International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 322-327 www.ijprajournal.com ISSN: 2456-4494

Novel Drug Delivery System in Opthalmic Diseases.

Miss. Darshana Ashok Shambharkar[1*]
Swati S. Pardhi, Pragati B. Hasbe, Suraj R. Sadawarte.
Student of Ishwar Deshmukh Institute of Pharmacy,Digras, Maharastra, India.

Submitted: 01-07-2022 Accepted: 14-07-2022

ABSTRACT:
Occular drug delivery system (ODDS) is a dosage form, vehicle or system intende for instilling, administration or delivering to eye against any disorder involving or affecting vision.Ideal ophthalmic drug delivery must be able to sustain the drug release.
Eye is a unique and complex organ, the major challenge faced by today's pharmacologist and formulation science is ocular drug delivery. Controlled drug delivery to eye is one of the most challenging fields of pharmaceutical research. Topical eye drop is the most convenient and patient compliant route of drug administration, for the treatment of anterior segment diseases. Occular drug delivery system has always been aimed, where the bioavailability of a drug is maintained for a longer period of time and the enhancement of bioavailability .These novel drug delivery system on the benefits of various ocular drug delivery system, likes microemulsion, liposomes, nanoparticle, ocular inserts, implants, gels and use of viscosity enhancers, eye ointments, etc. The route of choice for the treatment of ophthalmic diseases is by the topical route because of the blood ocular barrier. The most commonly utilized preparations of ophthalmic dosages forms are the solution, suspension and ointments. The data presented in this review will act as a good information resources for the develop ocular drug delivery system for sustain release and control the drug in the anterior or posterior segment of the eye and also enhances the bioavailability of the drug.
KEYWORDS: Enatomy of the eye, Barriers, Formulasions.

I. INTRODUCTION

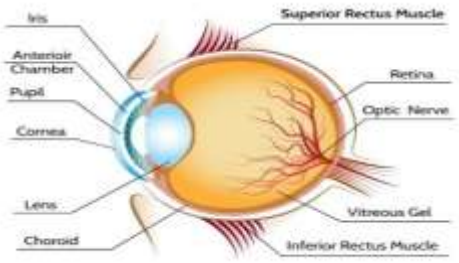
Human eye is the complex structure with an unique anatomy and physiology. eye is the most easily accessible site for topical administration of a medication. Human eye has a spherical shape (23mm diameter). The structure of human eye can be divided into two main part: Anterior segment
Posterior segment

Anterior segment of the eye occupies approximately one third and portion is occupied by the posterior segment.Anterior segment include cornea, conjunctiva, aqueous humor, iris, ciliary body and lens.
Posterior segment of the eye include; sclera, choroid, retinal pigment epithelium, neural retina, optic nerve and vitreous humor.The anterior and posterior segment of eye is affected by various vision threatening diseases.

Structural components of eyeball divided into three layer:
Outermost layer: Transparent cornea and opaque sclera.
Middle layer: Iris anteriorly, choroid posteriorly and sclera.
Inner layer: Retina **Composition of an eye:**
Water- 98%, solid- 1.8%, organic element(protein)- 0.067%, sugar- 0.65%, NACL- 0.66, other mineral elements sodium, potassium and ammonia- 0.79.

Different eye parts:

a. Pupil:Pupil generally appears to be the dark center of the eye, control the amount of light entering the eye.
b. Cornea: act as principal refractive element of an eye. Surface of the adult cornea has a radius of approximately 8mm.



c. Ciliary boby:Located behind the iris, which focuses the lens.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 322-327 www.ijprajournal.com ISSN: 2456-4494

d. Retina:The nerve layer lining the back of the eye. It is sensitive the light.
e. Sclera:White outer coatof eye, surrounding the iris.
f. Vitreous humor:The clear, gelation substance filling the central cavity of the eye.
g. Iris:Focuces light rays onto the retina.
h. Choroid: Layer containing blood vessel that lines the back of eye and is that located between the retina.

Aim of the optimization of ocular drug delivery system:

i. Improving sustain the drug release. ii. Increases the retention time of drug. iii. Enhancing site specification.
iv. Minimal systemic side effects.

