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Study of Dialyzer Membrane (Polyflux 210H) and Effects of Different Parameters on Dialysis Performance

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ABSTRACT

Problems frequently encountered in kidney malfunction include abnormal fluid levels in the body, increased acid levels, abnormal levels of Urea, Glucose, Endothelin, β2-Microglobulin and Complement Factor D. Parameters characterizing the structure of dialyzers are very important because they decide overall clearance of toxin molecules and at the same time should allow retaining useful molecules in the blood. In this paper, a cross sectional image of the dialyzer membrane with details of the porosity is presented. A multilayered membrane model with different porosity for each layer, describes the actual structure of Polyflux 210H membrane. This model is developed using Finite Element Software—COMSOL Multiphysics 4.3. A blood flow with substances like—Urea, Glucose, Endothelin, β2-Microglobulin, Complement Factor D and Albumin is introduced. For a certain blood flow rate, the toxins diffuse through the membrane and on the other side of the membrane a dialysate flow removes the toxins. Here, different parameters, such as flow rate of blood and dialysate, length and radius of the fiber are changed to simulate how these changes affect toxin clearance and the removal of useful molecules.

Keywords: Simulation, Dialysis; Axisymmetric Model; 3-Layered Membrane; Effective Diffusivity; Parameters; COMSOL Multiphysics 4.3

1. Introduction

A substantial amount of research has been performed regarding homogeneous dialyzer membranes. These homogeneous dialyzer membranes are mostly made of cellulose. These membranes have a uniform pore structure from the inner to the outer side of the membrane. The surface of such membranes was not very biocompatible, because exposed hydroxyl groups would activate complement in the blood passing by the membrane. Therefore, these days dialyzer membranes are made from synthetic materials, using polymers such as polyarylethersulfone, polyamide, polyvinylpyrrolidone, polycarbonate and polyacrylonitrile. These synthetic membranes activate complement to a lesser degree than cellulose membranes [1]. They have a structure which is known as asymmetric. This actually means that the shape of a pore gradually changes from inner to outer surface of the membrane. Synthetic membranes can be made in either low- or high-flux configuration, but most are high-flux. Polyflux 210H is an example of such high flux asymmetric polymer membrane. Sakai *et al*. [2] studied and captured the images of inner and outer surface images of such an asymmetric membrane. They calculated the surface porosity based on those photomicrographs. These give an idea of the surface porosity. But to what extend that porosity continues from one surface to another is not sure. Taking cross sectional image of the membrane and calculating the porosity from that image allow a better description of it. Experimental studies [3,4] have been done to determine whether increasing the dialysate or blood flow rate leads to better clearance or not. But these studies did not consider the structure of the membrane. Also these studies were limited to clearance of Urea only. A reasonable concern for doctors, in these days, is whether the necessary elements like Albumin are diffused through the membrane during the dialysis or not. Most of the experimental studies are done with dialyzers which are commercially available. So they actually give a comparison between different dialyzers. But which parameters of dialysis process are really important to have a better overall clearance of toxin molecules and at the same time retain useful molecules is not clear. Also

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how the change of those parameters will affect the clearance is important and will be investigated in this work.

2. Polyflux 210H Dialyzer Membrane

In one dialyzer of Polyflux 210H, there are approximately 12,000 fibers. These fibers are made of Polyamix which is a blend of Polyarylethersulfone, Polyvinylpyrrolidone and Polyamide [5]. Polyflux 210H fiber has a porous structure. A single fiber has a length of 270 mm.

The fibers used in this research were fixed using a mixture of 2.5% glutaraldehyde and 2% paraformaldehyde in a 0.1 M phosphate buffer. A series of mixtures of pure ethanol and distilled water in different ratios were used to dehydrate the fibers. To investigate the internal surface of the fibers, some fibers were placed on a carbon double sided adhesive scanning electron microscopy (SEM) tape glued from the other side to an SEM stub. The SEM stub with the fibers glued to its surface was transferred for viewing under the stereoscopic optical microscope. The fiber walls were dissected longitudinally using a surgical scalpel. Then a 250 Å layer of gold (purity 99.991%) is applied to render the surfaces of the capillaries conductive for observation under the Scanning Electron Microscope (SEM) and the Field Emission Scanning Electron Microscope (FESEM). The SEM used here is a Joel-6010LV and the FESEM is a SU6600 Hitachi.

