Molekul, Vol. 19. No. 3, November 2024: 480 – 488

MOLEKUL
eISSN: 2503-0310

Articles
https://doi.org/10.20884/1.jm.2024.19.3.10436

A Preparation and Characterization of Chitosan-Silica Membranes and Applications for Creatinine and Urea Transport

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Received December 18, 2023; **Accepted** August 19, 2024; **Available online** November 20, 2024

ABSTRACT. The main organ that of the urinary system after the main organ functions to filter waste products from the body's metabolism that must be removed through the excretion process is the kidneys. The remaining metabolite compounds that accumulate in the blood are caused by the kidneys being unable to filter and remove uremia toxin compounds such as urea and creatinine from the body. One indication of kidney damage can be seen from levels of creatinine and urea in the blood that exceed normal limits. Urea and creatinine levels can be lowered by improving kidney function, namely by the blood washing process (hemodialysis). In the hemodialysis technique, the price of an artificial kidney or hemodialyzer is very expensive so that kidney failure sufferers require very large costs for treatment. To overcome this problem, alternative natural materials are needed to make membrane artificial kidneys. The aim of the research is (1) to analyze the synthesis and characteristics of membranes and, (2) to apply them for the transport of creatinine and urea using silica chitosan membranes. Characterization includes functional group testing using an Fourier-Transform Infrared (FTIR) spectrophotometer, water absorption test (swelling test), tensile test, and morphology with Scanning Electron Microscope (SEM). The membranes were applied for creatinine transport with varying concentrations of 70, 100, and 130 mg/L. It was also used for transporting urea at various concentrations of 500, 1000, and 1500 mg/L. This study disclosed a window of opportunity to produce novel hemodialysis membranes using bio-based materials.

Keywords: Biocompatibility, chitosan, creatinine, hemodialysis, membrane, silica, urea

INTRODUCTION

Globally, Chronic Kidney Disease (CKD) ranks as the sixteenth most common cause of death. Primary care physicians must conduct appropriate screening, diagnosis, and management in order to prevent the negative consequences of CKD, such as end-stage renal disease, cardiovascular disease, and mortality. Hemodialysis (HD) is usually performed to treat kidney failure (Teresa et al., 2019).

Since the early 20th century, dialysis technology has been developed across several decades. Georg Haas treated six dialysis patients with hirudin, an anticoagulant, in 1928 using a cellulose membrane (Paskalev, 2001). Because of the inexperienced technique, there was no patient survival in the end. The first practical dialyzer, or rotating drum kidney, was created in 1943 by Dutch physician Willem Kolff. It consisted of a 20-meter revolving cellophane tube that was wound around a 2-meter horizontal drum as a semipermeable membrane. The rotating drum kidney was a successful treatment for acute kidney failure in a 67-year-old patient who had an exacerbation of a bile duct infection. The patient did not experience any further impairment to their kidneys. Because gravitational pressure does not create enough transmembrane pressure to achieve ultrafiltration, this device can remove uremic poisons but not excessive bodily fluid. It was therefore still not possible to treat renal failure associated with fluid overload, such as pulmonary edema or hypertension, using the rotating drum (Tang et al., 2022). The HD technique is very expensive, many kidney failure sufferers cannot undergo dialysis treatment which results in very high mortality rates. The high cost of HD is due to the high cost of HD technical instruments, especially the price of an artificial kidney or hemodialyzer (Wenten, 2016). The use of nature is carried out to overcome the expensive HD technique. Cellulose membrane is a natural polymer that is often used for the HD process (Azhar et al., 2021). Within the same high-flux hemodialyzer module, Hemodialysis Therapy (HDF) combines the convection of soluble middle-sized toxins, like β2-microglobulin, with the diffusion of mostly low molecular weight uremic toxins, which are known from conventional HD. Because HDF is better than HD at eliminating large- and middle-sized uremic toxins, clinical trials have shown that HDF is the most advanced renal replacement therapy currently available. Furthermore, HDF has the potential to enhance difficult clinical outcomes, and the results of clinical trials are extremely encouraging (Free, 2014; Ronco, 2015).

Cellulose membranes have the advantages of cheap production costs, thin walls and abundant availability in nature. Cellulose membranes have the weakness of being immunoreactive which causes an inflammatory response in patients, available in low flux form, only small molecules can pass, while molecular weights above 5000 pass very little through the membrane, only withstand a pH range of 2-8, and a temperature of 30- 40°C. Modification of cellulose membranes with acetate, diacetate, and triacetate was carried out to overcome the weaknesses of cellulose membranes. However, this membrane has a weakness, namely that it is less compatible with blood, causing protein adsorption to occur on the membrane surface (Eo et al., 2016).

