ISSN (print) : 2589-9120
ISSN (online) : 2589-9139

International Journal of Medical Science and Applied Research (IJMSAR)

Available Online at: https://www.ijmsar.com

Volume – 2, Issue –6, November – December - 2019, Page No. : 33 - 38

Recent Advancement of Discosomes in Ocular Drug Delivery

[1]Shah Zeel, UG Student, Parul Institute of Pharmacy and Research, Parul University, Limda, Vadodara, Gujarat, India.

[2]Patel Bhavisha, Assistant Professor, Department of Pharmacognosy, Parul Institute of Pharmacy, Parul University, Limda, Vadodara, Gujarat, India.

Corresponding Author: Patel Bhavisha, Assistant Professor, Department of Pharmacognosy, Parul Institute of Pharmacy, Parul University, Limda, Vadodara, Gujarat, India.

Type of Publication: Original Research Article

Conflicts Of Interest: Nil

Abstract

Topical eye drop is most useful and patient adaptable route of administration, especially for treatment of anterior segment diseases. The ocular drug delivery is most challenging venture faced by pharmaceutical scientist during the past. Various preparations of eye such as suspension, solution, etc. now available has various disadvantages such as blurred vision various variability.[1] Eye is remarkable organ due to its drug disposition features. In past years, ocular drug delivery research has been advancing in making novel, safe and patient adaptable formulation and drug delivery techniques. Posterior ocular delivery researches were focusing on development of drug releasing devices and nano formulations for treating long term vitro retinal diseases. These novel devices are easy to formulate no irritation and have high precorneal residence, sustain release which enhances ocular bioavailability. Currently, nanotechnology formulation is made and also strategies employing insitu gels contact lens etc[2] So, ocular drug delivery is most interesting and exigent venture and the challenge to formulator is to make protective obstruction without damaging the tissue.

Keywords: Ocular drug delivery, Conventional drug delivery system Nano Micelles, Eye emulsions, Discosomes.

Introduction

Eye is the most interesting organ consists of two parts: anterior and posterior segment. Anterior chamber of eye has iris, cornea, conjunctiva, aqueous humor, etc and posterior chamber of eye has sclera, choroid retina, optic nerve, vitreous humor etc. Diseases that affect anterior part are glaucoma, cataract and from posterior part includes diabetic retinopathy and age- related muscular degeneration. Topical is more preferred over systemic administration, any drug molecule is administered by the ocular route to cross the precorneal barriers.[3,4] Eye is the first barriers that slow penetrate of active ingredient into eye. The ocular bioavailability is low with topical administration. Various anatomical and physiological limitations like drainage, blinking, and ocular static and impede deeper ocular drug permeation. Different route of administration periocular, systemic and intravitreal in which intravitreal is mostly used to treat posterior ocular diseases. Repeated eye puncture done with intravitreal has side effects like hemorrhage, endophthalmitis. The transscleral drug delivery with periocular is alternative mode of drug delivery. Ocular obstruction to transscleral drug delivery include: RPE, episclera, choroid,etc.

To overcome the ocular drug delivery barriers and improve ocular bioavailability, various drug delivery systems are:

1. Conventional drug delivery includes eye drop, suspensions, aqueous, isotonic solution gels, ointment.

2. Acute corneal permeability of drug is low and small corneal contact time of 1- 2 minute in order to overcome, nanoparticle, liposome, nanosuspension.

3. Nanocarriers based delivery system includes microspheres and nanoparticle, Liposomes, Niosomes, pharmacosomes.

4. Emerging new drug delivery system such as micro emulsion, polymers, hydro gels, collagen shield.

New approach for treatment of macular degeneration including intravitreal small interfering RNA and inherited retinal degeneration. Also has nano technology, stem cell therapy, gene therapy, ribozyme therapy.[5]

To optimize the ocular drug delivery system:

1. Good corneal penetration.
2. Prolong contact time with corneal tissue.
3. Simplicity of instillation for the patient.
4. Non irritant and comfortable form suitable rheological preparation and concentration of viscous system.

Non-homogeneity, caking, settling, etc. Newer drug suspension includes microspheres which has small polymeric particles which are present in liquid carrier medium.

