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Review of Ocular Drug Delivery System

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ABSTRACT :

Developing an Ocular Drug Delivery System (ODDS) is one of the most difficult problems pharmaceutical researchers encounter. The capacity to sustain a therapeutic level of the drug at the site of action for an extended period of time is one of the primary obstacles in ocular therapy. About 70% of the eye dose formulations on the market are eye drops and ointments, making them the most widely accessible ophthalmic medicines. However, tear flow and lachrymal nasal drainage cause these preparations to be quickly drained from the ocular chamber after being placed in the cul-de-sac. Frequent dosage is necessary since just a tiny amount is available for its therapeutic impact. Newer pharmaceutical opthalmic formulations, including liposomes, nanosuspensions, nanoparticles, and innovative techniques, have been created to address these issues by increasing the drug's bioavailability in a regulated and sustained way. This review concentrated on a number of potential drug delivery pathways into the ocular tissues as well as controlled and sustained drug delivery, which is now the norm in contemporary pharmaceutical design.

Keywords: ocular Drug Delivery System, nanoparticles, nano suspension, controlled and sustained drug delivery

Introduction:

The peculiarities of the eye's drug disposition make it the most fascinating organ. Due to its ease of use and safety, topical medication administration is typically the preferred approach for ocular chemotherapy . Avoiding irreversible tissue damage while evading the eye's protective shields is a major difficulty for the formulator. Ocular delivery systems with excellent therapeutic efficacy are still being produced thanks to the development of innovative therapeutic substances and more advanced, sensitive diagnostic tools.Achieving the ideal medication concentration at the active site for the right amount of time is the specific goal of therapeutic system design[1].

.A variety of precorneal, dynamic, and static ocular factors limit the delivery of medications to the targeted ocular tissues... Furthermore, target tissues do not retain therapeutic medication levels for extended periods of time. Over the last twenty years, research on ocular drug administration has made significant progress in creating innovative, safe, and patient-friendly drug delivery methods and technologies that could potentially overcome these obstacles and sustain drug levels in tissues. [2]

.•The primary issue with ocular medicine delivery systems is the quick and thorough removal of traditional eye drops from the eye. This issue leads to a significant loss of medication. Merely a small quantity of medication can get through the corneal layer and reach the inner tissue of the eye. Lachrymal drainage and medication dilution through tears are the primary areas of drug loss

- This indulgence causes toxicity and unfavorable side effects in addition to reducing the ocular bioavailability.[3]

.The enhancement of ocular contact time-improving permeability of the corneal and the specificity of the site.[4]

1. When it comes to drug administration, the eye offers special potential as well as difficulties. One of the most fascinating and difficult tasks facing pharmaceutical chemists is ophthalmic medication delivery. The eye is remarkably resistant to external chemicals due to its unique architecture, physiology, and biochemistry. The formulator's difficulty is to get past the eye's protective layers without permanently harming the tissue.The development of an effective medication is the aim of pharmacotherapeutics.focus for the necessary amount of time at the targeted point of action[5].

- Topical ocular eye drops are typically used to treat the anterior part of the eye, which includes the cornea, conjunctiva, sclera, and anterior uvea. Only a little quantity (1–3%) of an eye drop actually reaches the intraocular tissue, and drops frequently remove quickly within five to six minutes of delivery, regardless of the injected volume .As a result, maintaining a sufficient medication concentration in the precorneal region is challenging.In clinical therapies, systemic administration, periocular, or intraocular injections of pharmaceuticals are typically used because topical medications typically do not reach the posterior part of the eye (retina, vitreous, or choroid).Nevertheless, the eye's distinct

physiology and architecture, as well as its defenses, prohibit the medications entering the target tissues due to the eye's distinct architecture, physiology, and protective barriers. Drug delivery systems (DDSs) for the posterior portion of the eye are currently gaining a lot of attention. In order to provide long-term, continuous medication release, a polymeric depot device is increasingly being injected or implanted directly into the vitreous.[6]

- Overview Lachrymal drainage and medication dilution by tears are the primary areas of drug loss. This superfluity causes unintended toxicity and adverse effects in addition to decreasing systems has received significant attention throughout the past 20 years. Such a system's goal is to improve drug effectiveness by avoiding dose frequency through localization to the site of action.[7]

- Conventional eyedrops cannot administer drugs to the posterior region of the eye with the required therapeutic concentration because of the limitations of standard dosage forms.Considering the aforementioned considerations, new methods that enable significant medication absorption into the eye are continuously being researched. Approaches based on nanotechnology have demonstrated their effectiveness in overcoming the limitations of conventional dosage forms, which include improving drug penetrability through a variety of static and dynamic barriers, extending the duration of the drug's action through controlled release, and reducing adverse effects.[8]
- **Benefit Benefits of the Ocular Medication Delivery**

Method

1) The following are some advantages

1)They give the dosage rate precision and consistency. Conventional systems can prevent pulsed dosing.

