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Modelling Urea and Creatinine Concentration Distribution in Hollow Fiber Membranes for Hemodialysis Applications

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ABSTRACT: Humans are dynamic creatures who continue to follow developments over time. This development also has a big impact on changes in habits and has an impact on the health of everyone, which needs special attention in this era of globalization. One of the treatments for kidney failure patients is kidney function replacement therapy, namely haemodialysis. Haemodialysis therapy is a high technology to replace the function of the kidneys in removing metabolic waste (air, sodium, potassium, hydrogen, urea, creatinine, uric acid and other substances) through a semi-permeable membrane as a separator for blood and dialysate fluid in an artificial kidney (dialyzer). where the processes of diffusion, osmosis, and ultrafiltration occur. In this study, a hollow fiber type dialyzer was used which consisting of three main components: the shell (which directs dialysate flow), the porous membrane, and the tube (which carries blood). In general, this research will be carried out theoretically by developing a mathematical model of mass transfer in hollow fiber membranes in the haemodialysis process to study the distribution of urea and creatinine concentrations in the tube, membrane, and shell axial and radial section, the effect of pore area of membrane on urea and creatinine clearance, and the influence of dialysate flowrate on urea and creatinine clearance. The mathematical modeling successfully illustrates the distribution of urea and creatinine concentrations within the hollow fiber membrane both axially and radially, with a concentration decrease from blood to dialysate, influenced by diffusion and convection mechanisms. Simulation results indicate that increasing dialysate flowrate enhances haemodialysis efficiency, but its effect diminishes after reaching a certain threshold. Meanwhile, increasing the membrane surface area from 1.3 m^2 to 1.8 m^2 results in only a slight reduction in the urea concentration from 16.67 mol/m^3 to 16.62 mol/m^3 and creatinine from 8.85 mol/m^3 to 8.83 mol/m^3, demonstrating that membrane surface area has a smaller impact.

Keywords: Blood; Dialysate; Hemodialysis; Hollow Fiber; Membrane.

1. Introduction

In 2021, the American Society of Nephrology, the European Renal Association, and the International Society of Nephrology reported that more than 850 million people worldwide suffer from kidney disease, twice as many as people with diabetes and 20 times as many as people with cancer. Hemodialysis is a key renal replacement therapy for managing chronic kidney disease (CKD). In hemodialysis, one of the main components in the dialyzer is the dialysis membrane, which determines the ability of ultrafiltration and the efficiency of removing uremic toxins in the body of patients with renal failure. Dialysis membrane performance is influenced by characteristics such as average pore (porosity), thickness, and tortuosity ratio. Ultrafiltration membranes have pore sizes that are between macrofiltration and nanofiltration membranes, with a pore size range between α 0.05 μm on the macrofiltration side to ±1 nm on the nanofiltration side.

The dialysis membrane, which is in direct contact with the patient's blood extracorporeally, must be able to eliminate etiological substances such as serot2-microglobulin without leaking important substances such as albumin. In hollow fiber membranes, mass transfer processes occur through diffusion and ultrafiltration mechanisms. In addition, dialysates used in hemodialysis therapy play an important role in maintaining plasma osmotic pressure, carbohydrate metabolism, as well as electrolyte and acid-base balance. The dialysate creates the concentration gradient necessary for diffusion phenomena, one of the principles of mass transfer in hemodialysis, along with ultrafiltration and adsorption. To achieve optimal

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dialysis efficiency, the concentration gradient between the blood and the dialysate must be maintained so that it does not reach equilibrium. The dialysate is used continuously in a single flow system in the opposite direction to the blood flow, with a flow rate of about 500 ml/min. Given that the volume of dialysate used in one therapy session reaches 120-150 liters, a machine is needed that can continuously supply dialysate with a stable concentration, sufficient solubility, as well as the ability to remove harmful substances. Hemodialysis process depends on the removal efficiency of urea and creatinine within the hollow fiber membrane. However, research on the simulation or modeling of urea and creatinine concentration distribution along the hollow fiber membrane is still limited. Therefore, this study will analyze the effect of dialysate flow rate and membrane area on the distribution of urea and creatinine concentrations along the hollow fiber membrane in the hemodialysis process.

