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OPHTHALMIC DRUG DELIVERY SYSTEMS FOR CONJUNCTIVITIS

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ABSTRACT: Ophthalmic drug delivery is greatly onerous for a better remedial response in any type of disease state for instance, conjunctivitis, more commonly published as pinkeye, is an inflammation of the conjunctiva, a clear membrane that envelopes the outmost lamina of the eye and the inside surface of the eyelids. Usually, conjunctivitis is of the following classes depending on their origins of contagion as like (Allergic conjunctivitis, viral conjunctivitis, Bacterial conjunctivitis, and Irritant and Chemical conjunctivitis). It possibly will cause a number of symptoms grounded on their causative reason, for example Itchiness, body aches, sensitiveness to light, uneasiness in the eye, redness of the eye or inward eyelids, discharge as well as tearness. Discharge may give rise to eyelids crusting and stick together while sleeping and swelling of the eyelids.

INTRODUCTION:

Eye Anatomy: Eye is one of the significant delicate structure of the human body. It's veritably sensitive additionally pregnable to miscellaneous disorders. Therefore, safekeeping with prevention is essential to maintenance the eye unharmed and in good shape.

Eye Ball: Eyeball (*Bulbus oculi*) is almost a globe-shaped organ with a circumference of nearby 24 mm. It's somewhat smoothened from over down. The eyeball is constructed of two segments, an anterior part and a posterior part. The anterior part is short and assembles one-sixth of the eyeball. The posterior part is bigger and constitutes five-sixth of the eyeball. Radius of this region is roughly 8 mm.

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The light-sensitive fabric coats the posterior wall of this segment called the retina. The Midpoint of the eyeball's anterior arc is titled anterior pole, and the core of the rear curve is named as posterior pole. Line combining both poles is titled optical axis. The line joining a point in cornea, little medium to anterior pole and fovea central is, positioned side posterior pole is known as visual axis. Light shafts pass through the visual axis of eyeball; Optic nerve leaves the eye, a little medium to posterior pole [1].

Orbital Cavity: In orbital depression, except for anterior one-sixth, the eyeball is positioned in a bony depression known as orbital depression or eye socket. A thick subcaste of areolar towel is interposed between bone and eyeball. It serves as a bumper to cover the eyeball from external force. Eyeballs are attached to orbital depression by the optical muscles [2].

Eyelids: Eyelids screen the eyeball from foreign pieces approaching in contact with its surface and cut down the light in the course of sleep. Eyelids are opened and closed voluntarily, as well as by

kickback action. Perimeters of eyelids possess sensitive hair named the cilia. Each cilium originates from a follicle, encompassed by a sensitive whim-whams super system. When dust flyspeck approaches cilia, these sensitive jitters are actuated, executing in rapid-fire eyelids blinking. It restrains the dust pieces from hitting the eyeball. There are nearly 100 to 150 cilia in the upper eyelid and approximately 50 to 75 cilia in the lower eyelid. Meibomian glands and several sebaceous glands are also arranged up in the eyelids. These glands open into the follicles of cilia. Contagion of these glands initiates the progression of usual eye ailment, leading to vision failure. Opening amid the two eyelids is termed palpebral chink. In grown-ups, it's near 25 mm long. Its range is around 12 mm to 15 mm, while opened [3].

Conjunctiva: Conjunctiva is a slim mucus membrane, that masks the bare region of the eye. Following covering the anterior face, the conjunctiva is exhibited inside the internal shells of eyelids. Part of the conjunctiva covering the eyeball is named bulbar portion. The region covering the eyelid is termed as a palpebral portion. In the course of the check or opening of eyelids, the contrary segments of conjunctiva slide over each other. The surface of the conjunctiva is waxed by thin sheet of gash buried by the lacrimal gland [4].

Lacrimal Gland and Tear: Lacrimal gland is placed in the sanctum of bone that embraces the posterior five sixth of the eye. The Antecedent it's nonstop with the cornea. White stringy tissues and elastic fibers assemble Sclera. The posterior part of the sclera, where the optical nerve pierces it is thin with perforations [5]. It's termed as the lamina crib Rosa forming upper and external border of the wall of the eye socket. From the lachrymal gland, tear flows over the surface of conjunctiva and drains inside the nose through lachrymal tubes, lacrimal sac, and nasolacrimal duct. The tear is a hypertonic fluid. Owing to its around-the-clock washing and lubrication, the conjunctiva is remained wet and is safeguarded from infection. Tear additionally embraces lysozyme that neutralizes bacteria. Discharge of tears is regulated by the parasympathetic fibers of the facial (VII cranial) nerve [6].

Wall of the Eye Ball:

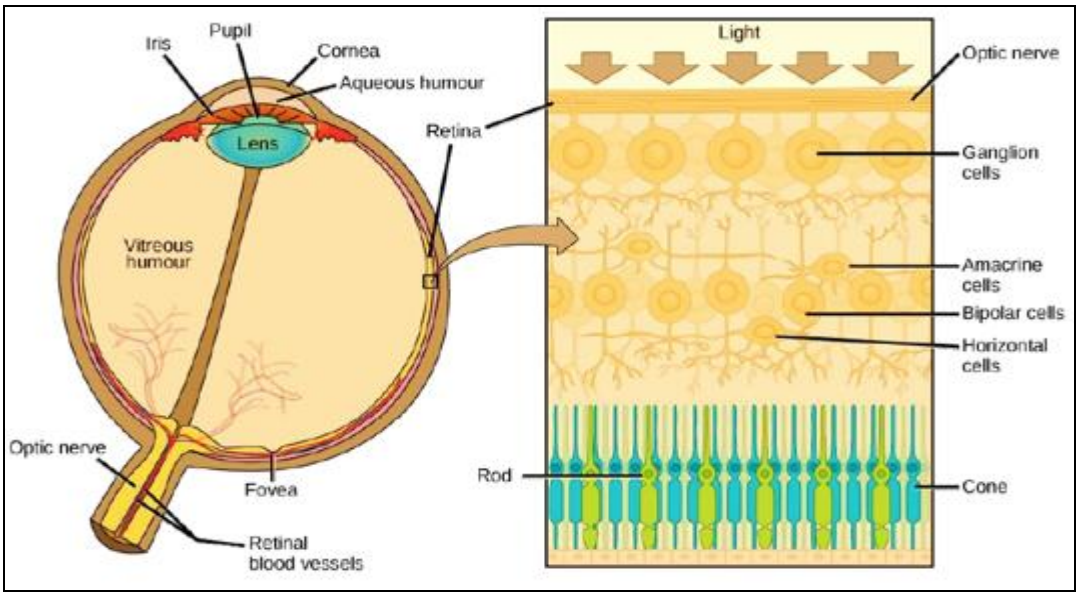


FIG. 1: STRUCTURE OF EYE BALL WALL

Wall of the eyeball is composed of three layers:

- Outer layer, which includes cornea and sclera
- Middle layer, which includes the choroid, ciliary body and iris
- Inner layer, the retina

Outer Layer or Tunica Externa or Tunica Fibrosa: Outer layer preserves the shape of the eyeball. Posterior five sixth of this coat is opaque and it is called the sclera Anterior one sixth is transparent [7].

