



## Review Article

# Ocular Inserts: A Rate Controlled Drug Delivery System – A Review

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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. 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. Newer ocular drug delivery systems are being explored to develop extended duration and controlled release strategy. 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.

**Key Words:** Ocular inserts, Controlled release strategy, Rate Controlled drug delivery, Bioavailability

## INTRODUCTION

Ocular inserts are defined as sterile preparations, with a thin, multilayered, drug-impregnated, solid or semisolid consistency devices placed into cul-de-sac or sac of conjunctiva and whose size and shape are especially designed for ophthalmic application. These inserts are placed in lower fornix and less frequently, in upper fornix or on the cornea. They are usually made up of polymeric vehicle containing drug and are mainly used for topical therapy.

Ocular drug delivery is one of the most fascinating and challenging tasks facing the Pharmaceutical researchers. 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 anatomy, physiology and biochemistry of the eye render this organ exquisitely impervious to foreign substances. The challenging to the formulator is to circumvent the protective barriers of the eye without causing permanent tissue damage. The development of newer, more sensitive diagnostic techniques and therapeutics agents renders urgency to the development of maximum successful and advanced ocular drug delivery systems.

The therapeutic efficacy of an ocular drug can be greatly improved by prolonging its contact with the corneal surface. For achieving this purpose, viscosity-

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enhancing agents are added to eye drop preparations or the drug is formulated in a water insoluble ointment formulation to sustain the duration of intimate drug-eye contact. Unfortunately, these dosage forms give only marginally maximum sustained drug-eye contact than eye drop solutions and do not yield a constant drug bioavailability. Repeated medications are still required throughout the day.

These practical issues have stimulated the search for alternative methods for ocular drug delivery. Much of the work recently devoted to ocular inserts, which serves as the platform for the release of one or more active substances. It has become clear, however that the development of an ocular insert that reliably combines controlled release with absence of any irritation to the patient, poses a formidable technical challenge.

In order to overcome the constraints placed by these conventional ocular therapies viz.

- Short residence time
- Pulsed dosing of drug.
- Frequent instillation
- Large drainage factors

Newer ocular drug delivery systems are being explored to develop extended duration and controlled release strategy. 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.

### 1. Characteristics of Ocular Inserts:

- Bio stable & Biocompatible with tissue of eye
- Nontoxic & Non carcinogenic
- Retrievable & Release at a constant rate.
- Non immunogenic & Non mutagenic
- Good mechanical strength
- Free from drug leakage
- Easily sterilizable
- Easy and inexpensive to manufacture
- Applicability to variety of drugs
- Non-interference with vision and oxygen permeability

### Approach

Ocular insert is defined as a preparation with solid or semisolid consistency, whose size and shapes are especially designed for ophthalmic application (i.e., rod or shield). 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 therapy. The main objective of the ophthalmic inserts is to increase the contact time between the preparation and the conjunctival tissue to ensure a sustained release suited to topical

or systemic treatment. In comparison with the traditional ophthalmic preparation i.e., eye drops, the solid ophthalmic devices presents some advantages .

### **Advantages of Ocular Inserts:**

In comparison with the traditional ophthalmic preparation i.e., eye drops, the solid ophthalmic devices presents some advantages :

- Increasing contact time and thus improving bioavailability.
  - Possibility of providing a prolong drug release and thus a better efficacy.
  - Reduction of systemic side effects and thus reduced adverse effects.
  - Reduction of the number of administrations and thus better patient compliance.
  - Reduction in systemic absorption
  - Possibility of targeting inner ocular tissues through non-corneal (conjunctival sclera) routes
  - Possibility of incorporation of various novel chemicals and technological approaches such as pro-drug, mucoadhesives, permeation enhancers, microparticulate, salts acting as buffers.
- Of course not all benefits listed above can present in single, ideal device. Each type of inserts represents compromise between desirable properties inherent by solid dosage forms and negative constraints imposed by structure and components of insert itself, by

fabrication cost, as well as by the physical/physiological constrains of application site.

### **2. Disadvantages of Ocular Inserts:**

- A capital disadvantage 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.
- Their movement around the eye, in rare instances, the simple removal is made more difficult by unwanted migration of the inserts to upper fornix.
- The occasional inadvertent loss during sleep or while rubbing the eyes.
- Their interference with vision, and
- Difficult placement of the ocular inserts (and removal, for insoluble types).

