Review Article

Recent trends in ocular drug delivery

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ABSTRACT

The eye preparations are sterile, isotonic solution, and buffered solutions. They are used for instant action. They cannot retain for the long time period. It is the major drawback with the conventional eyes dosage form; they are not able to maintain a therapeutic level. Ophthalmic preparation should be free from non-irritant and physiological properties of the material should not affect the physiological condition of the eye, not shown any type blurred vision. To attain the therapeutic effect with prolong action, this can be possible with novel drug delivery system. Ocular insert name is given to preparations which are controlled in the release as well as maintain the therapeutic level of drug in the eye conventional, mostly eye drops are used but due to lack of longer action preparations are modified in the form of ocular inserts. Various novel drug delivery systems have been developed to attain the better therapeutic effect of the drug. This article will cover the recent advancement of ocular to exploit better patient compliance and improved therapeutic efficacy.

Keywords: Bioavailability, BODS, corneal permeability, eye, new ophthalmic delivery system, particulate system, polymer, topical inserts

INTRODUCTION

For the treatment of the eye problem, the formulation is needed to deliver the eye with the minimum administration of the drug.[1] Ocular drug delivery has been a major challenge to pharmacologists and drug delivery scientist due to its unique anatomy and physiology . static barriers (different layers of cornea, sclera and retina including blood aqueous and blood-retinal barriers), dunamic barriers (Choroidal and conjunctival blood flow, lymphatic clearance and tear dilution) and efflux pumps in conjunction pose a significant challenge for a delivery of a drug alone or in a dosage form, especially to the posterior segment. Mostly used conventional ophthalmic preparations are eye drop, eye solution, eye gel, eye ointment, and eye injection. The mostly used formulations are eye drop, eye gel, and eye ointment. The conventional ophthalmic preparations have several drawbacks such as poor patient compliance, frequent administrations, the release of the drug is unpredictive, blurred vision, and even irritation also occurred. Bioavailability of drug is very low due to drainage of drug.[4,5] In case of corticosteroid, the minimum dose of the drug is six administration patient feels the burden, they may skip the prescribed dose, it leads to a poor pharmacological response of drug; therefore, frequent administration of the drug is required which leads to increase the risk of toxicity.[6] Various approaches are designed to achieve the more contact time with an eye like enhancement of viscosity, increasing the polymer concentration, but it leads to blurred vision patient acceptance is less, so need to designed a such type of carrier with maximum bioavailability and maximum patient acceptance which are discussed in later portion.[7,8] Before the development of formulation, we must know about the adsorption, distribution, metabolism, and excretion of the eye.[9] Bioavailability of the drug is important to attain the therapeutic effect, various novel approaches are used such as nanotechnologies and microsprays, for safer, effective, and better bioavailability, novel system is comfortable and easy to use.[10] There are several factors which determine the activity of drug as the all factors are define in Figure 1 which shows precorneal factors which effect bioavailability of the topically applied ophthalmic drug.

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ANATOMY AND PHYSIOLOGY OF EYE

The eye is one of the most complex organs in the human body. In the human eye, three layers can be distinguished. The outer region consists of the cornea and the sclera. The cornea refracts and

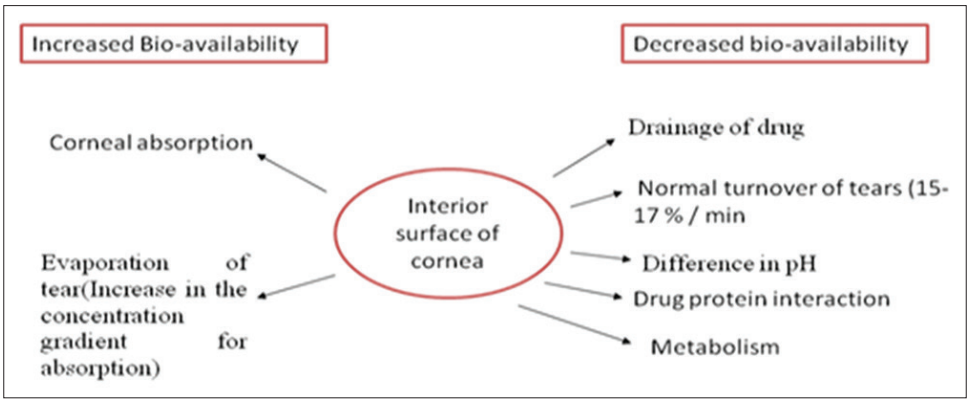

Figure 1: Precorneal factors which effect bioavailability of the topically applied ophthalmic drug

