



A Review On Ophthalmic Formulation

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ABSTRACT

Due to the complexity of the eye's structure and barriers, drug delivery experts and ophthalmologists find ocular drug delivery to be an extremely difficult field. The ocular drug delivery system is regarded as important and complex since it is tough to administer drugs there. Additionally, the traditional ophthalmic formulations have limited absorption and a brief pre-corneal residence time. Ophthalmic products are sterile preparations that can be administered onto the surface of the eye. The slightest inflammation in the eyes can cause intense soreness and cause eye infections. Quality control of ophthalmic preparations includes identification, potency, purity, sterility particulate matter, and dissolution testing.

Keywords: Ocular Diseases, Contact lenses, Eye drop, Eye ointments, Ophthalmic solution.

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INTRODUCTION

The ocular globe may be segmented in two chief parts—the anterior and posterior portions. According with the segment of the eye elicited, several diseases can be pointed out. In the last years, a significant number of Nano sized formulations were introduced in the market. (1)The eyeball is an important organ that allows humans to observe and interact with their surroundings. The anterior segment of the eyeball contains the cornea, iris, lens, conjunctiva, ciliary body and aqueous humour. The posterior segment consists of sclera, choroid, retinal pigment epithelium, optic nerves and vitreous humour (Monkhouse, 2007). (2) Ophthalmic Preparation (eye preparation) are the sterile products meant for instillation into the eye. Products must be sterile and are prepared under the same conditions and by the same methods as other parenteral preparations. Ophthalmic drug delivery may also offer equal or higher bioavailability with inside the eye. (3)Ocular drug delivery has remained as one of the most challenging tasks for pharmaceutical scientists. The unique structure of the eye restricts the entry of drug molecules at the required site of action. Most of the topically applied drugs are washed off from the eye by various mechanisms resulting in low ocular bioavailability of drugs.(4) Eye-drops are the conventional dosage forms that account for 90% of currently accessible ophthalmic drug formulations. Despite the acceptance by patients, one of the major problems encountered is rapid drug-delivery failure. Hydrogels generally offer a moderate improvement of ocular drug bioavailability with the disadvantage of blurring vision.(5) As contact lens technology develops, more people are using them for indications beyond the correction of refractive error. A soft lens has been approved for slowing the progression of myopia, potentially increasing the use of contact lenses in paediatric patients.(6)

Anatomy and Physiology of Eye

One of the body's most intricate organs is the eye. Human Eye can be distinguished into three layers. The cornea and sclera make up the outer region. The iris, ciliary body, and choroid make up the middle layer of the eye. The inner layer of the eye is the retina, a complex, layered structure of neurons that capture and process light. Blood/aqueous and blood/retinal barriers make up the blood ocular barriers. They are obvious barriers separating the blood from the eye, which is crucial for drug penetration, drug breakdown through ocular pathways, and homeostatic control preservation. The blood retinal barriers are a back segment barrier made up of an exterior barrier in the retinal pigment epithelium and an internal barrier in the endothelial membrane of the retinal vessel. (7)