Chronic kidney disease is a medical condition characterized by a progressive decline in kidney function, often requiring renal replacement therapies such as hemodialysis or kidney transplantation. In 2021, over 850 million individuals globally were reported to suffer from CKD, twice the prevalence of diabetes and 20 times higher than cancer cases (American Society of Nephrology et al., 2021). Hemodialysis serves as a high-technology therapy to perform blood purification, mimicking kidney function by removing metabolic wastes (e.g., urea, creatinine) and excess electrolytes via a semi-permeable membrane known as a dialyzer.

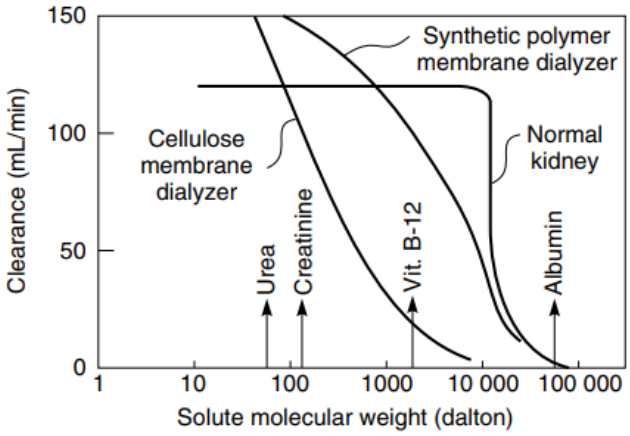

Figure 1. Clearance, a measure of membrane permeability as a function of Molecular Weight for hemodializers and Normal Kidneys

The key component in hemodialysis is the semi-permeable membrane. The efficiency of the dialyzer depends significantly on membrane properties, including pore size, thickness, and tortuosity. Ultrafiltration membranes, with pore sizes ranging between ±0.05 µm and ±1 nm, provide an optimal balance for filtering toxins such as urea (9.16 ± 4 nm) and creatinine (9.08 ± 2 nm) while retaining essential blood proteins like albumin (Rahmawati & Ambarwati, 2017). Hollow fiber membranes are particularly favored due to their high surface area, low blood flow resistance, and efficient mass transfer (Goodarzi & Mohebbi-Kalhori, 2022).

Based on Figure 1, it is known that the cellulose membrane can efficiently remove the main metabolites, urea and creatinine, from the blood, but metabolites with molecular weights between 1,000 and 10,000 Dalton are poorly eliminated. Mass transfer in hemodialysis occurs via diffusion and ultrafiltration mechanisms. Diffusion is driven by a concentration gradient across the membrane, facilitating the removal of small solutes like urea and creatinine into the dialysate. Ultrafiltration, on the other hand, involves fluid movement induced by a transmembrane pressure gradient, which also aids in solvent drag for larger molecules.

$$J = D.\frac{(C_b - C_d)}{\delta} \quad (1)$$

$$M_{urea} = J.A.t \quad (2)$$

The efficiency of these processes is influenced by factors such as dialysate flow rate, membrane porosity, and the operational configuration of countercurrent flow within the dialyzer (Mohanty & Purkait, 2011).

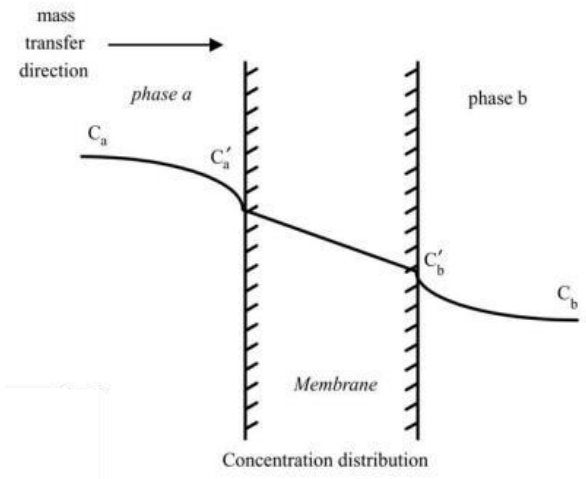

Figure 2. Mass Transfer Mechanism Of Hemodialysis (Yeh & Chang, 2005)

In the porous membrane, mass transfer occurs within it. Diffusion and ultrafiltration are the two mechanisms of mass transport in the membrane shown in Figure 2. Dialysate composition is critical for maintaining osmotic balance, electrolyte correction, and acid-base stability in patients. Continuous flow of dialysate counter to blood flow helps maintain an effective concentration gradient for diffusion. Standard operational settings require a dialysate flow rate of approximately 500 ml/min, consuming 120–150 liters per session, with stringent requirements for chemical stability and biocompatibility to avoid adverse patient reactions (Locatelli et al., 2015; Unair, 2021).

