

Optimization of Chitosan–Carboxymethyl Chitosan Membrane Modification with PVA to Increase Creatinine and Urea Permeation Efficiency

Riska Nurfirda Annisa¹, Retno Ariadi Lusiana^{1,*}, Gunawan¹, Hasan Muhtar¹



¹ Department of Chemistry, Faculty of Science and Mathematics, Diponegoro University, Semarang 50275, Indonesia

* Corresponding author: retno.lusiana@live.undip.ac.id

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Abstract

Polyvinyl alcohol (PVA) modified chitosan-carboxymethyl chitosan (CMC) membrane has been successfully fabricated and used as a dialysis membrane. This research aims to examine the manufacturing process, characterization, and dialysis performance of CMC and PVA-modified chitosan membranes. The membrane used the phase inversion method in acetic acid solvent with 5 CS:CMC:PVA dope compositions. Based on FTIR data, the modification process did not produce new spectra. Furthermore, the interaction produces a membrane with higher physical characteristics in terms of porosity, swelling, water uptake, hydrophilicity, and pH resistance values, which increase by 1.5–115%. Meanwhile, chitosan modification makes the membrane structure different from the original, requiring a longer degradation time. The modification also increased the permeation ability of urea by 17–65% and creatinine permeation by 20–62%. Membranes have the ability to be used more than once.

1. Introduction

High levels of urea and creatinine in the blood indicate that the kidneys are failing and require an artificial kidney/dialyzer [1]. The most important component in dialysis equipment is the membrane, which functions to control the permeation of urea and creatinine from the blood out of the body without losing important blood proteins such as albumin and fibrinogen. The dialysis membrane must be inert, porous, high contact area, selective, permeative, do not adsorb protein, and biocompatible, and the pore size must match the size of the waste permeate [2, 3].

In general, dialysis membranes are made from polymers in the form of hollow fiber. This type of membrane has high competence in separation systems because of its high area/unit volume, flexibility, inertness, and low operational costs [4]. Some natural and synthetic polymers such as cellulose, chitosan (CS), alginate, polyethersulfone (PES), polysulfone (PSf), and cellulose acetate (CA) have been used as a membrane material [5, 6, 7, 8]. Chitosan membranes are starting to be developed for dialysis because they are compatible, pH

stable, mechanical strength, and chemically inert. However, pure chitosan membranes are dense and less permeative, so many species are trapped on the membrane surface, which results in membrane fouling [9]. This results in a decrease in permeation ability.

A series of studies have been carried out to increase the porosity and permeability of chitosan through modification, both through functional groups and membrane structure. Lusiana *et al.* [10] grafted heparin to increase the number of active sites in chitosan. Several researchers have carried out grafting to increase the active side of chitosan, including using citric acid, carboxymethyl cellulose, and graphene oxide [11, 12, 13]. In addition, membrane porosity can be increased through alloying using polyvinyl alcohol (PVA), polyvinylidene fluoride (PVDF), and polyvinyl pyrrolidone (PVP) [3, 14, 15]. In this research, chitosan was used as the main membrane material. To improve membrane performance, modifications were made using carboxymethyl chitosan, which functions to increase the number of active sites through the formation of electrostatic interactions, and the alloy uses polyvinyl alcohol (PVA) to increase membrane porosity [16].

2. Experimental

2.1. Materials

Chitosan (MW = 132.000, DD = 87%) and carboxymethyl chitosan (CMC) were supplied by Biotech Surindo Co., Indonesia. Other analytic reagents such as polyvinyl alcohol (PVA), acetic acid (CH₃COOH), sodium hydroxide (NaOH), p-Dimethylaminobenzaldehyde (DMAB), creatinine, picric acid, urea, and ethanol were purchased from Merck.

2.2. CS-CMC Membrane Modification

Chitosan (0.5, 1, and 2 g) was each dissolved in 100 mL acetic acid 5% with a stirring rate of 300 rpm for 24 h. CS solution (1% w/v) was added to the CMC solution. The mixed solution (15 mL) was poured into a petri dish, and the solvent was evaporated at 60°C. Then, 4 M NaOH solution was added until the membrane was separated from the petri dish and washed using distilled water until neutral and dried.

