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Review Article

REVIEW ON OPHTHALMIC INSERTS

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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. Ocular route of drug delivery is one of the most interesting and challenging endeavors facing the pharmaceutical scientist. One of the major barriers of ocular medication is to obtain and maintain a therapeutic level at the site of action for prolonged period of time. Therefore many ophthalmic drug delivery systems are available. These are classified as conventional and non-conventional drug delivery systems. The main purpose of preparing ocular insert is to increase ocular bioavailability of drug. Ocular inserts maintain the drug concentration within a desired range. Fewer administrations are required so they increase patient compliance. In the present update, the advantages, disadvantages and requirement for success of ocular inserts, and examine the few inserts which are available on the market or are being developed by pharmaceutical companies for drug delivery. In this review, we have focused on the present area of ocuserts helps in treating eye diseases.

Keywords: Ocuserts, ocular drug delivery system, eye diseases

INTRODUCTION

Ocular drug delivery is one of the most challenging and interesting tasks for the Pharmaceutical researchers. One of the major barriers of ocular medication is to maintain and obtain a therapeutic level at the site of action for desired period of time. The anatomy, biochemistry and physiology of the eye render this organ exquisitely impervious to foreign substances [1].

The eye as a portal for drug delivery is generally used for local therapy against systemic therapy to avoid the risk of eye damage due to high blood concentrations of the drug, which is not intended. The ocular organ impervious to foreign substances due to unique anatomy, physiology and biochemistry of the eye, thus presenting a constant challenge to the pharmaceutical formulator to circumvent the protective barriers of the eye without causing permanent tissue damage. Therefore, the target tissue absorbs a very less fraction of drug. Due to this reason, concentrated solutions and frequent dosing are required for the instillation to achieve an adequate level of therapeutic effect. Polymeric film ocular drug delivery systems/ocular inserts, which are gaining worldwide accolade, release drugs at a pre-programmed rate for a longer period by increasing the pre-corneal residence time with increase. [2, 3]

The advantage of ocular inserts, which are solid devices placed in the cul-de-sac of the eye in comparison with liquid formulations are numerous. Because of the prolonged retention of the devices and a controlled release, the effective drug concentration in the eye can be ensured over an extended time period. Dosing of the drug is also more accurate and the risk of systemic side effects is decreased. Furthermore, solid devices have an increased shelf life and the presence of additives such as preservatives is not required. Ocular delivery systems like inserts, biodegradable polymeric systems, and collagen shields are being developed in order to attain better ocular bioavailability and sustained action of ocular drugs.

A basic concept in ophthalmic review and development is that the therapeutic efficacy of an ophthalmic drug can be greatly improved by prolonging its contact with the corneal surface. Ophthalmic inserts offer many advantages over conventional dosages forms, like increased ocular residence, possibility of releasing drug at a slow and constant rate, accurate dosing, and exclusion of preservatives and increased shelf life. Design, construction and technology of ocular insert in a controlled and sustained ocular delivery device are gaining rapid improvement to overcome this constraint. [4]

ADVANTAGES OF OCULAR DRUG DELIVERY SYSTEMS

1. Accurate dosing is possible. To overcome the side effects of pulsed dosing produced by conventional systems.
2. To provide sustained and controlled drug delivery.
3. To increase the ocular bioavailability of drug by increasing the corneal contact time. This can be achieved by effective adherence to corneal surface.
4. To provide targeting within the ocular globe so as to prevent the loss to other ocular tissues.
5. To circumvent the protective barriers like drainage, lacrimation and conjunctival absorption.
6. To provide comfort, better compliance to the patient and to improve therapeutic performance of drug.
7. To provide better housing of delivery system.

OCULAR PHARMACOKINETICS

The drug pharmacokinetics from the eye follows the following paths

• Transcorneal permeation from the lacrimal fluid into the anterior chamber.
• Non-corneal drug permeation across the conjunctiva and sclera into the anterior uvea.
• Drug distribution from the blood stream via blood-aqueous barrier into the anterior chamber.
• Elimination of drug from the anterior chamber by the aqueous humor turnover to the trabecular meshwork and sclemm's canal.
• Drug elimination from the aqueous humor into the systemic circulation across the blood-aqueous barrier.
• Drug distribution from the blood into the posterior eye across the blood-retina barrier.
• Intra vitreal drug administration.
• Drug elimination from the vitreous via E.g. posterior route across the blood-retina barrier.
• Drug elimination from the vitreous via anterior route to the posterior chamber. [5]

