THEORETICAL EVALUATION OF ULTRAFILTRATION EFFECT ON THE CLEARANCE OF HOLLOW FIBER ARTIFICIAL KIDNEY

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Abstract—The diafiltration of a hollow fiber artificial kidney is simulated with a one-dimensional model. The model equations are solved to give an explicit formula for calculating the clearance increase due to ultrafiltration. The computed results are compared with the experimental data of Kunitomo et al. (1977). The simultaneous diffusion and convection processes occur as if they occur consecutively when the overall permeability is small. The relationship between clearance and ultrafiltration rate is not linear as previous investigators reported because the outlet concentrations are dependent on the ultrafiltration rate.

INTRODUCTION

The artificial kidney has provided the greatest successes in the application of membrane in medical devices. The hemodialysis is widely used in hospitals and homes throughout the world as a means of maintaining patients who would otherwise have died from chronic kidney failure.

Conventional dialysis depends on the diffusion process. Molecules and ions whose plasma concentrations are greater than normal will diffuse across the membrane into the dialysate while those species whose concentrations are higher in the dialysate will diffuse into the blood. The possibility of employing ultrafiltration during dialysis to aid the transfer of "middle" molecules with molecular weights above 1000 by the mechanism of bulk flow as well as by the normal mechanism of diffusion has been raised [1]. With the advent of new types of membranes and large surface area dialyzers such as a hollow fiber artificial kidney, larger ultrafiltration rates became important and their contributions to overall mass transfer rates could no longer be neglected, particularly for "middle" molecules.

Although mass transfer in hemodialysis has been fairly well investigated, the analyses on the hemodiafiltration have been reported by rather few investigators [2-6]. Popovich et al. [2] undertook investigation to determine the effects of ultrafiltration on the mass transfer in a paralled plate dialyzer and solved a two-dimensional model by the method of separation of variables. A one-dimensional model of simultaneous dialysis and ultrafiltration has been proposed by Ross et al. [3] They assumed that the flow rate decreases linearly along the channel length, i.e., the ultrafiltration rate is constant over the membrane. This corresponds to the fact that the pressure difference across the membrane in counter-current flow is not a function of position. However, the assumption is not valid at large pressure drop when the ultrafiltration rate is large and/or limited by the concentration polarization [7]. Jaffrin et al. [4] numerically analyzed parallel plate hemodialyzers by using a one-dimensional model with the variation of ultratfiltration rate along the membrane. It was found that the clearance increase little depends on the distribution of ultrafiltration rate along hemodialyzers. Chang and his associates [5, 6] performed a series of theoretical studies on the effect of ultrafiltration on the clearance in a few commercial dialyzers and on the estimation of urea and vitamin B_{12} concentrations in the body using two compartment model when the patients were treated with hemodialysis or hemodiafiltration.

In the present study we provide a one-dimensional model modified by the exponential decay of ultrafiltration rate and its explicit solution for a hollow fiber artificial kidney. Besides, the linear increase of clearance with ultrafiltration that is previously accepted by other investigators is reexamined by the present model equation.

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ONE-DIMENSIONAL MODEL OF ARTIFICIAL KIDNEY

The removal rate of solutes by the artificial kidney is measured by its clearance, analogous to the concept of renal clearance used for the natural kidney. The clearance, CL, is defined as the amount of solute removed from the blood phase per unit time divided by the incoming blood concentration. in terms of the symbols used in Fig.1, the clearance may be given by

$$CL = \frac{Q_{bi}C_{bi} - Q_{bo}C_{bo}}{C_{bi}} = Q_{bi} - Q_{bo}\frac{C_{bo}}{C_{bi}} \quad \cdots\cdots (1)$$

where

$$Q_{bo} = Q_{bi} - Q_f$$

For low ultrafiltration rates, $Q_{bo} = Q_{bi}$ and Eq.(1) is reduced to

$$CL_o = \frac{C_{bi} - C_{bo}}{C_{bi}} Q_{bi} \quad \cdots\cdots (2)$$

These definitions do not reveal any details of the solute removal process.

