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REVIEW ON OCULAR INSERTS: AN EVOLUTIONARY TREND FOR TARGETED DRUG DELIVERY

Kazi Wasim B.[1], Khadkutkar Vijayananda K.[1]* and Sanjay S. Dudhamal[2]

[1]Channabasweshwar Pharmacy College (Degree), Latur 413512, Maharashtra, India.
[2]Maharashtra Pharmacy Diploma Institute, Nilanga. Latur 413512, Maharashtra, India.

***Corresponding Author: Khadkutkar Vijayananda K.**

Channabasweshwar Pharmacy College (Degree), Latur 413512, Maharashtra, India.

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ABSTRACT

The eye is a sensory organ. It is difficult to study from a drug delivery point of view. An ocular insert is a novel approach for drug delivery into the eye it is an advanced technology in eye disease therapy. The most frequently used and easy to administer dosage form available is eye drops. Conventional ocular drug delivery has major disadvantages like fast precorneal loss which could be overcome by a novel approach like an ocular insert. In ocular inserts, the films are prepared and are directly placed in a cul-de-sac of the eye. Ocular inserts are defined as preparations with a solid or semisolid consistency, whose size and shape are specially designed for ophthalmic application. Treating ocular diseases require localized administration of the drug in the eye. In recent years, there has been using of polymer-based delivery is very popular. Utilization of the principle of controlled release by means of the ocular insert with the help of polymers offers an attractive approach to the problem of prolonging precorneal drug residence time. This review article discusses the anatomy of the eye, ocular insert as a novel dosage form and emphasizes on advantages of ocular insert, classification, and various methods available for formulating ocular insert and also evaluation parameters.

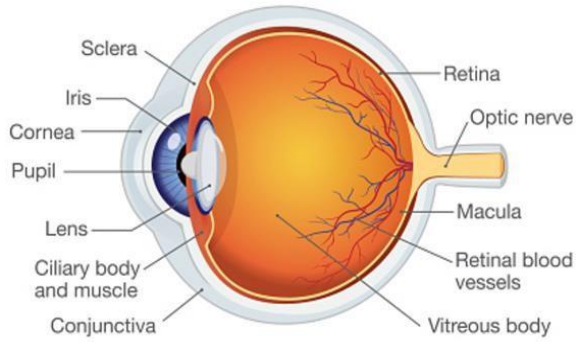
KEYWORDS: Eye, Films of preparation, Novel dosage form, Ocular insert.

INTRODUCTION

The eye is a unique organ with a complex structure and is highly resistant to foreign substances including drugs. Ocular drug delivery is one of the most challenging tasks faced by pharmaceutical researchers. The intraocular bioavailability of the drug through conventional dosage forms like eye drops is very poor because it is topically applied to the anterior portion of the eye and most of the applied dose is lost due to the defensive mechanism of the eye. The specific aim of designing an ocular insert is to deliver a drug without losing the dose of the drug and its therapeutic activity with prolonged or controlled release at a particular area. [1,2]

Structure of eye

The human eye has consisted of different parts and every part has its specific role in the eye.



The cornea is a very thin and transparent membrane in the eye. The cornea helps the eye to focus light so you can see clearly it is also known as the eyes of the window. The cornea contributes between 65-75% of the eye's total focusing power. The sclera is a white layer of the eye its main function is to protect the eye. Iris is the

colored part of the eye and the most visible part of the eye. Pupils are the black center of the eye. The lenses are transparent discs immediately behind the iris and pupil. The retina is a light-sensitive layer and contains light-sensitive cells.[1,3]

Diseases of eyes

The eye is a very sensitive organ in the human body Due to some external and internal factors eye causes diseases that are harmful to the eye which causes vision loss. Eye diseases are of a wide variety some diseases such as., Cataract, Glaucoma, Dry eye syndrome, Trachoma etc. A cataract is an opacity within the clear lens of the eye.

Glaucoma is the condition where increased intraocular pressure may result in damage to the optic nerve and the eyes become like glass.

Dry eye disease is a common condition that occurs when tears aren't able to provide adequate lubrication for the eyes.

Trachoma is an infection of the eyelids which causes the inside of the eyelid to rough and swell and they constantly rub the cornea when blinking the eye.

Such infection occurs due to when you live in polluted air, moving in polluted air, during road works cement particles and dust particles get into the eyes and cause an infection.

Fungal eye infections are extremely rare but they cause blindness the most common way to develop a fungal eye infection is as a result of eye injury, particularly if the injury was caused by plant material such as a stick or thorn.