At first the longitudinal image (**Figure 1**) of the fiber is taken from the outside.

A cross section of the fiber is showed in **Figure 2**.

Then images of the outer and inner side of the membrane are taken to get an idea of the pore size and porosity. The outer surface has a range of pore size which varies between 0.45 μm to 20.40 μm (**Figure 3**).

But for the inner surface the range is between 34 nm and 45 nm (**Figure 4**). Then to get a better idea of the porosity changes, cross sectional images of the membrane are taken. This gives a clear idea of the porosity changes across the thickness.

In **Figure 5**, a dialyzer membrane having a total thickness of 45 μm is divided into three different layers to calculate the porosity for each of the layer. The first layer (thickness of 8 μm) has a porosity of around 0.1, second layer (thickness of 12 μm) has a porosity of around 0.27 and third layer (thickness of 25 μm) has a porosity of around 0.4. Several photomicrographs from each of the layers are taken to calculate the porosity and then an average value of porosity is introduced for each layer.

3. Method of Developing Model

The configuration of a modern hollow fiber dialysis assembly can be seen in **Figure 6**. The blood flows through the fibers while the dialysate flows over the capillaries in a counter-current manner similar to a shell and tube heat exchanger. In this application the flow is laminar.

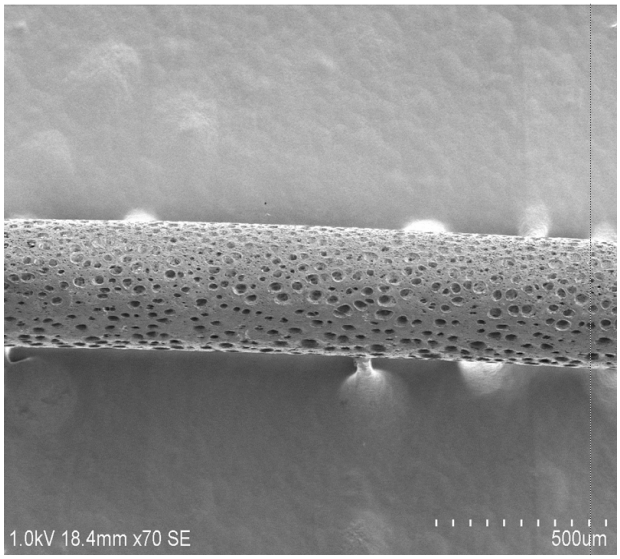

Figure 1. Longitudinal image of a fiber.

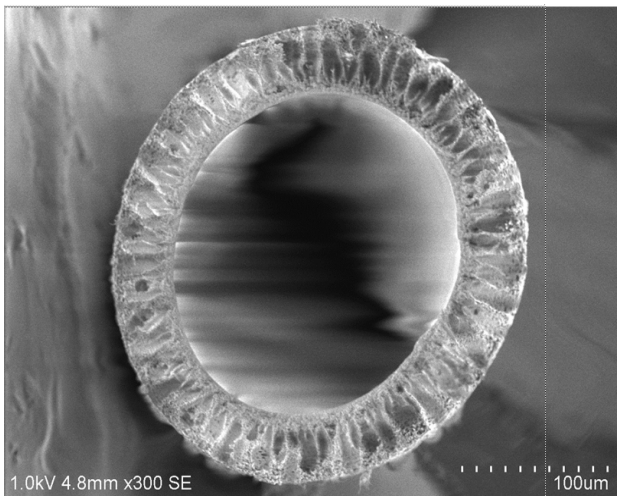

Figure 2. Cross section of the fiber.