Various Methods of Ocular Drug Delivery System:

1. Conventional Drug Delivery System: [6, 7, 8]

It is used in recent ocular disease treatment and prevention such as suspensions, solutions, Sterile preparation free from particles. Mostly used drugs in ocular therapy. Aqueous preparations made up of foreign active and inactive achieved by application of heat. The batch is made by final addition of sterile water. The stability of formulation is determined by shelf life and cessation dating of product. Ointments In spite of considerable criticism over the efficacy, limitation such as bioavailability, sterility. Major commercial products of this are available in pharmaceutical market.

A. Liquids

Pleasing state of dosage form of eye because the drug in dissolved state results in fastest inclusion from the eye surface.

B. Solution

Advantages

Simplicity of large scale manufacture.

Disadvantages

Rapid elimination so short time interval.

Poor bioavaibility.

Instability and necessity of dissolved drug.

C. Sprays

Use mydriatics alone or in combination in the form of eye spray. These are used for dilating the pupil.

D. Suspension [9]

Ophthalmic suspension is a part of ocular drug delivery which is best suited and has a sustained delivery of dose. Recently, developed drugs are hydrophobic poor solubility in water and other aqueous medium. It includes all excipients and these excipients have different properties. Suspending agents avoid sedimentation and affecting the rheological behavior of suspension. Suspending agents include methyl cellulose, hydroxymethyl cellulose etc. The formulation of ophthalmic suspension has errors.

E. Emulsion[10]

W/o type of emulsion are thermodynamically stable and optical isotropic colloidal system which has wetting property. When administered in eye ,they are converted into liquid crystalline state which causes sustained release of drug. Two types of emulsion:

1. Cationic emulsion: these emulsion increase residence time and decrease contact angle and increase spreading coefficient. In case of back of the eye, novagali designed cationic emulsion for painless topical direction which

causes drug to migrate to retina via Trans sclera route from cornea.

2. Anionic emulsion: This emulsion containing difluprednate has approved for treatment of ocular inflammation. Non- medicated anionic emulsion for eye lubricating purposes.

2. Novel Drug Delivery System Nanotechnology:[11,12,13]

It includes nanoparticle, micro emulsion, Liposomes which are used for various solubility problems. Nanocarriers are critical to exploit the emerging pharmaceutical field and new gene therapy in treatment of ocular diseases.

Microemulsion

It is a dispersion of water and oil that formulated the surfactants and co – surfactants to stabilize surface tension. They are used in ophthalmic preparation as they are easily equipped through emulsification process, stable, sterilized. Micro emulsion is most better than other as the surfactants and co- surfactants increases permeability and at same time increase bioavailability. As mechanism based on adsorption of nanodroplets which act as reservoir on cornea and decrease drainage limit.

Nanosuspension[14]

It is important strategy for hydrophobic delivery of drug because they not only increase rate and extent but also intensity of drug action. They are pure, hydrophobic and suspended in medium. This technology utilized for drug that form crystal which have high energy and are insoluble. Intrinsic solubility charge on drug in lachrymal fluid increase ocular bioavailability. Nanosuspension is incorporated with suitable hydrogen. Advancement in recent years causes desired release in polymeric nanosuspension. The bioerodible and water soluble has sustained and control release of drug. They are prepared by quasi-emulsion and solvent diffusion method.

3. Colloidal Or Vesicular System Of Drug Delivery: [15, 16, 17]

Liposome

Liposome is defined as a structure consists of one or more concentric spheres of lipid bilayer detach by water or buffer compartment. They enhance corneal drug absorption, their ability to contact with cornea and conjunctiva and are desirable for drugs that are poorly absorbed, partition coefficient and solubility due to increase molecular weight and thus increase the ocular drug absorption. Accumulation of drug in cornea could emerge by endocytosis of liposomes. In order to enhance it the dispersion of liposomes by mucoadhesive gel or coating with muco adhesive polymers. So, liposomes are potentially ocular drug delivery due to structural and versatility in unique physical components. But limitation is instability and technical problems to obtain sterile preparations.

Niosomes[18,19]

Niosomes overcome the problem faced in liposome i.e. instability by entrapping both hydrophilic and hydrophobic drugs. They are non –poisonous and do not require special handling. Niosomes are non- ionic surfactants which are useful in both hydrophilic as well as amphiphilic drug. Niosomes fulfill the ocular drug delivery system that not only convenience of drop, localize and maintain drug activity, sustained release and minimum frequency.

Discosomes[20, 21]

Disc shaped Niosomes are known as discosomes. Discosomes are large structures formed by

Solubilisation of Niosomes with a non-ionic surfactant.