MECHANISM OF OCULAR DRUG ABSORPTION [6, 7]

Topical delivery into the cul-de-sac is, by far, the most common route of ocular drug delivery. Absorption from this site may,

1. Corneal
2. Non-corneal

CLASSIFICATION OF OPHTHALMIC INSERTS

Ophthalmic inserts are aimed at remaining for a long period of time in front of the eye. These solid devices are intended to be placed in the conjunctival sac and to deliver the drug at a comparatively slow rate. Ophthalmic inserts are defined as sterile preparations, with a thin, multilayered, drug-impregnated, solid or semisolid consistency devices placed into cul-de-sac or conjuctival sac and whose size and shape are especially designed for ophthalmic application. They are composed of a polymeric support containing or not drug (s), the latter being incorporated as dispersion or a solution in the polymeric support. The inserts can be used for topical or therapy.

The advantages of these systems are:

1. Ocular contact time is increased.
2. Accurate dosing is possible. Constant and predictable rate of drug release can be achieved.
3. Systemic absorption can be reduced and side effects can be reduced.
4. Increased shelf life can be achieved
5. Better patient compliance.
6. Targeting to internal ocular tissues can be done. [8]

CLASSIFICATION OF OPHTHALMIC INSERTS

1. Non-erodible ocular insert: The Non-erodible ocular inserts include Ocusert, and Contact lens.

Ocusert was one of the earlier ocular inserts in use. The technology used in this is an insoluble delicate sandwich technology. In ocusert the drug reservoir is a thin disc of pilocarpine-alginate complex sandwiched between two transparent discs of micro porous membrane fabricated from ethylene-vinyl acetate copolymer. The micro porous membranes permit the tear fluid to penetrate into the drug reservoir compartment to dissolve drug from the complex.

Alza-ocusert: In this Pilocarpine molecules are then released at a constant rate of 20 or 40 μg/h for 4 to 7 days. Used in the management of glaucoma The use of pre-soaked hydrophilic contact lenses was used for ophthalmic drug delivery. Therapeutic soft lenses are used to aid corneal wound healing in patients with infection, corneal ulcers, which is characterized by marked thinning of the cornea.

An alternative approach to pre-soaked soft contact lenses in drug solutions is to incorporate the drug either as a solution or suspension of solid particles in the monomer mix. The polymerization is then carried out to fabricate the contact lenses. This technique is promising longer release up to 180 h as compared to pre-soaked contact lenses.

Disadvantages of these non-erodible ocular inserts are

1.Complexity and difficulty of usage is noticed particularly in self administration.

2.Tolerability in the eye is poor, due to rigidity, size or shape.

3.Foreign body sensation and they are to be removed at the end of the dosing period. [9]

2. Erodible ophthalmic insert: The marketed devices of erodible drug inserts are Laciserts, SODI, and Minidisc.

a. Lacisert: It is a sterile rod shaped device made up of hydroxyl propyl cellulose without any preservative is used for the treatment of dry eye syndromes. It weighs 5 mg and measures 12.7 mm in diameter with a length of 3.5 mm. Lacisert is useful in the treatment of keratitis whose symptoms are difficult to treat with artificial tear alone. It is inserted into the inferior fornix where it imbibes water from the conjunctiva and cornea, forms a hydrophilic film which stabilizes the tear film and hydrates and lubricates the cornea. It dissolves in 24 hours.

b. Sodi: Soluble Ocular Drug Insert is a small oval wafer developed for cosmonauts who could not use eye drops in weightless conditions. It is sterile thin film of oval shape made from acrylamide, N-vinylpyrrolidone and ethylacrylate called as ABE. It weighs about 15-16 mg. It is used in the treatment of glaucoma and trachoma. It is inserted into the inferior cul-de-sac and gets wets and softens in 10-15 seconds. After 10-15 min the film turns into a viscous polymer mass, after 30-60 minutes it turns into polymer solutions and delivers the drug for about 24hours. [10]

c. Minidisc: The minidisc consists of a contoured disc with a convex front and concave back surface in the contact with the eyeball. It is like a miniature contact lens with a diameter of 4-5mm. The minidisc is made up of silicone based prepolymer-α-ψ-bis (4-methacryloxy) butyl polydimethyl siloxane. Minidisc can be hydrophilic or hydrophobic to permit extend release of both water soluble and insoluble drugs. [11]

Classification of Patented Ocular Inserts (Based upon their solubility behavior)

1) Insoluble inserts
2) Soluble inserts
3) Bio-erodible inserts

Insoluble ophthalmic inserts

The insoluble inserts have been classified into three groups:-

i. Diffusion systems
ii .Osmotic systems
iii. Hydrophilic contact lenses.