Inflammation or infection of the cornea is known as Keratitis and inflammation or infection in the eye is called endophthalmitis. [10,12]

Classification of ocular insert[17,18]

The inserts are classified according to their solubility as Insoluble, Soluble, or Bioerodible inserts are classified as follows:

Insoluble inserts:

Insoluble inserts are solid or semisolid preparations that include a diffusion system in which a drug reservoir is inserted between the rate-controlling polymers for providing the drug in a controlled manner. In the reservoir system, the drug is dispersed or dissolved in a polymer in form of liquid, a gel, a semisolid, or a solid matrix.

The polymer which is used as a carrier may be hydrophobic, hydrophilic, organic, inorganic, naturally occurring, or synthetic material in nature.

Soluble inserts:

Soluble Inserts belong to the oldest class of ocular inserts. They offer a great advantage as they are entirely soluble so they do not need removal from the site of administration. The soluble inserts quickly lose their solid integrity and are squeezed out of the eye movement after blinking. This insert does not to be removed at the end of its use.

Components of soluble inserts containing synthetic polymers[12]

1. Soluble synthetic polymers	Cellulose derivatives- hydroxypropyl methylcellulose, hydroxyethylcellulose, hydroxypropyl cellulose Polyvinyl Alcohol,
2. Additives	
i. Plasticizer	Polyethylene glycol, Glycerin, Propylene Glycol
ii. Bioadhesives	Polyacrylic acids
iii. Complexing agent	Polyvinyl pyrrolidine
iv. Enteric-coated polymer	Cellulose acetate phthalate,

Bioerodible inserts

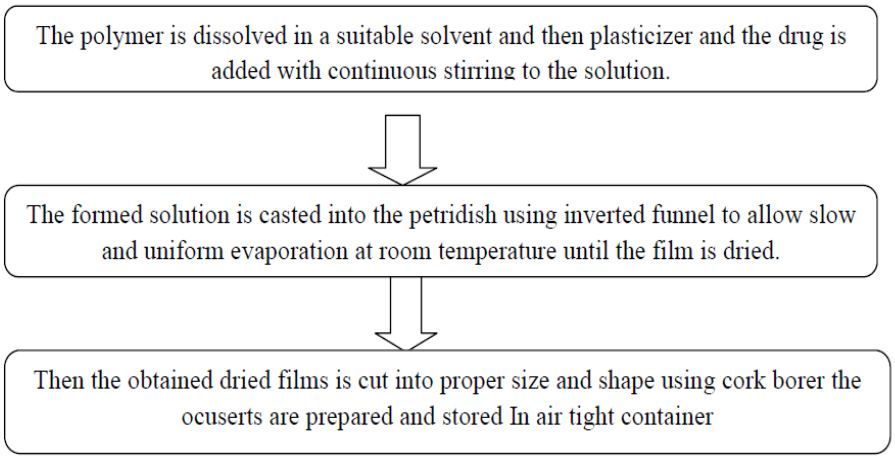
The bioerodible inserts are composed of homogeneous dispersion of a drug with or without a hydrophobic coat which is made of bioerodible polymers, which are impermeable to the drug. Which indicates the presence of bioerodible polymer in the formulation of an insert. Successfully used Bioerodible materials are poly (orthoesters) and poly (orthocarbonates). The release of these systems depends on the contact of the device with tear fluid showing apparent bioerosion of the matrix.

Formulation methods for ocular inserts[5,19]

The ocular inserts are prepared by various methods as follows:

1. Solvent casting method

This method is a more popular and easy method used for the preparation of ocular inserts. The process of this method is given below in a flow chart



