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OCULAR DRUG DELIVERY: AN UPDATE REVIEW

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ABSTRACT

The purpose of this review is to provide an update on the current knowledge within this field of ocular drug delivery. Drug delivery to eye has always been a daunting task in the field of pharmaceutical research due to distinctive anatomy and physiology of the eye. One of the major problems encountered by usual ocular dosage forms include rapid precorneal drug loss due to nasolacrimal drainage, tear turnover and drug dilution resulting in poor bioavailability. Therefore to improve the ocular drug bioavailability, considerable amount of research has been focused in developing controlled drug delivery systems. These hard works led to development of new drug delivery dosage forms such as nanoparticles, liposomes, hydrogels, ocuserts and mucoadhesive formulations. Controlled drug delivery systems offer many advantages over usual dosage forms in terms of improving drug bioavailability, reducing toxicity and decreasing dosage frequency.

KEYWORDS: Ocular drug delivery, Controlled and sustained drug delivery, Ocular barriers, Anatomy of eye, drug diffusion.

INTRODUCTION

The eye-ball is an organ protected from exogenous substances and external pressure by various barriers (Figure 1), therefore, therapeutic drugs must be transported across several defensive barriers regardless of which administration route is utilized, such as eye-drops and sub conjunctival, sub-tenon's and intravitreal injection and/or implant.

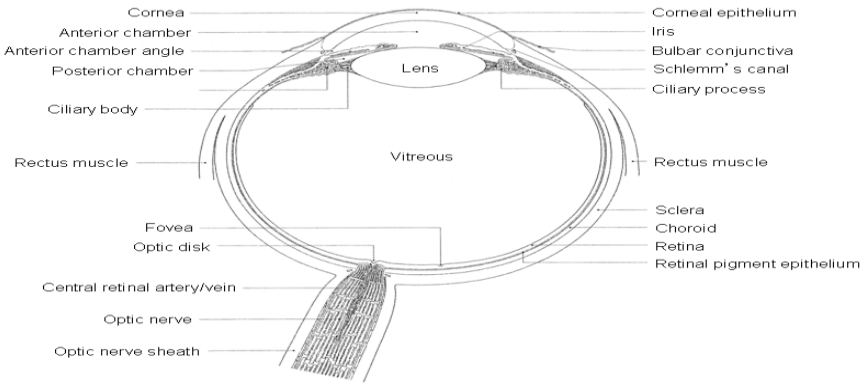


Figure 1: Schematic of the eye-ball structure.

For the treatment of the anterior part of the eye (cornea, conjunctiva, sclera), 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.[1] Thus, it is difficult to provide and maintain an sufficient concentration of drug in the precorneal area. More than 75% of applied ophthalmic solution is lost via nasolachrymal drainage and absorbed systemically via conjunctiva, hence ocular drug availability is very low.[2] To increase ocular bioavailability and prolong the retention time on the ocular surface, many ophthalmic vehicles such as viscous solutions, suspensions, ointments, aqueous gels and polymeric inserts, have been investigated for topical application to the eye.

In general, topical applied drugs do not attain the posterior part of the eye (retina, vitreous, choroid), therefore, systemic administration, periocular or intraocular injections of drugs are normally applied in clinical therapeutics.[3,4] However, the exclusive anatomy and physiology of the eye and its defensive barriers avoid the administrated drugs from penetrating into the objective tissues. Currently there is also rapidly increasing interest in drug delivery systems to the posterior part of the eye. This development is toward a polymeric depot system implanted or injected directly into the vitreous, to obtain long-term, sustained release of drugs, as described in Figure 2.

Compliance is also problematic, particularly among patients who have constant diseases such as glaucoma and refractory chorioretinal diseases, including uveitis, macular edema, neovascular (wet) and atrophic (dry) age-related macular degeneration (AMD) and retinitis pigmentosa (RP). It has been reported nearly 50% of glaucoma patients discontinued all topical ocular hypotensive therapy within six months.[5] Relatively, for the treatment of

neovascular AMD and macular edema secondary to retinal vein occlusion (RVO), standard therapy is intravitreal injections of ranibizumab, an anti-vascular endothelial growth factor (VEGF) monoclonal antibody fragment (Lucentis®, Genentech, Inc., South SanFrancisco, CA, U.S.) once a month.[6] The monthly cost of Lucentis® is about $2,000 and that means efficient treatment by Lucentis® faces a serious social problem.[7,9] In addition, frequent intravitreal injections might cause complications, such as endophthalm it is and retinal detachment. Therefore, DDSs for increasing patient's and doctor's convenience are also urgently needed.