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Research on the modeling and simulation of urea and creatinine distribution within hollow fiber membranes has gained attention due to its potential to optimize dialyzer design. Prior studies highlight that increasing the blood or dialysate flow rate enhances solute clearance, though excessive rates may pose risks (Goodarzi & Mohebbi-Kalhori, 2022; Cancilla et al., 2022).

$$\langle v_2 \rangle \frac{\partial c_A}{\partial z} = D_{AB}\left[\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial c_A}{\partial r}\right)+\frac{\partial^2 c_A}{\partial z^2}\right] \quad (3)$$

However, gaps remain in understanding radial and axial concentration profiles of solutes within hollow fiber membranes, particularly under varying operational conditions.

$$D_{A-membrane}\left[\frac{\partial^2 c_{A-membrane}}{\partial r^2}+\frac{1}{r}\frac{\partial C_{A-membrane}}{\partial r}\right]=0 \quad (4)$$

2. Materials and Methods

This study was conducted theoretically using a mathematical modeling approach to simulate the distribution of urea and creatinine concentrations in the hollow fiber membrane in the hemodialysis process. Modeling is based on the principle of mass transfer, assuming steady-state and laminar flow in the blood and dialysate. Numerical simulations were completed using MATLAB software version R2023b. The variables used in this study are divided into fixed variables, variable changes, and response variables. Fixed variables include membrane physical parameters, solute diffusivity, as well as operating temperature, as summarized in Table 1.

Table 1. Fixed Variable

Parameters	Value	Unit	Description
Temperature	37	^{0}C	Standard human body temperature
Radius in membrane	0.1	Mm	Hollow fiber Dimension (Mulder,1996)
Out radius membrane	0.14	Mm	Hollow fiber Dimension (Mulder, 1996)
Diffusivity urea in blood	1.4x10	M^2/s	Brunner (2010)

Variable changes in this study include variations in dialysate flow rate (200, 300, 400, and 500 mL/min) and membrane surface area (1.3, 1.5, and 1.8 m^2). The selection of variables is based on the boundary conditions observed in the field and the size of the existing commercial membrane surface area. Response variables are changes in urea and creatinine concentrations along the membrane, both axially and radially. Mathematical modeling is applied to describe the distribution of urea and creatinine concentrations in the hollow fiber membrane. The mass balance equation in this system is described in three main domains.

Table 2. Boundary Conditions

Domain	Condition	Location	Description
Tube	$C=C_0$	Z=0	Initial blood concentration
Membrane	$C=C_m$	$r_1<r<r_2$	Diffusion in membrane
Shell	C=0	z=L	Concentration in the end

3. Results and Discussion

3.1. Effect of Blood Flow Rate on Urea and Creatinine Concentrations Radially

Figures 3, 4, and 5 show the effect of blood flow rate on urea and creatinine concentrations radially in the tube, membrane, and shell.

