"Mathematical Modeling Of Drug Transport From Contact Lens To Anterior Segment Of The Eye"

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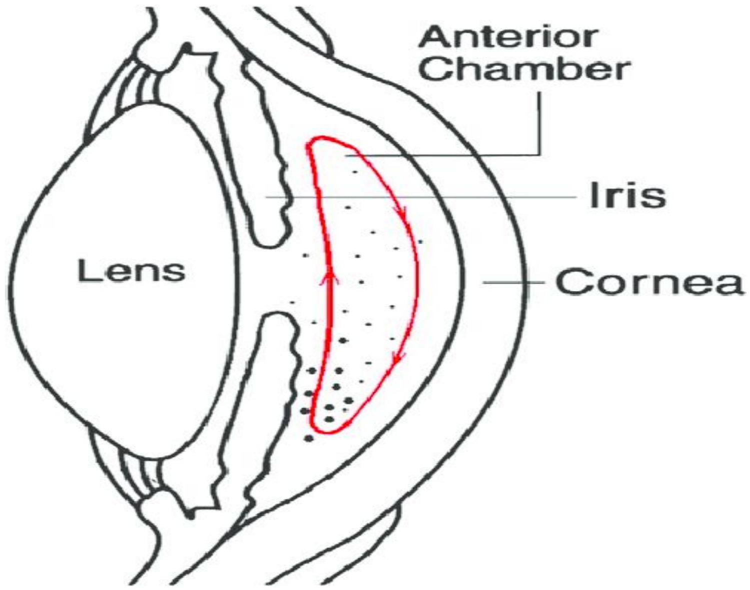
Abstract: The motive of this paper,to show the overview of drug delivery from contact lens to anterior segment via pre corneal area , cornea.We use the diffusion based mathematical model in which parameters can be adjusted ,based on experimental result obtained under controlled conditions.The contact lenses drug delivery system have been developed a model to increase the time of drug availability at the surface of eye.

Keywords : Contect Lens, Drug delivery, Biological Tissue, Anterior Chember, Hydrogel,Transport Phenomena.

I. INTRODUCTION

The use of contact lenses increasingly laboratories for in vivo animals retinal concept and preclinical studies. A flexible method to fabricate customized hydrogel contact lens. We observe that the fabricated gel has maximum transparency with refractive index range $1.42 - 1.45$ nano meter and in spectra range $400 - 800\ nm$[1].The soft contact lenses are made of hydrogel ,capable of absorbing requisite volume of medium of aqueous. The cornea remains in contact with high concentration of drug for long period and drug penetration is more efficient. The drug reservoir ability depends on the water contents , thickness of lenses and molecular weight of drug. Controlled and release drug delivery have moved phenomenally in recent years and open new ways in the field of drug delivery system. In this paper, Mathematical model that elucidates the joint process of drug release from polymeric matrix [5] and consequent transport of drug particles in biological tissue. In present investigation, the mathematical modeling and biological physiology for the sake of bridging the gap between biological perspective and transport phenomena. Therapeutic contact lenses for the sake of increase of ocular bioavailability of ophthalmic medicines together dermal and transdermal delivery [3,4].



Fig(1)
Schematic diagram of Eye

In mathematical point of view ,the FAQ that how can we predict of drug concentration in anterior chamber of the eye.Here mathematical models describing the behavior of drug concentration across the Precorneal and cornea. When a drug dropped on contact lens then the absorption of drug depend on the concentration of lens. The mathematical modeling of the different mechanism responsible for controlled released from hydrogel such as diffusion is well described in literature. The aim of this work to describe and characterize the diffusion based mathematical model to design of multilayered drug load lenses. Contact lenses are emerging as an alternative ophthalmic drug delivery system to resolve the weakness of conventional topical method[2].

Model:

In this model we will find the concentration of contact lens,precorneal Area , Cornea and Anterior chember by using mathematical calculations.