Sclera: Sclera is known as cornea Sclera is the tough white fibrous outer layer of eyeball.

Cornea: Cornea is the transparent convex anterior portion of the outer layer of eyeball, which covers the iris and pupil.

Middle Layer or Tunica Media or Tunica Vasculosa: Middle layer surrounds the eyeball completely, except for a small opening in front known as pupil. This layer comprises of three structures [8].

1. Choroid
2. Ciliary body
3. Iris

Choroid: Choroid is the thin vascular layer of eyeball positioned between sclera and retina. It forms posterior five sixth of middle layer. Choroid is extended to the insertion of ciliary muscle (the position of ora serrate). Choroid is separated from sclera by peri-choroidal space. Antecedent, this space is limited by the insertion of ciliary muscle into sclera, anteriorly, this space ends at a short distance from the optical nerve. Inner surface of choroid faces the colour epithelium (in most sub caste) of retina Choroid is composed of rich capillary super system, multitudinous small arteries and veins [9].

Ciliary Body: Ciliary body is the thickened anterior part of middle layer of eye, positioned between choroid and iris. It's positioned) in front of ora serrate. It's in the form of a ring.

Its external surface is separated from sclera by pre-choroidal space, Inner surface of ciliary body faces the vitreous body and lens. Suspensory ligaments from the lens are attached to the ciliary body Anterior surface of ciliary body faces towards the centre of cornea. From the surface, the iris arises Ciliary body has three parts [10].

Orbiculus Ciliaris: It is continuous with choroid and it forms the posterior two third of ciliary body. It is about 4 mm broad.

Ciliary Body Proper: It is made up of two sets of ciliary muscles, namely outer longitudinal and inner circular muscles. The parasympathetic fibres of oculomotor nerve innervate ciliary muscles.

Ciliary Processes: Ciliary processes are the finger-like projections from the inner surface of ciliary body. There are about 70 ciliary processes. Projecting towards the central axis of the eye to form radial fringes called corona ciliary.

Iris: Iris is a thin coloured curtain- the suchlike structure of an eyeball. Located in front of the lens. It forms a thin indirect diaphragm with an indirect opening in the center called pupil. Iris is formed by muscles.

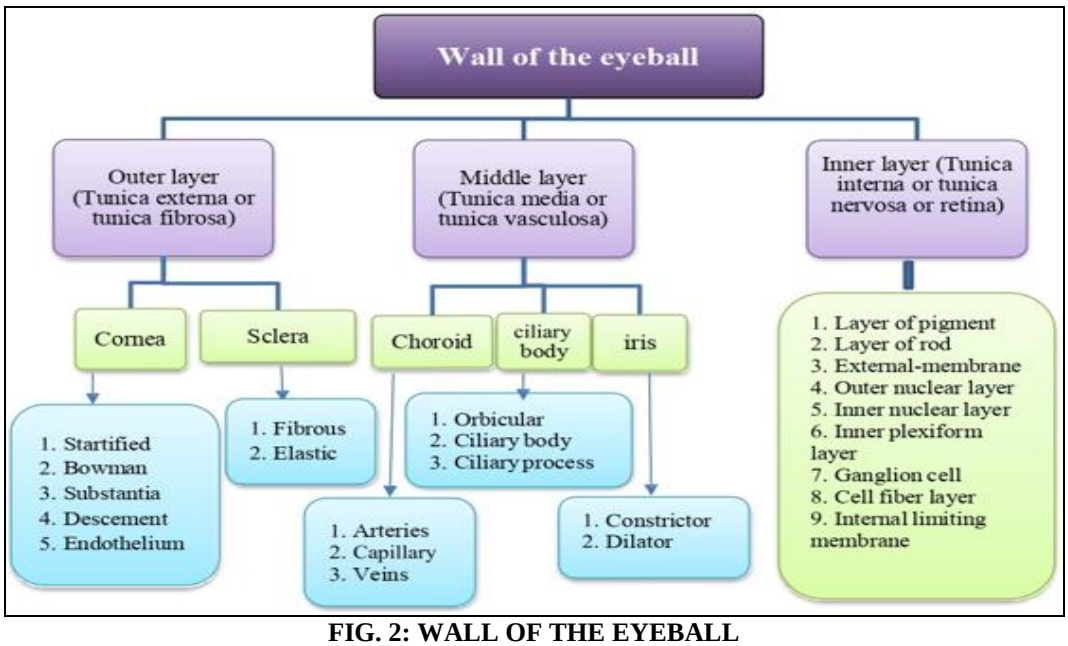


FIG. 2: WALL OF THE EYEBALL

Constrictor papillae or iris sphincter muscle or pupillary constrictor muscle. It's formed by indirect muscle fibres. Compression of this muscle causes compression of pupil. Dilator papillae or pupillary dilator muscle radial muscle fibres form it. Compression of this muscle causes dilatation of pupil Conditioning of these muscles increases or drop the periphery of pupil and regulates the amount of light entering the eye. Therefore, iris acts like the diaphragm of a cornea Iris separates the space between the cornea and lens, into two chambers, namely anterior and posterior chambers. Both chambers communicate with each other through pupil. The side border of anterior chamber is angular in shape. It's called iris angle or angle of anterior chamber [11].

Fundus oculi: Fundus oculi is the posterior part of interior eyeball. It's also called fundus in living subjects, fundus is examined by ophthalmic scope Fundus has two important structures:

A. Optic disk

B. Macula luteal with fovea centralism

Optic disk-Blind Spot: Optic disk is a pale disk, positioned near the centre of the posterior wall of eyeball. It's also called optical papilla. It's formed by the confluence of axons from ganglion cells, while forming the optical nerve. Optic disk contains all the layers of retina, except rods and cones. Thus, it's a sleep to light, Le; the object is n't foreseer, if the image falls upon this area. Because of this, the optical disk is known as eyeless spot [12].

Macula Lutea: Macula lutealisa small unheroic area, positioned a side to the optical disk in retina. It's also called unheroic spot. Unheroic colour of macula lutealis due to the presence of a unheroic pigment. Macula luteal has fovea centralism in its centre.

Fovea Centralis: Fovea centralis misa nanosecond depression in the centre of macula luteal. Then, all the layers of retina are veritably thin. Circuit of fovea is only about 0.5mm. Fovea eyeball is the region of utmost acute vision because it contains only cones [13].

Artery:

1. Vein

2. Optic disk

Intraocular Fluid: Intraocular fluid (fluid in eyeball) is responsible for the maintenance of shape of the eye ball. Intraocular fluid is of two types:

1. Vitreous humour

2. Aqueous humour.

Vitreous Humor: Vitreous humour is a thick fluid present behind lens, in the space between lens and retina. It's also known as vitreous body. It's a largely thick and glutinous substance that's formed by a fine fibrillary net work of proteoglycan moles. Major substances in vitreous humoura real buminand hyaluronic acid. These substances enter vitreous body from blood, by means of diffusion. Vitreous humour helps to maintain the shape of eyeball [14].

