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A Comprehensive Review on Ocular Drug Delivery System

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Abstract

Since the eyes are protected by a special architecture and physiology, the transport of medications administered using conventional dosage forms is restricted to the eye, and therapeutic drug concentrations in the target tissues are not sustained for an extended period of time. Various droppable items to extend the retention duration on the ocular surface have been introduced to the market for the treatment of the anterior portion of the eye. For the treatment of chronic vitreoretinal disorders, direct intravitreal implants made of biodegradable or non-biodegradable polymers have been extensively studied. The treatment of chronic diseases urgently requires the development of ocular drug delivery systems that offer controlled release and promote patient and physician convenience while lowering the frequency of dosage and intrusive treatment. This article reviews the development of ocular medication delivery systems that are now through clinical trials and late stages of experimentation.

Keywords: Anatomy and physiology of eye, Cornea, Contact lens, Barriers of ocular drug delivery, Drug delivery system for anterior and posterior segment of eye, Implants, Liposomes, Microemulsion

Introduction

Pharmaceutical and medical sciences face significant obstacles in the delivery of ophthalmic drugs. Progress has been made over several decades to improve the current dose formulations. Ocular disorders are difficult to cure, and ocular forms must be safe, non-allergic, and sterile. 90% of the indicated formulation is in topical form [1]. In topical application, tear fluid turnover, nasolacrimal drainage, corneal epithelium, and blood-ocular barriers reduce local bioavailability and ocular surface residence duration. Only 5% to 10% of the medication passes through the corneal barriers [2]. Furthermore, when compared to oral medication delivery, ocular drug delivery provided similar or greater bioavailability, controlled release, and therapeutic impact in the eye [3, 4].

Antibiotics, antibacterials and antimicrobials are a class of medications that are commonly used in ophthalmic administration to treat a variety of ocular illnesses (microbial keratitis, conjunctivitis, meibomian gland dysfunction, and dry eye) [5]. Antibacterial medicines can be delivered to the eye by topical, subtenon, intraocular, or subconjunctival routes. Antibiotics

typically used in the treatment of eye infections include tetracyclines, fluoroquinolones, amino glycosides, and penicillin's [6]. Antimicrobial resistance refers to bacteria's ability to resist the effects of antibiotic therapy. Antimicrobial formulation efficacy was investigated in vitro and in vivo. Different formulations and forms are being researched to improve antibiotic bioavailability, resident time in the eye, and therapeutic response. In situ gelling systems, liposomes, nanoparticles, niosomes, nanoemulsions, and microemulsions are among the new ocular drug delivery types they can extend precorneal residence time and decrease drug loss owing to tear with the right recipients. In a second section, topical formulations such as eye drops, ointments, hydrogel, contact lenses, and ophthalmic inserts are produced to introduce ocular administration and clarify the existing marketed dosage form. [7]

The Anatomy of the Eye

The human eye, exquisite in its intricacy and design, serves as a portal to the process known as vision. The eyeball is spherical in shape and measures around 1 inch across. It houses a number of structures that work together to improve visibility. The human eye is made up of layers and internal components, each of which serves a specific purpose. Below is a detailed description of each eye part.

Components of an Eye

A. Sclera

The sclera (white component of the eye) is the strong white sheath that comprises the ball's outer coat. It is a tough fibrous membrane that keeps the eye in an almost globe shape. It is substantially thicker in the back/posterior of the eye than at the front/anterior of the eye [7].

B.Conjunctiva

The conjunctiva is a thin transparent mucous epithelial barrier that borders the inside of the eyelids and covers one-third of the eyeball's anterior surface. The palpebral and bulbar conjunctiva is the separate portions of the conjunctiva. The conjunctiva is made up of two layers: the outer epithelium and inner stroma (substantia propria). The conjunctiva contributes to the development of the tear film by secreting significant electrolytes, fluid, and aqueous humor.

