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. : 01 - 05

Blood-ocular breakdown using Nanoparticle

[1]Namami Rathod, UG Student, Parul Institute of Pharmacy and Research, Parul University, Vadodara, India.

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

Corresponding Author: Bhavisha Patel, Assistant Professor, Department of Pharmacognosy, Parul Institute of Pharmacy and Research, Parul University, Vadodara, India**.**

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Many drug delivery systems have been developed for overcoming and improving ocular bioavailability. Administration of drug which can directly reach the systematic circulation is done due to blood-ocular barrier. The system known as nanotechnology have been developed to overcome ocular physiological barriers. This review suggests the use of blood-ocular breakdown thus allowing the drugs to reach systemic route via nanotechnology. Different ways to breakdown blood-ocular barrier like acute inflammation (by surgery) ,induced ocular hypotony, using inflammatory mediators. We discussed the different nano methods and its advantages over other conventional methods.

Keywords: Blood-ocular, Nanotechnology, Hypotony, Micro solutions

Introduction

Solutions, suspensions or ointments used are as topical preparations but have some drawbacks. These formulations have poor ocular bioavailability because of many physiological barriers in the eye. Oral and IV routes are preferred more because satisfactory drug concentration is achieved in intraocular tissues.

Blood aqueous barrier and blood retinal barrier combines to form blood ocular barrier. The functions of blood ocular barrier are: (i) protecting eye from entry of toxic substances. (ii) maintaining the homeostatic control. Components of blood aqueous barrier are: (i) non pigmented epithelium of ciliary body (ii) the posterior iris epithelium (iii) the endothelium of the iris vessels with tight junction of the leaky type (iv) the endothelium of Schlemm's canal. The components of blood retinal vessels : (i) the retinal pigment epithelium (outer barrier) (ii) the endothelial membrane of the retinal vessels (inner barrier). Function of blood aqueous barrier and blood retinal barrier is restrict the movement of blood elements to intraocular chambers. The drugs that are administered orally or intravenously reaches therapeutic levels in intraocular tissues hardly.

Blood brain barrier and blood ocular barrier have similar barrier properties. Protein like microperoxidase are capable of entering the peroximal space but not the retina. Thus indicating that the intercellular junctions of retinal endothelium are sealed with overabundant amount of zonulaeoccludentes contribute to form the bulk of blood retinal barrier. Effective tight junctions are not found in retina amd in brain capillaries of ciliary body of rabbit eye. Because of molecular diffusion blood aqueous barrier is not as active as blood retinal barrier. Substance such as insulin, Chloride, sucrose, phosphate, potassium, sodium, urea, proteins and some antibiotics when injected intravenously were found on the anterior side of vitreous humor because

of ciliary circulation, but didn't reached the retina due to blood retinal barrier.

Discussion

Ocular injury and ocular hypotonia can cause breakdown of blood retinal barrier. Other situations causing breakdown of blood retinal barrier are surgical and non-surgical traumas, intraocular inflammation (e.g. uveitis, scleritis), vascular disorder (e.g. M.coats, M.eales), systemic disorders (e.g. diabetes) and intraocular tumours (e.g. retinoblastoma, uvael melanoma) which can result in a variable inward movement of inflammatory cells and blood plasma constituents such as proteins, cytokines and growth factors.

When IOP is lower than episcleral venous pressure, breakdown of blood ocular barrier may occur due ocular hypotony, thus leading to reversion of the flow direction of the ocular fluids with plasma proteins entering the anterior chamber from blood filled Schlemm's canal.

Drug administration for ocular routes is topical, local, and systemic. But these routes have some limitations. Topical route causes toxicity in cornea, conjunctiva and nasal mucosal. An Intravitreal injection causes retinal toxicity and infections. The drugs cannot enter into posterior segment of eye because of blood retinal barrier.

The use of nanoparticle in drug delivery system can be done to overcome the limitations of systemic treatment of ophthalmic disorders.

