

EYE DISORDERS, DISEASES AND TREATMENT – AN OVERVIEW

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ABSTRACT

Eye is a sensitive organ and is easily injured and infected. Delivery of drugs into eye is complicated due to removal mechanism of precorneal area results decrease in therapeutic response. Conventional ocular delivery systems like solution, suspension, ointment shows some disadvantages such as rapid corneal elimination, repeated instillation of drug and short duration of action. In situ polymeric delivery system will help to achieve optimal concentration of drug at the target site, thereby helps to achieve the desired therapeutic concentration. There are various novel ocular drug delivery systems such as In-situ gel, dendrimers, niosomes, nanoparticulate system, collagen shield, ocular iontophoresis suspension and ocusert etc. In situ gelling systems are liquid upon instillation and undergo a phase transition to form gel due to some stimuli responses such as temperature modulation, change in pH and presence of ions. Various attempts have been made towards the development of stable sustained release in-situ gels. Newer research in ophthalmic drug delivery systems is directed towards an incorporation of several drug delivery technologies, that includes to build up systems which is not only extend the contact time of the vehicle at the ocular surface, but which at the same time slow down the removal of the drug. This is a review based on ocular in situ gels, characterization, techniques and evaluation of in situ ophthalmic drug delivery systems.

KEYWORDS: Diabetic retinopathy, dendrimers, niosomes, ocular in situ gels, conjunctivitis, etc.

INTRODUCTION

Ophthalmic preparations are sterile products that may contain one or more pharmaceutical ingredient (s) administered topically, or by subconjunctival or intraocular (e.g. intravitreal and intracameral) injection in the form of solution, suspension, or Ointment.

The ocular drug delivery system is considered as most crucial and challenging as human eye is an isolated organ where the delivery of drug is quite difficult. Moreover, the conventional ophthalmic formulations unveil a short pre-corneal

residence time and poor bioavailability due to rapid and extensive elimination of drugs from pre-corneal lachrymal fluid by solution drainage, lachrymation, and non-productive absorption by conjunctiva.

In order to surpass the drawbacks associated with the conventional ophthalmic formulations, various attempts have been made towards the development of stable sustained release in-situ gels. Newer research in ophthalmic drug delivery systems is directed towards an incorporation of several drug delivery technologies, that includes to build up systems which is not only extend the contact time of the vehicle at the ocular surface, but which at the same time slow down the removal of the drug. In situ gel system is formulated as liquid preparation suitable to be instilled into eyes which upon exposure to the physiologic environment changes to gel results in in-situ gel, thus increasing the precorneal residence time of the delivery system, and enhances the ocular bioavailability of the drug.^[1]

The formation of gels depends on factors like change in a specific physicochemical parameter (pH, temperature, ion-sensitive) by which the drug gets released in a sustained and controlled manner. These systems were evaluated for drug content, clarity, pH, gelling capacity, viscosity, in vitro drug release studies, texture analysis, sterility testing, isotonicity evaluation, accelerated studies and irritancy test. FT-IR spectroscopy was used to know drug and polymer incompatibilities.^[2]

There are various new dosage forms like in situ gel, collagen shield, minidisc, ocular film, ocusert, nanosuspension, nanoparticulate system, liposomes, niosomes, dendrimers, ocular iontophoresis etc. These are the six main properties of ophthalmic preparations: Sterility, Preservation, Particle Limitations, pH, Stability, and Eye comfort. The main requirement is sterility, it is very important to make sure that medications applied to the eye should be sterile. If there are any abrasions in the eye, it is very easy for microorganisms to penetrate that area and cause an eye infection of *Pseudomonas aeruginosa* can lead to rapid onset of blindness (2-3 d) as a result of exposure to contaminated ophthalmics. It is possible to sterilize products using either autoclaving (for heat stable drugs) or membrane filtration with a 0.22 micrometer filter (for heat-labile drugs). Membrane filtration is very effective because it sterilizes the solution as well as removes particulate matter. Tear fluid is isotonic with blood and other tissues, so the drug solutions need to be isotonic to reduce tearing and irritation. Irritation of the eye leads to increased tearing which washes away the drug and leads to less being absorbed. 0.9% sodium chloride and 1.9% boric acid are isotonic with the tears. Typically, the eye can tolerate solutions with tonicity values ranging from equivalents of 0.5% to 1.6% sodium chloride without discomfort. There are even some therapeutic drug concentrations that are hypertonic, but they are applied in such small amounts that the eye can tolerate them. Antioxidants, chelating agents, and surfactants are all used to stabilize ophthalmic products. Lastly adjuvants are added to provide lubrication and protection against drying and cracking. Emollients provide oil to the tears to prevent them from evaporating.³ This is particularly important in patients with dry eyes. Demulcents have the ability to hold water and keep the membranes of the eyes in a hydrated form. All of these properties of ophthalmic are very important to the sterility, stability, and comfort of the product once applied to the eye.



