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Diffusion Equation Model for Determining the Concentration of Urea in Artificial Kidney

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***Abstract*—** *In medicine, dialysis is primarily used to provide an artificial replacement for lost kidney function (renal replacement therapy) due to renal failure. Dialysis may be used for very sick patients, who have suddenly but temporarily lost their kidney function (acute renal failure) or for quite stable patients who have permanently lost their kidney function. We present a model, which consist of partial differential equation defining the process of diffusion in artificial kidney and finally get the solution of this equation in the form of concentration of urea in blood by using the finite difference approach. The graph drawn between concentration and radial distance shows the variation between these two quantity. Dialysis treatments replace some of these functions through diffusion (waste removal) and ultrafiltration (fluid removal).*

***Keywords*—** *Coil dialyzer, kiil dialyzer, Interstitial fluid, Henle and Vasa-recta loops*.
AMS Subject Classification – 92B05

I. INTRODUCTION

The kidneys maintain the body's internal equilibrium of water and minerals (sodium, potassium, chloride, calcium, phosphorus, magnesium, sulphate) and removes the daily metabolic load of fixed hydrogen ions from the blood. The kidneys are the filtering device of blood because it removes waste products from metabolism such as urea, uric acid and creatinine by producing and secreting urine. The kidneys also help in maintaining homeostasis by regulating the concentration and volume of body fluid.

Dialysis is the artificial process of getting rid of waste and unwanted water from the blood. This process is naturally done by our kidney. And "Hemodialysis is the treatment option for kidney failure.

The basic principle of the artificial kidney is to pass blood through minute blood channels bonded by a thin membrane. On the other side of the membrane in a dialysing fluid into which unwanted substances in the blood pass by diffusion, and this rate of movement of solute across the dialysing membrane depends on the following factors,

(i) The concentration gradient of the solute between the two solutions.
(ii) The permeability of the membrane.
(iii) The surface area of the membrane.
(iv) Time length, that blood and fluid remains in the contact with the membrane

The maximum rate of solute transfer occurs initially when the concentration gradient is greatest and slow down as concentration gradient is dissipated. In flowing systems, as in the case with hemodialysis, in which blood and dialyzate fluid flow through the artificial kidney the dissipation of the concentration gradient can be reduced and diffusion of solute across the membrane can be optimized by increasing the flow rate of blood, the dialysing fluid or both.

A comparison of coil and kiil dialyzer was made by Down et al. [1]. To assess the comparative efficiency, safety and cost of maintenance dialysis, the treatment of 13 patients with a kiil dialyzer was compared with that of 11 patients using a coil dialyzer. Kiil and coil dialyzers proved equally satisfactory from a medical standpoint and equally acceptable to the patients.

Previous work by some investigators indicates that erythrocytes urea and creatinine in uremic whole blood leaving the hemodialyzer do not move down the concentration gradients established by loss of these solutes across the dialyzer membrane. This puzzling disequilibrium is at odd with work indicating ready movement of both solutes across the erythrocyte membrane of nonuremic erythrocytes studied in vitro. Urea movement across erythrocyte membrane during artificial kidney treatment was discussed by Cheung et al [2] and this study shows that contact with the dialyzer does not noticeably alter the erythrocyte membrane of the uremic patient, so that urea distribution between plasma and erythrocyte water is the same as that in the blood of normal control subjects. Furthermore, urea does not show disequilibrium in concentration across the erythrocyte membrane in response to 50 percent dilution with a modified Ringer's solution but rather equilibrates swiftly and completely".

"The simulation of continuous arteriovenous hemodialysis with a mathematical model in which model predicts the performance of continuous arteriovenous hemodialysis was given by Pallon et al. [4]. The model was tested by perfusing a circuit with bovin blood under conditions of pure ultrafiltration, zero net ultrafiltration and dialysis, or combined ultrafiltration and dialysis. Model predictions regarding the relative contributions of diffusion and convection to urea clearance were explored. Under condition of nearly perfect equilibration of urea between blood and dialysate at the blood inlet, the model predicts that the diffusive clearance of urea will increase with increasing rate of filtration and may exceed the rate of dialyzate inflow".

"For the health care personnel, the use of hemodialyzers did not entail any increased risk of infection or exposure to toxic substances, if proper controls measures were taken. Baris et al. [5] evaluate the safety and potential cost savings of

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hemodialyzer reuse". For patients there was no evidence to suggest any excess risk of complications or death as long as precise and appropriate procedures are observed.

