A REVIEW ON: OCULAR INSERT DRUG DELIVERY SYSTEM

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Abstract: Eye is the most unique organ of the body. Various drug delivery system are used to delivery drug into eyes are used but there are various limitations researchers are finding new ways by which contact time. Bioavailability and residence time can be enchained as well as patient discomfort and frequency of dose can be reduced. An ocular insert represents and advanced technology in disease therapy. In spite of extensive pharmacological and clinical data pointing to the usefulness and advantages of solid device for topical drug delivery to the eye, liquid and to a smaller extent gel-type preparation appears to enjoy the continued inserts of manufactures and ophthalmologists. In the present update the authors discuss the advantage, disadvantages and examine the few insert which are available on the market or are being developed by pharmaceutical companies for drug delivery. In this review various new drug delivery system applied in eye like inserts. In-site gel, liposomes, noisome, nanoparticles, iontophoresis, corneal shield drug embedded, contact lenses, ocular wafers and films etc., are discussed. The present review is an attempt to present a brief information about ocular insert.

Keywords: Ocular insert, eye disease therapy, ophthalmologists, bioavailability, advantages and disadvantages, liposomes, liposomes, nanoparticles, noisome, In-site gel.

Introduction:
Ocular inserts are defined as sterile, thin, multilayered, drug-impregnated, solid or semisolid consistency device 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 may or may not contain a drug. Ocular drug delivery is one of the most challenging tasks faced by pharmaceutical review. Ocular inserts as an ocular sustained release drug delivery system. Increased ocular residence hence, prolonged drug activity and higher bioavailability with respect to standard vehicles. Release of drug at a slow, constant rate. To overcome the ocular drug delivery barriers and improve ocular bioavailability various conventional and novel drug delivery system have been developed such as emulsion, suspension, aqueous gels, nanoparticles, Nano micelles, liposomes, implants, contact lenses, etc.

Ocular inserts as an ocular sustained release drug delivery system-
1) Increased ocular residence hence, prolonged drug activity and higher bioavailability with respect to standard vehicles.
2) Release of drugs at a slow constant rate.
3) Reduction of systemic absorption.
4) Possibility of targeting internal ocular tissues through non-corneal (conjunctival scleral) routes.
5) Increased shelf life with respect to aqueous solutions.

Ocular drug delivery system is a dosage from vehicle or system intended for instilling administering or delivery drug medicine to eye against any ointment or disorder involving or affecting vision. All of the benefits listed above cannot be present in a single ideal device.

Use to drug delivery into the eye:-
Intravitreal injection is the most common and widely recommended route of drug administration to treat posterior ocular disease. Through the need of repeated eye puncture with intravitreal injections causes several side effects such as endophthalmitis, hemorrhage retinal detachment and poor patient tolerance.

Classification of Patented Ocular Inserts:
( Based upon their solubility behavior)
1) Insoluble inserts
   a) Diffusion based
   b) Osmotic based
   c) Soft contact lenses
2) Soluble inserts
3) Bio erodible inserts

Different type of ocular drugs-
Topical
Local ocular s
Systemic
The most appropriate method of administration depends on the area of the eye to the medicated.

1) **Topical liquid/solutions eye drops.**
   - (1) Topical ocular drug delivery has been considered to be an ideal route of administration for treatment of ocular diseases related to the anterior segment of the eye.
   - (2) Topical drops are the most convenient safe immediately active patient compliant and noninvasive mode of ocular drug administration.
   - (3) An eye drop solution provides a pulse drug permeation post topical drop instillation after which its concentration rapidly declines.

2) **Local Ocular.**
   - (1) Local ocular anesthesia is indicated in that subset of ophthalmologic surgeries in which general anesthesia is not needed and particularly for those surgeries requiring patient co-operation.
   - (2) The local anesthesia usually lasts for 2-3 hours although it can last longer,(up to6-8 hours) depending upon the type of anesthetic drug used.
   - (3) Local anesthesia also called local anesthetic is usually a onetime injection of medicine that numbs a small area of the body.

3) **Systemic.**
   - (1) While this article does not include an exhaustive list common systemic medication cause ocular side effects include.
   - (2) Bisphosphonates, cyclosporine and tacrolimus, minocycline, hydroxychloroquine, ethambutol, topiramate, tamsulosin, amiodarone, anticholinergics, erectile dysfunction drugs, blood pressure.
   - (3) Systemic drug therapy involve treatment that affects the body as a whole or that acts specifically on systems that involve the entire body such as the cardiovascular respiratory, gastrointestinal or nervous systems. Mental disorder also are treated systemically.

**Composition of eye:**
The eye is made up of three coats, which enclose the optically clear aqueous humor lens and vitreous body. The outermost coat consists of the cornea and the sclera; the middle coat contains the main blood supply to the eye and consists; from the back forward of the choroid the ciliary body and the iris.

