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A REVIEW ARTICLE ON OPHTHALMIC INSERTS

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ABSTRACT

Administering drugs to the eyes is one of the most challenging tasks that pharmacists face. The main barriers to eye medication are the ability to maintain a therapeutic level of the drug at the site of action over a long period of time. The ophthalmic preparations are available as a sterile, buffered isotonic solution. Different types of dosage forms are used as a delivery system for eye delivery of drugs. The most commonly prescribed dosage form is the eye drop solution because drops are easier to administer. Suspensions, gelled systems and ointments are also used to extend the therapeutic effect. The properties of eye preparations should not irritate the eye tissue. Homogeneous, i.e. Particles that are evenly distributed smooth and free of lumps or agglomerates. Relatively non-greasy. Shouldn't cause blurry vision. Should not cause an unbearable feeling of foreign bodies. Sterile and sufficiently preserved. Physically and chemically stable. Effective. New systems for administering medicinal products to the eye: The administration of medicinal products with eye drops requires frequent use. Prolonged drug release can be achieved with ophthalmic inserts with fixed devices placed in the eye. However, the inserts must be removed when they are no longer needed. Ocuserts are the new drug delivery systems designed to release the drug at predetermined and predictable rates, eliminating the need for frequent drug delivery. The systems generally include bio-erodible implantable elements with controlled, delayed and / or delayed release with multiple layers of different materials and / or different material concentrations. The elements generally comprise an inner layer or core containing a therapeutic agent and one or more outer layers made of polymeric materials, for example essentially pure polymeric materials. Important efforts in the area of topical eye administration relate to the design and conception of new ophthalmic drug delivery systems that can extend.

KEYWORD: Bio erodible, diffusion membrane, ocular inserts.

INTRODUCTION

Ophthalmic drug delivery is one of the most challenging tasks for pharmaceutical researchers. The eye offers unique opportunities and challenges when dispensing drugs.[1] The anatomy, physiology and biochemistry of the eye make this organ extremely impervious to foreign substances.[2]

The therapeutic effectiveness of an ophthalmic drug is said to be significantly improved by prolonging its contact with the surface of the cornea. To achieve this purpose, eye drop preparations are added with viscosity or enhancing agents or other drugs, or formulated in a water-insoluble ointment formulation to maintain the duration of intimate drug eye contact. However, these dosage forms result in only minimal persistent eye contact as an eye drop solution and do not result in constant bioavailability and repeat the medication all day long.[3]

Such practical problems have stimulated the search for alternative methods of dispensing drugs to the eye. This work recently focused on ophthalmic inserts that serve as a platform for the release of more than one active ingredient. However, this has made it clear that this development of an ophthalmic insert, which reliably combines controlled release with the absence of any irritation for the eye patient, represents a tremendous technical challenge.

The conventional eye dosage forms such as eye drops in suspension and solution) as well as eye ointments etc.[4], in which the intraocular bioavailability of the drug through the conventional eye drops is very poor due to factors such as tear flow, tear flow and tear flow. Drug thinning with trace fluid tear and conjunctiva absorption.[5] Binding of the drug to the protein also contributes to loss of the drug through corneal parallel elimination loss pathways. Therefore, a tiny amount of the drug actually penetrates the cornea and reaches the intraocular tissue.[6]

Dosage forms are contained in the suspension which are eluted by water-insoluble active substances in order to avoid the high toxicity caused by saturated solutions of water-soluble active substances.[7]

Newer ophthalmic or ocular drug delivery systems are being researched to develop a longer duration and also a controlled release of biodegradable polymer systems, such as collagen shields.

Some of the newer sensitive and successful delivery systems developed to improve eye bioavailability and long-term effects of eye drugs.

The following current trends are present
i) Mucoadhesive dosage forms
ii) Eyepiece inserts.
iii) Collagen shield or corneal shield.
iv) Artificial tear drops.
v) Phase transition system
vi) Microspheres and nanoparticles.[8]

AIM AND OBJECTIVE OF THE STUDY

Ophthalmic inserts are sterile preparations with a solid or semi-solid consistency, the size and shape of which have been specially developed for ophthalmic use. The inserts are placed in the lower fornix and less often in the upper fornix and in the cornea. Eyepiece inserts can overcome the disadvantages reported with conventional methods. Ophthalmic systems such as eye drops, suspensions and ointments. The typical pulse input type drug delivery behavior seen with eye drops, suspensions, and ointments is replaced by controlled, sustained, and continuous drug delivery using a controlled release drug delivery system in the eye. Interest in polymer-based dispensers has skyrocketed in recent years, adding another dimension to topical drug delivery, promoting the use of polymers such as collagen and fibrin, which have been processed into erodible inserts for dead end placement. The use of the principles of controlled release, as embodied by eye inserts, offer an attractive approach to the problem of prolonging the retention time of corneal drugs. Eyepiece inserts also offer the potential benefit of improving patient compliance by reducing the frequency of dosing.