Currently, research on the use of natural polymers as membranes, especially for hemodialysis, is being developed. Chitosan is the second most abundant natural polymer after cellulose. Chitosan structure and cellulose is almost the same, the only difference is the group attached to the C-2 atom position. The C-2 group of cellulose is a carboxyl group and the C-2 of chitosan is an N-acetyl group (Sugita et al., 2009). Chitosan has bioactive, biocompatible, anti-bacterial and biodegradable properties (Gomez & Cecilia, 2020). However, chitosan membranes also have weaknesses, namely low mechanical properties which is indicated by the value tensile strength, percent elongation, and a low Young's Modulus (Liu et al., 2017; Yeh et al., 2007). Chitosan membrane modification is expected to produce membranes with better characteristics, for example increasing membrane stability (Jin et al., 2018), reducing the size of membrane pores so that the separation of molecules or rejection of macromolecules from a solution by the membrane is more effective. Chitosan crosslinking is a solution offered to overcome the problem of the mechanical properties of chitosan (Wang, 2020). Therefore, it is necessary to modify the surface of chitosan before using it as a hemodialysis membrane. Several materials have been used as materials to modify chitosan as a hemodialysis membrane, including: pectin, alginate, polysulfone-polyethylene glycol (Ayuni & Siswanta, 2013; Kaban, 2006; Lusiana et al., 2016).

The success of the separation process using a membrane depends on the quality of the membrane produced. The permeability, selectivity and mechanical properties of the membrane depend on the pore structure of the composite membrane, this is what really determines the quality of the composite membrane. Silica particles are reported to be an ideal porogen used to make chitosan membranes that have controlled porosity and have good mechanical properties (Liu et al., 2017). In its formation, the pore structure of the composite membrane is influenced by several factors, including polymer concentration, wall-forming materials which are deliberately added to improve the mechanical properties of the membrane (Tan & Rodrigue, 2019).

The urgency of this research is that the hemodialysis technique is very expensive, so many people with kidney failure do not able to undergo treatment resulting in death. The high cost of dialysis treatment comes from this from the high cost of dialysis membranes. The high cost of dialysis membranes continues to encourage researchers to do so innovation and optimization to produce membranes that can be used properly by kidney failure patients. So far the materials used include cellulose, polysulfone, polyamide, polyacrylonitrile, and polymethyl methacrylate thus needs to be searched for other materials that can be used as a membrane hemodialysis.

Based on the previous description, it is deemed necessary to make efforts to synthesize chitosan-silica membranes for the transport of creatinine and urea. Chitosan-silica membranes were made with a ratio of 2% chitosan: silica. The membrane will be used for transport of creatinine with concentrations of 70, 100, 130 mg/L and urea with concentrations of 500, 1000, 1500 mg/L. The results of creatinine and urea transport were measured using an ultraviolet-visible (UV-Vis) spectrophotometer so that the transport efficiency value of the membrane was known. It is hoped that this membrane can be an alternative to a hemodialysis membrane.

EXPERIMENTAL SECTION

Materials and Instruments

This research are a series of transport tools, a magnetic stirrer, analytical balance, magnetic stir bar, thickness gauge, petri dish, supporting equipment in the form of glassware, manual Shimadzu UV mini-1240 spectrophotometry (UV-Vis) and Shimadzu 8201PC FTIR spectrophotometer. The materials used in this research were chitosan (pro analysis, Aldrich), silica (technical grade), glacial acetic acid, 2% NaOH, urea, dimethyl amine, 96% ethanol, HCl, PVA, phosphate buffer, creatinine (pro analysis, Merck), universal indicator and distilled water.

Synthesis and Characterization of Chitosan-Silica Membranes

Chitosan from the main material was carried out according to the procedure used (Liu et al., 2017) with several modifications. A total of 0.5 g of chitosan was dissolved in 50 mL of 2% acetic acid and 1.5 g of silica was dissolved in 50 mL distilled water (0.5:1.5, membrane type 1). Stirring was carried out continuously for 24 hours at room temperature until a homogeneous solution was produced. Once the solution was homogeneous, the solution was poured slowly onto a glass plate and leveled using a rod stainless steel. Next, the resulting chitosan membrane was left in the open air overnight to evaporate the solvent. After the composite was dry, it was dipped in 5% NaOH for 5 minutes and then washed using distilled water to remove residual solvent. The resulting chitosan composite was stored in a desiccator. The same procedure was used for variations of 2% chitosan: silica (1:1, membrane type 2), (1.5:0.5, membrane type 3).