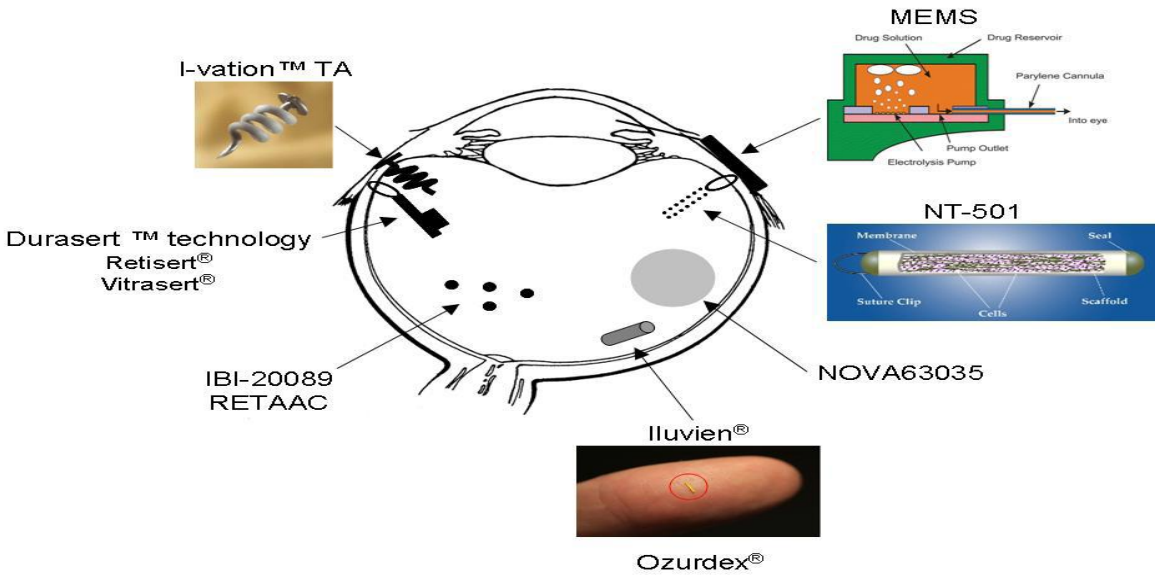
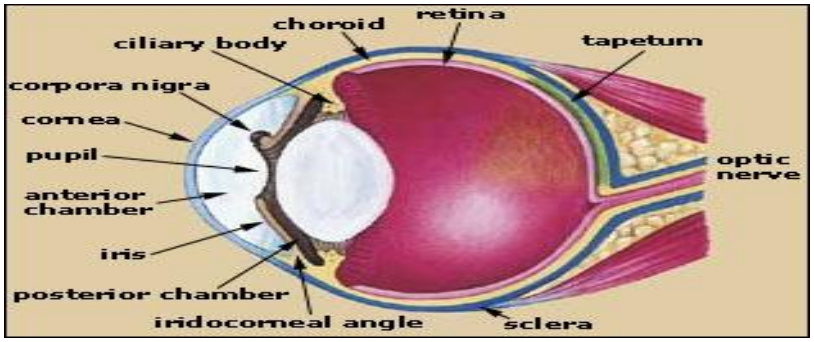


Figure 2: Example of intravitreal drug delivery systems for vitreoretinal diseases.

The function of ocular barrier systems is described and then development of ocular drug delivery system under clinical trials and in late experimental phase is reviewed.