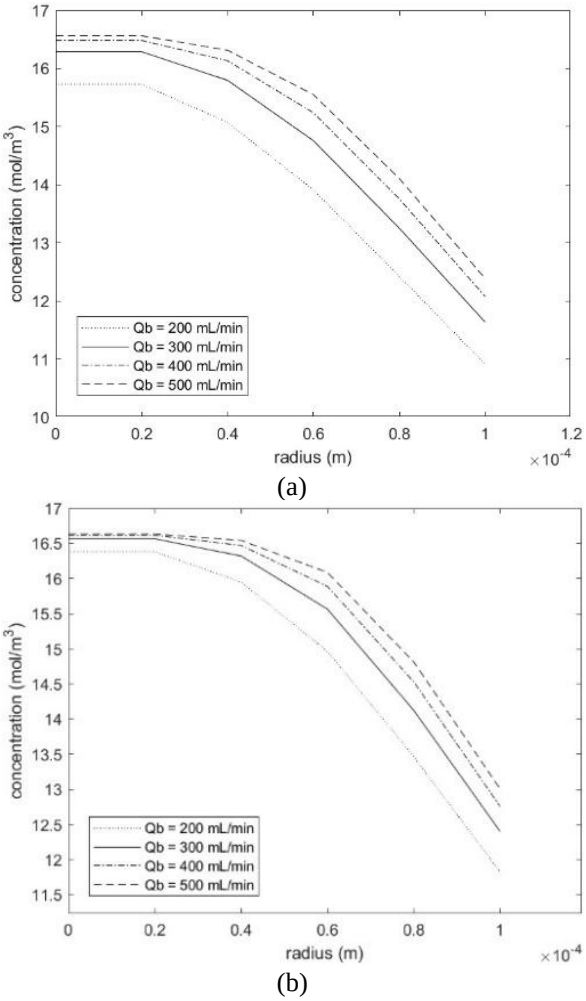

Figure 3. Effect of Blood Flow Rate on the Concentration of (a) Urea and (b) Creatinine in Tube Section

The flow rate of the synthesis solution used is 200, 300, 400, and 500 mL/min. It was found that the smaller the flow rate of the synthesis solution, the greater the concentration of urea and creatinine output at the shell (r = r3).

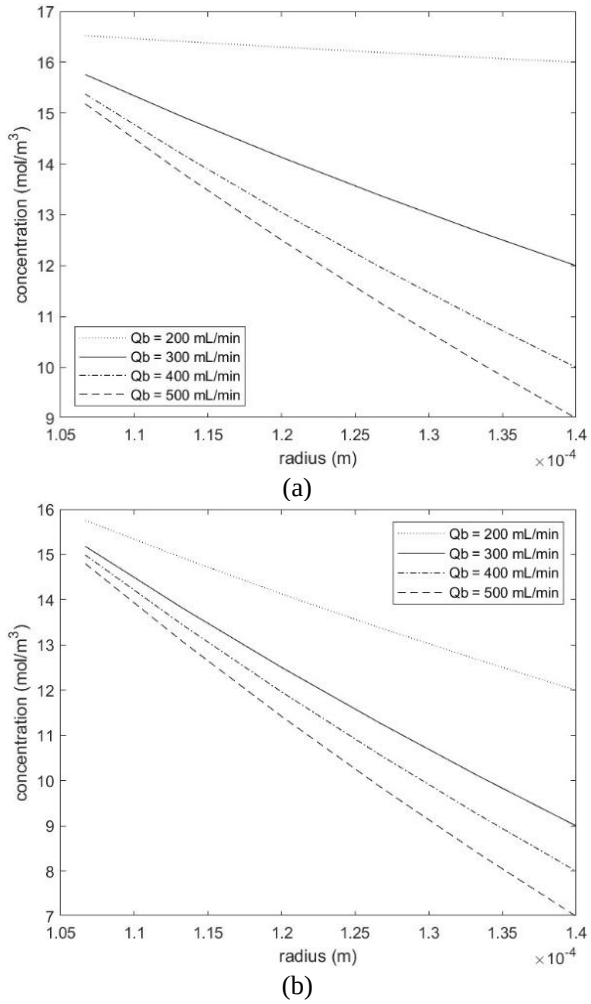

Figure 4. Effect of Blood Flow Rate on the Concentration of (a) Urea and (b) Creatinine in the Membrane Section

Similarly, at r = r2, the smaller the blood flow rate, the greater the concentration of urea and creatinine coming out of the membrane to the shell. This is because with the increasing blood flow rate, the concentration of urea and creatinine coming out of the tube is also getting bigger so that the concentration of urea and creatinine coming out of the shell is getting smaller. This statement is in accordance with research conducted by Goodarzi & Kalhori, 2022. In addition, overall, the concentration of urea and creatinine from r = 0 to r = r3 decreases for all variations in the flow rate of the synthesis solution.

