International Journal of Frontiers in
Biology and Pharmacy Research
Journal homepage: https://frontiersrj.com/journals/ijfbpr/
ISSN: 2783-0454 (Online)

(RESEARCH ARTICLE)

Check for updates

"DURYSTA" the first biodegradable sustained release implant for the treatment of open-angle glaucoma

Shabab Akbar and Sapna Ratan Shah *

Bio-Mathematical Lab 34, School of Computational and Integrative Sciences Jawaharlal Nehru University, New Delhi-110067, (India).

International Journal of Frontiers in Biology and Pharmacy Research, 2021, 01(02), 001–007

Publication history: Received on 28 August 2021; revised on 07 October 2021; accepted on 09 October 2021

Article DOI: https://doi.org/10.53294/ijfbpr.2021.1.2.0042

Abstract

A study for "DURYSTA" in the treatment of open angle glaucoma has been done in this work. A angle between the cornea and iris is open whereas the trabecular meshwork is partially blocked, that obstructs the outflow of aqeous humor and lead to vision loss and damage the optic nurve that is known as open angle glucoma. This model presented the study for outflow of watery clear liquid called aqueous humor from the eye through the trabacular meshwork into the Schlemm's Canal in the human eye. This circular lymphatic-like vessel which is called Canal of Schlemm is modeled as a permeable flexible canal with a trabecular meshwork that keeps it open. Aqueous humor seeps through trabacular meshwork and reaches to Schlemm's canal. The inner wall of the canal is porous and it is considered that between two collecting channels the segment of canal is assumed as a circular cross-section tube. In this model, the flow and pressure characteristics of the aqueous fluid are drawn, and the effect of the main limitations and parameters on these profiles is extracted and explained. The effects of "DURYSTA" on these parameter have also been extracted and shown.

Keywords: DURYSTA; Circular cross-section; Open Angle Glaucoma; Aqueous Humor; Schlemm's Canal

1. Introduction

A clear watery liquid produced by a ciliary muscles or ciliary body that fills anterior chamber as it progresses through the orifice of the pupil known as aqueous humor. Eventually it flows through the trabecular meshwork, a fine mesh at the cornea-sclera-iris junction, and then it reaches to Schlemm's canal and subsequently to the venous structure.

Aqueous humor, which functions similarly to water by providing nutrients and removing unused products of metabolism from the clear cornea and lens, both of which lack blood flow [1], has a comparable characteristic. DURYSTA consistently delivers medicine to the eye to help reduce high eye pressure. Eye drops must be taken at regular intervals but sometimes patients may forget taking the drops or are unable to take them due to age and other reasons. This causes fluctuations in the IOP. When Durysta is implanted in the eye, it releases medication continuously for 24 hours a day seven days a week, which keeps the eye pressure stable and eventually lowers the IOP. This offers relief for the patients as well as caregivers for glaucoma patients. Normal people have a fluid pressure range of 10 to 20 mm Hg due to the constant creation of aqueous humor and drainage through the trabecular meshwork. This pressure helps preserve the shape and optical function of the eye. The trabecular meshwork in some people can become obstructed suddenly or over time, causing an increase in intraocular pressure in the anterior chamber of the human eye.

* Corresponding author: Sapna Ratan Shah
Bio-Mathematical Lab 34, School of Computational and Integrative Sciences Jawaharlal Nehru University, New Delhi-110067, (India).