2)Drugs can be released in a controlled and sustained manner.

3)They improve the ocular bioavailability of medications by lengthening the corneal contact time, which is accomplished by the drug's efficient adhesion to the corneal surface.

i. Targeting within the ocular globe is necessary to prevent the loss of ocular tissues.

ii. In addition to improving patient compliance, providing comfort, and enhancing therapeutic drug performance, they also circumvent protective ocular barriers like drainage, lacrimation, and conjunctival absorption, improve delivery system housing, and enable self-administration of medications.

- Absorption is quicker and there are fewer systemic and ocular side effects. [9]
    - **Disadvantages of Ocular Medication Delivery Method**
        - The following are the main disadvantages of ocular medication delivery systems
        - 1) Themedication solution and the ocular surface have a brief contact time.
        - 2) Drug instability when dissolved
        - 3) Utilizing preservatives [10].

Anatomy of the Eye:

Structure of the Eye [1]

1) The layers and internal structures that make up the human eye each have specific roles to play.
2) Anterior parts of the eye they are as follows
3) 1) cornea
4) 2) Lens.
5) 3)Iris
6) 4)Ciliary body
7) •
8) Posterior parts of eye they are as follows:
9) 1.Retina.

10) 2. Optic nerve

11) 3. Choroid

12) 4. Sclera

13) 5. Fovea

14) 6.viterous•

- Anterior parts of eye:

1. Cornea: In the anterior of the eye, there is a prominent, transparent bulge called the cornea. The adult cornea's surface has a radius of about 8mm . Cornea is upper part of eye, in obverse of the iris and pupil. The cornea of human has horizontal diameter upto 11.5mm and vertical is 10.5mm. There are five layers of human cornea: epithelium, Bowman's membrane, laminar stroma, Descemet's membrane, endothelium membrane. The shell of the cornea is field with the tear film. The tear film "safeguards" it protects from chemical, toxic material and from microbial infection .

2. Lens: The eye lens is biconvex, translucent, and avascular structure .Lens purpose is to transmit and focus light onto the retina. The lens is the primary controller of the eye and it has the highest protein and tissue content. The collagenous capsule that surrounds the lens serves as a barrier to diffusion and aids in accommodating the lens by giving the lens its shape. . The collagen capsule molds the flexible lens into more spherical shape with greater refractive power process known as accommodation .

3. Iris: Iris is located behind the cornea and in front of lens. It controls the size of pupil . In the structure iris it having four layer they are: anterior border layer, stroma, anterior epithelium, posterior pigmented epithelium . Iris is the color part of the eye and they have the different shades like as green, blue, brown, hazel or grey .

4. Ciliary body: Ciliary body is present behind the iris. From the exterior view the ciliary body is not seen. It is constructed from the inner wall's tissue ring .The ciliary body is built of the tissue, so the function is tissue interactions that occurs at certain stage in the normal development of eye .[11] .Posterior part of eye:

1. Retina: Retina is located at the backside of the eye .Retina is connected to the optical nerve [11]. Cover the inner portion of the posterior two-third globe of the eye wall. In the structure of retina there is the rods and cones present which is of purplish-red color. The rods are made up of Rhodopsin, derivatives of vitamin A, this are the visual pigment of the rods. The rods and cones are same, but only the protein moiety is different .

2. Optic nerve: The optic nerve is composed of 1 million nerve fibers . This are in charge for the transmitting nerve signal from the eye to the brain. The signal is responsible for the image which is imagine or signal by the nerve to the brain. The topical surface of the nerve, which is visible upon the retina, is called the optic disk .The optic nerve is made of visual fibers [80%] and afferent pupillary fiber [20%]

3. Choroid: Choroid layer is existed behind the retina and it nourishes the retinal quantities also absorbs unused radiations. In the structure of the choroid there is maximum blood flows .