"Solute fluxes in different treatment modalities were governed by Leypoldt [7]. The principles governing solute flux or transport in different artificial kidney modalities are reviewed here. Solute clearance profiles were calculated for identical artificial kidney membranes during hemodialysis, hemofiltration and hemodiafiltration. It was also shown that the clearance of small solutes depends largely on the dialyzate flow rate and is similar when using either hemodialysis or hemofiltration. In contrast, clearance of middle molecules, especially low molecular weight proteins, depends largely on convective transport induced by high ultrafiltration rates and is maximized when using either hemofiltration or hemodiafiltration. Optimal fluxes for both small solutes and middle molecules can be achieved by using post dilution hemodiafiltration. In this work the reduction in plasma concentration was used, even after normalization for changes in extracellular volume during therapy, is not an exact measure of β_2-mocroglobulin (a kind of low molecular weigth protein) clearance. It is proposed that β_2-mocroglobulin plasma clearance be reported in failure studies instead of the normalized reduction in β_2-mocroglobulin plasma concentration. Additional studies are necessary to determine the effects of postdialysis rebound on the calculated clearance for β_2-mocroglobulin and other high molecular mass uraemic toxins".

"Grenier et al. [10] gave the functional MRI of the kidney. Functional MR imaging of the kidney has a great potential of development because the functional parameters, which can be approached non-invasively, are multiple: glomerular filtration, tabular concentration and transit, blood volume and perfusion, diffusion and oxygenation. Until now, its limitations in clinical applications are due to the difficulties in obtaining reproducible and reliable information in this mobile organ and sometimes in understanding the physiologic substrate of the signal changes observed. These approaches require other either endogeneous contrasts agents, such as water protons (for perfusion and diffusion) or deoxyhemoglobin (for oxygenation) or exogeneous contrasts agents such as gadolinium chelates (for filtration and perfusion) or iron oxide particles (for perfusion). Clinical validation of these methods and evolution of their clinical impact are now worthwhile before diffusing them in clinical practice".

"Dialyser manufactures only provide limited information about mass removal under well-defined flow and solute conditions in commercially available dialysers for hemodialysis. This computational study aimed at assessing the solute transport efficiency in a dialyser for different geometries. Optimization of solute transport in dialysers using a three dimensional finite volume model was developed by Eloot et al. [11], which is of a single fibre in a high flux polysulphone dialyser. Different equations describe blood and dialyzate flow (Navier-Stokes), radial filtration flow (Darcy) and solute transport (Convection diffusion). Fluid and membrane properties were derived from in vitro and in vivo tests as well as from literature data. Urea was used as marker to simulate small molecule removal, while middle molecule transport was modeled using vitamin B12 and inulin. Keeping the fluid velocity in the single fiber constant, fiber diameter and length were changed in a wide range for evaluation of solute removal efficiency. Clearances were found enhanced by 13 % (Urea), 50 % (Vitamin B12) and 89 % (Inulin) for a fiber diameter of 150µm instead of 200 µm. The impact of fiber dimensions were more pronounced for the middle molecules compared to urea".

"Charra [12] discussed about the fluid balance, dry weight and blood pressure in dialysis. The total amount of the sodium present in the body controls the extracellular volume. In advanced renal failure, sodium balance becomes positive and the extracellular volume expands. This leads to hypertension, and vascular changes leads to adverse cardiovascular consequences in dialysis patients. Controlling the body sodium content and the extracellular volume allows one to better control hypertension and its consequences. This can be achieved by reducing the sodium input and/or by increasing the sodium output. The discontinuous naturoze of hemodialysis causes saw-tooth volume fluctuations. This has led to the concept of dry weight, a crucial component of dialysis adequacy. Assessment and achievement of dry weight is feasible on pure clinical grounds. But its relative lack of accuracy has led to several non-clinical methods of assessing dry weight in an effort to improve the assessment of fluid status in dialysis patients".

Most artificial kidney can clear urea from the plasma at a rate of 1000 ml/m in to 225 ml/min, while urea clearance through kidney is only 70 ml/min. The efficiency of a dialyzer is measured by the clearance,

$$Cl = \frac{C_{in} - C_o}{C_{in}} W_b \ \text{(ml/min)}$$

where C_{in} and C_o are the concentrations of the metabolite at the inlet and outlet points and W_b is blood flow volume.

II. BASIC EQUATIONS

"The diffusion equation is derived by considering concentration gradient. Therefore at any point (x, y, z), some solute is having concentration c per unit volume at time t. Due to the concentration gradient (grad c) there is a flow of solute atoms from higher concentration to lower concentration which is given by the density vector at that time considered as j. Then according to Fick's first law we have

$$J = -D \text{ grad } c = -D\Delta c \quad (1)$$

The negative sign in the above equation shows that flow is towards the low concentration.