In Figure 3, we can see the effect of blood flow rate on the concentration of urea and creatinine along the radius of the tube. Higher blood flow rates lead to lower concentrations of urea and creatinine exiting the membrane, indicating increased clearance efficiency on the tube, so that the clearance value of urea and creatinine is smaller on the tube. This is because the faster the flow rate of blood, the thinner the film formed between the blood and the membrane. Therefore, the shorter the contact time of blood with the membrane so that urea and creatinine diffuse through the membrane is also less and the concentration of urea and creatinine that comes out on the tube is greater.

Figure 4 illustrates the effect of blood flow rate on the concentration of urea and creatinine along the radius of the membrane section. Higher blood flow rates lead to lower concentrations of urea and creatinine exiting the membrane, indicating increased clearance efficiency.

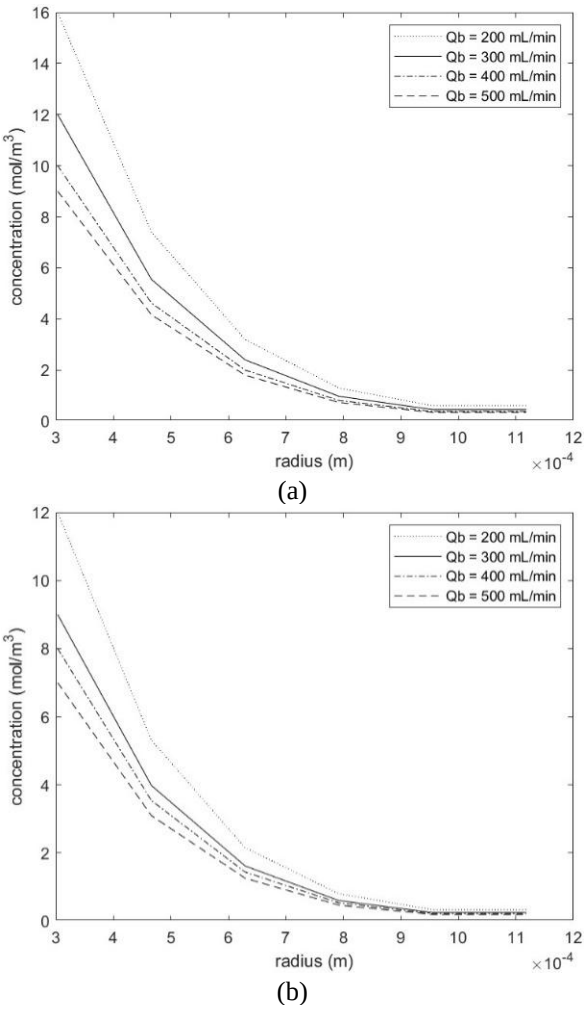

Figure 5. Effect of Blood Flow Rate on the Concentration of (a) Urea and (b) Creatinine in Shell Section

Then, in Figure 5, we can see the effect of blood flow rate on the concentration of urea and creatinine along the radius in the shell section. Higher blood flow rates lead to lower concentrations of urea and creatinine exiting the membrane, indicating increased clearance efficiency. However, as shown in the figure, the change in urea and creatinine concentration at the end is not very significant in each variation of blood flow rate.

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3.2. Effect of Blood Flow Rate on Axial Concentration of Urea and Creatinine

In Figure 7, the effect of blood flow rate on urea concentration axially in the shell (r = r3) can be seen. Dialysate enters the shell at z = L (z = 0.25 m) so that the concentration of urea is 0 mol/m3 at all flow rate variations. Then dialysate comes out at the z = 0 part, it is found that the smaller the flow rate, the greater the concentration of urea that comes out at the dialysate part. This is in accordance with the previous statement that the greater the blood flow rate, the greater the concentration of urea that comes out of the tube so that the concentration of urea that comes out in the shell is smaller.