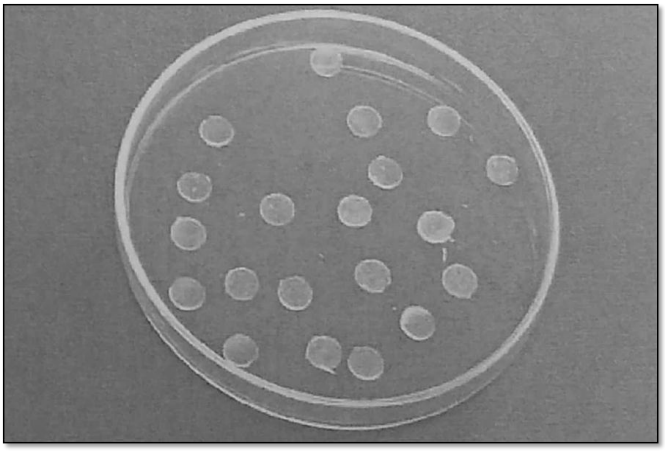
2. Glass substrate technique

In this method the polymer is soaked in 1%v/v Acetic acid solution for about 24hrs, to get a clear solution. Then the above solution is filtered and the required amount of drug is added and vortex mixer for 15 minutes to dissolve the complex in the polymer solution. The plasticizer is added to the above solution. The viscous solution is obtained and kept aside for 30 minutes until air bubbles are removed from the solution and rate-controlling films are formed. The films are cast on a leveled glass mold and allowing it to dry at room temp. for 24hrs. the dried films are cut into definite shapes and sizes then, the matrix is sandwiched between the rate-controlling membranes using gum which is non-toxic, non-irritating, and water-insoluble. They are wrapped in aluminum foil separately and stored in a desiccator.

3. Melt extrusion technique

In this method, the drug and the polymer are passed through a sieve having a mesh size of 60#, weighed, and blended. In this mixture, the plasticizer is added. The blend is then discharged to the container of the melt flow rate apparatus and ejected. The ejected was cut into accurate size and packed in polyethylene lined aluminum foil, heat-sealed, and sterilized by gamma radiation.

The formulated ocular insert is look as follows:



Evaluation parameters of ocular inserts [13,14,15,16]

The prepared inserts were evaluated for various parameters are as follows:

1) Uniformity of weight

All the prepared films were weighed separately on a digital balance. Then the average weight of the film is calculated from the mean value.

2) Thickness

The thickness of each film is measured using a Vernier calliper instrument for making accurate measurements and the average thickness of all the films is calculated.

3) Percentage moisture absorption

For calculating percentage moisture absorption, the inserts are weighed and placed in desiccators containing 100ml of a saturated solution of aluminium chloride. Ocular inserts are reweighed after three days.

The formula for calculating percentage moisture absorption is:

= Final weight – Initial weight/Initial weight x 100.

4) Swelling index

A small amount of film is cut and weighed initially and then it is soaked in pH 7.4 tear fluid for 1 hour. After 1 hour, the film is reweighed. The swelling index is calculated by the following formula.

Swelling index = Initial weight/ final weight × 100

5) Drug content uniformity

A small amount of inserts is cut and dipped in 7 ml tear fluid. Then it is taken in a centrifuge tube and centrifuged for 15 min. then is analyzed in UV spectrometry and the concentration of a drug is calculated using a standard plot.

6) Surface pH

Inserts are placed in a closed Petri plate in distilled water for half-hour. After this, the swelling of the insert occurred. Swollen insert is then placed in a digital pH meter to determine surface pH.

7) Folding endurance

The film is started to fold from one side and again folded several times until the tearing of the film is to be done. The number of folds that are occurred in the film is its folding endurance till its breakage. The folding endurance of all the films is measured.

8) IN Vitro diffusion studies

An in vitro diffusion study of the ocuserts is done by using the Franz diffusion cell apparatus. The study of permeability of drug is carried out by using Franz diffusion cell. It consists of mainly the two-compartment one is the donor compartment in which the dosage form i.e., ocuserts is added and another is the receptor compartment which is filled with 7.4 tear fluid to simulate tear fluid in the eye.

Both compartments are separated by a membrane which may be a semi permeable dialysis membrane or egg membrane. The instrument is started, RPM and temp.is adjusted. Ocusert is placed in the donor compartment and tears fluid in the receptor compartment. 1ml sample is withdrawn after a fixed time interval and after making a suitable dilution sample is analyzed in a U.V spectrophotometer and drug release is calculated.

CONCLUSION

Ocular inserts have been found to be advantageous technology regarding the delivery of drugs in the eye with achieving the target and eliminating side effects of conventional dosage forms like., frequent administration of the drug which causes patient compliance as well as the formation of crystalline deposits on the cornea due to its pH-dependent solubility which is very low. Ocular inserts increase the contact time of the drug also controlled release of the drug is also achieved thus improving bioavailability. The systemic side of the drug taken can be could be decreased by utilizing the ophthalmic insert approach. Various classes of ocular inserts have been developed with different methods erodible, non-erodible, and bio erodible and can be evaluated with different parameters. Ocular inserts are a novel approach to drug delivery in the eye which reduces the frequency of administration leading to patient compliance with eye disease therapy.

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