C. Cornea

The cornea is a prominent transparent protrusion at the front of the eye. The adult cornea's surface has a radius of about 8mm. It serves a key optical function by refracting light that enters the eye and then travels through the pupil and onto the lens (which focuses the light onto the retina). The cornea, a non-vascular structure (it lacks blood vessels), obtains nutrition via capillaries that finish in loops around its perimeter. These infiltrate the cornea's layered tissue. As a result, it is exceedingly sensitive.

D. Aqueous humor

The aqueous humor is a jelly-like material found in the eye's outer/front chamber. It is a watery fluid that fills the "anterior chamber of the eye" which lies directly

behind the cornea and in front of the lens. The aqueous humor is a mildly alkaline salt solution containing trace amounts of sodium and chloride ions. Schlemm's canal (also known as the scleral venous sinus) is a circular conduit that receives aqueous humour from the anterior chamber and transports it to the circulation via the anterior ciliary canal veins. It is situated at the intersection of the cornea and the sclera. The rate of aqueous humor turnover in humans is around 1% - 1.5% of the anterior chamber volume per minute. Pressure dependent and pressure independent routes exist in aqueous humor [8].

E. Pupil

The pupil appears to be the dark "centre" of the eye, but it is actually the circular aperture in the center of the iris through which light enters the eye. The pupillary reflex (also known as the "light reflex") regulates the size of the pupil (and thus the amount of light admitted into the eye).

F. Iris

The iris is a thin circular contractile curtain positioned behind the cornea but in front of the lens. The iris is a variable-size diaphragm that regulates the quantity of light let into the eye by adjusting the size of the pupil. It is the colored part of the eye (shades can vary, such as blue, green, brown, hazel, or grey).

G. Ciliary Muscle

The ciliary muscle is a ring of striated smooth muscles in the middle layer of the eye that regulates the flow of aqueous humour into Schlemm's canal and controls accommodation for viewing objects at different distances. The muscle is innervated by both parasympathetic and sympathetic nerves. The curvature of the lens is altered by the contraction and relaxation of the ciliary muscle.

H. Lens

The lens is a clear structure encased in a thin clear capsule. It is situated behind the pupil of the eye and is surrounded by ciliary muscles. It aids in the refraction of light passing through the eye (which is initially refracted by the cornea). The lens focuses light onto the retina, creating an image. It is able to do so because the shape of the lens changes depending on the distance of the object(s) from the person's eye.

I. Vitreous Humour

The vitreous humour (also known as the vitreous humor) is a vast region in the human body that occupies approximately 80% of each eye. The vitreous humour is a clear, thin jelly-like material that fills the chamber behind the eye's lens. It is an albuminous fluid that is surrounded by a fragile translucent membrane known as the hyaloids membrane.

J. Retina

The human retina is placed in the back of the eye. The retina is the "screen" on which an image is generated by light that has gone into the eye via the cornea, aqueous humour, pupil, lens, and lastly the vitreous humour. The purpose of the retina's function is not only to be a screen, onto which an image can be generated, but also to collect the information contained in that image and convey it to the brain in a form that the body can use.

K. Macula

The macula is the center of the retina. The macula is densely packed with photoreceptor cells, which turn light into nerve signals. With the macula, humans can perceive small details

such as newspaper due to the high concentration of photoreceptors. The fovea, or center of the macula, is the place of our clearest eyesight.

L. Choroid

The choroid layer is placed behind the retina and collects unneeded radiation as well as nourishing the retina's outer sections. It is a thin, dark brown membrane that is extremely vascular (it contains blood vessels) and contains a pigment that absorbs excess light, preventing impaired vision (due to too much light on the retina). The choroid has the highest blood flow rate in the body and the lamina fusa connects the choroid to the inner surface of the sclera.

M. Optic nerve

The optic nerve (a network of about one million nerve fibers) is in charge of sending nerve impulses from the eye to the brain. These nerve signals carry information on an image for the brain to process. The optic disk is the visible front surface of the optic nerve on the retina [9].