transmits the light to the lens and the retina and protects the eye against infections and structural damage to the deepest layer of the eye.[11] The sclera forms a connective tissue coat that protects the eye from internal and external forces and maintains its shape. The cornea and the sclera are connected at the limbus.[12] The visible part of the sclera is covered by a transparent mucous membrane, the conjunctiva. The middle layer of the eye is composed of the iris, the ciliary body, and the choroid.[13] The iris controls the size of the pupil and thus the amount of light reaching the retina; the ciliary body controls the power and shape of the lens and is the site of aqueous production, and the choroid is a vascular layer that provides oxygen and nutrients to the outer retinal layers.[14] The inner layer of the eye is the retina, a complex, layered structure of neurons that capture and process light. The three transparent structures surrounded by the ocular layers are called the aqueous, the vitreous, and the lens.

THE EYEBALL

The main part of the eye is the eyeball. Each eye is shaped like a ball and its full size is about 2.5–3 cm (1 inch) in diameter.[15] The inside of the eye contains a clear, jelly-like fluid that helps support the eye and maintains its shape. In the front or upper of the eye, this fluid is more watery and called aqueous humour. The fluid in the back or in middle of the eye is called vitreous humour.[16]

THE CORNEA

The cornea is the most anterior part of the layer of the eye, presents in front of the iris and pupil. It is the most densely innervated tissue of the body, and most corneal nerves are sensory nerves, derived from the ophthalmic branch of the trigeminal nerve. The cornea of an adult human eye has an average horizontal diameter of about 11.58 mm and is located in the center of the cornea, anterior to the pupil, and in photopic conditions.[17] The cornea is avascular and the branches of the anterior ciliary arteries stop at the limbus where they form arcades that supply the peripheral cornea. The optic zone (prepupillary cornea), which provides most of the cornea's refractive function, has a diameter of 4 mm. Therefore, the peripheral and central cornea are very distinct in terms of physiology and pathology.[18]

THE RETINA

The retina is the tissue that lines the inner surface of the eye, surrounding the vitreous cavity. During embryogenesis, the vertebral retina develops from the optic cup. The latter is formed by invagination of the optic vesicle, which is an outgrowth of the embryonic forebrain.[19] The inner wall of the optic cup (surrounding the vitreous cavity) ultimately becomes the neural retina; the outer wall (surrounded by the choroid and sclera) becomes the retinal pigment epithelium (RPE). The retina is protected and held in the appropriate position by the surrounding sclera and cornea.[20]

Sclera

The sclera is the white of the eye. It is made up of tough connective tissue and covers most of the eyeball. The sclera is the protective covering of the eyeball. Muscles that control the movement of the eye attached to the sclera.[21]

Iris

The iris is the thin, muscular colored part of the eye. It is located between the cornea and the lens. The muscles of the iris change the size of the pupil (the small, black, and central area of the eye) to control the amount of light that enters the eye. The iris has melanocytes, the cells that make a pigment called melanin. The amount of melanin in the iris is what gives the eye its color.[22] Figure 2 shows the various parts of eye.

