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A REVIEW ARTICLE ON OCCULAR DRUG DELIVERY SYSTEM

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Abstract:

The scientist's faced many challenges in Ocular drug delivery system due to unique anatomy and physiology of eye. In ocular drug delivery system there are two types of barriers static and dynamic barrier. Static barriers consist of different segment of eye such as cornea, sclera, retina and blood- retinal barriers. In other way dynamic barriers consists choroidal and conjunctival blood flow, lymphatic clearance, and tear dilution. These both barriers affect the bioavailability of drugs. In recent year some new concept of drug delivery such as iontophoresis, liposome bio adhesive gels, ocular insert, contacts lenses etc. Has been developed to overcome problems associated by static and dynamic barriers. These formulation-based approaches have high capacity to carry maximum concentration of drug at targeted site of eye.

Therefore, a demand for improved cell culture that can replace animal experimentation with an adequate reproducibility is mandatory. Corneal epithelial cell culture models are the longer-considered strategy to study in vitro ocular drug delivery. From these, rabbit and human cell lines are the most frequently used. Primary cells have been employed that were transformed by using some chemicals or viruses to establish continuous/immortalized cells. Alternatively, original immortalized cells because of a tumour were also employed. Additionally, some attempts have been made to develop a tridimensional corneal structure.

Key Words: *Ocular Drug Delivery System, Intra Ocular Barriers*

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INTRODUCTION:

Most ocular treatments call for the topical administration of opthamically active drugs to the tissues around the ocular cavity. Several types of dosage forms can be applied as the delivery systems for the ocular delivery of drugs. The most prescribed dosage form is the eye drop solution, for example, ocular decongestant eye drops and aqueous antiglaucoma pilocarpine solutions.

The eye drop dosage form is easy to instil but suffers from the inherent draw- back that the majority of the medication it contains is immediately diluted in the tear film as soon as the more eye drop solution is instilled into the cul-de-sac and is rapidly drained away from the precorneal cavity by constant tear flow, a process that proceeds intensively in inflamed than in the normal eyes, and lacrimal-nasal drain-age. Therefore, only a very small fraction of the instilled dose is absorbed into the target tissues (e.g., 1.2% is available to the aqueous humour), and relatively concentrated solution is required for instillation to achieve an adequate level of therapeutic effect. The frequent periodic instillation of eye drops becomes necessary to maintain a continuous sustained level of medication. This gives the eye a massive and unpredictable dose of medication, and unfortunately, the higher the drug concentration in the eye drop solution, the greater the amount of drug lost through lacrimal-nasal drainage system. Subsequent absorption of this drained drug, if it is high enough, may result in undesirable systemic side effects. Furthermore, the intraocular concentration of medication surges to a peak every- time eye drops are instilled; the drug level then declines rapidly at an exponential pattern as time passes. A plot of intraocular drug concentration versus time yields a series of peaks of drug level, which may surpass the toxic threshold of the drug, separated by extended valleys of drug level below the critical level required to achieve the desired therapeutic efficacy.

Suspension-type pharmaceutical dosage forms have also been widely used for ocular medication; hydrocortisone acetate and prednisolone acetate are typical of drugs currently marketed as suspensions. Suspension formulations also have some inherent drawbacks. For example, they are generally formulated with relatively water-insoluble drugs to avoid the intolerably high toxicity created by saturated solutions of water-soluble drugs. However, the rate of drug release from the suspension is dependent upon the rate of dissolution of the drug particles in the medium, which varies constantly in its composition with the constant inflow and outflow of lacrimal fluid.

A basic concept shared by most scientists in ophthalmic research and development is that the therapeutic efficacy of an ophthalmic drug can be greatly improved by prolonging its contact with the corneal surface. For achieving this purpose, viscosity-enhancing agents, such as methylcellulose, are added to eye drop preparations, or the ophthalmic drug is formulated in a water-insoluble ointment formulation to sustain the duration of intimate drug-eye contact. Unfortunately, these dosage forms give only marginally more sustained drug-eye contact than eye drop solutions and do not yield a constant drug bioavailability as originally hoped. Repeated medications are still required throughout the day.

