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Review Article

Ocuserts: A Review

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ABSTRACT

Ocular inserts are sterile preparations, with a thin, multilayered, drug-impregnated, solid or semisolid consistency devices placed into cul-de-sac or conjunctiva sac. They are usually made up of polymeric vehicle containing drug. Ocular drug delivery is one of the most fascinating and challenging tasks facing the Pharmaceutical researchers. Ocular drug delivery has been a major challenge to pharmacologists and drug delivery scientists due to its unique anatomy and physiology 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. The therapeutic efficacy of an ocular drug can be greatly improved by prolonging its contact with the corneal surface. Novel drug delivery strategies such as bioadhesive gels and fibrin sealant-based approaches were developed to sustain drug levels at the target site. Designing noninvasive sustained drug delivery systems and exploring the feasibility of topical application to deliver drugs to the posterior segment may drastically improve drug delivery in the years to come . Some of the newer, sensitive and successful 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.

INTRODUCTION

The eye as a portal for drug delivery is generally used for local therapy against systemic therapy to avoid the risk of eye damage from high blood concentrations of the drug, which is not intended. The unique anatomy, physiology, and biochemistry of the eye render this organ impervious to foreign substances, thus presenting

a constant challenge to the formulator to circumvent the protective barriers of the eye without causing permanent tissue damage. Most ocular treatments like eye drops and suspensions call for the topical administration of ophthalmically active drugs to the tissues around the ocular cavity. These dosage forms are easy to instill but suffer from the inherent drawback that the majority of the medication they contain is immediately diluted in the tear film as soon as the

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eye drop solution is instilled into the cul-de-sac and is rapidly drained away from the pre-corneal cavity by constant tear flow and lacrimo-nasal drainage. Therefore, the target tissue absorbs a very small fraction of the instilled dose. For this reason, concentrated solutions and frequent dosing are required for the instillation to achieve an adequate level of therapeutic effect. One of the new classes of drug delivery systems, 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 Ocular inserts are defined as preparations with a solid or semisolid consistency, whose size and shape are especially designed for ophthalmic application (i.e., rods or shields). These inserts are placed in the lower fornix and, less frequently, in the upper fornix or on the cornea. They are usually composed of a polymeric vehicle containing the drug.

History of ocular inserts

The first solid medication (precursors of the present insoluble inserts) was used in the 19th century, which consisted of squares of dry filter paper, previously impregnated with dry solutions atropine sulphate, pilocarpine (e.g., hydrochloride). Small sections were cut and applied under eyelid. Later, lamellae, precursors of the present soluble inserts, were developed. They consisted of glycerinated gelatin ophthalmic containing different drugs. Glycerinated gelatin 'lamellae' were present in official compendia until the first half of the present century. However, the use of lamellae ended when more stringent requirements for sterility of ophthalmic preparations were enforced. Nowadays, growing interest is observed for ophthalmic inserts as demonstrated by the

increasing number of publications in this field in recent years.

Merits of ocular inserts

there are several merits of ocular insert.

- a. Increased contact time, hence a prolonged drug activity and a higher bioavailability with respect to standard vehicles;
- b. Possibility of releasing drugs at a slow, constant rate;
- c. Accurate dosing (contrary to eye drops that can be improperly instilled by the patient and are partially lost after administration, each insert can be made to contain a precise dose which is fully retained at the administration site);
- d. Reduction of systemic absorption (which occurs freely with eye drops via the nasolacrimal duct and nasal mucosa);
- e. Better patient compliance, resulting from a reduced frequency of administration and a lower incidence of visual and systemic sideeffects;
- f. Possibility of targeting internal ocular tissues through non-corneal (conjunctival scleral) routes:
- g. Increased shelf life with respect to aqueous solutions;
- h. Exclusion of preservatives, thus reducing the risk of sensitivity reactions;
- i. Possibility of incorporating various novel chemical/technological approaches.

