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A REVIEW ON OCUULAR DRUG DELIVERY

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ABSTRACT

Ocular drug delivery is maintenance of an adequate concentration of drug in the pre-corneal area. Ocular administration of the drug is primarily associated with the need to treat ophthalmic diseases. Topical application of drugs to the eye is the well-established routes of administration for the treatment of various eye diseases like dryness, conjunctiva, and eye flu etc. Conventional topical ocular delivery systems include various dosage forms such as solutions, suspensions, emulsions, ointments, gels, erodible inserts, non-erodible inserts which shows drawbacks such as rapid pre-corneal elimination, blurred vision, abrasion, irritation to eye, tissue fibrosis, matted eyelids after use and patient discomfort etc. In order to overcome these, vesicular system for drug delivery are used such as Liposomes Niosomes, Pharmacosomes and discomes.Various ocular drug delivery devices are used that can deliver drug to eye such as Matrix-type drug delivery systems, Capsular type drug delivery systems, Implantable drug delivery pumps etc .The field of ocular delivery is one of the most interesting and challenging Endeavours facing the pharmaceutical scientist.

KEYWORDS: Ocuular Drug Delivery System, Anatomy and Physiology of Eye, Conjunctivitis.

INTRODUCTION

Optical administration of the medicine is primarily associated with the need to treat ophthalmic conditions. Topical operation of medicines to the eye is the well- established

routes of administration for the treatment of colorful eye conditions like blankness, conjunctiva, and eye flu etc. Conventional topical optical delivery systems include colorful lozenge forms similar as results, dormancies, mixes, ointments, gels, erodible inserts,non-erodible inserts which shows downsides similar as rapid-firepre-corneal elimination, blurred vision, bruise, vexation to eye, towel fibrosis, matted eyelids after use and case discomfort etc. In order to overcome these, vesicular system for medicine delivery are used similar as Liposomes, Niosomes, Pharmacosomes and discomes. colorful optical medicine delivery bias are used that can deliver medicine to eye similar as Matrix- type medicine delivery systems, Capsular type medicine delivery systems, Implantable medicine delivery pumps etc. The field of optical delivery is one of the most intriguing and grueling Endeavours facing the pharmaceutical scientist. This is significantly bettered over once many 10- 20 times. In the earlier period, medicine delivery to the eye has been limited to topical operation, re-division into the eye following systemic administration or directs intraocular/ peri optical injections. Lozenge forms are administered directly to the eye for localized ophthalmic remedy. Topical operation of medicines to the eye is the well- established route of administration for the treatment of colorful eye conditions like blankness, conjunctiva, eye flu etc. thus retailed ophthalmic lozenge phrasings are classified as conventional and non-conventional (newer) medicine delivery systems. There are most generally available ophthalmic medications similar as drops and ointments about 70 of the eye lozenge phrasings in request. Topical operation of medicines to the eye is the most popular and well- accepted route of administration for the treatment of colorful eye diseases. Topical administration is generally considered the favored route for the administration of optical medicines due to its convenience and affordability. medicine immersion occurs through corneal and non-corneal pathways. utmost on-corneal immersion occurs via the nasolacrimal conduit andleads to non-productive systemic uptake, while utmost medicines transported through the cornea is taken up by the targeted intraocular towel Unfortunately, corneal immersion is limited by drainage of the inseminated results, lacrimation, gash development, metabolism, gash evaporation ,non-productive immersion/ adsorption, limited corneal area, poor corneal permeability, binding by the lacrimal proteins, enzymatic declination, and the corneal epithelium itself. These medications when inseminated into eye they're fleetly drained down from the optical face, only a small quantum of medicine is available for its remedial effect performing occasional dosing operation to the eye. Ophthalmic conditions are most generally treated by topical eye- drop instillation of waterless products. These phrasings, still, raise specialized problems (e.g., solubility, stability, and preservation) and clinical issues (efficacy, original

toxin and compliance). It leads to development of advanced ways for optical remedy those include particulate delivery system which improves the pharmacokinetic and pharmacodynamic parcels of colorful types of medicine motes and new controlled medicine delivery systems similar as dendrimers, micro mixes, muco- tenacious polymers, hydrogels.

