CHAPTER - III

ANALYSIS OF ION TRANSPORT IN HUMAN EYE
3.1 INTRODUCTION

Ocular avascular tissues derive their nutrients from the blood in direct or indirect manner. The tissues in the contact of vascular system receive directly nutritional elements while the tissues far from the vasculcular system, i.e. not direct in contact, do the same through a fluid environment in aqueous or vitreous environment. The aqueous humour, the principal fluid of the eye, plays the most important role in ion exchange processes between blood vessels and the aqueous fluid chambers as well as between fluid chambers and avascular tissues and between other fluid systems. Movement of ions between blood vessels and the intraocular fluids or between the fluids and the ocular tissues generally takes place across membranes which offer varying degrees of resistance from ion to ion and from substance to substance.

Movement of ions between blood vessels and the intraocular fluids is mainly responsible for the maintenance of homeostasis of aqueous humour concentration which is essential for normal supply of nutrients to the tissues e.g. the lens and cornea [Cole (1961) Cunha-vaz, Shakib and Ashton (1966)]. The movement is controlled mainly by the interfacing morphological systems (i.e. cellular membranes) between the blood and fluid known as blood-aqueous barriers and interfacing structures between the aqueous and tissues regulate accumulation and steady state distribution of ions in the posterior
and the anterior aqueous. The aqueous humour is produced from the blood by ciliary processes and is accumulated into the posterior chamber and escape through the pupillary aperture into the anterior chamber from the posterior chamber, thence flows out of the eye through trabecular meshwork.

Some percent of the total aqueous produced flows through the vitreous. The lens and ciliary body receive their nutritional substances from the posterior aqueous and the cornea from the anterior aqueous [Davson and Spaziani (1961), Cole (1960)]. A knowledge of the accumulation and steady state distribution of ions in the posterior & anterior aqueous and the trabecular meshwork is very useful for understanding solute exchange phenomena in the aqueous humour.

The homeostasis of the posterior and anterior aqueous concentration is necessary and essential for living of avascular tissues — the lens and cornea. Its disturbance has detrimental effects on the normality of these tissues which may cause a loss of vision by interrupting optical functions of the eye [Bito, Davson, Levin, Murray and Snider (1965)]. Also, the aqueous homeostasis is mainly dependent on the transport activity of blood-aqueous barriers, interfacing systems between the aqueous environment and the tissues [Miller (1965)]. An analytical study of transient concentration distribution in the posterior and anterior aqueous humour and in the trabecular meshwork and the effect of physiological parameters of the interfacing systems on the
distribution may provide a significant understanding of the nature of ion and solute transport for maintaining the homeostasis [Kinsey and Reddy (1964) and Kinsey (1972)].

Present study is concerned with the transient penetration of various ions, in particular Na\(^+\) and Cl\(^-\) in aqueous humour filling the posterior and anterior chambers and the trabecular meshwork taking into consideration of various factors i.e. electrochemical osmosis contributing in the transport phenomena of ions.

3.2 FORMULATION OF THE PROBLEM:

Most of experimental studies of solute transfer in the anterior and posterior chambers have been concerned with the estimation of the quantity of ions that enter and leave the posterior and anterior aqueous by passive diffusion and unidirectional flow. It is appropriate to accomplish a mathematical analysis of the ion penetration in the posterior and anterior aqueous humour and trabecular meshwork.

We assume that ion movement from ciliary body stroma to the posterior chamber occurs by passive diffusion and unidirectional flow and ion transfer across posterior chamber and vitreous interface takes place by diffusional processes. The transfer of substances from posterior aqueous to the anterior aqueous is due to flow of aqueous humour. The rate of accumulation of substances in the posterior chamber
is described by the equation:

\[
\frac{dC_h}{dt} = K_{fh}(C_s - C_h) + K_{dh}(C_s - a_f C_h) - K_{fa}(C_h - C_a) - K_{dv}(C_h - C_v)
\]  

(3.1)

It is also assumed that transfer of substances from the anterior chamber into the cornea is due to the diffusion and outflow of aqueous humour in the trabecular meshwork. The contribution of each of these factors to the rate of accumulation of substances in the anterior chamber is described by the equation:

\[
\frac{dC_a}{dt} = K_{fa}(C_h - C_a) + K_{dI}(C_I - C_a) - K_{da}(C_a - C_c) - K_{fTm}(C_a - C_{Tm})
\]  

(3.2)

It is assumed that the transfer of substances from the trabecular meshwork into episcleral veins takes place only through unidirectional flow:

\[
\frac{dC_{Tm}}{dt} = K_{fTm}(C_a - C_{Tm}) - K_{fE}(C_{Tm} - C_E)
\]  

(3.3)