Limitations of Conventional Systems in Ocular Drug Delivery

Despite various limitations, conventional drug delivery systems used for dosage form instillation are very convenient and straightforward to use by all age groups. When eye drops are applied to the inferior fornix of the conjunctiva, only a small portion of the dose reaches the intraocular tissues, with the majority being washed away with the lachrymal fluid or absorbed systemically in the nasolacrimal duct and pharyngeal sites [10]. Another barrier is the drug's limited permeability from the epithelial surface of the cornea. One of the primary causes of blindness is posterior segment eye disease. Because eye drops are administered topically, they remain in the front region and do not deliver drugs to the posterior part of the eye. As a result, there is a need for safe, effective, and convenient drug delivery systems that deliver the medicine to the intended areas [11].

Ocular Pharmacokinetics

The drug pharmacokinetics from the eye follows the paths shown below.

- Lacrimal fluid transcorneal penetration into the anterior chamber
- Non-corneal drug penetration into the anterior uvea via the conjunctiva and sclera
- Drug delivery from the bloodstream into the anterior chamber via the blood-aqueous barrier.
- The aqueous humor transition to the trabecular meshwork and Schlemm's canal removes the medication from the anterior chamber.
- The passage of drugs from the aqueous humor into the systemic circulation via the blood-aqueous barrier
- Drug delivery from the bloodstream to the posterior eye via the blood-retina barrier
- Drug administration intravitreal.
- Drug elimination from the vitreous via posterior route across the blood-retina barrier via the anterior pathway [12, 13].

Barriers for Ocular Delivery

1**. Drug loss from the ocular surface**

Following instillation, the flow of lacrimal fluid removes the injected substances from the eye's surface. Despite the fact that the lacrimal turnover rate is only about 1 l/min, the surplus volume of the injected fluid is rapidly transported to the nasolacrimal duct in a few of minutes. Another source of

ineffective medication removal is systemic absorption rather than ocular absorption. Systemic absorption can occur directly from the conjunctival sac via local blood capillaries or after the fluid has flowed into the nasal cavity.

2. Lacrimal fluid-eye barriers

The medication absorption from the lacrimal fluid into the eye is limited by the corneal epithelium. Tight connections occur between ocular epithelial cells, limiting paracellular drug permeation. As a result, lipophilic medications often have at least an order of magnitude more permeability in the cornea than hydrophilic pharmaceuticals. In general, the conjunctiva is more permeable to the epithelium is larger than the cornea, and its surface area is about 20 times larger**.**

3. Blood-ocular barriers

Blood-ocular barriers protect the eye from xenobiotics in the bloodstream. These barriers are divided into two parts: the blood-aqueous barrier and the blood-retina barrier. The endothelial cells in the uvea form the anterior blood-eye barrier. It is made up of the iris, the ciliary body, and the choroid. This barrier inhibits plasma albumin from entering the aqueous humor and also limits the entry of hydrophilic medicines from plasma into the aqueous humor. The retinal pigment epithelium (RPE) and the tight walls of retinal capillaries form the posterior barrier between the bloodstream and the eye. Drugs can easily enter the Choroidal extra vascular space, but their distribution into the retina is hampered by the RPE and retinal endothelial cells [14].