Fig. 1: Human Eye.

Eyes are round in shape. But the Eye Lashes cover most of the structure of the eye. Hence, we can see the eye as in a convex structure. But the Eye Lashes are not part of the eye. There are some components in the eye. Those structures together build the anatomy of the Eye. Also, along with the components, there is the secondary structure which helps the eye to smoothly look around an eye is a spherical structure with a wall made up of three layers: the outer part sclera, the middle parts choroid layer, ciliary body and iris and the inner section nervous tissue layer retina. The sclera is tough fibrous coating that protecting the inner tissues of eye which is white except for the transparent area at the front, that is cornea allows light to enter to the eye. The choroid layer, situated in the sclera, contains many blood vessels that modified at front of the eye as pigmented iris the colored part of the eye (blue, green, brown, hazel, or grey). The front part of the eye (the part you see in the mirror) includes: The iris, cornea, pupil, sclera, conjunctiva. Just behind the iris and pupil lies the lens, which helps to focus light on the back of the eye. 80% of the eye is filled with a clear gel called as vitreous. Light passes through the pupil and the lens then it will reaches back of the eye. The inner part of the eye is protected by special light-sensing cells are together known as retina. The retina transforms light into electrical impulses. Behind the eye, the optic nerve conveys these impulses to the brain. The macula is a small extra-sensitive area which is present in retina that gives central vision. This is located in the center of the retina and contains the fovea, a small depression or pit at the middle of the macula that gives the clear vision.^[4]

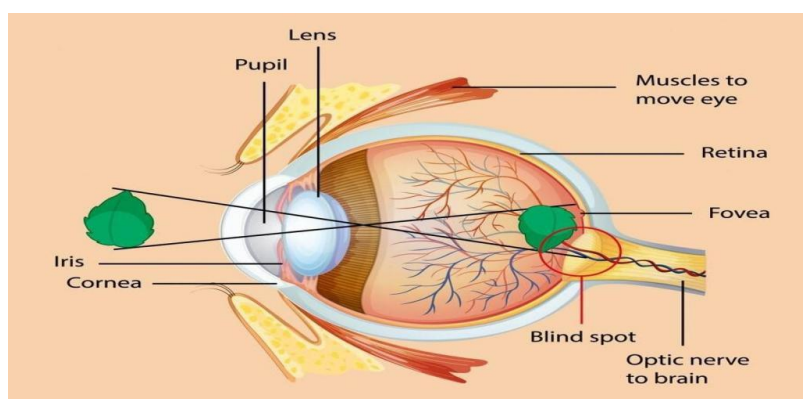


Fig. 2: Internal Structure of Human Eye.

PRIMARY COMPONENT OF EYE

- 1) Cornea - It is the circular structure present in front of the eyes. We can't able to see the cornea directly from the outside. As it is circular, we can't able to identify its position normally. It is just situated at the front of the eye. It is completely transparent. There are no blood vessels present at all in this area. It is a highly sensitive region.

- 2) Sclera - This is the whitest region found in the eye. It covers most of the eye portion which we can look at from the outside. Aqueous It is the jelly-like structure present between the Cornea & the lens. There is 99% of water in this portion. Nearly 1% is vitamin, protein & other materials may present. As the name suggests "Aqueous" means the water. And it defines the watery nature of this area.^[5]
- 3) Iris - It is made with a fiber-like structure. It is the circular region present in the middle of the eye. There are some pigments present. According to the inheritance, these pigments are inherited from the parents of any individual. These pigments may be Black, Blue, Brown, etc. as per the heredity. That is why Iris may differ from individuals as per the availability of the pigments.
- 4) Pupil - This is the circular hollow position present in the center of the Iris.
- 5) Lens - It is olive shape structure present behind the Pupil. It is enclosed in a transparent capsule. There are no blood vessels in this area. This is the main component of the eye.
- 6) Retina - This is another main component of the eyes. Inside the wall of the eyes, the retina is present all over the wall. This is the receipting component of the eye. But the Retina consists of two different kinds of cells. They are Rod Cells & Cone Cells. Around 130 million cells are present here. Also, only this part has the blood vessels. Also, this part is connected with the nerve.^[6]

