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Review article

Advanced approaches of ocular drug delivery system

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Key words: Ophthalmic Irritancy, advanced ocular therapy, Ocular Drug Delivery, safety evaluation.

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Abstract

Eye is the most select organ of the body and different medication conveyance frameworks are utilized to convey tranquilize into eye yet there are different impediments like fast precorneal sedate loss of customary frameworks. Visual attitude and disposal of a helpful operator is reliant upon physicochemical, microbiological, pharmaceutical properties and ophthalmic irritancy properties of visual measurement shapes and also the significant visual life structures and physiology. To enhance visual medication contact time, bioavailability and home time, and to decrease the patient distress, recurrence of measurements, and additionally to back off the end of the medication there are critical endeavours concentrating towards more up to date tranquilize conveyance frameworks for ophthalmic organization. This audit concentrates on the different new medication conveyance frameworks connected in eye like supplements, in-situ gel, the recently created particulate and vesicular frameworks like liposome, pharmacosomes and discomes, niosomes, nanoparticles, iontophorosis, corneal shields, tranquilize installed contact focal points, visual wafers and so on and the latest progressed methodologies of the occular drug delivery like the conveyance of the qualities and proteins to the inside structures which were utilized as a part of treating the sicknesses brought on because of hereditary transformation, alongside security assessment of ocular medication conveyance details with some contextual investigations.

Introduction

Ocular drug delivery has stayed as a standout amongst the most difficult charge for pharmaceutical researchers. In developing a drug delivery approach, issues of absorption, distribution, metabolism, elimination (ADME) must be considered [1]. Ocular disposition and elimination of a therapeutic agent is dependent upon its physicochemical properties as well as the relevant ocular anatomy and physiology. The improvement of more up to date, more delicate demonstrative procedures and helpful operators renders direness to the advancement of greatest fruitful and advanced ocular drug delivery systems. Eye, as an entryway for medication conveyance is by and large utilized for the neighborhood treatment as against systemic treatment with a specific end goal to maintain a strategic distance from the danger of eye harm from high blood groupings of medication which are not planned for eye. The conventional ocular dosage forms are eye drops, eye ointments, eye gels, eye solutions, eye injections, eye irritation solutions, eye suspensions, sol to gel systems. The most widely used are eye drops, eye ointments and gels, which constitute 80% of the total ophthalmic preparations. Successful treatment of visual ailments is a ghastly test for researchers in the field, particularly as a result of the way of infections and nearness of the visual boundaries particularly in back visual portions. In order to remove the constraints placed by these conventional ocular therapies. A newer approach for ocular drug delivery systems are being explored to develop extended duration and controlled release strategy. These reviews focus briefly on different drug delivery systems for ocular therapy along with their safety evaluation of ocular drug delivery formulations case studies [2].

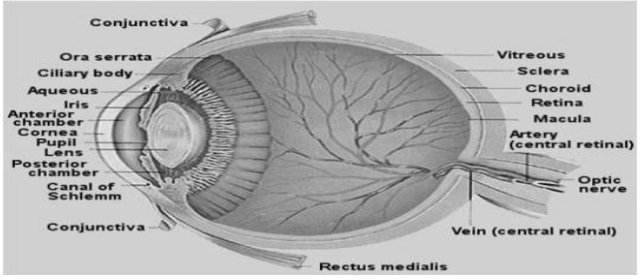

Figure 1. Structure of Eye

Composition of eye [3]

Ocular drug delivery is a standout amongst the most alluring and requesting experimentation confronting by the pharmaceutical researcher. The primitive ophthalmic arrangements, suspensions and balm measurements structures are certainly no more extended agreeable to battle some flow destructive ailments. The proportionate rates were 62.4% in spoil of arrangements, 17.4% for salves and 8.7% for suspensions. Disregarding the imperatives of quick end from the precorneal cavity of eye, visual plans as arrangements are still conceded most astounding priority by formulators in light of the fact that they are relatively uncomplicated to get ready, refine and sterilize. Water 98%, Solid 1.8%, Organic components proteins 0.67%, sugar 0.65%, Sodium chloride 0.66%, other mineral component sodium, potassium and smelling salts 0.79%.

Ocular Anatomy and Physiology

The human eye is a testing organ for topical organization of medications. The premise of this can be found in the anatomical course of action of the surface tissues and in the porousness of the cornea [1].

A. Eyeball: The mass of the human eyeball (globe) is made out of three concentric layers.

1. The external stringy layer. The sinewy layer is comprised of two sections.
    a. Posterior (5/sixth) is obscure and called the sclera.
    b. Anterior (1/sixth) is straightforward and called the cornea.
2. A centre vascular layer – the uvea or uveal tract comprising of the choroid, the ciliary body and the iris.
3. An apprehensive layer-the retina.