Membrane characterization includes functional group analysis, water absorption test, and tensile test. Characterization of functional group membranes was analyzed using an FT-IR spectrophotometer. The sample was weighed at approximately 1-2 mg, then added to approximately 200 mg of pure KBr powder and stirred until smooth. The sample and KBr powder were mixed, placed in a mould, and pressed using a mechanical pressure device. Then, the sample was analyzed. The water absorption test was carried out by measuring the difference in membrane weight before and after being immersed in phosphate buffer. Dry weight (W_k) measured from membranes dried for 24 hours at room temperature. Wet weight (W_b) measured from a membrane soaked in water for 6 hours. The swelling test of the synthesized membrane was calculated by Equation 1.

$$\%WU = \frac{W_b - W_k}{W_k k} \times 100\% \quad (1)$$

The tensile test was carried out and the mechanical stability of the membrane was measured using a Strograph VG 10-E. The membrane to be tested was first cut to a size of 0.1 mm. The strain rate used was 10 mm/minute with a tensile strength of 100 N. Measurements were carried out at room temperature.

Membrane Analysis Performance Test

Creatinine transport using chitosan-silica membranes

Membrane attached to chamber which separates the receiver phase and the source phase can be seen in **Figure 1**. Chamber of the source phase, 50 mL of creatinine was added with concentrations of 70, 100 and 130 mg/L respectively for creatinine transport and in the receiving phase, 50 mL of distilled water was added. Each phase was equipped with a magnetic stir bar and then stirred for 6 hours. Two mL of creatinine and water were taken every 2 hours in the source and receiver phases. In the source phase and receiver phase, for creatinine analysis, 8.8 mM picrate solution in 0.4 M NaOH was added and then left for 36 minutes. The membrane resulting from transport and which has been left to rest was then analyzed using UV Vis spectrophotometry at a wavelength of 492 nm (Lusiana et al., 2016).

Urea transport using chitosan-silica Membranes

The membrane was carefully attached to a chamber, serving as a barrier between the receiving phase and the source phase, a key component of the experimental setup. 50 mL of urea was added to chamber as the source phase and 50 mL of distilled water was added to the receiving phase, pH 7.4 buffer was added to each phase which was equipped with a magnetic stir bar, then stirred for 6 hours with every 2 hours each solution being taken 2 mL in the source phase and receiver phase. The source and recipient phases were added with a color reagent consisting of dimethylamine solution (1 g of dimethyl amine dissolved in 50 mL of 96% ethanol) and 3 M HCl (3:1). Urea concentration was analyzed using a UV spectrophotometer UV-Vis at a wavelength of 425 nm. The same procedure was carried out for urea concentrations of 1000 and 1500 mg/L.

RESULTS AND DISCUSSION

Synthesis and Characterization of Chitosan-Silica Membranes

The membrane in this study was made using the phase inversion method. Phase inversion is the method most widely used in making polymer membranes for the separation process. The successfully synthesized chitosan-silica membrane can be seen in **Figure 2**.

Functional Group Using FTIR Spectrophotometer

The infrared spectrum of the chitosan-silica membrane shown in **Figure 3** shows the absorption of the Si-O-Si functional group which appears at wave numbers 897-894 cm^{-1} which indicates the formation of silica polymer which interacts with chitosan on the membrane. The absorption intensity of the Si-O-Ti functional groups on the membrane decreases in line with the decreasing ratio of the amount of silica nanosol in the composite.