Nano system

The particles or system which lies in nanoscale is defined as nanosystem. Nanoparticles (nanospheres and nanocapsules), liposomes, dedrimers, nisomers, are included on Nanosystem.Nanoparticles lies in size range of 10mm to 1 micrometer. The API can be encapsulated/entrapped, dissolved or distributed to a nanoparticle matrix.Nanoparticle can reach the capillaries by overcoming physiological barriers. Liposomes consists of phospholipid or cholesterol bilayers. They carry the drug into the core or into the bilayer. Depending on their chemical composition they may be positive, negative or neutral surface charge.

After systemic administration Light-targeted liposomal delivery was employed. In this system a liposomal formulation of light sensitive delivery system was selectively withheld in neovascular areas of the eye for treatment of age related mascular degeneration. This therapy was not completely successful in its purpose of destroying abnormal blood vessels without causing damage to normal surrounding tissues.

Applications of Nanosystem in Opthalmolgy

Drug delivery system which increases bioavailability, prolonged drug release , compatibility with ocular tissues, ease of use in form of eye drops causing no blurred vision or irritation and fewer instillations to obtain the intended therapeutic effect have been developed.

Ciclosporinloaded nanoparticles are also used for the treatment of extraocular disease, such as keratocunjuctivitissica. Topical instillation of cyclospori-A-loaded chitosan nanoparticles into rabbits, it was possible to achieve therapeutic concentrations in external ocular tissues during at least 48 h while maintaining negligible cyclosporine-A levels in inner ocular structures.

Systemic Administration

Reseaches have been made to develop drug delivery systems to administer drugs systemically in order to clear these barriers.

The challenges for effective systemic nanodelivery into tissues are limited penetration across the vascular endothelium and the uptake by reticuloendotheial systems are considerable factors.the present nanodelivery system depends on transvascular exchange and tissue accumulation, which require high dose to create large concentrations gradients to drive nanoparticles passively across the blood-tissue interface. Only fractional dosage of

nanoparticles penetrating into target tissues are passively accumulated. This diminishes therapeutic efficacy and worsen the side effects. Delivery of targeted nanoparticles across the vascular endothelium could increase the desired therapeutic index with fewer side effects. Dilution and degradation of the drugs before reaching the target site limits the systemic application.

Nanoparticle having high selectivity for the target tissue is a challenge to be achieved to improve systemic administration. Targeting systems are needed to transport molecues to deeper layers of the eye, overcoming the blood-ocular barrier.No toxicity was found in retinal, endothelial cells, astrocytes, and retinoblastoma cells. Another study has demonstrated that transferrin, arginine-glycine-aspartic acid peptide, or dual functionalized polynanoparticlescarrying anti-VEGF intraceptor plasmid, administered intravenously, were able to reach choroidal neovascularization lesions. Due to broken blood-retinal barrier as a result of choroidal neovascularization in the laser treated rat eye.

Systemically administered nanoparticles have ability to pass through the ocular barrier. Dalargin a hexapeptideanalog of leucine-enkephalin containing D-alanine, which produces central nervous system analgesia, can cross BBB when conjugated with polynanoparticlesand accumulate in the brain of mice. But when it was administeredwithoutpolynanoparticles it was not able to cross BBB.

Kinetics of systematically administered Nanoparticles

The study of bioavailability of nanoparticles in vivo is wide field of research. There is no standardized characterization of possible interaction of nanoparticles with proteins and immune cells.

Toxicity of nanoparticle system

The polymer used in nanoparticle system causes toxicity. Also it can induce change in organ of human body, such alterations in blood clinical chemistry, liver function, kidney function,Blood cell count, and other known side effects. The side effects depends upon systemic configuration, specific materials used, frequency of administration and other factors.

The models and studies for nanotoxicology need to be encouraged. Recent studies have been made for modifications of nanoparticle to prolong blood circulation and enhance treatment efficacy.According to recent studies it has been found that microparticles administered periocularlyin rabbits remained at the periocular site for long time without causing local side effect.