Recently, drug-pre-soaked hydrogel contact lenses and pledgets have gained some popularity in an attempt to bypass the need for repetitive drug dosing and to avoid the peak-and-valley activity-time curves resulted from periodic applications of eye drops and ointments (2-5). A micro pump-type delivery system has also been developed for the continuous administration of fluid to dry eyes or medications to infected eyes. These drug delivery systems have succeeded in significantly reducing the frequency of dosing and also in remarkably improving the therapeutic efficacy of ophthalmic drugs.

Anatomy of eye

- Eye is a spherical structure with a wall consisting of three layers the outer sclera, the middle choroid layer and the inner retina. The sclera is a tough fibrous coating that protects the inner layers.
- It is white except for the transparent area at the front, the cornea which allows light to enter the eye.
- The choroid layer situated inside the sclera contains many blood vessels and is modified at the front of the eye as the pigmented iris.
- The biconvex lens is situated just behind the pupil.
- The chamber behind the lens is filled with vitreous humour a gelatinous substance occupying 80% of the eye ball.

The anterior and posterior chambers are situated between the cornea and iris and lens respectively and filled with aqueous humour. At the back of the eye is light detecting retina.

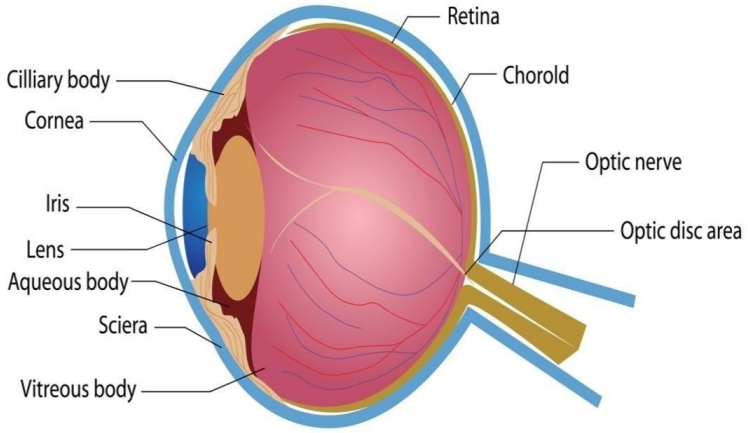


Fig. 1.1 Anatomy of eye

Intra ocular barriers:

1. **Tear;** The precorneal barrier is tear film which reduces the effective concentration of the administrated drugs due to dilution by the tear turn over (1µl/min), accelerated clearance and binding of the drug molecule to the tear proteins. The dosing volume of instillation is generally 20–50 µl whereas the size of cul-de-sac is only 7–10 µl. The excess volume may spill out on the cheek or exit through the naso lacrimal duct.
2. **Cornea;** The cornea consists of three layers such as epithelium, stroma and endothelium and a mechanical barrier to inhibit transport of exogenous substances into the eye. Each layer possesses a different polarity and a rate limiting structure for drug permeation. The corneal epithelium is lipophilic nature and tight junctions are formed to restrict paracellular drug permeation from the tear film. The stroma is composed of collagen fibrils. The highly hydrated structure of the stroma acts as a barrier to permeation of lipophilic drug molecules. Corneal endothelium is the innermost monolayer of hexagonal shaped cells and acts as a separating barrier between the stroma and aqueous humour. The endothelial junctions are leaky and facilitate the passage of macromolecules between aqueous humour and stroma.
3. **Conjunctiva;** Conjunctiva of eyelids and globe is a thin and transparent membrane which is involved in the formation and maintenance of the tear film. The conjunctiva or episclera is highly supplied with capillaries and lymphatics. Hence administered drugs in the conjunctival space may be cleared through blood and lymph. The conjunctival blood vessels do not form a tight junction barrier which means drug molecules can enter into blood circulation by pinocytosis and convective transport through paracellular pores in the vascular endothelial layer.