Physiology of Eye

The eye consists of transparent cornea, lens, and vitreous body without blood vessels. The oxygen and nutrients are transported to this non-vascular tissue by aqueous humor which is having high oxygen and same osmotic pressure as blood. The aqueous humor in human is having volume of 300 µl that fills the anterior cavity of the eye which is in front of lens. It is shown in **figure 2.**



The cornea is covered by a thin epithelial layer continuous with the conjunctiva at the cornea-sclerotic junction. The main bulk of cornea is formed of criss-crossing layers of collagen and is bounded by elastic lamina on both front and back. Its later surface is covered by a layer of endothelium. The cornea is richly supplied with free nerve endings. The transparent cornea is continued posteriorly into the opaque white sclera which consists of tough fibrous tissue. Both cornea and sclera with stand the intra ocular tension constantly maintained in the eye.[11] The eye is constantly cleansed and lubricated by the lacrimal apparartus which consists of four structures. lacrimal glands, lacrimal canals, lacrimal sac, nasolacrimal duct. The lacrimal fluid secreted by lacrimal glands is emptied on the surface of the conjunctiva of the upper eye lid at a turnover rate of 16% per min. It washes over the eye ball and is swept up by the blinking action of eye lids. Muscles associated with the blinking reflux compress the lacrimal sac, when these muscles relax; the sac expands, pulling the lacrimal fluid from the edges of the eye lids along the lacrimal canals, into the lacrimal sacs. The lacrimal fluid volume in humans is 7 µl and is an isotonic aqueous solution of bicarbonate and sodium chloride of pH 7.4. It serves to dilute irritants or to wash the foreign bodies out of the conjuctival sac. It contains lysozyme, whose bactericidal action reduces the bacterial count in the conjuctival sac. The physiological barriers to diffusion and productive absorption of topically applied drug exist in the precorneal and corneal spaces. The precorneal constraints that are responsible for poor bioavailability of conventional ophthalmic dosage forms are solution drainage, lacrimation, tear intensity, tear turn over and conjuctival absorption.[12]

Accessory Organs of the Eye

The eye is protected by several structures.

- Eyebrows
- Eyelids and eyelashes
- Lacrimal apparatus

Eyebrows protect the anterior feature of eyeball from sweat, dust and foreign bodies. The eyelids have various layer of tissue including conjunctiva which protects the slight cornea and front of the eye. When eye drops are administered, they are placed in lower conjunctival sac. The lacrimal glands secrete tears composed of water, mineral salts, antibodies and lysozyme, a bactericidal enzyme. Drainage of the eye drops through nasolacrimal system into gastrointestinal tract begins instantly on instillation. This takes place when either reflex tearing or the dosage form causes volume of fluid in peripheral tissue to exceed the normal lacrimal volume of 7-10 µl. The excess fluid volume enters the superior and inferior lacrimal puncta, moves down the canalicula into the lacrimal sac and continues into the gastrointestinal tract.[13]

Routes of Ocular Drug Delivery

There are several possible routes of drug delivery into the ocular tissues. The selection of the route of administration depends primarily on the target tissue.

Topical route

Typically, topical ocular drug administration is accomplished by eye drops, but they have only a short contact time on the eye surface. The contact and thereby duration of drug action, can be protracted by formulation design (e.g. m gels, gelifying formulations, ointments and inserts).

Subconjunctival administration

Usually subconjunctival injections have been used to deliver drugs at improved levels to the uveitis. Currently this mode of drug delivery has gained new energy for various reasons. The development in materials sciences and pharmaceutical formulation have provided new exciting possibilities to develop controlled release formulations to deliver drugs to the posterior part and to guide the curative process after surgery.

Intravitreal administration

Direct drug administration into the vitreous offers distinct advantage of more simple access to the vitreous and retina. It should be noted; however that delivery from the vitreous to the choroid is more complex due to the barrier by the RPE (Retinal Pigment Epithelium) barrier. Small molecules are able to disperse rapidly in the vitreous but the mobility of large molecules, particularly positively charged, is restricted.[14]

Barriers for Ocular Delivery

Drug loss from the ocular surface

After instillation, the flow of lacrimal fluid removes instilled compounds from the surface of eye. Even though the lacrimal proceeds rate is only about 1 µl/min the excess volume of the instilled fluid is flown to the nasolacrimal duct rapidly in a couple of minutes. Another source of non-productive drug removal is its general absorption instead of ocular absorption. Systemic absorption may take place either directly from the conjunctival sac via local blood capillaries or after the solution flow to the nasal cavity.

Lacrimal fluid-eye barriers

Corneal epithelium limits drug absorption from the lacrimal fluid into the eye. The corneal epithelial cells form rigid junctions that limit the paracellular drug permeation. Therefore, lipophilic drugs have normally at least an order of magnitude higher permeability in the cornea than the hydrophilic drugs. In general, the conjunctiva is leakier epithelium than the cornea and its exterior area is also nearly 20 times greater than that of the cornea.