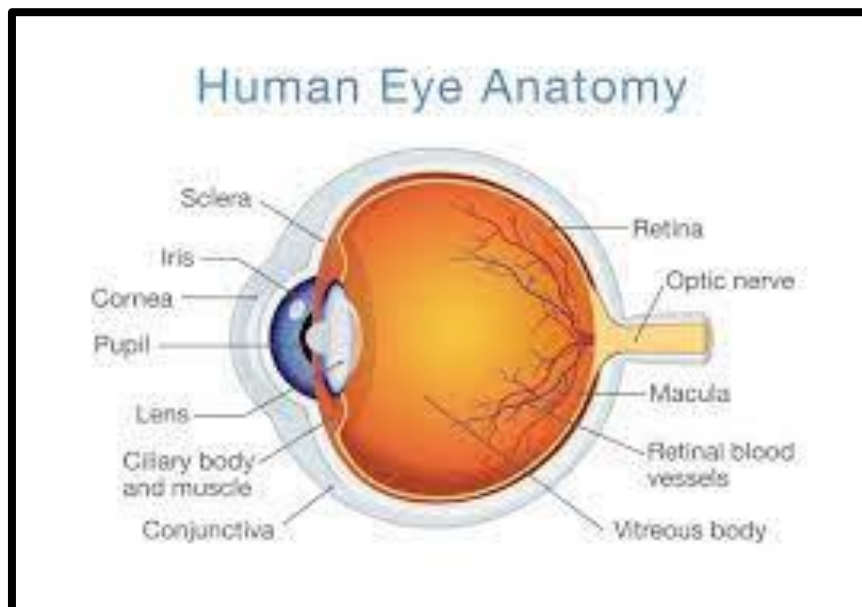


Figure Human eye anatomy

Barriers In Ocular Drug Delivery (8)

Many different eye disorders have been treated with drug delivery by non-invasive methods, such as oral drugs, eye ointments, and topical eye drops, but most of these are ineffectual and only useful for early, moderate symptoms(9). Additionally, the bioavailability of these non-invasive treatments is frequently constrained by the physiological barriers of the eye. For instance, the corneal epithelial barrier lowers the drug concentration in the eye when ointments and eye drops are applied to the ocular surface, and the blood-retinal barrier (BRB) prevents oral delivery from reaching the systemic circulation. Short medication retention time due to fast removal of topical eye drop from ocular surface. Because of the corneal epithelial barrier and nasolacrimal duct drainage, typically less than 5% of the medicine injected is retained on the ocular surface. Although these therapies were more tolerable for the patients, it is challenging to get topical drugs to the cornea and retina because of limited bioavailability caused by ocular barriers.

Barrier in the anterior part of the eye (8)

The tear film on the ocular surface is the initial and outermost barrier of the eye after topical instillation of a medication. In a few minutes, the medication is transported from the ocular surface to the nasolacrimal duct by the flow of lacrimal fluid. Lacrimal turnover occurs at a rate of about 1 L/min. Due to this tear drainage process, topical medication administration has low drug bioavailability. The cornea, which is about 500 m thick and can be seen in Figure 1, is another barrier. The cornea, which has five layers in a healthy cornea, is transparent, clear, and avascular. These layers are the corneal endothelium, Bowman's layer, corneal stroma, and

corneal epithelium. Due to the tight connections and lipophilic nature of the corneal epithelium, the penetration of hydrophilic substances is constrained.

The cornea's deepest layer is the corneal endothelium, a monolayer of hexagonal endothelial cells that serves as a barrier between the cornea and aqueous humour and controls water influx into the cornea. These qualities make the cornea a significant barrier and a problem for drug delivery to the eye's anterior portion. The conjunctiva is a mucous membrane made of vascularized epithelium that covers the outside of the cornea and the posterior aspect of the eyelids. It aids in the production and maintenance of the tear film and shields the ocular surface from external infections. Tight connections on the corneal and conjunctival epithelia prevent foreign objects from entering the eye. Additionally, the mucus layer in the eye prevents both particles and medications from entering, which are then expelled via the lacrimal system. The blood-aqueous barrier (BAB), is the additional barrier to drug delivery in the anterior region of the eye. The BAB, which is made up of endothelial cells in the iris's veins and non-pigmented ciliary epithelial cells from the ciliary body, includes the ciliary epithelium and capillaries of the iris. The BAB's purpose is to restrict the free flow of chemicals from iridial vessels.

Barriers in the posterior part of the Eye(8)

The anterior and posterior regions of the eye are connected by the sclera, which encircles the globe's outermost layer (Figure 1III). To keep the ball shape, it is made of extracellular matrix, which includes collagen fibrils and glycoproteins. Hydrophilic compounds are easily able to pass through the sclera. As seen in Figure 1IV, the choroid is the pigmented layer that lies in the midst of the sclera and the retina. It is a highly vascularized coat that covers 80% of the eye's posterior external segment. Since it supplies blood containing oxygen and nutrition to the outer retina as well as the retinal pigmented epithelial (RPE) layer, the choroid also helps to maintain ocular equilibrium and intraocular pressure (IOP).