### Barriers for ocular insert drug delivery system:

| Barriers for ocular insert drug delivery system: |
|------------------------------------------------|
| **1) Static barriers** | Different layers of cornea, sclera and retina including blood aqueous and blood retinal barriers. |
| **2) Dynamic barriers** | Choroidal and conjunctival blood flow, lymphatic clearance and tear dilution. |

**New drug delivery system applied in eye:**
In-site gel, Liposomes, Noisome, Nanoparticles, Corneal shield, Contact lenses, Ocular wafers and films etc.

**Advantages of ocular insert drug delivery system:**
1) Release of drugs at a slow, constant rate.
2) Accurate dosing.
3) Reduction of systemic absorption.
4) Increased shelf life.
5) Better patient compliance.
6) No addition of preservative.
7) Low dosing frequency.

**Disadvantages of ocular insert drug delivery system:**
1) The very short time the solution stays at the eye surface.
2) Its poor bioavailability.
3) Foreign body sensation.
4) Difficult to handle.
5) This may constitute a difficult physical and physiological barrier to patient compliance.
6) Movement around eye might occur.
7) Interference with vision.
Major classes of drug used are

| Category of drug | Examples                                      |
|------------------|-----------------------------------------------|
| Anesthetics      | Tetra Caine                                   |
| Anti-inflammatories | Corticosteroids                         |
| Mydriatics       | Atropine                                      |
| Cycloplegics     | Atropine                                      |
| Miotics          | Pilocarpine HCl                               |
| Anti-infectives  | Antibiotics, Antivirals, and Antibacterial     |
| Diagnostic drugs | Sodium fluorescein                            |
| Surgical adjuncts | Irrigating solutions                         |
| Glaucoma drugs   | Pilocapine HCl                                |

Eye disease therapy:
You may choose to have surgery to correct your vision. If you already have glasses, you may need a stronger prescription. Other more serious condition also happen as you age. Eye diseases like macular degeneration, glaucoma and cataracts can cause vision problems.

Ocular drug delivery bioavailability:
Highly lipophilic biological membrane has much lower affinity towards hydrophilic cyclodextrins. Therefore, cyclodextrins remain in aqueous solution and the hydrophobic drug is absorbed by the biological membrane. Optimal bioavailability was achieved for eye drops with cyclodextrins of <15%.

Ocular drug bioavailability from topically applied liposomes:
During the past decade liposomes have been investigated extensively for their ability to improve drug utilization by the body, first in the area of chemotherapeutics and most recently in the area of ophthalmology. Liposomes are vesicle-like mestructures with a concentric series of alternating compartments of aqueous spaces and phospholipids bilayers. To date, liposomes have been found to both promote and reduce ocular drug absorption, indicating that a definite needs exists for further studies to evaluate the interplay of drug, liposomes, and the corneal surface in determining the effectiveness of liposomes as vehicles for topically applied ophthalmic drugs. The purpose for this review is place is to place in perspective the role of liposomes in topical ocular drug delivery.

Mechanism Of Drug Release From Ocular Inserts:
**Diffusion:** In this mechanism the drug is released continuously at a controlled rate through the membrane. If the insert is formed of a solid non-erodible body having pores and drug is in a dispersed form, the drug release takes place via diffusion through the pores.

**Osmosis:** In the osmosis mechanism, the insert is made up of a transverse impermeable elastic membrane which divides the interior of the insert into two compartments first and second the first compartment is surrounded. Osmosis is a phenomenon of paramount significance for the transport of water and solute through biological membranes. It accounts for fluid transport out of kidney tubules and the gastrointestinal tract, into capillaries, and across cell membranes. The thermodynamic equations for osmosis are well established but, despite the fundamental significance for biological fluid transport, an understanding of osmosis at the molecular level has been lacking.

**Bio erosion:** Bio erosion is defined as erosion, i.e., removal and transport of material by the action of organisms. Bio abrasion refer to removal by mechanical means: scraping, rasping, and drilling. Bio corrosion refers to removal by chemical means: etching, dissolving, boring.

**Evaluations test for ocular insert:**
1. Thickness
2. Folding Endurance
3. Surface pH
4. Weight Uniformity
5. Drug Content Uniformity
6. Tensile Strength
7. In Vitro Drug Release Study
8. Ex Vivo Trans corneal Permeation Study
9. Drug Release Kinetics
10. Accelerated Stability Study
Conclusion:
Ocular insert drug delivery has to overcome unique barriers. However, several approaches have been shown, experimental to improve ocular drug absorption. Constantly increasing understanding of the absorption process offers new possibilities in the future. It seems that new tendency of research in ocular drug delivery system is directly towards a combination of several drug delivery technologies. Solution or suspension drops and ointment still remain the first line approach to treatment in standard therapies. Small, ocular dosage forms, in particular gel-forming erodible inserts, show interesting in vivo performance and allow for therapeutics levels to be obtained over an extended period of time in the tear film and anterior chamber. Mucoid adhesive inserts are promising ocular insert drug delivery system to treat external and intraocular eye infection, and diseases that require frequent eye drops instillation in order to maintain therapeutic drug levels.

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