### **Classification of Ocular Inserts:**

#### **A. Insoluble ocular inserts:**

The insoluble inserts have been classified into three groups:-

- I. Diffusion systems
- II. Osmotic systems
- III. Contact lenses.

The first two classes include a reservoir in contact with the inner surface of the rate controller and supplying drug there to. 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. The reservoir contains a liquid, a gel, a colloid, a semisolid, a solid matrix or

a carrier-containing drug. The third class including the contact lenses. The insolubility of these devices is their main disadvantages, since they have to be removed after use.

### I. Diffusion controlled ocular inserts

The diffusion systems are compares 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. This consists of medicated core prepared out of a hydro gel polymer like alginates, sandwiched between two sheets of transparent, lipophilic, rate controlling polymer like ethylene /vinyl acetate copolymer membrane designed to the required geometry suitable for insertion in to the cul-de-sac. When the device is placed in a cul-de-sac the drug molecule penetrates through the rate controlling membranes at zero order rate process as defined :

$$Dq/dt = dp_{km} (cr-ct)/dm.$$

A typical In vivo release rate profile of pilocarpine from the ocusert pilo-20.

During the first hour the system releases pilocarpine at a rate, which is three times higher than the programmed rate i.e. 20 microgram per hour. Ocular inserts of this type have been reported for various other ophthalmic therapeutic agents like carbonic anhydrase inhibitors, epinephrine, anesthetics, antibiotics, anti inflammatory steroids etc.

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

### II. Osmotic Inserts:

The osmotic inserts are generally compared of a central part surrounded by a peripheral part. The 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.

Water permeable matrix Ethylene - vinyl esters copolymers, Divers-plasticized polyvinyl chloride (PVC), polyethylene, cross-linked (PVP) poly vinyl pyrrolidone.

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.

### **III. 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<sup>8</sup>. 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.

This type of device substantially prolongs the drug /eye contact time and thus increases bioavailability. Some of the polymers that could be used for preparing the device are 2-hydroxyethylmethacrylate, vinyl pyrrolidone acrylic co polymer etc. When contact lenses are used as device, the lenses are presoaked in the drug solution for sufficient time for equilibration and are then inserted just like a contact lenses

## B. Soluble ocular 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 agent is preferably absorbed by soaking the insert in a solution containing the drug, drying and rehydrating it 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 release of the drug from such a 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 is still controlled by diffusion. The release rate,  $J$ , derived from Fick's law yields the following expression

When  $A$  - Surface area of the membrane.

$K$  – Diffusion coefficient of the drug

$L$  – Membrane thickness

$C_s$  – 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 soluble insert made of cellulose derivatives can be sterilized by exposure to gamma radiation without the cellulose components being altered.

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.

C. Bioerodible ocular inserts:

This type of device is fabricated from bio-erodible or bio- degradable polymer of hydro gel or non hydro gel type. The mechanism of drug release in this system is dependent on rate of erosion or rate of degradation. Several erodible type of ocuserts have been prepared using polymer like carboxymethyl cellulose, poly vinyl alcohol, collagen etc. containing drug like pilocarpine, gentamicin etc in the form of

disc and wafers. Some of the products are also marketed recently as,

- Lacrisert
- Soluble ocular drug insert, (SODI)
- Ocular therapeutic system or (minidisk)
- Corneal collagen shield
- **LACRISERT :**
  - It is sterile rod shaped device made of hydroxypropyl cellulose without any preservative. i.e. used for the treatment of dry eye syndrome.
  - It weighs 5 mg & measures 1.27 mm in diameter with a length of 3.5 mm.
  - It is inserted into the inferior fornix where it imbibes water from conjunctiva and forms a hydrophilic film which stabilizes the tear film and hydrates & lubricates the cornea.
  - Day long relief from dry eye syndrome has been reported from a single insert placed in the eye early in the morning.

Advantages :-

Replacement of 4 times an hr regimen by once or twice daily regimen is the benefit achieved by this dosage forms.

- **SODI:(Soluble Ocular Drug Inserts)**
  - The insert is small oval wafer.
  - It is in the form of sterile thin film of oval shaped Weighing 15-16 mg
  - After introduction into the inferior cul-de-sac where wetted by tear film , it softens in 10-15 seconds and assumes the curved configuration of globe.

