Intravitreal implants for treatment of posterior segment diseases

Essay
Submitted for partial fulfillment of M.Sc. degree in Ophthalmology

By

Zaid Ali Hassan Al-Sharafi
M.B. B.Ch.
Faculty of medicine
Cairo university

Under supervition of

Dr. Karim Adly Raafat
Professor of ophthalmology
Faculty of medicine
Cairo university

Dr. Mohammed Abdelmonaem Hassaballah
Professor of ophthalmology
Faculty of medicine
Cairo university

Dr. Nahla Borhan Abuhussein
Associate professor of ophthalmology
Faculty of medicine
Cairo university

Faculty of medicine
Cairo university
2012

Acknowledgement

I would like to express my deep and sincere gratitude to Pro. Dr. Karim Adly Raafat professor of ophthalmology, faculty of medicine, Cairo university. Also with immense gratitude that I acknowledge the support of Pro. Dr. Mohammed Abdelmonaem Hassaballah professor of ophthalmology, faculty of medicine, Cairo university. Also I would like to express my deep and sincere gratitude to assistant Pro. Dr. Nahla Borhan Abuhusssein, assistant professor of ophthalmology, faculty of medicine, Cairo university without their efforts, supervision, encouragement and guidance this work would not have been possible.

Abstract

AIn the ongoing armamentarium against sight threatening diseases not only the drug composition is a determining factor but also the way of delivery is a crucial point to consider. Novel methods of ophthalmic drug delivery are being developed to facilitate treatment of a variety of eye diseases.

In order to develop novel methods of ophthalmic drug delivery certain aspects should be considered.

The anatomy and the functional physiology of the eye plays an important role in ocular drug delivery and distribution.

The blood ocular barriers affect the extent of drug absorption and distribution intended to be delivered to the posterior segment of the eye.

Key Words :

Cerium oxide - *Cytomegalo virus* - *Inner oBRB* .

List of content

List of abbreviations

AMD	*Age-related macular degeneration*
ARPE-19	*Activated retinal pigment epithelium*
BCVA	*Best corrected visual acuity*
BM	*Bruch’s membrane*
BRB	*Blood retinal barrier*
BRVO	*Branch retinal vein occlusion*
(CeO_2)	*Cerium oxide*
CME	*Cystoid macular edema*
CMT	*central macular thickness*
CMV	*Cytomegalo virus*
CNTF	*Ciliary neurotrophic factor*
CRVO	*Central retinal vein occlusion*
3D	*3 dimensional*
DDS	*Drug delivery system*
DME	*Diabetic macular edema*
DMSB	*Dexamethasone sodium m-sulfobenzoate*
DNA	*Double stranded nucleic acid*
DSMT	*donut-shaped minitablet*
EBV	*Epstein barr virus*
ECT	*Encapsulated cell technology*
EVA	*Ethylene vinyl acetate*
FAME	*Flucinolone acetonide in diabetic macular edema*
FDA	*Food and drug administration*
Fig	*Figure*

Gd-DTPA	*Gadolinium diethylene triamino pentaacetic acid*
kda	*atomic mass unit*
iBRB	*Inner oBRB*
ILM	*internal limiting membrane*
IOP	*Intraocular pressure*
MEMS	*microelectromechanical systems*
MRI	*Magnetic resonance imaging*
NY	*New York*
oBRB	*Outer oBRB*
PGA	*Polyglycolic acid*
PLA	*Polylactic acid*
PLGA	*Polylactic co-glycolic acid*
PMM 2.1.2	*Polymethylidene malonate*
PVA	*Polyvinyl alchol*
REETAC	*Intravitreal bioerudivel controlled-release triamcilinone microsphere system*
RPE	*Retinal pigment epithelium*
SVH	*simulated vitreous humor*
TA	*Triamcilinone*
USA	*United States of America*
VA	*Visual acuity*
VEGF	*Vascular endothelial growth factor*
VZV	*Varicella zoster virus*

List of tables

List of figures

Introduction

The unique anatomy and physiology of the eye renders it difficult to achieve an effective drug concentration at the target site. Therefore, efficient delivery of a drug past the protective ocular barriers accompanied with minimization of its systemic side effects remains a major challenge **(Rupenthal and Alany, 2007).**

Diseases affecting the posterior segment of the eye are difficult to treat and take longer to combat by employing conventional topical or systemic drug delivery **(Maurice, 2001).**

Research has been directed at specialized drug delivery technologies to the tissues of the posterior segment of the eye **(Visor, 1994).**