The main goal of the ophthalmic inserts is to increase the contact time between the preparation and the conjunctiva tissue to ensure a sustained release suitable for topical or systemic treatment. They consist of a polymer carrier with or without active substances, the latter being incorporated into the polymer carrier as a dispersion or solution.[9]

HISTORY OF OPHTHALMIC INSERTS

The first solid drug (precursor to the present insoluble inserts) was used in the 19th century, consisting of squares of dry filter paper that had previously been impregnated with dry solutions (such as atropine sulfate, pilocarpine hydrochloride). They are applied using a small section under the eyelid. Later, lamellar precursors to the present soluble inserts were developed. They consisted of glyceride gelatin, which contained various ophthalmic medicines. Glyceride gelatin slats were available in official compendia until the first half of the 20th century. The use of lamellae, however, ended when stricter sterility requirements were imposed on the ophthalmic preparation. A growing interest in ophthalmic inserts is now being observed.[10]

TYPES OF OPHTHALMIC INSERTS

The eye inserts are classified as
Based on their solubility behaviour:
Mainly divided into three classes:
1. Insoluble
2. Soluble
3. Bio erodible

(1) Insoluble
a) Diffusion
b) Osmotic
c) Contact lens

(2) Soluble
a) Based on natural polymers, e.g. collagen
b) Based on synthetic or semi-synthetic polymers, e.g. Cellulose derivatives such as HPMC, HPC, MC.

(3) Bio erodible
a. Insoluble Ocuserts
Only the insoluble types can typically deliver drugs at a predetermined rate using a variety of methods, but must be removed from the eye when empty.

b. Soluble Ocuserts
Soluble inserts, generally defined as erodible (E), monolithic polymeric devices that experience gradual dissolution as the drug is released and need not be removed. Real dissolution occurs primarily through swelling of the polymer, while erosion corresponds to a chemical or enzymatic hydrolytic process. In source-controlled devices, the active ingredient is homogeneously dispersed in a glass-like polymer; glass-like polymers are essentially drug-impermeable, so that there is no diffusion through the dry matrix. When the liner is inserted into the eye fluid from the tear fluid, it begins to penetrate the matrix, then swelling and consequent relaxation of the polymer chain and drug diffusion to release its drug content.

I. Insoluble eyepiece inserts
Insoluble polymer inserts can be divided into two categories:
A. Reservoir systems
B. Matrix systems
A. Reservoir systems: Each class of insert shows different drug release profiles. The reservoir systems can release drugs either by diffusion or by an osmotic process. Each contains a liquid, a gel, a colloid, a semi-solid, a solid matrix or an active substance containing a

carrier. Carriers consist of hydrophobic, hydrophilic, organic, natural or synthetic polymers.

They were divided into
1. Diffusion inserts
2. Osmotic inserts.

1. Diffusion insert: It is a new type of drug delivery system for the eye that is based on a porous membrane. The release of the drug from diffusion inserts is based on a diffusion release mechanism. It consists of a central drug reservoir enclosed in a specially designed micro porous membrane that enables the drug to diffuse out of the reservoir at a precisely determined rate.

As highlighted by Urquhart, the pilocarpine eye therapy system developed by Alza Corporation is remarkable for several reasons. This product was the first speed controlled, speed specific drug for which the strength of the label is indicated by the rate (s) of drug delivery in vivo rather than the amount of drug contained. It offers predictable, time-independent drug concentrations in the target tissue, a performance that cannot be achieved with conventional, quantity-specific ophthalmic drugs with pulse input. The almost constant concentration of active substances in the eye tissue significantly improves the selectivity of pilocarpine. A major benefit is that two interfering side effects of the drug, meiosis and myopia, are significantly reduced, while the reduction in intraocular pressure (IOP) is fully maintained in glaucoma patients. There are two types of diffusion inserts available: the Pilo-20 and the Pilo-40. The former delivers the drug at a rate of 20 µg / h for 7 days and the latter at a rate of 40 µg / h for 7 days. This device, which is certainly well known to the readers of this review, has been described and discussed in detail in a number of specialist articles. In short, it consists of a reservoir containing pilocarpinalginate, which is enclosed at the top and bottom by thin EVA (ethylene vinyl acetate) membranes. The insert is surrounded by a retaining ring made of the same material and impregnated with titanium dioxide. The dimensions of the elliptical device are (for the 20 µg / h system): main axis 13.4 mm, secondary axis 5.7 mm, thickness 0.3 mm. The membranes are the same in both systems, but in order to obtain a higher release rate, the reservoir of 40µ contains g / h system about 90 mg.