The vitreous body, which has a volume of about 4 mL, is primarily made up of a water-based gel structure (99%); fibrillin-1, opticon, and VIT1 are non-collagenous proteins; types I, V, IX, and XI of collagen are collagens; hyaluronic acid (HA); proteoglycans of chondroitin sulphate; and heparan sulphate; and they are Maintaining ocular wholeness and transferring nutrients between the retina are the fundamental duties of the vitreous body. The diffusion of molecules from the vitreous humour to the retina is significantly constrained because the vitreous humour is filled with a thick gel. Due to their tendency to aggregate, the large, charged molecules might interact with negatively charged HA and anionic collagens, which can lead to the precipitation of molecules in the vitreous humour.

The inner portion of the blood-retinal barrier (BRB), which separates the blood from the retina, is made up of tight connections between the monolayer of RPE cells and retinal capillary endothelial cells. The BRB's anatomical position effectively prevents molecules from travelling from the choroidal blood circulation to the posterior portion of the eye. Furthermore, the RPE layer, which is a tightly packed monolayer limiting the movement of molecules, is difficult to pass through the BRB layer, which also plays a significant role in regulating the environment of the neural retina in contrast to the choroidal vasculature's high blood flow and leaky walls where molecules easily enter the choroidal extracellular gap.

Routes of Administration (10)

Topical and parenteral administration are the typical drug delivery methods for the eye. To obtain the desired drug concentrations at the target tissue, these pathways must overcome a number of obstacles. Several other drug administration strategies are suggested to get over these obstacles.

Table 1: Routes of administration

Routes of Administration	of Target site	Used in
Intravitreal Injection	Posterior Segment	Retinal detachment, cataract, hyperemia, and endophthalmitis
Subconjunctival Route	Beneath The conjunctival membrane	For dilating Pupil
Retrobulbular route	Retrobulbular Spec	Delivery of anesthetic agents
Peribulbular Route	Intraorbital Structure	Cataract surgery
Sub-Tenon Route	Between Tenons capsule and sclera	For delivering anesthesia
Intracameral Route	Anterior Chamber	Delivering antibiotics

Ophthalmic Dosage Form

Eye Drop

Eye drops are available as water and oil solutions, emulsions, or suspensions of one or more active substances. If stored in multipurpose packaging, these eye drops may also contain preservatives(20) Drugs with antiseptic, anaesthetic, anti-inflammatory, mydriatic, or meiotic characteristics are frequently found in them. An appropriate preservative, which is both a bactericide and a fungicide, is present in aqueous eye drops, unless they are single-dose. The ideal pH for eye drops must be 7.4%, which is the same as tear fluid. (7)Eye drop supplied for use in:

- Multiple-dose amber fluted eye dropper bottles that are either sold separately or include the rubber teat as part of the closed container.

- Plastic containers with a necessary dropper A breakable seal implies that the dropper or cap hasn't been taken off before first usage.(21)

The most practical, non-invasive, and patient-acceptable topical ocular medicines are eye drops. Pahuja, Arora, and Pawar point out a few obstacles that eye drops in treatment must overcome. According to the study, many patients had trouble administering the drops.(22)

Eye Ointments (3)

These sterile, semi-solid preparations are meant to be injected into the eye's conjunctival sac or lid border. These typically contain mydriatic, miotic, antiseptic, anti-inflammatory, or antibacterial chemicals. They include one or more medications that have been dissolved or dispersed in a suitable base, and they appear to be homogeneous. (7)

Although they are widely tolerated and safe, eye ointments have certain drawbacks, including the tendency to impair vision and occasionally induce annoying side effects, which is why they are typically used at night.(20)

Ointment is a mixture of semisolid and solid hydrocarbons, such as paraffin, that is non-irritating to the eye and melts at body temperature, according to Rathore & Nema (2009). Commonly, there are two different kinds of ointments: simple-based ointments, which consist of a single continuous phase, and compound-based ointments, which have two phases like an emulsion. The ointment will shatter into tiny drops when applied to the eye, and these drops will linger in the conjunctival sac for a longer amount of time (Baranowski, Karolewicz, Gajda, & Pluta, 2014). This results in the ointment's main benefit, which is that it acts as a drug depot in the conjunctival sac, enhancing and extending the absorption of the medication(22).

