An Insight into Ocular Drug Delivery System

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Abstract: Ocular drug delivery has been a major challenge for the researchers. Therapeutic concentration in the target tissues are not maintained for a long duration due to complex structure of the eye. Most of the treatments call for the topical administration directly to the eye for localized therapy. There are several barriers to restrict the intraocular drug transport by which retention time to the eyes decreases. Pharmaceutical researchers has been developed new dosage forms for the ocular delivery like hydrogels, ocuserts, duraserts, in-situ gels etc to increase the residence time of the active ingredient into the ocular site. Hydrogels generally offer a moderate improvement of ocular drug bioavailability with the disadvantage of blurring of vision. Intravitreal implants, using various biodegradable or non-biodegradable technologies have been widely investigated for the chronic vitreoretinal diseases.

Key words: Eye drops · Hydrogels · Ocular Drug Delivery · Ocuserts · Nasolacrimal Drainage

INTRODUCTION

Eyes, a beautiful and sensitive part with complex structure among all the parts in our body and delivery of drugs through this route are also the most challenging endeavors for the pharmaceutical scientists [1]. Many parts of the eyes are not accessible to systemically administered drug so that in most of the cases topical drug delivery remains the preferred route for delivery of the drug. Eyes are easily and simply reachable site for the topical drug delivery [2]. Use of minimum concentration of preservative with effective packaging founds to be more attractive approach for process development in ophthalmic preparations. Fate of ophthalmic drug delivery system (Figure 1) describes the absorption and elimination of the drug from the eyes. In conventional drug delivery of ophthalmic solutions droppers are used by which about 45-65 ìl dosage form delivered to the eyes. Due to blinking of the eyes, the dosage form drains out of the eyes and that’s why very small portion of drug reaches to the inner tissue and the corneal region of the eyes. Only small amount of drug reaches to the intraocular tissues i.e. about 10% of the drug reaches to the cornea because of such low permeability of the drug to the cornea [3].

Physiology of the Eye: The human eye is the most essential and sensitive part of the body with the complex anatomy. It is slightly asymmetrical globe, about an inch in diameter. The structure of eye and its different parts (Figure 2). The front part of the eyes includes:

- The sclera
- The conjunctiva
- The cornea
- The pupil
- The iris

Around the outside of the eyeball, there is tough white sheath called as sclera and consist of the membrane that gives attachment to the extrinsic muscles of the eyes. The conjunctiva is vascularized and thin mucous membrane that lines the outer region of the cornea and eyelids. It is also involved in maintenance & formation of...
Fig. 1: Fate of ophthalmic drug delivery system

Fig. 2: The structure of eye and its different parts

The Precorneal tear film. Cornea, a clear transparent epithelial membrane that conveys images to the back of the eyes and it also covers the one sixth part of total surface area of the eye-ball [4]. The aperture through which light enters the eyes and hence we see images called as pupil. The visible colored part of the eyes that extends anteriorly from the ciliary body. The constriction and dilation of the pupil occurs by the parasympathetic and sympathetic nerves that are supplied to the iris. The color is created by the amount and type of pigment in the iris.

**Nasolacrimal Drainage System:** The Nasolacrimal drainage system (Figure3) serves as drain for tear flow from the external eye to the nasal cavity. It mainly consists of three parts:

**The Secretory System:** It consist of secretors that are stimulated by blinking and temperature change and reflex secretors that have an efferent nerve supply i.e. parasympathetic nerve and secretes in response to emotional and physical stimulation.

**The Distributive System:** Around the lid edges of the open eyes there is eyelids and tear meniscus that spreads tears over the ocular surface.

**The Excretory Part:** It consists of lacrimal sac, canaliculi, lacrimal punctum and Nasolacrimal duct. The corners of the eyes normally holds around 7-10 µl of tears. The pH of the tears is maintained at 6.5-7.5 and flow rate is about 1 µl min⁻¹ [5].
Fig. 3: The Nasolacrimal Drainage System

Ideal Characteristics of Ocular Drug Delivery System [6]: An ideal ocular drug delivery system must possess following characteristics-

- Easy to self-administer.
- Not induce bad taste after administration.
- Should be sterile.
- Possess more local activity than systemic effects.
- Deliver the drug to the right place.
- Reduce the number of administration per day.
- Should be non-irritative.
- Good corneal penetration.
- Prolong the contact time of the drug with the corneal tissue.

Advantages of Ocular Drug Delivery System [7, 8]:

- Provide controlled and sustained drug delivery.
- Accurate dosing.
- Self medication i.e. no need have trained personnel for application of drug.
- Needle free drug delivery.
- Penetration of low molecular weight, hydrophilic drugs can be obtained.
- Avoidance of hepatic first pass metabolism.
- There is rapid absorption due to high vascularization and large surface area.

Disadvantages of Ocular Drug Delivery System [9, 10]:

- Short duration of action due to rapid elimination of the drug through eye blinking and tear flow.
- Required frequent dosing.
- Unwanted systemic side effects due to drainage of administered dose into the lacrimal duct.
- Use of preservative is necessary.

Ophthalmic Disorders [11, 12]:

- Dry eye syndrome: In this syndrome, there is wetting of the ocular surface.
- Glaucoma: When the aqueous humour fails to drain properly then there is formation of pressure in the chambers of choroid layers.
- Conjunctivitis: It is a viral or bacterial infection causes inflammation of the conjunctiva.
- Keratitis: It is a viral, bacterial or fungal infection causes inflammation of cornea.
- Iritis: Pain and inflammation to the eyes.
- Blepharitis: Inflammation of the eyelids near the eyelashes.
- Stye: Bacteria infect the skin on the edge of the eyelid.
- Cataract: Blurred vision due to clouding of the internal lens of eyes.