Aqueous Humor: Waterless humouris a thin fluid present in front of retina. It fills the space between lens and cornea. This space is divided in to anterior and posterior chambers by iris. Both the chambers communicate with each other through pupil. Volume of Waterless humour is 0.13ml & pH of 7.5. Waterless humour measure of intraocular pressure is an important part of eye examination. It's measured by to no meter. When intraocular pressure increases to about 60 to 70 mm Hg. glaucoma occurs. It contains Water-98.7 & Solids-1.3 [15].

Lens: Lens of the eye ball is crystallinein nature it's positioned behind the pupil. It's a biconvex, transparent and elastic structure. It's a vascular and receives its nutrition substantially from the waterless humour. Lens refracts light rays and helps to concentrate the image of the objects on retina. Focal length of mortal lens is 44 mm and its refractory power is 23D Lens is supported by the suspensor ligaments (zonular fibres), which are attached with ciliary bodies. Lens Capsule is a largely elastic membrane that covers with membrane. The process by diffusion, ultrafiltration and active transport through the epithelial cells lining the ciliary processes [16].

1. Capsule After formation, aqueous humour reaches the posterior.

2. Anterior epithelium chamber by passing through the suspensor ligaments.

Muscles of the Eyeball: Muscles of the eyeball are of two types;

1. Intrinsic muscles
2. Extrinsic muscles.
3. Intrinsic muscles

Intrinsic muscles are formed by and are controlled by autonomic nerves. Intrinsic muscles of eye are contain [17].

1. Constrictor papillae
2. Dilator papillae
3. Ciliary muscle.

Extrinsic Muscles: In general, the term optical muscles 'referst of oreign eyeball muscles. Foreign muscles are formed Oculomotor Nerve by cadaverous muscle fibres and are controlled by the physical nerves. Eyeball moves with in the orbit by six foreign cadaverous muscles. One end of each muscle is attached to the eyeball and the other end to the wall of orbital cavity. There are four straight muscles (rectus) and two oblique muscle [18].

Extrinsic Muscles are:

1. Superior rectus
2. Inferior rectus
3. Medial or internal rectus
4. Lateral or external rectus
5. Superior oblique
6. Inferior oblique

Actions of constrictor papillae and dilator papillae are already explained along with iris Contraction of muscle increases the anterior curvature of lens during accommodation [19].

Parts of Human Eye: Humaneye is divided in the following parts, which has given below;

1. Anterior chamber
2. Posterior chamber
3. Pupil
4. Iris
5. Lens
6. Vitreous humour
7. Retina
8. Sclera
9. Cornea [20]

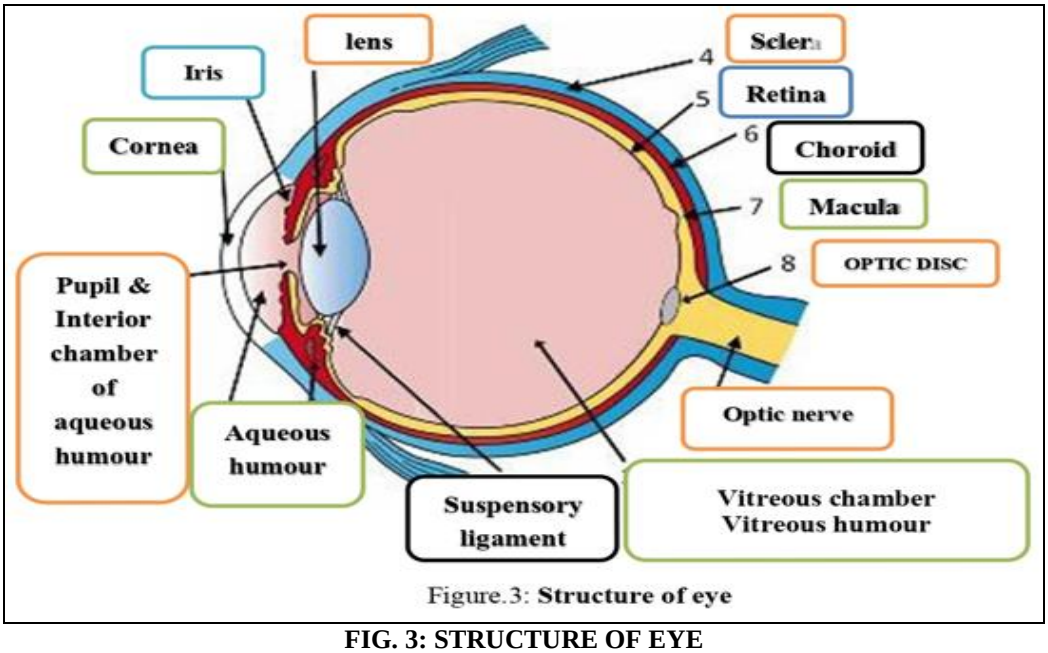


Figure.3: **Structure of eye**

FIG. 3: STRUCTURE OF EYE

Conjunctivitis: Conjunctivitis, further generally known as pink eye, is an inflammation of the conjunctiva, a clear membrane that covers the remotest layer of the eye and the inner surface of the eyelids [21]. Conjunctivitis generally looks and feels worse than it, and while the pronounced redness can be relatively intimidating at first, conjunctivitis infrequently infrequently causes long-term visual damage.

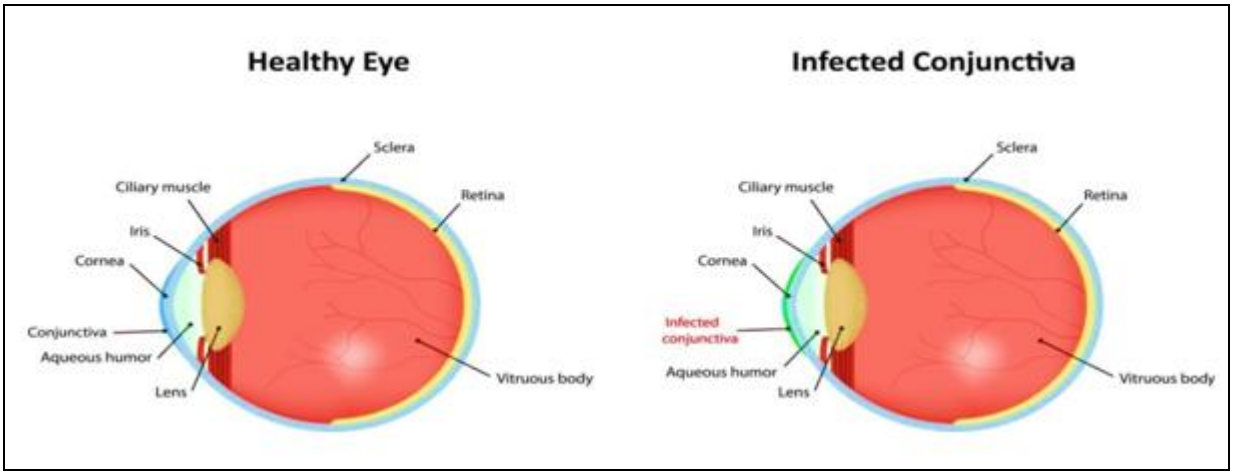


FIG. 4: HEALTHY EYE AND INFECTED CONJUNCTIVA EYE

Generally, conjunctivitis is the following types based on the sources of infection.