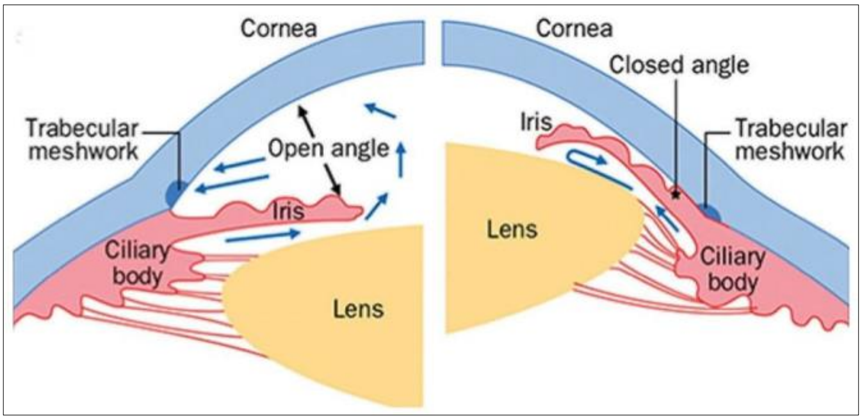

Figure 1 Flow of aqueous humor in eye

This increased intraocular pressure passes to the retina, causing it to lose its function and become one of the main causes of glaucoma. Aqueous humor is a fluid which provides the nutrition and maintain all the all activities of eye. It is secreted at a rate of 2-3 μL/minute by the epithelium of ciliary and reaches the area between the iris and lense, passes through the pupil to the area between lense and cornea and finally reaches the trabecular meshwork which is kind of spongy tissue in the anterior chamber. Nourishes the anterior and posterior chamber tissues while eliminating metabolic waste [2]. Aqueous humor is a necessary fluid which helps eye to maintain normal IOP levels and provide all nutritions to the eye. The trabecular meshwork is made up of collagen fibers and elastic spongy tissue that is covered with cells and drains aqueous humor into Schlemm's canal. These cells can create metalloproteinase matrix enzymes, matrix extracellular components, and individual increase factors and have phagocytic activity.

Impaired aqueous humor drainage caused by amplified resistance within the trabecular meshwork, particularly in the juxtacanalicular region, is the mechanism of IOP increase in open-angle glaucoma. Schlemm's canal is a single endothelium-lined canal that surrounds the cornea. Schlemm's channel cells have characteristics that are similar to blood and lymphatic vessels, as well as molecular similarities between the two cell types [3]. With three views, the size of the cross section of Schlemm's canal was estimated at 1709 m; The cross-sectional area is now expected to vary between 4064 and 7164 m, with many branching water channels. Because Schlemm's canal is little short in the anteroposterior duct than the trabecular meshwork, there is no Schlemm's canal near the external aspect of a portion of the trabecular meshwork (without filtration). The main role of canal of Schlemm is to supply aqueous humor to the collection channels [4]. Both the outer and inner walls of Schlemm's canal include endothelial cells with different expressions of cell-specific markers, specialized cell organelles, shapes, and functions. These anatomical variations between the inner and outer wall endothelium can be influenced by the biomechanical aspects. The endothelium of Schlemm's Canal is linked to trabecular meshwork. Schlemm's canal endothelium and trabecular lamella procedures adhere to juxtacanalicular cellular processes, forming a cellular contact between the Schlemm's canal endothelium and the trabecular lamellae. Desmosomes that are suitable for maintaining cellular stress lie between the junctions of the cellular process and distribute pressure across the cytoskeleton of the involved cell [5].

In the eye there is a canal like a circular lymphatic tube which is known as schlem's canal that is responsible for to collects aqueous humor from the anterior chamber and conducts it through aqueous veins to episcleral blood vessels. Friedrich Schlemm (1795-1858), a German anatomist, was the inspiration for the name. The channel resembles a lymphatic channel because it is lined with endothelium. The trabecular meshwork is located inside the canal, closer to the aqueous humor; This region is the one that contributes the most to the resistance to the outflow of aqueous humor. Schlemm's canal was previously thought to be a blood canal, however studies published in 2014 revealed that its molecular identity is extremely similar to that of the lymphatic vasculature. Glaucoma is the second leading cause of permanent blindness, affecting more than 80 million people worldwide. The imbalanced value of intraocular pressure is the only sign for the diagnosis and progression of glaucoma. The generation and output of aqueous humor in the human eye are balanced to monitor and control intraocular pressure [6]. Aqueous humor progresses through the spongy tissue, trabecular meshwork and juxtacanalicular connective tissue like mussels, Schlemm's canal, collecting canals traversing the sclera, and finally episcleral veins in the conventional outflow tract [7].