The solute mass balances are given by

$$\frac{d}{dx}(Q_bC_b) = -(K_oA/\ell)(C_b - C_d) + (dQ_b/dx)sC_b \quad (3)$$

$$-\frac{d}{dx}(Q_dC_d) = (K_oA/\ell)(C_b - C_d) - (dQ_b/dx)sC_b \quad \cdots(4)$$

where K_o and s stand for the overall membrane permeability and sieving coefficient respecitively. * The boundary conditions are

$$C_b = C_{bi} \qquad \text{at } x = 0$$
$$C_d = C_{di} \qquad \text{at } x = \ell$$

* Sieving coefficient has different values for different solutes. When $s = 1$ there is no reflection, and the solute particles pass through like water. When $s = 0$ all the solute particles are reflected.

The solvent flux is represented

$$-\frac{dQ_b}{dx} = L_p(P_b - P_d)A/\ell \quad \cdots\cdots (5)$$

were L_p represents hydraulic permeability.

Applying the Poiseuille's law to pressure drop along hollow fibers, we obtain the expressions for pressure distribution:

$$P_b(x) = P_{bi} - a\int_o^x Q_b\,dx \quad \cdots\cdots (6)$$
$$P_d(x) = P_{di} - b\int_x^\ell Q_d\,dx \quad \cdots\cdots (7)$$

where a and b are proportional constants that may be calculated by the Poiseuille law or determined by experiments.

Overall conservations of solvent and solute give

$$Q_{bi} - Q_b = Q_{do} - Q_d \quad \cdots\cdots (8)$$

$$Q_{bi}C_{bi} - Q_bC_b = Q_{do}C_{do} - Q_dC_d \quad \cdots\cdots (9)$$

SOLUTION OF THE MODEL EQUATION

In order to obtain the flow rate as a function of axial coordinate, Eqs.(5) through (8) are used. The resulting solutions are

$$Q_b(x) = I + Je^{mx} + Ke^{-mx} \quad \cdots\cdots (10)$$
$$Q_d(x) = I' + Je^{mx} + Ke^{-mx} \quad \cdots\cdots (11)$$

where:

$$I = -\frac{b}{a+b}(Q_{do} - Q_{bi})$$

$$I' = \frac{a}{a+b}(Q_{do} - Q_{bi})$$

$$J = \{(Q_{bo} - I)e^{m\ell} - (aQ_{bi} + bQ_{do})/(a+b)\}/(e^{2m\ell} - 1)$$

$$K = \{-(Q_{bo} - I)e^{m\ell} + (aQ_{bi} + bQ_{do})e^{2m\ell}/(a+b)\}/(e^{2m\ell} - 1)$$

$$m = \{(a+b)L_pA/\ell\}^{1/2}$$

Insertion of Eq. (9) into Eq. (3) leads to a first order differential equation

$$\frac{dC_b}{dx} + f(x)C_b = g(x) \quad \cdots\cdots (12)$$

were:

$$f(x) = \frac{1}{Q_b}\left(\frac{K_oA}{\ell}\frac{Q_{do} - Q_{bi}}{Q_b + Q_{do} - Q_{bi}} + (1-s)\frac{dQ_b}{dx}\right)$$

$$g(x) = \frac{1}{Q_b}\left(\frac{K_oA}{\ell}\frac{Q_{do}C_{do} - Q_{bi}C_{bi}}{Q_b + Q_{do} - Q_{bi}}\right)$$

Solving Eq. (12) using Eq. (10), we obtain

$$\frac{C_b}{C_{bi}} = \frac{1}{P(x)}\frac{K_oA}{\ell}\frac{S(x)C_{bo}Q_{bo}}{C_{bi}(Q_{bi} - Q_{do})} + \frac{P(o)}{P(x)} \quad \cdots\cdots (13)$$

where:

$$P(x) = Q_b^{1-S}\exp(P_1(x) - P_2(x))$$

$$P_1(x) = -W\left(\frac{K_2A}{m\ell}\right)[I_2 - 4JK]^{*1/2}$$
$$\ln\left(\frac{e^{mx} + I/2J + ([I^2 - 4JK])^{1/2}/2[J]}{e^{mx} + I/2J - ([I^2 - 4JK])^{1/2}/2[J]}\right)$$
$$\text{for } I^2 - 4JK > 0$$

$$W\left(\frac{2K_oA}{m\ell}\right)\tan^{-1}\left(\frac{e^{mx} + I/2J}{([I^2 - 4JK])^{1/2}/2[J]}\right)/(I^2 - 4JK)^{1/2}$$
$$\text{for } I^2 - 4JK < 0$$