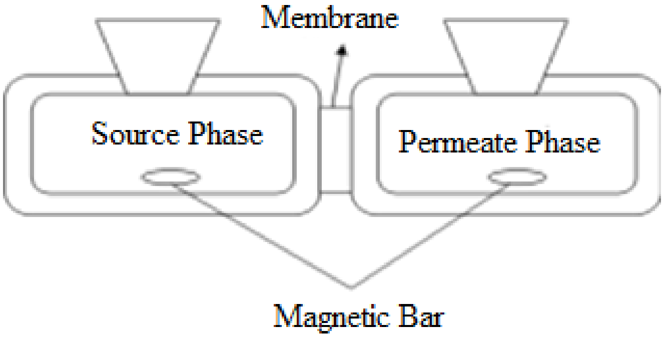


Figure 1. Circuit of creatinine and urea transport equipment

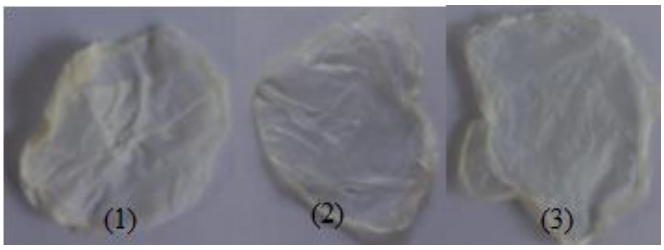


Figure 2. The result of membrane synthesis chitosan: silica

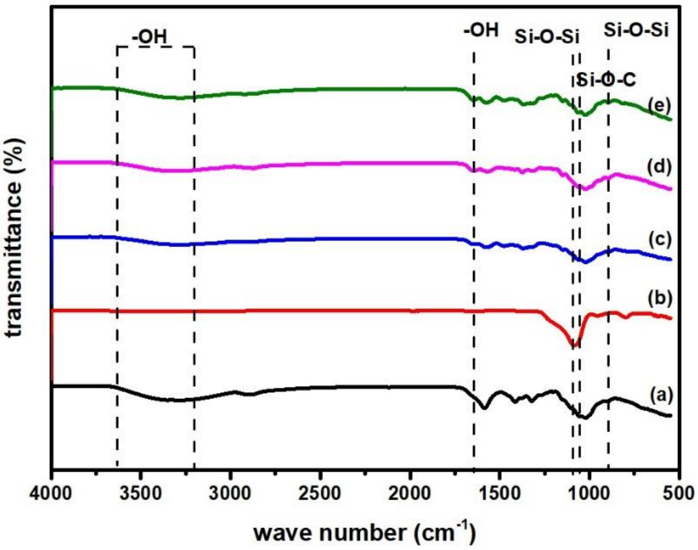


Figure 3. FTIR spectrum (a) chitosan (b) silica and chitosan:silica membrane (c) 1, (d) 2,(e) 3.

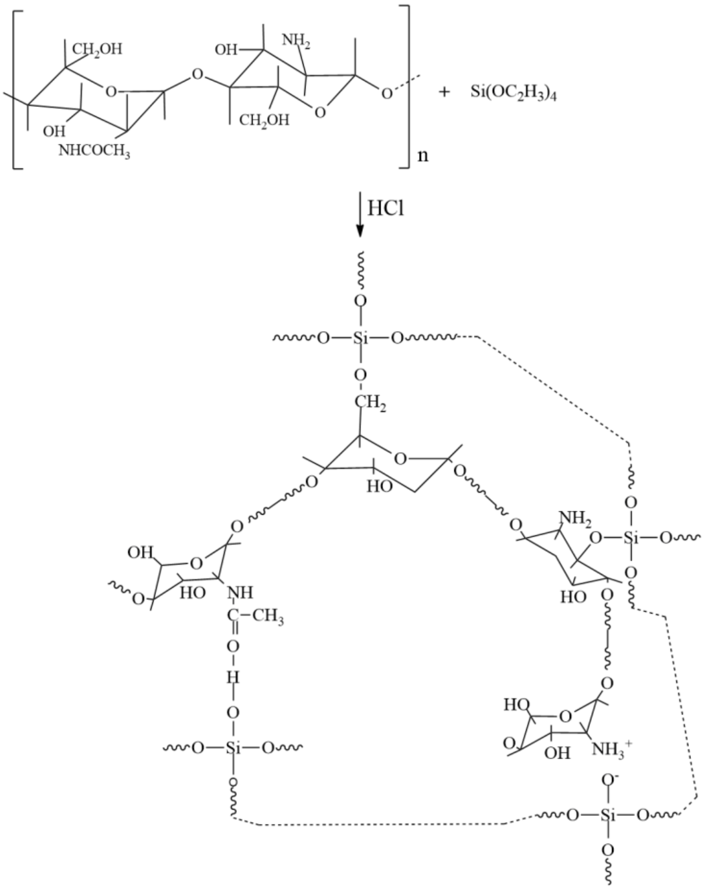


Figure 4. The interaction between chitosan and silica in the membrane ((Silva et al., 2011)

