REVIEW ON OCULAR DRUG DELIVERY SYSTEM AND ITS DEVICES

Available online at www.ijdra.com

REVIEW ARTICLE

Nikhil Gulati*, Vanya Dwivedi.

Department of Pharmaceutics, Jamia Hamdard, New Delhi, India

**Corresponding Author's E-mail: nikhil.gulati@outlook.com*

ABSTRACT

Ocular drug delivery system for the treatment of eye diseases has become popular and feasible in the past few years. Improving ocular contact time, enhancing corneal permeability and site specificity are the key points for the optimization of ocular drug delivery. Use of polymers such as ethylene vinyl acetate copolymer can increase the solution viscosity and decrease the drainage of solution, thereby increasing the contact time and its bioavailabilty. There are various types of ocular drug release system such as ocusert, contact lenses, diffusional inserts which falls under the category of non-erodible ocular controlled release system, lacrisert, soluble ocular delivery implant(SODI),minidisc which falls under the category of erodible ocular controlled release system; nanoparticles; liposomes.

Episcleral, intrascleral and suprachoroidal routes have the advantage of bypassing the main barriers to topical drug penetration. This type of delivery system provides a controlled release of drug for a long period of time. This type of delivery system has good patient compliance. Acuvue, lacrisert; biomedics are the most common marketed products of ocular drug delivery system.

This manuscript will review the recent research advances on ocular drug delivery system and their types.

Keywords: ocular drug delivery system, bioavailability, ethylene vinyl acetate copolymer; episcleral, intrascleral and suprachoroidal routes of drug delivery; erodible and non erodible ocular controlled release system.

INTRODUCTION

Key points for the optimization of ocular drug delivery

- Improving ocular contact time
- Enhancing corneal permeability
- Enhancing site specificity

Mechanism of ocular absorption

The two mechanisms are as follows :Non corneal absorption : Penetration across Sclera and Conjunctiva into Intra Ocular tissue. It is non-Productive because penetrated drug is absorbed by general circulation.

Corneal absorption: Outer Epithelium: rate limiting barrier, with pore size 60å, only access to small ionic and lipohilic molecules.

Trans cellular transport: transport between corneal epithelium and stroma. (1)

Factors affecting intraocular bioavailability

- Inflow and Outflow of Lacrimal fluids
- Efficient naso-lacrimal drainage.
- Interaction of drug with proteins of lacrimal fluid.
- Dilution with tears

Role of polymers in ocular drug delivery system: polymers increase the Solution Viscosity thereby decreasing the solution drainage.

Polymer Mucoadhesive Vehicle: Retained in the eye due to non-covalent bonding between with conjuctival mucine. Mucine is capable of picking of 40-80 times of weight of water.

Role of mucoadhesive in ocular drug delivery system

- Mucoadhesive retained in eye by non covalent bonding.
- Extends pre ocular residence time
- Better ocular absorption

Classification of ophthalmic dosage form

Ophthalmic dosage form is classified into two categories (2):

Based on route of administration: **Topical Solution**: Multiple Dose container With Preservatives.

Intra-ocular Solution: For Surgery, Single dose, without preservative.

Ophthalmic Solution Injections: Intra-ocular injection, given in eye tissues, without preservative.

Based on physical form:

- Aqueous Solution.
- Suspension
- Ointments.
- Gels.
- Eye Lotions.
- Solid Insert

Ophthalmic inserts: Solid or semisolid in nature placed in a lower fornix composed of polymeric matrix containing a drug.

Advantages:

1. Accurate dosing.
2. Absence of preservative.
3. Increase in shelf life due to absence of water.

Disadvantages:

1. Perceived by patient as foreign body.
2. Movement around the eye.
3. Occasional loss during sleep or while rubbing eyes.
4. Interference with vision.
5. Difficulty in placement and removal. (3)

Types of ocular controlled release system

1) **Non erodible**
   - Ocuserts
   - Contact lenses
   - Diffusional inserts
2) **Erodible**
   - Lacrisert
   - SODI
   - Minidisc
3) **Nanoparticles**
4) **Liposomes**

Non erodible

Ocuserts:

- Developed by Alza Corporation.
- Oval flexible ocular insert
- Release Rate: 20-40 micrograms/hour for 7 days. It consists of annular ring impregnated with Ti02 for Visibility.
- Merits of Ocuserts: controlled rate of delivery, greater drug absorption.
- Demerits of Ocuserts: Patients uncomfort.
- Placement and removal of inserts. (4)

Contact lenses:

Pre-soaked Hydrophilic lens.
Drug Release: within first 30 minutes.
Alternate approach: incorporate drug either as solution or suspension of solid monomer mixture.

Release rate is up to 180 hours.

Diffusional Inserts:

Central reservoir of drug enclosed in Semi permeable or micro porous membrane for diffusion of drug. Diffusion is controlled by lacrimal fluid penetrating through it. It prevents continues decrease in release rate due to barrier. (4)

Release follows: Zero order kinetics

Erodible inserts

Lacrisert: Sterile, Rod Shaped device.