The high resistance to the outflow of aqueous humor causes an increase in IOP, which is diagnostic of eye disease which is known as open-angle glaucoma. Juxtacanalicular connective tissue and the inner wall of Schlemm's canal, which are generally considered the main sites of resistance to outflow [8], have been the focus of most studies of resistance to outflow. Resistance to flow forms in Schlemm's canal and collecting canals as intraocular pressure increases, especially in the former [9, 10]. Aqueous humor in the area between the lense and the iris, anterior chamber (AC) passes through a multilayer trabecular meshwork (TM) and into Schlemm's canal in the conventional aqueous humor outlet canal (Trabecular) (SC; located along the limbus). The aqueous humor then passes through the collecting channels (CC) into an intrascleral venous plexus, finally reaching the aqueous and episcleral veins, where it joins the venous circulation that travels to the right side of the heart. The uveoscleral outflow was discovered as a second drain for fluid to leave the eye after the conventional outflow was found to be the initial drain.

2. Mathematical Formulation of the Problem:

When aqueous humor (AH) progresses Schlemm's canal, it has to travel a certain depth to reach a collecting canal. To understand the flow behaviour of aqueous humor in this complex channel area inbetween two gather collector channels the tube is considered as circular cross section, for this we have created a simple mathematical fluid model. The liquid aqueous humor approches to channel area and reaches this collection to the right of the midpoint inbetween two accumulator, while the next half approaches the collector on the onother side. As a result, the flow in the middle, z = 0, is zero. The flow of aqueous humor is considered fluid through a circular channel due to symmetry [11].

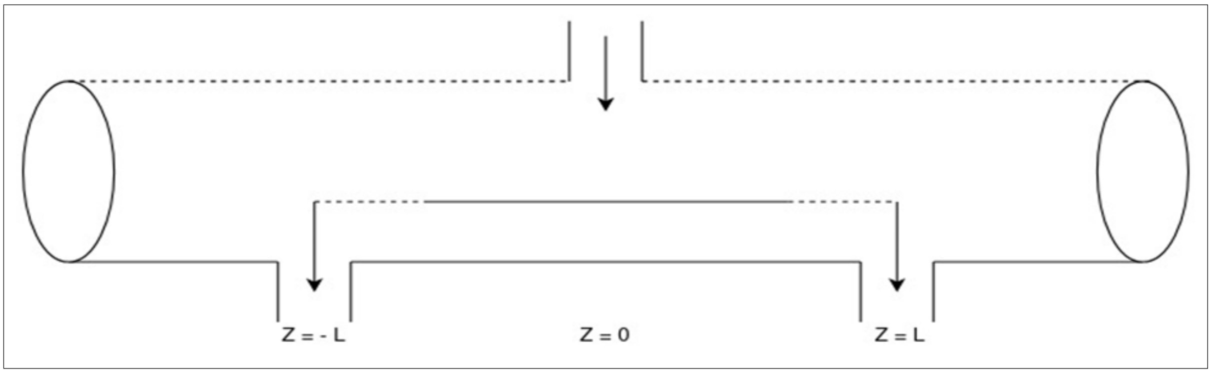

Figure 1 Canal Segment as an circular cross section with upper wall permeable

3. The Governing Equation of fluid Mechanics in Circular Cross-Sectional Tube

$$\rho \frac{Dv}{Dt} = -\nabla p + \mu\nabla^2 + f$$

Where $\frac{Dv}{Dt}$ = Instantenious acceleration

$$\mu\nabla^2 v = \text{Shear viscosity term}$$

$$f = \text{External force}$$

$$\rho = \text{Density}$$

After inserting the assumption indicated above, the governing Navier-Stokes equation takes the forms-