Advantages:

• Large size (12-60 μm) prevents their drainage into the systemic pool.

• Better adherence of the system to the cornea.

• Disc shaped provides for a better fit in the cul-de-sac of the eye.

Non-ionic surfactant-based discoidalniosomes (discosomes) of timolol maleate have been reported to be promising systems for the controlled ocular administration of water-soluble drugs, with zero order drug release.

In vivo studies showed that discosomes released the contents in a biphasic profile if the drug was loaded using a pH gradient technique. Discosomes may act as potential drug delivery carriers as they released drug in a sustained manner at the ocular site.

Microneedle [22]

Alternative to topical route to deliver drug to posterior segment shown prominent invtro penetration into sclera and fast dissolution of coating solution after insertion while in vivo drug level higher than the level observed.

4. Advanced Ocular Drug Delivery System.[23, 24, 25]

Gene Therapy

Front line biomedical research to treat blindness arising from corneal diseases. While the second only to cataract which cause vision loss. Various virus such as retro virus, adenovirus are used for gene therapy. Topical delivery to eye is most beneficial way for ocular drug delivery. Retroviral are worn which has high efficacy, do not aptitude to transducer non dividing cell. this drug delivery system prolong contact time with surface of eye and enhance transgenic expression.

Term Cell Therapy

Cell therapies have been emerging for restoration of sight of eyes on two areas such as cornea and retina. Current status are used for management of ocular condition consists of eliminating injurious agents. Another important is use of limbal stem cell transplanted from the source to another patient for renewal of corneal epithelium.

Scleral Plug Therapy[26]

Scleral plug can be implanted painlessly at the parsplana region of eye, made up of biodegradable polymers and drugs and releases effective doses for several months. These sclera plug are effective in treating vitroretinal diseases such as proliferative vitreoretinopathy respond to repeated intravitreal injection and for vitreoretinal disorders.

Ribozyme Therapy

Ribozyme are three dimensional structures having single stranded RNA molecules exhibits catalytic activity and induce cleavage ,ligation and polymerization of nucleotides. Main function is binding to the target RNA moiety and inactivate by removing phosphodiesterase backbone. A disease named, Autosomal dominated retinitis pigmentosa (ADRP) caused by mutation of genes by mutated proteins that leads to apoptotic death of photoreceptor cells.

SiRNA THERAPY[27,28]

Feasibility of using SiRNA for action on choroidal revascularization has been done using SiRNA against vascular endothelial growth factor (VEGF) they are tested in clinical trials. This VEGF or its receptors are for topical delivery to repress corneal revascularization. SiRNA is tool for various potential roles in ocular diseases. SiRNA has been useful in treating and developing various ocular deliveries both in vivo and invitro. Viral gene delivery is also useful but presently it lacks selectivity on target cell type. Therapeutic effects and approaches using SiRNA has been useful in future in modern medicine. New encapsulated SiRNA is developed using liposome, coupled- antibodies and other vesicles.

Future Perspectives

Treatment of ocular chronic diseases has always remained a challenge for the health practitioners and the patients alike. The advent of nanotechnology and its use in devising

newer and effective ocular systems has added impetus to ocular therapy. However the need of the hour is to create stable as well as non-toxic systems which are able to be used for chronic therapies. The futuristic system is essentially be needed to be equipped with better efficacy, controlled release, non-toxic and also cost effective.

Conclusion

New ophthalmic delivery drug system consists of ocular films and inserts, collagen shields, disposable lens and other novel drug delivery system likes nanoparticle ,micro emulsion, Niosomes 20 . An ideal system has efficient and better drug concentration at target tissue for limited period of time with minimum systemic effect. Patient compatibility and acceptance is very important criteria for the design of ocular drug delivery system. Major improvements are required in system like stability, sustained release of drug, large scale manufacturing and many other. A newer drift to the permutation of drug delivery technologies like improving the therapeutic responses of non–efficacious drug. This will give superior dosage forms to the topical ophthalmic application. Among all the drug delivery system, only few commodities have to be commercialized.