During the following 10-15 min. the film is turn into viscous polymer mass, there after in 30-60 min it becomes a polymer solution.

Advantages:

Single SODI application has been reported to replace 4-12 drops instillation or 3-6 applications of ointment for treatment of glaucoma & trachoma.

- **MINIDISC: (Ocular Therapeutic System)**
  - Consist of countered disc with a convex front & concave back surface in contact with eyeball.
  - It is like a miniature contact lenses with a diameter of 4-5mm.
  - The major component of it is silicone based prepolymer.
  - The OTS can be hydrophilic or hydrophobic to permit extended release of both water soluble and insoluble drugs.

• **Corneal Collagen Shield:**

Prepared by molding collagen mixed with the drug into a contact lens configuration is dehydrated and sterilized by gamma radiation and packed. Drugs like antibiotics, steroids have been reported (Bloomfield, 1978)

The biodegradable inserts are composed of 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.

### Evaluation of Ocular Inserts:

1. Film thickness
2. Content uniformity
3. Uniformity of Weight
4. Percentage moisture absorption
5. Percentage moisture loss
6. In-vitro drug release
7. In-vivo drug release
8. Accelerated stability studies.
9. Compatibility study.

#### 1. Thickness of Film:

Film thickness is measured by using dial caliper at different points and the mean value was calculated. Reading were taken over an circular film of area of 38.5 mm square. The standard deviation in thickness was computed from the mean value.

#### 2. Drug Content Uniformity:

To check the uniformity of the drug in the cast film inserts are cut at different places in the cast films and each film is place in vials containing 5 ml of pH 7.4 phosphate buffer and shaken to extract the drug from patch. 1 ml from above resulting solution is taken and dilute. The solution is analyzed by spectrophotometer using pH 7.4 phosphate buffer as blank. The drug

content was calculate using the following formula:

$$\text{Mg of drug in one patch} = \frac{\text{As} \times \text{Cr}}{\text{Ar}}$$

Where:

As =Absorbance of sample solution.

Ar =Absorbance of standard solution.

Cr =Concentration of drug in Standard solution.

Same procedure is adopts for all the batches of cast films in triplicates and mean drug content and standard deviation of variance are calculate.

#### 3. 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.

**4. 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. The percentage moisture absorption is calculate using the formula

Percentage moisture absorption =



$$\frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

### 5. Percentage Moisture Loss:

The percentage moisture loss is carried out to check integrity of the film at dry condition. Ocular inserts are weighed and kept in a desiccator containing anhydrous calcium chloride. After 3 days, the ocular inserts are taken out and reweighed, the percentage moisture loss is calculated using the formula Percentage moisture loss =

$$\frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

### 6. In-vitro drug Release:

To simulate the actual physiological conditions prevailing in the eye an in-vitro dissolution is used in the present work.

In-vitro release studies are carried out using bi-chamber donor-receiver compartment model design using commercial semi-permeable membrane of transparent and regenerated cellulose type (sigma dialysis membrane). It is tied at one end of the open cylinder, which acts as the donor compartment. The ocular insert is placed inside the donor compartment. The semi permeable membrane is used to simulate ocular in vivo condition like corneal epithelial barrier in order to simulate the tear volume, 0.7 ml of distilled water is placed and maintained at the same level throughout the study in the

donor compartment. The entire surface of the membrane is in contact with reservoir compartment, which contains 25ml of pH 7.4 phosphate buffers and stirred continuously using a magnetic stirrer. Samples of 1ml are withdrawn from the receptor compartment at periodic intervals and replaced with equal volume of distilled water. The drug content is analyzed at 246 nm against reference standard using pH 7.4 phosphate buffer as blank on a UV/visible spectrophotometer.

### 7. In-vivo Drug Release Rate Study:

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 placed in UV sterilization chamber (hood).

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

The male albino rabbits, weighing between 2.5-3.0 kg are required for the experiment. The animals are housed 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 is also recording throughout the experiment. After one week of wash period the experiment is repeating for two times as before.

### **8. Accelerated Stability Studies:**

The accelerated stability studies are carries out to predict the breakdown that may occur over prolong periods of storage at normal shelf condition. The films of the formulation are taken in a separate Petri dish and are keep at three different temperatures 400C, 500C and 600C and the period for break down or degradation of the ocular inserts is check. When ocular inserts show degradation the time in days is note and subject to determine the drug

content of each individual film using the drug content uniformity procedure.