Hypothesis

The blood ocular barrier can be breakdown if there is acute inflammation. If the blood ocular barrier breaks than the drug administered systematically can penetrate. Other factors causing breakdown of blood ocular barrier are intra ocular surgeries and ocular inflammation.

Blood ocular Barrier breakdown

Ocular surgeries

The intra ocular surgery can cause breakdown of the blood ocular barrier. This can increase protein content in aqueous humor and edema of sensory retina.Vasodilation, increased blood flow, increased permeability of blood vessels, edema, increased tissue pressure are the events of ocular trauma.

Release of endogenous mediators such as prostaglandins, leukotrins, interleukins, tumor necrosis factor can cause breakdown of blood ocular barrier.

Induced ocular hypotony

Currently to induce ocular hypotonyparacentesis is being performed.This process has been widely used in ophthalmic microsurgery. Immediate anterior chamber paraentesis, combined with antiglaumatous drugs give relief insymtoms f acute primary angle closure glaucoma.

Transient hypotonia presents no functional sequelae while acute hypotonia can cause structural changes. To decrease

the intraocular pressure without causing collapse of anterior chamber leakage of aqueous through corneal paracentesis should be quick.

Drugs having short life could not be used because repitativeparacentesis can caus infection. Thus hypotony can cause opening of natural vascular fenestrations. The risks of infections are less in paracentesis.

Inflammatory Mediators

Inflammatory mediators cause breakdown of blood ocular barrier. Leuktrins, prostaglandins, platelet activating factor, interleukin-1 etc are inflammatory mediators. The accumulation of these mediators increase the vascular permeability, thus breakdown of blood ocular barrier.Tumor necrosis factor causes breakdown of blood retinal barrier.

Measuring the blood ocular breakdown

Breakdown of aqueous blood barrier causes inward movement of plasma constituents to cells anterior chamber. Tyndallometry method is used measure the integrity of blood aqueous level.

Conclusion

The purose of this article is to take advantage of breakdown of blood ocular barrier for systemic route administration. The breakdown can occur with the help of sugerytoo.To facilitate systemic administration of drug breakdown of blood ocular barrier is an interesting factor. Adminstrations of drugs using nanosytem can ive much effective results for breakdown of blood ocular barrier. Reversion of breakdown of blood ocular barrier can be achieved using anti-inflammatory and Antihypetensive.

References

1. Gunda, S.; Hariharan, S.; Mandava, N.; Mitra, A.K. Barriers in Ocular Drug Delivery. In Ocular Transporters in Ophthalmic Diseases and Drug Delivery; Tombran-Tink, J., Barnstable, C.J., Eds.; Humana Press: Totowa, NJ, USA, 2008; Chapter 21, p. 399.
2. Cunha-Vaz, J.G. The blood-ocular barriers. Doc. Ophthalmol. 1976, 41, 287–327.
3. Worakul, N.; Robinson, J.R. Ocular pharmacokinetics/pharmacodynamics. Eur. J. Pharm. Biopharm. 1997, 44, 71–83.
4. Cunha-Vaz, J.G. The blood-ocular barriers. Surv. Ophthalmol. 1979, 23, 279–296.
5. Muh-Shy, C.; Hou, P.K.; Tong-Yuan, T.; Lin, B.J. Blood-ocular barriers. Tzu Chi Med. J. 2008, 20, 25–34.
6. Smith, R.S.; Rudt, L.A. Ocular vascular and epitelial barriers to microperoxidase. Invest. Ophthalmol. 1975, 14, 556–560.
7. Peyman, G.A.; Bok, D. Peroxidase diffusion in the normal and laser-coagulated primate retina. Invest. Ophthalmol. 1972, 11, 35–45.
8. Cunha-Vaz, J.G. The blood-retinal barriers. Doc. Ophthalmol. 1976, 41, 287–327.
9. Green, K.; Pedersno, J.E. Effect of 1-tetrahydrocannabinol on aqueous dynamics and ciliary body permeability in the rabbit. Exp. Eye Res. 1973, 15, 499–507.
10. Schmack, I.; Völcker, H.E.; Grossniklaus, H.E. Phthisi bulbi. In Ocular Disease Mechanisms and Management; Levin, L.A., Albert, D.M., Eds.; Saunders Elsevier: Maryland Heights, MO,USA, 2010; Chapter 54, p. 420.
11. Völcker, H.E.; Naumann, G.O.H. Morphology of uveal and retinal edemas in acute and persisting hypotony. Mod. Probl. Ophthalmol. 1979, 20, 34–41.
12. Raviola, G. The structural basis of the blood-ocular barriers. Exp. Eye Res. 1997, 25, 27–63.