Now, if we consider a surface S with volume V, then the rate of change of the amount is given by

$$\frac{\partial}{\partial t}\int_v c(x,y,z,t)dax dy dz \quad (2)$$

and the amount of the solute which comes out to the surface S per unit time is

$$\frac{\partial}{\partial t}\int_s j.\hat{n}\,dS \quad (3)$$

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where $\hat{n}$ is the unit normal vector to the surface.

If there is no sink and source inside the volume, then by equations (2) and (3), we get

$$\frac{\partial}{\partial t}\int_V c(x,y,z,t)\,dxdydz = -\int_S j.\hat{n}\,dS$$

$$= \int_S (D\,grad\,c)\hat{n}\,dS = \int_V div(D\,grad\,c)\,dxdydz$$

Hence

$$\int_V \left[\frac{\partial c}{\partial t} - div(D\ grad\ c)\right] dxdydz = 0 \tag{4}$$

Since equation (4) hold for all volume, we get the Fick's second law of equation as

$$\frac{\partial c}{\partial t} = div(D\ grad\ c)$$

Further D is assumed to be a constant and known as diffusion coefficient than we get the diffusion equation

$$\frac{\partial c}{\partial t} = div(D\ grad\ c) = D\Delta^2 c \tag{5}$$

Where $\Delta^2 = \left(\frac{\partial}{\partial x^2} + \frac{\partial}{\partial y^2} + \frac{\partial}{\partial z^2}\right)$

Hence the equation in three dimensional forms becomes,

$$\frac{\partial c}{\partial t} = D\left(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2} + \frac{\partial^2 c}{\partial z^2}\right) \tag{6}$$

and also known as heat conduction equation"[3].

III. Advancement in the Diffusion Equation

Equation (6) represents diffusion equation when there is no source and sinks generating or destroying the solute. However if there is solute that generates at a rate Q(c) per unit time, then (6) becomes

$$\frac{\partial c_i}{\partial t} = D\Delta^2 c + Q(c) \tag{7}$$

If there are a number of substances diffusing together in a medium, then

$$\frac{\partial c_i}{\partial t} = D\Delta^2 c + Q_i(c_1, c_2 ..... c_n) \tag{8}$$

D_i is the coefficient of diffusion of the i^{th} substance and Q_i rate of its generation per unit time. These two equations (7) and (8) are called diffusion reaction equations. Similarly some other advancement of diffusion and diffusion reaction equations are available.

IV. Diffusion Equation For Artificial Kidney

Assuming a straight duct without any sagging, the steady state laminar Newtonian fluid flows with constant physical properties. In all of these circumstances the diffusion equation with the convection term is the basic partial differential equation,

$$D\left(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r} + \frac{\partial^2 c}{\partial z^2}\right) = v\frac{\partial c}{\partial z} = v_m\left(1 - \frac{r^2}{R^2}\right)\frac{\partial c}{\partial z} \tag{9}$$

where

c(r,z) - Concentration of urea in the blood, v(r) - Velocity in the fully developed flow

v_m - Maximum velocity, R - Radius of the duct, D - Diffusion coefficient

The magnitude of the convective term as compared to the magnitude of the longitudinal diffusion term is given by the dimensionless Picklet number,

$$Pe = \frac{v_m R}{D}, \tag{10}$$

which may be as large as 15,000 for hemodialyser so that the longitudinal diffusion term can be neglected, therefore

$$D\left(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r}\right) = v_m\left(1 - \frac{r^2}{R^2}\right)\frac{\partial c}{\partial z} \tag{11}$$

Now the boundary conditions:

I. $c = c_i$ at $z = 0; 0 \le r \le R$

II. $\frac{\partial c}{\partial r} = 0$ at r=0

III. $-D\frac{\partial c}{\partial r} = P(c - c_d)$ at r=R (12)

where the permeability P and c_d is assumed to be constant in the dialyzate and the first condition shows the constant entry concentration while, the other defines that flow is symmetric about the axis.