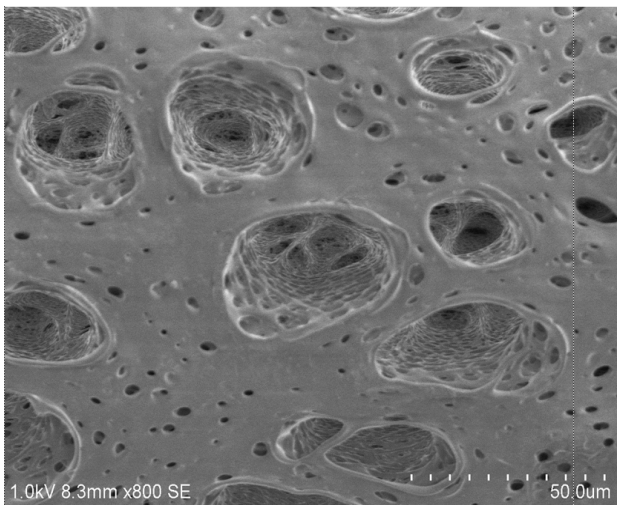

Figure 3. Outer surface of the dialyzer membrane.

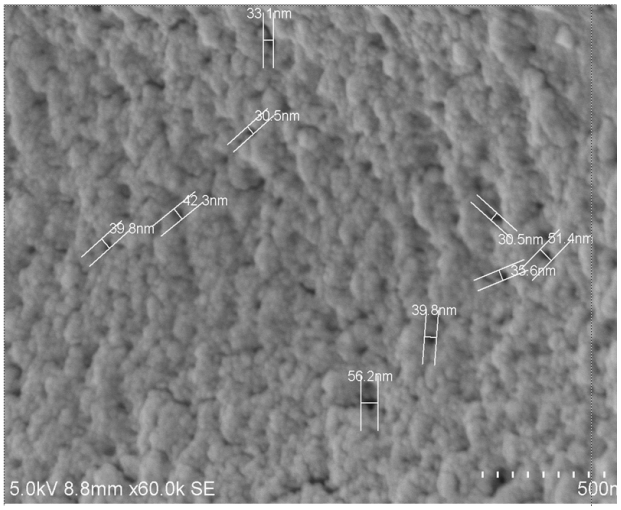

Figure 4. Inner surface of the dialyzer membrane.

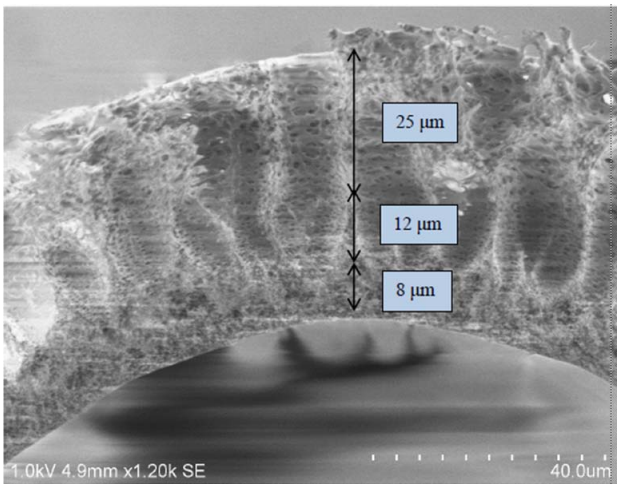

Figure 5. Cross section of the membrane.

Figure 7 shows the three sections of the axisymmetrical domain: the domain on the left represents the blood flow in the fiber, the small domain in the middle with three layers represents the membrane, and the domain on the right represents the outer dialysate flow in the shell.

4. Equations

The following simplified PDE (Partial Differential Equation) describes the convective and diffusion processes in the blood and the dialysate [6].

$$\nabla \cdot \left(-D_i \nabla c_i + c_i u\right) = 0 \qquad (1)$$

where c_i denotes the concentration of the toxin (mol/m^3) in the respective phase, D denotes the diffusion coefficient (m^2/s) in the liquid phases and u denotes the velocity (m/s) in the respective liquid phase.