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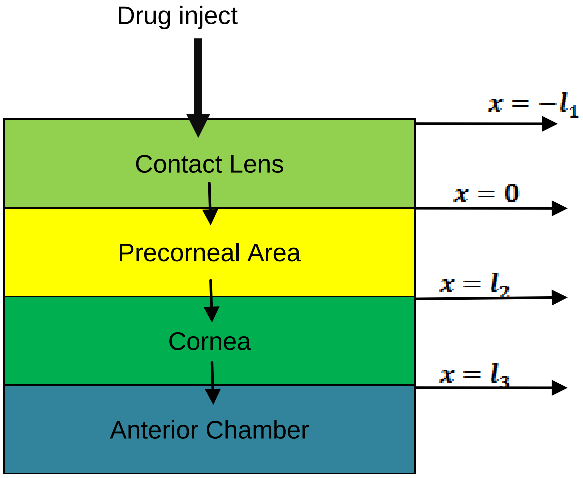


Fig:2 *Schematic diagram of the drug transport from a therapeutically contact lens.*

Drug Transport in Lens
Governing equations:

$$\frac{\partial c_L}{\partial t} = D_L \frac{\partial^2 c_L}{\partial x^2} - \delta_0 c_L \dots \dots \dots \dots \dots (1)$$ [4]

$$c_L(x,t) = \left[c_1 \cos\left(\sqrt{\frac{p^2-\delta_0}{D_L}}\right) x + c_2 \sin\left(\sqrt{\frac{p^2-\delta_0}{D_L}}\right) x \right] c_3 e^{-p^2 t} \dots\dots (1)^*$$

Where p is constant and δ_0 is also a constant depends the behavior of contact lens.
Solution of pre Corneal Area equations:

$$\frac{dc_t}{dt} = \frac{-F_p f_p A_p - F_q f_q A_q - S c_t}{V_L + V_i e^{-k_d t}} \dots\dots\dots\dots (2)$$

Now equation 1 can be written as

$$\frac{dc_t}{dt} + \frac{S}{V_L + V_i e^{-k_d t}} c_t = \frac{-F_p f_p A_p - F_q f_q A_q}{V_L + V_i e^{-k_d t}} \dots\dots\dots\dots (3)$$

We observe that 2 is linear differential equation so

I.F.$= \left(e^{k_d} + \frac{V_i}{V_L}\right)^{\frac{S}{k_d V_L}}$

Then solution of equation (3) is

$$c_t(t) = \left[-\frac{(F_p f_p A_p + F_q f_q A_q)}{S} \left(e^{k_d t} + \frac{V_i}{V_L}\right)^{\frac{S}{V_L k_d}} + c_4 \right] \dots\dots\dots\dots (4)$$

Solution of Corneal Area equation

$$\frac{\partial C_c}{\partial t} = D_c \frac{\partial^2 C_c}{\partial x^2} - \frac{V_c C_c}{k_r + C_c} \dots\dots\dots\dots (5)$$

Here $C_c \ll k_r$ now the reaction term which approximate

by $k_1 C_c$ (Kaku ji ,1988)

So equation (4) reduce as

$$\frac{\partial C_c}{\partial t} = D_c \frac{\partial^2 C_c}{\partial x^2} - k_1 C_c \dots\dots\dots\dots (6)$$

Solution of equation (5) is

$$C_{c_{\alpha_i}}(x,t) = \left[c_5 \cos\left(\sqrt{\frac{p^2-k_1}{D_{\alpha_i}}}\right) x + c_6 \sin\left(\sqrt{\frac{p^2-k_1}{D_{\alpha_i}}}\right) x \right] c_7 e^{-p^2 t} \dots\dots (7)$$

Where $i = 1, 2, 3$

$$C_{c_{\alpha_i}}(x,t) = \left[\sum_{n=1}^{\infty} a_n \cos\theta_i x + \sum_{n=1}^{\infty} b_n \sin\theta_i x \right] e^{-p^2 t} \dots\dots\dots\dots (8)$$

Where $C_{c_{\alpha_i}}$ is the concentration of corneal layers

Where $a_n = c_5 c_7$ and $b_n = c_6 c_7$ and $\theta_i = \left(\sqrt{\frac{p^2-k_1}{D_{\alpha_i}}}\right)$

Then

$$C_{c_{\alpha_1}}(x,t) = \sum_{n=1}^{\infty} [a_n \cos\theta_1 x + b_n \sin\theta_1 x] e^{-p^2 t} \dots\dots\dots\dots (9)$$

Where $\theta_1 = \left(\sqrt{\frac{p^2-k_1}{D_{\alpha_1}}}\right)$

$$C_{c_{\alpha_2}}(x,t) = \sum_{n=1}^{\infty} [c_n \cos\theta_2 x + d_n \sin\theta_1 x] e^{-p^2 t} \dots\dots\dots\dots (10)$$