OCULAR BARRIERS

The transport of fluids and solutes in the eye is controlled by several membranes and barriers. These barriers can hamper the delivery of topical ocular drugs (i.e., eye drops) and systemically (i.e., orally or intravenously) administered drugs.[23] Topical ocular drugs, mostly given as eye drops, are the most frequently used dosage forms for treating ocular diseases. The first barrier to cross for these drugs is the tear film, which rapidly removes instilled compounds from the eye, resulting in low bioavailability.[24] Other membranous barriers are located in the cornea, the conjunctiva, the iris-ciliary body,

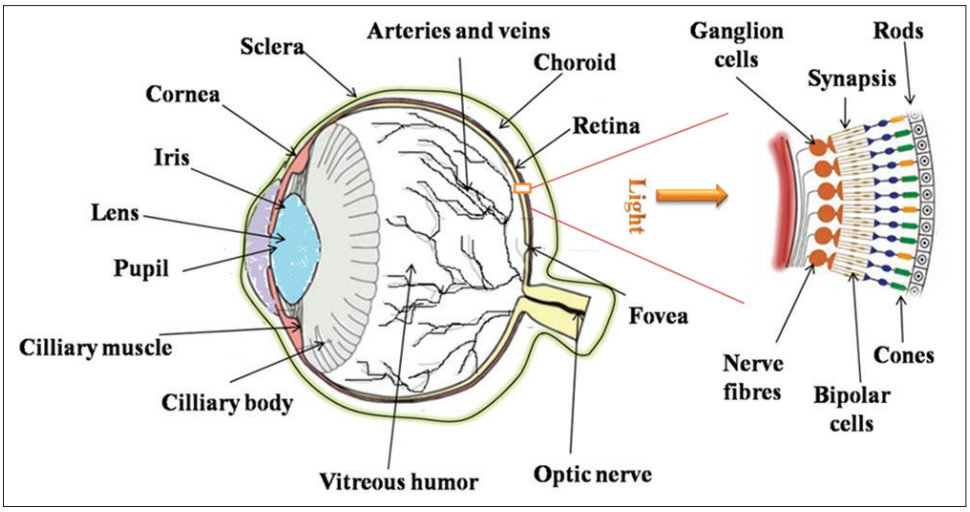

Figure 2: Various parts of the eye

and the retina. Depending on the physiochemical characteristics of the compounds, delivery of drugs can occur through the corneal route and/or the conjunctival/scleral route.[25] The corneal route is the main route for delivery of drugs to the anterior chamber. Permeation of hydrophilic drugs and macromolecules through the corneal epithelium is limited by the presence of tight junctions between adjacent outer superficial epithelial cells.[26] The abundant presence of hydrated collagen in the stroma may hamper the diffusion of highly lipophilic agents. The endothelium is more permeable and allows the passage of hydrophilic drugs and macromolecules between the aqueous and the stroma due to the presence of "leaky tight junctions" called desmosomes or macula adherents. The passage of topical ocular drugs through the corneal route depends on their lipophilicity, molecular weight, charge, and degree of ionization. Particularly, small lipophilic drugs can easily permeate through the cornea. After crossing the cornea, the drug diffuses into the aqueous and to the anterior uvea.[3]

Lens

The lens is transparent disc-shaped structure present in the inner part of the eye. It lies directly back to the cornea and iris. The lens changes its shape to allow the eye to focus on near or far objects. Light rays pass through the lens and are focused on the retina to create images of objects at different distances from the body.[27]

Choroid

The choroid is a thin layer of tissue that lies between the sclera and retina. It contains many tiny blood vessels that supply oxygen and nutrients to the retina.[28] The choroid contains many melanocytes. The melanocytes in the choroid absorb light to help lessen light reflection in the eye.[29]

Ciliary body

The ciliary body is a muscular ring of tissue at the junction of the iris and the choroid. Muscle fibers in the ciliary body help the eye to focus on near or far objects by changing the shape of the lens. The ciliary body also has cells that make aqueous humor, the jelly-like fluid in the front of the eye between the cornea and lens.[30]

Figure 3 shows the barriers affecting the ocular drug delivery.