For different toxins the diffusion coefficient is different and it can be calculated from [7]

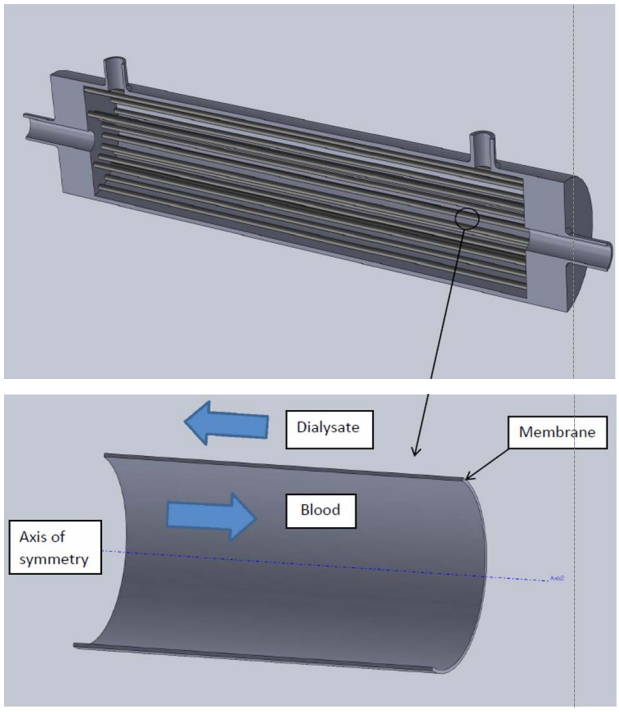

Figure 6. Diagram of dialysis hollow-fiber dialyzer.

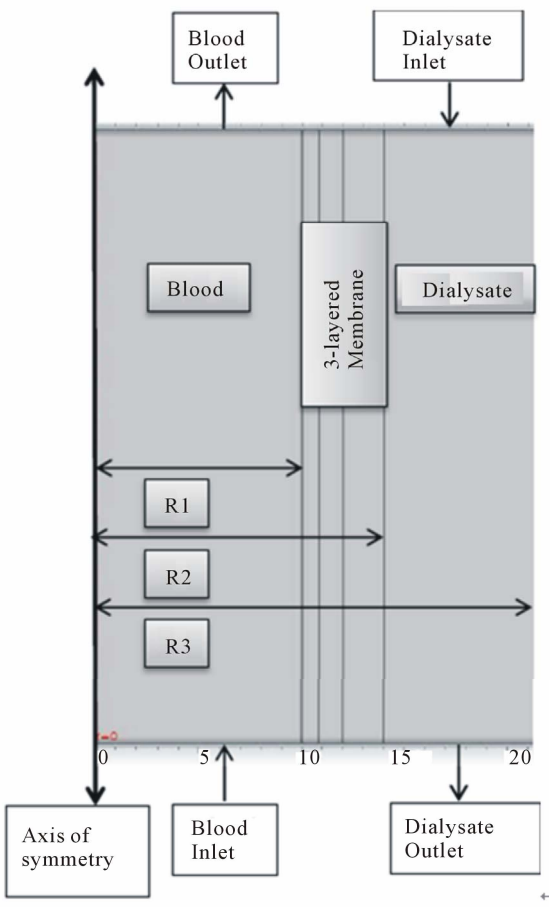

Figure 7. Model Geometry with R1, R2, R3.

$$D = 1.62 \times 10^{-4} \left(MW \right)^{-0.552} \quad (2)$$

where MW is the molecular weight of the respective toxin.

Both the blood and dialysate flow is considered fully developed laminar flow. For an inlet velocity of blood along the axial direction [8],

$$v_B = \left(\frac{2Q_B}{\pi R_1^2 n} \right) \left[1 - \left(\frac{r}{R_1} \right)^2 \right] \quad (3)$$

where Q_B is the volume flow rate of blood, R_1 is the inner radius of the hollow fiber, r is the radial coordinate and n is the number of fibers in a dialyzer which is 12,000 for Polyflux 210H dialyzer.

For the phenomenon of diffusion through the membrane, the following equation has been used-

$$\nabla \cdot \left(-D_{e,i} \nabla c_i \right) = 0 \quad (4)$$

where c_i denotes the concentration of the molecules (mol/m^3) in the respective phase, D denotes the diffusion coefficient (m^2/s) of the molecules and D_e denotes the effective diffusion coefficient of the molecules in the porous media.