Blood-ocular barriers

The eye is protected from the xenobiotics in the blood stream by blood-ocular barriers. These barriers have two parts: blood-aqueous barrier and blood-retina barrier. The anterior blood-eye barrier is composed of the endothelial cells in the uveam (The middle layer of the eye beneath the the sclera. It consists of the iris, ciliary body and choroid).

This barrier prevents the access of plasma albumin into the aqueous humor and also restrictions the access of hydrophilic drugs from plasma into the aqueous humor. The posterior barrier between blood stream and eye is comprised of retinal pigment epithelium (RPE) and the tight walls of retinal capillaries. Unlike retinal capillaries the vasculature of the choroid has wide blood flow and leaky walls. Drugs easily gain access to the choroidal extravascular space, but there after distribution into the retina is partial by the retinal pigment epithelium and retinal endothelia.[15]

Diseases of Eye

The eye is a sensory and receptive organ which is situated on the surface of the body, is easily injured and infected.

According to the location of diseases, ocular disorders are grouped as 1. Periocular diseases, 2. Intraocular diseases.

The periocular diseases are explained as follows

Conjuctivitis: It is a condition where redness of the eye and the presence of a foreign body sensation are clear. There are many causes of conjunctivitis, but the great majorities are the result of acute disease or allergy. Bacterial conjunctivitis is the most common ocular infection.

Keratitis: The condition in which patients have a decreased vision, ocular pain, red eye and often a cloudy/opaque cornea. Keratitis is mainly caused by bacteria, viruses, fungi, protozoa and parasites.

Trachoma: The conjunctival inflammation is called "active trachoma" and usually is seen in children, specially pre-school children. It is characterized by white lumps in the undersurface of the superior eyelid and by non-specific inflammation and thickening often associated with papillae. This is caused by the organism Chlamydia trachomatis. Active trachoma will often be irritating and have a watery discharge.

Dry Eye: If the composition of tears is changed, or an insufficient volume of tears is produced, the symptom of dry eye will result. Dry eye conditions are not just a cause for ocular uneasiness where it also results in corneal damage. Periocular diseases such as these are relatively easily treated using topical formulations.

The intraocular diseases are explained as follows

One of the intraocular diseases is intra ocular infection which includes intraocular infections: i.e.

Infections in the inner eye, including the aqueous humor, iris, vitreous humor and retina. They are more complicated to manage and occur commonly after ocular surgery, trauma or may be due to endogenous causes. Such infections carry a high risk for damage to the eye and also afford the possibility of spread of infection from the eye into the brain. Other common intraocular disease is glaucoma, considered to be one of the major ophthalmic clinical harms in the world. More than 2% of the populations over the age of 40 have this disease, in which an increased intraocular pressure (IOP) greater than 22 mm Hg ultimately compromises blood flow to the retina and therefore causes death of the peripheral optic nerves. This process

results in visual field loss and ultimately blindness.[16] Apart from these common harms of eye are cataract and macular deterioration and sometimes diseases which may be of a universal origin such as diabetes or hypertension result the eye.

Ideal Characteristics of Ophthalmic Drug Delivery System

• Good corneal diffusion.
• Maximizing ocular drug inclusion through prolong contact time with corneal tissue.
• Simplicity of instillation for the patient.
• Reduced regularity of administration.
• Patient compliance.
• Lower toxicity and side effects.
• Minimize precorneal drug failure.
• Nonirritative and easy form should not cause blurred vision.
• Relatively nongreasy.
• Suitable rheological properties and concentrations of the viscous system.

Classification of Ocular Drug Delivery Systems

A large amount of ocular dosage forms are available for delivery of drugs to the eye. These can be classified on the basis of their physical forms as follows:

1. Liquids: - Solutions, Suspensions, Sprays
2. Solids: - Ocular inserts, Contact lenses, corneal shield, artificial tear inserts, Filter paper strips
3. Semi-solids: Ointments, Gels
4. Miscellaneous: Ocular iontophoresis, Vesicular systems, Muco-adhesive dosage forms, Particulates.

1. Liquids: - Liquids are the most accepted and pleasing state of dosage forms used for the eye. This is because the drug absorption is fastest from this state. The slow discharge of the drug from the suspended solids provides a sustained effect for a short duration of time.