The non- dimensionalization of the governing equation is as follows.

$$c^* = \frac{c - c_d}{c_i - c_d}, r^* = \frac{r}{R}, z^* = \frac{z}{RPe^2}, Pe = \frac{v_m R}{D} \tag{13}$$

therefore the system of equation using dimensionless variable.

$$\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r} = \left(1 - r^2\right)\frac{\partial c}{\partial z}, \tag{14}$$

and the boundary conditions becomes:

I. c=1 at $z = 0; 0 \le r \le 1$ (15)

II. $\frac{\partial c}{\partial r} = 0$ at $r = 0, z > 0$ (16)

III. $\frac{\partial c}{\partial r} + Sh_n c = 1$ at r=1 with $Sh_n c = \frac{PR}{D}$ (17)

V. Numerical Results and Discussion

In hemodialysis, the patient's blood is pumped through the blood compartment of a dialyzer, exposing it to a semipermeable membrane. The cleansed blood is then returned via the circuit back to the body. Ultrafiltration occurs by increasing the hydrostatic pressure across the dialyzer membrane. This usually is done by applying a negative pressure to the dialysate compartment of the dialyzer. This pressure gradient causes water and dissolved solutes to move from blood to dialysate, and allows the removal of several litres of excess fluid.

As far as the concentration of the urea at a point (r, z) is concerned, then the value of this concentration is obtained by the equation (14), along with the initial and boundary

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conditions of equation (15), (16), (17) by using the finite difference approach.

Graphs show a variation of concentration with respect to time and radius. Figure 1 presents a view of concentration vs radius, which indicates that as the radius increases the concentration going to be decreases, whereas Figure 2 is plotted for concentration vs time at the initial boundary, which again indicates the loss in concentration as time decreases. On the other hand Figure 3 defines the increase in concentration at the boundary.

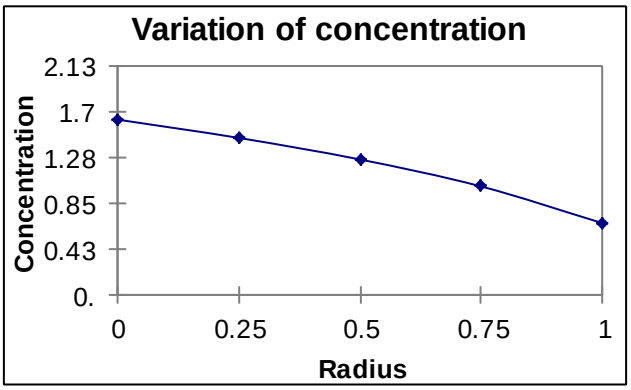

Fig. 1. Variation of concentration with respect to radius.

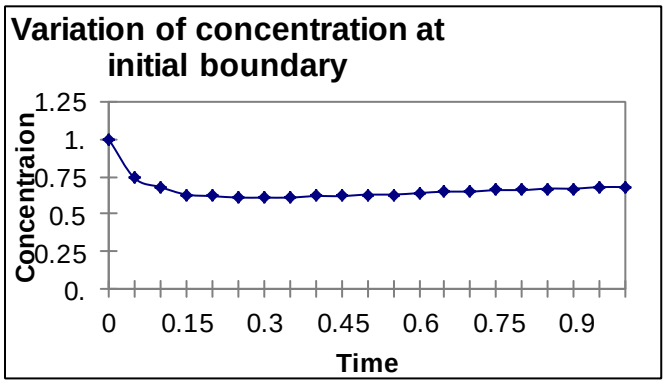

Fig. 2. Variation of concentration with respect to time.

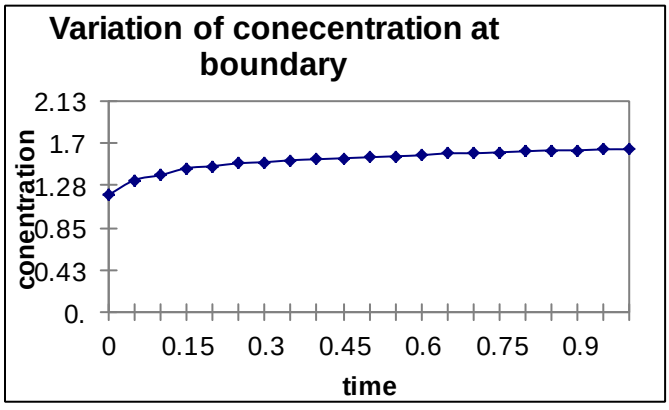

Fig. 3. Variation of concentration with respect to time.

The action of the kidneys is vital and so kidney failure is serious. However, if one kidney fails, the other enlarges to take over its function. A patient with two defective kidneys may still continue near-normal life with the aid of dialysis using a kidney machine or continuous ambulatory peritoneal dialysis (CAPD), or by a kidney transplant.

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