### **8. Polymer Systems in Ocular Inserts:**

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.

Polymers used in ocular inserts can be of natural, synthetic or semi synthetic in nature. Further, they can be either water soluble polymers with linear chains or water insoluble polymers joined by cross linking agents. Most commonly used polymer groups include nonionic polymer such as hydroxypropylmethylcellulose (HPMC); polycationics such as chitosan, DEAE-dextran and polyanionics like polyacrylic acid (PAA) derivatives e.g. carbopols, polycarbophils, carboxy-methylcellulose.

Earlier sustained release ocular dosage form included lamellae or disks of glycerinated gelatin and sterile drug impregnated paper strip. The aqueous tear fluids dissolve the lamella and the drug is released for absorption.

#### **A. Cellulose polymers:**

Cellulosic polymers such as methyl cellulose; hydroxyethylcellulose (HEC);

hydroxypropylmethylcellulose (HPMC); hydroxypropylcellulose(HPC) were introduced as viscolizers into artificial tear preparations to retard canalicular drainage and improve contact time. All cellulose-ethers impart viscosity to the solution, have wetting properties and increase the contact time by virtue of film forming properties.

Drug release was found to be better in terms of extent and amount. Controlled release has been observed with various beta-blockers from HPM inserts with improved ocular bioavailability and reduced toxicity and dosing frequency. HPC, HPMC, PVP and PVA were also used in different ratios to prepare the ocular films with the objective to reduce the frequency of drug administration, patient compliance, controlled drug release and greater therapeutic efficacy for ocular infections such as conjunctivitis, keratitis, kerato-conjunctivitis and corneal ulcers.

#### **B. Polyvinyl Alcohol (PVA):**

Alginic acid and derivatives PVA was introduced into ophthalmic preparations and reported to have a superior corneal contact time. PVA lowers the surface tension of water reducing interfacial tension at an oil/water interface and enhances tear film stability. This film-forming property together with ease of sterilisation, compatibility with a range of ophthalmic drugs and an apparent lack of

epithelial toxicity lead to use of PVA as a drug delivery vehicle and artificial tear preparation. Polyvinylalcohol (PVA) has been used as a carrier to formulate polymeric inserts and were found to enhance bio-availability in comparison to solutions

#### **C. Poly (ethylene oxide) (PEO):**

Poly Ethylene Oxide(PEO) exhibits good compressibility and thus is easy for the manufacturing of matrix tablets. In contact with an aqueous medium, poly(ethylene oxide) hydrates and gels superficially, the polyether chains of PEO forming strong hydrogen bonds with water. Drug release from poly(ethylene oxide) matrices is controlled by polymer swelling and erosion, or drug diffusion through the gel, or by both processes. Various release patterns can be achieved depending on the poly(ethylene oxide) molecular mass and physicochemical properties of the drug. Good mucoadhesive properties and lack of irritancy to the rabbit eye has been reported. It points that this polymer can be an interesting candidate material for controlled release erodible ocular inserts.

#### **D. Pluronic, Poloxamer F127**

Sustained drug delivery can also be achieved by use of a polymer that changes from solution to gel at the temperature of the eye (33 to 34o C). An example of this type of polymer is poloxamer F127, which consists of linked polyoxyethylene and

polyoxypropylene units. At room temperature, the poloxamer remains as a solution. When the solution is instilled onto the eye surface, the elevated temperature causes the solution to become a gel, thereby prolonging its contact time with the ocular surface.

#### **E. Collagen**

Collagen is widely used for biomedical applications. It accounts for about 25 % of the total body protein in mammals and is the major protein of connective tissue, cartilage and bone. Importantly, the secondary and tertiary structures of human, porcine, and bovine collagen are very similar, making it possible to use animal-sourced collagen in the human body. Collagen shields are designed to be sterile, disposable, temporary bandage lenses that conform to the shape of the eye and protect the cornea. Their dissolution time on cornea ranges from 12-17 hrs and is controlled by varying degree of cross-link of the polymer.