Types of Conjunctivitis:

1. Allergic Conjunctivitis
2. Viral Conjunctivitis
3. Bacterial Conjunctivitis
4. Irritant and Chemical Conjunctivitis

Allergic Conjunctivitis: Allergic conjunctivitis is caused by an allergen-induced inflammatory response in which allergens interact with IgE bound to sensitized mast cells resulting in the clinical ocular allergic expression. The pathogenesis of allergic conjunctivitis is predominantly an IgE-mediated hypersensitivity reaction [22-23]. Generally, this conjunctivitis often has a seasonal element and occurs more frequently during spring and seasonal changes. Other common allergens are dust, pollen, cosmetics, perfume, or medication; allergic symptoms of pink eye often affect both eyes, and severe itchiness swellings are common [24].

Allergic conjunctivitis is also divided in types.

A. Seasonal conjunctivitis

B. Perennial conjunctivitis:

C. Giant papillary conjunctivitis

D. Contact dermato conjunctivitis

E. Vernal conjunctivitis

F. Atopic conjunctivitis

FIG. 5: ALLERGIC CONJUNCTIVITIS

Viral Conjunctivitis: Viral conjunctivitis is caused by a virus that is either contracted through the air or in direct contact. Viruses that beget the common cold wave, acute respiratory infections, or complaints similar to measles or herpes are frequently the causes of viral conjunctivitis. A herpes infection is relatively common, especially the herpes simplex contagion, which causes cold blisters on the lips and mouth area. Exposure to the sun and high sicknesses are triggers for causing these cold lumps. This type of conjunctivitis, and it's fairly contagious [25].

FIG. 6: VIRAL CONJUNCTIVITIS

Bacterial Conjunctivitis: Bacteria similar to Staphylococcus, Streptococcus, and Haemophilus are the common culprits that beget this type of conjunctivitis which is largely contagious and fluently spread, especially amongst children. However, including those related to STDs, caused your pinkeye, If bacteria. You may need to apply eye drops or ointments to the inside of your eye lid three to four times a day for 5 to 7 days. For furthers tub born infections or for rare cases of pinkeye caused by gonorrhea or Chlamydia, you might get an oral antibiotic. You would take capsules for several days. The infection should a meliorate within a week. Take or use the drugs as instructed by your doctor, indeed after the symptoms go down [26].

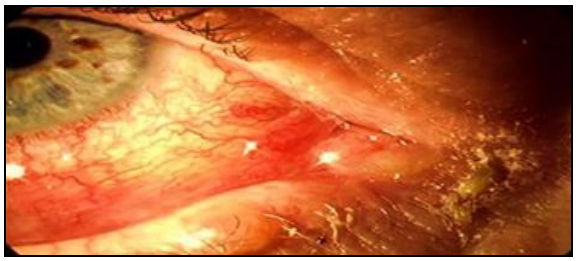
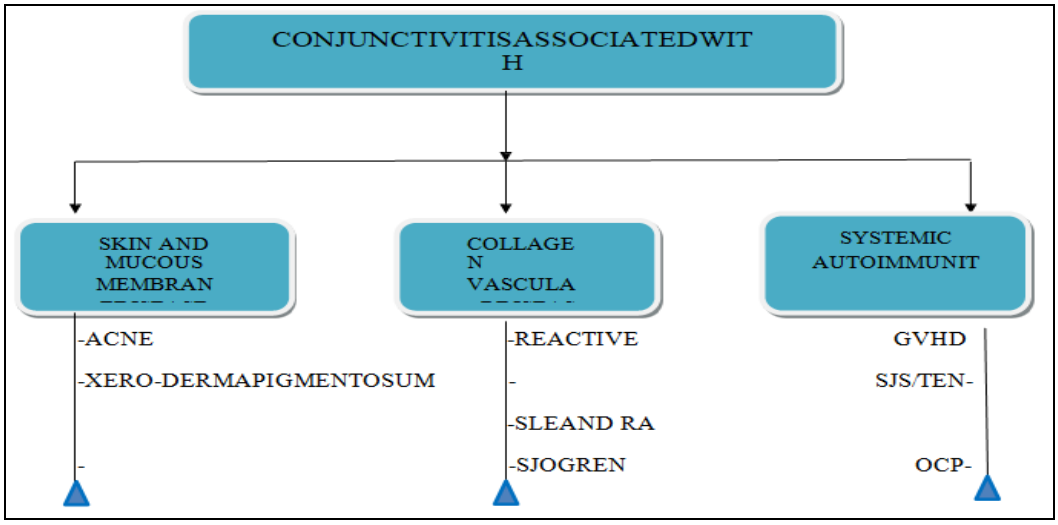


FIG. 7: BACTERIAL CONJUNCTIVITIS

Irritant and Chemical Conjunctivitis: Certain irritants to the eye, similar as flame burns, some plant saps, irritant gases or chemicals, and environmental toxins, can all beget irritant conjunctivitis. For pinkeye caused by a prickly substance, use water to wash the substance from the eye for 5 eye blinks. Your eyes should begin to ameliorate within 4 hours. However, incontinently wash the eyes with lots of water and call your doctor if your conjunctivitis was caused by acid or alkaline material similar to bleach [27].

FIG. 8: IRRITANT AND CHEMICAL CONJUNCTIVITIS

Conjunctivitis as Sociated with Systemic Disease:



Full form: Stevens-Johnson syndrome (SJS), Toxic epidermal necrolysis (TEN).

Symptoms: Pink eye is caused by infections (from bacteria or toxins), allergies, or certain irritants that come in to contact with the eye; therefore the different types of conjunctivitis tend to beget different. Tender-heartedness of the eye, or pain (which can be severe in the cases of irritant conjunctivitis).

1. Itchiness
2. Body aches
3. Sensitivity to light
4. Discomfort in the eye
5. Redness of the eye or inner eyelids
6. Discharge and tearness
7. Discharge may cause eyelids to crust and stick together while sleeping
8. Swelling of the eye lids
9. Infection usually begins with one eye, but can quickly spread too there eye in cases of viral or bacterial conjunctivitis
10. In most cases of pink eye, pain, photophobia and blurred vision are not very common and should they occuritis important to seek medical at tention to rule out other diseases such as glaucoma, uveitis, keratitis or even meningitis [28].