Mechanism of ocular drug absorption: topically applied drug can be absorbed from, two mechanisms are follows:-

A. Corneal absorption:- Drug through cornea. It is the outermost layer of anterior segment of eye. It is the rate limiting barrier.Transcellular transport is the major mechanism between corneal epithelium and stroma.corneal absorption for lipophilic drug. pore size 60a, only access to small ionic and hydrophilic molecular appear to gain access to the anterior chamber through paracellular pathway.
B. Non-cornealabsorption:- It involves penetration across the sclera and conjunctiva into intra ocular tissue. This mechanism of absorption is usually non-producive because penetrated drug is absorption by general circulation. Significant for permeability.

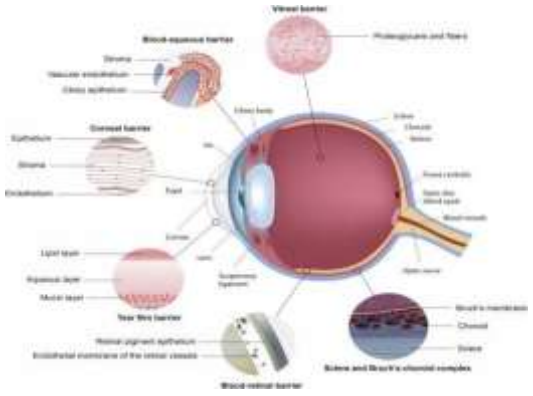
Factors affecting intraocular drug molecules with poor corneal bioavailability:- 1.Non-productive absorption.
2. Inflow & outflow of lacrimal fluids.
3. Corneal barrier.
4. Active ion transport at cornea.
5. Naso-lacrimal drainage.
6. Interaction of drug with protein of lacrimal fluids. **Advantages of ocular drug delivery system:-** 1.They have quick absorption and effect.
2. Less visual & systemic side effect.
3. Better patient compliance.
4. It can be easily administered
5. Reduces dose frequency.
6. Sustain & control release of drug can be achived. **Disadvantage of ocular drug delivery system:-** 1.Poor bioavailability.
2. Instability of the dissolved drug.
3. Residence time of drug at eye surface is less.
4. Short contact time of drug solution. **Limitations of ocular drug delivery system:-** 1.Interference with vision.
2. Termination of the dosage form is not possible during an emergency.
3. Faces difficulty in placement & removal dosage. **Ideal characteristics of ocular drug delivery system:-** 1.It should be stable.
2. Buffer – pHadjustment.
3. Easy of manufacturing.
4. Non-irrigation.
5. It should be isotonic to body fluid.
6. It should be sterile.
7. Lack of explosion.

Barriers to ocular drug delivery:-It is difficult to achieve relevant therapeutic doses within the eye is primarily due to the presence of multiple barriers. These barrier can be broadly classified as anatomical &physiological barriers. Ocular drug delivery suffers from the following barrier effects:-

1.**Anatomical barriers**: When a drug is topically administered, there are two routes of absorption.
- Cornea route
- Non- corneal route

Cornea route:-The cornea is multilayered tissue that is mainly composed of five sections:- ✓Endothelium ✓Browman's membrane
- Descemet's membrane
- Epithelium- principle barrier ✓Stroma- multiple layer of collagen fibers. Non- corneal route:- bypass the cornea.

Conjunctiva:- it is more permeable than cornea for hydrophilic molecules.



2. **Physiological barriers:-**Bioavailability of topically administered drug is reduces by precorneal factors. Precorneal factor are tear

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 322-327 www.ijprajournal.com ISSN: 2456-4494

dilution, solution drainage, increased lacrimation & tear turnover. The eye's primary line of defense is it's tear film.

3. **Blood ocular barrier**:- Blood ocular barrier are used for the protection the eye from xenobiotics. It is present in the bloodstream. It comprises of two parts:

i. Blood- aqueous barrier : It is composed endothelial cells i. e. Present in the middle layer of the eye below iris, ciliary body, sclera & choroid. It is used to prevent the entry of hydrophilic drug present in plasma to the aqueous humar. ii.Blood – retina barrier:- Non – fenestrated capillaries of the retina circulations & tight junctions between retinal epithelial cells preventing passage of larger molecules from chorio- capillaries into retina.