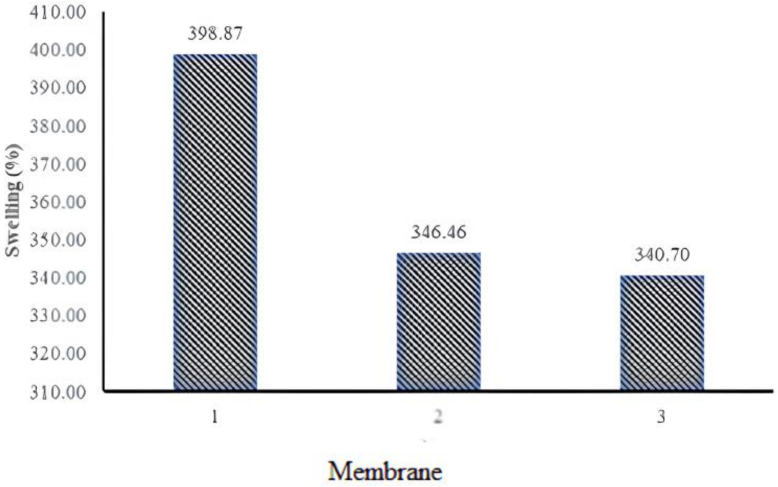


Figure 5. Swelling Test Chitosan-Silica Membranes

The infrared spectrum (**Figure 3**) shows bands at 1110 to 1000 cm^{-1} corresponding to Si-O-R asymmetric stretching and hydroxyl groups (3700-3400 cm^{-1}). Other characteristic bands were observed at 950 cm-1 (Si-O-Si axial deformation). These results indicate that in The chitosan-silica membrane contains an active site, (Si-O- groups) which are able to bond with metal ions. The interaction between chitosan and silica in the membrane shows in **Figure 4**.

Swelling Test

The swelling test aims to predict the size of substances that can diffuse into the membrane. Swelling also indicates that there are voids between the bonds in the polymer. The results of testing the water absorption capacity of the chitosan-silica membrane are explained in **Figure 5**.

The addition of silica to chitosan in a composite membrane can significantly affect the swelling behavior. Chitosan is inherently hydrophilic due to its abundant hydroxyl and amine groups, which can readily interact with water molecules, leading to significant swelling. Silica is also hydrophilic, but its presence in the composite can influence the extent and rate of water absorption. It can also be seen that the less silica added to the membrane, the higher the percentage yield of swelling. Lower silica content or higher chitosan concentration makes the distance between the molecules in chitosan closer, reducing the pores formed in the membrane. As a result, the water diffusivity into the membrane, making it difficult for water to diffuse into the membrane, which causes decreasing its ability to expand.

Tensile Test

The mechanical strength of the hemodialysis membrane needs to be evaluated to provide an illustration of how well the membrane can withstand fluid pressure. In **Table 1**, the mechanical strength of the chitosan-alginate membrane is presented. The tensile strength at break (tension) decreases with decresing chitosan concentration, this is because the more chitosan content, the tighter the pores.