The term effective diffusivity is defined [9] as

$$D_e = Df\left(q\right) S_D A_k \quad (5)$$

$$q = \frac{r_s}{r_p} \quad (6)$$

$$f\left(q\right) = \frac{1 - 2.1050q + 2.0865q^3 - 1.7068q^5 + 0.72603q^6}{1 - 0.75857q^5} \quad (7)$$

$$S_D = \left(1 - q\right)^2 \quad (8)$$

Where D is the diffusion coefficient of molecule, $f(q)$ the friction coefficient, S_D the steric hindrance factor at the pore inlet in diffusion, A_k the membrane porosity, q is the ratio of solute radius r_s to pore radius r_p. Here, the porosity values of the three layers of the membrane are used for A_k.

The six molecules that are considered in this paper are listed in **Table 1** with their molecular weight [10], diameter [11] and diffusion coefficient.

5. COMSOL Multiphysics 4.3

COMSOL Multiphysics 4.3 is used for developing and simulating the model of Polyflux 210H dialyzer. COMSOL Multiphysics is a finite element analysis, solver and simulation software / FEA Software package for various physics and engineering applications, especially coupled phenomena or multiphysics.

After developing the model with necessary inlet, outlet and boundary conditions, simulations are done for changes of different parameters. A post processing result is showed in **Figure 8**.

Table 1. Six molecules with their molecular weight, diameter and diffusion coefficient.

Molecule	Molecular weight (Da)	Diameter (nm)	Diffusion coefficient (x 10^{-8} cm^2/s)
Urea	60	0.48	1690.35
Glucose	180	1.0	921.73
Endothelin	4282.8	2.60	160.25
β2-Microglobulin	11800	3.88	91.59
Complement Factor D	24000	5.12	61.89
Albumin	66000	7.8	35.41

6. Validation

At first, the clearance rate of Urea at different blood flow rate is compared with the experimental results provided by the manufacturer [5].

From **Figure 9**, it can be concluded that the clearance rate of Urea at different blood flow rate is in good agreement with the data provided by the Polyflux 210H manufacturer.

7. Results

7.1. Effects of Blood Flow Rate on Clearance Rate

For the blood flow rate of Q_B = 300, 400 and 500 ml/min and dialysate flow rate of Q_D = 500ml/min, the clearance rate for six molecules is calculated.

As it can be seen from **Figure 10**, with the increasing blood flow rate, the clearance rate of both Urea and Glucose increase rapidly. Specially, for Urea, when the blood flow rate increases from 300 to 500 ml/min, the clearance rate almost gets doubled. And from **Figure 11**, it is evident that the clearance rate of Albumin remains almost constant.

7.2. Effects of Dialysate Flow Rate on Clearance Rate

The blood flow rate, Q_B= 400 ml/min is kept constant and the dialysate flow rate, Q_D is gradually increased.

From **Figures 12** and **13**, it can be said that at a constant blood flow rate, the increasing dialysate flow rate ensures further clearance of Urea and Glucose.

7.3. Effects of Length of the Dialyzer Fiber on Clearance Rate

The length of the dialyzer fiber is varied from 270 to 540 mm when Q_B = 300 ml/min and Q_D = 500 ml/min.

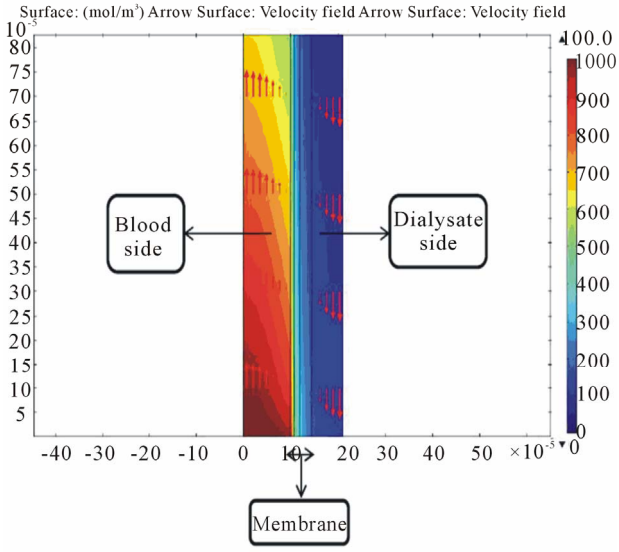

Figure 8. Concentration of Urea at both blood and dialysate side along the membrane (axisymmetric).