Solutions and Suspensions.

Solutions

Solutions are the pharmaceutical forms most extensively used to administer drugs that must be active on the eye surface or in the eye after passage through the cornea or the conjunctiva.

The drug in the solution is in the dissolved state and may be instantly active. This form also have disadvantages; the very short time the solution stays at the eye surface, its poor bioavailability (a major portion i.e. 75% is lost via nasolacrimal drainage), the instability of the dissolved drug, and the necessity of using preservatives. A considerable disadvantage of using eye drops is the rapid removal of the solution and their poor bioavailability. This rapid removal is due to solution state of the preparation and may be influenced by the composition of the solution. The release of a solution in the eye is partial by viscosity, hydrogen ion concentration, the osmolality and the instilled volume. Extensive work has been done to prolong ocular retention of drugs in the solution state by enhancing the viscosity or changing the pH of the solution.[18,19]

Suspensions

Suspensions are called as dispersion of finely divided comparatively insoluble drug substances in an aqueous vehicle which contains suitable amount of suspending and dispersing agents. Because of a tendency for the particle to be retained in the cul-de-sac, the contact time and duration of action of a suspension exceed those of a solution. While the retention increases with an increase in the particle size, so does the irritation of the eye. The rate of the dissolution of the suspended drugs increases with decreasing particle size. Thus an optimum particle size has to be selected for each type of drug and it is recommended that the particles in an ophthalmic suspension should be not more than 10 μm in size.

Sprays[20,21]

Although not usually used, some practitioners use mydriatics or cycloplegics alone or in combination in the form of eye spray. These sprays are used in the eye for dilating the pupil or for cycloplegics examination.

2. Solids: - The concept of using solids for the eye is based on providing sustained release characteristics.

Ocular inserts

Ocular inserts are aseptic, thin, multilayered, drug loaded, solid or semisolid dosage forms placed into the cul-de-sac or conjunctival sac, whose dimension as well as build are specifically planned future for ophthalmic application and can conquer the hindrance stated with conventional ophthalmic systems. The ocular inserts assert an efficient drug concentration within the intended tissue.[22] Ocular inserts tender an appealing optional

advent to the formidable difficulty of bounded pre-corneal drug residence time[23]; another promising benefit of insert therapy is the potentiality of endorsing non-corneal drug penetration, consequently enlarging the effectiveness of a number of hydrophilic drugs that are dreadfully absorbed via cornea.

The inserts are classified according to their solubility as insoluble, soluble, or bio-erodible inserts. The release of drug from the insert depends upon the diffusion, osmosis and bioerosion of the drug.[24],[25]

Contact lenses

Contact lenses are shaped structures and originally used for vision correction. Their use has been extended as potential drug delivery devices by presoaking them in drug solutions. The main benefit of this system is the possibility of correcting vision and releasing drug simultaneously. Refojo has proposed a subdivision of contact lenses into 5 groups.

a) Rigid

b) Semi-rigid

c) Elastomeric

d) Soft hydrophilic

e) Bio-polymeric

Rigid contact lenses have the drawback of being composed of polymers (e.g., poly methyl methacrylic acid) hardly permeable to moisture and oxygen, a difficulty which has been overcome by using gas permeable polymers such as cellulose acetate butyrate. However, these systems are not suitable for prolonged delivery of drugs to the eye and their rigidity makes them very uncomfortable to wear. For this reason, soft hydrophilic contact lenses were developed for prolonged release of drugs such as pilocarpine, chloramphenicol and tetracycline prednisolone sodium phosphate. The most commonly used polymer in the composition of these types of lenses is hydroxy ethyl methylmetacrylic acid copolymerized with poly (vinyl pyrrolidone) or ethylene glycol dimethacrylic acid (EGDM). Poly (vinyl pyrrolidone) is used for increasing water of hydration, while EGDM is used to decrease the water of hydration. The soft hydrophilic contact lenses are very popular because they are easy to fit and are tolerated better. The drug incorporation into contact lenses depends on whether their structure is hydrophilic or hydrophobic. When contact lens (including 35 to 80% water) is flooded in solution, it absorbs the drug. Drug release depends markedly on the amount of

drug, the soaking time of the contact lens and the drug concentration in the soaking solution.[26]

Artificial tear inserts[27]

A rod shaped pellet of hydroxypropyl cellulose without preservative is commercially available (Lacrisert). This device is designed as a sustained release artificial tear for the treatment of dry eye disorders. It was developed by Merck, Sharp and Dohme in 1981.