The first two classes include a reservoir in contact with the inner surface of the rate controller and supplying drug thereto. The reservoir contains a liquid, a gel, a colloid, a semisolid, a solid matrix or a carrier-containing drug homogeneously or heterogeneously dispersed or dissolved therein. Carriers can be made of hydrophobic, hydrophilic, organic, inorganic, naturally occurring or synthetic material.The third class includes the contact lenses. The insoluble of these devices is their main disadvantages, since they have to be removed after use.

Diffusion inserts: The diffusion systems are compared of a central reservoir of drug enclosed in specially designed semi permeable or micro porous membranes, which allow the drug to diffuse the reservoir at a precisely determined rate.

The drug release from such a system is controlled by the lachrymal fluid permeating through the membrane until a sufficient internal pressure is reached to drive the drug out of the reservoir. The drug delivery rate is controlled by diffusion through the membrane, which one can be controlled. [12]

Table 1: Components of diffusional inserts

Central reservoir	Glycerin, ethylene glycol, propylene glycol, water, methyl cellulose mixed with water, sodium alginate, poly (vinylpyrrolidone), poly ox ethylene stearate.
Micropores membrane	Polycarbonates, polyvinyl chloride, polysulfones, cellulose esters, crosslinked poly (ethyl oxide), cross-linked polyvinylpyrrolidone, and cross-linked polyvinyl alcohol.

Osmotic inserts [13]

The osmotic inserts are generally compared of a central part surrounded by a peripheral part. The first central part can be composed of a single reservoir or of two distinct compartments.

In first case, it is composed of a drug with or without an additional osmotic solute dispersed through a polymeric matrix, so that the drug is surrounded by the polymer as discrete small deposits. In the second case, the drug and the osmotic solutes are placed in two separate compartments, the drug reservoir being surrounded by an elastic impermeable membrane and the osmotic solute reservoir by a semi permeable membrane. The second peripheral part of these osmotic inserts comprises in all cases a covering film made of an insoluble semi permeable polymer. The tear fluid diffuse into peripheral deposits through the semi permeable polymeric membrane wets them and induces their dissolution. The solubilized deposits generate a hydrostatic pressure against the polymer matrix causing its rupture under the form of apertures. Drug is then released through these apertures from the deposits near the surface of the device which is against the eye, by the sole hydrostatic pressure. This corresponds to the osmotic part characterized by zero order drug release profile.

Table 2: Components of osmotic inserts.

Water permeable matrix	Ethylene - vinyl esters copolymers, Divers-plasticized polyvinyl chloride (PVC),polyethylene, cross-linked polyvinylpyrrolidone(PVP)
Semi permeable membrane	Cellulose acetate derivatives, Divers – Ethyl vinyl acetate (EVA), polyesters of acrylic and methacrylic acids (Eudragit ®).
Osmotic agents	Inorganic – magnesium sulfate, sodium chloride, potassium phosphate dibasic sodium carbonate and sodium sulfate. Organic- calcium lactate, magnesium succinate and tartaric acid. Carbohydrates – Sorbitol, mannitol, glucose and sucrose.

Soft contact lenses

These are shaped structure made up of a covalently crosslinked hydrophilic or hydrophobic polymer that forms a three-dimensional network or matrix capable of retaining water, aqueous solution or solid components.

When a hydrophilic contact lens is soaked in a drug solution, it absorbs the drug, but does not give a delivery as precise as that provided by other non-soluble ophthalmic systems. The drug release from such a system is generally very rapid at the beginning and then declines exponentially with time. The release rate can be decreased by incorporating the drug homogeneously during the manufacture or by adding a hydrophobic component. Contact lenses have certainly good prospects as ophthalmic drug delivery systems.