4. Sclera; The sclera mainly consists of collagen fibres and proteoglycans embedded in an extracellular matrix. Sclera permeability depends on the molecular radius and it decreases roughly expontially with molecular radius. The posterior sclera is composed of a looser weave of collagen fibres than the anterior sclera and the human sclera is relatively thick near the limbus (0.53 ± 0.14 mm), thin at the equator (0.39 ± 0.17 mm) and much thicker near the optic nerve (0.9-1.0mm). The increase of hydrophobic/lipophilic character drugs shows lower permeability in sclera. Hydrophilic drugs may diffuse through the aqueous medium of proteoglycans in fibre matrix pores more easily than lipophilic drugs. The charge of drug molecule may affect its permeability across the sclera. Positively charged drugs may exhibit poor permeability due to their binding to the negatively charged proteoglycan matrix.

5. Choroid/Bruch's membrane: Choroid is one of the most highly vascularized tissues of the body to supply the blood to retina. The choroidal capillary endothelial cells are fenestrated and in humans are relatively large in diameter (20-40 µm). Bruch's membrane (BM) causes thickening with age. These changes cause increased calcification of elastic fibres increased cross linkage of collagen fibres and increased turn over glycosaminoglycans. The advanced glycation end products and lipofuscin accumulate in BM. Thickness changes of choroid and BM might affect drug permeability from sub conjunctiva space into the retina and vitreous.

6. Retina; The barriers restricting drug penetration from the vitreous to the retina is the internal limiting membrane (ILM).The ILM separates the retina and

the vitreous and is composed of 10 distinct extracellular matrix proteins. Drug transport across the retinal pigment epithelium (RPE) takes place by transcellular and paracellular routes. The driving forces of outward transport of molecules from the subretinal spaces are hydrostatic and osmotic and small molecules may transport through the paracellular inter RPE cellular clefts and by active transport through the transcellular route.

7. Blood-Retinal Barrier: Blood retinal barrier (BRB) restricts drug transport from blood into the retina.BRB is composed of tight junctions of retinal capillary endothelial cells and RPE called iBRB for the inner and oBRB for outer BRB respectively. The function of iBRB is supported by Muller cells and astrocytes. The retinal capillary endothelial cells are not fenestrated and have apaucity of vesicles. The functions of these endothelial vesicles are reported as endocytosis or transcytosis that may be receptor mediated or fluid phase requiring adenosine triphosphate. Muller cells support neuronal activity and maintain the proper functioning of iBRB under normal conditions. Therefore oBRB (RPE) restricts entry of drugs from the choroid into the retina.RPE is a monolayer of highly specialized hexagonal shaped cells located between sensory retina and the choroid. The tight junctions of the RPE efficiently restrict intercellular permeation into sensory retina

DRUG DELIVERY TO EYE:

Anatomical and Physiological features of the Eye:

The eye is a very sensitive organ of the body. There are many anatomical and physiological features which affect the administered drug.
These are as follows:

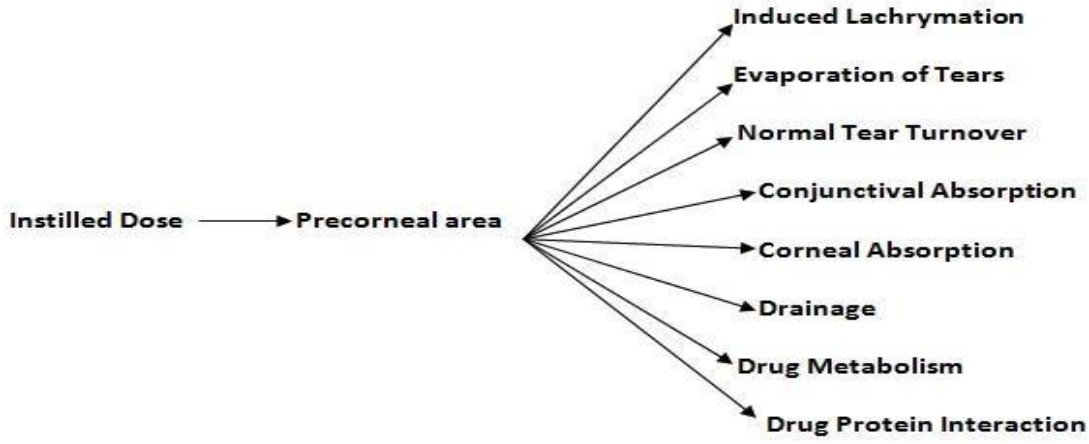
- Blinking of eye
- Tear secretion
- Nasolacrimal drainage