Filter paper strips[27]

Sodium fluorescein and rose Bengal dyes are commercially available as drug impregnated filter paper strips. These dyes are used diagnostically to disclose corneal injuries and infections such as herpes simplex, and dry eye disorder.

3. Semi solids

Gel

Gel formation is a severe case of viscosity enhancement through the use of viscosity enhancers which leads to slight extended precorneal residence time. It has advantage like reduced systemic exposure. Despite the extremely high viscosity, gel achieves only a limited enhancement in bioavailability and the dosing occurrence can be decreased to once a day at most. The high viscosity, however, results in blurred vision and matted eyelids, which substantially reduce patient acceptability.

The aqueous gel typically utilizes such polymers as PVA, polyacrylamide, poloxamer, HPMC, carbomer, poly methyl vinylethermaleic anhydride and hydroxypropyl ethylcellulose. Swellable water insoluble polymers, called hydrogel, or polymers having peculiar characteristics of swelling in aqueous medium give controlled drug delivery systems. The release of a drug from these systems occurs via the transport of the solvent into the polymer matrix, leading to its swelling. The final step involves the diffusion of the solute through the swollen polymer, leading to erosion/dissolution. Poly (acrylic acid) hydrogel has been reported to augment appreciably the ocular bioavailability of tropicamide in humans, with respect to both a viscous solution and a paraffin ointment.[28] Pilopine HS® gel, commercialized in 1986 by Alcon and more recently Merck's Timoptic-XE®.

Ointments

Ointments are typically formulated using mixtures of semisolid and solid hydrocarbons (paraffin) which have a melting or softening point close to body temperature and are nonirritating to the eye. Ointments may be simple bases, where the ointment forms one constant phase, or compound bases where a two-phased system (e.g., an emulsion) is employed. The medicinal agent is added to the base either as a solution or as a finely micronized powder. Upon instillation in the eye, ointments break up into small droplets and remain as a depot of drug in the cul-de-sac for extensive periods. Ointments are therefore useful in improving drug bioavailability and in sustaining drug release. Although safe and well-tolerated by the eye, ointments suffer with comparatively poor patient compliance due to blurring of vision and occasional irritation.[29]

4. Miscellaneous

Ocular iontophoresis

Iontophoresis is a current non-invasive approach specifically designed for ocular drug delivery.[30] Theoretically, iontophoresis is limited to drugs of a small size, an ionic nature and with low molecular weight. The practice of iontophoresis implies assigning an electric current to an ionizable material to step-up its transportability across a surface, a theory that dates back to the 18th century. The initial transscleral iontophoretic effort for vitreal drug delivery was proclaimed in 1943.[31] Subsequent, David Maurice performed a vital function in upgrading the utilization of iontophoresis to intensify ocular drug delivery.[32,33] If the drug molecules hold a positive charge, they are driven through the tissues at the anode; whether negatively charged, at the cathode. Ocular iontophoresis overtures a drug-delivery system that is rapid, pain free and secure; furthermore, in the majority of cases, it consequences in the delivery of a high concentration of the medicament to a particular site. Implementation of iontophoresis approach in case of antibiotic's delivery to ocular route may heighten their bactericidal activity and may diminish the acuteness of disorder; correspondingly, solicitation of anti-inflammatory agents might stave off or curtail vision intimidating side effects.[34]

Vesicular systems

Vesicular systems have been developed to provide improvement in ocular contact time, providing sustained effect and reducing side effects of the drug(s) entrapped.

Liposome's

Liposome's are phospholipids-lipid vesicles for targeting the drugs to the specific sites in the body. Because of their structural versatility they can incorporate any kind of drug substance regardless of its solubility. They provide the controlled and selective drug delivery and improved bioavailability and their potential in ocular drug delivery appears greater for lipophilic than hydrophilic compounds. Liposomes are vesicles composed of a lipid membrane enclosing an aqueous volume. Liposome's offer the advantage of being completely biodegradable and relatively nontoxic but are less stable than particulate polymeric drug delivery systems. Liposome's were found to be potential delivery system for administration of a number of drugs to the eye.[35,38]

Niosomes

In order to circumvent the limitations of Niosomes.