- **Drug Delivery Systems to Anterior Segment of the Eye**

1. Eye-Drops

Anterior DDSs for eye-drops are being developed to increase the retention period of topically given pharmaceuticals by leveraging the interaction between the drug carrier and the physiological milieu of the cornea and/or subconjunctiva. Dura site DDS is based on a polycarbophil aqueous solution (InSite Vision Inc., Alameda, CA, USA) [15]. Polycarbophil is polyacrylic acid cross-linked with divinyl glycol, and it creates hydrogen bonds with mucus, corneal and conjunctival epitheliums, all of which are negatively charged, to prolong the effects of the medicine for several hours. Broad-spectrum antibiotic, Azithromycin ophthalmic solution made with Dura site (Aza Site, Inspire Pharmaceuticals Inc., Durham, NC, U.S.), was released in the United States in 2007.Durasite, a combination of Azithromycin and dexamethasone (DEX) (ISV-502; Aza Site Plus TM, In Site Vision Inc.), is currently in Phase III trials for the treatment of blepharoconjunctivitis [16]. Dura Site (ISV-303, In Site Vision Inc.) contains bromfenac, which is in Phase I/II trials to minimize inflammation and pain after ocular surgery [17]. The critical solution temperature (LCST) of methylcellulose (MC) is around 50 °C, and a sol-gel phase transition occurs. Because the ocular surface temperature is 32-34 °C [18], LCST must be lower to gel MC solution at the ocular surface fast after instillation as eye-drops. In general, excessive electrolyte concentrations cause salting-out and gelation of MC [19].

Amberlite IRP-69 is a polystyrene sulfonic acid resin cross-linked with divinyl benzene that is a strong cationic ion exchange resin. Betoptic S, which has been on the market since 1990 (Alcon Laboratories, Inc., Fort Worth, TX, USA), and whose active

ingredient is betaxolol for glaucoma therapy, is made up of this resin [20]. Positively charged betaxolol binds to the resins negatively charged sulfonic acid groups. When betaxolol-bound resin is applied to the eye, cationic ions in the tear fluid, such as Na+ or K+, cause the release of betaxolol molecules from the resin matrix into the tear film, resulting in betaxolol penetration across the cornea [21].

2. Contact Lens

Soft contact lens-based DDSs have been investigated by several approaches: (1) Soak and absorption of drug solution [22]; (2) piggyback contact lens combined with a drug plate or drug solution [23]; (3) surface-modification to immobilize drugs on the surface of contact lenses [24]; (4) incorporation of drugs in a colloidal structure dispersed in the lens [25]; (5) ion ligand-containing polymeric hydrogel [26]; and (6) molecularly imprinting of drugs [27,28]. The soft contact lens based drug delivery devices are being developed by the following two companies, but details have not been disclosed. Vistakon Pharmaceuticals, LLC (Philadelphia, PA,A multinational Phase III clinical trial for a contact lens presoaked to release an antihistamine medication, ketotifen, to prevent allergic conjunctivitis in contact lens wearers has been completed [29,30]. SEED Co., Ltd. (Tokyo, Japan) and Senju Pharmaceutical Co., Ltd. (Osaka, Japan) have collaborated to prduce a one-day disposable soft contact lens containing integrated sodium cromoglicate. Clinical studies for allergic conjunctivitis will be done in Japan in 2010 [31].

3. Cul-de sac Inserts

TM is an eye hypotensive medication that delivers consistent regulated release (20 or 40 g/hour for 7 days) and was first introduced in 1974 [32]. Ocuserts is made up of two ethylene-vinyl acetate copolymer (EVA) exterior layers and an inner layer containing pilocarpine in alginate gel within di-(ethylhexyl) phthalate for a release enhancer sandwiched between EVA layers [33]. However, Ocuserts has not been extensively adopted due to poor IOP control caused by a variety of factors such as difficulties inserting the device, ejection of the device from the eye, and discomfort during insertion [34].Although numerous inserts, including collagen shield, Ocufit SR, New Ophthalmic Delivery System, and Minidisc ocular therapeutic system, have already been developed [35].

4. Punctal Plugs

Inhibiting drainage through the nasolacrimal system with a punctal plug into the pancta has long been used to lengthen retention time and boost absorption and efficacy following eye-drop instillation [36]. The effectiveness of an ocular hypotensive drug in eye drops in conjunction with punctual occlusion via punctual plug has been studied. Although punctal occlusion considerably reduced IOP in the plugged eyes by roughly 2 mmHg (p 0.001), it was not established that this IOP decrease is clinically meaningful [37, 38]. QLT (Vancouver, Canada) and Vistakon Pharmaceuticals, LLC, respectively, have developed punctal plugs as DDSs for latanoprost and bimatoprost. QLT Inc. has presented Phase II results for a punctual plug with 44 g, 81 g, and two separate 95 g release rates. Based on available data from 185 eyes with 12 weeks of follow-up in conjunction with previous research, the retention rate was 81%, although no dose-response for IOP

reduction was identified [39]. QLT Inc. intends to conduct a clinical trial of a punctal plug containing the antihistamine medication olopatadine to treat allergic conjunctivitis.