2.3. CS-CMC/PVA Membrane Modification

A 1 g of PVA was dissolved in 100 mL distilled water at 60°C with a stirring rate of 300 rpm for 2 h. Then, the CS-CMC and PVA solutions were heated at 60°C with a stirring rate of 300 rpm for 24 h, as in Table 1. The mixed solution (15 mL) was poured into a petri dish, and the solvent was evaporated at 60°C. Then, 4 M NaOH solution was added until the membrane was separated from the petri dish and washed using distilled water until neutral and dried.

2.4. Membrane Characterization

Membrane chemical characterization includes functional groups using FTIR (Fourier Transform-Infra Red, Agilent Cary 630), crystallinity using XRD (X-ray Diffraction, Rigaku Miniflex 600), membrane surface morphology using FESEM (Field Emission Scanning Electron Microscopy, Thermo Scientific Quattro S), and creatinine and urea permeation tests using a UV-Vis spectrophotometer (PG T60). The resulting membranes were also characterized based on physical properties, including mass and thickness, porosity, swelling, water uptake, hydrophilicity, pH resistance, and biodegradation.

2.4.1. Mass and Thickness

The membrane mass of each composition was weighed using an OHAUS analytical balance. Membrane thickness was measured using a Mitutoyo thickness

gauge. Membrane mass and thickness measurements were carried out three times for each membrane.

2.4.2. Porosity

All dry membranes were weighed, soaked in 10 mL of distilled water for 24 h, dried and weighed using an analytical balance. The porosity value of each membrane was calculated using Equation (1).

$$\text{Porosity (\%)} = \frac{w_{\text{wet}} - w_{\text{dry}}}{v \times \rho_w} \times 100\% \quad (1)$$

where v is the membrane volume, and ρ is the density of water.

2.4.3. Swelling

The dry membrane diameter was measured using a ruler with five predetermined points. Then, the membrane was soaked in 10 mL for 24 hours, and the diameter was measured again. The value of the degree of expansion for each membrane was determined using Equation (2).

$$\text{Swelling (\%)} = \frac{w_{\text{wet}}}{w_{\text{dry}}} \times 100\% \quad (2)$$

2.4.4. Water Uptake

All dry membranes were weighed and then soaked in distilled water (20 mL) at room temperature for 1-6 h. Every 1 h, the membrane was removed, wiped with tissue, and weighed. The water absorption percentage was calculated using Equation (3).

$$\text{Water uptake (\%)} = \frac{w_{\text{wet}} - w_{\text{dry}}}{w_{\text{dry}}} \times 100\% \quad (3)$$

2.4.5. Hydrophilicity

All dry membranes with flat surfaces were dropped with a drop of water from the surface of the membrane. Then, the contact angle was determined based on the resulting image to calculate the hydrophilicity of the membrane.

2.5. Stability of membrane

2.5.1. Resistance to pH

The resistance of the membrane to pH is determined by immersing it in various types of pH solutions, namely acidic, neutral, and basic. All dry membranes were weighed. The membrane was soaked in 10 mL of various pH solutions, including 3, 5, 7, 9, and 11, for 24 h. The mass of the membrane immersed in solutions of various pH was weighed. The resistance of the membrane to pH was determined using Equation (4).

$$\text{pH} = \frac{w_{\text{dry}} - w_{\text{wet}}}{w_{\text{dry}}} \times 100\% \quad (4)$$

Table 1. Composition of dope chitosan, carboxymethyl chitosan, and polyvinyl alcohol

Membrane type	Composition of dope (w/w, %)		
	Chitosan	Carboxymethyl chitosan	PVA
CS	1	0	0
CS-CMC	1	1	0
CCP1	1	0.5	1
CCP2	1	1	1
CCP3	1	2	1