Upon reflex blinking lid closure provides protection against external problems. Tears wash the surface of eye. It contains lysozyme and immunoglobulin which exert an anti-infectious activity to eye. The lachrymal fluid drained out through nasolacrimal rout, pharynx and oesophagus. In addition binding of drug to conjunctival mucin and tears proteins also inactivate the drug

Corneal Absorption:

In terms of corneal absorption of drug, the cornea consists of three layers which are responsible for its poor permeability. These are as follows:

- ✓ The superficial layer of epithelium, which is lipophilic in nature.
- ✓ The stroma, which is hydrophilic in nature this layer is mostly responsible for thickness of cornea.
- ✓ The inner endothelium consisting of a single layer of trampled epithelium like cells. Since, the cornea has both hydrophilic and lipophilic structures. It presents an efficient obstruction to the absorption of both hydrophilic and lipophilic compounds. Some formulation based approaches used for improvement of ocular bioavailability of drugs. The duration of ophthalmic drug can be divided in to two categories. The first category based on controlled release and continuous delivery of drugs. The second category based on prevention of pre-corneal loss of drug. Some necessities of controlled drug delivery system to eye.



Eye Penetration of Drugs Administered Local; In ocular drug delivery, if drug is not act on outer surface of eye then the active drug substance has to enter the internal tissue of eye. The most important route for drug delivery is Tran's corneal but non corneal route has also contributed significant to bioavailability of some drugs such as insulin and timolol 12. In other way sclera has high permeability for some β- blockers 13. In human eye hydrophilic-lipophilic nature of cornea indicates the absorption of active ingredient depends on both hydrophilic-lipophilic nature of drug. Secretion of tear spread by blinking of eyelids and keeps the cornea clean, moist and healthy.

Eye Penetration of Systemically Administered Drugs; Because of blood-eye-barriers it is interested to reflect penetration of the systematic administration of anti- infectious and anti- inflammatory drugs. The ciliary epithelium produces aqueous humour. These acts as ultra-filtrate and restrict the entry of macro molecules such as antibiotics and plasma proteins. Drug delivery to the posterior site and retina is very difficult because of blood-retina barriers complicated by high viscosity, prevents diffusion of drugs in the posterior pole of the eye.

Drug Delivery to the Internal Regions of the Eye; The aim of pharmacotherapeutics is to treat a disease in a reliable and conventional approach. A supposition is made that a correspondence exists between the concentration of a drug at its proposed site of action and the consequential pharmacological effect. Following factors have to be considered during drug delivery to the intraocular tissues.

- Pinpoint the pharmacodynamics action at the eye and lessen drug action on other tissues.

- Traverse the blood-eye fence (systemic to ocular) or cornea (external to ocular) to get to the site of action.

- Lengthen the duration of drug action such that the rate of recurrence of drug administration can be condensed.

Pre-Ocular Retention: It has been anticipated that the human eye can embrace just about 35µl of an ophthalmic solution without dribble over or spillage at the outer angle 14, while the amount delivered by most marketable ophthalmic eye drop dispensers is more or less than 45µl. Thus a large fraction of the drug is shattered due to administration of a surfeit volume. Following the removal of the surfeit solution from the front of the eye, a second mechanism of clearance prevails. The eye has a competent system for tear turnover (1µl/min). The two mechanisms of clearance result in a biphasic profile for an instilled solution with a quick initial clearance phase due to exclusion of surfeit fluid followed by a slower second phase due to tear turnover.