Microemulsion

The fundamental characteristics and distinctive architectures of microemulsions. They are auto-emulsified and then simply sterilized before use. These preparations can effectively degrade medicines and have good stability. These characteristics contribute to its high bioavailability. Absorption is the drug's primary mode of action. Nanodroplets in the interior phase of the micro emulsion reserve the drug substance on the cornea's outer surface and lessen drug discharge. (7)

Ophthalmic Solution

Ophthalmic solutions are hydrated, sterile liquids that are used for a variety of things, including cleaning and rinsing the eyes. Excipients that control the PH, osmotic pressure, and consistency of the formula may be present in ophthalmic solutions. If the ophthalmic solution is kept in multiuse packaging, further preservatives may be added to the mixture. (7)




Contact Lenses Coated With Drugs


These are circular structures, and the inclusion of drugs relies on whether the structure is hydrophilic or hydrophobic. Dye addition may occur during polymerization. The number of studies reported in recent years has increased, reflecting the importance of contact lenses which is continually increasing. Timolol, ciprofloxacin, dexamethasone, and cyclosporine are a few examples of medications whose medicinal accessibility from contact lenses. Using techniques like imprinting, straightforward soaking, and colloidal nanoparticles, the drug fusion is satisfied. The initial contact lenses were composed of glass, but the introduction of polymethylmethacrylate prevented the hard lens from expanding and improved patient comfort by blocking the passage of oxygen. For the past three decades, silicone hydrogel has mostly been used in the production of contact lenses. There are two varieties of contacts:

- Hard Contact Lenses
- Soft Contact lenses(7)

Regardless of their intended function, all contact lenses are medical devices that are governed by the US FDA. Prior to a Senate measure from 2005 that supported this assertion, decorative plano contact lenses were exempt from the medical device classification on the grounds that their use was only meant to alter eye appearance.(23)

Table 2: Ophthalmic dosage form

Diseases	Products	Brand name	Mfg. by	Dosage form	Picture
A] Dry Eye [704946]	diclofenac sodium & ketorolac	SANDOZ	AdvaCare	Eye Drop	
B] Conjunctivitis (5)	Benzalkonium Chloride	BIPREVE	Ista	Eye drop	
C] Glaucoma (5)	Betaxolol hydrochloride	BETAXOLOL	Alcon	Eye Drop	

D] Uveitis	Emulsion of difluprednate	AJANTA	Advacare	Eye Drop	
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Ocular Sustained Drug Delivery System

Several methods, including in situ gelling, the utilization of mucoadhesive polymers, polymer-coated nanoparticles, and liposomal distribution, are used in the innovative drug delivery system.

LIPOSOME

Liposomes are natural lipid-based lipid vesicles with a diameter of 25–10,000 nm that are biocompatible and biodegradable. They are presently the likelihood of ocular medication absorption is increased by intimate contact with the corneal and conjunctival surfaces, which is advantageous for pharmaceuticals that are poorly absorbed, those with low partition coefficient, poor solubility, or those with medium to high molecular weights. A thin layer of negatively charged mucin covers the corneal epithelium, and this mucin can bind to the positive charged surface of the liposomes.

Table 3: Liposome

Drug	Result	Year	Ref
1.GCV	In vitro transcorneal permeation and in vivo ocular pharmacokinetics was improved	2007	(24)
2.Tacrolimus	maintained for 2 weeks and reduced drug related toxicity	2010	(25)
3.Levofloxacin	Drug was released following first-order kinetics for more than 6 days and formulation had showed activity against <i>S. aureus</i> .	2007	(26)

Implant

Implants are a successful drug delivery technique for chronic ocular illnesses including cytomegalovirus (CMV) retinitis. Previously, non-biodegradable

Although polymers were utilized, their insertion and removal required surgical procedures. In the vitreous cavity, biodegradable polymers like Poly Lactic Acid (PLA) are currently safe and efficient drug delivery systems that exhibit no adverse effects. Fluocinolone acetonide intravitreal implants were created for the treatment of the posterior segment and were found to be effective at reducing retinal ocular inflammation.