B. Sclera: Contains the microcirculation, which supports the tissues of this front section and is typically white.

C. The Iris nervous coat is called retina, which contains photosensitive receptors. The eyeball houses an optical device which comprises, in successions of the precorneal film, the cornea, the fluid diversion, the student, the crystalline focal point, the vitreous amusingness and the retina. The watery and vitreous humours are layers of clear liquid or gel like material intervened between the strong structures. The crystalline focal point is a refractive component with variable power controlled and bolstered by a muscle fused in the ciliary body

D. Conjunctiva: The conjunctival layer covers the external surface of the white segment of the eye and the inward parts of the eyelids. It is appended freely and consequently allows free development of the eyeball. Aside from the cornea, the conjunctiva is the most uncovered bit of the eye.

Structure and function of the eye [4]

1. The eye comprises of a few sections that take after a camera.
2. Sclera - The eye's white external defensive coat, typically observed as the "white of the eye" Cornea - the straightforward, bended structure at the front of the eye
3. Iris - the shaded part of the eye - blue, cocoa, green, dim and so on - that can be seen through the cornea.
4. Pupil - the dark part of the eye amidst the iris. It contracts or widens as indicated by the measure of light going through it.
5. lens - the straightforward circle (with both sides being raised) promptly behind the iris and student.
6. Aqueous silliness- The straightforward liquid (with consistency like water) that courses behind the cornea and before the focal point.
7. Vitreous silliness - The material (like straightforward jam) that fills the eyeball between the focal point and the retina.
8. Retina - the light-touchy layer of a large number of nerve cells that line the back of the eyeball. The phones comprise of two principle bunches, called bars and cones because of their appearance under the magnifying instrument.
9. Rods - increasingly various, spread out over the whole retina with additional toward external edge, react to low levels of light.
10. Cones - far less, focused around the retina's inside, react to shading and to subtle elements. Macula - the little focal point of the retina, in charge of perusing vision.
11. Retinal shade epithelium - This is a dim hued layer of cells at the back of the retina in charge of giving oxygen and different supplements to the poles and cones.
12. Choroid - an expansive system of veins (behind the retina) that vehicle oxygen and different supplements to the retinal colour cells.
13. Optic circle - a little yellow oval structure in the retina, to which nerve cell associations go from every one of the poles and cones.
14. Optic nerve and past - the "string" of nerve cell associations that go from the eyeball to goals all through the mind.

Function of the eye

1. When you see a question, the light goes from that protest the cornea, then goes through the fluid cleverness, student, focal point and vitreous amusingness to achieve the retina.

2. During this entry, the light gets to be distinctly engaged onto the macula. At the macula, the light cause's concoction responses in the cones, that subsequently send electrical messages from the eye to the cerebrum.
3. The mind perceives these messages and demonstrates to you that this specific protest has been seen.
4. The cones are hence in charge of you having the capacity to perceive hues and to peruse.
5. The bars are fundamental for you to find oblivious, and to identify items to the sides, above and underneath the protest on which you are straightforwardly engaged.
6. This work keeps you from catching snags when moving around.
7. All the retinal cells (bars and cones) are given oxygen and different supplements from the retinal shade cells (epithelium), which are kept provided by the rich system of veins in the choroid.

Routes of Drug Delivery in Eye

There are a few conceivable routes of drug delivery into the ocular tissues. The determination of the route of administration depends essentially on the target tissue [20].

a. **Topical course:** Regularly topical visual medication organization is expert by eye drops, yet they have just a short contact time on the eye surface. The contact, and along these lines length of medication activity, can be delayed by plan outline (e.g. gels, gelifying definitions, balms, and additions).

b. **Subconjunctival organization**: Customarily subconjunctival infusions have been utilized to convey drugs at expanded levels to the uvea. Presently this method of medication conveyance has increased new energy for different reasons. The advance in materials sciences and pharmaceutical plan have given new energizing conceivable outcomes to create controlled discharge details to convey medications to the back fragment and to direct the mending procedure after surgery.

c. **Intravitreal organization:** Direct medication organization into the vitreous offers particular preferred standpoint of more clear access to the vitreous and retina. It ought to be noted; however that conveyance from the vitreous to the choroid is more muddled because of the deterrent by the RPE (Retinal Shade Epithelium) boundary. Little atoms can diffuse quickly in the vitreous however the portability of substantial particles, especially emphatically charged, is limited.

Factors affecting intra Ocular Bio-availability:

Factors that influence the bioavailability of topically instilled drug are mentioned below.

1) **Lacrimal Fluid:** At the point when the eye drops are ingrained in the cul-de-sac, the tranquilize arrangement get weakened with the lacrimal liquid. This could with consistent tear stream diminish the volume and grouping of medication achieving the objective locales.

2) **Nasolacrimal Drainage:** This waste framework is likewise dependable the contact time of the medication arrangement with the corneal surface.

3) **Molecular size:** Small size particle like mannitol (mol.wt =182) can easily pass through an intact cornea when compared to large sized particle like insulin and dextran.

4) **Partition Coefficient:** Corneal membrane being lipophilic is highly permeable to lipophilic drug while hydrophilic drug experience greater resistance from the epithelium for penetration .through the epithelium of the cornea via the following two major pathways.
   a. Movement of drug molecules through transcellular route while is a partition controlled pathway.
   b. Passage of molecules through the intercellular spaces.