Where $\theta_2 = \left(\sqrt{\frac{p^2-k_1}{D_{\alpha_2}}}\right)$

$$C_{c_{\alpha_3}}(x,t) = \sum_{n=1}^{\infty} [e_n \cos\theta_3 x + f_n \sin\theta_1 x] e^{-p^2 t} \dots\dots\dots\dots (11)$$

Where $\theta_3 = \left(\sqrt{\frac{p^2-k_1}{D_{\alpha_3}}}\right)$

Equation of Anterior chamber

$$\frac{d}{dt}(V_a C_a) = -F_p f_p A_p - Cl_a C_a \dots\dots\dots\dots (12)$$

Equation 8 can be written as

$$\frac{dC_a}{dt} + \frac{Cl_a C_a}{V_a} = -\frac{F_p f_p A_p}{V_a} \dots\dots\dots\dots (13)$$

Solution of equation (13) is given by

$$C_a(t) = -\frac{F_p f_p A_p}{Cl_a} + C_8 e^{-\frac{Cl_a}{V_a} t} \dots\dots\dots\dots (14)$$

Boundary Conditions:

$$\frac{\partial C_L}{\partial x} = 0 \ at \ x = -l_1 \dots\dots\dots\dots (a)$$

$$C_t(t) = C_0 \ at \ t = 0 \dots\dots\dots\dots (b)$$

$$C_{\alpha_i}(x,t)_{t=0} = 0 \dots\dots\dots\dots (c)$$

$$-D_{\alpha_1} f_1 A_1 \left(\frac{\partial C_{\alpha_1}}{\partial x}\right)_{x=0} = \varphi_1 \left[(C_t)_{x=0} - (C_{\alpha_1})_{x=0} \right] \dots\dots\dots\dots (d)$$

$$\left(\frac{C_{\alpha_2}}{\varphi_2}\right)_{x=L_1} = \left(\frac{C_{\alpha_1}}{\varphi_1}\right)_{x=L_1} \dots\dots\dots\dots (e)$$

$$D_{\alpha_2} f_2 A_2 \left(\frac{\partial C_{\alpha_2}}{\partial x}\right)_{x=L_2} = D_{\alpha_1} f_1 A_1 \left(\frac{\partial C_{\alpha_1}}{\partial x}\right)_{x=L_2} \ldots\ldots\ldots\ldots (f)$$

$$\left(\frac{C_{\alpha_3}}{\varphi_3}\right)_{x=L_1} = \left(\frac{C_{\alpha_1}}{\varphi_1}\right)_{x=L_2} \ldots\ldots\ldots\ldots (g)$$

$$D_{\alpha_3} f_3 A_3 \left(\frac{\partial C_{\alpha_3}}{\partial x}\right)_{x=L_3} = D_{\alpha_2} f_2 A_2 \left(\frac{\partial C_{\alpha_2}}{\partial x}\right)_{x=L_2} \ldots\ldots\ldots\ldots (h)$$

$$-D_{\alpha_3} f_3 A_3 \left(\frac{\partial C_{\alpha_3}}{\partial x}\right)_{x=L_3} = \varphi_1\left[(C_t)_{x=L_3} - (C_a)_{x=L_3}\right] \ldots\ldots\ldots\ldots (i)$$

$$(C_a)_{t=0} = 0 \ldots\ldots\ldots\ldots (j)$$

Now applying the boundary condition (a) on equation (1^*) we get

$$c_L(x,t) = \left| b_n \left[\cos\left((l_1 - x)\sqrt{\frac{p^2-\delta_0}{D_L}}\right) x\right] \frac{e^{-p^2 t}}{\sin\left(\sqrt{\frac{(p^2-\delta_0)}{D_L}}\right) l_1} \right| \ldots\ldots\ldots\ldots (15)$$

Where $\boldsymbol{b_n = -c_2 c_3}$

Again apply the boundary condition (b) on equation (4) we get

$$C_t = \left| \frac{(F_p f_p A_p + F_q f_q A_q)}{S} \left[\left(\left(1 + \frac{V_i}{V_L}\right)^{\frac{S}{V_L k_d}} - \left(e^{k_d t} + \frac{V_i}{V_L}\right)^{\frac{S}{V_L k_d}}\right) + C_0 \ldots\ldots\ldots\ldots (16)\right]\right|$$