- **Subconjunctival/Episcleral Implants**

LX201 (Lux Biosciences Inc., Jersey City, NJ, United States) is a silicone matrix episcleral implant that is designed to administer cyclosporine A to the ocular surface for one year. The implant has a flat bottom in touch with the episclera and a rounded top in contact with the anterior surface. The LX201 is available in two lengths: 0.5 and 0.75 inches. Each implant measures 0.08 inch wide by 0.04 inch high [40]. The episcleral cyclosporine implant provided continuously possibly therapeutic cyclosporine levels to the lacrimal gland in preclinical tests employing rabbits and dogs, and demonstrated efficacy in a keratoconjunctivitis model [41]. LX201 is currently being studied in Phase III to prevent corneal transplant rejection [42]**.** A silicone episcleral implant produced by 3T Ophthalmic (Irvine, CA, USA) looks like a little bathtub and is less than 1.0 cm long. It can be refilled with pharmaceuticals in a variety of forms, including solution, gel, and matrix [43]. In animal studies using a model compound (sodium fluorescein), the episcleral implant facilitates fluorescein diffusion through the sclera, resulting in high levels in the retina and posterior vitreous, and tissue levels are significantly higher than with periocular fluorescein injection [44].

Drug Delivery Systems to Posterior Segment of the Eye

Intravitreal Implants

1. Durasert™ Technology System

The Durasert TM technology system (pSivida Corp., Watertown MA, USA) employs a drug core surrounded by one or more polymer layers to deliver medications for predefined time periods ranging from days to years. The permeability of the polymer layers governs drug release [45] Using the Durasert TM system, an antiviral drug, ganciclovir (GCV)-loaded intravitreal implant (Vitrasert, Bausch & Lomb Inc., Rochester, NY, U.S.) has been developed as the first intravitreal DDSs that avoids systemic side effects and does not require frequent intravitreal injections for the treatment of cytomegalovirus retinitis. This implant is comprised of EVA and PVA and releases GCV for 6-8 months by passive diffusion through a small aperture in EVA at the device's base [46,47] Retisert (Bausch & Lomb Inc.), an intravitreal implant containing fluocinoloneacetonide (FA) [48,49], has been approved by the FDA for the treatment of non-infectious posterior uveitis. The implant's composition and drug release time differ from those of Vitrasert. The implant contains 0.59 mg of FA and is intended to deliver the medicine for up to 1,000 days. The Retisert implant is made up of a central core of FA compressed into a 1.5 mm diameter tablet [50]. Each FA tablet is housed in a silicone elastomer cup with a release opening. A semi-permeable layer of PVA coats the tablet inside the cup reservoir near the release orifice, forming a membrane between the tablet and the aperture that serves as an additional barrier for drug release.

2. Novadur™ Technology

Ozurdex (Allergan, Inc., Irvine, CA, United States) is an intravitreal implant containing 0.7 mg of DEX composed of PLGA (length: 6.5 mm, diameter: 0.45 mm) that was