$P_2(x)$ = the same as $P_1(x)$ except that I is replaced by I' where

$$S(x) = \int_o^x P(x)(Q_b^{-1} - Q_d^{-1})\,dx$$

$W = \text{sign}(J)$

When the ultrafiltration rate is small enough to assume

that $m \ll 1$, Q_b Q_d and C_{bo} become

$$Q_b = I + J + K + (J-K)mx = Q_{bi} - Q_f x/\ell \quad \text{..... (14)}$$

$$Q_d = I' + J + K + (J-K)mx = Q_{do} - Q_f x/\ell \quad \text{..... (15)}$$

$$C_{bo} = X_1 C_{bi}/(1 + X_1 X_2 Q_{bo}) \quad \text{..... (16)}$$

where:

$$X_1 = (1 - Q_f/Q_{bi})^{(K_o A/Q_f - 1 + s)} (1 - Q_f/Q_{do})^{-(K_o A/Q_f)}$$

$$X_2 = \frac{K_o A}{Q_{bi} Q_{do}} \int_o^{\ell} (1 - Q_f y/Q_{bi})^{-(K_o A/Q_f + s)} (1 - Q_f y/Q_{do})^{(K_o A/Q_f - 1)} dy$$

Eqs. (14) and (16) were established by Ross et al. [3] Thus it is seen that the one-dimensional model formulated by Ross et al. is the limiting case of the present model.

When there exists negligible ultrafiltration, m becomes zero. In this case X_1 and X_2 in Eq. (16) have the following limiting values.

$$\lim_{Q_f \to 0} X_1 = \exp(-K_o A(Q_b^{-1} - Q_d^{-1}))$$

$$\lim_{Q_f \to 0} X_2 = \exp(K_o A(Q_b^{-1} - Q_d^{-1}) - 1)/(Q_d - Q_b)$$

Hence the outlet concentration C_{bo} can be represented by

$$C_{bo}/C_{bi} = \frac{\exp(-K_o A(Q_b^{-1} - Q_d^{-1}))}{1 + Q_b(1 - \exp(-K_o A(Q_b^{-1} - Q_d^{-1})))/(Q_d - Q_b)} \quad \text{..... (17)}$$

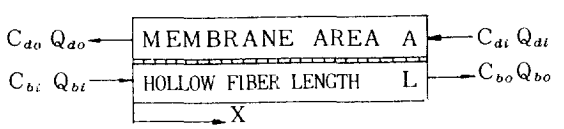


Fig. 1. Two phase model and notations for hollow fiber artificial kidney

RESULTS AND DISCUSSION

In this section a set of data reported by Kunitomo et al. [8] is compared to the present model. The characteristics of polymethylmethacrylate hollow fiber units (Filtryzer Type A-1, Toray Industries, Inc., Tokyo, Japan) are given in Table 1. Overall membrane permeability for urea and vitamine B_{12} can be calculated at blood and dialysate flow rates of 200 and 500 ml/min, respectively with the clearance data obtained from the conventional dialysis experiment. Using the clearance data in Table 2 and Eqs. (2) and (17), we obtain the overall membrane permeability K_0.

Table 1 Hollow Fiber Artificial Kidney Characteristics

Model	Filtryzer A-1
Area(A)	1.15 m^2
Length(l)	0.19 m
Hydraulic Permeability(L_p)	2.5^{-11}m/Pa.s
Pressure Drop Parameter (a,b)	1.9×10^9 kg/m^5.s

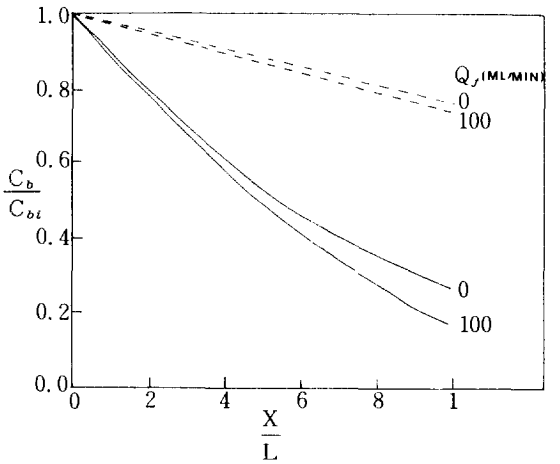


Fig. 2. Concentration distribution in hollow fiber artificial kidney with and without ultrafiltration; —:urea; ···:vitamine B_{12}