Note: CCP : CS-CMC/PVA

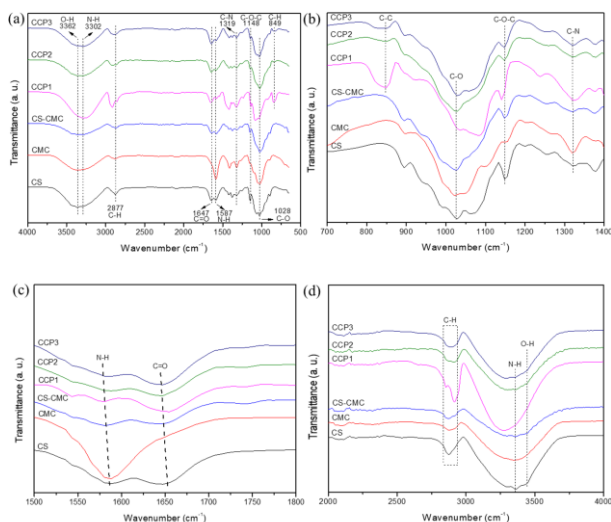


Figure 1. FTIR spectra of pure chitosan, CMC, CS-CMC and CCP at (a) 4000–500 cm⁻¹, (b) 700–1400 cm⁻¹, (c) 1500–1800 cm⁻¹, and (d) 2000–4000 cm⁻¹

2.5.2. Biodegradation

All dry membranes were weighed and then planted in soil that had been given fertilizer for 8 weeks. Every week, the membrane mass was weighed to determine the decrease in membrane mass. Membrane biodegradation was calculated using Equation (5).

$$\text{Biodegradation (\%)} = \frac{W_{\text{initial}} - W_{\text{final}}}{W_{\text{initial}}} \times 100\% \quad (5)$$

2.6. Membrane Permeability Test

The membrane permeation test on urea and creatinine solutions was carried out using transport equipment consisting of two cylindrical chambers of glass connected and in the middle placed the membrane to be analyzed. The source phase was filled with 1.5 mg/dL (creatinine solution) or 25 mg/dL (urea solution), and the acceptor phase was filled with phosphate buffer solution (PBS) with a volume of 45 mL each. The permeation process lasted for 6 h with 2 mL of solution taken from both the source and acceptor phases every hour, then mixed with 2 mL of complexing reagent, and the absorbance was measured using a UV-Vis spectrophotometer at a wavelength of 486 nm for the creatinine-picric acid complex and 425 nm for the urea-DMAB complex. The clearance value was used to compare urea or creatinine levels at the initial time with the final time.

3. Results and Discussion

3.1. Membrane Characterization

The membranes were assessed through various analyses. Structural analysis and interaction modes were characterized using FTIR. XRD analysis was conducted to determine the membrane's phase, while FESEM analysis provided insights into its surface morphology. Additionally, the physicochemical properties of the membrane, including mass, thickness, porosity, degree of swelling, water uptake, and hydrophilicity, were also evaluated.

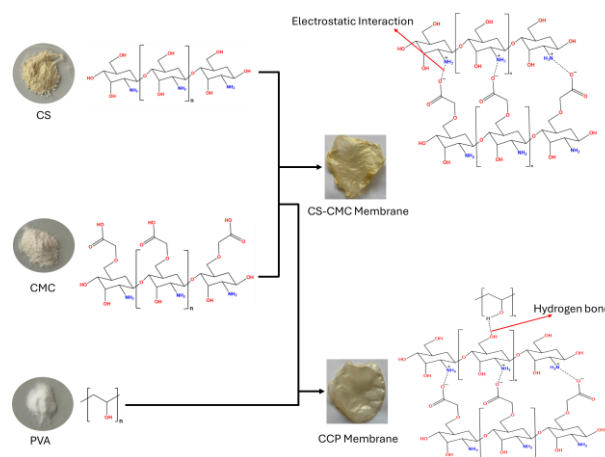


Figure 2. Proposed structure and interaction of chitosan-carboxymethyl chitosan/polyvinyl alcohol