Prescribed initial conditions are

\[
C_a(0) = 0
\]  

(3.4)

\[
C_h(0) = 0
\]  

(3.5)

\[
C_{Tm}(0) = 0
\]  

(3.6)

where \(K_{fh} \), \(K_{fa} \), \(K_{fT} \) and \(K_{fE} \) are transfer coefficients for
flows from plasma to the posterior chamber, from the posterior chamber to the anterior chamber, from the anterior chamber to the trabecular meshwork and from the trabecular meshwork to the episcleral veins respectively. $K_dh$, $K_{da}$, $K_{dv}$ and $K_{di}$ are the transfer coefficients by diffusion from plasma to the posterior chamber, from the anterior chamber to the cornea, from the posterior chamber to the vitreous body and from the iris to the anterior chamber respectively.

3.3 SOLUTION TO THE PROBLEM:

The problem consisting of the differential equations (3.1, 3.2, 3.3) and initial and boundary conditions (3.4 - 3.6) has been solved by using Picard's type iterative procedure, we obtain the solution in the form

$$C_h = A_4 t + B_1 \frac{t^2}{2} + 3 B_2 \frac{t^3}{6} + B_3 \frac{t^4}{24} + B_4 \frac{t^5}{120} + B_6 \frac{t^6}{720}$$ (3.7)

$$C_a = A_2 t + [A_1 A_2 + K_{da} A_4 + K_{FT} A_6] t^2/2 + [B_1 K_{fa} - A_1 K_{fa} A_4$$

$$+ A_2 K_{FT}^2] t^3/6 + [B_2 + K_{fa} K_{FT} A_4] t^4/24 + B_3 t^5/120$$

$$+ B_5 t^6/720 + B_6 \frac{t^7}{5040}$$ (3.8)

$$C_{Tm} = A_6 t + (-A_5 A_6 + K_{FT} A_2) t^2/2 + [A_5 A_3 K_{ft} + K_{FT}$$

$$(A_1 A_2 + K_{fa} A_4 + K_{FT} A_6)] t^3/6 + [-A_5 A_4 K_{fa} + (A_2 K_{FT}$$

$$+ B_3 K_{fa} - A_1 A_4 K_{fa})] \frac{t^4}{24} + [K_{FT} B_2 + K_{fa} K_{FT} A_4]$$
\[
\frac{t^5}{120} + K_{fT} \frac{t^6}{720} + K_{fT} B_4 \frac{t^7}{5040} + K_{fT} B_5 \frac{t^8}{40320} \tag{3.9}
\]

where

\[
A_1 = K_{fa} + K_{dI} + K_{da} + K_{fT}
\]
\[
A_2 = K_{dI} C_I + K_{da} C_c
\]
\[
A_3 = K_{fh} + K_{dh} + K_{fa} + K_{dV}
\]
\[
A_4 = K_{fh} C_s + K_{dh} C_s + K_{dV} C_v
\]
\[
A_5 = K_{fT} C_{fE}
\]
\[
A_6 = K_{fE} C_E
\]
\[
B_1 = A_4 B_3 + A_2 K_{fa}
\]
\[
B_2 = A_3 (-A_3 A_4 + K_{fa} A_2) - A_1 A_2 K_{fa} + A_6 K_{fT}
\]
\[
B_3 = A_2 K_{fT}^2 - A_4 A_4 K_{fa}^2 + K_{fa} A_2
\]
\[
B_4 = A_4 (K_{fa} + K_{fT}) K_{fa}
\]
\[
B_5 = A_4 K_{fa}^2
\]

The computational results for the concentration of penetrating Isotopes \( {^{24}}\text{Na}^+ \) and \( {^{35}}\text{Cl}^- \) in the posterior and anterior aqueous humour for experimentally determined values of parameters (Table 3.1) are presented in the following section.
Table 3.1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Numerical value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$K_{da}$ (Cl)</td>
<td>0.0125 min$^{-1}$</td>
</tr>
<tr>
<td>$K_{dh}$ (Cl)</td>
<td>0.0325 min$^{-1}$</td>
</tr>
<tr>
<td>$K_{fa}$ (Cl)</td>
<td>0.0135 min$^{-1}$</td>
</tr>
<tr>
<td>$K_{ft}$ (Cl)</td>
<td>0.109 min$^{-1}$</td>
</tr>
<tr>
<td>$K_{fh}$ (Cl)</td>
<td>0.019 min$^{-1}$</td>
</tr>
<tr>
<td>(Cl)</td>
<td>0.972 µmol/gm</td>
</tr>
<tr>
<td>$K_{da}$ (Na)</td>
<td>0.0125 min$^{-1}$</td>
</tr>
<tr>
<td>$K_{dh}$ (Na)</td>
<td>0.065 min$^{-1}$</td>
</tr>
<tr>
<td>$K_{fa}$ (Na)</td>
<td>0.0125 min$^{-1}$</td>
</tr>
<tr>
<td>$K_{fh}$ (Na)</td>
<td>0.0625 min$^{-1}$</td>
</tr>
<tr>
<td>$\alpha$ (Na)</td>
<td>1.096 µmol/gm</td>
</tr>
</tbody>
</table>