#### **F. Eudragit**

The polymer system avoids of any irritant effect on cornea, iris and conjunctiva up to 24 h after application and seems to be a suitable inert carrier for ophthalmic drug. Similarly, In another study, Eudragit RL100 polymer nanoparticle system loaded with cloricromene polymer matrix was prepared and characterized on the basis of physicochemical properties,

stability and drug release features by topical administration in the rabbit eye and was compared with an aqueous solution of the same drug.

#### **G. Poly(Lactic Acid) /Poly ( Glycolic Acid )**

Polymers such as poly (lactic acid) or poly (glycolic acid) undergo hydrolytic degradation in the body and become monomers of lactic acid or glycolic acid. These monomers can be metabolized and eliminated from the tissues. It is possible to incorporate drugs in the matrix of these polymers. The polymer containing the drug releases the drug for a sustained period and undergoes degradation simultaneously. These polymers have been used as materials of absorbable surgical sutures for many years and proved to be safe and biocompatible. Feasibility of delivering drugs to the retina and vitreous as well as the subconjunctival space using the microspheres of biodegradable polymers has been reported.

#### **H. Alginate and derivatives**

Alginate is a linear co-polysaccharide isolated from brown seaweeds and certain bacteria. Chemically it is a (1-4)-linked block copolymer of  $\alpha$ -D-mannuronate (M) and its C-5 epimer R-L-guluronate (G), with residues arranged in homopolymeric sequences of both types and in regions which approximate to the disaccharide repeating structure (MG) Commercially

alginate is widely used as a gelling agent not only in foods but also in other industries such as pharmaceutical, biomedical, and personal care). As it is easy to prepare alginate ionotropic gels at mild conditions, it is possible to entrap drugs and living cells in alginate gels, which allow a wide application of alginate as scaffolds for tissue engineering, drug delivery systems, and cell encapsulation and transplantation. Drug release from such matrices may be controlled by polymer swelling or erosion or drug diffusion in hydrated gel or by these processes all together. All these properties and applications are ultimately dependent on the molecular architecture and gelling mechanism. Recently alginate-chitosan ocular inserts has been studied as an efficient means of delivering antibiotics (gatifloxacin).

### Recent Trends:

The following recent trends are in existence:

- a) Membrane-bound ocular inserts (biodegradable and non-biodegradable)
- b) Mucoadhesive dosage forms (ocular films or sheath, ophthaCoil, polymer rods, HEMA hydrogel, Dispersion, polysulfone capillary fiber)
- c) Collagen shields, cyclodextrine based system, ophthalmic rods.
- d) Filter paper strips (drug-impregnated filter paper strips for staining agent-

sodium fluorescent, lissamine green and rose Bengal)

- e) Soft contact lenses, implants, flexible coils and cotton pledgets (Drug presoaked hydrogel type, polymeric gels)
- f) Phase Transition systems (in-situ gel formation system: ion- activated based, pH changed based, temperature change based).
- g) Nanoparticles (Microspheres, nanosuspension, Amphiphilogs, Niosomes, Liposomes, Dendrimers and Quantum dots)
- h) Ocular Iontophoresis and pumps
- i) Chemical delivery systems vesicular systems

Utilization of the principal of controlled release as embodied by ocular inserts therefore offers an attractive alternative approach to the difficult problem of prolonging pre-corneal drug residence time.

### SUMMARY:

In summary the ideal ocular inserts as a therapeutic system should be bio stable, biocompatible with minimal tissue-implant interaction, stable, nontoxic, non carcinogenic, retrievable and should release the drug at a constant programmed rate for a predetermined duration of medication. As ocular inserts release the drug for prolong period, so it reduces the no. of administrations and increases

patient complaience.

The concept of ocular inserts as a drug delivery system to the eye though conceived long back was commercialized only after the uses of bio-compatible polymers as described earlier were developed. Different categories of a drugs like antiglaucoma, antibacterials, antivirals, anaesthetics, NSAIDs can be loaded through the ocular inserts for the treatment of eye disorders. The use of Pilocarpine for glaucoma treatment in the form of ocular inserts is the most widely used technique in ocular therapeutics.

In spite of this investigation development of an ideal and bio-compatible polymer free from toxic and allergic manifestation is yet to be brought about. However, with the available polymer a reasonably good ocular insert device with minimal tissue interaction, nontoxic, non carcinogenic, have been developed commercially.

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