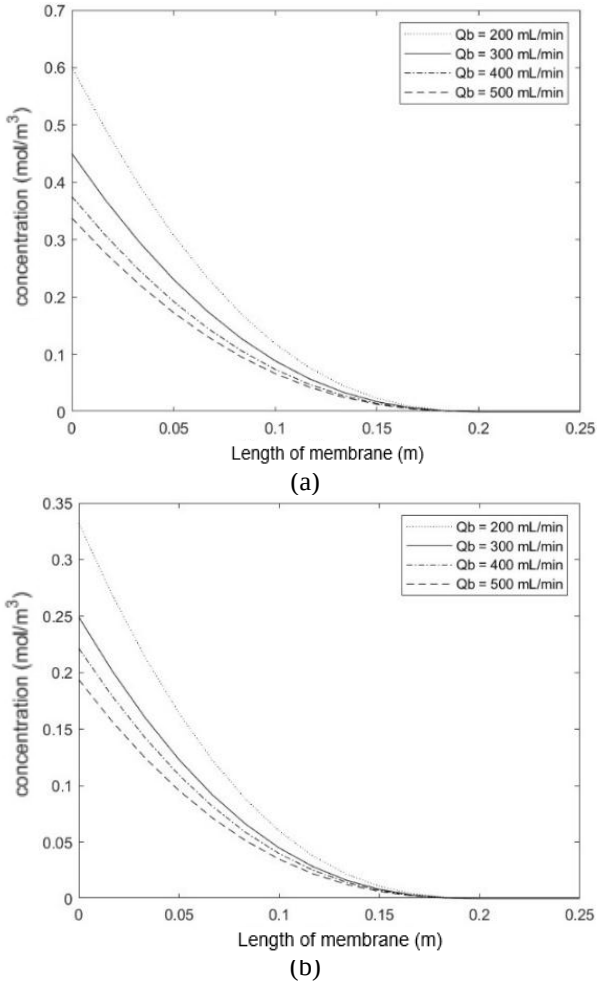


Figure 6. Effect of Blood Flow Rate on Concentration of (a) Urea and (b) Creatinine in the Shell (r = r3)

Furthermore, the effect of blood flow rate on the concentration of urea and creatinine axially in the tube (r = r1) can be seen in Figure 8. Blood enters the tube at z = 0 and exits at z = L (z = 0.25 m). Therefore, at z = 0 the concentration of urea and creatinine is the same at all variations of flow rate, which is 16.65 mol/m3. The decrease in concentration is still seen the same at all flow rates up to z = 0.018 m. Then the larger the flow rate, the greater the concentration of urea and creatinine that comes out of the tube. Overall, the concentration of urea and creatinine from z = 0 to z = L in the tube section decreased for all variations in flow rate.

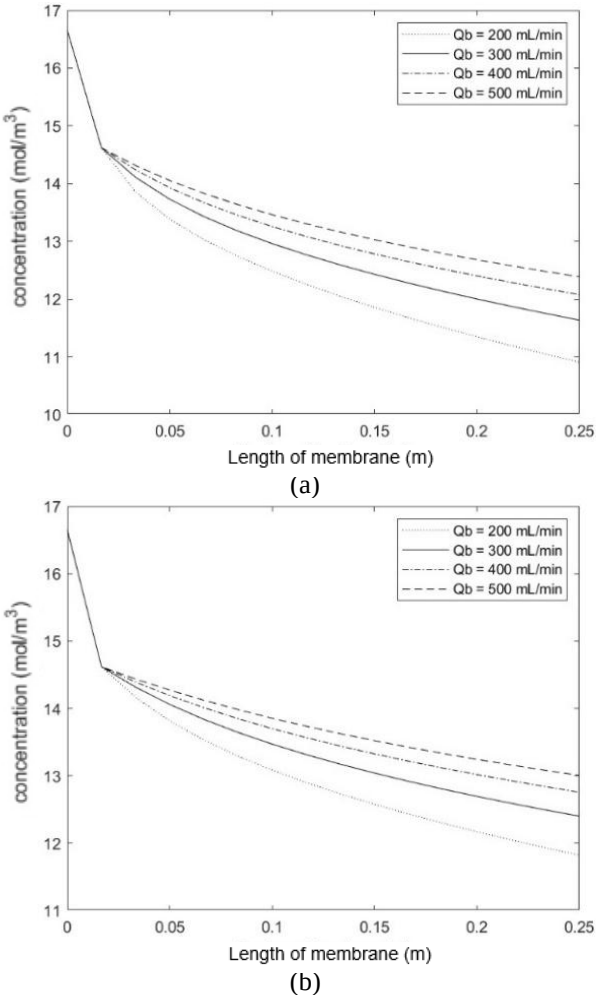
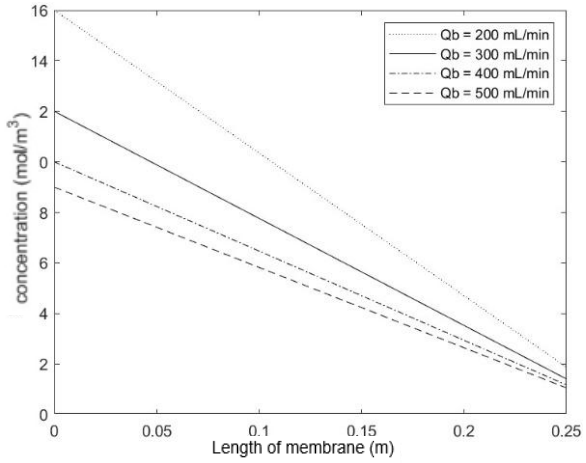