Composition: HPC without preservative.
Weight: 5mg
Dimension: Diameter: 12.5mm, Length: 3.5mm
Use:-Dry eye treatment, Keratitis Sicca.

SODI(soluble ocular delivery insert)

Small water soluble developed for Cosmonauts by soviet scientists who could not use their eye drop in weightless conditions.

Composition: Acryl amide, Vinyl Pyrolidone, Ethylacrylate.

Weight 15-16 mg.

In 10-15 sec Softens; in 10-15 min. turns in Viscous Liquids; after 30-60min. Becomes Polymeric Solution.(4)

Advantages of SODI:

Single SODI application replaces 4-12 eye drops Instillation or 3-6 application of Ointments.

Once a day treatment of Glaucoma and Trachoma

Minidisc: It is made up of counter disc with convex front and concave back surface in contact with eye ball.

Composition:

- Silicon based pre polymer.
- Hydrophilic or Hydrophobic.
- Drug release for 170 hr.
- Further increase in gentamycin sulphate to 320 hrs.

Gamma irradiation and heat exposure may decrease release rate due to additional cross linking of polymer matrix.

Nanoparticles : For water soluble drugs.

- Size: 10-1000nm
- Drug is Dispersed Encapsulated or Absorbed.
- Produced by Emulsion Polymerization
- Chemical initiation,
- Gamma irradiation, visible light
- Polymerization is carried out by:
- Emulsifier stabilizes polymer particle
- Polymer used is Biodegradable.

E.g.:- Nanoparticle of Pilocarpine enhances Miotic response by 20-23%.

Liposomes: Biodegradable, Non-toxic in nature.

- Vesicle composed of lipid membrane enclosed in an aqueous volume.
- Formed when matrix of phospholipids is agitated in aqueous medium to disperse two phase.
- Phospholipids used are: Phophotidylcholine, Phophotidicacid, Sphingo -myline, Phosphotidyleserine, Cardiolipine.(4)

Advances in ocular drug delivery system

Ophthalmic gel for pilocarpine

• Poloxamer F127 (low viscosity, optical clarity, mucomimetic property)

• Solution at room temp but forms gel when instilled into eye thereby enhancing time of contact. (1)

Ophthalmic prodrug

• Dipivalyl epinephrine (Dipivefrin)
• Lipophilic drug increase in corneal absorption.
• Esterase within cornea and aqueous humour.

Continuous delivery system based upon the osmotic property

• Thin flat layer, contoured three-dimensional unit.
• Conform to the space of the upper conjuctival fornix.
• Delivery of diethyl carbamazine in ocular onchocerciasis

Gel delivery system

• Biodegradable polyisobutyl-cyano acrylate (PIBCA) colloidal particulate system of pilocarpine to incorporate it into a Pluronic F127 (PF 127)-based gel delivery system.

Mucoadhesive Polymer.

• Mucoadhesive polymer, the tamarind seed polysaccharide as a delivery system for the ocular administration of hydrophilic and hydrophobic antibiotics. (5)

NANOPARTICLES

Study using nanosphere done on system constituted of pilocarpine-loaded nanosphere of polymethylmethacrylate acrylic acid copolymer by Gurny et al.developed pH sensitive

nanoparticles for pilocarpine and result found to be promising.In another study binding of pilocarpine to poly butyl cynoacrylate nanoparticles enhanced the miotic response by about 22 to 33 %. (6)

CONCLUSION

•Very few advanced ocular drug delivery systems have been commercialized.

•The performance of these new products, however, is still far from being perfect.

•More clinical studies are necessary to provide further information and insight to these advanced ocular drug delivery systems.

ACKNOWLEDGEMENT

We would like to acknowledge the support of our faculty who helped us in every aspect. We are grateful to the teachers who have motivated us for choosing this topic and spent extra time for helping us to achieve clearer structure.

CONFLICT OF INTEREST

Author declares that there are no conflicts of interest.

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. Available from: http://www.japtr.org/temp/JAdvPharmTechRes13291-3119373_083953.pdf
3. Remington G. The science and practice of pharmacy.1st ed. Pennsylvania: Mack publication Company: 1563-1567.
4. Tangri P, khurana S. Basis of ocular drug delivery system. Int J Pharm Biomed Res [Internet]. 2011 Oct [cited 2014 Jul 05]; 2(4):1540-1541.Available from: http://www.ijrpbsonline.com/files/RV15.pdf
5. Patel V, Agarwal YK, Current status and advanced approaches in ocular drug delivery system. J Global Trends Pharm. Sci [internet]. 2011 Apr [cited 2014 July 14]; 2(2):131-48. Available from : http://www.jgtps.com/Patel.pdf
6. Rathore KS. Review on insitu-gelling opthalmic drug delivery system. Int J Pharm Pharm Sci [Internet]. 2010 Aug [cited 2014 Jul 10]; 2(4):30-4. Available from: http://www.ijppsjournal.com/Vol2Suppl4/875.pdf