   It has been found that drugs with a distribution coefficient of 100-1000 exhibited optimum permeation. The following equation derived by Schoenwald and Huang relates the distribution coefficient with the permeability of beta-blocker.

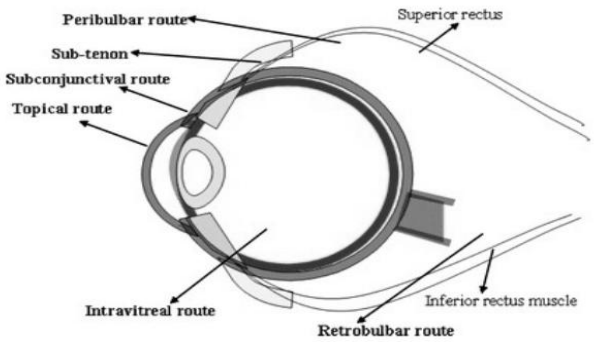

Figure 2: **Routes of delivery of the eye**

Figure 2. Routes of delivery of the eye

$$\text{Log } p = 0.623(\log K_{oct/buffer}) - 0.108 (\log K_{oct/buffer})^2 - 5.0263$$

Where,

P = Permeability coefficient

$K_{oct/buffer}$ = Distribution coefficient

However, this relation does not hold good for low molecular weight and water soluble compounds like mannitol, methanol etc., as these are transferred via pores rather than the two major pathways mentioned above.

5) **Protein Binding:** Endless supply of the medication arrangement, proteins in the lacrimal liquid spot with the medication particles. Just free or unbound medication particles can experience corneal penetration. In the cornea, free medication atoms experience tranquilize protein connections have found to diminish the pharmacological action of the medication [25-30].

6) **Charge:** Surface of the corneal epithelium is adversely charged and henceforth it supports the assimilation of emphatically charged medication particles.

Types of Ocular Controlled Release System

1. **Non erodible**
   a. Ocuserts
   b. Contact lenses
   c. Diffusional inserts

2. **Erodible**
   a. Lacrisert
   b. SODI
   c. Minidisc

3. **Nanoparticles**

4. **Liposome**

1. **Non erodible**

a. **Ocuserts:** Ocular insert (ocusert) are sterile preparation that prolong residence time of drug with a controlled release manner and negligible or less affective by nasolacrimal damage. Ocusert system is a novel ocular drug delivery system based on porous membrane. The release of drug from diffusional inserts/Ocusert is based on a diffusional release mechanism. It consists of a central reservoir of drug enclosed in specially designed microporous membrane allowing the drug to diffuse from the reservoir at a precisely determined rate. The ocusert pilocarpine ocular therapeutic system, developed by Alza Corporation.

Merits of Ocuserts: controlled rate of delivery, greater drug absorption.

Demerits of Ocuserts: Patientsun comfort, Placement and removal of inserts.

b. **Contact Lens :**
   1. Presoaked Hydrophilic lens.
   2. Drug Release: within 1st 30 Min.
   3. Alternate approach: incorporate drug either as solution or suspension of solid monomer mixture.
   4. Release rate is up to: 180 hr.

c. Diffusional Inserts:
   1. Central reservoir of drug enclosed in Semi permeable or micro porous membrane for diffusion of drug.
   2. Diffusion is controlled by Lacrimal Fluid penetrating through it.
   3. It prevents continues decrease in release rate due to barrier.
   4. Release follows: Zero Order Kinetics.

2. Erodible Inserts [15-19]

Erodible supplements defeat the negative marks of non-erodible embeds as they don't need to be expelled from the eye furthermore give more prominent level of solace and passableness in the eye. However inspite of offering comfort in application, erodible embed can show changeability in the discharge energy of medications from patient. This is on the grounds that patients vary from each other as far as rate of tear creation and level of metabolic compounds in the lacrimal liquid.

a. **Lacrisert:** Lacrisert is non-sedated, sterile, pole moulded erodible embed which is produced using hydroxypropyl cellulose. It is without any additive and is valuable in the treatment of dry eye disorder. It is set in the sub-par fornix, where it gets hydrated to from a hydrophilic film, which thus hydrates the cornea.

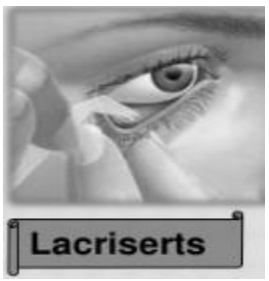

Figure 3. Lacriserts

b. **SODI (soluble ocular delivery inserts):** Small water-soluble developed for cosmonauts by soviet scientists who could not us their eye drop in weightless conditions.
   1. Composition: Acryl amide, Vinyl Pyrolidone, Ethylacrylate.
   2. Weight 15-16 mg.
   3. In 10-15 sec Softens; in 10-15 min. turns in Viscous Liquids; after 30-60min becomes Polymeric Solution.
   4. Advantages: Single SODI application replaces 4-12 eye drops Instillation or 3-6 application of Ointments. Once a day treatment of Glaucoma and Trachoma.

c. **Minidisc:** It is made up of counter disc with convex front and concave back surface in contact with eye ball.
   1. Composition**:** Silicon based pre polymer.
   2. Hydrophilic or Hydrophobic.
   3. Drug release for 170 hr.
   4. Further increase in gentamycin sulphate to 320 hrs.
   5. Gamma irradiation and heat exposure may decrease release rate due to additional cross linking of polymer matrix.