Demerits of ocular inserts

The demerits-of ocular inserts are as follows:



- a. A capital demerit of ocular inserts resides in their 'solidity', i.e., in the fact that they are felt by the (often oversensitive) patients as an extraneous body in the eye. This may constitute a formidable physical and psychological barrier to user acceptance and compliance.
- b. Their movement around the eye, in rare instances, the simple removal is made more difficult by unwanted migration of the insert to the upper fornix,
- c. The occasional inadvertent loss during sleep or while rubbing the eyes,
- d. Their interference with vision, and
- e. Difficult placement of the ocular inserts (and removal, for insoluble types).

Mode of action of Drug Release

The mechanism of controlled drug release into the eye is as follows:

A. Diffusion, B. Osmosis, C. Bio-erosion.

A.Diffusion

In the Diffusion mechanism, the drug is released continuously at a controlled rate through the membrane into the tear fluid. If the insert is formed of a solid non-erodible body with pores and dispersed drug. The release of drug can take place via diffusion through the pores. Controlled release can be further regulated by gradual dissolution of solid dispersed drug within this matrix as a result of inward diffusion of aqueous solutions. In a soluble device, true dissolution occurs mainly through polymer swelling. In swelling-controlled devices, the active agent is homogeneously dispersed in a glassy polymer. Since glassy polymers are essentially drug-impermeable, no

diffusion through the dry matrix occurs. When the insert is placed in the eye, water from the tear fluid begins to penetrate the matrix, then swelling and consequently polymer chain relaxation and drug diffusion take place. The dissolution of the matrix, which follows the swelling process, depends on polymer structure: linear amorphous polymers dissolve much faster than cross-linked or partially crystalline polymers. Release from these devices follows in general Fickian 'square root of time' kinetics; in some instances, however, known as case II transport, zero order kinetics has been observed.

B.Osmosis

In the Osmosis mechanism, the insert comprises a membrane transverse impermeable elastic dividing the interior of the insert into a first compartment and a second compartment; the first compartment is bounded by a semi-permeable membrane and the impermeable elastic membrane, and the second compartment is bounded by an impermeable material and the elastic membrane. There is a drug release aperture in the impermeable wall of the insert. The first compartment contains a solute which cannot pass through the semipermeable membrane and the second compartment provides a reservoir for the drug which again is in liquid

When the insert is placed in the aqueous environment of the eye, water diffuses into the first compartment and stretches the elastic membrane to expand the first compartment and contract the second compartment so that the drug is forced through the drug release aperture.

C.Bioerosion

In the Bioerosion mechanism, the configuration of the body of the insert is constituted from a matrix of bioerodible material in which the drug is



dispersed. Contact of the insert with tear fluid results in controlled sustained release of the drug by bioerosion of the matrix. The drug may be dispersed uniformly throughout the matrix but it is believed a more controlled release is obtained if the drug is superficially concentrated in the matrix. In truly erodible or E-type devices, the rate of drug release is controlled by a chemical or enzymatic hydrolytic reaction that leads to polymer solubilization, or degradation to smaller, watersoluble molecules. These polymers, as specified may undergo bulk or surface by Heller, hydrolysis. Erodible inserts undergoing surface hydrolysis can display zero order release kinetics; provided that the devices maintain a constant surface geometry and that the drug is poorly watersoluble.

Classification of Ocular Inserts

The inserts have been classified, on the basis of their physico-chemical behavior, as soluble (S) or insoluble

- I. Insoluble ocular inserts;
- II. Soluble ocular inserts;
- III. Bio-erodible ocular inserts.

I. Insoluble ocular inserts

Inserts made up of insoluble polymer can be classified into two categories:

A. Reservoir systems;

B. Matrix systems.

A. Reservoir systems

Each class of inserts shows different drug release profiles. The reservoir systems can release drug either by diffusion or by an osmotic process. It contains, respectively, a liquid, a gel, a colloid, a semisolid, a solid matrix, or a carrier containing drug. Carriers are made of hydrophobic, hydrophilic, organic, natural or synthetic polymers.

They have been sub-classified into:

- 1. Diffusional inserts, e.g., 'Ocuserts';
- 2.Osmotic-inserts.