Controlled drug delivery devices made of biodegradable or non-biodegradable polymers are known as intraocular implants. The ocular pars plana, which is situated anterior to the retina and

posterior to the lens, is where these are often inserted into the vitreous. The advantages of implants exceed the disadvantages of the implantation procedure despite the invasive nature of the implantation approach. One of these benefits is the removal of the blood-retina barrier, which enables therapeutic drug delivery directly to the target site; another is prolonged drug delivery; and a third is a decrease in the side effects that are frequently associated with intravitreal injections and systemic administration.(27)

Dendrimers

Large, intricate molecules with a clearly defined chemical structure are called dendrimers. Dendrimers can be utilised successfully for a variety of medication delivery systems. administration and claimed to have improved bioavailability, biocompatibility, and water solubility. The solutions containing dendrimers with carboxylic and hydroxyl surface groups have longer residence times. For regulated ocular drug administration, Vandamme et al. constructed and assessed poly (amidoamine) dendrimers containing fluorescein. They also identified the effects of dendrimer size, molecular weight, and the number of amine, carboxylate, and hydroxyl surface groups in various series. The solutions containing dendrimers with carboxylic and hydroxyl surface groups have a longer residence time.

The use of systemic administration in pharmacological therapy for the eyes is uncommon. Although it would remain straightforward and affordable while addressing some patient compliance issues with topical delivery, efficiencies are even lower. Blood flow in the anterior segment rate is exceedingly low, even when compared to the tissue's size. Even though the posterior portion is heavily vascularized, the blood-retina barrier prevents direct access to the retina and concentrates almost all of it in the choroid. While some substances can be administered systemically to the eye, the doses required to achieve therapeutic efficacy frequently cause many of the same negative effects as those associated with topical administration.(28)

Micro Emulsion

In order to lower interfacial tension, water and oil are dispersed in microemulsions, which are often characterized by tiny 100 nm droplet size, greater thermodynamic stability, and clarity. The choice of the organic phase, aqueous phase, and surfactant/co-surfactant systems are crucial factors that can impact the system's stability.

Theories of Microemulsion Formation:

Here, the interfacial or mixed film theory, solubilization theory, and thermodynamic theory the three primary theories of ME formation—are briefly reviewed. According to the thermodynamic

theory of stabilization, ME arises spontaneously because to the low interfacial tension caused by surfactant diffusion in the interfacial layer and the significant entropy contribution caused by the mixing of one phase in the other in the form of many tiny droplets. According to the mixed film hypothesis, the interfacial film behaves differently toward the aqueous and oily portions of the interface. According to the solubilization idea, ME is thought of as swelling micellar systems in which water or oil is dissolved into reverse micelle structures to create a one-phase system.(29)

Nanosuspension

Water and oil are dispersed in microemulsions, which are frequently characterized by minuscule 100 nm droplet size, improved thermodynamic stability, and clarity, in order to reduce interfacial tension. The selection of the aqueous phase, organic phase, and surfactant/co-surfactant systems is a critical element that can affect the stability of the system. Stabilizers: Provide steric or ionic barriers; thoroughly moisten the drug particles; prevent Ostwald's ripening and agglomeration of nanosuspensions.

Formulations of Nano suspension :(30)

Stabilizers

Thoroughly wet the drug particles; use steric or ionic barriers to stop Ostwald's ripening and agglomeration of nanosuspensions. Lecithin's, Poloxamers, Polysorbate, Cellulosics, and Povidones are a few examples.

Cosurfactants-

When creating nanosuspensions from micro emulsions, cosurfactants might affect phase behaviour. Examples include bile salts, dipotassium glycerine, transcitol, glycofurol, ethanol, and isopropanol.

Organic solvent

A less dangerous, pharmaceutically acceptable solvent used in formulation preparation. Examples include Benzyl alcohol, Methanol, Ethanol, Chloroform, Isopropanol, Ethyl Acetate, Ethyl Format, Butyl Lactate, Triacetin, and Ethyl Acetate.

Other additives

Depending on the needs of the administration method or the characteristics of the medication moiety. For instance, cryoprotectant, buffers, salts, polyols, and osmogens.