Soluble Ophthalmic inserts

Soluble inserts correspond to the oldest class of ophthalmic inserts. They offer the great advantage of being entirely soluble so that they do not need to be removed from their site of application thus, limiting the interventions to insertion only.

Types

a) Based on natural polymers e.g. collagen.

b) Based on synthetic or semi synthetic polymers.

The therapeutic agents is preferably absorbed by soaking the insert in a solution containing the drug, drying and rehydrating in before use on the eye. The amount of drug loaded will depend upon the amount of binding agent, upon the concentration of the drug solution into which the composite is soaked, as well as the duration of the soaking.

The soluble ophthalmic inserts containing synthetic/semi synthetic polymers

Offers the additional advantages of being generally of a simple design.

a) Based on products well adopted for ophthalmic use.

b) Easily processed by conventional methods – slow evaporating extrusion, compression or injection molding.

The release of the drug from such system is by penetration of tears into the insert which induces release of the drug by diffusion and forms a gel layer around the core of the insert, this external gelification induces the further release, but still

controlled by diffusion. The release rate, J, is derived from Fick's law yields the following expression.

$$J = \frac{AdkCS}{L}$$

A- Surface area of the membrane
K – Diffusion coefficient of the drug
L – Membrane thickness
CS – Drug solubility in water
D- Diffusion coefficient of the ocuserts membrane.

Since all the terms on the right hand side of the above equation are constant, so is the release rate of the device. The other factors affecting drug release from these Ocuserts include:

• Penetration of the inclusion.
• Swelling of the matrix.
• Dissolution of the drug and the polymers.

The soluble insert made of cellulose derivatives can be sterilized by exposure to gamma radiation without the cellulose components being altered. A decreased release rate is obtained by using a component of the matrix a polymer normally used for enteric coatings or by introducing a suitable amount of hydrophobic polymer capable of diminishing the tear fluid penetration and thus of decreasing the release of the drug without modifying the solubility of the insert when added in proper proportion.

Table 3: Components Of Soluble Inserts Containing Synthetic Polymers.

Soluble synthetic polymers	Cellulose derivatives –Hydroxypropyl cellulose methylcellulose, hydroxyethyl cellulose and hydroxypropyl cellulose. Divers – Polyvinyl alcohol, ethylene vinyl acetate copolymer.
Additives	Plastisizer – Polyethylene glycol, glycerin, propylene glycol Enteric coated polymer –Cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate. Complexing agent – Polyvinyl pyrrolidone. Bioadhesives – Polyacrylic acids.

Biodegradable ophthalmic inserts

The biodegradable inserts are composed of material homogeneous dispersion of a drug included or not into a hydrophobic coating which is substantially impermeable to the drug. They are made of the so-called biodegradable polymers. Successful biodegradable materials for ophthalmic use are the poly (orthoesters) and poly (orthocarbonates). The release of the drug from such a system is the consequence of the contact of the device with the tear fluid inducing a superficial diversion of the matrix.

The use of solid ophthalmic devices will certainly increase owing to the development of new polymers, the emergence of new drugs having short biological half lives or systemic side effects and the need to improve the efficacy of ophthalmic treatment by ensuring an effective drug concentration in the eye over an extended period of time. [12, 14]

OCUSERTS USING IN VARIOUS EYE DISEASES:

1. Glaucoma: Glaucoma refers to a group of eye conditions that lead to damage to the optic nerve. This nerve carries visual information from the eye to the brain. In most cases, damage to the optic nerve is due to increased pressure in the eye, also known as intraocular pressure (IOP).

Medication available but having side effects: Ophthalmic pilocarpine is used to treat glaucoma, a condition in which increased pressure in the eye can lead to gradual loss of vision. Pilocarpine is in a class of medications called miotics. It works by allowing excess fluid to drain from eye.

The amount of the drug administered in pilocarpine eye drops is substantially in excess of that needed for IOP control. The need to avoid this problem and the inconvenience of administering drops are leading to the development of a variety of alternative methods for drug delivery to the eye. Pilocarpine needs to be administer four times a day which do not provide a constant therapeutic effect of the medication while leading the side effects of blurred or fluctuating vision and also not been tolerated by patients under the age of 40 and leeds to the fluctuation of intraocular pressure.

Other Side Effects:

1. Prostaglandin Analogs: possible changes in eye color and eyelid skin, stinging, blurred vision, eye redness, itching, burning.