References

1. Ding S ,Tien W, Olejnik O.US Patent ,1995;5:474-979.
2. Lang JC, Roehrs RTE ,Jani R . Opthalmic preparation . Lippincott Williams and Wilkins 2005 :1(21):25-35.
3. Gaudana R, Jwala J , Boddu SH, Mitra AK. Recent perspectives in ocular drug delivery. Pharma res.2009;26: 1197-1216.
4. Gallarate M, Chirio D, Bussano R, Peira E , Battaglia L, Baratta F, Trotta M .Development of O/W nanoemulsion for ophthalmic administration of timolol. Int J pharm. 2013;440:126-134.
5. Tajika T, Isowaki A, Sakaki H. Ocular distribution of difluprednate ophthalmic emulsion 0.05% in rabbits. J Ocul Pharmacol Ther.2011;27: 43-49.
6. Lang J , Roehrs R, Jani R, Remington : the science and practice of pharmacy .21 philadelphia : Lippincott Williams & Wilkins ;2009 . ophthalmic preparations ;p .856.
7. Gupta H , Aqil M,Khar RK, Ali A, Bhatnagar A ,Mittal G .Biodegradable levofloxacin nanoparticles for sustained ocular drug delivery. J Drug Target.2011 ;19 : 409 -417.
8. Rajoria G ,Gupta A. In-situ Gelling system : A Novel Approach for Ocular Drug Delivery. AJPTR.2012;2:24-53.
9. Patravale VB, Date AA, Kulkarni RM .Nanosuspension : a promising drug delivery strategy. J Pharm Pharmacol. 2004 ;56 :827 -840.
10. Urtti A. Challenges and obstacles of ocular pharmacokinetics and drug delivery. Adv Drug Delivery Rev. 2006; 58(11):1131-35.
11. Patel A, Cholkar K, Agrahari V, Mitra AK. Ocular drug delivery systems: An overview. World J Pharmacol. 2013; 2(2): 47-64.
12. Del Amo EM, Urtti A. Current and future ophthalmic drug delivery systems. A shift to the posterior segment. Drug Discov Today. 2008; 13(3-4): 135-43.
13. Sahoo SK, Dilnawaz F, Kumar SK. Nanotechnology in ocular drug delivery. Drug Discov Today. 2008; 13(3-4): 144-51.
14. Bourlais CL, Acar L, Zia H, Sado PA, Needham T, Leverge R. Ophthalmic drug delivery systems - recent advances. Prog Retin Eye Res. 1998; 17(1):33- 58.
15. Shell JW. Cut. & Ocular Toxicol. journal of toxicology 1982;1(1):49-53.
16. Patton TF, Robinson JR. Journal of pharmaceutical sciences., 1975; 65:125-135

17. Wood RW, Lee VHE, Kreutzer J , Robinson JR. International Journal of Pharmaceutics., 1985;23:175-183.
18. Kaur IP, Garg A, Singla AK, Aggarwal D. ―Vesicular systems in ocular drug delivery: an overview‖, International Journal of Pharmaceutics., 2004; 269:1-14.
19. Wadhwa S, Paliwal R, Paliwal SR, Vyas SP. ―Nanocarriers in ocular drug delivery: An update review‖,Current Pharmaceutical Design., 2009; 15: 24-50.
20. Hui HW , Robinson.JR. International Journal of Pharmaceutics., 1985; 26:203-213.
21. Banker GS, C.T. Rhodes, Dekker. M. Modern Pharmaceutics 2007:415-43.
22. Yusuf AaK, Lehmussaari H. ―Industrial Perspective in Ocular Drug Delivery‖, Advanced Drug Delivery Reviews., 2006; 58: 58-68.
23. Ali A, Sharma SN. ―Modified the same apparatus by introducing jacketed flask and eye‖, Ind JHospPharm.,1991; 28:165-169.
24. David NM, Farr SJ HJ, IW. K. ―Evalution of mucoadhesive polymer in ocular drug delivery. I.Viscous solution‖, Pharmaceutical research., 1991; 8:1039-1043.
25. Bhargava HN, DW N, BJ. O. ―Topical suspensions Pharmaceutical dosage forms:. Disperse systems‖, Marcel Dekker 1996;2:183–241.
26. Udwig A, van ootengm M. ―Influence of viscolyzers on the residence of ophthalmic solution evaluated by slit lamp fluorometry‖, Pharmaceutical science., 1992; 2:81-87.
27. Rishna N, J. BFA. Ophthalmol., 1964; 57:99. Release Thermosensitive In-Situ Fast Gelling Vehicles for Ocular Delivery of Ketorolac.
28. Ding S , Tien W, Olejnik O. US Patent., 1995;5:474-979.