Commonly eye diseases and their treatment

Eye diseases can be occurred for any reason such as inflammation, pain, allergy, dry eye, glaucoma, conjunctivitis, keratitis, blepharitis, and iritis cataract.[31] Pain and inflammation are generally resulting from ophthalmic surgery such as vitreoretinal, cataract, and glaucoma procedure. These all are treated with corticosteroid or by nonsteroidal anti-inflammatory drugs eye drop, market formulations are durezol (difluprednate), lotemax (loteprednol etabonate), and nevanac (nepafenac).[32]

MECHANISM OF DRUG RELEASE INTO THE EYE

The drug is released by three following mentioned mechanism:

I. Diffusion
II. Osmosis
III. Bioerosion.

Diffusion

In the diffusion mechanism, release of the drug is continuously acted as predefined controllable manner. When ocular inserted into the eye, the fluid of eye enters into the insert and causes swelling of the polymer which leads to relaxation of chain and drug diffusion occur.

Osmosis

In the osmosis, the insert is divided into two parts as internal and external when eye fluid comes in contact with eye insert diffuse and stretched.

Bioerosion

When ocular insert comes in contact with tear fluid, it leads to release the drug in a sustained manner by erosion of matrix. The drug is

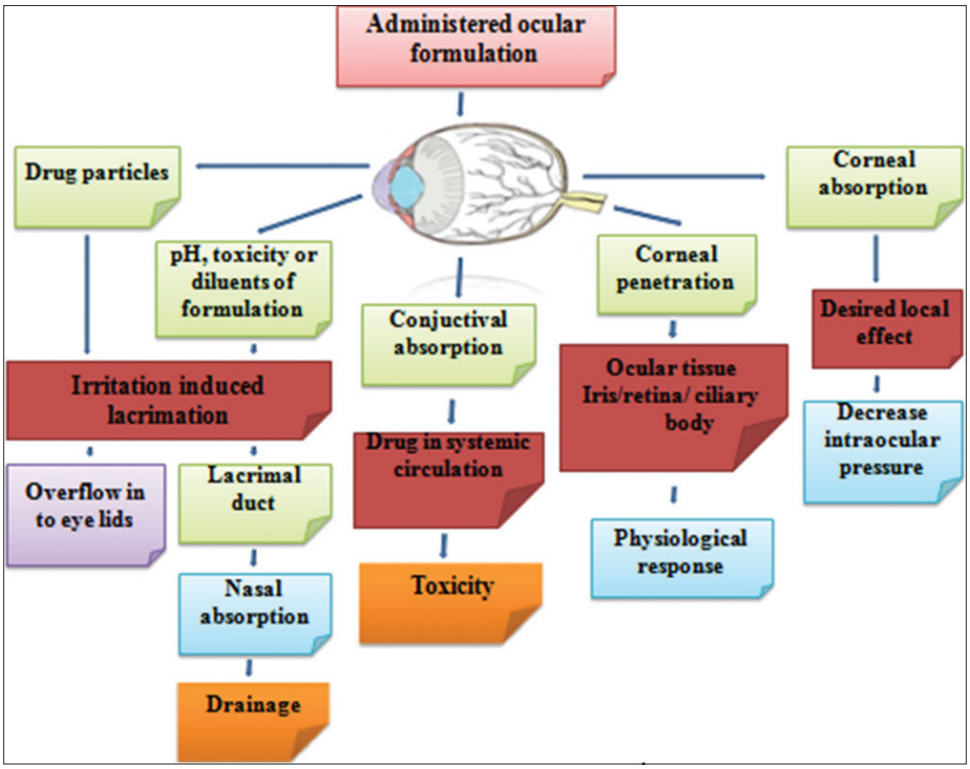

Figure 3: Barriers effecting the ocular drug delivery

available as dispersing in the ocular insert, through in the matrix it is believed that drug release in more in controlled form if it is available in the superficial concentrated in the matrix form.[33,34]