1. Diffusional insert or Ocuserts

Ocusert system is a novel ocular drug delivery system based on porous membrane. The release of drug from diffusional inserts/Ocusert is based on a diffusional release mechanism. It consists of a central reservoir of drug enclosed in specially designed microporous membrane allowing the drug to diffuse from the reservoir at a precisely determined rate. As pointed out by Urquhart, the Occusert pilocarpine ocular therapeutic system, developed by Alza Corporation, is notable for several reasons. This product was the first ratecontrolled, rate specified pharmaceutical for which the strength is indicated on the label by the rate(s) of drug delivery in vivo, rather than by the amount of contained drug. It provides predictable, timeindependent concentrations of drug in the target tissues, a feat impossible to achieve with conventional, quantity-specified, pulse entry ophthalmic medications. The near-constant drug concentration in ocular tissues markedly improves the selectivity of action of pilocarpine. A major advantage is that two disturbing side effects of the drug, miosis and myopia, are significantly reduced, while reduction of intraocular pressure (IOP) in glaucoma patients is fully maintained.

2.Osmotic-insert



The osmotic inserts are generally composed of a central part surrounded by a peripheral part and are of two types:

Type 1: The central part is composed of a single reservoir of a drug with or without an additional osmotic solute dispersed throughout a polymeric matrix, so that the drug is surrounded by the polymer as discrete small deposits. The second peripheral part of these inserts comprises a covering film made of an insoluble semi-permeable polymer. The osmotic pressure against the polymer matrix causes its rupture in the form of apertures. Drug is then released through these apertures from the deposits near the surface of the device.

Type 2: The central part is composed of two distinct compartments. 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 is similar to that of type 1. The tear diffuse into the osmotic compartment inducing 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 aperture.

B.Matrixsystems

The second category, matrix system, is a particular group of insoluble ophthalmic devices mainly represented by contact lenses. It comprises of covalently cross-linked hydrophilic or hydrophobic polymer that forms a three dimensional network or matrix capable of retaining water, aqueous drug solution or solid components. The hydrophilic or hydrophobic polymer swells by absorbing water. The swelling

caused by the osmotic pressure of the polymer segments is opposed by the elastic retroactive forces arising along the chains or crosslinks are stretched until a final swelling (equilibrium) is reached.

1.Contact-lenses

Contact lenses are shaped structures and initially used for vision correction. Their use has been extended as potential drug delivery devices by presoaking them in drug solutions. The main advantage of this system is the possibility of correcting vision and releasing drug simultaneously. Refojo — has proposed a subdivision of contact lenses into 5 groups.

- a. Rigid
- b. Semi-rigid
- c. Elastomeric
- d. Soft hydrophilic
- e. Bio-polymeric

Rigid contact lenses have the disadvantage of being composed of polymers (e.g., poly methyl methacrylic acid) hardly permeable to moisture and oxygen, a problem which has been overcome by using gas permeable polymers such as cellulose acetate butyrate. However, these systems are not suitable for prolonged delivery of drugs to the eye and their rigidity makes them very uncomfortable to wear. For this reason, soft hydrophilic contact lenses were developed for 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 hydroxy ethyl methyl metacrylic acid copolymerized with poly (vinyl pyrrolidone) or ethylene glycol dimethacrylic acid (EGDM). Poly (vinyl pyrrolidone) is used for

increasing water of hydration, while EGDM is used to decrease the water of hydration. The soft hydrophilic contact lenses are very popular because they are easy to fit and are tolerated better. The drug incorporation into contact lenses depends on whether their structure is hydrophilic or hydrophobic. When contact lens (including 35 to 80% water) is soaked in solution, it absorbs the drug. Drug release depends markedly on the amount of drug, the soaking time of the contact lens and the drug concentration in the soaking solution.

II. Soluble ocular inserts

These soluble inserts offer the advantage of being entirely soluble so that they do not need to be removed from their site of application, thus limiting the intervention to insertion only.

They can be broadly divided into two types, the first one being based on natural polymers and the other on synthetic or semi-synthetic polymers.

A.Natural-polymers

The first type of soluble inserts is based on natural polymer. Natural polymer used to produce soluble ophthalmic inserts is preferably collagen. The therapeutic agent is preferably absorbed by soaking the insert in a solution containing the drug, drying, and re-hydrating it before use on the eye. The amount of drug loaded will depend on the amount of binding agent present, the concentration of the drug solution into which the composite is soaked as well as the duration of the soaking. As the collagen dissolves, the drug is gradually released from the interstics between the collagen molecules.