Table 2 Clearance Data

Solute	M.W.(daltons)	Clearance (ml/min)	Sieving Coefficient
Urea	60	147	1
Vitamine B_{12}	1355	48	0.92

Fig. 2 shows the concentration distribution calculated by Eq. (13) along the fibers. The decrease of urea concentration is more prominent than that of vitamine B_{12} which is attributed to higher permeability of urea. The further decrease of solute concentrations upon ultrafiltration is not readily explained. However, rearranging Eq. (3) assuming s = 1, we have

$$\frac{dC_b}{dx} = \frac{-(K_o A/\ell)(C_b - C_d)}{Q_b} \quad \text{..... (18)}$$

From Eq. (18) it becomes clear that decreasing Q_b will result in a larger rate of decrease for C_b along x. Physically it means that a smaller Q_b will have a longer residence time during which more solute will be remov-

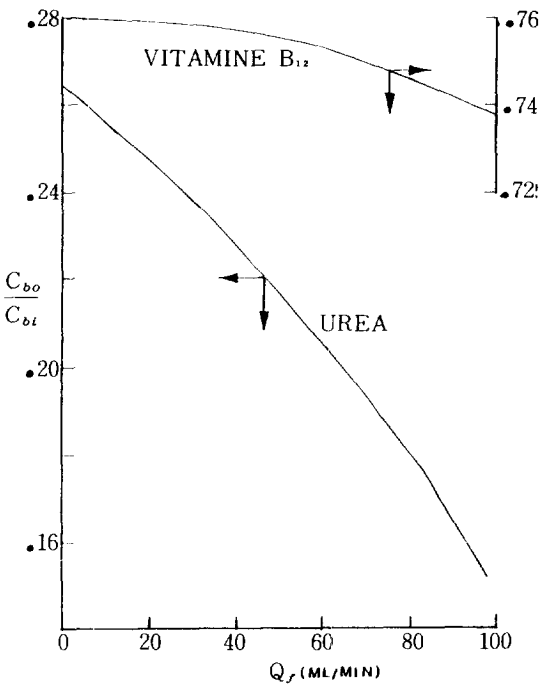


Fig. 3. Outlet concentration as a function of ultrafiltration rate

ed. The rate of removal is proportional to permeability, which explains the enhanced ultrafiltration effect of urea over vitamin B_{12}. The outlet concentrations of the two solutes are given in Fig. 3 as a function of ultrafiltration rate. The variation in the concentration of vitamin B_{12} is less than that of urea. This indicates that the diffusion process of high molecular weight solutes is less dependent on the convection process, i.e., the ultrafiltration and the diffusion are mutually less inter fered.

Werynski [9] compared two forms of clearance, one of which is Eq. (1) and the other is

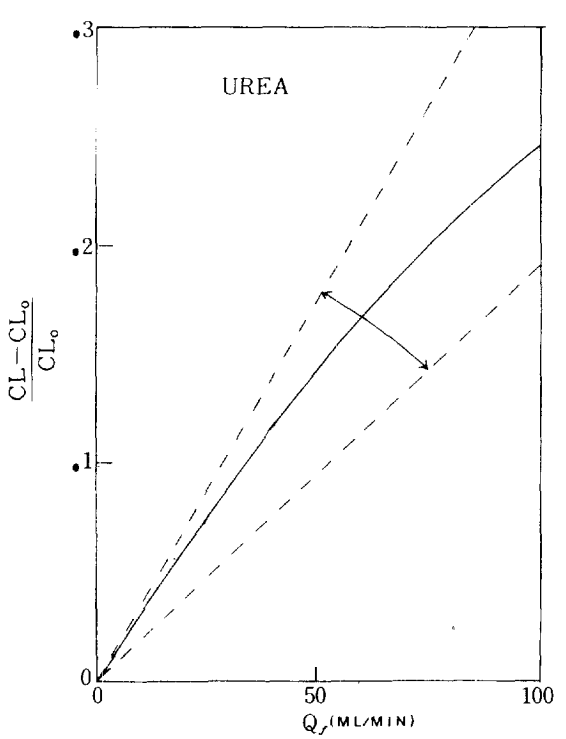
$$CL = CL_o + M'Q_f \quad \text{.....(19)}$$

where CL_o is represented by Eq. (2) and M' is a constant coefficient obtained from the slope of the graph for CL vs. Q_f.