FORMULATION APPROACHES TO IMPROVE BIOAVAILABILITY

Prodrug approach

Prodrug concept has tum out to be an important part of the ocular drug design and delivery. Synthesizing prodrugs which accomplish most if not all requirements of an ideal formulation are very challenging. Functional group approach is one of the most commonly used ocular prodrug strategies. The common functional groups that have been utilized in ophthalmic prodrug design are carboxylic, hydroxyl, amine, and carbonyl groups. Modification of these functional groups which include esters, carbamates, phosphates, and oximes results in ophthalmic prodrugs. Transporter-targeted prodrug approach is also there. Recent progress in transporter identification has greatly contributed to the field of prodrug derivatization. Various transporters have been explored and recognized for transferring exogenous and endogenous nutrients across the cell membranes. A major role of these influx transporters is to deliver essential nutrients which can be utilized to deliver therapeutic molecules across various ocular barriers. The third one is the receptor-targeted prodrug approach. Receptors useful for prodrug targeting have been identified in the various regions of the eye. Receptors are responsible for the internalization of nutrients such as folate, Vitamin B12, and transferrin. Due to the importance of these receptors, numbers of investigator have examined the use of drug-receptor conjugation for drug delivery and drug targeting. Internalization of such conjugates has been achieved successfully by receptor-mediated endocytosis. Lipid prodrug is also a type of the prodrug approach. Molecules can cross cell membranes through passive diffusion. In the eye, drug absorption takes place either through corneal route (cornea-aqueous humor-intraocular tissues) or non-corneal route (conjunctiva-sclera-choroid/RPE). Due to lipophilic nature of cornea and other intraocular tissues, both hydrophilic and hydrophobic drugs take the transcellular pathway to cross the ocular membrane. To improve lipophilicity of hydrophilic drug molecules and hence to improve corneal permeation, the lipid prodrug approach has been developed. Lipid prodrugs diffuse readily across the cell membrane by facilitated diffusion and thereby result in improved cellular absorption.

Ocular preparation and formulations

Ointment is better known for sustain release bioavailability of the drug, it acts as a reservoir for the drug, with the help of ointment base drug having low bioavailability can be delivered to the eyes. The drug release of ointment in the eye reported as 2–4 or more even more than 8 h.[35]

Penetration enhancer

With the help of penetration enhancer, penetration of drug toward to corneal epithelial membrane increased by increase the transiently against the membrane corneal epithelial made up of tight transport tissue. With the help of various agents such as tween 20, parabens, ethylenediaminetetraacetic acid, benzalkonium chloride, saponins, azone, and fusidic acid in different formulations, these all show significant enhancement in the corneal absorption of drug.[36]

Colloidal system

Collidal system act as carrier for drug delivery. They provide sustain and prolong release of drug, it excretes the frequent dosing of the medicament. They can also target the medicament to particular site. The nature of the carrier should be non-irritant, biocompatible, and biodegradable.[37]

Liposome

They are made up of phospholipids and cholesterol and other small molecules having diameter range of 80–100 nm. They can release both types of drug, i.e.,: Hydrophilic and lipophilic (−). The absorption of the drug can be enhanced by liposomes. They enhance the intimate contact with conjunctival and corneal surface. The earlier research indicates that liposome, when associated with idoxuridine, is quality to the solution form of the drug for the treatment of herpes simplex keratitis in rabbits. If we talk about the size of liposome, they are available as small unilamellar vesicles (10–100 nm) and large unilamellar vesicles (100–3000 nm) in size. The composition of liposome matter it might have a positive, negative, or neural charge on the surface. Liposomes having positive charge highest drug concentration in the eye site which will helpful in the better treatment of chroditis and iritis.[38]

Niosomes

In case of liposome having several drawbacks such as cost, degradation of phospholipids, and chemical instability, this problem can be sorted out by the development of niosomes having relatively stable and osmotically active.[39] Niosomes have been reported as a better ophthalmic carrier. The drug timolol malate with non-ionic-based noisome (discomer) for the central rules of the water-soluble drug, as name discomer they are disc shape and large size of discomer makes it drainage preventive into the systemic pool, gives more better release in the cul-de-sac of the eye.[40]

Cubosomes

Cubosomes are defined as nanoparticles of a liquid crystalline phase with cubic crystallographic symmetry formed by the self-assembly of amphiphilic or surfactant-like molecules. One of the most common surfactants used to make cubosomes is monoglyceride glycerol monoolein. Gan *et al.* investigated cubosomes as an ophthalmic delivery system for dexamethasone, to improve ocular retention and ocular bioavailability. Dexamethasone cubosome particles were produced by fragmenting a cubic crystalline phase of monoolein and water in the presence of the stabilizer poloxamer 407. The apparent *in vitro* permeation coefficient of dexamethasone administered in cubosomes showed a 4.4-fold and 3.5-fold increase compared with that of dexamethasone sodium phosphate eye drops.