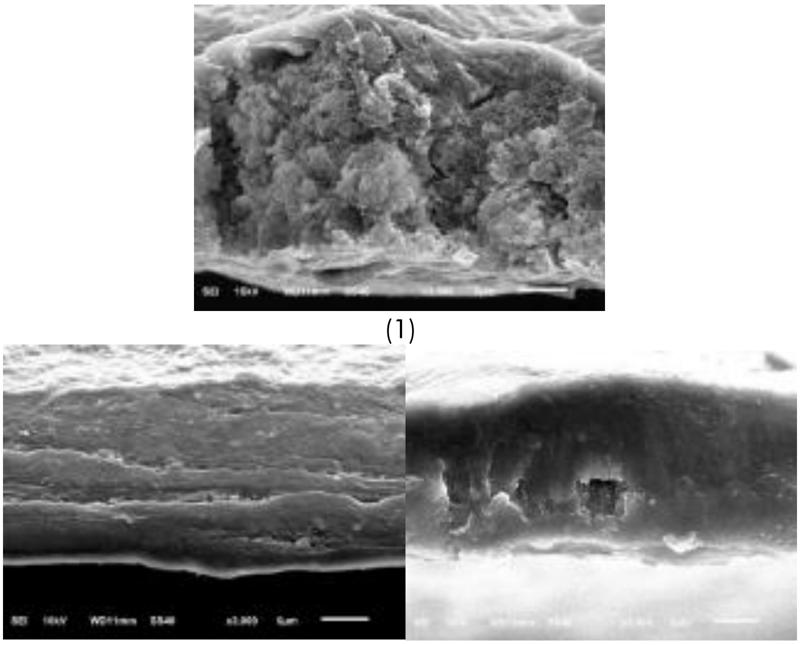
Morphological Analysis with SEM

The addition of the chitosan-silica composition has an influence on the resulting membrane pores, where the greater the chitosan-silica composition used in the membrane manufacturing process. This is proven using SEM testing which is presented in **Figure 6**.

As the silica content increases (**Figure 6.1**), the surface morphology changes significantly. The SEM images reveal a rougher surface with a higher density of silica particles. These particles may appear as clusters or agglomerates, depending on their dispersion within the chitosan matrix. At higher silica ratios, there is a tendency for silica particles to agglomerate. SEM images may show larger, irregularly shaped clusters of silica, indicating poor dispersion. This agglomeration can lead to heterogeneities in the composite's microstructure, affecting its mechanical and swelling properties. At low silica concentrations (**Figure 6.2-3**), the SEM images typically show a relatively smooth surface dominated by the chitosan matrix. Small, evenly distributed silica particles may be visible, but their impact on the overall morphology is minimal.

Table 1 Tensile Test Results

Membrane Variations	Tensile Strenght (MPa)	Strain (%)
1	31.74	10.37
2	18.28	5.57
3	14.92	4.08


(1)

(2) (3)

Figure 6. Morphology analysis of chitosan:silica membrane

Transport Studies Using Chitosan-Silica Membranes

Creatinine

Chitosan-silica membrane used for creatinine transport. The carrier compound is a determining factor in the separation performance from the source phase to the permeate phase. Creatinine transport was chosen because the molecular weight of creatinine (molecular weight 113 g/mol) is higher than urea so that if creatinine can be transported then urea (molecular weight 60 g/mol) can also be transported. A larger molecular weight can be analogous to a large molecular size. Creatinine transport can occur due to the presence of active groups on the membrane. Creatinine transport results are shown in **Figures 7-8**.

Creatinine transport on the chitosan-silica membrane reached maximum transport at the sixth hour. The highest transport for each type of membrane was at a concentration of 100 mg/L. This results was obtained that optimal creatinine transport was carried out on membrane type 1 with a creatinine transport percentage of 48.60%. The result of this type of membrane is due to the existence of a match between the number of active groups forming hydrogen bonds in the carrier compound and the density between the active groups of the carrier compound (cavities formed) in the membrane.

Urea

The amount of urea that interacts with the polymer is one of the important things that will determine the performance of the membrane when used for transport applications. **Figures 9-10** explain the results of urea transport with membrane variations, it can be seen that urea transport has the same tendency as creatinine transport. The more chitosan, the less urea that is transported to the acceptor phase in the same time. Membranes with higher silica content may exhibit reduced urea transport rates due to lower swelling and smaller pores, which restrict the movement of urea molecules.