4. **Drug & dosage from related factors:**- The rate absorption depend on the physical properties of drug molecules.

i. Solubility:-Solubility is dependent on the pKa of the drug &pH of lachrymal fluid. Hence cationic species rate to their anionic counter parts.

ii. Lipophillicity:- Lipophilic drug easily permeate through epithelial layer of cornea. lipophilicity and corneal permeability display Sigmoidal relationship. Thise is because of the differential permeability of the different layer of cornea towards lipophilic drugs.

iii. Molecular weight& size:-Molecules having diameter less than 2 nm. Molecular weight less than 500 doltons readily permeate through cornea.the weight & size of molecules play a critical role in deciding its overall permeability through paracellular route.

Methods to overcomes barriers to ocular drug delivery:- Drug delivery through topical or systemic route feces a number of challenges limiting their success. To overcome barriers in ocular drug delivery, two distinct yet complimentary approaches can be used. The first approach involve using alternative delivery route to convential ones allowing for more direct access to intended target site. Second approach involve development of novel drug delivery system providing better permeability and controlled release at target site.

Alternate drug delivery system:-

1. Intra – vitreal injection:- In this route, the medication is delivered injections in the vitreous humor of the eye. Formulation such as; solution, suspension or a depot formulation can be administered through this route. Avoid both cornea & sclera blood vessels. Drug elimination occurs either through the retina or the anterior chamber through the aqueous humor following a first order rate of decline. This rate elimination has a linear correlation with the molecular weight of the drug. IVI administration is associated with advers effect such as; retinal detachment, cataract, hyperemia. Sustained release drug delivery system can help by lowering frequency of administration and thus allow for better patient complains.
2. Subconjunctival injection:- The drug is delivered beneath the conjunctival membrane to each sclera. The drug is administered to the mucus membrane, open space of the eyelids. Avoid both cornea & conjunctiva allowing the drug. excellent route for delivering hydrophilic drug. it has lesser side effect than IVI.
3. Intracameral injection:- Intracameral route is similar to intravitreal injection, but this injection delivers drug to the anterior & posterior chambers. It can be demonstrated by injecting an anesthetic agent into the anterior chamber of the eye , usually during surgery. It is an efficient & often a more cost effective method of delivering antibiotics.
4. Retrobulbar &Peribulbar route:-Retrobulbar injection is given through eyelid and orbital fascia and place the drug into retrobulbar space. Thise route is especially applicable for the delivery of anesthetic agent. It may damage the optic nerveand thus required proper expertise and equipment.

Peribulbar injection is given above or below the globe. It is used for delivering anesthesia in cataract surgery. It is a safer route compared to the retrobulbar route with reduced risk of injury. rise in IOP have been reported.

Formulations for ocular drug delivery system:-

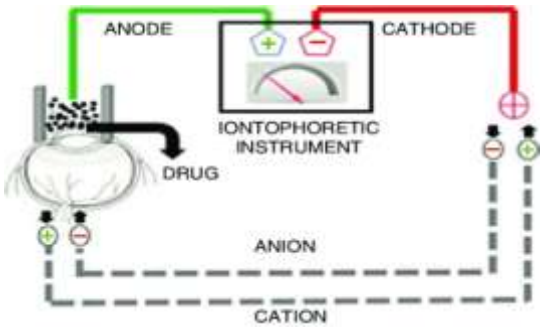
1. Conventional delivery system
a. Eye drops
b. Ointment and gels
c. Ocuserts and lacriserts
2. Vesicular system
a. Liposomes
b. Niosome
3. Controlled delivery system
a. Implants
b. Iontophoresis
c. Dendrimers
d. Microemulsion
e. Nanosuspension
f. Microneedle
g. Mucoadhesive polymers

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 322-327 www.ijprajournal.com ISSN: 2456-4494

