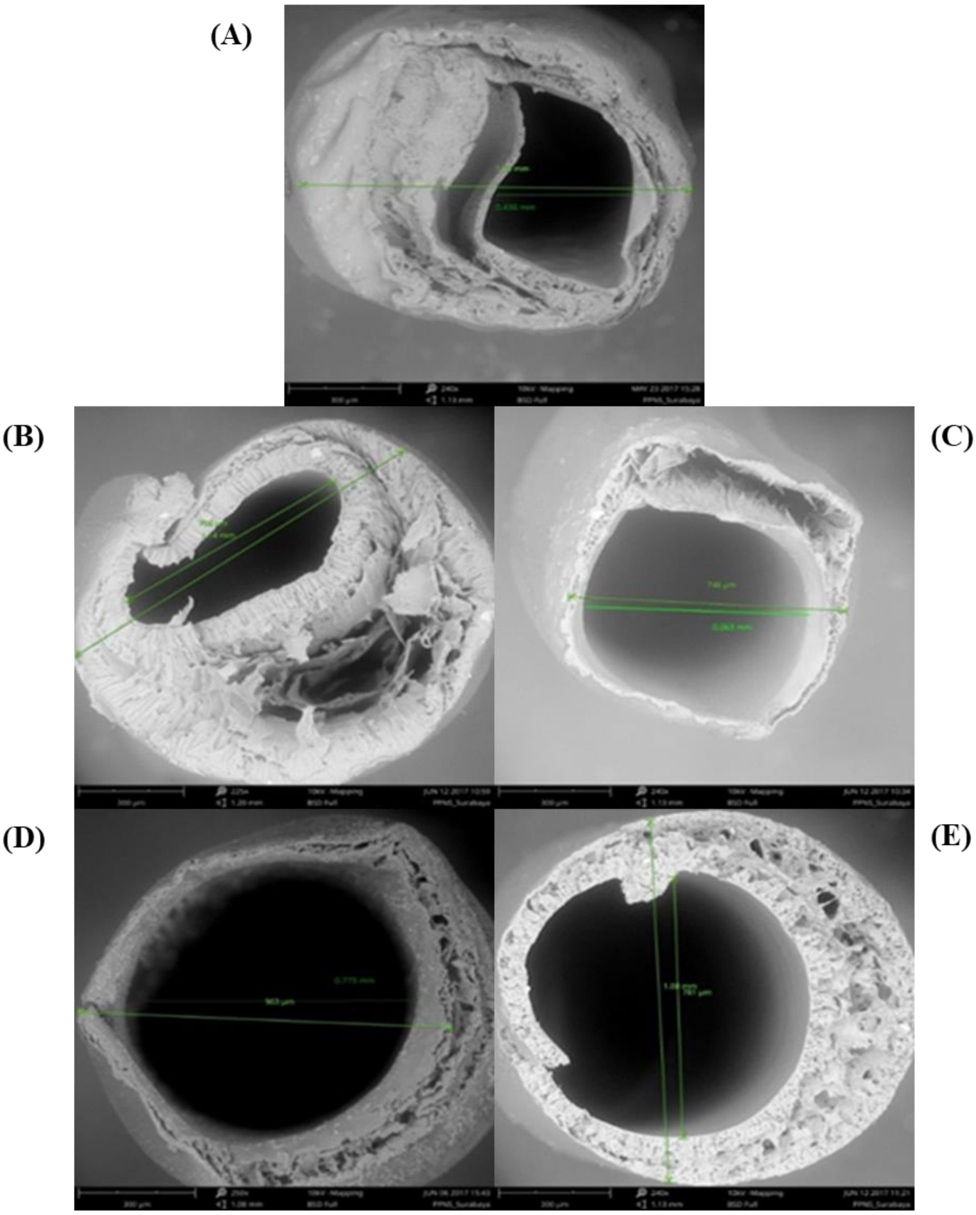

Figure 2: Cross section shape and diameter size of membrane Hollow Fiber PES-PVP with PVP variation: (A) 0%; (B) 3%; (C) 6%; (D) 9%; (E) 12%.

Table 2: Morphological test results outer diameter (D) and in (d).