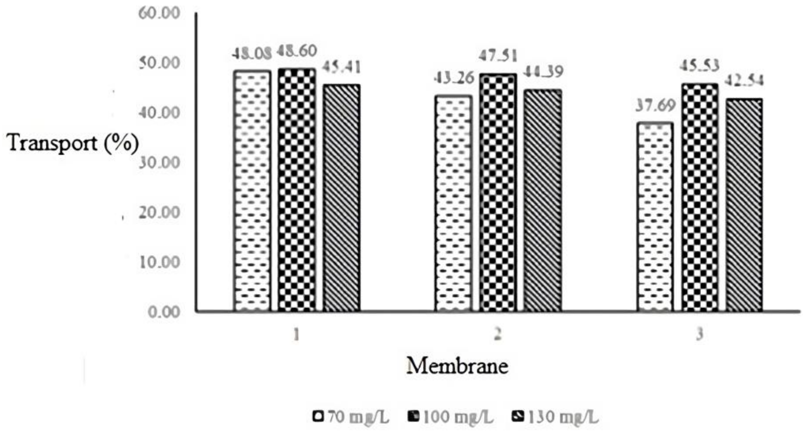
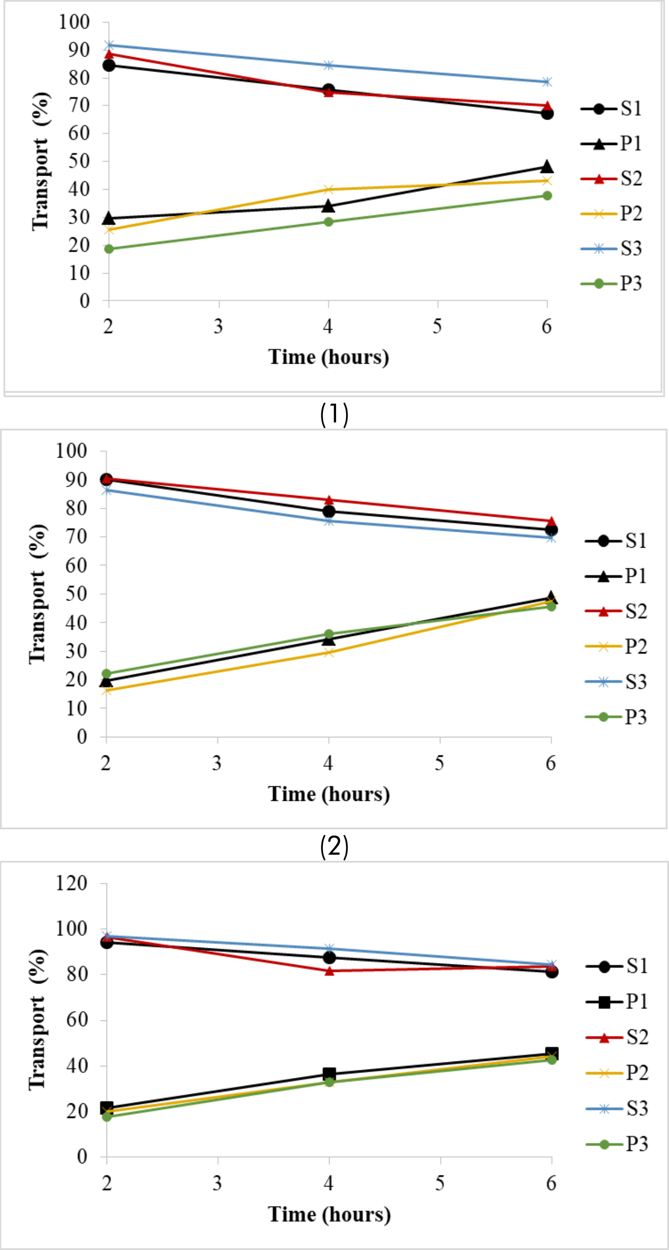


Figure 7. Results of creatinine transport of chitosan:silica membrane.



(1)

(2)

(3)

Figure 8. Results of creatinine transport of chitosan:silica membrane (**1**) 70 mg/L, (**2**) 100 mg/L, (**3**) 130 mg/L (S1 =source phase of membrane 1, P1 = permeat phase of membrane 1, S2 =source phase of membrane 2, P2 = permeat phase of membrane 2, S3 =source phase of membrane 3, P3 = permeat phase of membrane 3)