13. Schubert, H.D. Postsurgical hypotony: Relationship to fistulization, inflammation, chorioretinal lesions, and the vitreous. Surv. Ophthalmol. 1996, 41, 97–125.
14. Bill, A.; Philips, C. Uveoscleral drainage of aqueous humor in human eyes. Exp. Eye Res. 1971, 12, 275–281.
15. Salminen, L.; Chioralia, G.; Scheiber, S. Effect of acute ocular hypotony on the blood-ocular barrier. Trans. Ophthalmol. Soc. (UK) 1977, 97, 621–622.
16. Servatt, J.J.; Bernardino, C.R. Effects of common topical antiglaucoma medications on the ocular surface, eyelids and periorbital tissue. Drugs Aging 2011, 28, 267–282.
17. Baudouin, C. Detrimental effect of preservatives in eyedrops: Implications for the treatment of glaucoma. Acta Ophthalmol. 2008, 86, 716–726.
18. Baudouin, C.; Labbé, A.; Liang, H.; Pauly, A.; Brignole-Baudouin, F. Preservatives in eyedrops: The good, the bad and the ugly. Prog. Retin. Eye Res. 2010, 29, 312–334.
19. Cho, J.H.; Kwun, Y.S.; Jang, H.S.; Kang, J.M.; Won, Y.S.; Yoon, H.R. Long-term use of reservatives on rat nasal respiratory mucosa: Effects of benzalkonium chloride and potassium sorbate. Laryngoscope 2000, 110, 312–317.
20. Reardon, G.; Kotak, S.; Schwartz, G.F. Objective assessment of compliance and persistence among patients treated for glaucoma and ocular hypertension: A systematic review. Patient Prefer Adherence 2011, 5, 441–463.
21. Reardon, G.; Schwartz, G.F.; Mozaffari, E. Patient persistency with topical ocular hypotensive therapy in a managed care population. Am. J. Ophthalmol. 2004, 137, S3–S12.
22. Jaycock, P.D.; Mather, C.M.; Ferris, J.D.; Kirkpatrick, J.N. Rectus muscle trauma complicating sub-Tenon's local anaesthesia. Eye (Lond) 2001, 15, 583–586.
23. Faure, C.; Faure, L.; Billotte, C. Globe perforation following no-needle sub-Tenon anesthesia. J. Cataract Refract. Surg. 2009, 35, 1471–1472.
24. Kumar, C.M.; Eid, H.; Dodds, C. Sub-Tenon's anaesthesia: Complications and their prevention. Eye (Lond) 2011, 25, 694–703.
25. Penha, F.M.; Rodrigues, E.B.; Maia, M.; Furlani, B.A.; Regatieri, C.; Melo, G.B.;Magalhães, O.; Manzano, R.; Farah, M.E. Retinal and ocular toxicity in ocular application of drugs and chemicals—Part II: Retinal toxicity of current and new drugs. Ophthalmic Res. 2010, 44, 205–224.
26. Jager, R.D.; Aiello, L.P.; Patel, S.C.; Cunningham, E.T., Jr. Risks of intravitreous injection: A comprehensive review. Retina 2004, 24, 676–698.
27. Sampat, K.M.; Garg, S.J. Complications of intravitreal injections. Curr. Opin. Opthalmol. 2010, 21, 178–183.