3.1.1. Chemical Structure and Binding Mode Analysis

Figure 1a shows the FTIR spectra of chitosan (CS), carboxymethyl chitosan (CMC), chitosan-carboxymethyl chitosan (CS-CMC), and CCP at various dope compositions. The spectral characteristics of chitosan are specifically shown in the 1587 and 1647 cm⁻¹ areas, which are the primary vibrations of N-H (amide I) and C=O (amide II); the C-N stretch in chitosan is observed in 1319 cm⁻¹ [17]. The sharp peak of CMC in 1587 cm⁻¹ indicates the presence of N-H (amide I) primary vibrations [18]. The characteristic peak of polyvinyl alcohol is evident at an absorption of 849 cm⁻¹, which corresponds to the presence of C-C stretching [19]. Absorptions found in the range of 3362, 3302, 2877, 1148, and 1028 cm⁻¹ across all membranes are attributed to O-H stretching, N-H stretching, C-O-C asymmetric stretching, and C-O stretching, respectively [20]. The modification of chitosan (CS) with carboxymethyl cellulose (CMC) does not result in any new peaks, indicating that the mixing reaction between CS and CMC involves only electrostatic interactions rather than the formation of new chemical bonds [21].

Figure 1b shows the appearance of a new peak in the 849 cm⁻¹, which is related to the C-C strain due to the addition of PVA. This indicates the presence of strong miscibility in the CCP membrane. The peaks of C-O and C-O-C strain in the 1028 and 1148 cm⁻¹, respectively, experienced a shift. Figure 1c shows the N-H bending shift (1587 cm⁻¹) and C=O stretching (1647 cm⁻¹), along with the mixing reaction between chitosan with CMC and PVA. This intensity shift indicates an electrostatic interaction that causes a change in characteristics.

In addition, a decrease in intensity occurs in the 1647 cm⁻¹ (C=O strain) as the concentration of CMC added increases. Figure 1d shows that the N-H (3362 cm⁻¹) and O-H (3302 cm⁻¹) strain peaks on the CS-CMC and CCP membranes experienced widening and shifting towards higher wavenumbers. The peak in 2877 cm⁻¹ is the C-H stretching, which is found in all membranes. The interaction between chitosan, CMC, and PVA is illustrated in Figure 2.

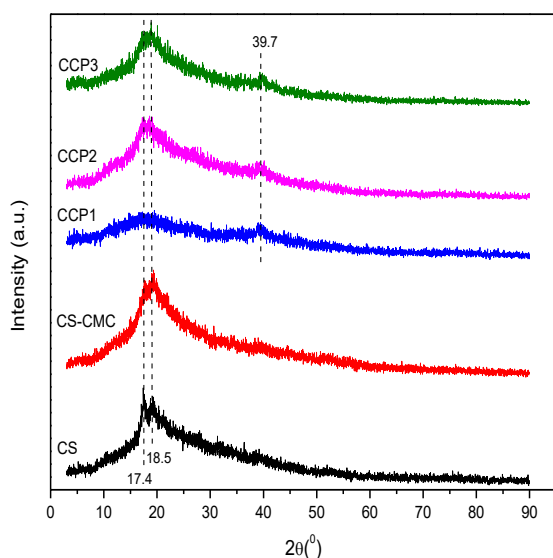


Figure 3. XRD patterns of pure chitosan, CS-CMC, and CCP

3.1.2. XRD Analysis of Membrane

Crystallinity analysis using XRD was carried out on all membranes presented in Figure 3. Crystal peaks at 2θ of 17.38° and 18.5° were found in the XRD pattern of pure chitosan. The broad peaks observed in the XRD pattern around 10° of 2θ indicate the average intermolecular distance of the amorphous part, and small peaks are centered at around 20° of 2θ [22]. The new crystal peak at 2θ is 39.7° (which indicates the PVA peak) found in the CCP membrane pattern [23]. The CCP membrane pattern consists of characteristic reflections of CS, CMC, and PVA. The peak intensity decreases and becomes broader, implying that CS, CMC, and PVA are complex and can mix well and form a homogeneous mixture. This indicates that pure chitosan, CS-CMC, and CCP are amorphous.

3.1.3. Surface Structure of Membrane

According to Figure 4a, the pure chitosan membrane contains fewer pores and exhibits non-uniformity. In contrast, the CS-CMC membrane (Figure 4b) shows more pores distributed across the membrane body, resulting in a smoother and denser surface. The incorporation of PVA into the CCP membrane increases the asymmetry of the pores on the membrane surface [24]. Thus, the CCP membrane (Figure 4c-e) becomes more hydrophilic and has low fouling, high mechanical strength, and strong pH stability. This shows that modifying chitosan with CMC and PVA enhances the membrane's porosity.