Advantages of occular drug delivery system

- Increased accurate dosing. To overcome the side effects of pulsed dosing produced by conventional delivery.
- To increase the ocular bioavailability of drug by increasing the corneal contact time.
- To circumvent the protective barriers like drainage, lacrimation and conjunctively absorption.
- To provide better housing of delivery system.
- Reduction of the number of administration and thus better patient compliance.
- Reduction of systemic side effects and thus reduced adverse effects.
- Possibility of targeting internal ocular tissue through non-corneal routes.
- Administration of an accurate dose in the eye, which is fully retained at the administration site, thus a better therapy.
- Increases the bioavailability and decreases the adverse effects.
- Iontophoresis of charged nanoparticles as drug carriers, providing a long duration.
- Therapeutic activity.
- Topical ophthalmic preparation and easy to apply.
- Good drug penetration to the anterior and posterior segments of the eye bytopically.
- May combine to other drug delivery system.
- Good acceptance by the patients.

Disadvantages of occular drug delivery system

- The physiological restriction is the limited permeability of cornea resulting into low absorption of ophthalmic drugs.
- A major portion of the administered dose drains into the lacrimal duct and thus can cause unwanted systemic side effects.
- The rapid elimination of the drug through the eye blinking and tear flow results in a short duration of the therapeutic effect resulting in a frequent dosing regimen.
- A capital disadvantage of ocular inserts reside in their ‘solidity’, i.e., in the fact that they

are felt by the (often oversensitive) patients as an extraneous body in the eye .

- Their movement around the eye, in rare instances, the simple removal is made more difficult by unwanted migration of the inserts to upper fornix.
- The occasional inadvertent loss during sleep or while rubbing the eyes.
- Their interference with vision.
- Difficult placement of the ocular inserts (and removal, for insoluble types).
- The insert may be lost immediately.
- Sometimes the insert twists to form ‘a figure eight’, which diminishes the delivery rate. A leakage may occur Dislocation of the device in front of the pupil.

ANATOMY AND PHYSIOLOGY OF EYE

The eye is a spherical structure with a wall made up of three layers; the outer part sclera, the middle parts choroid layer, Ciliary body and iris and the inner section nervous tissue layer retina. The sclera is tough fibrous coating that protects the inner tissues of eye which is white except for the transparent area at the front, and the cornea allows light to enter to the eye. The choroid layer, situated in the sclera, contains many blood vessels that modified at front of the eye as pigmented iris, the colored part of the eye (blue, green, brown, hazel, or grey). The clear transparent bulge cornea situated at the front of the eye conveys images to the back of the nervous system. The adult cornea has a radius of approximately 7- 8mm that covers about one-sixth of the total surface area of the eye ball that is a vascular tissue which provides nutrient and oxygen, supplied via lachrymal fluid and aqueous humour as well as from blood vessels of the junction between the cornea and sclera. The cornea is made of five layers as epithelium, bowman’s layer, stroma, descemet membrane and endothelium that is main pathway of the drug permeation to eye. The epithelium made up of 5 to 6 layers of cells.

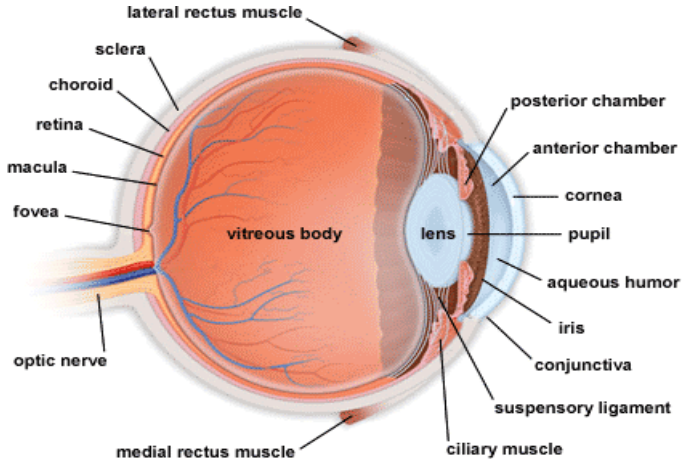

Figure 1: Schematic cross section through a human eye.

COMMON EYE INFECTION

Bacteria are the causative pathogens for a large number of eye infections. In addition virus, fungus and protozoans also cause eye infections. As such, eyes are prone to number of diseases but more commonly found are mentioned here.

CONJUNCTIVITIS

Conjunctivitis, commonly known as pink eye as shown in Fig 1, is a clear membrane that covers the white part of the eye and lines the inner surface of the eyelids. The inflamed\ conjunctiva will usually make the eye appear red or pink because the tiny blood vessels that are normally within the conjunctiva get irritated and enlarged. It usually affects both eyes at the same time although itmay start in one eye and spread to the other after a day or two days. It may be asymmetrical, affecting one eye more than theother. Pink eye can be infectious or noninfectious

There are many causes for conjunctivitis, Including.