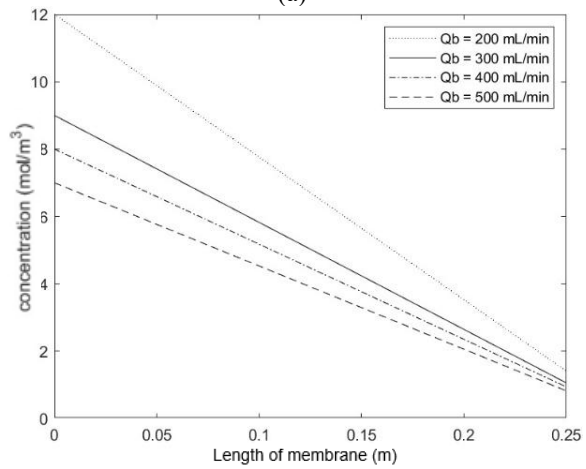
Figure 7. Effect of Blood Flow Rate on Concentration of (a) Urea and (b) Creatinine in the Tube (r = r1)

The effect of blood flow rate on the concentration of urea and axial creatinine in the membrane (r = r2) can be seen in Figure 9. The relationship between blood flow rate and urea and creatinine concentrations in the membrane is the same as that of the shell, that is, the greater the flow rate, the smaller the concentration of urea and creatine. Overall, the concentration of urea and creatinine from z = 0 to z = L in the membrane decreased for all variations in flow rate.

From Figures 3-8, it can be said that the increasing blood flow rate, the greater the clearance value of urea and creatinine. This aligns with Ward's 2017 theory, which states that urea clearance increases as the blood flow rate rises. This indicates that blood flow rate affects urea clearance, as illustrated in the following graphs.



(a)



(b)

Figure 8. Effect of Blood Flow Rate on Concentration of (a) Urea and (b) Creatinine in the Membrane (r=r2)

From the simulation conducted to study the influence of blood flow rate on the concentration of urea and creatinine both radially and axially, the results obtained are consistent with the theory by Goodarzi & Mohebbi-Kalhori (2022).

