OCULAR INSERTS

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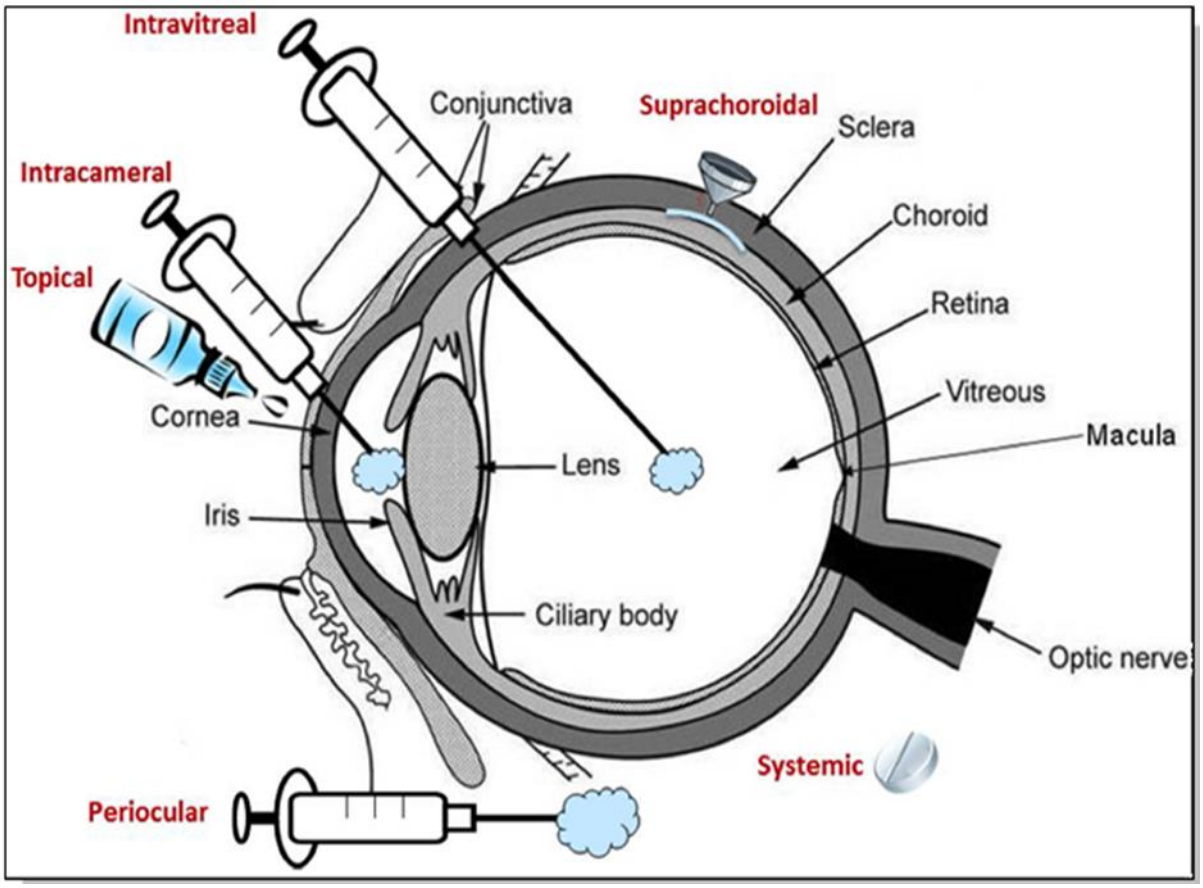
***Abstract*: The ocular insert represents a significant advancement in the therapy of eye disease. Ocular inserts are defined as sterile, thin, multilayered, drug-impregnated, solid or semisolid consistency devices placed into the cul-de-sac or conjunctival sac, whose size and shape are especially designed for ophthalmic application. They are composed of a polymeric support that alter release of the drug. The drug can later be incorporated as dispersion or a solution in the polymeric support. They have several advantages as increased ocular residence and sustained release of medication into the eye. The insert includes a body portion sized to position within a lachrymal canaliculus of the eyelid. The inserts are classified according to their solubility as insoluble, soluble, or bioerodible inserts. The release of drug from the insert depends upon the diffusion, osmosis and bioerosion of the drug, and this article is an attempt to present a brief about this newer drug delivery system.**

Keywords*: *Bioerosion, diffusion, membrane, ocular inserts

Introduction

Ocular Drug Delivery System (ODDS) is a dosage form, vehicle, or system intended for instilling, administering, or delivering drug/medicine to eye against any aliment or disorder involving or affecting vision. The ocular drug delievery system will increase ocular resistance, improve bioavailability, prolong drug release, reduce the side effects, better patient compliance, increase shelf life and have less visual and systemic side effects. Precision dosing with controlled release avoids pulsate drug delievery, reduces administration frequency, can target conjuctival/several route.