- Bacterial conjunctivitis – staphylococci, streptococci.
- Viral conjunctivitis (often associated with the common cold) – adenovirus.
- Chlamydial conjunctivitis – Chlamydia trachomatis.
- Allergic conjunctivitis –allergic disease such as hay fever, asthma and eczema and by antigens like pollen, dust mites or cosmetics.
- Reactive conjunctivitis or irritant conjunctivitis – chemicals, smoke, fumes etc.
- Sign and symptoms of conductivities
- The blood vessels over the white of the eye are more visible and swollen.
- The lining of the eyelids also looks red or pinker due to inflammation.
- Eye is sticky, with a heavy discharge and tearing that may cause the lids to stick together, especially after sleeping.
- Inflammed and swollen eyelids.
- Blurred vision.

BARRIER IN EYE

Loss of drug from the ocular surface; after instillation, the flow of lacrimal fluid removes instilled compounds from the surface of the eye. Even though the lacrimal turnover 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 systemic 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.

Anyway, most of small molecular weight drug doses absorbed into systemic circulation rapidly in few minutes. This contrasts the low ocular bioavailability of less than 5%. Drug absorption into the systemic circulation decreases the drug concentration in lacrimal fluid extensively. Therefore, constant drug release from solid delivery system to the tear fluid may lead only to ocular bioavailability of about 10%, since most of the drug is cleared by the local systemic absorption anyway.

Lacrimal fluid eye barriers Corneal epithelium limits drug absorption from the lacrimal fluid into the eye. The corneal barrier is formed upon maturation of the epithelial cells. They migrate from the limbal region towards the centre of the cornea and to the apical surface. The most apical corneal epithelial cells form tight junctions that limit the paracellular drug permeation. Therefore, lipophilic drugs have typically at least an order of magnitude higher permeability in the cornea than the hydrophilic drugs. Despite the tightness of the corneal epithelial layer, trans corneal permeation is the main route of drug entrance from the lacrimal fluid to the aqueous humor. In general, the conjunctiva is leakier epithelium than the cornea and its surface area is also nearly 20 times greater than that of the cornea. Drug absorption across the bulbar conjunctiva has gained increasing attention recently, since conjunctiva is also fairly permeable to the hydrophilic and large molecules .Therefore, it may serve as a route of absorption for larger bio-organic compounds such as proteins and peptides. Clinically used drugs are generally small and fairly lipophilic. Thus, the corneal route is currently dominating. In membranes, cornea and conjunctiva, principles of passive diffusion have been extensively investigated, but the role of active transporters is only sparsely studied.

Blood- ocular barrier The eye is protected from the xenobiotic 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 uveitis barrier prevents the access of plasma albumin\ into the aqueous humor, and limits also the access of hydrophilic drugs from plasma into the aqueous humor. Inflammation may disrupt the integrity of this barriercausing the unlimited drug distribution\ to the anterior chamber. In fact, the permeability of this barrier is poorly characterized. 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 extensive blood

flow and leaky walls. Drugs easilygain access to the choroid extravascular space, but thereafter distribution into the retina is limited by the RPE and retinal endothelia. Despite its high blood flow the choroidal blood flow constitutes only a minor fraction of the entire blood flow in the body. Therefore, without specific targeting systems only a minute fraction of the intravenous or oral drug dose gains access to the retina and choroid. Unlike blood brain barrier, the blood-eye barrier shave not been characterized in terms of drug transporter and metabolic enzyme expression. From the pharmacokinetic perspective plenty of basic research is needed before the nature of blood-eye barriers is understood.

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MACHANISM OF DRUG RELEASE

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 release of drug cans 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 are homogeneously dispersed in 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; in some instances, however, known as case II.

Transport, zero order kinetics has been observed.

B. OSMOSIS

In the Osmosis mechanism, the insert comprisesa 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 isbounded by an impermeable material and the elastic membrane. There is a drug releaseaperture in the impermeable wall of the insert. The first compartment contains a solute which cannot pass through the semi-permeable membrane and the second compartment provides reservoir for the drug which again is in liquid or gel form. When the insert is placed in the aqueous environment of the eye, water diffuses into the first compartment and stretches the elasticmembrane to expand the first compartment and contract thesecond compartment so that the drug is forced through the drug release aperture.

C. BIOEROSION

In the Bio erosion mechanism, the configuration of the body of the insert is constituted from a matrix of bio erodible material in which the drug is dispersed. Contact of the insert with tear fluid results in controlled sustained release of the drug by bio erosion of the matrix. 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 orenzymatic 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.

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