approved by the FDA in June 2009 for the treatment of macular edema caused by branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO) [51]. Ozurdex is injected into the vitreous cavity using a specially developed injector with a 22-gauge needle. Two multicenter, 6-month sham-controlled clinical trials [52] looked at 1,267 individuals who had visual loss due to macular edema caused by BRVO or CRVO. Patients received a single treatment with a 0.7 mg DEX-intravitreal implant (n = 427), a 0.35 mg implant (n = 414), or a sham injection (n = 426). The time it takes for patients to acquire a result after one therapy In both groups receiving the DEX-intravitreal implant, the BCVA improvement of 15 letters or more was substantially less than it was in the sham-assigned individuals (P 0.001). At 30 to 90 days, both DEX-intravitreal implant groups significantly outperformed the sham implant group in terms of the proportion of eyes with a BCVA improvement of at least 15 letters (P 0.001) At all follow-up visits, the proportion of eyes with a BCVA loss of at least 15 letters was substantially lower in the groups receiving the DEX-intravitreal implant 0.7 mg than in the sham group (P 0.036). At all follow-up time periods, both DEX-intravitreal implant groups improved mean BCVA more than the sham group did (P 0.006). Both patients with BRVO and those with CRVO experienced improvements in BCVA following DEX-intravitreal implant therapy; however the patient response patterns varied. IOP 25 mm Hg was present in 16% of the eyes treated with the DEX-intravitreal implant at day 60 (for both dosages), and by day 180, there was no difference between the treated eyes and the control eyes. FDA most recently authorized Ozurdex for posterior non-infectious A Phase III clinical trial for DME is now underway with Ozurdex [53].

- **Injectable Particulate Systems**

1. IBI-20089

IBI-20089 containing TA is being developed by Icon Bioscience, Inc. (Sunnyvale, CA, U.S.) using the Verisome TM drug delivery platform technology. The Verisome TM is a clear fluid. Saline and IBI-20089 combine to generate a milky, somewhat opaque solution that solidifies into gel. IBI-20089 might be a TA solution in biodegradable benzyl benzoate, according to Icon's patent [54]. With just one intravitreal injection, IBI-20089 is intended to last up to a year. For cystoids macular edema linked to BRVO or CRVO, a Phase I open label trial has been finished [55, 56].

2. Retaac

Human studies of PLGA microspheres with TA (RETAAC system) were described by Cardillo et al. [57]. Patients with diffuse DME received intravitreal injections of RETAAC, and their effectiveness was compared to that of bare TA injections. For a full 12 months, eyes treated with RETAAC displayed a noticeable reduction in retinal thickness as well as increased visual acuity. In comparison to uninjected TA eyes, this study showed greater long-term pharmacologic performance. The retina was proven to tolerate RETAAC without any adverse effects. In this investigation, no adverse medication or procedure-related effects were found. The central macular edema evaluated by OCT in a Phase I/II research of 21 patients with DME unresponsive to laser photocoagulation showed a decrease from baseline surpassing 59% at 3 months

following RETAAC injection, which maintained at 6 months or year, although no appreciable improvement in visual acuity was made.

3. Cortiject

The preservative-free emulsion Cortiject (NOVA63035, Novagali Pharma S.A.) contains a target tissue-activated corticosteroid prodrug inside of an oily carrier [58]. A retina-specific esterase de-esterifies the released DEX palmitate before it is activated to become DEX. Over the course of 6–9 months, a single intravitreal injection produces sustained release. Details of the open-label Phase I research for DME, which is presently underway, are not made public [59].

4. Eye-Drops

Poor redispersibility and caking of weakly water-soluble medicines in aqueous suspension might decrease bioavailability due to dosage error, and the large variety of particle sizes makes filtering sterilizing challenging. These concerns are resolved by difluprednate emulsion, which also penetrates intraocular tissues more readily than its suspension [60]. Comparing sub-tenon's injection of TA with difluprednate emulsion eye drops (DurezolTM, Alcon Laboratories, Inc.) approved by the FDA for the treatment of inflammation and pain associated with ocular surgery was done in a non-randomized clinical research for refractory DME following vitrectomy [61]. The mean retinal thickness evaluated by OCT in the group receiving eye drops (11 eyes in 7 patients) dropped from 500.6 207.7 m at baseline to 341.2 194.8 m at three months. The mean retinal thickness for the sub-tenon's TA group (11 eyes in 10 patients) dropped from 543.3 132.6 m at baseline to 378.6 135 m at three months. Between difluprednateeye drops (73%) and sub-tenon's TA (84%) there was no significant difference in the rate of effective improvement in retinal thickness (Fisher's exact test: P = 1)

- **Routes of Ocular Drug Delivery**

There are numerous ways to deliver drugs to the tissues of the eye. The target tissue plays a major role in the choice of administration route various routes used in ocular drug delivery like topical route, subconjunctival, intravitreal, intra camera, peril ocular and Supera choroidal [62-65].