3. Nanoparticles:

Nanoparticles are the particulate drug delivery sy stem 10 to 1000nm in size in which the drug may be dispersed, encapsulated or absorbed.
   1. For water soluble drugs.
   2. Size: 10-1000nm
   3. Drug is Dispersed Encapsulated or Absorbed.
   4. Produced by Emulsion Polymerization
   5. Chemical initiation,
   6. Gamma irradiation, visible light
   7. Polymerization is carried out by:
   8. Emulsifier stabilizes polymer particle
   9. Polymer used is Biodegradable. E.g.- Nanoparticle of Pilocarpine enhances Miotic response by 20-23%.

4. Liposome: A liposome is a circular vesicle having no less than one lipid bilayer. The liposome can be utilized as a vehicle for organization of supplements and pharmaceutical medications. Liposome can be set up by disturbing natural layers, (for example, by sonication).

Advantages of Ocular Drug Delivery

1. Increased contact time and thus improved bio-availability.
2. Possibility of providing a prolonged drug release and thus a better efficacy.
3. Administration of an accurate dose in the eye and thus a better therapy.
4. Reduction of systemic side effects and thus reduced adverse effects.
5. Ease of handling and insertion.

Disadvantages of Ocular Drug Delivery

1. The insert may be lost immediately.
2. The necessity of using preservative.
3. Its poor bioavailability.
4. The instability of dissolved drug.
5. The very short time the solution stays at the eye surface

Recent formulation Trends in ocular drug delivery system

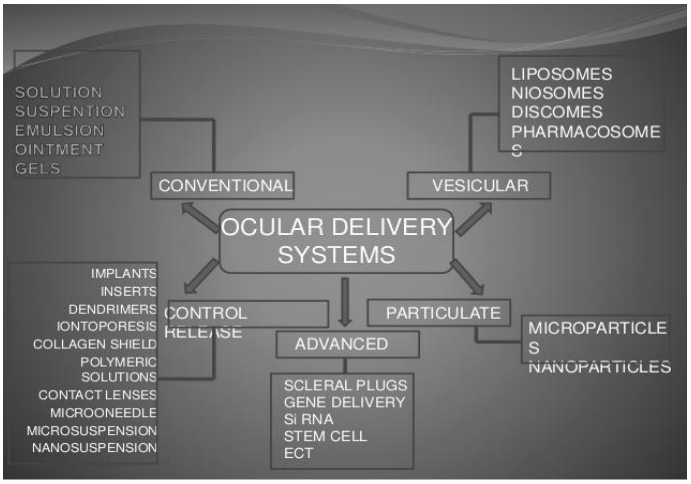

Figure 4. Different drug delivery systems for ocular therapy.

Conventional Delivery Systems [6]

Solution eye drops: An eye drop arrangement gives a heartbeat sedate pervasion post topical drop instillation, after which its fixation quickly decreases. The energy of medication fixation decrease may take after a rough first request. In this manner, to enhance medicate contact time, pervasion and visual bioavailability; different added substances might be added to topical eye drops, for example, consistency enhancers, penetration enhancers and cyclodextrins.

Suspensions: Suspensions are another class of non-intrusive visual topical drop medicate bearer frameworks. Suspension might be characterized as scattering of finely isolated insoluble Programming interface in a watery dissolvable comprising of an appropriate suspending and scattering specialist. At the end of the day, the transporter dissolvable framework is a soaked arrangement of Programming interface.

Emulsions: An emulsion based plan approach offers favorable position to enhance both solvency and bioavailability of medications. There are two sorts of emulsions which are monetarily abused as vehicles for dynamic pharmaceuticals: oil in water (o/w) and water in oil (w/o) emulsion frameworks.

Ointment and Gels: Prolongation of medication contact time with the outer visual surface can be accomplished utilizing ophthalmic balm vehicle however, the significant disadvantage of this measurement shape like, obscuring of vision and tangling of eyelids can limits its utilization.

Vesicular System

Liposome: Liposome are biocompatible and biodegradable lipid vesicles made up of characteristic lipids and around 25–10 000 nm in distance across. They are having a cosy contact with the corneal and conjunctiva surfaces which is alluring for medications that are ineffectively consumed, the medications with low parcel coefficient, poor dissolvability or those with medium to high sub-atomic weights and in this manner expands the likelihood of ocular drug absorption.