B. Synthetic and semi-synthetic polymer

The second type of soluble insert is usually based on semi-synthetic polymers (e.g., cellulose derivatives) or on synthetic polymers such as polyvinyl alcohol.- A decrease of release rate can be obtained by using Eudragit, a polymer normally used for enteric coating, as a coating agent of the insert . Saettone et al . have observed in rabbits that Eudragit coated inserts containing pilocarpine induced a miotic effect of a longer duration, compared to the corresponding uncoated ones. However, the inherent problems encountered with these soluble inserts are the rapid penetration of the lachrymal fluid into the device, the blurred vision caused by the solubilization of insert components and the risk of expulsion due to the initial dry and glassy consistency of the device. Ethyl cellulose, a hydrophobic polymer, can be used to decrease the deformation of the insert and thus to prevent blurred vision. As for the risk of expulsion, several authors have incorporated carbomer, a strong but well tolerated bio-adhesive polymer. The soluble inserts offer the additional advantage of being of a generally simple design, of being based on products well adapted for ophthalmic use and easily processed conventional methods. The main advantage is decreased release rate, but still controlled by diffusion.

III. Bio-erodible ocular inserts

These inserts are formed by bio-erodible polymers (e.g., cross-linked gelatin derivatives, polyester derivatives) which undergo hydrolysis of chemical bonds and hence 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 addition of anionic or cationic surfactants. A cross-linked gelatin insert was used by Attia *et al*. to increase bioavailability of dexamethasone in the rabbit eye. The dexamethasone levels in the



aqueous humor were found to be four-fold greater compared to a dexamethasone suspension. However, erodible systems can have significantly variable erosion rates based on individual patient physiology and lacrimation patterns, while degradation products and residual solvents used during the polymer preparation can cause inflammatory reaction. In the following paragraphs, some important ocular inserts are discussed which are available commercially (SODI) or in advanced states of development (collagen shields, Ocufit, NODS, and Minidisc).

Soluble ophthalmic drug inserts

Soluble ophthalmic drug insert (SODI) is a small oval wafer, which was developed by soviet scientists for cosmonauts who could not use eye weightless conditions. drops in SODI is together with the collagen shields, the first modern revival of the gelatin 'lamellae', which disappeared from pharmacopoeias in the late forties. The SODIs are the result of a vast collaborative effort between eminent Russian chemists and ophthalmologists, and led eventually (in 1976) to the development of a new soluble copolymer of acrylamide, N-vinyl pyrrolidone and ethyl acrylate (ratio 0.25: 0.25: 0.5), designated ABE. A comparison of medicated eye films prepared with different polymers, showed that ABE produced the highest concentration of rabbit ocular drugs in tissues. After large-scale preclinical and clinical testing, the ABE copolymer was used for the industrial manufacture of the SODI in the form of sterile thin films of oval shape (9 x 4.5 mm, thickness 0.35 mm), weighing 15-16 mg, and color-coded for different drugs (over 20 common ophthalmic drugs, or drug combinations). After introduction into the upper conjunctival sac, a SODI softens in 10-15 s, conforming to the shape of the eyeball. In

the next 10-15 min the film turns into a polymer clot, which gradually dissolves within 1 h while releasing the drug. The sensation of an 'extraneous body' in the eye disappears in 5-15 min.

Collagen Shields

Collagen is the structural protein of bones, tendons, ligaments, and skin and comprises more than 25% of the total body protein in mammals. This protein, which is derived from intestinal collagen, has several biomedical applications, the main of which is probably catgut suture. Bloomfield et al. are credited for first suggesting, in 1977 and 1978, the use of collagen inserts as tear substitutes — and as delivery systems for They compared the levels of gentamycin. gentamycin in tears, cornea, and sclera of the rabbit eye after application of a collagen insert, drops, an ointment or following subconjunctival administration. After 3 h, they found that the collagen insert gave the highest concentration of gentamycin in the tear film and in the tissue. Other treatments using collagen shields impregnated with gentamycin and dexamethasone have been described. In rabbits, aqueous humor levels of dexamethasone and gentamycin achieved with shields were collagen compared subconjunctival injections. The authors concluded that the use of collagen shields impregnated with gentamycin-dexamethasone was comparable to the subconjunctival delivery of these drugs over a 10-h period. Some drawbacks of these devices, however, need mentioning. To apply the collagen shield, the cornea is anaesthetized while the physician uses a blunt forceps to insert the hydrated or unhydrated shield. Contrary to medicated contact lenses, collagen shields often produce some discomfort and interfere with vision. In rabbits, collagen shields have been found to exacerbate ulcerations of alkali-burned A new preparation referred to as corneas.