$\boldsymbol{Where\ C_0 \approx 1}$

Now apply the boundary conditions (d-h) on equation (7) we get

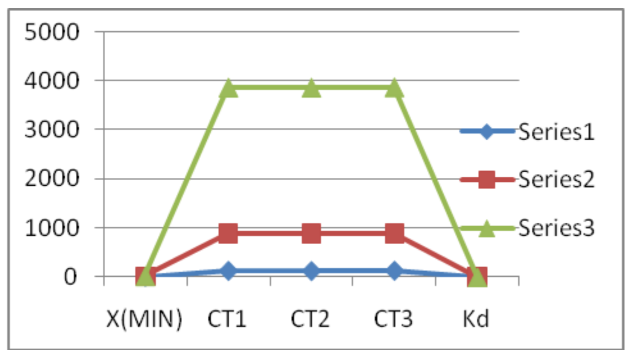
$a_n = \rho_1$

Apply the boundary condition (j) on the equation (10) we get

$$C_a(t) = \left| \frac{F_p f_p A_p}{Cl_a} \left(e^{-\frac{Cl_a}{V_d} t} - 1\right) \right| \ldots\ldots\ldots\ldots (17)$$

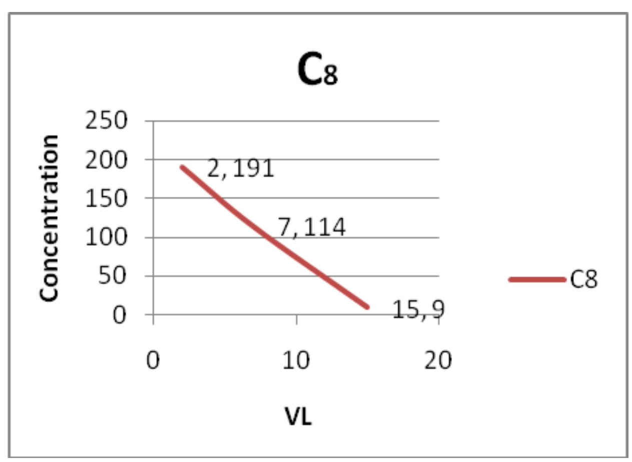
Table(1)[6,3]

$D_{\alpha_i}\ (i = 1,2,3)$	Diffusion Coefficient of Corneal layers(Storma, Epithelium, endothelium)	2.81×10^{-5}, 1.77×10^{-5}, $.49 \times 10^{-5}$	$\frac{cm^2}{s}$
F_p	Fickian diffusion flux of drug across p^{th} corneal layer	7.8-7.6 (For open Eyes) 6.0-6.2(For closed Eyes)	$\mu l \frac{cm^2}{hrs}$
F_q	Fickian diffusion flux of drug across q^{th} conjectiva.	4-6	$\mu l \frac{cm^2}{hrs}$
k_d	Solution of drainage rate constant	1.45(Normaly)	$\frac{1}{min}$
V_L	Normal tear volume	7.0	μl
S	Tear Secretion rate	1.2	$\frac{\mu l}{min}$
A_p	Corneal surface area	1.04	cm^2
A_q	Conjectiva surface area	17.65	cm^2
V_d	Volume distribution in anterior chamber	$1500 - 3000$	μl
Cl_a	Clearance rate in anterior chamber	1-30	$\frac{\mu l}{min}$
f_p	The fractions of Ap occupied by the diffusional route being considered	1	
f_q	The fractions of Aq occupied by the diffusional route being considered	1	



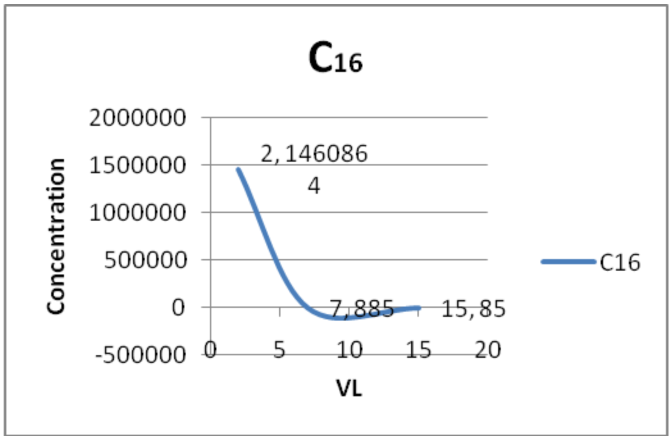
Ct change according to $\boldsymbol{k_d}$