Table 2. Mass and thickness of pure chitosan and modified membranes

Membrane type	Mass ($\times 10^{-1}$ g)	Thickness ($\times 10^{-3}$ mm)
CS	2.33	1.26
CS-CMC	2.19	1.21
CCP1	2.28	1.15
CCP2	2.24	1.13
CCP3	2.23	1.11

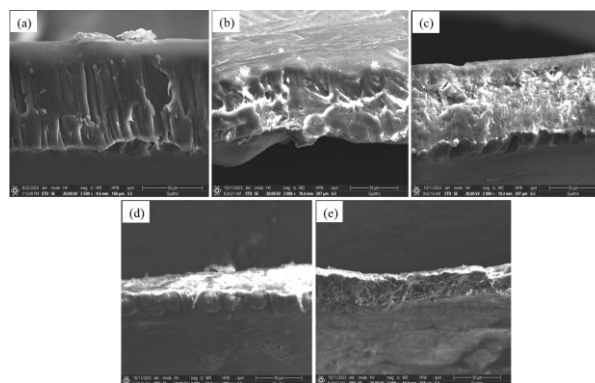


Figure 4. Membrane morphologies of (a) pure chitosan, (b) CS-CMC, (c) CCP1, (d) CCP2 and (e) CCP3

3.1.4. Physicochemical Properties of Membranes

The mass and thickness values of the membrane indicate the uniformity of its composition [25]. The more composition that makes up the membrane, the higher the mass and thickness values of the membrane. The mass and thickness of pure chitosan and modified membranes are presented in Table 2. Membrane porosity is a crucial factor in determining permeation performance and water flux during dialysis [26]. Greater membrane porosity results in improved permeation and water flux. The pores create spaces that can be filled by water, so larger membrane pores provide more opportunities for water absorption [27].

The porosity of pure chitosan and modified membranes is shown in Table 3. The data in Table 3 indicates that membrane porosity increases with modification. The significant increase in porosity demonstrates that CMC and PVA integrate into the chitosan structure, forming pores throughout the membrane body. This observation aligns with Salmasi *et al.* [28], who stated that incorporating highly hydrophilic CMC and PVA into the membrane structure enhances membrane porosity.

The degree of swelling indicates the membrane's ability to expand within a solution system. Water-filled cavities within the membrane influence its expansion ability as the membrane size increases [29]. The swelling of pure chitosan and modified membranes are presented in Table 3. Based on Table 3, it can be seen that the swelling of the membrane has increased with modification. The porous structure of the membrane body due to the inclusion of CMC and PVA in the membrane body affects the ability of the membrane to adsorb water in the membrane environment [30].

Table 3. Porosity, swelling, water uptake, and contact angle of pure chitosan and modified membranes

Membrane type	Porosity (%)	Swelling (%)	Water uptake (%)	Contact angle ($^\circ$)
CS	6.52	102.45	5.55	59.45
CS-CMC	10.55	103.94	8.77	48.65
CCP1	10.14	103.48	8.49	51.53
CCP2	12.67	104.77	10.04	32.33
CCP3	16.59	110.37	11.97	28.20

Table 4. Creatinine and urea permeation

Membrane type	Permeation (%)	
	Creatinine	Urea
CS	23.68	27.81
CS-CMC	31.87	33.68
CCP1	28.57	32.73
CCP2	33.88	38.22
CCP3	38.50	46.04

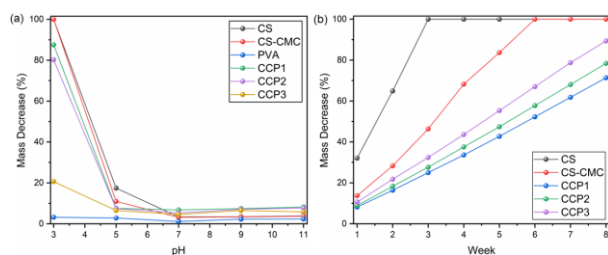


Figure 5. (a) decreased mass of pure chitosan and modified membranes under various pH conditions (b) degradation mass of pure chitosan and modified membranes

The water absorption capacity of pure chitosan and modified membranes is presented in Table 3. The water absorption value increases with increasing concentrations of CMC and PVA. The highest water absorption capacity was obtained on the CCP3 membrane, which was equal to 11.97%. The water uptake capacity value can be influenced by the active groups and the distribution of pores on the membrane surface. The carboxyl group (-COOH) in CMC facilitates interaction between the membrane and water molecules [31].