Noisome and Discomes: Noisome are artificially steady when contrasted with liposome and can capture both hydrophobic and hydrophilic medications. They are non poisonous and don't require uncommon taking care of procedures. Noisome are non-ionic surfactant vesicles that have potential applications in the conveyance of hydrophobic or amphiphilic drugs. Non-ionic surface dynamic operators based discoidal vesicles known as (discomes) stacked with timolol maleate were figured and portrayed for their in vivo parameters. Discomes may go about as potential medication conveyance transporters as they discharged medication in a supported way at the visual site.

Pharmacosomes: This term is utilized for immaculate medication vesicles framed by the amphiphilic drugs. Any medication having a free carboxyl gathering or a dynamic hydrogen particle can be esterifies (with or without a spacer gathering) to the hydroxyl gathering of a lipid atom, hence creating an amphiphilic prodrug. The amphiphilic prodrug is changed over to pharmacosomes on weakening with water. The pharmacosomes indicate more noteworthy rack soundness, encouraged transport over the cornea, and a controlled discharge profile.

Control Delivery Systems

Implants: For endless visual sicknesses like cytomegalovirus (CMV) retinitis, inserts are powerful medication conveyance framework. Prior non biodegradable polymers were utilized yet they required surgical methods for inclusion and expulsion. Right away biodegradable polymers, for example, Poly Lactic Acid (PLA) are sheltered and powerful to convey sedates in the vitreous depression and give no dangerous suggestions.

Iontophoresis: In Iontophoresis coordinate current drives particles into cells or tissues. Emphatically charged of medication are crashed into the tissues at the anode and the other way around. Visual Iontophoresis conveyance is quick, effortless and protected as well as convey high grouping of the medication to a particular site.

Dendrimers: Dendrimers are effectively utilized for various courses of medication organization and have better water-solvency, bioavailability and bio-compatibility. Vandamme and colleagues have created and assessed poly (amidoamine) dendrimers containing fluoresce in for controlled visual medication conveyance.

Collagen Shield: Collagen shield fundamentally comprise of cross connected collagen, manufactured with fetal calf skin tissue and created as a corneal wrap to advance injury recuperating. Topically connected anti-toxin conjugated with the shield is utilized to advance mending of corneal ulcers. Tear liquid makes these gadgets delicate and frame a thin malleable film which is having disintegration rate up to 10, 24 or 72 hours. In view of its basic solidness, great biocompatibility and natural latency, collagen film demonstrated as a potential transporter for ophthalmic drug delivery system

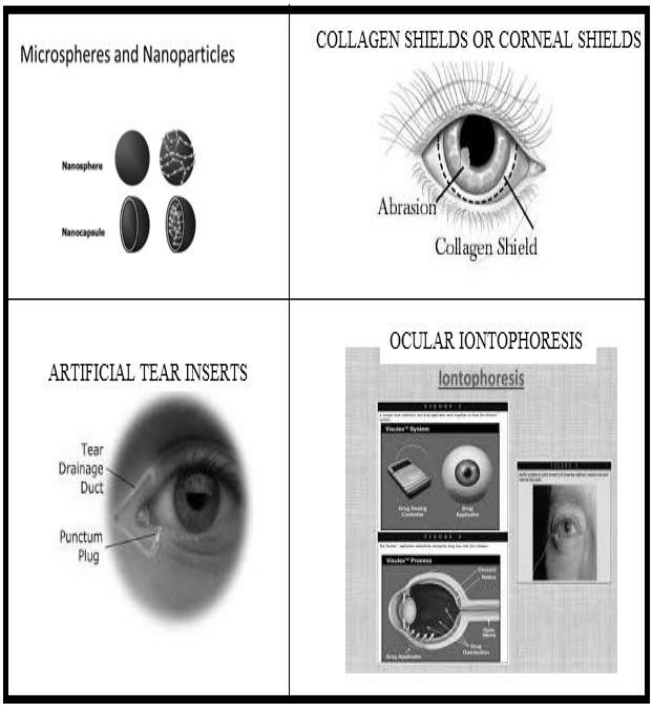

Figure 5. Control Drug Delivery System

Advanced Delivery System

Stem cell Therapy: The most successful ocular application has been the utilization of limbal undifferentiated cells, transplanted from a source other than the patient for the reestablishment of corneal epithelium. The wellsprings of limbal cells incorporate benefactors, auto grafts, corpse eyes, and (as of late) cells developed in culture. Undifferentiated cell Therapy has shown incredible accomplishment for specific diseases of the front section.

Sclera Plug therapy: Sclera plug can be embedded utilizing a basic strategy at the standards plane district of eye, made of biodegradable polymers and medications, and it step by step discharges compelling measurements of medications for a while upon biodegradation. The fittings are viable for regarding vitreoretinal illnesses, for example, proliferative vitreoretinopathy; cytomegalovirus retinitis reacts to rehashed intravitreal infusions and for vitreoretinal issue that require vitrectomy [35-40].

Particulates (Nanoparticles and Microparticles): - The greatest size cut-off for micro particles for ophthalmic organization is around 5-10 mm. Nanoparticles are readied utilizing bio adhesive polymers to give managed impact to the captured drugs. That is the reason microspheres and nanoparticles are promising medication transporters for ophthalmic application.