4. **Sclera**: The sclera is the white portion of the eye, which is the first layer of the eye. The sheath is firm. This is done by the tight fibrous membrane to maintain the eye's shape

. 5. Fovea: The most important part of the retina is the fovea. High visual acuity and color vision are functions of the fovea

6. Vitreous: vitreous is present in the center of the retina and lens. The vitreous is in the transparent form like gel and that conquers the inner most part of the eye. The function of the vitreous is to provide the support and proteins to the retina from the ciliary body. The vitreous is attached to the optic disc, detachment caused non-vison threatening.[12]

Physiological barriers to ocular Drug Delivery system [13].

1)The precorneal and corneal gaps contain physiological barriers that prevent the diffusion and

effective absorption of drugs applied topically. The precorneal limitations that cause conventional drugs to have low ocular bioavailability solution drainage, lacrimation, tear dilution, tear turnover, and conjunctival absorption are all examples of ophthalmic dose forms.

2)It has been demonstrated that the most important component in decreasing the drug's contact time with the cornea and, as a result, the ocular bioavailability of topical dose forms is drug solution drainage away from the precorneal area.

3). Within two minutes of administration, the administered dosage in humans departs the precorneal region. 50–75 µl of the eye drops are delivered by the ophthalmic dropper. The eye may contain roughly 30 µl without overflowing across the cheek if the patient does not blink. The cul-de-sac's volume naturally tends to decrease to 7–10 µl6. Nevertheless, the majority of the medication is quickly eliminated through nasolacrimal drainage right after dosage. The medication can enter the systemic circulation through the nasal mucosa thanks to the discharge. The loss is substantial because the conjunctiva has a comparatively high surface area—five times that of the cornea. It has been suggested that the primary possible locations for systemic absorption of medications administered topically are the conjunctival and nasal mucos[13].

Mechanism of Drug release into the Eye[14].

The medication is released via the three mechanisms listed below

1. Diffusion
2. osmosis
3. Bioerosion
4. **Diffusion** : The medicine is continually released through the diffusion mechanism in a predetermined, regulated manner. The fluid from the eye enters the insert when the ocular is inserted, causing the polymer to inflate and causing the chain to relax and the medicine to diffuse.

Osmosis: When eye fluid comes into touch with the diffused and stretched eye insert, the osmosis insert splits into internal and external portions.

Bioerosion: The medicine is released gradually by the erosion of the matrix when the ocular insert comes into touch with tear fluid. The medication is available for dispersion in the ocular insert; however, if it is present in the superficial concentrated form within the matrix, it is thought that drug release will occur in a more regulated manner.[14]

CLASSIFICATION OF OCULAR DRUG DELIVERY SYSTEM .[15]

Type –I and Type -||

Type-| are divided into different type

9. Drug Delivery Systems to Anterior Segment of the Eye – e.g.
    a. Eye-Drops

2)Contact Lens

3)Cul-de sac Inserts

4)Punctual plugs

5)Subconjunctival/Episcleral Implants

2) Drug Delivery Systems to Posterior Segment of the Eye 1.Intravitreal Implants

2. Injectable Particulate Systems

3. Eye-Drop

3) Physical Devices

1. Iontophoresis

2. Micro-Electromechanical Intraocular Drug Delivery Device

Type-II are divided into different t

1)Conventional delivery systems

1. Eye drop

2. Ocuserts and Lacrisert

2) vesicular system

Liposomes.

2.Pharmacosomes

3.Nisosomes andDiscomes

3.Control delivery systems

1) Implant

2) Dendrimer

3)Nanosuspensions

4) Microneedle

5) Iontophoresis

6)Mucoadhesive polymer

4) particulate (Nanoparticles and micro particles)

5)Advanced delivery system

1) cell encapsulation

2)stem cell therapy

3) protein and peptide therapy .[15]

Approaches to Improve Ocular Bioavailability are :