Linear enhancement of clearance resulting from applying ultrafiltration was also reported by Kunitomo et al. [8] and the experimental results were correlated in the following form

$$\frac{CL - CL_o}{CL_o} = MQ_f \quad \text{.....(20)}$$

The theoretical value was evaluated by varying the ultrafiltration rate and putting the data in Table 1 and K_o's into Eq. (13). The comparisons of the theoretical



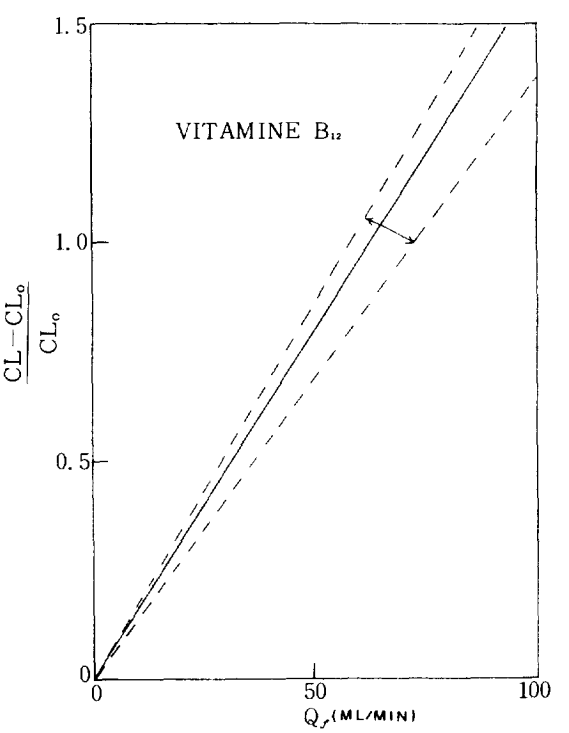


Fig. 4. Increase of clearance due to ultrafiltration; (a) urea; (b) vitamine B_{12}; ···experimental data range; —theoretical value.

and the experimental clearance increases for urea and vitamine B_{12} were made in Fig. 4(a). and 4(b). It was found that the clearance enhancement is more noticeable with the increase of molecular weight. The theoretical lines are not straight but become concave downward. This implies that in Eq. (1), C_{bo}/C_{bi} is not independent of the ultrafiltration rate but coupled through the simultaneous diffusion and convection. The theoretical curve in case of vitamine B_{12} is closer to a straight line because the change of outlet concentration with the increase of ultrafiltration is not so large as in urea. The set of experimental data scattered so broadly that the trend of curve flattening at high ultrafiltration rate could not be observed.

CONCLUSIONS

A more general model for predicting the ultrafiltration effect on clearance was developed to consider the variation of ultrafiltration rate along hollow bifers in an artificial kidney.

This model showed that the increase of clearance with ultrafiltration was not linear contrast to the result of previous investigators. The curves representing the relationship between clearance increase and ultrafiltration become concave downwards as the ultrafiltration increases.

Experimental data adapted to compare with theoretical results was so scattered that the results were inside the error range of the experimental data.

NOMENCLATURE

a : proportional constant defined by Eq. (6), $kg/m^5.s$
A : membrane area, m^2
b : proportional constant defined by Eq. (7), $kg/m_{5}.s$
C : concentration, mol/m^3
CL : clearance defined by Eqs. (1) and (2), cm^3/min
I,I′ : constant defined by Eqs. (10) and (11), respectively
J,K : constant defined by Eq. (10), m^3/s
K_o : overall membrane permeability, m/s
ℓ : length of hollow fiber, m
L_p : hydraulic permeability, m/Pa.s
m : parameter defined by Eq. (10), 1/m
M : proportional constant defined by Eq. (20), s/m^3
P(x) : function defined by Eq. (13), m^3/s
Q : volumetric flow rate, m^3/s
s : sieving coefficient (C_f/C_b)
S(x) : function defined by Eq. (13), m
x : axial coordinate, m
X_1, X_2 : constants defined by Eq. (16)

Subscripts

b : blood phase
d : dialysate phase
f : filtrate
i : inlet
o : outlet

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