Niosomes are bilayered structural vesicles made up of nonionic surfactant which are capable of encapsulating both lipophilic and hydrophilic compounds. Niosomes reduce the systemic drainage and improve the residence time, which leads to increase ocular bioavailability. They are nonbiodegradable and nonbiocompatible in nature. In a recent approach to deliver cyclopentolate, niosomal formulation was developed. It released the drug independent of pH, resulting in important improvement of ocular bioavailability. Niosomal formulation of coated (chitosan or carbopol) timolol maleate exhibited significant IOP lowering effect in rabbits as compared with timolol solution.[39]

Nanoparticles

Nanoparticles are solid, submicron, colloidal particles ranging in dimension from 10 to 1000 nm, in that drug molecules may be present in dissolved, entrapped, adsorbed or covalently attached form.[40] Based on formulation approaches nanoparticles can be acquired with distinct properties and release attributes for the capsulized drug.[41,42] These colloidal particles can be assigned in the liquid form just like eye drops and diminishes unease provoked by application of semisolid ointments. They are patient friendly owing to less frequent application, extended duration of retention in the extra ocular portion destitute of blurring vision. Nanoparticles have been established to be the most talented of all the formulations developed over the past a couple of years of marked navigate in ocular therapeutics, payable to their sustained release and prolonged therapeutic concern. Polymeric nanoparticles are additionally capable in the targeting of ailments in the posterior segment of the eye.[43]

Nanoparticles made of biodegradable polymer that combines the capabilities of stimulus response and molecular recognition hold a pronounced aptitude in ocular drug delivery. Biodegradable polymers formulated as colloidal systems hold significant promise for ophthalmic drug delivery. Supplementally, surface altered nanoparticulate carriers may use to acclimatize a sort of actives.[44,45]

The serious concerns with regard to the formulation of nanoparticles understand stability, particle size homogeneity, control of drug release rate and sizeable production of uncontaminated preparations.[46] Nanocarries possessing polyethylene glycol or surface-segregated chitosan have been established to be correspondingly stable as well as proficient at overcoming mucosal barriers.[47]