Ophthalmic spray

About 4% solution of drug pilocarpine is used to treat intraocular miosis through spray (single application). It was found to be beneficial drug delivery for intraocular miosis.[41]

Pharmacosomes

The amphiphilic drug in the presence of water converted into pharmacosomes. It provides better control release of drug and shelf stability. Drugs having free carboxyl group or might be active hydrogen atom, these can be esterified into a hydroxyl group which will lead to the formation of amphiphilic prodrug.[42]

Nanoparticles

From the past decades, nanoparticles are most widely studies colloidal system. The colloidal particles having a size range of 10 nm–1 mm, the drug is placed in the carrier by entrapment method.[43] Nanoparticle has better bioadhesive property, therefore, increases the residence time of drug, and it leads to more biological responses. Several researchers concluded that better efficiency of nanoparticle due to their bioadhesive property. By researchers found that 5 times more corneal concentration of cyclosporine. Nanoparticles have a better effect than the nanosphere it can diffuse the drug at a higher rate into the eye site.[44]

Chemical delivery system (CDS)

In this system, chemical modification of the drug agent with the help of metabolism here prodrug phenomena is also applicable in the form of the CDS. On administration of CDS, they undergo several enzymatic transformations with inactive intermediates and in the end by active species to target the site.[38] This method consists of a modification of drug molecule and chemical structure that makes it more selective toward site specific, safe drug delivery to eye site. Prodrug formulation of epinephrine gives 10-time fold penetration, with the help of ion-pair lipophilicity and corneal absorption is enhanced, other drugs with enhanced permeability by prodrug, i.e., albuterol, timolol, tilisolol, and pilocarpine.[45]

Implantable system

Due to the requirement of minor surgery for placing the polymer system to the eye, therefore, the implantable system is less popular, with zero order of drug release selection of drug is increased, repetitive administration of the drug is decreased. In case of cytomegalovirus (CMV), the ocular implant of drug ganciclovir has been developed this implant release the drug directly to the retina up to 5 months. The benefit of this approach is with the help of zero-order release rate selectivity action of drug take place.[46,47]

Cell therapies

Encapsulated cell technology (ECT), developed by Cumberland – based neurotech pharmaceuticals , is aiming to solve the challenge of delivering large molecular weight drugs to the retina over extended period of time. With the help of semi-permeable recombinant protein is encapsulated in the carrier.[48] Patient with AIDS-associated cytomegalovirus retina infection implanted with intraocular non-biodegradable drug delivery devices. The device is produced by coating of poly(vinyl alcohol) (PVA) on the drug ganciclovir, pellets were coated with ethylene vinyl acetate except on its top surface. This device release the drug to the retina for 4–5 months and shows responses in case of CMV retinitis.[49]

Topical inserts

They are placed under the eyelid, release the medicament for a longer period of time. They are made up of drug contain polymers, which are non-invasive in nature.[50] This type of insert is developed by Menlo Park based on sight vision. It has just completed the Phase II clinical trial compared with timolol in a patient with glaucoma (NCTOIP15940). As per the website of the company, they have mentioned this insert is also effective for seasonal allergy and dry eye.[51]

Contact lens

Contact lens are a good carrier for the ocular delivery of medicines, patient acceptance is better due to decrease in the mixing with tear and increase in the bioavailability. It provides sustained release of the drug, the only drawback of contact lens is drug loading and is less and difficult to control the release of drug for a longer time period of time.[52] Different methods were employed by various research groups to diminish this challenge such as encapsulation nanoparticles immobilizing drug one more carrier has been developed which release the drug on enzyme degradation named as a nanodiamond gel. These efforts have shown better drug release during the clinical trials.[53]