Sample	Variation of PVP Composition (wt%)	D (mm)	d (mm)
A	0	1,05	0,436
B	3	1,14	0,708
C	6	0,746	0,663
D	9	0,963	0,775
E	12	1,08	0,781

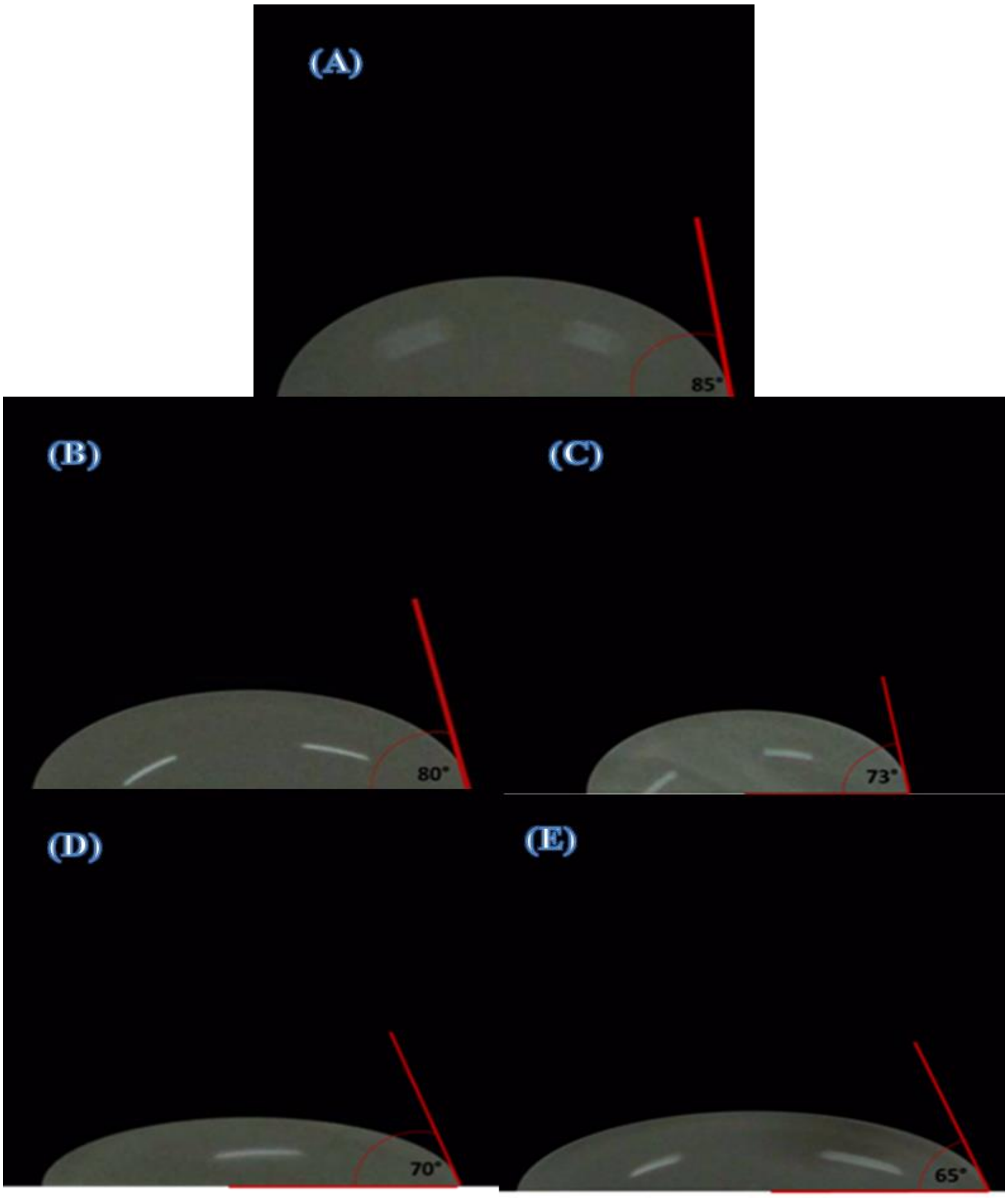

Figure 3. Water Drop Profile on Hollow fiber PES-PVP Membrane with PVP Variation : (A) 0%; (B) 3%; (C) 6%; (D) 9%; (E) 12%.

Table 3. Mechanical test results : Elongatioan and Tensile Strength.