3.4 RESULTS AND DISCUSSION

Figure 3.1 represents the penetration of isotope $^{24}$Na injected in the plasma into the posterior and anterior aqueous humour. It is observed from the graphs that the concentration in the posterior aqueous initially rises rapidly and after some time this rise begins to decrease. We also observe a rapid decrease in the rise at the first instant and then the rise continues to decrease gradually with time. Initial rise in the concentration in the anterior
Fig. 3.1 Effect of parameters on the $^{24}\text{Na}$ concentration-time curves in posterior and anterior chamber aqueous humour for $K_{da} = 0.0125 \text{min}^{-1}, K_{fh} = 0.0625 \text{min}^{-1}$
aqueous humour is rapid but less than that in the posterior aqueous. The rise in the anterior aqueous goes on decreasing with time. Thus initially, $^{24}\text{Na}$ concentration in the anterior aqueous is smaller than that in the posterior aqueous. But after some time concentration in aqueous increases with that in the anterior chamber and finally over shoots so that at a later stage the concentration in the anterior aqueous becomes higher. At the initiation of $^{24}\text{Na}$ penetration, there are no losses through the lens-vitreous interface. As the time increases, losses to the vitreous reduces the concentration in the posterior chamber. The transport of $^{24}\text{Na}$ from iris to the anterior chamber increases its concentration in later stages.

The effects of transfer coefficients $K_{dh}$ and $K_{fa}$ on the penetration in the posterior and anterior aqueous have also been brought out. $K_{dh}$ does not affect considerably the penetration of $^{24}\text{Na}$ while $K_{fa}$ has greater effects than $K_{dh}$. An increase in $K_{fa}$ causes increase in concentration in the anterior aqueous. Similar results were obtained by Kinsey (1962).

In Fig. 3.2, we have plotted relative concentration of $^{24}\text{Na}$ in the posterior aqueous humour with time, and the effects of various parameters on the penetration have also been depicted. Evidently, a decrease in $K_{rh}$ causes a decrease in the concentration and an increase in electrochemical equilibrium coefficient, $\alpha$, increases.
Fig. 3.2 Effect of different parameters on the $^{24}$Na concentration-time curves in posterior chamber aqueous humour.
the concentration in the anterior aqueous humour. A decrease in transfer coefficient due to flow from the posterior chamber into anterior chamber, $K_{fh}$, decreases the influx of $^{24}\text{Na}$ from the ciliary body to the posterior aqueous leading to a decrease in the concentration in the posterior aqueous. We assume that increase in it is due to only increase in potential difference. An increasing potential increases influx of sodium. An increase in $\alpha$ augments influx of $^{24}\text{Na}$ in the posterior chamber and therefore the concentration increases.

Figure 3.3 depicts the concentration of penetrating $^{24}\text{Na}$ into the anterior aqueous humour and effects of transfer coefficient due to flow into the trabecular meshwork from the anterior chamber, $K_{fT}$, and transfer coefficient due to diffusion from the posterior chamber into the anterior chamber on the concentration. The concentration decreases with increase in $K_{fT}$ while an increase in $K_{da}$ makes arise in the concentration. These results are justified due to the fact that increasing $K_{fT}$ increases the loss of ion and increasing $K_{da}$ increases $^{24}\text{Na}$ ion penetration in the anterior aqueous from the iris vessels.

In Fig. 3.4, we have shown the concentration of penetrating $^{35}\text{Cl}$ into the posterior and anterior aqueous humours. It is evident from the graphs that the concentration in the anterior chamber rises linearly in the beginning, but after some time, there is nonlinear decrease in the rise with
Fig. 3.3 Effect of parameters on the $^{24}\text{Na}$ concentration time curves in the anterior chamber aqueous humour for $K_{fa} = 0.01 \text{ min}^{-1}$. 