	$-\frac{\partial p}{\partial x} = 0$	(1)
	$-\frac{\partial p}{\partial y} = 0$	(2)
	$-\frac{\partial p}{\partial z} + \mu\nabla^2 v_z = 0$	(3)

And the continuity equation is

	$\frac{\partial v_z}{\partial z} = 0$	(4)

	$w(z)dz = q(z + dz) - q(z)$	(5)

where $q(z)$ Represent the aqueous volume flux in the channel. Now by using $q(z + dz)$ Taylor series:

	$\frac{dq(z)}{dz} = w(z)$	(6)
where	$q(z) = \iint v_z \, dxdy$	(7)
	$w(z) = G[P_I - p(z)]$	(8)

The physically acceptable and mathematical boundary conditions are provided:

	$v_z = 0$ about the inner perimeter,	(9)
	$p(z = L) = P_0$	(10a)
	$\frac{dp}{dz_{z=0}} = 0$	(10b)

where, P_0 is the pressure.

Table 1 Representative values for aqueous humor

Parameters	Values
Dynamic viscosity of aqueous humor (μ)	$0.75cp$
Pressure between the area cornea and iris (P_0)	$12mmHg$
Distance between two collector channels ($2l$)	$1200\mu m$
Filtration constant (G)	$8.28182e - 009 \; mm^2 s/g$
The value of (r)	$0.005mm$

4. Results and discussion

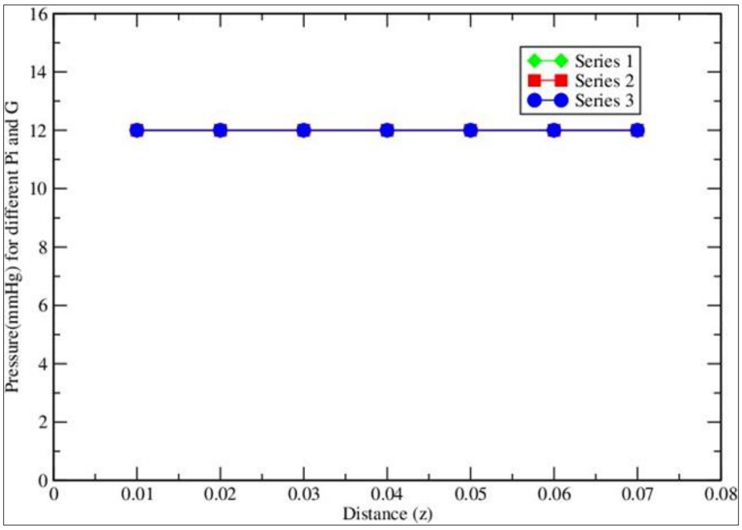

Figure 2 Variation of intraocular pressure with filtration constant

The ideal values of the different constants have been provided in Table 1. The investigated result of the projected work provided for the flow of aqueous humor in Schlemm's Canal has been achieved using the graphs for the situation when the inner linning wall of the canal is stiff and maintained similar to a circular cross-sectional tunnel. The consequence of essential constants like, filtration constant (G) and the Intraocular Pressure (IOP) for the outflow patterns through the canal, have explored by figs 3-5, for the case of circular cross-sectional tubes in human eye. It is obvious from figure 3 that the pressure is linear for increasing value of distance. Figure 4 shows the result for the volume flux and pressure. It is shown in this figure that the vilume flux is increasing as distance increases as well as pressure increases. Figure 5 shows the variation of volume flux for different values of filtration constant. It may be seen from the figure that the volume flux increases as the filtration costant increases. Figure 6 shows the result for the intraocular pressure with axial distance. This figure shows that in the presence of durysta the intraocular pressure is decreasing fastly due to continuous delivery of medicine to the eye.