Sample	Variation of PVP Composition (wt%)	*Elongation* (%)	Tensile Strength (N/m^2)
A	0	8.1%	8.902
B	3	7.3%	9.397
C	6	5.3%	10.652
D	9	5.7%	17.234
E	12	3.7%	20.148

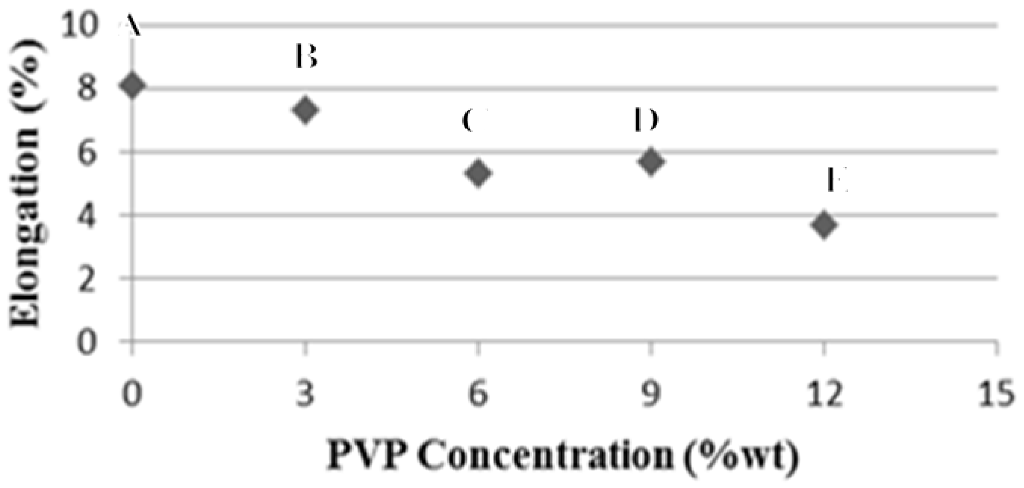

Figure 4: Water Drop Profile on Hollow fiber PES-PVP Membrane with PVP Variation : A. 0%; B. 3%; C. 6%; D. 9%; E. 12%.

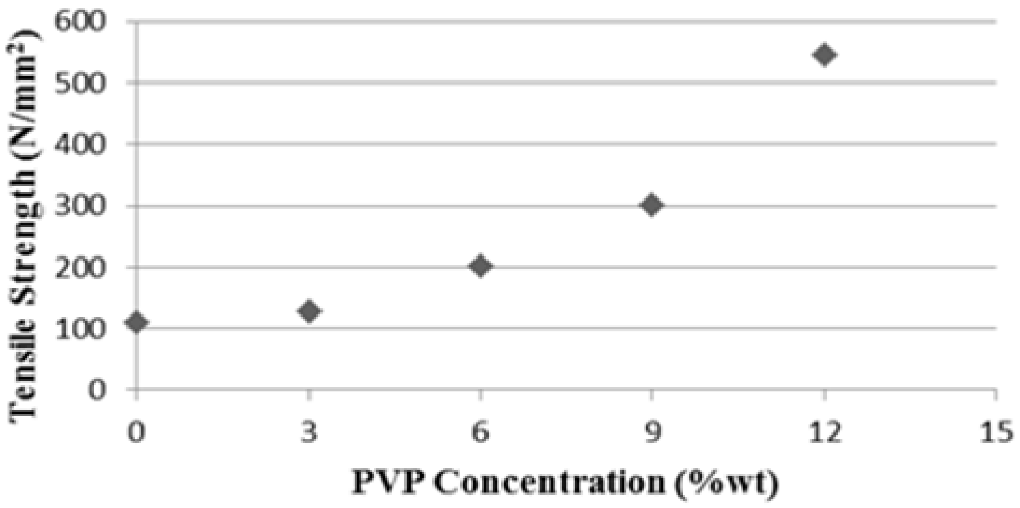

Figure 5: The higher concentration of PVP causes the tensile strength to increase.