2. Beta Blockers: low blood pressure, reduced pulse rate, fatigue, shortness of breath; rarely: reduced libido, depression. **3. Alpha Agonists:** burning or stinging, fatigue, headache, drowsiness, dry mouth and nose, relatively higher likelihood of allergic reaction.

4. Carbonic Anhydrase Inhibitors: in eye drop form: stinging, burning, eye discomfort; in pill form: tingling hands and feet, stomach upset, memory problems, depression, frequent urination.

New advanced ocusert system

Ocular inserts of Timolol maleate: Controlled release of timolol maleate ocusert avoids the pulse-entry with which side-effects are associated. These systems can be based on any of several different mechanisms, and include both erodible and nonerodible matrices, wafers. Timolol maleate was the first β-blocker to be used as an anti-glaucoma agent and to date remains as the standard because none of the newer beta blockers were found to be more effective. Timolol maleate has the longest record of safety and efficacy to lower IOP and is administered via eye drops one or more times per day. They lengthen the extent of drug action by enhancement of corneal absorption.

Pilocarpine ocusert: A matrix-dispersed pilocarpine soluble insert avoids some of the problems of administration of pilocarpine by drops. It has shown an effective lowering of the IOP with a duration of at least 24 hours.The insert is, in effect, a device for prolonging the contact time of the dispersed drug with the corneal tear film. It is therefore analogous to the use of agents which increase tear film viscosity, such as methylcellulose and polyvinyl alcohol, without the disadvantage inherent in the removal of a drug- soaked carrier such as the cotton pledget. Since there is a limit to the effectiveness of increasing viscosity on drug penetration, the duration of effect seen with these inserts can be attributed to prolonged release with the slow dissolution of the device.

1. **Herpes Simplex Eye Disease:** The most common herpes simplex eye disease caused is an infection of the cornea, which can potentially threaten sight. The infection varies in duration, severity and response to treatment, depending in part on which of several different strains of HSV type I caused the original infection. It can be considered a "cold sore" or "fever blister" of the eye.Herpes simplex keratitis (HSK) remains a common cause of unilateral corneal disease.

Medication available but having side effects: Acyclovir, an antiviral is effective against human Herpes Simplex viruses, commercially available as a 3 % w/w eye ointment to be applied 5 times a day in the eye. The poor therapeutic response exhibited by conventional ophthalmic ointments due to rapid pre corneal elimination of the drug.

New advanced ocusert system

Acyclovir ocular inserts: They were prepared using solvent casting method said promising formulation would be able to offer benefits such as increase residence time, prolonged drug release, reduction in frequency of administration and thereby may help to improve the patient compliance.

1. **Eye Allergies:** Eye allergies often are hereditary, and occur due to processes associated with other types of allergic responses. When an allergic reaction takes place, your eyes may be overreacting to a substance perceived as harmful, even though it may not be. These substances are called allergens. For example, dust that is harmless to most people can cause excessive production of tears and mucus in eyes of overly sensitive, allergic individuals.

Medication available but having side effects: The disadvantage with Systane eye drops, use in eye allergies, especially with the gel formula, is that when first applied the eyes, people may experience a blurry vision for about 20 to 30 seconds. It can also cause a little feeling of burning and stinging sensations around the eyes but not to the point that it will cause redness and further irritations to the eyes. Additionally, although it s a very rare case, at the initial application of the Systane eye drops, some people may experience pain in the eyes, changes in vision orientation and swelling and irritation.

Blurred vision, headache, and increased tear production; swelling of the cornea and iris; temporary burning, irritation, pain, redness, stinging, or swelling of the eye are the side effects.

New advanced ocusert system: Ketorolac tromethamine ocuserts were prepared using different polymers such as hydroxy propyl methylcellulose, ethyl cellulose, methylcellulose and polyvinyl pyrrolidone in different proportions. [15]

1. **Blepharitis:** An infection of lid tructures (usually by staphylococcus aureus) with concomitant seborrhoea, rosacea, a dry eye and abnormalities in lipid secretions.

Medication available but having side effects: The poor bioavailability and therapeutic response exhibited by Ofloxacin conventional ophthalmic

solutions due to rapid pre-corneal elimination of the drug.