METHODS TO OVERCOME BARRIERS:

I. Physical methods

1. Iontophoresis,
2. Sonophoresis
3. Micro needles

I. Physical methods

Physical force-based methods, initially utilized in transdermal drug delivery, generally require a power driven physical device to deliver energy to the barriers, thereby enhancing transient drug transport.

1. Iontophoresis: It is the process in which direct current drives ions into cells/tissues. Iontophoresis, application of a low-intensity electrical current, enhances drug delivery across biological membranes by causing electro repulsion and electro-osmosis of the drug molecule. Electro repulsion primarily applies to the movement of ionic drugs, while electro-osmosis can enhance the transport of both neutral and charged molecules by convective solvent flow. The relative contribution of electro repulsion and electro-osmosis depends on both the physicochemical characteristics of the drug (e.g. size, charge and charge to molecular-weight ratio) and the electrical properties of the biological membrane. Ocular iontophoresis offers a drug delivery system that is fast, painless, Safe and in most cases result in the delivery of high concentration of drug at specific site.

2. Sonophoresis /Ultrasound: It involves the application of a sound field at frequencies higher than 20 kHz to improve drug transport across biological membranes, including ocular barriers. The mechanisms for ultrasound enhanced drug delivery take into account non-thermal (e.g. cavitation, acoustic streaming and mechanical stress) and thermal effects with ultrasound parameters, co-administration of micro bubbles and drug characteristics, all having an effect on delivery efficacy. Cavitation is generally considered the predominant factor for enhanced drug delivery and is defined as the formation of micro bubbles due to an acoustic pressure gradient within the coupling medium. Corneal permeability enhancement is generally a result of stable cavitation at low ultrasound intensities, whereas both stable and inertial cavitations play important roles at higher ultrasound strengths.

3. Micro needles: Micro needles (MLs) are micrometre sized needles, or arrays of such, fabricated by adapting microelectronics tools. Applying MLs to biological membranes can create tiny transport pathways, thereby allowing drugs to permeate across these barriers. To date, numerous ML fabrication approaches have been utilized, resulting in a variety of shapes, sizes, materials and configurations. Enhanced drug delivery into the cornea and anterior segment of the eye can be achieved by insertion of MLs across the corneal epithelium. Various polymeric MLs have found great use in intrascleral drug delivery. According to their delivery mechanism, ocular MLs can be categorized into four types such as solid micro needles, drug-coated micro needles, dissolving micro needles and hollow micro needles.

II. Chemical approaches

Chemical modification of drugs to improve therapeutic efficacy and to enhance various physicochemical properties such as solubility, stability, permeability, and evasion of efflux pump is an established approach in therapeutic drug delivery. The metabolic activity of ocular tissues provides an opportunity of utilization of chemically modified drugs that have a predictable metabolic bioconversion in the eye.

The most important strategies in chemical approaches for ocular delivery are

- Designing ocular drugs that are inactive at sites other than the eye (prodrugs)
- Designing drugs that undergo sequential metabolic conversion and finally reach the target (retro metabolic design)
- Chemical modification of a known inactive metabolite or analog to restore the therapeutic activity that transforms back into the inactive metabolite in a predictable one-step biotransformation (SD)

OCULAR FORMULATIONS

I. Drug delivery systems to anterior segment of the eye
II. Drug delivery systems to posterior segment of the eye
III. Advanced delivery system
IV. Vesicular drug delivery system

I. Drug delivery systems to anterior segment of the eye:

1. Eye-Drops; Drugs which are active at eye or eye surface are widely administered in the form of solutions, emulsion and suspensions conjunctivitis. Generally eye drops are used for anterior segment disorders as adequate drug concentrations are not reached in the posterior tissues using this drug delivery method. Various properties of eye drops like hydrogen ion concentration, osmolality, viscosity and instilled volume can influence retention of a solution in the eye. Eye drop forms hydrogen bonding with the mucus and corneal and conjunctival epitheliums which are all negatively Novel Drug Delivery System Page 12 charged to extend the effects of drug to several hours. Azithromycin ophthalmic solution is formulated with Durasite (Inspire Pharmaceuticals Inc.) can be used for the treatment of bacterial conjunctivitis.