Prevention of Conjunctivitis: First line of defence is to avoid the cause of conjunctivitis as viral and bacterial conjunctivitis spread fluently others. Then are some tips to avoid spreading the conjunctivitis orre-infecting your- self. Which are following [29].

Wash hand completely before you use the drug sin your eye, after using the drug in your eyes.

1. Wash any clothing touched by infected eyes
2. Clothes
3. Towels
4. Pillow cover
5. Avoid shaking hands.
6. Do not share eye drops or cosmetics as eyeliner, eye shadow. Replace them after you healed, to avoid re-infection.
7. Disinfect surfaces such as doorknobs and counters with diluted bleach solution.
8. Do not swim (some bacteria can spread in warm water).
9. Wear black sunglasses, when among others.
10. Do not touch the infected eye because the infection will spread to the good eyes.
11. Repeatedly wash the eyes with clean water.
12. To avoid allergic conjunctivitis [30].
13. Keep windows in your home and car closed during the pollen season, use air conditioning instead.
14. Dust and vacuumed frequently to alleviate potential allergens at home.
15. Avoid outdoor activities such as moving the lawn or gardening, especially in the morning and early afternoon when pollen release at its height.

Non-pharmaceutical Management:

Avoiding rubbing the eyes.

Using cool compresses, eyebaths and preservative-free lubricants may be soothing.

Avoiding wearing contact lenses/prostheses until symptoms and signs resolve.

If lenses are essential, consider using daily disposable lenses.

Allergen avoidance is often tricky but should be the primary aim. Consider introducing air conditioning, reducing pet contact, and bedding change.

Artificial tears can be helpful in mild cases (they dilute the allergen).

Contact lenses should not be worn if conjunctivitis is present, ordering a course of topical therapy [31].

Different Therapies Use in the Conjunctivitis:

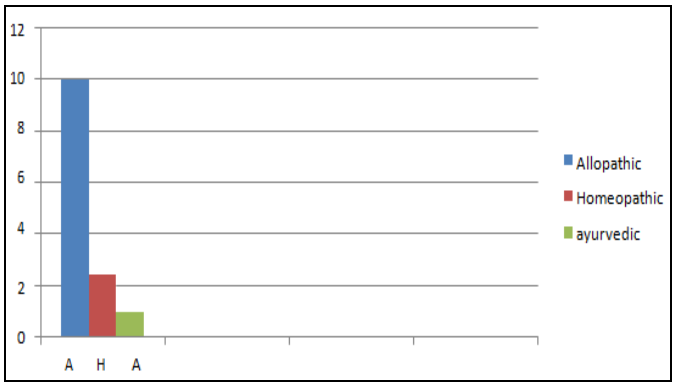


FIG. 9: GRAPHICAL REPRESENTATION OF DIFFERENT THERAPIES IN THE TREATMENT OF CONJUNCTIVITIS

Pharmaceutical Management: There are a number of compound use for treatment of conjunctivitis which are classify below.

1. Topical mast cell stabilizers- e.g., sodium Cromoglycate:
2. Topical antihistamines (other than in contact Derma to conjunctivitis which is unresponsive to these). The topical ocular antihistamines, Antazoline, Azelastine,
3. Combined antihistamine/vasoconstrictor drops –e.g. Antazoline with Xylometazoline.
4. Diclofenac eye drops are also licensed for seasonal allergic conjunctivitis.
5. Oral antihistamines such as Loratadine or Chlorphenamine may be used.
6. Topical corticosteroids (e.g, Betnesol) can be used if symptoms are very severe but there must be absolutely no doubt about the diagnosis.
7. Oralsteroids in a short (five-day) course may be used in severe cases where there is no doubt about the diagnosis.
8. Ophthalmologists may use them in severe cases.
9. Bacterial conjunctivitis is usually treated with antibiotic eye drops or ointments that cover abroad range of bacteria [29].

Example: Trimethoprim with polymycin-B, Gentamicin, Tobramycin, Neomycin, Ciprofloxacin, Ofloxacin, Gatifloxacin, Erythromycin.

Moxifloxacin: Bacterial conjunctivitis is generally treated with moxifloxacin antibiotic an eyedrops or ointments that covera broad range of bacteria. It's a synthetic fluoroquinolone antibiotic used to treat colourful bacterial infections. Bayer AG developed the medicine (originally called BAY12-8039) and it's retailed worldwide (as the hydrochloride) under the brand name Avelox (in some countries also Avalox) for or altreatment [30].

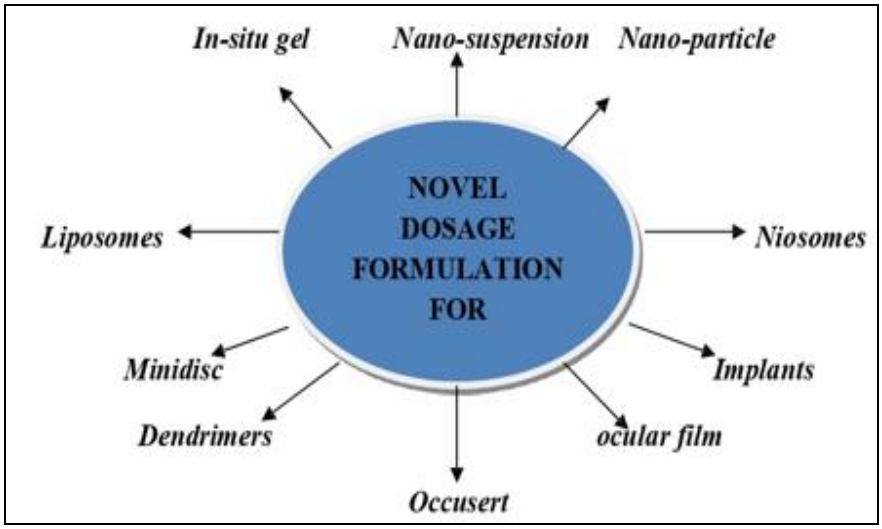


FIG. 10: VARIOUS NOVEL SYSTEMS FOR EYE

Moxifloxacin is administered topically to the eyes. It also given through oral routes absorption following topical administration of moxifloxacin. Moxifloxacin is used to treat microbialeye infections. It works by stopping the growth of certain types of microbes. This drug treats only microbial eye infections. It'll also work for other types of eye infections [31]. Newer Exploration in

ophthalmic medicine delivery systems is directed towards objectifying several medicine livery technologies, including makeup systems which not only extend the contact time of the vehicle at the optical surface but also decelerate down the elimination of the medicine. Which are following new dosage forms. eg. (*In-situ* gel, Nano--particulate--ion---film, Implants, Ocuserts *etc* [32].

Challenges or constraints occur during the Application of the Convention Alophthalmic Delivery System: The conventional ophthalmic formulations parade shortpre-corneal residence time and poor bioavailability due to rapid-fire and expansive elimination of medicines from pre-corneal lachrymal fluid by result drainage, lachrymation, and non-productive absorption by conjunctiva [33].