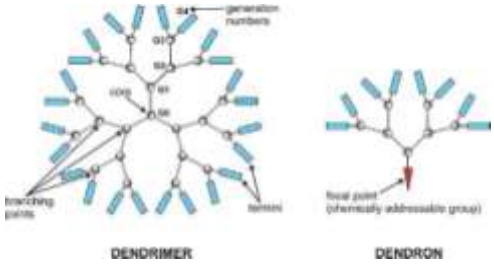
h. Contact lenses

- **Eye drops :-**
  - Administered as solutions, emulsion and suspention.
  - Retention is affected by properties like hydrogen ion conc., osmolality, viscosity and instilled volume.
  - Low absoption of dose .
  - The dose is mostly absorption via the conjunctival and nasal blood vessels.
- **Ointment and gels:-**
  - Semisolids are useful for prolongation of drug contact time with the external ocular surface.
  - The major drawback of thisdosage form like, blurring of vision & matting of eyelids can lit its use.
- **Liposomes:-**
  - Biodegradable, non –toxic and amphiphilic delivery system, consists of phospholipids & cholesterol.
  - Offers better permeability of entrapped drug.
  - Sustained release of drug into vitreous and retina-choroid compeartment and avoids non-targeted tissue.
- **Niosomes and discomes:-**
  - These are bilayer structure which can entrap both hydrophilic and lipophilic drugs.
  - Exhibit low toxicity and are chemically stable.
  - Discomes contains non-ionic surfactant.
  - These system not to pass through systemic circulation. **▪Implant:-**
  - Effective for cytomegalovirus retinitis.
  - Non-biodegradable polymers need surgery.
  - Biodegradable polymer (poly lactic acid) are safe & effective to deliver drug in vitreous cavity and show no toxic signs.

- **Ocular Iontophoresis**:-
  - Direct current drives charged molecules of the drug into cell or tissue.
  - Positively charged drug are driven into the tissue at the anode & vice versa.
  - It is fast, painless and safe but it can also deliver high conc. of the drug to a specific site.

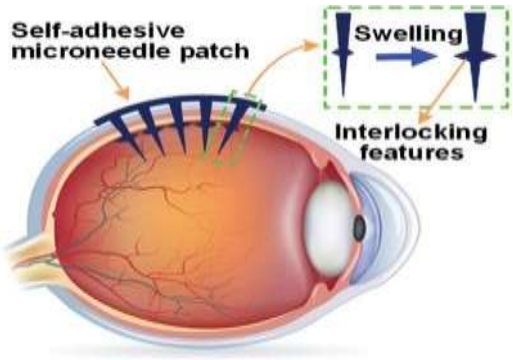


- **Dendrimers:-**
  - Tree-like," nano-structured polymers and have better water-solubility, bioavailability and biocompatibility.
  - They are attractive system for ocular drug delivery due to their nanosized range, ability to display multiple surface group that allows for targeting and easy preparation.



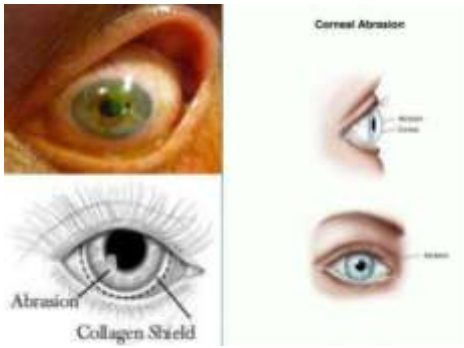
- **Microemulsion:-**
  - Thermodynamically stable-phase transition system, which possess low surface tension and small droplet size (5200nm).
  - Offer high drug absorption and permeation, and provides drug delivery to posterior segment of eye.
- **Nanosuspensions:-**
  - Efficient delivery of hydrophobic drug and enhanced the rate and extent of ophthalmic drug absorption.
  - The intensity of drug action with significant extended duration of drug effect.
- **Microneedles:-**
  - Minimally invasive, and a feasible vehicle for sustained drug delivery.
  - Delivery drug into the sclera (posterior segment) to treate diseases and avoid the complications associated with intraocular injection and systemic administration.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 322-327 www.ijprajournal.com ISSN: 2456-4494



- **Collagen shields:-**

- Disposable,cross-linked, shortterm therapeutic bandages lens for cornea that conformsto shape of eye.
- Shield are sterilized by gamma irradiation, deliver drugs and promote corneal epithelial healing.
- Soaked in a water-soluble antibiotic and steroid solution prior to their placement and biocompatible.