Di (2-ethylhexyl) phthalate as a flux enhancer.

2. Osmotic Insert The osmotic inserts generally consist of a central part surrounded by a peripheral part and are of two types:
Type 1: The central part consists of a single reservoir of a drug with or without an additional osmotic solute, which is distributed in a polymer matrix so that the drug is surrounded through the polymer as discrete small deposits. The second peripheral part of these inserts comprises a cover film made of an insoluble semi-permeable polymer. The osmotic pressure against the polymer matrix causes it to break in the form of openings. The drug is then released from the deposits near the surface of the device through these openings.

Type 2: The central part consists of two different subjects. The drug and the osmotic solutes are arranged in two separate compartments, the drug reservoir being surrounded by an elastic impermeable membrane and the osmotic dissolved reservoir by a semipermeable membrane. The second peripheral part is similar to that of type 1. The crack diffuses into the osmotic compartment and induces an osmotic pressure that stretches the elastic membrane and contracts the compartment, including the drug, so that the active component is forced through the single drug release orifice.

B. Matrix Systems The second category, the matrix system, is a certain group of insoluble ophthalmic devices that are mainly represented by contact lenses. It consists of a covalently cross-linked hydrophilic or hydrophobic polymer that forms a three-dimensional network or a three-dimensional matrix that can retain water, aqueous drug solution or solid components. The hydrophilic or hydrophobic polymer swells when water is absorbed. The swelling caused by the osmotic pressure of the polymer segments is opposed by the elastic reaction forces occurring along the chains, or the crosslinks are stretched until a final swelling (equilibrium) is reached.

1. Contact lenses
Contact lenses are shaped structures and are initially used for vision correction. Their use as potential drug delivery devices has been expanded by soaking them in drug solutions. The main advantage of this system is the ability to correct vision while releasing medication. Refojo suggested dividing the contact lenses into 5 groups.
a) Rigid
b) Semi-rigid
c) Elastomer
d) Softly hydrophilic
e) Biopolymer

Rigid contact lenses have the disadvantage that they consist of polymers (e.g. poly-methyl meth acrylic acid) that are hardly permeable to moisture and oxygen, a problem that was overcome by the use of gas-permeable polymers such as cellulose acetate butyrate. However, these systems are not suitable for prolonged drug delivery to the eye and their stiffness makes them very uncomfortable Wear. For this reason, soft hydrophilic contact lenses have been developed for the prolonged release of drugs such as pilocarpine, chloramphenicol and tetracycline prednisolone sodium phosphate. The most commonly used polymer in the composition of these types of lenses is hydroxylethylmethyl meth acrylic acid, which is copolymerized with poly (vinyl pyrrolidone) or ethylene glycol dimethacrylic acid

(EGDM). Poly (vinyl pyrrolidone) is used to increase the water of hydration, while EGDM is used to reduce the water of hydration. The soft hydrophilic contact lenses are very popular because they are easy to assemble and are better tolerated. The incorporation of the drug into contact lenses depends on whether their structure is hydrophilic or hydrophobic. If contact lenses (including 35 to 80% water) are soaked in solution, they will absorb the medicine. The drug release depends heavily on the amount of drug, the soak time of the contact lens and the drug concentration in the soak solution.

II. Soluble Eye Inserts These soluble inserts offer the advantage that they are completely soluble so that they do not have to be removed from their place of use, which means that the intervention is restricted to insertion. They can be roughly divided into two types, the first based on natural polymers and the other based on synthetic or semi-synthetic polymers.

A. Natural Polymers The first type of soluble insert is based on natural polymer. Natural polymer used to make soluble ophthalmic inserts is preferably collagen. The therapeutic agent is preferably absorbed by soaking the insert in a solution containing the drug, drying and rehydrating before use on the eye. The amount of drug loaded depends on the amount of binder present, the concentration of drug solution in which the composite is soaked, and the duration of soaking. As the collagen dissolves, the drug is gradually released from the spaces between the collagen molecules.