Retro Metabolic Delivery System

This medication configuration approach were assigned as retro metabolic to accentuate the way that metabolic pathways are outlined going in reverse contrasted with genuine metabolic procedures.

Retro metabolic sedate plan joins two noteworthy deliberate methodologies: The outline of soft drug (SDs) and Chemical Delivery Systems (CDSs).

Both expect to outline new, safe medications with an enhanced remedial list by incorporating auxiliary movement relationship (SAR) and basic digestion system connections (SMR).

Evaluation of Ocular Drug Delivery System

Ocular drug delivery system at preclinical stage should be tried for their security and adequacy to empower in their movement to clinical stage. For assessing a particular visual medication conveyance framework, it is important to pick fitting contraption, system and creature tissues. A portion of the strategies for assessment are portrayed beneath.

Uniformity of Thickness

This test is applicable to ocular films, inserts, lenses etc. Five films are selected from each batch and the thickness of each clip is measured using a micrometer screw gauge.

Uniformity of Weight

Five films are selected from each batch and each film is weighted on an electronic balance and the mean weight of each formulation is noted.

Drug Contain Uniformity

This test for ocular inserts require the use of simulated tear fluid (STF) with the following composition and pH of 7.4

Sodium chloride	-0.67g
Sodium bicarbonate	-0.2g
Hydrated calcium chloride	-0.008g
Purified water	-quantity sufficient 100g

Each dose form is ground in a glass mortar and pestle to which to which the tear fluid is added to obtain a suspension. This is then filtered and the filtrate is subjected to spectrophotometer analysis to determine the drug content.

Determination of Surface pH

In this, initially as agar solution is prepared by dissolving suitable quantity of agar in simulated tear fluid and then pouring it in a Petri dish. The dosage form is placed in the petri dish and left for 5 hours to swell at room temperature. After this time period, pH of the surface is measured using and electrode.

% Moisture Absorption

The dosage form are initially weighted and placed in a desiccators containing 100 ml of saturated solution of $AlCl_3$. Humidity is maintained at 79.5%. Dosage form are removed after three days and weighted again. The % of moisture absorbed is determined by the following formula.

% moisture absorbed

$$= \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

% Moisture Loss: Dosage forms are initially weighted and that place in a desiccators containing anhydrous calcium chloride. The dosage forms are removed after a period of three days, reweighted and % moisture loss is calculated from the following formula [5].

% moisture loss

$$= \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Swelling Index

For this test, three beakers are taken and each is filled with 4ml simulated tear fluid. Three dosage forms which have been previously weighted are added to each beaker and left to swell for five minutes. After this period, the dosage forms are removed and excess water is removed by using a filter paper. These are weighed and the water is continued to be removed until there is no increasing weight. Swelling index is then calculated from these data.

Folding Endurance

Typically, dispensable glass vessels of 1ml limit are utilized for examining. The examples are gathered from the negligible tear piece of the rabbits. Outrageous care must be taken to stay away from any corneal contact and conceivable incited lacrimation. To pull back watery silliness, rabbits are anesthetized with ketamine and fluid funniness around 200ml is pulled back from the front load utilizing 1ml syringe with 26 gage needle. Vitreous specimens are likewise acquired with 20 gage needle. The whole cornea, focal point, and iris-ciliary body are additionally expelled and broke down for the medication content.

In-Vitro Evaluation Methods [7]

Bottle method: In this strategy, dose structures are put in the way of life jugs containing phosphate cradle at pH 7.4. The way of life jugs are shaken in a thermostatic water shower at 37°C. A specimen of medium is taken out at fitting interims and broke down for medication substance.

Diffusion method: A suitable test system device is utilized as a part of this technique. Tranquilize arrangement is set in the contributor compartment and cradle medium is put in the receptor compartment. A fake layer or goat cornea is put in the middle of benefactor and receptor compartment. Medicate diffused in receptor compartment is measured at different time interims.

Modified rotating basket method: In this technique, measurement frame is put in a wicker bin get together associated with a stirrer. The get together is brought down into a jacketed measuring glass containing support medium. The temperature of framework is kept up at 37°C. An example of medium is taken out at suitable time interims and broke down for medication content.

Modified rotating paddle apparatus: In this technique, dispersion cells (those that are utilized for examination of semi-strong plans) are put in the flagon of pivoting oar contraption. The support medium is set in the jar and oar is turned at 50 rpm. The whole unit is kept up at 37+0.5° C. Aliquots of tests are expelled at suitable time interims and broke down for medication content.