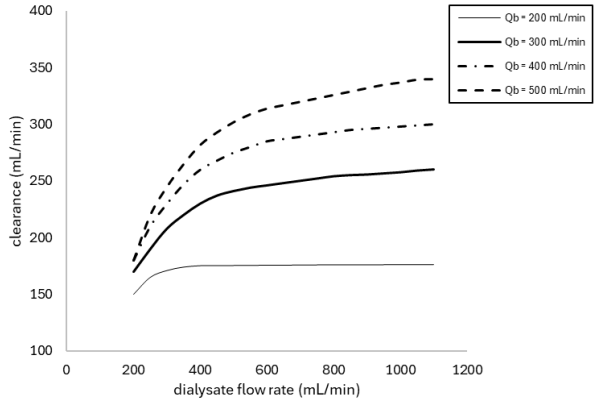
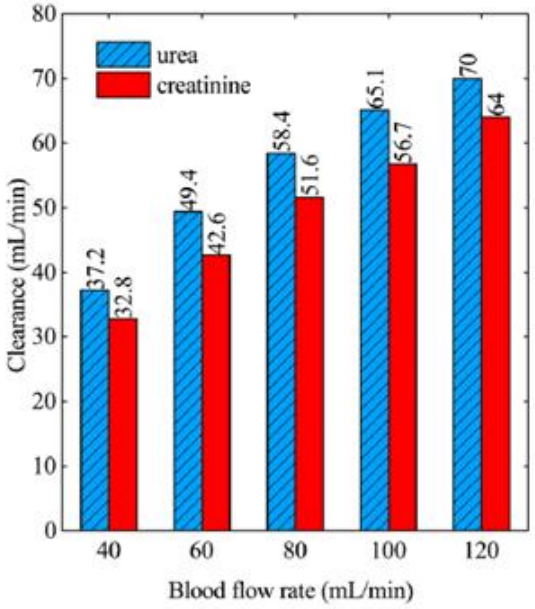
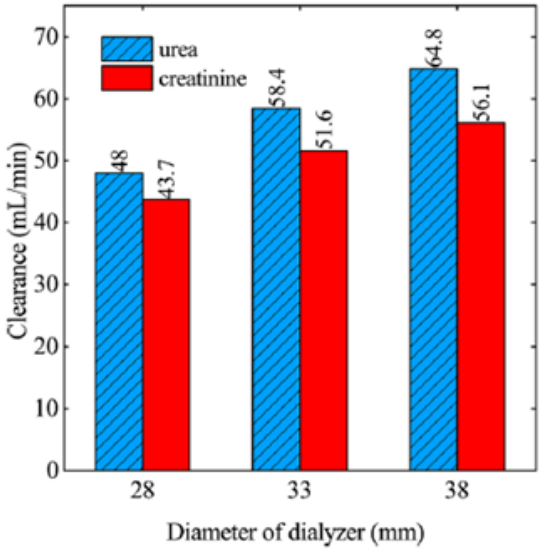


Figure 9. Effect of Blood Flow Rate and Dialysate Flow Rate on Urea Clearance

It states that an increase in blood flow rate along the radial and axial directions of the tube, membrane, and shell results in greater clearance. This indicates that blood flow rate affects urea clearance, as shown in the following graph.



(a)



(b)

Figure 10. Effect of (a) Blood Flow Rate and (b) Diameter of Dialyzer on the Clearance

4. Conclusions

This study shows that the efficiency of the hemodialysis process is greatly influenced by the distribution of urea and creatinine concentrations in the hollow fiber membrane. The developed mathematical model is able to describe mass transfer through diffusion and ultrafiltration mechanisms in three main domains: tube, membrane, and shell. The simulation results showed that the dialysate flow rate and membrane surface area played a significant role in

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increasing the clearance of urea and creatinine. Higher dialysate flow rates increase concentration gradients, while larger membrane surface areas provide effective areas that support more optimal removal of uremic toxins. From this simulation, the increase in membrane surface area from 1.3 m^2 to 1.8 m^2 did not result in a significant change in the exit concentrations of urea and creatinine compared to the initial concentrations. At a flow rate of 3.33×10^{-6} m^3/s, the urea concentration only slightly decreased from 16.67 mol/m^3 (initial) to 16.6303 mol/m^3 (A = 1.3 m^2) and 16.6163 mol/m^3 (A = 1.8 m^2), while the creatinine concentration decreased from 8.85 mol/m^3 (initial) to 8.8381 mol/m^3 (A = 1.3 m^2) and 8.8337 mol/m^3 (A = 1.8 m^2). A similar trend occurred at other flow rates, indicating that although the membrane surface area increased, the reduction in concentration remained small.

By detailing the axial and radial concentration distributions, this study offers valuable insights for optimizing dialyzer design, especially in adjusting to optimal operating conditions. This simulation is also the first step in developing a more efficient and individualized approach in hemodialysis therapy, so that it is expected to improve the quality of life of kidney failure patients.

Acknowledgments

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Credit authorship contribution statement

Please refer to https://credit.niso.org/

Melinda Nur Fauziah: Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Investigation, Formal analysis, Conceptualization. **Yeni Rahmawati:** Writing – review & editing, Validation, Resources, Formal analysis, Conceptualization. **Siti Nurkhamidah:** Validation, Resources, Project administration, Visualization**. Fadlilatul Taufany:** Conceptualization, Resources, Funding acquisition, Supervision. **Ali Altway**: Conceptualization, Validation, Resources, Software. **Susianto**: Methodology, Data curation, Validation, Supervision.

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