1. **dendrimer:**dendrimers have a multibranched, nanoscale polymeric web that resembles a star. they also differ and range in molecular weight. to create a system that is cost-effective to use in the context of drug transporting, these systems must optimize their primary properties, such as functional groups, molecular geometry, charge of surface, and molecular weight. lipophilic or hydrophilic medications may be encapsulated due to the unique structure of dendrimers. dendrimers with poly(amidoamine) (pamam) as its structural foundation are frequently used for ocular route purposes. pilocarpine nitrate and tropicamide were created as pamam dendrimers for the medications' ocular miotic and mydriatic effects, respectively.[16]
2. **2)in situ -forming gel :** the droppable gels react to changes in the environment by becoming liquid when they are injected and then changing into a viscoelastic gel in the ocular cul-de-sac. the degree of patient acceptability is increased. it increases the drug's ocular bioavailability and prolongs its duration in the eye. the phase transition of droppable gels can be influenced and initiated by a number of variables, including ph, temperature, and ionic strength. a change in temperature can result in poloxamers, methyl cellulose, and smart hydrogeltm; a change in ionic strength can result in gelrite and alginate; and a change in ph can result in cap latex cross-linked polyacrylic acid and its derivatives, carbomers, and poly-carbophil.[17]
3. **niosomes:** bilayer vesicles called niosomes are made up of nonionic surfactants. outstanding customization of hydrophilic and lipophilic compounds. niosomes change visual bioavailability, promote more time spent at home, and reduce alkaline drainage. chitosan and the polymer carbopol coat the niosome levels.[18]
4. **ocular inserts:** by maintaining an appropriate medication center in the target tissues, ocular augmentations provide more regulated, sustained, and continuous drug delivery. it lowers the necessary prescription maintenance. it results in cautious prescription dosage. various technologies were used to organize different visual augmentations to provide hydrogel, nonerodible, erodible, and dissolvable enhancements.[18]
5. **microspheres and nanoparticles:** due to their substantially slower rate of ocular particle removal, microspheres and nanoparticles greatly improve medication absorption in the eye as compared to eye drop solutions. nanoparticles may be a particularly comfortable ophthalmic prolonged action delivery technology since patients tolerate smaller particles better than larger ones. however, it has been documented that albumin microspheres produce negative eye reactions.[19].
6. **liposomes**: phospholipids called liposomes are utilized to direct medications to particular bodily locations. they enhance bioavailability and offer prolonged, regulated medication administration.[20]
7. **mucoadhesive substances :**macromolecular hydrocolloids having a variety of hydrogen-bonding hydrophilic functional groups (such as carboxyl, hydroxyl, amide, and sulfate groups) are the most widely utilized bioadhesives. hui and robinson were the first to show how bioadhesive polymers may be used to increase progesterone's ocular bioavailability.[21]

Niosomes [23].

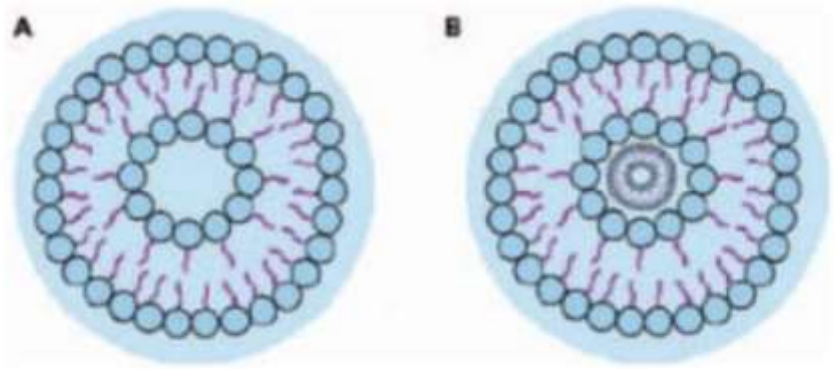

Figure 3. Schematic representation of unilamellar liposome (a) and multilamellar liposome (b).

8. **Microneedle:**. A blunt needle is fastened to a flexible, tapered tube, which is equipped with a microneedle or micropipette at the end for insertion into tiny blood vessels. These needles can be used to apply a drug or carrier system to the sclera or the "suprachoroidal space," which is the tiny area between the sclera and choroid.[[23]]

Conclusion:

The ocular insert is a major improvement in the treatment of eye diseases. Numerous benefits are offered by this occusert system, including improved patient compliance through decreased dosage frequency, prolonged and regulated medication delivery, and lower dosages, which lessen side effects. Consequently, it seems logical to examine nonconventional techniques such as nanotechnology, microspheres, liposomes, suitable prodrug in situ forming gel, and iontophoresis for successful delivery and to further optimize ocular absorption and reduce side effects.

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