- $k_{da} = 0.013 \text{ min}^{-1}, k_{fT} = 0.019 \text{ min}^{-1}$
- $k_{da} = 0.0125 \text{ min}^{-1}, k_{fT} = 0.019 \text{ min}^{-1}$
- $k_{da} = 0.0125 \text{ min}^{-1}, k_{fT} = 0.02 \text{ min}^{-1}$
Fig. 3.4 Effect of parameters on the $^{35}$Cl–concentration-time curves in posterior and anterior chamber aqueous humour for $K_{da} = 0.125 \text{ min}^{-1}$, $K_{dh} = .03 \text{ min}^{-1}$.
the time. The concentration in the posterior aqueous humour shows initially a steep rise. In the later stages of the process, there is a rapid fall in the rise of concentration in the posterior fluid and this fall is almost linear. We observe that the concentration in the posterior aqueous is greater than that in the initial stage. But in the later stages, it becomes lower i.e. in the latter stages of the process the concentration in the anterior aqueous overtakes the concentration in the posterior aqueous. From figures 3.1 and 3.4 we notice that the falling in the rise of concentration of Cl\(^{-}\) ion in the posterior aqueous is much more profound than that of 24Na.

We have also shown the effects of \(K_{fa}\) and \(K_{fh}\) on the concentration. The concentration in the anterior aqueous decreases with decrease in \(K_{fa}\) as a decrease in \(K_{fa}\) reduces the influx in the anterior chamber. A decrease in \(K_{fh}\) leads to a decrease in the concentration in the posterior aqueous humour. These results are fairly in agreement with that of Kinsey (1972).

In Fig. 3.5, we have shown the effects of \(K_{ft}\) and \(K_{da}\) on the penetration of 35Cl in the posterior and anterior aqueous humour. The concentration decreases with decrease in \(K_{da}\). Decreased \(K_{da}\) reduces the penetration of Cl\(^{-}\) in the anterior fluid from the iris blood vessels. An increase in \(K_{ft}\) increases the out flow of aqueous humour from the anterior chamber and the concentration of ions is
Fig. 3.5 Effect of parameters on the $^{35}$Cl concentration time curves in the posterior chamber aqueous humour for $k_{fa} = 0.130$ min$^{-1}$
decreased with increase in $K_{fT}$. Similar results are found from the graphs in Fig. 3.5.

A decrease in $K_{dh}$ causes a decrease in the influx of penetration from the ciliary body stroma in the posterior aqueous humour and so the concentration decreases with decrease in $K_{dh}$. Such results are observed from the graphs in Fig. 3.6. It is also observed that a decrease in $\alpha$ decreases the concentration. A decrease in $\alpha$ implies that potential difference is decreased which causes a decrease in penetration of ions into the posterior aqueous humour.

In Figure 3.7, the characteristic curves of concentration of $^{24}\text{Na}$ penetrating in the trabecular meshwork of the eye have been plotted. The effects of the model parameters $K_{fT}$, $K_{fE}$ on the penetration have also been shown. An examination of the curves clearly shows that the concentration of $^{24}\text{Na}$ increases rapidly in the initial stage of process. After some time a decrease in the increase in concentration is observed. This decreasing trend continues till steady state is attained. An increase in $K_{fT}$ causes an increase in the concentration. This observation is supported by the fact that as the aqueous outflow coefficient $K_{fT}$ increases, the aqueous in-flux increases and so increased amount of $^{24}\text{Na}$ is carried by the increased aqueous flux. Which results in an increase in the concentration.
Fig. 3.6 Effect of parameters on the $^{35}\text{Cl}^-$ concentration accumulation in posterior chamber aqueous humour for $k_{fh} = 0.06 \text{ min}^{-1}$.
Fig. 3.7 Effect of parameters on the $^{24}\text{Na}$-concentration time curves in the trabecular meshwork aqueous humour for $k_{fa} = 0.010 \text{ min}^{-1}$ and $k_{da} = 0.0125 \text{ min}^{-1}$
Figure 3.8 depicts the influence on the characteristic curves of concentration of penetrating $^{35}\text{Cl}$ in the trabecular meshwork of the flow coefficients $K_{fT}$ and $K_{fE}$. Evidently, the concentration of $^{35}\text{Cl}$ increases with time. In the initial stage of penetration process, the increase in concentration is rapid. After some time, a decrease in increase is observed. The concentration of $^{35}\text{Cl}$ increases with increasing $K_{fT}$ while the concentration decreases with increasing $K_{fE}$. An increase in $K_{fT}$ causes an increase in influx of aqueous in the trabecular meshwork and so more $^{35}\text{Cl}$ is carried in the trabecular meshwork. An increase in $K_{fT}$ results in more out flux of aqueous humour from the trabecular meshwork and so a decrease in the concentration of $^{35}\text{Cl}$.
Fig. 3.8 Effect of parameters on the $^{35}$Cl$^-$ concentration time curves in the trabecular meshwork aqueous humour for $k_{fa} = 130 \text{ min}^{-1}$ and $k_{da} = 0.125 \text{ min}^{-1}$