Particulate system

Mucus-penetrating particles utilized by Waltman-based Kala Pharmaceuticals used to enhance the drug delivery and avoid clearance of mucous. For the treatment of post-operative cataract inflammation, Kala Pharmaceutical is already in the clinical trial for the lead compound.[54,55]

Soluble ophthalmic drug inserts (SODIs)

SODI is made up of soluble polymers acrylamide, n-vinyl pyrrolidine, and ethyl acrylate. It is available as a sterile and thin film. These are oval in shape having (weight) 15–17 mg. After insertion of soda in the conjunctiva, the soda becomes soften within 10–15 s and takes a shape of eye ball and allows the drug dissolved in the fluid of eye.[35] Pilocarpine dose of 2.7 mg is used in the treatment of glaucoma. A single dose of soda gives long-term effect of the drug; it will replace the repetitive doses of eye drop.[56]

Iontophoresis

This is a way to deliver the drug across biological membrane with the help of slight electrical current. EyeGate Pharma has developed an ocular device based on iontophoresis for safer delivery of dexamethasone phosphate.

Bioadhesive ophthalmic drug inserts

In the conventional formulation, major drawback is the expulsion of drug from the site of absorption, and the drug is unable to reach the site specific. To tackle this problem, new carriers have been developed which provide site-specific action they need to remove from the site after the release of the drug.[57]

Collagen shields

Collagen shields are prepared from the porcine sclera tissue. They are having the same composition as the cornea. Collagen is hydrated before place in the eye site; the drug is loaded into the collagen shield by soaking the collagen in the drug. It forms a clear, firm having 0.1 mm in thickness approximately which release the drug up to 72 h.[58]

New ophthalmic delivery system (NODS)

NODS consists of 6 mm strips containing water soluble, which is separately coated with a film of PVA in which the drug is placed. Drug is released from the system as they coming contact with tears.[59] This gives an opportunity for a drug which is sparingly soluble in water and unstable on physiological pH. It provides 8-fold more bioavailability than the standard eye drop of pilocarpine. Nods are formulated to release the drug at a particular site with long-lasting effect.[60]

Osmotic inserts

These consist of the central part enclosed by the help of peripheral part, basically, they are of two types:

Type-A: Drug is surrounded by the polymer matrix which allows the drug release; it consists of the single reservoir with or without the addition of solvent. In the second layer of these inserts containing film which is an insoluble and semi-permeable polymer.[61]

Type-B: The midpart surrounded by two compartments osmotic solution and drugs are placed in the separated compartment, the tears diffuse to an osmotic compartment with osmotic pressure; it leads to stretches the elastic membrane and removal of drug.[62]

Bioerodible ocular insert

The cross-linked gelatin and polyester are used in the bioerodible system, which goes hydrolysis of chemical bond and dissolution. The major effect of bioerodible is modulating their erosion by the change in the final structure or by addition of surfactant, i.e., Anionic and cationic surfactants.[63] The ocular insert releases the drug in predetermined and predictive rates also eliminate the frequent dosing of eye drop, in case of ocular insert bioerodible material is used having different layers with different concentrations of the material to control the release of the drug. It consists of inner core and an outer layer of the formulation. More addition of ophthalmic preparation is the particle completely or uniformly disperse. Comparatively non-greasy in nature, at the same time, they cannot cause foreign body sensation in the eye.[64] Before the development of delivery of drug to the ophthalmic preparation must know about the unique properties of eyes, which gives more challenges and opportunities to work in this organ. The approach of the novel controlled drug delivery system gives control release of drug which cannot be maintained by the conventional eye drop.[65]

Ocufit

They are rod-shaped, sustained release device produced by the help of elastomer solution. This was patented in 1992. They are assembled to

Table 1 : Various ocular drug delivery technologies which are in development phase