EYE CONDITIONS

Amblyopia (lazy eye)

One eye sees better than the other as a result of not using the other eye during childhood. The weaker eye may or may not "wander." The weaker eye is called the "lazy eye."

Astigmatism

A defect that causes an inability to properly focus light onto the retina. Astigmatism causes blurry vision that can be corrected with glasses, contact lenses, or, in some cases, surgery.

Black eye

Swelling and discoloration (bruise) around the eye as a result of injury to the face.

Blepharitis

Inflammation of the eyelids near the eyelashes. Blepharitis is a common cause of itching or a feeling of grit in the eyes.

Cataract

A clouding of the natural internal lens of the eye, which can cause blurred vision.

Chalazion

An oil-making gland gets blocked and swells into a bump.

Conjunctivitis

Also known as "pinkeye," conjunctivitis is an infection or inflammation of the conjunctiva, the clear layer that covers the front of the eye. It is usually caused by allergies, a virus, or a bacterial infection.

Corneal abrasion

A scratch on the clear part of the front of the eye. Pain, light sensitivity, or a feeling of grit in the eye is the usual symptoms.

Diabetic retinopathy

High blood sugar damages blood vessels in the eye. Eventually, weakened blood vessels may start leaking or overgrow the retina, threatening vision.

Diplopia (double vision)

Seeing double can be caused by many serious conditions. Diplopia requires immediate medical attention.

Dry eye

Either the eyes don't produce enough tears, or the tears are of poor quality. Dry eye can be caused by medical problems such as lupus, scleroderma, and Sjogren's syndrome.

Glaucoma

Progressive loss of vision usually associated with increased pressure inside the eye. Peripheral vision is lost first, often going undetected for years.

Hyperopia (farsightedness)

Inability to see near objects clearly. The eye is "too short" for the lens, or certain eye muscles have weakened with age.

Keratitis: Inflammation or infection of the cornea. Keratitis typically occurs after germs enter a corneal abrasion.

Myopia (nearsightedness)

Inability to see clearly at a distance. The eye is "too long" for the lens, so light isn't focused properly on the retina.

Optic neuritis

The optic nerve becomes inflamed, usually from an overactive immune system. Painful vision loss in one eye typically results.

Pterygium

A thickened conjunctival mass usually on the inner part of the eyeball. It may cover a part of the cornea, causing vision problems.

Retinal detachment

The retina comes loose from the back of the eye. Trauma and diabetes are common causes of this problem, which often requires urgent surgical repair.

Retinitis

Inflammation or infection of the retina. Retinitis may be a long-term genetic condition or result from an infection.^[7]

OPHTHALMIC PRODUCTS

There are various types of ophthalmic products

It includes.

- 1) Eye Drops
- 2) Eye lotions
- 3) Eye suspensions
- 4) Contact lens solution
- 5) Ophthalmic inserts
- 6) Gels
- 7) Emulsion

1) Eye drops

Eye drops or eyedrops are liquid drops applied directly to the surface of the eye usually in small amounts such as a single drop or a few drops. Eye drops usually contain saline to match the salinity of the eye. Drops containing only saline and sometimes a lubricant are often used as artificial tears to treat dry eyes or simple eye irritation such as itching or redness. Eye drops may also contain one or more medications to treat a wide variety of eye diseases. Eye drops are a type of medication that are administered directly into the eye. They are used to treat a variety of conditions such as dry eyes, allergies, infections, and glaucoma.^[8]



Fig. 3: Eye Drop.

2) Eye lotion

Definitions of eye-lotion. lotion consisting of a solution used as a cleanser for the eyes. synonyms: collyrium, eyewash. type of: application, lotion. Liquid preparation having a soothing or antiseptic or medicinal action when applied to the skin. Eye lotions. Powders for eye drops and powders for eye lotions. Semisolid eye preparations (ointments, creams and gel Eye lotions are sterile aqueous solution used for washing of the eye The eye lotions are supplied in concentrated form and are required to be diluted with warm water immediately before use.