Examples; Eye Drops, Eye-Ointment *etc*.

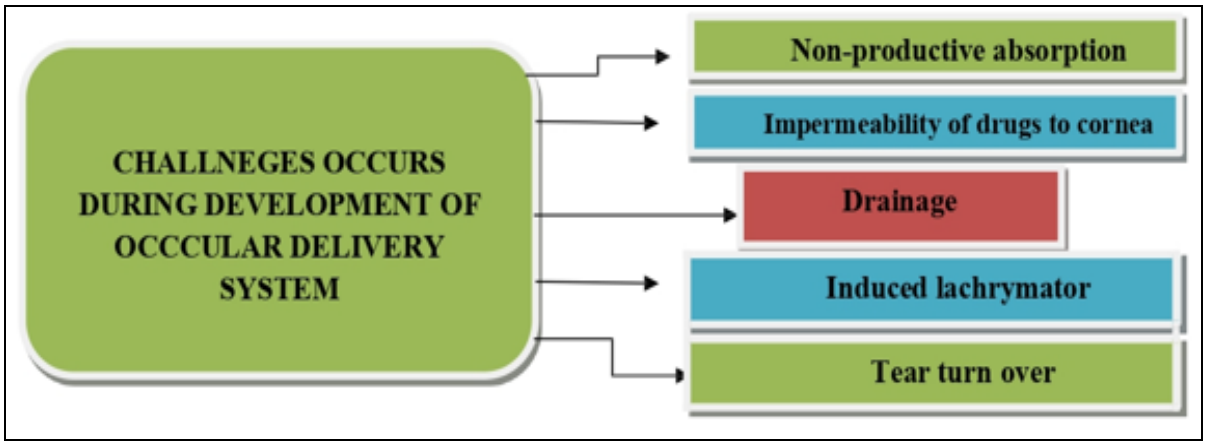


FIG. 11: CONSTRAINT OF CONVENTIONAL OPHTHALMIC DELIVERY SYSTEM

The development of ocular drug delivery systems has always been challenging because of the ocular route-like drawbacks. Topical application of drugs to the eye is the well-established route of administration for treating various ocular diseases.

Ophthalmic Gel: Generally, Opthalmicgel is Available in the following.

Ophthalmic gels are divided into Two Categories:

A. Geleye drops

B. *In-situ* gels

Gel Eye Drops: Gel eye drops are simple thick formulations that don't suffer any changes after their administration. They're substantially applied as tear substitutes in the treatment of dry eye because they present multitudinous down sides, which limit their use for the of ophthalmic medicines. Gel eye drops don't allow accurate and reproducible medicine administration and can beget blurred vision, encrusting on the eyelids and tearing [33].

Brands Name: Cytoryn

***In-situ* Gels:** The *in-situ* gellingsy stem represents one of the most intriguing strategies and a promising approach to increase the residence time of medicines on the optical surface After instillation of the waterless solution containing polymers sensitive to external stimulants, a thick and muco-adhesive gel is formed on the surface of the eye, with a consequent increase in the optical retention time and bioavailability of the medicines administered [34-35].

Brands Name: Isotine plus, Avizor lacrifresh

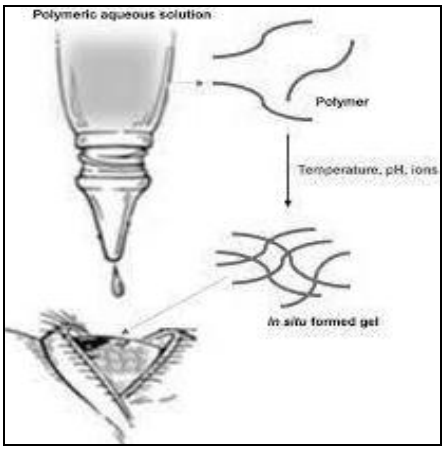


FIG. 12: *IN-SITU* GELLING SYSTEM

Gelation System: The gelation system can be caused by colorful external stimulants similar to temperature, pH, and ions.

Temperature: gelatinizing system is grounded on the use of polymers that are in liquid form below their low critical solution temperature (LCST) and come gels when the ambient temperature is equal to or above the LCST.

pH Convinced: *In-situ* gels correspond of polymers that retain acidic or alkaline functional groups. They gel during the transition from a low pH environment to a high Ph environment.

Ionic Systems: The polymer undergoes a sol- gel transition due to changes in ionic concentration, which are generally touched off by mono or divalent cations present in tear fluid, similar as Na, Mg2, and Ca2 ion [37].

Mechanism of *In-situ* Gels:

- *In-situ* gelling system based on two basic mechanisms:
- Based on physical mechanisms;

1. Swelling
2. Diffusion
3. Based on the chemical reaction mechanism

Grounded on Physical Medium: Swelling In this system of In situ gel conformation material absorbs water from the ringing environment and expands to asked space. For sample glycerol mono-oleate, a polar lipid, swells in water to form lyotropic liquid crystalline phase structures. It has some bio-adhesive properties and can be degraded *in-vivo* by enzymatic action [38].

Diffusion This method involves the diffusion of solvent from polymer result into girding towel, which results in the rush or solidification of the polymer matrix. N- Methyl pyrrolidone (NMP) is a useful solvent for a similar system.

Grounded on chemical reaction mechanism Chemical reactions that results in situ gelation may involve precipitation of inorganic solids from supersaturated ionic solutions, enzymatic processes, and print-initiated processes.

General Method of Preparation the *In-situ* Gelling Solution:

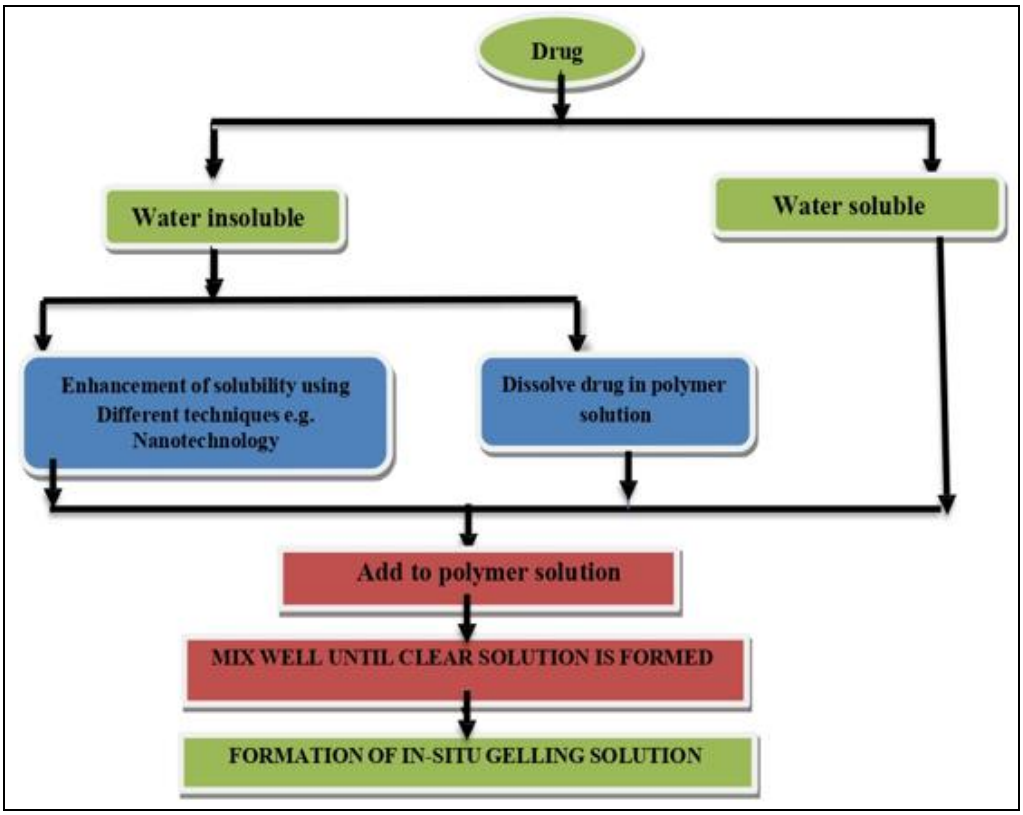


FIG. 13: GENERAL METHOD OF PREPARATION OVERVIEW OF GEL FORMATION [39]

Factor affecting *In-situ* Gelling Formation:

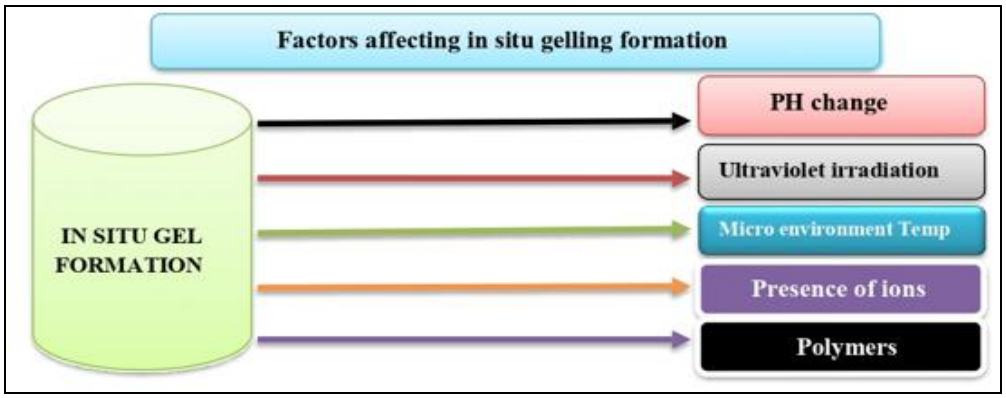


FIG. 14: FACTOR AFFECTING *IN-SITU* GELLING FORMATION

Physicochemical Characterization of *In-situ* Gel:

1. Viscosity using viscometer
2. Visual Appearance and Clarity
3. PH
4. Drug content uniformity
5. Zeta potential
6. *In-vitro* drug release study
7. Surface morphology of in situ gel using Tem
8. Sterility and Isotonicity testing
9. Ocular irritancy test (*In-vitro* human hemoglobin denaturation test)
10. Stability study [40-41]

Advantages of *In-situ* Gel Formulation: *In-situ* gel has the following advantages over other conventional ocular formulations.

1. Simple manufacturing process,
2. The ease of administration,
3. The delivery of an accurate dose(42-43)
4. Reduced frequency of applications hence improved patient compliance and comfort.
5. Generally more comfortable than insoluble or soluble insertion
6. Improved local bioavailability due to increased pre-corneal residence time and absorption.
7. Its production is less complex and thus lowers the investment and manufacturing cost.
8. Less blurred vision as compared to ointment.
9. Decreased nasolacrimal drainage of the drug which may cause undesirable side effects due to systemic absorption [44-45].
10. Sustained, Prolonged drug release and maintaining relatively constant plasma profile [46].

CONCLUSION: Most viral conjunctivitis cases are due to adenoviruses, and the rapid-fire antigen test to diagnose adenoviral conjunctivitis may present an applicable strategy to avoid the overuse of antibiotics. Bacterial pathogens are isolated in half of the cases of conjunctivitis, and roughly 60 of culture-positive cases are known to be tone-limited conjunctivitis is to rule out serious optical conditions that present with “red eye”, mimicking conjunctivitis. Antipathetic conjunctivitis is an inclusive term that encompasses different clinical entities grounded on the assumption that the classical. Type I hypersensitivity mechanism is responsible for all clinical forms of antipathetic eye complaint. Still, IgE and non-IgE-mediated mechanisms are involved in developing optical antipathetic disorders.

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REFERENCES:

1. Valerie C: Scanlon, Essential of anatomy and physiology, fifth edition, Chapter: 9, the senses. Published by F.A. Davis 2007; 202-210.