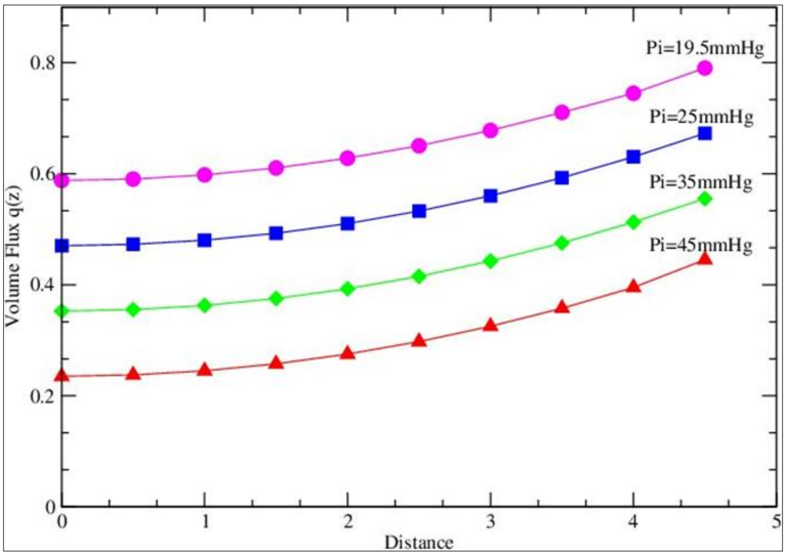

Figure 3 Variation of volume flux with distance for different values of IOP

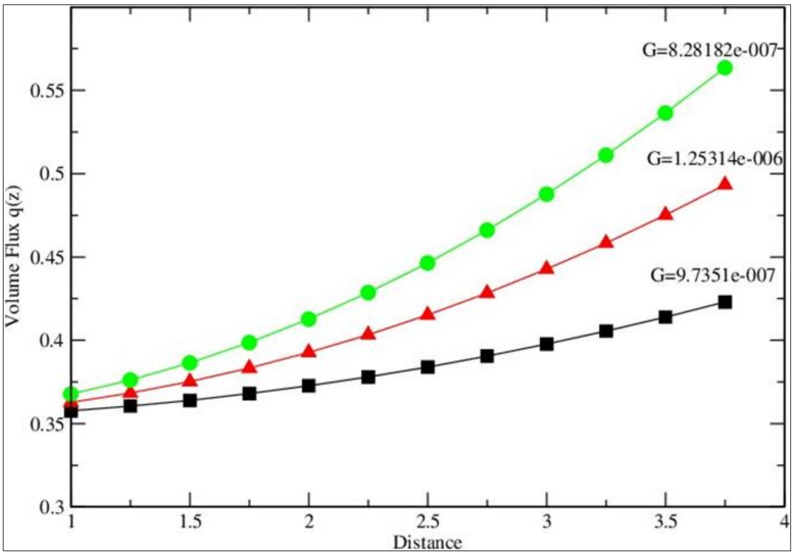

Figure 4 Variation of volume flux with distance for different values of filtration constant in a circular canal