collasomes consists of small pieces (1 mm x 2 mm x 0.1 mm) of collagen suspended in a 1% methylcellulose vehicle. Kaufman and co-workers recently reported that collasomes provide the same therapeutic advantages of the shields (high and sustained levels of drugs and/or lubricants to the cornea), while not presenting their disadvantages.

Ocufit

The Ocufit is a sustained release, rod shaped device made of silicone elastomer, patented in 1992 and currently developed by Escalon Ophthalmics Inc. (Skillman, NJ). It was designed to fit the shape and size of the human conjunctival fornix. Accordingly, it does not exceed 1.9 mm in diameter and 25-30 mm in length, although smaller sizes for children and newborn babies are planned. The superiority of the cylindrical shape can be traced in an earlier paper by Katz and Blackman. They reported the effect of the size and shape of the inserts on tolerance and retention by human volunteers. - These workers found that expulsion of rod shaped units was significantly (P < 0.01) less frequent than expulsion of oval, flat inserts. A typical example of a rod-shaped insert is the Lacrisert (Merck and Co., Inc.), a cellulosic device used to treat dry-eye patients. The insoluble Ocufit reportedly combines two important features, long retention and sustained drug release. When placed in the upper fornix of volunteers, placebo devices were retained for 2 weeks or more in 70% of the cases. Moreover, active disease (bacterial, allergic and adenoviral conjunctivitis, trachoma, episcleritis, anterior uveitis, corneal ulcers or scars) did not overtly affect the ability of the patients to retain the inserts. Tetracycline-loaded inserts released in vitro 45% of the drug over the 14-day period with an initial burst in the first day followed by a constant rate remaining over the period.

The Minidisc ocular therapeutic system

This monolytic polymeric device, originally described by Bawa et al. (Bausch and Lomb, Rochester, New York) - and referred to as Minidisc ocular therapeutic system (OTS), is shaped like a miniature (diameter 4-5 mm) contact lens, with a convex and a concave face, the latter conforming substantially to the sclera of the eye. The particular size and shape reportedly allow an easy placement of the device under the upper or lower lid without compromising comfort, vision or oxygen permeability. When compared with another standard insert, the Lacrisert, the Minidisc was reported to require less time and less manual dexterity for insertion. Different versions of the device have been evaluated, such as, non-erodible hydrophilic, non-erodible hydrophobic erodible. *In vitro* tests showed that the hydrophilic OTS (based on poly hydroxyl methyl methacrylate) released sulfisoxazole for 118 h, while the hydrophobic unit (based on a proprietary and Lomb pre-polymer) released Bausch gentamycin sulfate for more than 320 h. Clinical trials on placebo units demonstrated that the devices were well tolerated when placed either in the upper or lower conjunctival sac. In the eyes of healthy volunteers, the hydrophilic OTS released sulfisoxazole continuously for 3 days.

Various method of Evaluation parameter

- 1 Uniformity of Weight
- 2. Drug Content uniformity
- 3. . insert thickness
- 4. Percentage moisture absorption
- 5. Percentage moisture loss
- 6.Surface PH determination



- 7. In-vitro drug release
- 8. In-vivo drug release

Uniformity of Weight:

The weight variation test is carried out by weighing three patches cut from different places of same formulation and their individual weights are determine by using the digital balance. The mean value is calculate. The standard deviation of weight variation is compute from the mean value

Drug Content Uniformity:

Uniformity of the drug content is determined by assaying the individual insert . each insert is grounded in glass pestle mortar and STF is added to make a suspension.the suspension so obtained is filtered and the filtrate is assayed spectrophotometrically.