The contact angles of pure chitosan and modified membranes are shown in Table 3. According to Table 3, the modification reduces the membrane contact angle. This decrease becomes more pronounced with increasing amounts of CMC, resulting in the membrane becoming more hydrophilic [32, 33].

3.2. Stability of Membranes

3.2.1. Resistance to pH

The decrease in mass resistance of pure chitosan and modified membranes under various pH conditions is presented in Figure 5a. Chitosan-based membranes are damaged in acidic conditions (pH 3 and 5), except for those modified with PVA, which remain resilient against acidity. In neutral to alkaline environments (pH 7-11), all membranes exhibit only a slight reduction in mass, indicating their stability in these conditions. This aligns with the research by Ma *et al.* [34] that neutral and alkaline solutions that enter the membrane will cause deprotonation of the polymer at the amine group. As a result, the amine group acquires a negative charge, becoming more hydrophobic.

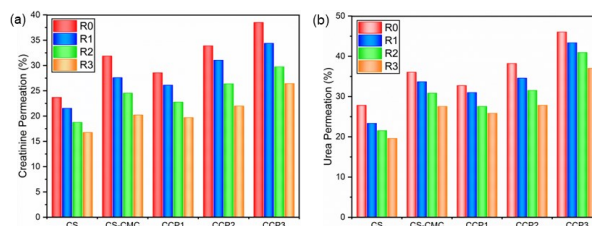


Figure 6. Test the repeatability of membrane used in the permeation process of (a) creatinine and (b) urea. R0: initial state of membrane, R1: first repetition, R2: second repetition, R3: third repetition

3.2.2. Biodegradation

Membrane biodegradation is the main benchmark for environmentally friendly membranes [35]. The degree of membrane decomposition can be influenced by the activity of soil microorganisms. Figure 5b shows the reduction in degradation mass for pure chitosan and modified membranes. The degradation rate of pure chitosan is faster compared to modified chitosan membranes. This aligns with research by Zong *et al.* [36] that chitosan is a biopolymer compound that can be degraded quickly. Meanwhile, modifications to chitosan make the membrane structure different from the original. These structural changes require microorganisms to spend more time recognizing and adapting their enzymes to degrade the membrane, which increases the time required for decomposition.

3.3. Membrane Permeability Test

The most important property in dialysis membranes is permeability. The results of creatinine and urea membrane permeation are shown in Table 4. Creatinine permeation increased by 20-62%, and urea permeation increased by 17-65% as the concentration of CMC in the membrane body increased. This enhancement in permeation demonstrates that the additional functional groups of CMC effectively recognize and bind urea and creatinine, facilitating their transport and subsequent release on the permeate side. In this study, the urea permeation value exceeded that reported in previous research conducted by Lusiana *et al.* [29]. Specifically, the urea permeation results using a sulfonated PEG/PVDF membrane were only 39.66%. This underscores the superior performance of the present investigation.

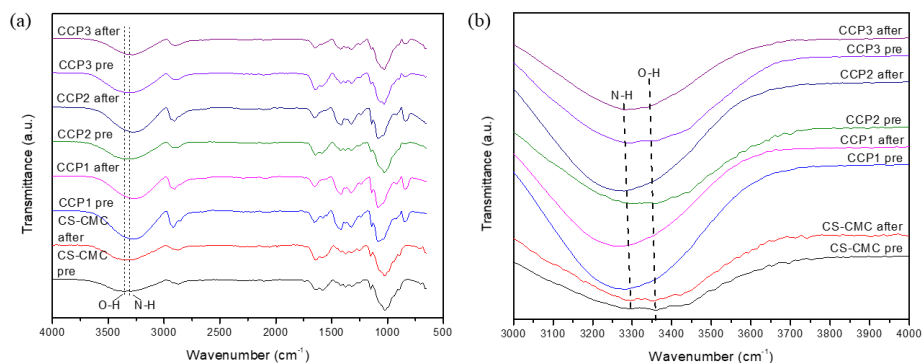


Figure 7. FTIR spectra of the membrane before and after the creatinine permeation process of (a) 4000–500 cm^{-1} and (b) 3000–4000 cm^{-1}