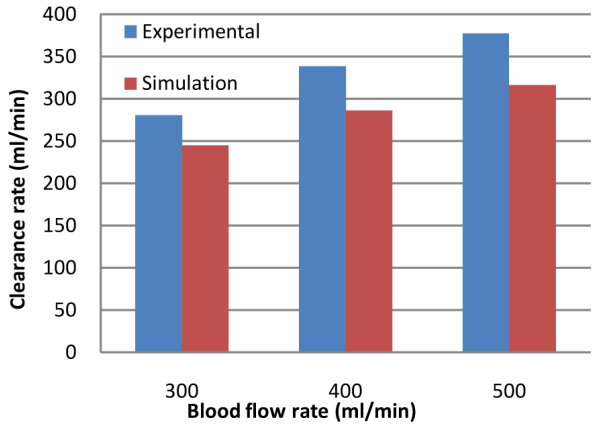

Figure 9. Clearance of Urea for both experimental and simulation cases at blood flow rate, QB = 300, 400 and 500 ml/min whereas dialysate flow rate, QD = 500 ml/min.

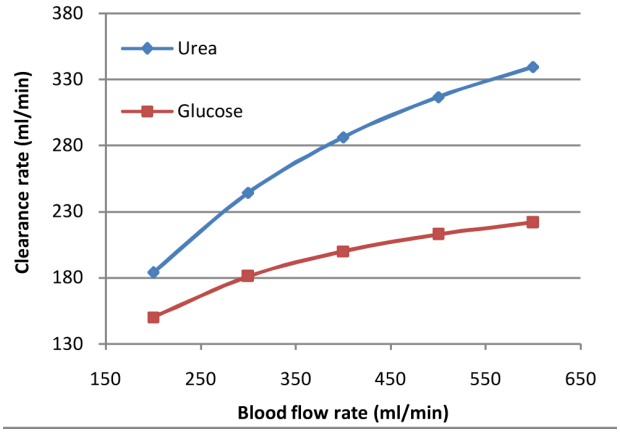

Figure 10. Clearance rate of Urea and Glucose at different blood flow rates when QD = 500 ml/min.

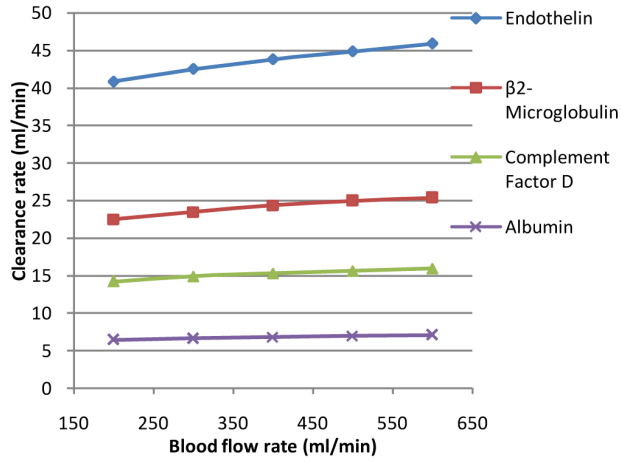

Figure 11. Clearance rate of Endothelin, *β*2-Microglobulin, Complement Factor D and Albumin at different blood flow rates when QD = 500 ml/min.

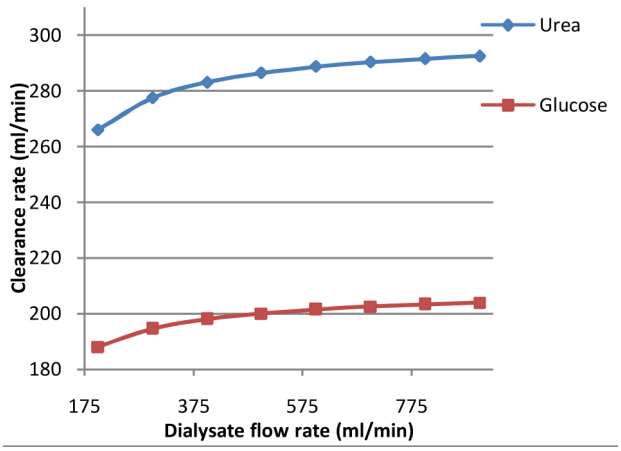

Figure 12. Clearance of Urea and Glucose at different Dialysate flow rates when QB = 400ml/min.