Routes and Different Drug Delivery Systems for Eyes:
Mainly there are three routes for delivery of the drug to the eyes i.e. topical, systemic and intraocular route of administration in which the topical route is the most preferred and common route to administer the medication to the eyes. Instilled dose to the corners of the eyes are usually drained quickly by blinking of eyes and thus precorneal region returns to its original volume. Modern formulations attempt to increase the retention time of the dose by using sustained release drug and thus increase bioavailability [13].

Eye Drops: Solutions, emulsions or suspensions forms are most widely used to administer the drugs that are active at eye or eye surface. In this delivery system, there is quite low absorption of drug in the posterior tissues so eye drops are mainly used to anterior segment disorders. Various types of viscosity enhancers and polymers are used to increase the retention time of instilled dose to the eyes (Table 1). If the viscosity of the eye drop solution is
Table 1: Various Polymers Used In Ophthalmic Preparation

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Name of Polymer</th>
<th>Performance</th>
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<tbody>
<tr>
<td>1.</td>
<td>Pectin</td>
<td>Poor</td>
</tr>
<tr>
<td>2.</td>
<td>Acacia</td>
<td>Poor</td>
</tr>
<tr>
<td>3.</td>
<td>Gelatin</td>
<td>Fair</td>
</tr>
<tr>
<td>4.</td>
<td>Hydroxypropylcellulose and Carbopol</td>
<td>Good</td>
</tr>
<tr>
<td>5.</td>
<td>Dextran</td>
<td>Good</td>
</tr>
<tr>
<td>6.</td>
<td>Polyacrylamide</td>
<td>Good</td>
</tr>
<tr>
<td>7.</td>
<td>Carbopol and EX 55</td>
<td>Good</td>
</tr>
<tr>
<td>8.</td>
<td>Polycarbophil</td>
<td>Excellent</td>
</tr>
<tr>
<td>9.</td>
<td>Carbopol</td>
<td>Excellent</td>
</tr>
<tr>
<td>10.</td>
<td>Carboxymethylcellulose</td>
<td>Excellent</td>
</tr>
</tbody>
</table>

about 15-150 mPaS then there is maximum corneal penetration of the drugs [14, 15]. Eye drops follow first order kinetics and there is rapid decline in drug concentration that provides a pulse entry of the drug to the eyes. Many patients like pediatrics and geriatrics finds difficulty in administration of eye drops and may not receive the correct dose [16].

Eye Ointments: Ointments are the semi solid preparation intended for external application to prolong the contact of drug to the external ocular surface. Ointments are useful in improving the drug bioavailability and in sustaining drug release. Blurred vision and sticking of eyelids are the main disadvantages of the eye ointments [17].

Ocuserts: An ocular insert is sterile preparation that prolongs the residence time of the drug to the eye with control release. Ocusert affects to a lesser extent by Nasolacrimal drainage and tear flow [18]. Ocusert® has not become widely used because of unsatisfactory Intra ocular penetration control due to various causes, including difficulty of inserting the device, ejection of the device from eye and irritation during insertion [19].

Lacrisert: Lacrisert is a rod-shaped, water-soluble cul-de-sac insert composed of hydroxpropylcellulose without preservatives and other ingredients and is indicated in moderate to severe dry eye syndrome. Although previously many inserts including collagen shield, Ocufit SR®, New Ophthalmic Delivery System and Minidisc ocular therapeutic system have been developed [20, 21].

Durasert: An intravitreal implant uses a drug core with one or more surrounding polymers layers and delivers the drugs for predetermined periods ranging from days to year. The permeability of the polymer layers are the main factor for controlling the drug release [22]. An antiviral drug, ganciclovir (GCV)-loaded intravitreal implant (Vitrasert®), for the treatment of cytomegalovirus retinitis has been developed as the first intravitreal Drug Delivery System that avoids systemic side effects and does not involve frequent intravitreal injections [23].

Aqueous Gels: It is also known as hydrogels and consists of high molecular weight, hydrophilic, cross-linked polymers that form a three-dimensional network with the water. These gels provide increased residence time with higher bioavailability in cul-de-sac. Now-a-days, in-situ forming gels are more acceptable for the patients since they are administered into the eye as solution, after which they undergo transition into a gel [24].

Eye drop solution is the most prescribed dosage form, which are easy to use but it suffers from disadvantage of drug loss and immediate dilution through nasolacrimal drainage. So, the maximum bioavailability of the intra ocular administration of drops may hardly be 1.2% to the aqueous humor. That’s why there is a demand of suitable intra ocular delivery system to increase bioavailability to a substantial level [25]. The sequences of transcorneal permeation of topical administered drug in the cul-de-sac can be outlined below in Figure 4.
Marketed Products [26-28]: Some marketed formulations of ocular drug delivery are given below in Table 2.

CONCLUSION

It can be concluded from the whole study that eye drops are still the drug delivery system of choice in ophthalmic drug delivery. Ocular drug delivery system offers the unique carrier system for many pharmaceuticals. After literature survey, it has been found that ocular delivery based formulations have great application for local treatment of eye diseases with lesser side effects.

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