Mechanism of Control Drug Release into the Eye

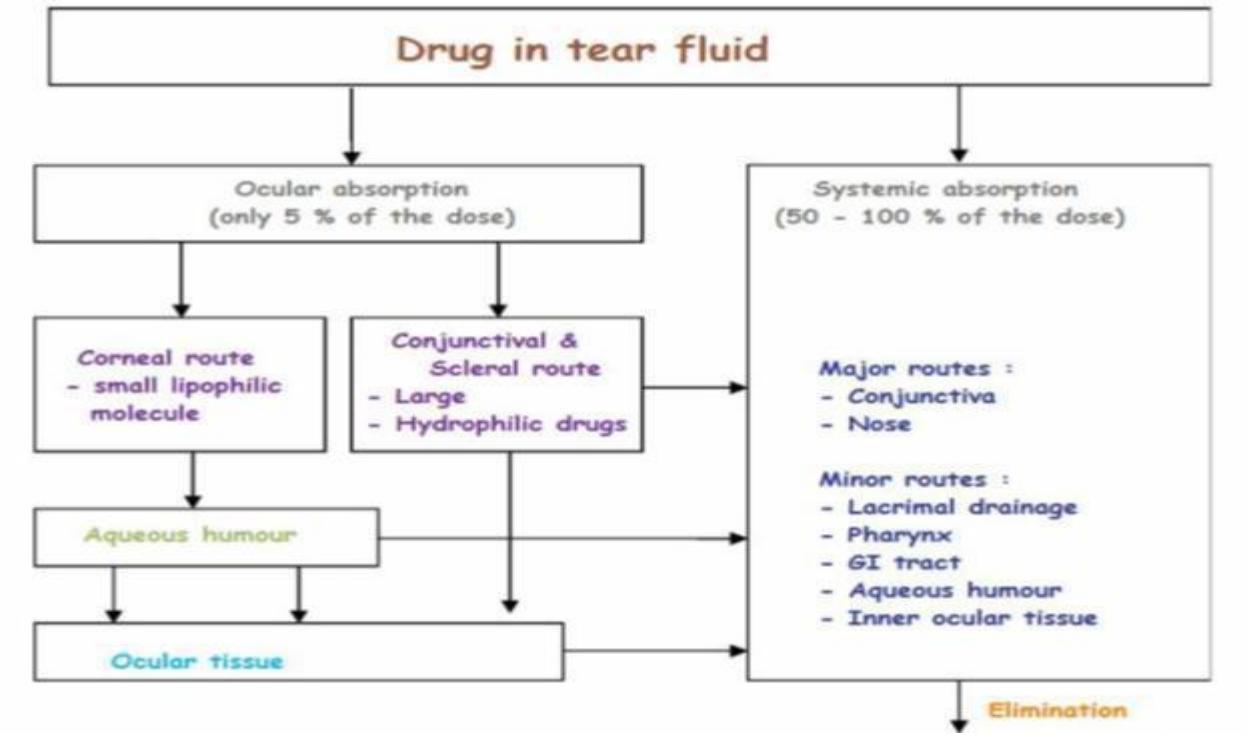


Fig. Ocular Drug Absorption.[48,49]

The mechanism of controlled drug release into the eye is as follows: A. Diffusion, B. Osmosis, C. Bio-erosion.

A. Diffusion

In the Diffusion mechanism, the drug is released continuously at a controlled rate through the membrane into the tear fluid. If the insert is formed of a solid non-erodible body with pores

and dispersed drug. The releases of drug can take place via diffusion through the pores. Controlled release can be further regulated by gradual dissolution of solid dispersed drug within this matrix as a result of inward diffusion of aqueous solutions. In a soluble device, true dissolution. occurs mainly through polymer swelling. In swelling-controlled devices, the active agent is homogeneously dispersed in a glassy polymer. Since glassy polymers are essentially drug impermeable, no diffusion through the dry matrix occurs. When the insert is placed in the eye, water from the tear fluid begins to penetrate the matrix, then swelling and consequently polymer chain relaxation and drug diffusion take place. The dissolution of the matrix, which follows the swelling process, depends on polymer structure:linear amorphous polymers dissolve much faster than cross-linked or partially crystalline polymers. Release from these devices follows in general Fickian 'square root of time' kinetics; insome instances, however, known as case II transport, zero order kinetics has been observed.

B. Osmosis

In the Osmosis mechanism, the insert comprises a transverse impermeable elastic membrane dividing the interior of the insert into a first compartment and a second compartment; the first compartment is bounded by a semi-permeable membrane and the impermeable elastic membrane and the second compartment is bounded by an impermeable material and the elastic membrane. There is a drug release aperture in the impermeable wall of the insert. The first compartment contains a solute which cannot pass during the semi-permeable membrane and the second section provides a reservoir for the drug which again is in liquid or gel form. When the insert is located in the aqueous environment of the eye, water diffuses into the first compartment and stretches the elastic membrane to expand the first compartment and contract the second compartment so that the drug is forced through the drug release aperture.

C. Bioerosion

In the Bioerosion mechanism, the configuration of the body of the insert is constituted from a matrix of bioerodible material in which the drug is isolated. Contact of the insert with tear fluid results in controlled sustained release of the drug by bioerosion of the medium. The drug may be dispersed uniformly throughout the matrix but it is believed a more controlled release is obtained if the drug is superficially concentrated in the matrix. In truly erodible or E-type devices, the rate of drug release is controlled by a chemical or enzymatic hydrolytic reaction that leads to polymer solubilization, or degradation to smaller, water-soluble molecules. These polymers, as specified by Heller, may undergo bulk or surface hydrolysis.

Erodible inserts undergoing surface hydrolysis can display zero order release kinetics; provided that the devices maintain a constant surface geometry and that the drug is poorly water-soluble.[50]

CONCLUSION

New ophthalmic delivery system includes ocular inserts, ocular films, disposable contact lens and other Novel drug delivery systems like nanoparticles. Newer trend is a combination of drug delivery technologies for humanizing the beneficial response of a non efficient drug. This can give a greater dosage forms for ophthalmic application. In the middle of these drug delivery systems, Patient acceptance is very important for the design of easy ophthalmic drug delivery system. Advancement in the field of ocular drug delivery has been established newly with controlled loading and constant release. Hence, competent drug delivery and targeting is faced by challenges to overcome these barriers.

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