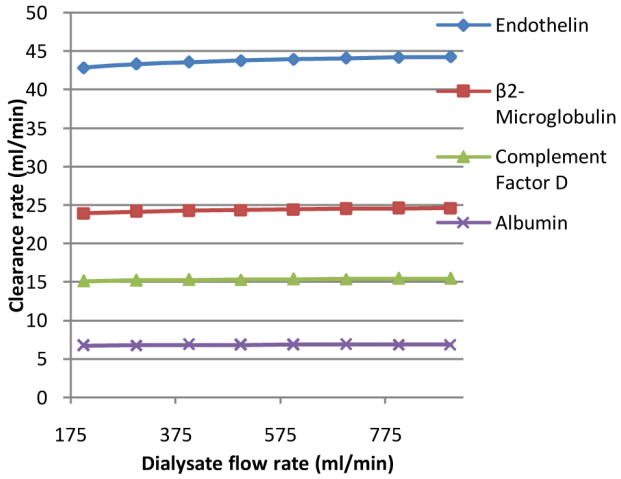

Figure 13. Clearance of Endothelin, *β*2-Microglobulin, Complement Factor D and Albumin at different Dialysate flow rates when QB = 400 ml/min.

From **Figure 14**, it can be seen that if the length of the dialyzer fiber is increased, the clearance rate of Glucose increases more rapidly than the clearance rate of Urea. For Endothelin and β2-Microglobulin (**Figure 15**) the clearance rate increases twice compared to the initial condition. Meanwhile, the clearance rate of Albumin does not change that much.

7.4. Effects of Radius of the Dialyzer Fiber on Clearance Rate

The radius of the dialyzer fiber is increased from 0.1 mm to 0.2 mm when Q_B = 300 ml/min and Q_D = 500 ml/min.

From **Figures 16** and **17** it is evident that the effect of increasing radius of dialyzer fiber is similar to that of increasing the length of the dialyzer fiber. However, if a case is considered where the clearance rate of Albumin is similar for length of 450 mm with a radius of 0.1 mm and radius of 0.17 mm with a length of 270 mm dialyzer fiber.

From **Table 2**, it is evident that for the same level of clearance rate of Albumin (or loss of Albumin), the dialyzer fiber with relatively higher length and lower radius shows better clearance of Urea, Glucose, Endothelin, β2-Microglobulin and Complement Factor D than the dialyzer fiber with relatively higher radius and lower length.

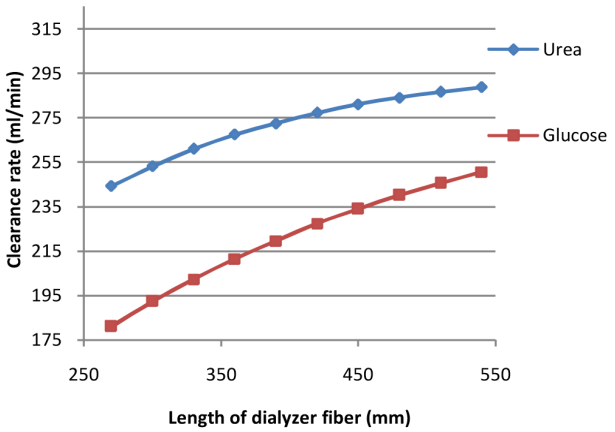

Figure 14. Clearance rate of Urea and Glucose at QB = 300ml/min and QD = 500 ml/min.