In-Vivo Evaluation Methods

1. The drug delivery systems can be evaluated for its pharmacokinetic and pharmacodynamic profiles [8].
2. The fundamental goal of the pharmacokinetic studies is to decide the medication discharge from the measurements frame to the eye.
3. Rabbit is utilized as a trial creature as a result of various anatomical and physiological visual likenesses furthermore because of bigger size of the eye.
4. Pharmacokinetic studies are performed by measuring drug focus in different eye tissues e.g.: focal point, cornea, iris, ciliary body, retina, sclera, watery and vitreous funniness in rabbits. The intraocular weight of the eye is measured with a monometer
5. Ocular pharmacokinetic studies can also be carried out by tear fluid sampling, which is a non-invasive technique.
6. Normally, expendable glass vessels of 1 ml limit are utilized for inspecting. The examples are gathered from the minor tear portion of the rabbits.
7. Extraordinary care must be taken to stay away from any corneal contact and conceivable incited lacrimation.
8. To pull back watery funniness, rabbits are anesthetized with ketamine and fluid diversion around 200 ml is pulled back from the front load utilizing 1 ml syringe with 26 gage needle.
9. Vitreous specimens are additionally gotten with 20 gage needle. The whole cornea, focal point, and iris-ciliary body are likewise expelled and dissected for the medication content.

Conclusion

The ocular insert represents a significant advancement in the therapy of eye disease. Ocular inserts are characterized as clean, thin, multilayered, medicate impregnated, strong or semisolid consistency gadgets set into the culde-sac or conjuctival sac, whose size and shape are particularly intended for ophthalmic application. They are made out of a polymeric bolster that might possibly contain a medication. Points of interest with ocuserts, for example, exact dosing Capacity to give at consistent rate and draw out medication discharge hence a superior adequacy. Expanding contact time and along these lines enhancing bioavailability. Conceivable diminishment of systemic absorption and in this manner lessened systemic antagonistic impacts. Lessened recurrence of organizations and therefore better patient consistence with lower occurrence of visual side effects. In this survey, we have focused on the advanced approaches in ocular drug delivery system [9,10].

Acknowledgement

The successful accomplishment of this seminar would not have been possible but by the timely help and guidance rendered by many people. I would like to mention few of them.