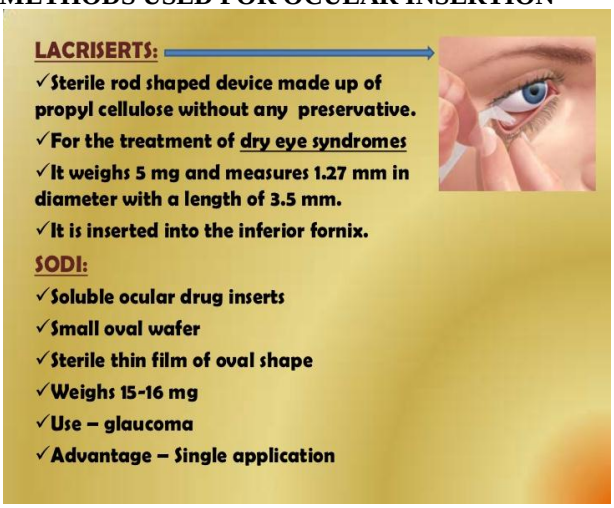
B. Synthetic and semi-synthetic polymer

The second type of soluble use is usually based on semi-synthetic polymers (e.g. cellulose derivatives) or on synthetic polymers such as polyvinyl alcohol. A reduction in the release rate can be obtained by using Eudragit, a polymer normally used for enteric coating, as the coating agent of the insert. Saettone et al. have observed in rabbits that pilocarpine-coated inserts coated with Eudragit induced a longer-lasting mitotic effect than the corresponding uncoated ones. However, the inherent problems with these soluble inserts are the rapid penetration of the tear fluid into the device, the blurred vision caused by the solubilisation of the insert components, and the risk of ejection due to the device's initial dry and glassy consistency. Ethyl cellulose, a hydrophobic polymer, can be used to reduce the deformation of the insert and thus prevent blurred vision. With regard to the risk of ejection, several authors have incorporated Carbomer, a strong but well-tolerated bio-adhesive polymer. The soluble inserts offer the additional advantage that they have a generally simple design, are based on products that are well suited for ophthalmic use and can be easily processed using conventional methods. The main advantage is a reduced rate of release, but it is still controlled by diffusion.

III. Bio erodible: eye inserts These inserts are formed by bio erodible polymers (e.g. cross-linked gelatine derivatives, polyester derivatives), which undergo hydrolysis of chemical bonds and thus dissolution. The great advantage of these bio erodible polymers is the possibility of modulating their erosion rate by modifying their final structure during synthesis and by adding anionic or cationic surfactants. A cross-linked gelatine insert was developed by Attica et al. to increase the bioavailability of dexamethasone in rabbit eyes. It was found that the dexamethasone levels in the aqueous humour were four times higher than in a dexamethasone suspension. However, erodible systems can have significantly variable erosion rates based on the patient's individual physiology and tear pattern, while degradation products and solvent residues used during polymer production can cause inflammatory reactions. The following sections discuss some important eye inserts that are commercially available (SODI) or in advanced stages of development (collagen shields, NODS, and Minidisc).

Soluble Ophthalmic Drug Use The Soluble Ophthalmic Drug Use (SODI) is a small oval wafer that was developed by Soviet scientists for cosmonauts who couldn't use eye drops under weightless conditions. Together with the collagen labels, SODI is the first modern revival of the gelatine slats that disappeared from the pharmacopoeias in the late 1940s. The SODIs are the result of extensive collaboration between well-known Russian chemists and ophthalmologists and finally (1976) led to the development of a new soluble copolymer of acrylamide, N-vinylpyrrolidone and ethyl acrylate (ratio 0.25: 0.25: 0.5). denotes ABE. A comparison of medical eye films made with different polymers showed that ABE produced the highest concentration of drugs in rabbit eye tissues. After large-scale preclinical and clinical tests, the ABE copolymer was used for the industrial production of SODI in the form of sterile thin films of oval shape (9 × 4.5 mm, thickness 0.35 mm) with a weight of 15-16 mg and Colour used - coded for various drugs (over 20 common ophthalmic drugs or drug combinations). After insertion into the upper conjunctiva sac, a SODI softens in 10-15 s, according to the shape of the eyeball. Over the next 10-15 minutes, the film turns into a polymer clot that gradually dissolves within 1 hour as the drug is released. The feeling of a "foreign body" in the eye disappears in 515 minutes.[10,11]

METHODS USED FOR OCULAR INSERTION[12]



Advantages of Ophthalmic Inserts[13,14]

1. It provides sustained and controlled drug delivery.
2. Ophthalmic inserts are used to overcome the side effects due to pulsed dosing of conventional dosage form.
3. Increasing the corneal contact time also increase the ocular bio availability.
4. To prevent the loss of other ocular tissues by provides targeting with in the globe.
5. Circumvent the protective barriers like drainage, and conjunctiva absorption.
6. Provide comfort, better compliance to the patient and to improve therapeutic performance of drug.
7. Provides better housing of delivery system.
8. Increased shelf life with respect to aq. solutions.