- They are usually applied with a clean eye-bath or sterilized fabric dressing and a large volume of solution is allowed to flow quickly over the eye.
- Eye lotions should be isotonic and free from foreign particles to avoid irritation to the eye. They are required to be prepared fresh and should not be stored for more than two days as the lotion may get contaminated.^[9]



Fig. 4: Eye lotion.

3) Eye suspension

Ophthalmic suspensions are used to deliver poorly soluble compounds and are sterile liquid preparations containing solid particles dispersed in a liquid carrier. Such suspensions must contain the drug in micronized form to prevent irritation and/or scratching cornea. CD Formulation's team are leading experts in all aspects of pharmaceutical dosage form development and dosage form optimization, and we can design suspension dosage forms based on the properties of the API and the client's development goals. CD Formulation can be your one stop shop for your suspension dosage form needs.

Ophthalmic solutions are sterile, aqueous solutions used for, among other things, cleansing and rinsing eyeballs. They may contain excipients, which, for example, regulate osmotic pressure, the pH, and viscosity of the preparation.



Fig. 5: Eye suspension.

Products that are designed for ophthalmic use are sterile, meaning that they are free of germs, as long as they are not open. Once open, they are at higher risk of becoming contaminated. In addition, improper storage or exposure to less-than-ideal conditions can have an impact on their quality.^[10]

4) Contact lens solution

Contact lens solution is used for effective cleaning of contact lenses helps maintain the quality of the lenses throughout their lives and, more importantly, helps protect the health of the eye. The disinfection process is simple and the most important thing is to find the right CL solution. purpose of contact lens solution.

- A good quality contact lens solution is the best friend for your eyes.
- It helps in cleaning, rinsing and disinfecting the contact lenses.
- All other contact lenses are stored in lens solution, other than daily disposable.^[11]

5) Ophthalmic inserts

Ophthalmic inserts are defined as sterile solid or semisolid preparations, with a thin, flexible and multilayered structure, for insertion in the conjunctival sac. Recently ophthalmic inserts impregnated with drug, have been developed to provide for the continuous release of the drug.

6) Gels

Ophthalmic gels are composed of mucoadhesive polymers that provide localized delivery of an active ingredient to the eye. Such polymers have a property known as bioadhesion meaning attachment of a drug carrier to a specific biological tissue. These polymers are able to extend the contact time of the drug with the biological tissues and thereby improve ocular bioavailability.

7) Emulsions

Topical ophthalmic emulsions generally are prepared by dissolving or dispersing the active ingredient(s) into an oil phase, adding suitable emulsifying and suspending agents and mixing with water vigorously to form a uniform oil-in-water emulsion. Each phase is typically sterilized prior to or during charging into the mixing vessel. High-shear homogenation may be employed to reduce oil droplet size to sub-micron size which may improve the physical stability of the oil micelles so they do not coalesce.^[12]

ADVANTAGES

- Increasing contact time and improving bioavailability.
- Providing a prolong drug release and thus a better efficacy.
- Reduction of adverse effects.
- Reduction of the number administrations and thus better patient compliance.^[13]

CONCLUSION

New ocular drug delivery systems have great potential to improve drug bioavailability in the eye. Limitations of the ocular barriers are major issues to solve for an optimal formulation. Active substance limitations are decreased with the choice of an adaptable form and composition. Patient compliance improves with a tolerable and non-irritating formulation; this parameter is primary for an acceptable administration.

This review showed various development studies of ocular delivery forms. Many studies explored the possibility to decrease the side effects of ocular barrier to prolong ophthalmic residence of the drugs in the eyes, to improve the bioavailability of the active substances and to enhance ocular penetration. Various antibiotics with different characteristics were tested with different delivery systems in order to improve their ophthalmic bioavailability. Antibiotic administration required optimal antimicrobial efficacy. These drugs are used in eye surgeries, anterior segment and posterior segment diseases. Some improvements to limit the impact of the antibiotic's disadvantages on the eye are under study and under development. Existing forms and new shapes make it possible to increase the ocular therapy efficacy. In the next few years, drug development allowing local action without the need for systemic passage will decrease the frequency of administration, dosage of the drug and improve patient compliance.

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