New advanced ocusert system: Ocular inserts were prepared with prolonged release of drug and minimum swelling within cul-de-sac using Ofloxacin. [16]

1. **Ocular Hypertension:** The term ocular hypertension usually refers to any situation in which the pressure inside the eye, called intraocular pressure, is higher than normal. Eye pressure is measured in millimeters of mercury (mm Hg). Normal eye pressure ranges from 10-21 mm Hg. Ocular hypertension is an eye pressure of greater than 21 mm Hg.

2. **Medication available but having side effects:**

Table 4:Medication for ocular hypertension having side effects.

Medication	Mechanism	Dosage form	Adverse effects
Acetazolamide	Carbonic Anhydrase Inhibitor	Systemic Administration	Diuresis, Loss Of Appetite
Timolol	B-Receptor Antagonist		Bradycardia Bronchoconstriction

New advanced ocusert system

Pilocarpine ocusert system for sustained control of ocular hypertension: A number of excellent drugs are available that are effective in reducing IOP. These drugs are typically applied as eye drops. However, patient adherence can be poor, thus reducing the clinical efficacy of the drugs. Several novel delivery systems designed to address the issue of adherence and to ensure consistent reduction of IOP are currently under development. A pilocarpine-containing, polymermembrane unit (Ocusert) was evaluated in 29 patients with open-angle glaucoma.Their potential is dependent on developing suitable delivery systems that can provide the drugs in a sustained, local manner to the retina and optic nerve. Drug delivery systems have the potential to improve patient adherence, reduce side effects, increase efficacy, and ultimately, preserve sight for glaucoma patients.

1. **Herpes Simplex Keratitis:** Herpes Simplex keratitis (HSK) is a viral infection that if left untreated can have devastating ocular consequences25. The keratitis caused by the herpes simplex virus (HSV) typically presents as a unilateral "red eye" with a variable degree of pain or ocular irritation. Photophobia and epiphora are common; however, vision may or may not be affected, depending upon the location and extent of the corneal lesion. You may see a vesicular skin rash and follicular conjunctivitis with the initial infection, but these are less common with recurrent HSV. A more common sign is secondary uveitis.

Medication available but having side effects: Adverse events associated with the use of ganciclovir ophthalmic gel may include, but are not limited to, the following:

1. Blurred Vision
2. Eye Irritation
3. Punctate Keratitis
4. Conjunctival Hyperemia

New advanced ocusert system

Idoxuridine ocular insert therapy: use in treatment of herpes simplex keratitis: Therapy of acute herpes simplex keratitis in rabbits with idoxuridine-releasing ocular inserts showed that an application rate of 30µg/hr gave significantly better results than conventional treatment with idoxuridine drops and ointment while exposing the eye to 40% less drug. Delivery rates lower than this were equal or not as effective as drop and ointment therapy and rates up to 100µg/hr did not produce significantly better results than rates of 30µg/hr. Serial viral cultures demonstrated the persistence of virus beyond the period of clinical resolution of disease in all treatment groups, indicating that therapy should be continued longer than apparent resolution of disease.

1. **Dry Eye Syndrome:** Dry eye is a disorder of the tear film due to tear deficiency or excessive tear evaporation which causes damage to the interpalpebral ocular surface (i.e. exposed eye surface) and is associated with symptoms of ocular discomfort. This definition of dry eyes was adopted by the National Eye Institute workshop on dry eyes. The eye becomes dry either because there is not enough tears being produced or because there is abnormally high rate of evaporation of tears.

New advanced ocusert system

Hydroxypropyl cellulose ophthalmic inserts for treatment of dry eye: There are various treatment modalities for dry eye syndrome available to eye care professionals, which can be used as monotherapy or in combination.

There is evidence to suggest that with proper use and adequate patient education, hydroxypropyl cellulose ophthalmic inserts are an effective and

safe treatment choice for dry eye syndrome. Most patients showed significant improvement in ocular symptoms and clinical signs, and many patients continued using hydroxypropyl cellulose ophthalmic inserts for several years alone or in conjunction with other dry eye therapies. There was no significant worsening in symptoms or any major long-term side effects of the medication. The inserts may be particularly helpful in patients who cannot tolerate preservatives or immunosuppressant drops, do not want to instill multiple artificial tears throughout the day, or still have an insufficient tear film despite other therapies. However, it is worth noting that several of the studies excluded patients with meibomian gland disease or blepharitis. It remains to be seen if the inserts help patients with evaporative aqueous tear loss due to meibomian gland dysfunction or blepharitis. One would think that both of these disease groups would benefit from using the inserts because there is often overlap of patients who also have dry eye syndrome. Nonetheless, hydroxypropyl cellulose ophthalmic inserts can be used effectively as monotherapy, or in conjunction with other therapies, and should be considered in the treatment of dry eye syndrome.