Insert thickness:

thick of the insert is measerd by dead weight thickness gauge.after initial setting the foot is lifted, with the help of the lifting lever fixed on the side of the dial gauge.insert is placed on the anvil such that the area where the thickness is to be measured lies below the foot.reading of the dial gauge are recorded after gentle lowering of foot.

Percentage moisture absorption: The percentage moisture absorption test is carried out to check physical stability or integrity of ocular inserts. Ocular inserts are weigh and place in a desiccators containing 100 ml of saturated solution of aluminum chloride and 79.5% humidity is maintain. After three days the ocular inserts are taken out and reweigh.

Percentage Moisture Loss:

The percentage moisture loss is carries out to check integrity of the film at dry condition. Ocular inserts are weighing and keep in a desiccators containing anhydrous calcium chloride. After 3 days, the ocular inserts are taken out and reweigh.

Surface PH determination: inserts are left to swell for 5 hr on agar plate prepared by dissolving 2%(w/v) agar in warm simulated tear fluid (STF; SODIUM CHLORIDE 0.670 g,sodium bicarbonate 0.200 g.

In vitro drug release

In-vitro release studies are carried out using bichamber donor-receiver compartment model using commercial semi-permeable design membrane of transparent and regenerated cellulose type (sigma dialysis membrane). It is tie at one end of the open cylinder, which acts as the donor compartment. The ocular insert is place inside the donor compartment. The semi permeable membrane is use to simulate ocular in vivo condition like corneal epithelial barrier in order to simulate the tear volume, 0.7 ml of distilled water is place and maintain at the same out the study in the donor level through compartment. The entire surface of the membrane is in contact with reservoir compartment, which contains 25ml of pH 7.4 phosphate buffers and stirs continuously using a magnetic stirrer. Samples of 1ml are withdrawn from the receptor compartment at periodic intervals and replace with equal volume of distilled water. The drug content is analyze at 246 nm against reference standard using pH 7.4 phosphate buffer as blank on a UV/visible spectrophotometer.

In vivo drug release-

The inserts are sterilized by using UV radiation before in-vivo study. Inserts are taken in a Petri dish along with 100 mg of pure drug, which are



spread to a thin layer. This Petri dish along with polyethylene bags and forceps are place in UV sterilization chamber (hood).

The inserts and other materials are exposing to UV radiation for one hour. After sterilization, inserts are transferee into polyethylene bag with the help of forceps inside the sterilization chamber itself. The pure drugs which are sterilized along with inserts are analyzing for potency by UV spectrophotometer after suitable dilution with pH 7.4 phosphate buffer.

The male albino rabbits, weigh between 2.5-3.0 kg are require for the experiment. The animals are house on individual cages and customized to laboratory conditions for 1 day. Receive free access to food and water. The ocular inserts containing drug are taken for in-vivo study which are previously sterilize on the day of the experiment and are place into the lower conjunctivas cul-de-sac. The inserts are inserting into 7 eyes at same time and each one eye of seven rabbits is serving as control.

Ocular inserts are removing carefully at 2, 4, 6, 8, 10, 12 and 24 hours and analyze for drug content as dilution mention in drug content uniformity. The drug remaining is subtracted from the initial drug content of inserts which will give the amount of drug release in the rabbit eye. Observation for any fall out of the inserts also recording throughout the experiment. After one week of wash period the experiment is repeating for two times as before.

CONCLUSION-

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 culde- sac or conjuctival

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. Advantages with ocuserts such as, Accurate dosing Capacity to provide at constant rate and prolong drug release thus a better efficacy. Increasing contact time and thus improving bioavailability. Possible reduction of systemic absorption and thus reduced systemic adverse effects.Reduced frequency of administrations and thus better patient compliance with lower incidence of visual side effects. Administration of an accurate in the eye and thus a better therapy Possibility of targeting internal ocular tissues through non-corneal conjuctival – sclera penetration routes; and Increased shelf life with respect to eye-drops due to the absence of water. Advantage of inserts as dosage form Ease of handling and insertion Lack of expulsion during Reproducibility of release kinetics wear Applicability to variety of drugs Non-interference with vision and oxygen permeability.

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