FIGURE: EYE – DIFFERENT ROUTES OF ADMINISTRATION



Classification of ocular inserts (Based on their solubility): The inserts are classified according to their solubility as soluble, insoluble or bioerodible inserts the release of drug from the insert depends upon the diffusion, osmosis and bioerosion of the drug.

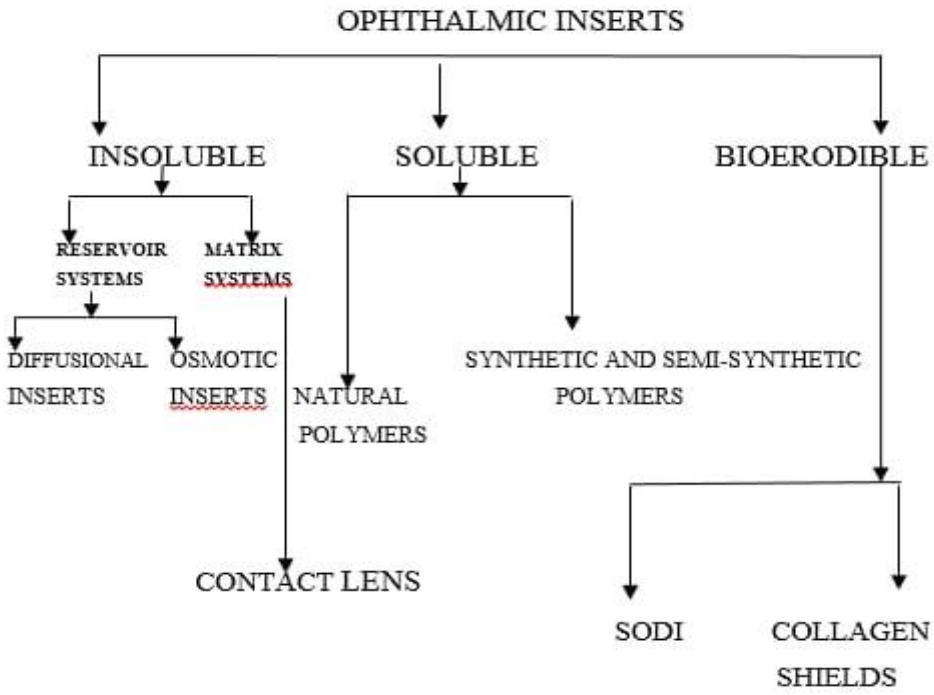


FIGURE: CLASSIFICATION OF OCULAR INSERTS

I. Insoluble ophthalmic inserts:

1. **Diffusion inserts** – The drug release from such a system is controlled by the lachrymal fluid, which permeates through the membrane. A sufficient internal pressure is achieved to drive the drug out from the reservoir. The drug delivery rate is controlled by diffusion through the membrane. **[1]**

Example:-ocuset pilo – 20

Insoluble inserts consist of medicated core prepared out of a hydrogen polymer like alginates, sandwiched between two sheets of transparent lipophilic rate controlling polymer.

2. **Osmotic inserts-** The release of drug through the osmotic insert follows the zero-order drug release profile. **[2]**

Generally composed of a central part (drug) surrounded by a peripheral part (osmotic solute)

Components of osmotic inserts-

Water permeablecomponent - Ethylene vinyl esters polymers
Semipermeable component – Cellulose acetate derivatives, polyesters of acrylic and metharylic acids
Osmotic agents –Inorganic**–** Magnesium sulfate**,** sodium chloride, potassium sodium carbonate
Organic – Tartaric acid
Carbohydrates – Sorbitol, sucrose, glucose.

II. Soluble ophthalmic inserts:

Soluble inserts correspond to the oldest class of ocular inserts, which offer the advantage of being wholly soluble, so the need not be removed from the site of application, thus, limitation the interventions to insertionly. **[3]**

Broadly divided into two types based on natural polymers and semisynthetic polymers

1. **Natural polymers –** Collagen derivatives like p-collagen, polyvinyl pyrrolidine
2. **Semisynthetic polymers –** Cellulose derivatives like hydroxypropyl cellulose, methyl cellulose

III. Bioerodible ophthalmic inserts:

Bioerodible inserts are composed of homogeneous dispersion of a drug which can be included in or not included in the hydrophobic coat made of bioerodible polymers, which is impermeable to the drug. Successfully used bioerodible materials are the poly (orthoesters) and poly (orthocarbonates). Drug release from such a system is due to the contact of the device with the tear fluid, including a superficial bioerosion of the matrix. **[4]**

Glaucoma:

Glaucoma is a group of eye conditions that damage the optic nerve, the health of which is vital for good vision. This damage is often caused by an abnormally high pressure in our eye. Glaucoma is one of the leading cause of blindness for people over the age of 60.