Pharmacokinetics describes the quantitative relationship between administered dose and tissue concentration over time, it is an important tool in drug development. To optimize drug concentration at the target sites, pharmacokinetic studies are useful **(Kim et al, 2004).**

Convential techniques as fluorescein, MRI and 3D simulation eye models are methods of assessing ocular drug distribution **(Li et al , 2008).**

A variety of approaches for drug delivery to the posterior segment of the eye have been explored over the last few decades. These approaches include direct intravitreal injections, drug loaded microparticle carriers as microspheres, nanospheres, and liposomes, transscleral drug delivery devices, and intravitreal devices using polymers **(Davis et al, 2004).**

The pharmaceutical world is becoming more and more aware of intraocular drug delivery challenges, and revolutionary therapeutic advances are being invented and implemented which may have the potential to vastly improve patient care and quality of life. Among these most promising developments are intravitreal drug delivery devices designed to deliver drugs with precision directly to the vitreous, retina, and choroid **(Ashton et al, 2000).**

An intraocular device can be designed as either bioerodable or non-bioerodable **(Choonara et al, 2010).**

With the continued development of more potent drugs combined with research into novel delivery methods, there is a realistic hope that optimal therapeutic drug delivery for diseases of the posterior segment will be available in the near future **(Shalin et al, 2010).**

Aim of the study:

To spotlights on the types, indications and complications of the intravitreal implants in the posterior segment of the eye and their future trends.

Anatomical and physiological review

The eye-ball is an organ protected from exogenous substances and external stress by various barriers ***(Figure 1),*** therefore, therapeutic drugs must be transported across several protective barriers regardless of which administration route is utilized, such as eye-drops, subconjunctival, sub-tenon's, intravitreal injection and/or implant. For the treatment of the anterior segment of the eye (cornea, conjunctiva, sclera and anterior uvea), usually topical ocular eye-drops are used. An eye-drop, irrespective of the instilled volume, often eliminates rapidly within five to six minutes after administration, and only a small amount (1–3%) of an eye-drop actually reaches the intraocular tissue **(Maurice and Mishima, 1984).**

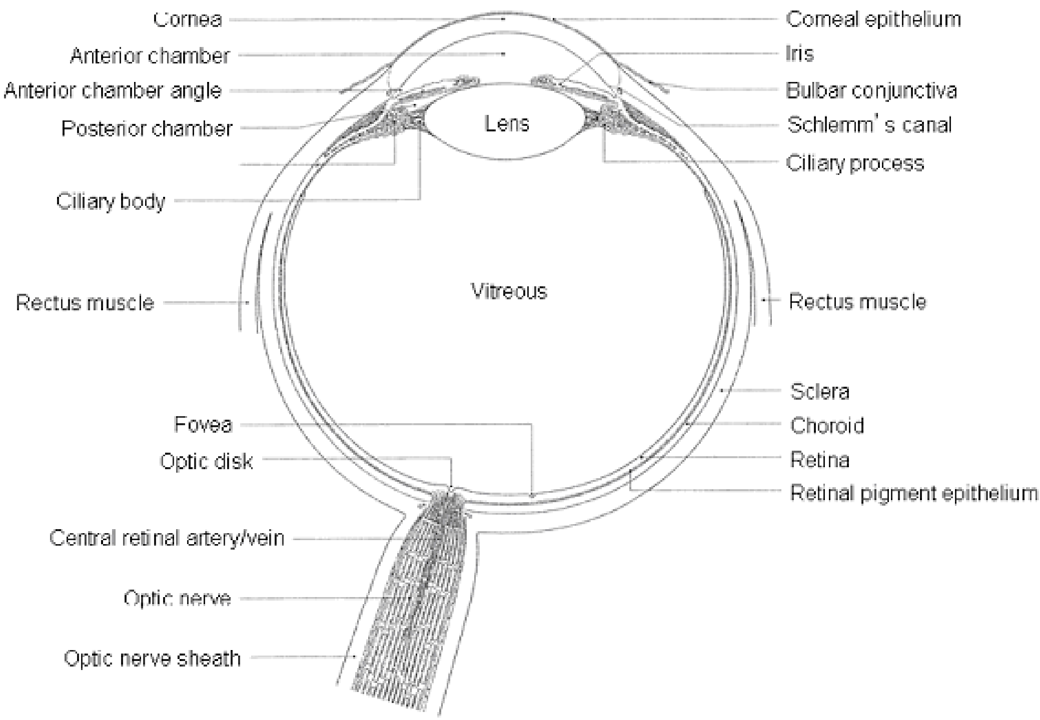

Fig. (1). Schematic of the eye-ball structure. (Kuno and Fuji , 2011).