Types of Ocular Drug Delivery System

Table 4: Ocular drug delivery system

Topical dosage forms	Conjunctival Inserts
	Contact Lenses
	Gels
	Nanoparticles
	Mucoadhesive Polymers
	Ointments
	Solutions
	Suspensions
Intraocular dosage forms	Implants
	Nanoparticles
	Inserts

Ophthalmic Manifestation of Corona Virus**Table 5: Ophthalmic manifestation of corona virus**

Disease	Symptoms
Conjunctiva(15),(16)	Eye redness, ocular irritation, eye soreness, eyelid swelling, congestion & chemosis
Episcleritis(17)	Eye redness, Photophobia or tenderness
Acute anterior Uveitis(18)	Pain, Redness
Oscillopsia(19)	Intractable vertigo, nausea & Vomiting
Epiphora	Redness, Soreness, sharp pain, eyelid swelling, blurred vision, light sensitivity
Nystagmus	Vertigo, Nausea, Vomiting
Orbit and Ocular Adnexa	Proptosis, visual loss, Motor Deficits, Eyelid oedema, Painful eye and Sinusitis

India's Growing Presence in the Global Pharmaceutical Market

With the E7 countries - Brazil, China, India, Indonesia, Mexico, Russia, and Turkey—accounting for around one-fifth of worldwide pharmaceutical sales by 2020, it is predicted that the global pharmaceutical market will more than double to US\$1.3 trillion at a 5% compound annual growth rate (CAGR). By incremental growth, India is probably in the top three pharmaceutical markets and ranks sixth overall in terms of market size. The pharmaceutical market had revenues of Rs. 10,029 crore (\$1.56 billion) in March 2018, an increase of 9.5% from the same month the previous year. India is ranked third in volumes yet it is tenth in the world in terms of value. India ranks third in volumes while placing tenth internationally in terms of value. This expansion will be influenced by factors such as the rise in middle-class households, the development of the healthcare system, and the prevalence of health insurance. India exported pharmaceutical items of Rs. 767.17 billion (\$11.90 billion) between April 2017 and February

2018, with the country expecting this figure to reach US\$40 billion by 2020. More than 200 nations throughout the world get Indian medications for export, with the US serving as the primary market, followed by Europe, Africa, and various Asian nations. India is the largest exporter of generic medications in the world, making up between 70 and 80 percent of domestic retail sales and 20 percent of all generic drug exports globally.(11)

The Pharmaceutical Ophthalmic Market

This is the market for ophthalmic therapeutic drugs. The size of the global market for ophthalmic pharmaceuticals was estimated at almost \$30 billion in 2016, and it is anticipated to increase to \$42 billion by 2023, indicating a 5.3% CAGR between 2017 and 2023. [8] Due in part to a growth in the number of elderly people there, North America contributes 35% of the total. Global demand for ophthalmic drugs is driven by those used to treat disorders related to the retina, cataract, and glaucoma: Diabetes retinopathy and ARMD

The introduction of new ocular medication delivery is the current topic of interest worldwide. With a growth in the development of innovative ocular drug delivery techniques such as nanoparticles, noisome, and dendrimers, multicompartiment drug delivery systems registered the highest CAGR of 8.0%. From roughly 1400 crores INR in 2014 to 2200 crores INR in 2018, India's pharmaceutical ophthalmic market increased. Currently, this market is expanding at a 6.4% annual rate (2018). The pharmaceutical market in India is dominated by glaucoma and tear substitutes (for dry eye).(11)