1. **Conjunctivitis:** Conjunctivitis is the inflammation of the conjunctiva (the membrane that lines the eyelids and covers the exposed surface of the eyeball).Conjunctivitis can be caused by allergies, bacteria, viruses, chemicals, or underlying health conditions. The eyes are susceptible to infection because they are not sterile. They rely on lysozyme (an enzyme found in the tears) to destroy bacteria. Bacteria line the surface of the eyelids (all the way down into the shaft of the eyelashes), which makes the conjunctiva predisposed to germs and conjunctivitis.

Medication available but having side effects Moxifloxacin hydrochloride ophthalmic solution used. Serious side effects are not expected to occur during treatment with this medication. Some eye burning, stinging, irritation, itching, dryness, redness, tearing; or blurred vision may occur.

Polymeric Controlled Release Natamycin Ocular Inserts: Ocular drug delivery system for Natamycin; a polyene antibiotic is highly useful for the treatment of conjunctivitis and keratitis. Natamycin, a polyene antibiotic is highly useful for the treatment of fungal blepharitis, conjunctivitis and keratitis. Natamycin when formulated as eye drops suffered the disadvantage of instillation of the dye drops for every 3-4 h and hence maximized patient non compliance, leading to ineffective therapy.

1. **Corneal Ulcers:** A corneal ulcer is an erosion or open sore on the surface of the cornea. The cornea is the transparent area at the front part of the eye that serves as a window through which we see. It also refracts light and offers protection to other parts of the eye. If the cornea becomes inflamed due to infection or injury, an ulcer may develop. A corneal ulcer is a serious condition that must be treated promptly to avoid lasting vision problems.

Medication available but having side effects Treatment for corneal ulcers needs to be aggressive, as some ulcers lead to vision loss and blindness. Treatment usually involves antibiotics as well as antiviral or antifungal medications. Steroid eye drops may also be given to reduce inflammation but having side effects like White precipitate and ocular discomfort (stinging and burning may occur upon application). For e.g. In patients with corneal ulcer or frequent administration of the drug, white precipitates have been observed, which resolved spontaneously with continued application The precipitate does not preclude continued use of CILOXAN Eye drops or CILOXAN Eye ointment, nor does it adversely affect the clinical course of the ulcer or the recovery process. [17]

New advanced ocusert system

Ocular inserts of Ofloxacin: Ocular inserts of ofloxacin were prepared with objectives of reducing the frequency of administration, obtaining controlled release and greater therapeutic efficacy in the treatment of corneal ulcers. Ofloxacin ocular inserts were prepared to overcome the problem of the excretion and low retention time into the eye. The prepared ocular inserts show the more retention time and less excretion through the eye secretions. The ocular inserts prepared were smooth and passed all the evaluation tests. Formulations show a maximum cumulative percentage drug release of 91.27 % at the end of 24 hours. Ocuserts formulated also passed the test for sterility. They showed zero-order release of the drug in the in vitro and in vivo release studies. The drug in the films was found to be active against selected

microorganisms as was proved by microbial efficacy studies. A high correlation coefficient was found between in vitro and in vivo release rate studies. Shelf-life of the product was found to be more than one year. [18]

Conclusion: Ocular drug delivery systems provide local as well as systemic delivery of the drugs. The limitations of existing medical therapies for ocular disorders include low drug bioavailability, no specificity, side effects, and poor treatment adherence to therapy. These limitations may be overcome through the use of sustained- release intraocular drug delivery systems. In the area of topical ocular administration, important efforts concern the design and the conception of new ophthalmic drug delivery systems able to prolong the residence time. The use of inserts, which are solid devices to be placed in the cul-de- sac or on the cornea, represents one of the possibilities to reach increased residence time. These solid ophthalmic devices present the advantage of avoiding a pulsed release due to multiple applications. Finally concluded that the present review work has been reveals that the ophthalmic disease and their treatment by using ocuserts.

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