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References

1. K. S. G. Arul Kumaran, K. Karthika and J. Padmapreetha: Comparative review on conventional and advanced ocular drug delivery. International Journal of Pharmacy and Pharmaceutical Sciences 2010; 2(4): 1-5.
2. S. W. Jacob and C. A. Francone: structure and function in man; 2nd edition, W. B. Sauder, Philadelphia, 1970, Chapter 17.
3. K. P. Sampath Kumar, Debjit Bhowmik, G. Harish, S. Duraivel, B. Pragathi kumar: Ocular Inserts: A Novel Controlled Drug Delivery System. The pharma innovation journal 2013; 1(12): 1-16.
4. Wolff, E: Anatomy of eye and orbit. Blakistone Company, New York and Toronto, 4th edition, 1954:207.
5. Stella, V.J; Mikkelson, T.J; Pipkin, J.D: Drug Delivery System: Characterictic and Biomedical application. Oxford university press; New York; 1996; 5th edition 112.
6. Brian GS: Safety Evaluation of Ocular Drug Delivery Formulations: Techniques and Practical Considerations, Toxicologic pathology 2008; 36:49-62.
7. Mitra AK: Fundamentals of ocular drug delivery. American Association of Pharmaceutical Scientists Journal 2010; 12(3):348-360.
8. Barar et al. Ocular novel drug delivery, impacts of membranes and barriers. Expert Opin Drug Deliv 2008; 5(5):567-8.
9. Kim et al.: Fundamentals of ocular drug delivery. Ophthalmic Res. 2007; 39:244-54.
10. Wadhwa S, Paliwal R, Paliwal SR, Vyas SP.: Nanocarriers in ocular drug delivery: Current Pharmaceutical Design 2009; 15: 2724-2750.
11. Mueller WH, Deardroff DL: Ophthalmic vehicles: The effect of methyl cellulose on the penetration of Homatropine hydro bromide through the cornea. American Association of Pharmaceutical Scientists Journal 1956; 334-341.
12. Maichuk YF: Ophthalmic drug inserts. Invest Ophthalmol 1975; 87–90.
13. MF Seattone: Solid polymeric inserts/disks as drug delivery devices. In: P Edman, ed. Biopharmaceutics of Ocular Drug Delivery. Boca Raton, FL: CRC Press 1993; 61–79.
14. Kaur IP, Garg A, Singla AK, Agarwal D: Vesicular systems in ocular drug delivery. International Journal of Pharmaceutical 2004; 269:1-14.
15. Vyas SP, Mysore N, Jaitely V, Venkatesan N: Discoidal niosome based controlled ocular delivery of timolol maleate. Pharmazie 1998; 53(7): 466-469.
16. Guinedi AS, Mortada ND, Mansour S, Hathout RM: Preparation and evaluation ofreverse-phase evaporation and multilamellarniosomes as ophthalmic carriers of acetazolamide. American association of pharmaceutical scientists journal 2005; 306:71-82.
17. Kaur IP, Kanwar M: Ocular preparations: The formulation approach. Drug developmentIndrustrial Pharmacy 2002; 28(5):473-493.
18. VHL Lee, JR Robinson. Review: Topical drug delivery: recent developments and future challenges. Journal Oculus Pharmacol. 1986; 2:67–108.
19. Saettone MF, Bucci G, Speiser P: Ophthalmic Drugs Delivery: Biopharmaceutical, Technological, Clinical Aspects. Fidia Research Series, Padova, Italia: Latvian Press 1987; 11.
20. VHL Lee: New directions in the optimization of ocular drug delivery. Journal ofOculPharmacol 1990; 6:157–164.
21. Edman P: Biopharmaceutics of Ocular Drug Delivery. Boca Raton, FL: CRC Press 1993.
22. AK Mithra: Ophthalmic Drug Delivery Systems. New York: Marcel Dekker 1993.
23. M Van Ooteghem: Preparations Ophtalmiques, Paris: Technique & Documentation 1995.
24. Frangie JP: Clinical pharmacokinetics of various topical ophthalmic delivery systems. Clin Pharmacokinetic 1995; 29:130–138.
25. Kimura H, Ogura Y, HashizoeM, Nishiwaki H, Honda Y, Ikad Y: A new vitreal drug delivery system using an implantable biodegradable polymeric device. Investigative Ophthalmology & Visual Science 1994; 35:2815-2819.
26. Hill JM, O'Callaghan RJ, Hobden JA: Ocular Iontophoresis. In: Mitra AK. Ophthalmic Drug Delivery Systems. New York: M. Dekker Inc; 1993; 331-354.
27. Rootman DS, Janssen JA, Gonzalez JR, Fischer MJ, Beuerman R, Hill JM: Pharmacokinetics and safety of transcorneal iontophoresis of tobramycin in the rabbit. Investigative Ophthalmology & Visual Science 1988; 29:1397-1401.
28. Callahan MC, Hobden JA, O'Callaghan RJ, Hill JM: Ocular drug delivery, A comparison of transcorneal iontophoresis to corneal collagen shields. International Journal of Dharma 1995; 123:173- 179.
29. Usayapant A, Karri AH, Narurkar MM: Effect of 2-hydroxypropyl-beta-cyclodextrin on the ocular absorption of dexamethasone and dexamethasone acetate. Pharmaceutical Research 1991; 8: 1495–1499.
30. Vainer M, Amidon G, Lindenbaum S, Haslam JL: Thermodynamic studies on the gelsol transition of some pluronic polyols. International Journal of Pharmaceutical 1984; 22: 207-218.
31. Vasantha R, Sehgal PK, Rao P: Collagen ophthalmic inserts for Pilocarpine drug delivery system. International Journal of Pharmaceutical, 1988; 47: 95-102.
32. Patravale VB, Date AA, Kulkarni RM.: Nanosuspensions: a promising drug delivery strategy. J Pharm Pharmacol 2004; 56: 827-840.
33. Jiang J, Gill HS, Ghate D, McCarey BE, Patel SR, Edelhauser HF, Prausnitz MR.: Coated microneedles for drug delivery to the eye. Investigative Ophthalmology & Visual Science 2007; 48:4038– 4043.
34. Green K, Chapman JM, Cheeks L, Clayton RM, Wilson M, Zehir A: Detergent penetration into young and adult rabbit eyes: comparative pharmacokinetics. Journal of Toxicology Cutaneous And Ocular Toxicology 1987; 6:89–107.
35. Ch'ng HS, Park H, Kelly P, Robinson JR: For oral controlled delivery II: Synthesis and evaluation of some swelling, water-insoluble bioadhesive polymers. Journal of Pharmaceutical Science 1985; 74:399-405.
36. Middleton DL, Robinson JR. Design and evaluation of an ocular bio adhesive delivery system. S.T.P. Pharma Sci 1991;1:200-206.
37. Gavini E, Chetoni P, Cossu M, Alvarez MG, Saettone MF, Giunchedi P: PGLA microspheres for the ocular delivery of a peptide drug, vancomycin using emulsification/spray-drying as the preparation method: In vitro/in vivo studies. Europen Journal of Pharmaceutical and Biopharmaceutical 2004; 57: 207–212.
38. Yasukawa T, Kimura H, Tabata Y, Ogura Y: Biodegradable scleral plugs for vitreoretinaldrug delivery. Advanced Drug Delivery Reviews 2001; 52(1): 25-36.
39. Selvam S, Thomas PB, Hamm-Alvarez SF, Schechter JE, Stevenson D, Mircheff AK, Trousdale MD: Current status of gene delivery and gene therapy in lacrimal gland using viral vectors. Advance drug delivery Research 2006; 58:1243–1257.
40. Klausner EA, Peer D, Chapman RL, Multack RF, Andurkar SV: Corneal gene therapy. Journal of Control Release 2007; 124: 107–133.
41. Campochiaro PA: Potential applications for RNAi to probe pathogenesis and develop new treatments for ocular disorders. Gene Therapy 2006; 13:559–562.
42. Levin LA, Ritch R, Richards JE, Borras T.: Stem- cell therapy for ocular disorders. Arch Ophthalmol 2004; 122(4): 621-627.
43. Tao W.: Application of encapsulated cell technology for retinal degenerative diseases. Expert Opinion on Biological Therapy 2006; 6: 717–7