Disadvantages of Ophthalmic Inserts[7,13,14]

1. A capital demerits of ocular inserts resides in their solidity that is experienced as a foreign body in the eye by the patient.
2. Their movement around the eye, in rare instance, the simple removal is made more difficulty by unwanted migration of the inserts to the upper fornix.
3. The occasional inadvertent loss during sleep of while rubbing the eyes.
4. Their interference with vision, any difficulty placement of ophthalmic inserts.

Recent Advancement In The Ophthalmic Inserts

The following recent trends are: The following newer approaches are developing sensitive, successful eye delivery systems with prolonged duration and controlled release, such as eye inserts, in order to achieve better bioavailability of the eye and a lasting effect of drugs on the eye. Applying the principle of controlled release, as embodied by eye inserts, therefore offers an attractive alternative approach to the difficult problem of extending the dwell time of corneal medication.[1,10]

- Mucoadhesive dosage forms.
- Eye inserts.
- Collagen or corneal shields.
- Artificial tear inserts.
- Hydrogel-type drug-impregnated contact lens.
- Eye iontophoresis.
- phase transition systems.
- Microspheres and nanoparticles.

1. Mucoadhesive polymers during drug delivery to the eye

This update on mucoadhesive eye dosage forms discusses the tremendous advances in mucin biochemistry, the development of new polymers, the use of drug complexes, and other technological advances. This review focuses on recent literature on mucoadhesive fluids (viscous solutions, particle systems), semi-solid (hydrogel, in-situ gelling system) and solid dosage forms, with particular emphasis on in vivo studies. Gel-forming mini tablets and inserts made from thiomers show an interesting potential for future applications in the treatment of eye diseases.[15]

2. Collagen eye inserts

Pepsin-treated telopeptide-poor fetal calf skin collagen was used as a carrier for a controlled release of pilocarpine nitrate. Three types of collagen pilocarpine nitrate drug delivery systems have been developed. The in vitro release of pilocarpine nitrate from these systems was investigated. The release studies showed that pilocarpine was released at a constant rate after an initial boost release after zero order kinetics. The release of the drug can be manipulated based on the type of modification made to the collagen carrier. The release rate of pilocarpine nitrate could be regulated from 5 to 15 days depending on the modification made to the collagen carrier. Due to its biological inertness, structural stability and good biocompatibility, the collagen film proved to be the most promising carrier for ophthalmic drug delivery systems.[16]

3. Artificial tear inserts

Treatment of patients with sicca keratoconjunctivitis (KCS) remains a problem. Different types of treatment are used to improve tear function. The closure of the

point helps prevent tears from flowing away, but usually supplementation with artificial tears is necessary. Numerous preparations are available, and trial and error can be used to find the most suitable for a particular patient. The most popular preparations are based on methyl cellulose or polyvinyl alcohol and replace the aqueous component of tears and help stabilize the tear film. The disadvantage of this therapy method is that it is short-lived and drops have to be administered regularly, especially in severely affected patients. No study has shown satisfactorily that the solutions remain in contact with the.[17]

CONCLUSION

The ophthalmic insert represents a significant advance in the treatment of eye diseases. Ophthalmic inserts are sterile, thin, multi-layer, drug-impregnated, solid or semi-solid consistency devices that are inserted into the sack or conjunctiva sack and whose size and shape are specially designed for ophthalmological use, they consist of a polymeric carrier, which may or may not contain a drug. Advantages with Ocuserts such as: Accurate dosing capacity to provide at a constant speed and to prolong drug release and thus a better effectiveness. there by extending the contact time and thus improving bioavailability. Possible reduction in systemic absorption and thus reduced systemic side effects. Reduced frequency of administration and thus better compliance of the patient with less frequency of visual side effects. Administration of an exact eye and thus a better therapy Possibility to target inner eye tissue via non-corneal conjunctiva-scleral penetration routes; and increased durability in relation to eye drops due to the absence of water. Advantage of use as a dosage form Easy handling and insertion Lack of emissions during wear Reproducibility of the release kinetics Applicability to various medicinal products Non-impairment of vision and oxygen permeability, sterility, stability, lightness of the manufacturer.

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