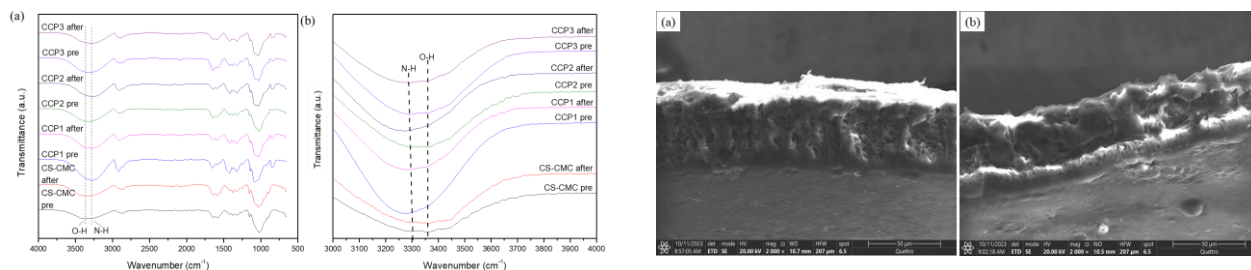


Figure 8. FTIR spectra of the membrane before and after the urea permeation process (a) 4000–500 cm^{-1} and (b) 3000–4000 cm^{-1}

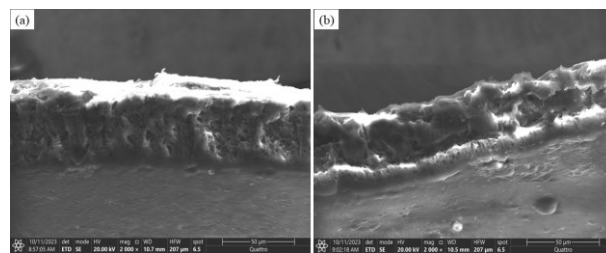


Figure 9. CCP3 membrane morphology after the permeation process of (a) creatinine and (b) urea

The repeatability test of the membrane used in the permeation process was conducted to evaluate the performance of membranes previously utilized. The membrane permeation process was repeated three times. Data on the repeatability of membranes used in the creatinine and urea permeation process are shown in Figure 6. An FTIR analysis was performed to assess the repeatability of the membrane during the permeation process, providing insight into functional changes in pure and modified chitosan membranes. These functional changes, observed after repeatability testing, are shown in Figures 7 and 8. Figure 6 shows a decline in the permeation repeatability of the used membrane. This is likely due to the fouling process, where the target compounds (creatinine in Figure 6a and urea in Figure 6b) become trapped on the membrane surface.

The spectra presented in Figures 7 and 8 reveal differences between the membrane spectra before and after use in the repeatability test. A significant shift occurs in the O-H and N-H group spectra, in the 3200–3400 cm^{-1} range. This shift is likely due to electrostatic interactions between urea and creatinine and the hydroxyl or amine groups. These shifts also suggest hydrogen bonding between the membrane, creatinine, and urea [26].

Figure 9 shows that the CCP3 membrane pores become fewer after the creatinine and urea permeation process. This indicates that fouling occurred during the permeation process. Target compounds (creatinine and urea) are trapped on the membrane surface of the filtration system, and the shelf life of the membrane [37].

4. Conclusion

Membranes made from chitosan with a mixture of CMC and PVA have been successfully prepared and physically and chemically characterized. Based on the SEM image, the membrane becomes more porous with modification. Modification with CMC and PVA can increase the porosity, swelling, water uptake, and hydrophilicity of the membrane. However, modification reduces the membrane degradability. CMC and PVA enter the chitosan structure homogeneously, not through chemical reactions but through electrostatic interactions. Membrane permeation increased with increasing concentration of added CMC. Urea permeation increased by 17–65%, and creatinine permeation increased by 20–64%. The membrane can be consistently used repeatedly but experiences a decrease in permeation of 10% from the first use.

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