2. Vinay Kuma and Abdul K Abbas: Jon Aster Robbins and Cotran pathologic basis of disease, Ninth edition, chapter 29, the eye. Published by James A.perkins MS.MFA. 2015; 1319-1324.
3. Sembulingum K: mp; Prema Sembulingum, Essential of medical physiology, sixth edition, Chapter:165, structure of the eye, published by Jypee Brother medical publisher private ltd 966-971.
4. American Academy of Ophthalmology — Fundamentals and Principles of Ophthalmology.
5. Snell R & A. Lemp, Clinical Anatomy of the Eye, second edition, published willey Black well 2013; 30-48.
6. Samar K Basak: Essentials of Ophthalmology, Seventh edition, Published by Jypee brother medical publisher private ltd 2019; 1-30.
7. Jie Zhu, Ellean Zhang, Katia Del Rio-Tsonis: Eye Anatomy, eLS & John Wiley & Sons, Ltd. 2012.
8. Barbosa-Sabanero K, Hoffmann A and Judge C: Lens and retina regeneration: new perspectives from model organisms. Biochemical Journal 2012; 447(3): 321–334.
9. Butt AM, Pugh M, Hubbard P and James G: Functions of optic nerve glia: axoglial signalling in physiology and pathology. Eye 2004; 18: 1110–1121.
10. Civan M: The Eye's Aqueous Humor. 2nd edn, Amsterdam: Academic Press of Elsevier2008.
11. To CH, Kong CW, Chan CY, Shahidullah M and Do CW: the mechanism of aqueous humour formation. Clinical and Experimental Optometry 2002; 85(6): 335–349.
12. Oyster CW: The Human Eye. Sunderland: Sinauer Associates 1999.
13. Wan QF and Heidelberger R: Synaptic release at mammalian bipolar cell terminals. Visual Neuroscience 2011; 28(1): 109– 119.
14. Whitehead AJ, Mares JA and Danis RP: Macular pigment: a review of current knowledge. Archives of Ophthalmology 2006; 124: 1038–1045.
15. Wyse JP and Spira AW: Ultrastructural evidence of a peripheral nervous system pattern of myelination in the avascular retina of the Guinea pig. Acta Neuropathologica 1981; 54: 203.
16. Land MC and Fernald RD: the evolution of eyes. Annual Review of Neuroscience 1992; 15: 1–29.
17. Lens Al: Ocular Anatomy and Physiology, 2nd edn. United States: SLACK Incorporated 2008.
18. Marmor MF and Wolfensberger TJ: The Retinal Pigment Epithelium: Function and Disease. New York, USA: Oxford University Press 1998.
19. Merbs SL and Nathans J: Absorption spectra of human cone pigments. Nature 1992; 356: 433–435.
20. Richards A and Guzman Cottrill JA: Conjunctivitis, Pediatr Review 2010; 31(5): 196-208.
21. Leonardi A, De Dominicis C and Motterle L: Immunopathogenesis of ocular allergy: a schematic approach to different clinical entities. Curr Opin Allergy Clin Immunol 2007; 7(5): 429–435.
22. Leonardi A: The central role of conjunctival mast cells in the pathogenesis of ocular allergy. Curr Allergy Asthma Rep 2002; 2(4): 325–331.
23. Baran GR, Kiana MF and Samuel SP: Chapter 2: Science, Pseudoscience, and Not Science: How Do They Differ, Healthcare and Biomedical Technology in the 21st. Century Springer 2014; 19–57.
24. Shang A, Huwiler Muntener K and Nartey L: Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of Homoeopathy and allopathy. Lancet 2005; 366(9487): 32-726.
25. Whorton JC: Oxford University Press US, ed. Nature Cures: The History of Alternative Medicine in America (illustrated Ed.). New York: Oxford University Press 2004; 18: 52.
26. Leonardi A, De Dominicis C and Motterle L: Immunopathogenesis of ocularallergy: a schematic approach to different clinical entities. Curr Opin Allergy Clin Immunol 2007; 7(5): 429–435
27. Beal C & Giordano B: Clinical evaluation of red eyes in pediatric patients. Journal of Pediatric Health Care 2016; 30: 506–514. 10.1016/j.pedhc.2016.02.001.
28. Miller D: Review of moxifloxacin hydrochloride ophthalmic solution in the treatment of bacterial eye infections. Clinical Ophthalmology 2008; 2: 77–91. 10.2147/opth.s1666.
29. Manne Reddy, Sajja Eswaraiah, Vetukuri Venkata Naga Raju, Rapolu Kumar, Ningam Srinivasreddy, Vedantham Ravindra, &quot Crystalline form III of anhydrous moxifloxacin hydrochloride and a process for preparation thereof." U.S. Patent US20050137227 issued June 2005; 23.
30. Alfonso SA, Fawley JD & XAL: Conjunctivitis. Primary Care 2015; 42: 325–345. 10.1016/j.pop.2015.05.001
31. Azari AA & Barney NP: Conjunctivitis: A systematic review of diagnosis and treatment. JAMA, 2013; 310: 1721–1729. 10.1001/jama.2013.280318.
32. Varshosaz J, Tabbakhian M and Salmani Z: Designing of a Thermo sensitive Chitosan/Poloxamer *in-situ* Gel for Ocular Delivery of Ciprofloxacin. The Open Drug Delivery Journal 2008; 2: 61-70.
33. Nalla A and Chinnala KM: *In-situ* ophthalmic drug delivery systems – An Overview Indo Am J Pharm Sci 2016; 3(3): 202-208
34. Shah J, Nair AB, Jacob S, Patel RK, Shah H and Shehata TM: Nanoemulsion based vehicle for effective ocular delivery of moxifloxacin using experimental design and pharmacokinetic study in rabbits. Pharmaceutics 2019; 11: 230.10.3390/pharmaceutics11050230.
35. Tauber S, Cupp G, Garber R, Bartell J, Vohra F and Stroman D: Microbiological efficacy of a new ophthalmic formulation of moxifloxacin dosed twice-daily for bacterial conjunctivitis. Advances in Therapy 2011; 28: 566–574. 10.1007/s12325-011-0037-x.
36. Prajapati PM: Droppable Gel (*In-situ* Gel) A Smart Approach for Ocular Drug Delivery Recent Advances and Innovations 2013; (5): 353–361.
37. Nerkar T and Gujarathi N: *In-situ* gel: novel approach in sustained and controlled drug delivery system. Pharma Science Monitor 2013; 4(4): 1–18.
38. Ginsburg AS, Hooper N, Parrish N, Dooley KE, Dorman SE, Booth J, Diener-West M, Merz WG, Bishai WR and Sterling TR: Fluoroquinolone resistance in patients with newly diagnosed tuberculosis. Clin Infect Dis 2003; 37(11): 1448-52. Epub 2003; 4.
39. Jethava JK and Jethava GK: Design, formulation, and evaluation of novel sustain release bioadhesive *in-situ* gelling ocular inserts of ketorolac tromethamine. International Journal of Pharmaceutical Investigation, 4, 2014226–232. 10.4103/2230-973X.14313
40. Srividya B, Cardaza RM and Amin PD: Sustained ophthalmic delivery of oflaxacin from a pH triggered in situ gelling system. J Controll Release 2001; 73: 205-211.
41. Che Marzuki N, WahabR and Abdul Hamid M: An overview of nanoemulsion: Concepts of development and cosmeceutical applications. Biotechnology &

Biotechnological Equipment 2019; 33: 779–797. 10.1080/13102818.2019.1620124.
42. La Rosa M, Lionetti E and Reibaldi M: Allergic conjunctivitis: a comprehensive review of the literature. Ital J Pediatr 2013; 39: 18.
43. Gambhire S, Bhalerao K and Singh S: *In-situ* hydrogel: Different approaches to ocular drug delivery. International Journal of Pharmacy and Pharmaceutical
44. Sciences 2013; 5(2): 27–36.
45. Deepak S and Singh TR: *In-situ* gel system for ophthalmic preparation. Innovare J of Health Science 2013; 1(1): 6-15.
46. Rathore KS: *In-situ* Gelling Ophthalmic Drug Delivery System: An Overview. International Journal of Pharmacy and Pharmaceutical Sciences 2010; 2(4): 30-34.
47. Kant A, Reddy S, Shankraiah MM, Venkatesh JS, Nagesh K: *In-situ* Gelling System – A Overview Pharmacologyonline 2011; 2: 28-44.
48. https://pubchem.ncbi.nlm.nih.gov/compound/Moxifloxacin #section=Names-and Identifiershttps://go.drugbank.com/drugs/DB00218
49. https://www.scbt.com/p/moxifloxacin-hydrochloride-186826-86-8

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