2. Ophthalmic Inserts; Ophthalmic inserts are sterile preparations with a solid or a semisolid consistency, and whose size and shape are especially designed for ophthalmic application. The inserts are placed in the lower fornix and less frequently, in the upper fornix or on the cornea.

Classification of ocular inserts; Based upon their solubility behaviour:

1) Insoluble inserts
2) Soluble inserts
3) Bio erodible inserts

3. Punctual Plugs: To prolong the retention time and increase absorption and efficacy after instillation of eye drops, inhibition of drainage through nasolacrimal system using punctual plug into the pancta is a long-standing approach. Efficacy of an ocular hyposensitive agent in eye drops in conjunction with punctual occlusion by punctual plug is reported.

4. Subconjunctival/Episclera Implants; Scleral plug can be implanted at the pars plana region of eye made of biodegradable polymers and drugs and it gradually releases doses of drugs for several months upon biodegradation. The release profiles vary with the kind of polymers used their molecular weights and the amount of drug in the plug. LX201 (Lux Biosciences, USA) is a silicone matrix episcleral

implant designed to deliver cyclosporine A to the eye surface for one year. The implant is flat on the bottom in contact with the episclera and the top is rounded in contact with anterior surface.

5. Ointment and Gels; Prolongation of drug contact time with the external ocular surface can be achieved using ophthalmic ointments and gels. Hence prolonging duration of action and enhancing ocular bioavailability of drugs is possible by gels and ointments. Ointment breaks up into small droplet and remains as a depot of drug in the cul de sac for extended periods. But blurring of vision and matting of eyelids can limits those use.

II. Drug delivery systems to posterior segment of the eye:

1. Intravitreal Implants; Intravitreal injection revolutionized posterior segment treatments by delivering drug directly to the site of disease. Because intravitreal implants release low doses of drug directly into the vitreous cavity over an extended period of time, they reduce systemic complications.

2. Injectable particulate systems; RETAAC can be injected intra vitreously into patients with diabetic macular edema (DME) and their efficacy compared to naked TA injections. RETAAC treated eyes showed decrease of retinal thickness as well as improved visual acuity for 1 year. It is safe and well tolerated by the retina.

III. Advanced delivery system

1. Cell encapsulation: The entrapment of immunologically isolated cells with hollow fibres or microcapsules before their administration into the eye is called encapsulated cell technology (ECT).It enables the controlled, continuous and long term delivery of therapeutic proteins directly to the posterior regions of the eye. The polymer implant containing genetically modified human RPE cells secretes ciliary neuotrophic factor into the vitreous humour of patient's eye. CT is used as a delivery system for chronic ophthalmic diseases like neuroprotection in glaucoma, antiangiogenesis in choroid neovascularization, and anti-inflammatory factors for uveitis.

2. Gene therapy: Along with tissue engineering gene therapy approaches are used to treat blindness arising from corneal diseases, cataract, glaucoma etc. Many viruses including adenovirus, retrovirus, Aden associated virus and herpes simplex virus are manipulated for use in gene transfer and gene therapy applications. Topical delivery to the eye is the most expedient way of ocular gene delivery. Retroviral vectors are used due to their high efficacy and lead to restrict their clinical use. The advanced delivery systems prolong the contact time of vector with the surface of the eye may enhance transgene expression thereby facilitate non-invasive administration.

3. Stem cell Therapy: Cell therapies are used for the restoration of sight that are critical for visual function, the cornea and the retina. The current method for management of ocular conditions consists of eliminating the injurious agent or attempting to minimize its effects. The limbal stem cells are used the most successful ocular application transplanted from a source other than the patient for the renewal of corneal epithelium. The sources of limbal cells include donors, auto grafts, cadaver eyes and cells grown in culture.

4. Protein and peptide therapy: The delivery of therapeutic proteins and peptides to eye plays a vital role for drug delivery. But several limitations such as membrane permeability, large size, metabolism and solubility restrict their efficient delivery. Poor membrane permeability of hydrophilic peptides may be improved by structurally modifying the compound thus increasing their membrane permeability. Ocular route is not preferred route for systemic delivery of such large molecules. Immunoglobulin G is effectively delivered to retina by Tran's scleral route with insignificant systemic absorption.