Acetazolamide

Acetazolamide belongs to a class of drugs, called anticonvulsants and it also a Carbonic anhydrase inhibitor which will reduce eye pressure by decreasing the production of intraocular fluid. So can be used to treat glaucoma. Acetazolamide is safe and effective in children younger than 12 years of age. Acetazolamide is used with other medicines to reduce edema (excess fluid retention) Acetazolamide and methazolamide are two Carbonic anhydrase inhibitors which can be derivatised by mannich-type derivatives to increase their solubility. **[5]** Acetazolamide is a carbonic anhydrase inhibitor is still the most effective drug for the treatment of glaucoma for many years, also it is used in the various forms of epilepsy. It is also used as diuretic and treat several illnesses. **[6]**

FDA-Approved indications [7]

- Glaucoma
- Idiopathic intracranial hypertension
- Congestive heart failure
- Altitude sickness
- Periodic paralysis
- Epilepsy

Non-FDA-Approved indications

- Central sleep apnea
- Dural ectasia in Marfan syndrome
- Methotrexate-included renal damage

Acetazolamide as oral and topical formulations are being available in the market for the reduction of Intra Ocular Pressure (IOP) in patients suffering from glaucoma by reducing aqueous humor production. Acetazolamide in the form of controlled release ocular inserts increase the amount of drug absorption into the aqueous humor when compared to eye drops. The conjuctival absorption coefficients calculated by the model and the AUC of the conjuctiva per mumol of delivered drug were found be 2.7 and 42 times higher, respectively for the ocular inserts as compared to eye drop administration**. [8]** In this way ocular inserts are having beneficiary advantage when compared with that of other routes of administration.

- **Barriers of ocular drug delievery system:**

These barriers can be broadly classified as

I. Anatomical barriers- are of two types:

1. **Corneal absorption** - Corneal route is important route for the ocular absorption of drugs. Absorption of the drug by the corneal leads it into the aqueous humor (target site). Corneal epithelium is the major barrrier to which prevents the transcorneal permeation of drugs. Due to its hydrophobic nature, water soluble drugs are not able to pass through it.

2. **Non-corneal absorption**- Non-corneal route refers to penetration of drugs across the conjuctiva and sclera. Drug upon reaching beyond the cornea is absorbed by small capillaries and transferred to the systemic circulation. This route represents as non productive route, as this route prevents the transfer of drug to the aqueous humor which is the actual site responsible for therapeutic efficacy.

II. Physiological barriers

In the eye's primary line of defense is it's tear film. Bioavailability of topically administred drug is further reduced by Precorneal factors such as solution drainage, tear dilution, tear turnover and increase lacrimation.

III. Blood ocular barriers

The blood ocular barrier normally kepts most drugs out of the eye. However, inflammation breakdown this barrier allowing drugs and large molecules to penetrate into the eye.

- **Methods to overcome barriers:**

To overcome the barriers for drug delievery through ocular inserts the following methods can be used.

I. Bioavailability improvement:

1. Viscosity adjustment-

- ✓ Increasing polymers are usually added to Opthalmic drug solutions. Increased vehicle viscocity should correspond to a slower elimination, from the preocular area.
- ✓ It improves precorneal residence time and greater transcorneal penetration of the drug into the anterior chamber.
- ✓ It has minimal effects in human, interms of improvement in bioavailability.

2. Prodrug-

- ✓ Prodrug is to enhance corneal drug permeability through modification of the Hydrophilicity or liphophilicity of the drug.
- ✓ Prodrug is either chemically or Enzymatically metabolized to the active parent compound.

Example:- Esterase

3. Penetration enhancers-

- ✓ The transport characteristics across the cornea can be maximised by increasing the permeability of corneal epithelial membrane.

II. Controlled release drug delivery:

Inserts- classified as two types

1. Non erodible inserts:

a. Ocusert- The ocusert release pilocarpine continuously at a study rate for seven days. Mainly used to treat glaucoma.

b. **Contact lens-** Hard contact lenses, soft contact lenses and intraocular are popular for correction of refractive errors of the eye and several kinds of polymers used for this preparation.

2. Erodible inserts:

a. Lacriserts- It is sterile rod shaped device made up of propyl cellulose without any preservative for the treatment of eye syndromes.

b. SODI (Soluble ocular drug inserts) – These are small oral water, sterile, thin film of oval shaped of polyacrylamide incorporating drug.

c. Minidisc- Centered disc with a convex front and a concave back surface, drug release-170 hours.

Conclusion:

The main efforts in ocular drug delievery during the past two decades has been on the design of systems, to prolong the residence time of topically applied drugs in the conjuctival sac by modifying the composition of inserts. One can has various new approaches like ocular inserts, non corneal route of ocular drug penetration to overcome the barriers of ocular drug delievery system are being developed by the pharmaceutical scientists. The advantages gained by ocular inserts are many for the treatment of eye related problems, but only few gain commercial acceptances. This is because of the high cost of this inserts and reluctance of the patient to use unfamiliar types of ophthalmic medication. Acetazolamide in the form of ocular insert is used to treat several eye related illness like glaucoma. So, there is further scope for the development of ocular inserts when compared with other formulation.

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