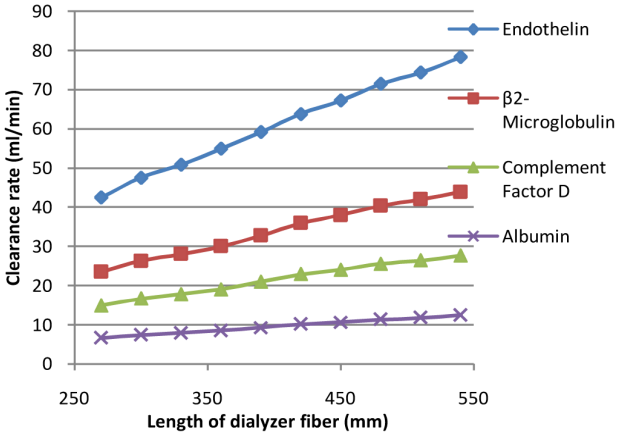

Figure 15. Clearance of Endothelin, β2-Microglobulin, Complement Factor D and Albumin at QB = 300 ml/min and QD = 500 ml/min.

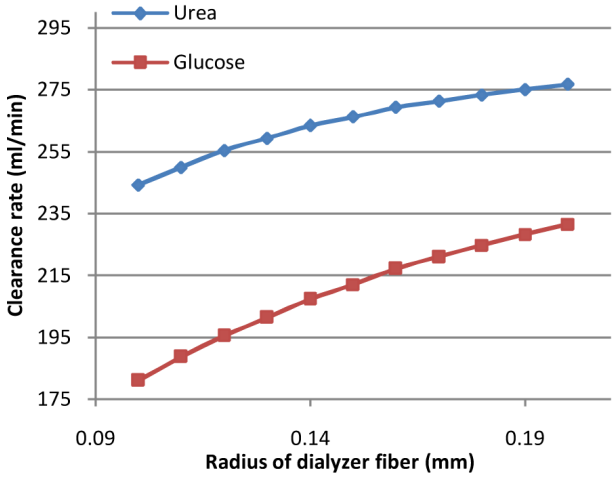

Figure 16. Clearance rate of Urea and Glucose at QB = 300 ml/min and QD = 500 ml/min.

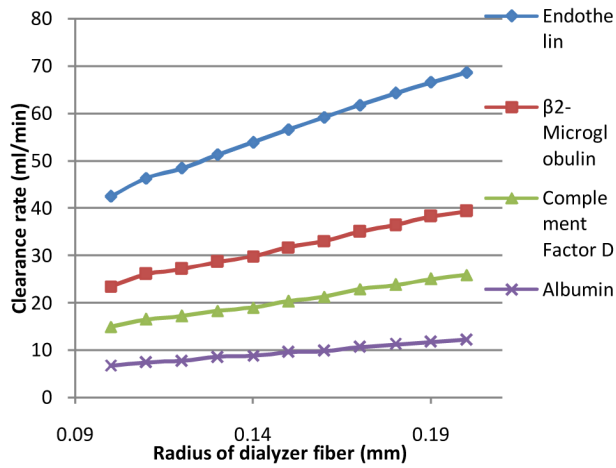

Figure 17. Clearance of Endothelin, β2-Microglobulin, Complement Factor D and Albumin at QB = 300 ml/min and QD = 500 ml/min.

Table 2. Clearance rate of different molecules for two dialyzer fibers consisting length = 450 mm, radius = 0.1 mm and length = 270 mm, radius = 0.17 mm.

	Length = 450 mm, Radius = 0.1 mm	Length = 270 mm, Radius = 0.17 mm
Urea	281.1	271.3
Glucose	234.1	221
Endothelin	67.21	61.8
β2-Microglobulin	37.97	35.05
Complement Factor D	24.04	22.92
Albumin	10.67	10.7

8. Conclusion

The clearance rate of Urea at different blood flow rate is in good agreement with the data provided by the Polyflux 210H manufacturer which ensures that the equations used to represent the phenomenon of dialysis process are reasonable. The clearance rate of small molecules—Urea and Glucose, increases rapidly with increasing blood flow rate while the clearance rate of Albumin is almost constant. Also increasing dialysate flow rate ensures further clearance of Urea and Glucose. Increasing the length or radius of the dialyzer fiber ensures better clearance of Glucose and middle molecules, such as Endothelin and β2-Microglobulin. Moreover, increasing the length of the dialyzer fiber shows better clearance than increasing the radius of the dialyzer fiber, in the case of same amount of Albumin loss.

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