5. Scleral plug therapy: Scleral plug can be implanted using a simple procedure at pars plana region of eye, made of biodegradable polymers and drugs. It releases effective doses of drugs for several months upon biodegradation. The release profiles vary with the kind of polymers used their molecular weight and the amount of drug in the plug. The plugs are effective for treating vitreoretinal diseases such as proliferative vitreoretinopathy, cytomegalovirus retinitis responds to repeated intravitreal injections and for vitreoretinal disorders that require virectomy.

6. SiRNA therapy: The siRNA therapy is used for the treatment of choroidal neovascularisation. The siRNA is directed against vascular endothelial growth factor (VEGF) or VEGF receptor 1(VEGFR1) and these approaches are used in clinical trials. Topical delivery of siRNA is directed against VEGF or its receptors are reported to suppress corneal neovascularisation. The siRNA therapy is also used for delivery of genes in ocular disease processes. It is reported that siRNA may be used in the pathogenesis and development of new treatments of ocular diseases based on in vivo and in vitro studies. New

encapsulated siRNA are developed using liposomes coupled antibodies or polymer vesicles.

7. Oligonucleotide therapy: Oligonucleotide (ON) therapy is based on the principle of blocking the synthesis of cellular proteins by interfering with either the transcription of DNA to mRNA or the translation of mRNA to proteins. The antisense molecules disrupt gene expression and inhibit protein synthesis. A number of factors are determined to contribute to the efficacy of antisense Oligonucleotide. The primary consideration is the length of the ON species. Lengths of 17-25 bases have reported to be optimal as longer ONs have the potential to partially hybridize with non-target RNA species. Biological stability is the major barrier to consider when delivering both DNA and RNA Oligonucleotide to cells. Protection from nuclease action can be achieved by modification of phosphate backbones, sugar moiety and bases.

8. Aptamer: Aptamers are Oligonucleotide ligands that are used for high affinity binding to molecular targets. It is isolated from synthetic nucleic acid by an iterative process of adsorption, recovery and reamplification. It binds with the target molecules at a very low level with high specificity. Pegaptanib sodium (Pfizer) is an RNA Aptamer directed against VEGF where VEGF is form primarily responsible for pathological ocular neovascularisation and vascular permeability.

9. Ribozyme therapy: RNA enzymes or Ribozyme are single stranded RNA molecules capable of assuming three dimensional conformations and exhibiting catalytic activity that induces site specific cleavage, ligation and polymerization of nucleotides involving RNA or DNA. It binds to the target RNA moiety and inactivates it by cleaving the phosphodiester backbone at a specific cutting site. The delivery of ribozymes in autosomal dominated retinitis pigmentosa (ADRP) shows positive action for controlling disease. ADRP is caused by mutations in genes that produce mutated proteins leading to the apoptotic death of photoreceptor cells.

IV. Vesicular system

1. Liposomes: Liposomes are vesicles composed of lipid membrane enclosing an aqueous volume. Lipophilic drugs can be delivered to the ocular system by liposomal drug delivery system. They are having an intimate contact with the corneal and conjunctival surfaces which is desirable for drugs that are poorly absorbed, the drugs with low partition coefficient, poor solubility. Hence it increases the ocular drug absorption.

2. Niosomes: Niosomes are non-ionic surfactant vesicles that have potential applications in the delivery of hydrophobic or amphiphilic drugs. They are more stable than liposomes. Hence they can target drug to eye very easily.

3. Pharmacosome: Pharmacosome are efficient tool to achieve desired therapeutic goals such as drug targeting and controlled release. Any drug possessing an active hydrogen atom (-COOH,-OH,-NH2, etc.) can be esterified to the lipid with or without spacer chain that strongly result in an amphiphilic compound which will facilitate membrane, tissue or cell wall transfer in the organism. These are defined as colloidal dispersions of drugs covalently bound to lipids and may exist as ultrafine vesicular, micellar, or hexagonal aggregates, depending on the chemical structure of drug-lipid complex. The pharmacosome show greater stability, facilitated transport across the cornea and a controlled release profile.