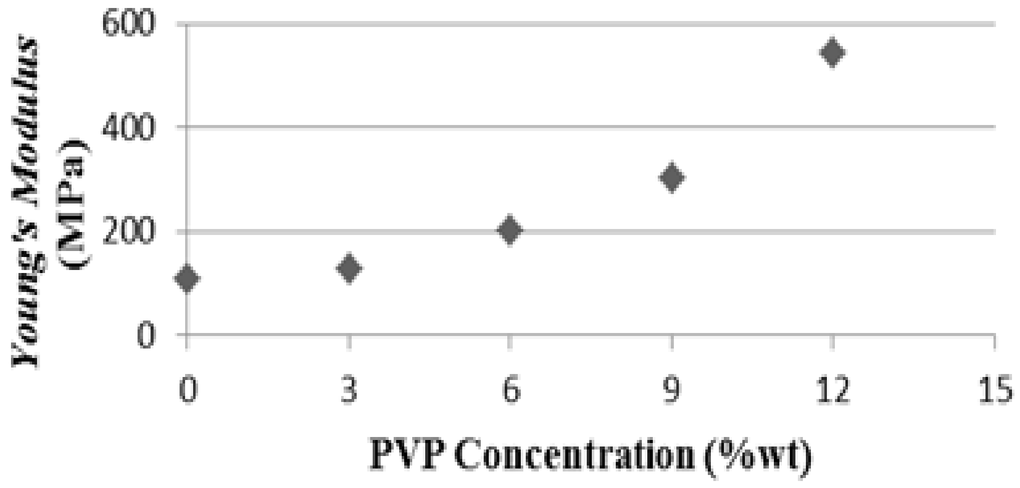

Figure 6: The higher concentration of PVP causes the young's modulus to increase.

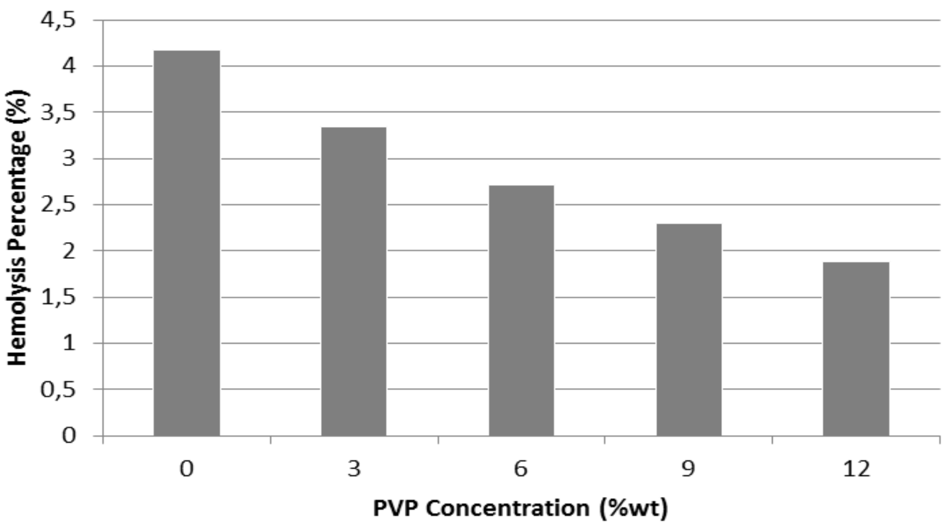

Figure 7: The influence of PVP concentrate variants on hemolysis assay, the higher concentration of PVP causes hemolysis to decrease.

Table 4: Test result of flux value of hollow fiber PES-PVP on PVP 12% wt.

Iteration	Permeate Volume (mL)	Surface Area (m^2)	Time (minute)	Fluks (mL/m^2 minutes)
1	50	0.343	1	145.772
2	53	0.343	1	154.518
3	50	0.343	1	145.772
Average				148.705

Table 5: Results of rejection value coefficient test of hollow fiber PES-PVP on PVP 12% wt.

Iteration	Dissolved Concentration in Permeat (C_p)	Dissolved Concentration in Feed (C_f)	Rejection (%)
1	0.1057	0.25	57.72
2	0.118	0.25	52.8
3	0.117	0.25	53.2
Average			54.57

4. Conclusions

PVP variant composition as an additive material on PES membrane influences the pore size, hydrophilicity, mechanistic, hemocompatibility, and membrane performance. The increase of PVP concentration influences pore size which keeps growing smaller, higher tensile strength, higher hydrophilicity, higher hemocompatibility, and higher membrane performance.

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