Technology	Description	Stage of development	Company	Indication
Refillable implants	Drug-containing reservoir	Phase I	Genetech	Wet AMD
	Refills implantation invasive	Phase I	Replenish	DME
	Can deliver the drug to posterior of the eye			
	Non-biodegradable			
Topical inserts	Non-elastomer	Phase II	Foresight vision 5	Glaucoma
	Drug-containing soft elastomer	Preclinical	Amorphex	No info available
	Non-invasive		Therapeutics	
	Anterior disease focused			
	Release drug over			
Iontophoresis	A wearable electrical device used to deliver the drug into ocular	Phase III	EyeGate Pharma	Anterior uveitis
	site	Phase III		Cataract surgery
	Non-invasive	Phase III		Dry eye
	Drug deliver to posterior			
Punctual plug	Might have biodegradable property	Phase II	Mati Therapeutics	Glaucoma
	Drug loaded polymeric device	Phase III	Ocular Therapeutix	Post-operative inflammation
	Non-invasive			Allergic conjunctivitis
Implant (polymeric)	Drug-containing the polymeric construct	Phase III	pSivida	Posterior uveitis
	Typically biodegradable	Phase I (with Pfizer)	Allergen	Glaucoma
	Implanted in subconjunctival or intravitreal to release the drug	Phase II		Geographic atrophy
	over time	Phase I/II		Retinitis pigmentosa
	Invasive	Phase II		Glaucoma
	Can release the drug to posterior of the eye	Phase III		
Encapsulated cells	Cell containing reservoirs	Phase II/III	Neurotech Pharmaceuticals	Retinitis pigmentosa
	Non-biodegradable	Phase II		Macular telangiectasia
	Invasive	Phase II		Type 2
	Can deliver the drug to posterior of the eye	Phase I/II		Wet AMD
		Phase I		Glaucoma
		Phase I		Ischemic optic
Gene therapy	Injected into ocular compartments to deliver genetic material	Phase I/II	Spark Therapeutics	Choroideremia
	Invasive	Phase III	Avalanche	Leber congenital
	Viral vector-based delivery system	Phase II	Biotechnologies	Wet AMD
		Phase I	Genzyme	Wet AMD
		Phase I	Oxford BioMedica	Stargardt disease
		Phase I/II (With Sanofi)		Usher syndrome
Particulate system	The various drugs containing particulate (liposomal/drug crystal	Phase III	Kala Pharmaceuticals	Ocular inflammation
	and polymeric)	Phase II		Post
				cataract surgery
				Dry eye
Contact lens	Drug-containing soft contact	Preclinical	Various research groups	Glaucoma
	Non-invasive			
	Anterior disease focus			
	Function as a contact lens and a drug reservoir to release the			
	drug over time			

easily fit in the eye shape and in size of conjunctiva. They are 1.9 mm in diameter and 25–30 mm in length. Rod-shaped insert example is Lacisert (Merk and Co., Inc.) used for the treatment of dry eye. Ocufit having insoluble property is combined for the two major features, sustained and long retention of the drug diseases such as allergic, bacterial and adenoviral conjunctivitis, corneal ulcer, and episcleritis does not affect on retention of the insert.[66]

Various ocular drug delivery technologies which are in development phase are given in Table 1.

CONCLUSION

The formulation for ocular is not easy due to the characteristic which makes the drug delivery difficult. However, the novel drug delivery system is trying to diminish the problem makes the use of formulation in a different way. The recent novel ocular formulation provides sustained release of drug at particular eye site. With the help of various polymers bioavailability of drugs can be enhanced. Combination of various drugs with polymer coating is a better way to deliver the drug in control manners. Long-term safety and efficacy need to be established. Many of the above-mentioned formulations are in clinical phase; we say that if some of them pass the clinical trial it will bring remarkable benefits for a patient with better acceptance and treatment. Of all these novel formulations, the ocular insert has great future. An attentive study of given methods in the development of ocular preparation leads to effective preparations. Ocular inserts provide a constant release of drug with accurate dosing, better efficacy. Systemic absorption of the drug is reduced which diminish the side effect, ease of handling, no interference with vision, stability, and sterility.

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