ADVANTAGES AND DISADVANTAGES

Advantages:

- They are easily administered by nurse.
- They are easily administered by the patient himself.
- Less visual and systemic side effects.
- Increased shelf life.
- Better Patient compliance.
- Combination therapeutic approaches.
- Increased residence time/bioavailability
- Reduction of systemic side effects.

Disadvantages:

- The very short time the solution stays at the eye surface.
- Its poor bioavailability.
- The instability of dissolved drug.
- Insertion technique is difficult and expulsion of shields may occur not individually fit for each patient.
- Shields are not fully transparent and thus reduce visual activity.
- Occasional inadvertent loss.
- Difficult to handle.
- Its poor bioavailability

REFERENCES:

1. Sasaki H, Yamamura K, Mukai T, Nishida K, Nakamura J, Nakashima M, Ichikawa M. Enhancement of ocular drug penetration. Critical Reviews™ in Therapeutic Drug Carrier Systems. 1999; 16(1).
2. Patel A, Cholkar K, Agrahari V, Mitra AK. Ocular drug delivery systems: An overview. World journal of pharmacology. 2013; 2(2):47.

3. Farkouh A, Frigo P, Czejka M. Systemic side effects of eye drops: a pharmacokinetic perspective. Clinical ophthalmology. 2016 Dec 7:2433-41.
4. Wadhwa S, Paliwal R, Paliwal SR, Vyas SP. Nanocarriers in ocular drug delivery: an update review. Current pharmaceutical design. 2009 Aug 1; 15(23):2724-50.
5. Maurice DM. The structure and transparency of the cornea. The Journal of physiology. 1957 Apr 4; 136(2):263.
6. Nickla DL, Wallman J. The multifunctional choroid. Progress in retinal and eye research. 2010 Mar 1; 29(2):144-68.
7. Lu C, Smith G. The aspherizing of intra-ocular lenses. Ophthalmic and Physiological Optics. 1990 Jan; 10(1):54-66.
8. Cholkar K, Dasari SR, Pal D, Mitra AK. Eye: Anatomy, physiology and barriers to drug delivery. In Ocular transporters and receptors 2013 Jan 1 (pp. 1-36). Wood head publishing.
9. Freddo TF, Civan M, Gong H. Aqueous Humor and the Dynamics of Its Flow: Mechanisms and Routes of Aqueous Humor Drainage. InAlbert and Jakobiec's Principles and Practice of Ophthalmology 2022 Apr 23 (pp. 1989-2033). Cham: Springer International Publishing.
10. Holland EJ, Mannis MJ, Lee WB. Ocular surface disease: cornea, conjunctiva and tear film: expert consult-online and print. Elsevier Health Sciences; 2013 May 17.
11. Meek KM. The cornea and sclera. In Collagen: structure and mechanics 2008 May 10 (pp. 359-396). Boston, MA: Springer US.
12. MacMonnies CW. Incomplete blinking: exposure keratopathy, lid wiper epitheliopathy, dry eye, refractive surgery, and dry contact lenses. Contact Lens and Anterior Eye. 2007 Mar 1; 30(1):37-51.
13. Crooke ST. Molecular mechanisms of action of antisense drugs. Biochimica et Biophysica Acta (BBA)-Gene Structure and Expression. 1999 Dec 10; 1489(1):31-43.
14. Sun H, Zhu X, Lu PY, Rosato RR, Tan W, Zu Y. Oligonucleotide aptamers: new tools for targeted cancer therapy. Molecular Therapy-Nucleic Acids. 2014 Jan 1; 3.
15. Sikandar MK, Sharma PK, Visht S. Ocular drug delivery system: an overview. International Journal of Pharmaceutical Sciences and Research. 2011 May 1; 2(5):1168.
16. Meisner D, Mezei M. Liposome ocular delivery systems. Advanced drug delivery reviews. 1995 Aug 1; 16(1):75-93.