Fig:3



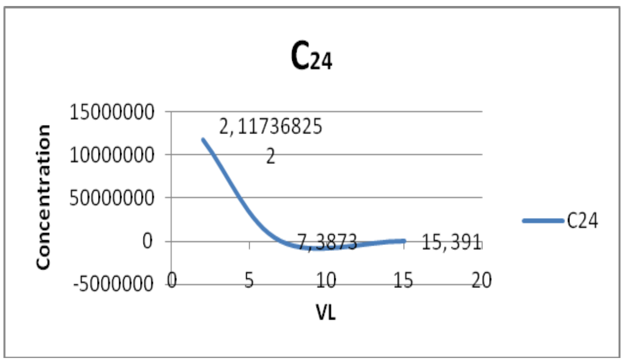
Graph Between Concentration and Tear Volume

Fig:4



Graph Between Concentration and Tear Volume

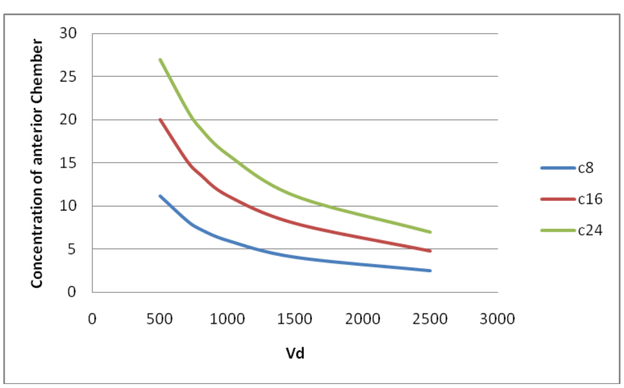
Fig:5



Graph Between Concentration and Tear Volume

Fig:6

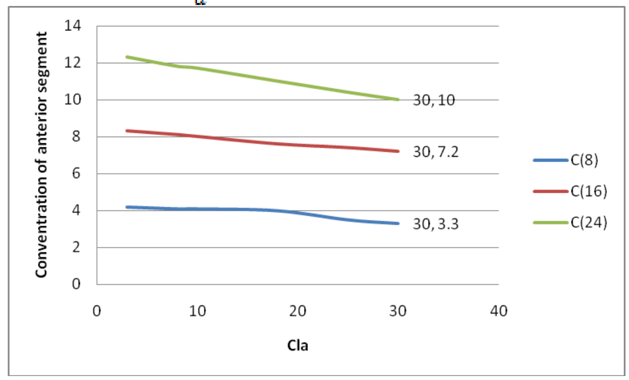
We observe from above graph C_t change according to V_L.The concentration of lens is very high and as soon as drug reached at last layer of lens that's decrease and also parameter effect on concentration of lens C_l &C_t also. It means that as drug inject on the contact lens surface than drug soaked by lens in maximum quantity of drug and reached at Precorneal surface. Also the effect of V_L over concentration is very high , as value of V_L increase then total concentration decrease .It is shows in Fig:3.



Change in Concentration according to Vd

Fig:7

According to fig. 4 we observe that the parameter effect on concentration of anterior segment, the concentration decrease as the value of V_d increase.



Graph between concentration and clearance of anterior chamber

Fig:8

According to above graph the effect of Cl_a shows that concentration is also little bit decrease as the value of Cl_a increase.

RESULT:

From fig 3,4,5 it is clear that the concentration increases as time increases and also if the value of V_L increase then concentration of Precorneal surface decrease. To increase the concentration of Precorneal surface we use contact lens. The concentration of cornea depends on the diffusion coefficient, permeability contact lens k_1. It is clear from all expression of concentration that concentration can't be negative. The concentration of anterior chamber is also decrease as the value of V_d increase. Also the concentration of anterior segments depends on the clearance. If clearance increase then less change in concentration of anterior segment from fig (8).

CONCLUSION:

By using of contact lens for therapeutically treatment may use many deficiencies seen with the typical administration of eye drop into eye. The resident time of drug at Precorneal surface area will be longer All most toxicity will be soaked by can lens. By using soft contact lens, we can control the eye diseases like glaucoma, dry eyes etc. The contact lens can also use for change eye color modification or treatment of diabetic eye diseases, we can provide best treatment of artificial cornea and corneal wound healing.

APPENDIX

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