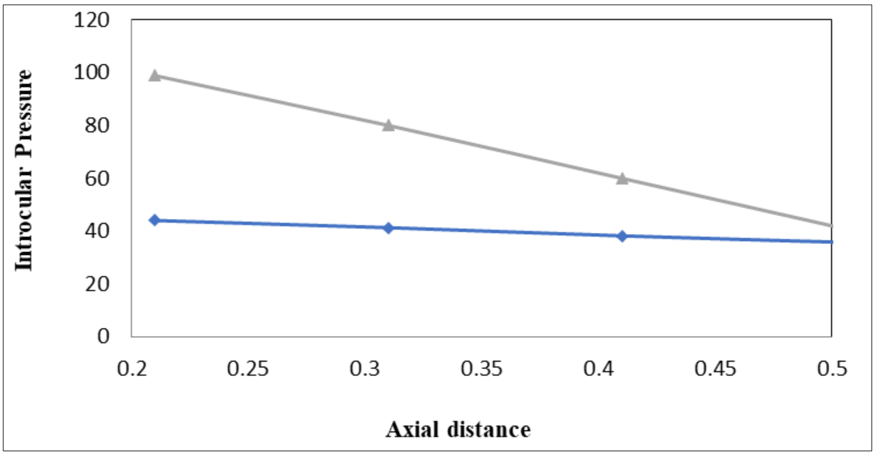

Figure 6 Variation of Intraocular pressure with axial distance for with durysta and without durysta

5. Conclusion

The main aim of this work is to notice the change in the flow variable in the Schlemm Canal modeled as circular tubes and its effects with "DURYSTA". It is observed in this work that current medical therapies are inadequate for lowering down the intraocular pressure. A rational approach to choosing antiglaucoma medications should minimize the number of medications and the probability of significant adverse effects. The ideal drug for treatment of POAG should have the following characteristics: (1) effectively lower IOP, (2) no adverse effects or systemic exacerbation of disease, and (3) inexpensive with once-a-day dosing. In this regard "DURYSTA" is the best way to deliver the 100% medicine to the eye. Durysta is implanted in the eye's anterior chamber that releases bimatoprost medicine directly to the target tissues to improve the drainage of aqueous humor and relieve intraocular pressure (IOP). On the other hand, when bimatoprost is administered through eye drops, hardly 5% of the medication is able to reach beyond the cornea, resulting in reduced efficacy when compared to the bimatoprost implant.

Compliance with ethical standards

Acknowledgments

We would like to express our thanks to the SCIS, JNU, New Delhi, for giving the facility of MATLAB.

Disclosure of conflict of interest

The corresponding author on behalf of all authors, states that there is no conflict of interest.

References

[1] JA Scott. A finite element model of heat transport in the human eye, Phys. Med. Biol. 1988; 33(2): 227–242.

[2] MC Johnson, RD Kamm. The role of Schlemm's canal in aqueous outflow from the human eye. Invest. Ophthalmol. Vis. Sci. 1983; 24(3): 320–325.

[3] AP Nesterov, Y Batmanov. Study on morphology and function of the drainage area of the eye of man, Acta Ophthalmol. 1972; 50(3): 337–350.

[4] F Yuan, AT Schieber, LJ Camras, PJ Harasymowycz, LW Herndon, R Rand Allingham. Mathematical modeling of outflow facility increase with trabecular meshwork bypass and schlemm canal dilation, J. Glaucoma. 2016; 25(4): 355–364.

[5] CR Canning, MJ Greaney, JN Dewynne, AD Fitt. Fluid flow in the anterior chamber of a human eye, Math. Med. Biol. 2002; 19(1): 31–60.

[6] AS Huang, BA Francis, RN Weinreb. Structural and functional imaging of aqueous humour outflow: a review, Clinical and Experimental Ophthalmology. 2018.

[7] RA Moses. Circumferential flow in Schlemm's canal," Am. J. Ophthalmol. 1979; 88(3): 585–591.

[8] R Avtar, R Srivastava. Aqueous outflow in Schlemm's canal, Appl. Math. Comput. 2006; 174(1): 316–328.

[9] RA Moses, WJ Grodzki, EL Etheridge, CD Wilson. Schlemm's canal: the effect of intraocular pressure., Invest. Ophthalmol. Vis. Sci. 1981; 20(1): 61–68.

[10] AP Nesterov. Role of the blockade of Schlemm's canal in pathogenesis of primary open-angle glaucoma, Am. J. Ophthalmol. 1970; 70(5): 691–696.

[11] AD Fitt, G Gonzalez. Fluid Mechanics of the Human Eye: Aqueous Humour Flow in The Anterior Chamber, Bull. Math. Biol. 2006; 68(1): 53.