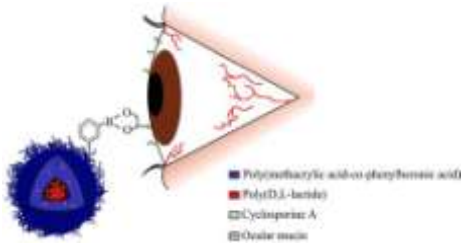


- **Contact lenses:-**

- Ocular contact lenses offers correction of refractive error of eye.
- Therapeutic lenses are often used to aid corneal wound healing in case of infection in prolonged manner.
- Increase residence time of drug in ocular region.
- Eg; Bionite

- **Mucoadhesive system:-**

- Macromolecular hydrocolloids having hydrophilic function group (hydroxyl, carboxyl, amide and sulphate) involve in electrostatic interactions.
- Mucoadhesive system containing levobetaxolol hydrochloride and poly acrylic acid have been developed for the treatment of glaucoma.

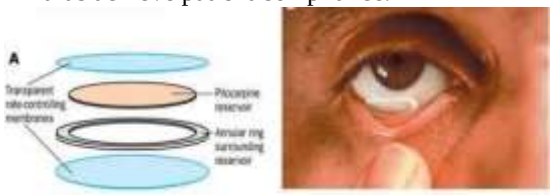


- **Ocuserts and lacrisert:-**

- Ocular insert (ocusert) is a sterile, thin, multilayered, solid or semisolid consistency sac.
- Prolong residence time of drug in controlled release manner.
- Delivers at constant rate by diffusion mechanism.
- Generally all type of ocuserts consist of three components namely:

1. A central drug reservoir
2. Rate controlling membrane
3. An outer annular ring meant for easy handling

- Ocuserts increase corneal contact time, prolong duration of action, improve bioavailability, reduces the frequency of administration and thus achieve patient compliance.



- Lacrisert is a sterile, rod shaped device to treat dry eye syndrome and keratitis sicca.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 322-327 www.ijprajournal.com ISSN: 2456-4494

II. CONCLUSION

New ophthalmic delivery system include ocular inserts, collagen shield, ocular film, disposable contact lens and other Novel drug delivery system for improving bioavailability. The novel advanced delivery system offer more protective and effective means of the therapy for various diseases of eyes. The primary requirement of a successful controlled release product focuses on increasing patient compliance. This types of dosage forms are used now a day in combat glaucoma, dry eye syndrome, etc.

REFERENCES

[1]. Vyas SP, Khar KR. Targeted and controlled drug delivery system. 1st ed. Delhi: CBS publishers and distributors; 2002.
[2]. Kumari A, Sharma PK, Garg VK. Advancement in therapy of eye diseases. Journal of Adv Pharma Tech. and res [internet]. 2010 Nov; [cited 2014 July 12];1(3):291-6.
[3]. Available from:
[4]. http://www.japtr.org/temp/JAdvPharmTechR e s13291-3119373_083953.pdf
[5]. Palani S, Joseph Nisha Mary, Goda CC, Zachariah Anish, Ayenew Zelalem. Ocular drug delivery : a review. Int J Pharm Sci Res 2010;1:1:-1.
[6]. Le Bourlais C, Aear L, Zia H, Sado PA, Needham T, Leverge R. Ophthalmic drug delivery system recent advances. Prog Retin Eye Res 1998;17:33-58.
[7]. Bawa, R., Ocular insert, IN: Ophthalmic drug delivery system, Marcel Dekker, Inc., New York (Mitra.A.K edr), 1993; 58:223.
[8]. Act by imbibing water from cornea and conjunctiva and from a hydrophilic film which lubricates the cornea.