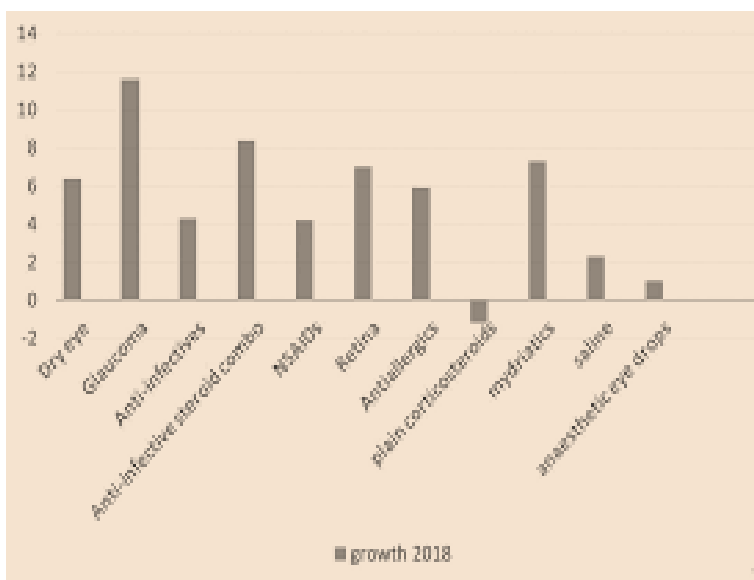


Figure Pharmaceutical ophthalmic market

FUTURE PROSPECT

Over three-quarters of the ophthalmic medication market is made up of branded generics, and this generic market will keep growing in every subsegment in line with the anticipated expansion of the ophthalmic pharmaceutical market in India. A sizeable portion of OTC sales go toward the eye drop category, which includes tear substitutes, antibiotics with and without steroids, and saline/salt preparations. In the near future, innovative brands are expected to be introduced in three different ophthalmic areas.

The introduction of medications like lifitegrast, lacritin, nasal tear stimulators, and sodium channel blockers may be seen in the dry eye segment. Formulation technology may also advance with the use of nanomicellar formulations, mucus penetration particle technology, and treatments for meibomian gland dysfunction.(12) The glaucoma market has already had two new USFDA approvals for latanoprostene bunod and Rho kinase inhibitors, with a third, trabodendoson (an adenosine A1 agonist), undergoing reevaluation. DARPins (ankyrin derivatives), non-biodegradable long-term fluocinolone-eluting implants, antiplatelet-derived growth factors, and a variety of monoclonal antibody medicines under development are expected to be visible in the retina section.(13)

This review provides a brief summary of the structure and growth trends of the Indian ophthalmic pharmaceutical market, as well as information on potential future developments of novel medications and advances in formulation and delivery technology.(14)

CONCLUSION

Ocular drug delivery has been a major challenge for scientists due to its unique anatomy and physiology. Different layers of the eye contain various types of barriers such as different layers of cornea, sclera and retina. Novel drug delivery strategies have been developed. The sterile products known as ophthalmic preparations are designed to be applied to the eye, any area nearby, and any spaces immediately surrounding the eye. The preparation may serve a variety of purposes, including therapeutic, preventative, or palliative ones. A therapeutic agent can be used for preparation purposes due to the dosage form's flexibility. Aqueous solution, aqueous suspension, ointments, and ocular inserts are only a few examples of the many ophthalmic formulations. To prevent microbial infection of the eyes, every ophthalmic product should be sterile in its final container. When compared to traditional drug delivery, the development of ocular drug delivery systems has been helpful. Similarly, developing effective ophthalmic medication delivery devices is difficult enough. The effectiveness of ophthalmic delivery systems has improved as a result of ongoing efforts to expand our understanding of the principles

and mechanisms driving ocular medication absorption and disposition. In-situ ocular gel formation is one such new strategy. Therefore, it makes sense to keep in mind non-conventional methods such as nanotechnology, microspheres, liposomes, appropriate prodrug in situ producing gel, and iontophoresis for effective transport as well as to improve ocular absorption and reduce side effects. Therefore, it makes sense to keep in mind non-conventional methods such as nanotechnology, microspheres, liposomes, appropriate prodrug in situ producing gel, and iontophoresis for effective transport as well as to improve ocular absorption and reduce side effects. A patient with upper respiratory and vestibular symptoms was diagnosed with a novel viral infection in the middle of a global pandemic. This case highlights the importance of having an index of suspicion for a COVID-19 infection in patients presenting with these symptoms, according to researchers at Cardiff University. Three ophthalmic segments are poised for introduction of innovator brands in the near future. Dry eye segment may show entry of drugs such as lifitegrast, lacritin, nasal tear stimulators and sodium channel blockers. Glaucoma segment has already shown two newUSFDA approvals in Rho kinase inhibitors and latanoprostenebunod.

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