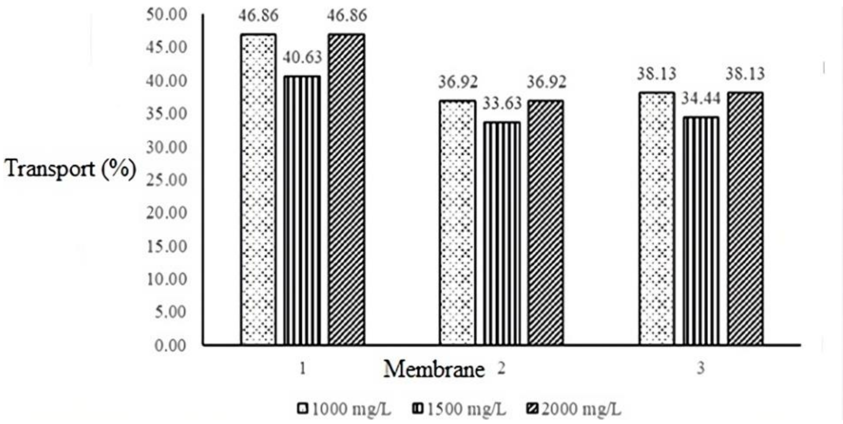
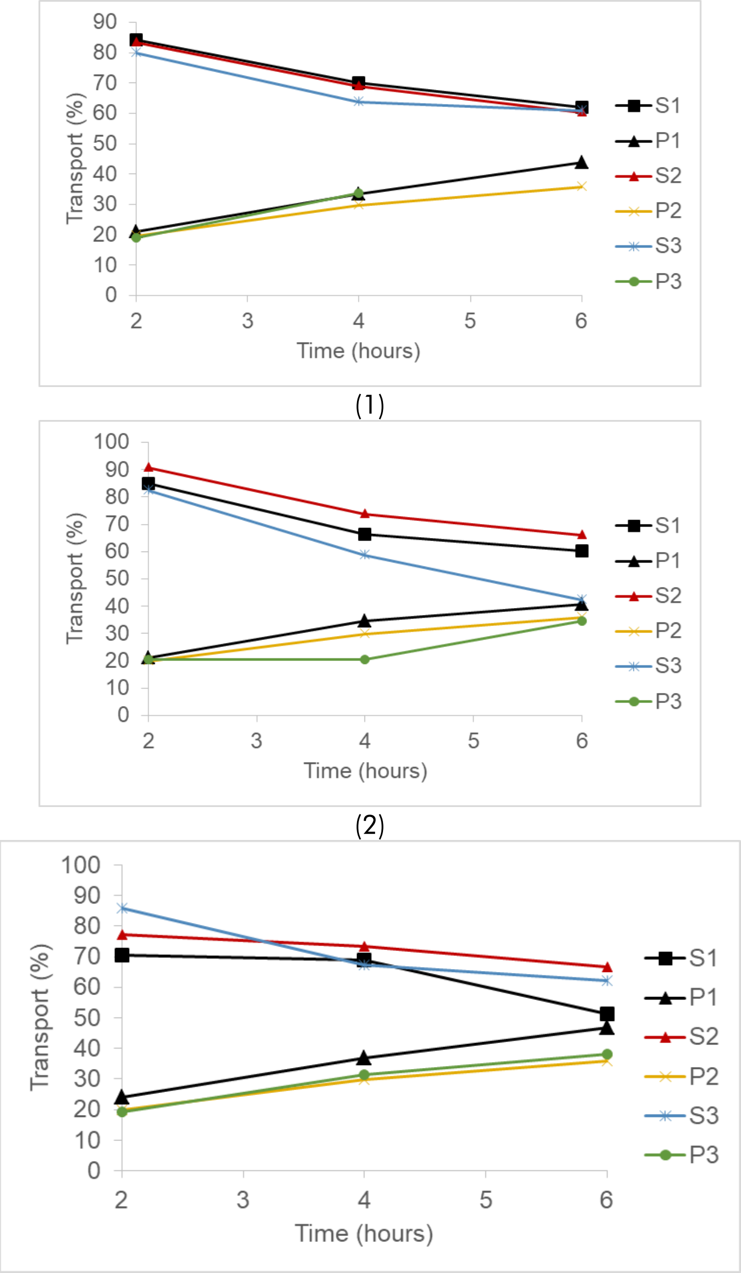


Figure 9. Results of urea transport of chitosan:silica membrane for 6 hours.



(1)

(2)

(3)

Figure 10. Results of urea transport of chitosan:silica membrane (**1**) 1000 mg/L, (**2**) 1500 mg/L, (**3**) 2000 mg/L (S1 =source phase of membrane 1, P1 = permeat phase of membrane 1, S2 =source phase of membrane 2, P2 = permeat phase of membrane 2, S3 = source phase of membrane 3, P3 = permeat phase of membrane 3)

CONCLUSIONS

Chitosan-silica membranes have been successfully characterized based on IR spectrum data, swelling test and stretch pull test. The results of the FTIR test showed the presence of a Si-O function cluster that appears at a wave number of 897-894 cm^{-1}, indicating the formation of silica polymers that interact with the chitosan on the membrane. The result of the six-hour swelling test was 398.87% and the results of the stretch pull test were 31.74 MPa and the membrane stretch was 10.37%. Creatinin transfer results on the chitosan-silica membrane with concentration variations of 70, 100 and 130 mg/L respectively with chitosan:silica membrane 1. Maximum creatinin transport efficiency results at a concentration of 70 mg/L Urea transport results on chitosane-silica membranes with concentrations variation of 500, 1000 and 1500 mg/L respectively chitosan:silica membrane 1. These results showed the potential as a hemodialysis membrane.

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