- **Novel approaches of ocular drug delivery systems**

1. Polymeric gels

These often use a similar technique to lengthen the drug's ocular residence duration. To enhance the viscosity of the fluid, these medications increase intraocular diffusion. There are two categories of polymeric gels, and they can be separated by there are two types of gels: in-situ gel formation and traditionally performed gels. Additionally, their in-situ forming gels are viscous liquids that change into a viscoelastic gel after being exposed to physiological conditions in a cul-de-sac.

2. Bio-adhesive hydrogels

In this, bio- adhesive hydrogels are frequently used excipients are the hydrophilic polymers belonging to different classes, including the cellulose derivatives of polyacrylic like carbomer, povidone, polyvinyl alcohol, sodium hyaluronate or sodium alginate, etc. The carbomer they have bio-adhesive properties which can be increased, and they can be broadly defined as the maintenance of contact for an extended period of two

materials, one of which when they installation frequency will be lower than with eye drops They are increasingly using hydrogels based on hyaluronic acid (HA) to treat dry eye condition.

3. In-situ forming hydrogel

It is anticipated that this ocular drug delivery system will use an easy-to-use device to provide a precise concentration of the medicine over a predetermined duration they try to combine the benefits of both gels and solutions in this novel medicinal dosing form. They are injected as a solution into their conjunctival sac in their in-situ gels, where they transition into the gel as a result of a change in either temperature or ion concentration vigilance or Ph. There are numerous polymers having these characteristics [66].

4. Combination of polymers

Combining different polymers holds more compliance and increases therapeutic effectiveness because some polymers have downsides when used alone. The polyacrylic acid (carbapol 940) in the ofloxacin's ocular delivery method is when combined with HPMC, which acts as a viscosity-improving agent. Lin and Sung created an ocular medication formulation of pilocarpine that contains carbapol, pluronic, or a mixture of the two, according to a US patent. This is the preferred carbapol and pluronic formulation, which contains a 0.3% and 14% carbapol mixture. As a result, the medication was retained more effectively than with the individual polymer solution [67].

5. Liposomes

Microscopic vesicles known as liposomes are made up of one or more concentric lipid bilayers. The water or aqueous buffer chambers are what separate them. This raises the likelihood that ocular drugs may be absorbed. Due in part to their surface charge, these liposomes have been found to be effective as an eye medication delivery mechanism. Liposomes are phospholipids with a specifiedviscosity that are employed in drugs to target specific sites of action. These primarily offer regulated and prolonged medication release while also enhancing drug bioavailability [66].

6. Microemulsion

The natural defense of the eye is present in microemulsions due to their intrinsic properties and specific structure; they are prepared by inexpensive processes through auto emulsification and they supply the energy; and they can be easily sterilized, so there is a stable and high capacity for dissolving the drug. These generally are in vivo results and preliminary studies on healthy volunteers Systems with lecithin propylene glycol, PEG200 as a surfactant or co-surfactant, and isopropyl myristate as the oil phase have typically been developed [68].

7. Niosomes

When compared to liposomes, they are typically more chemically stable. These are the nonionic surfactant's bilayers structural vesicles. They have the ability to enclose both hydrophilic and lipophilic molecules niosomes lessen the overall drainage and longer residence times result in a rise in ocular bioavailability. Since they are often harmless, special handling procedures are not necessary In general; these niosomes are not biocompatible or biodegradable. Niosomal formulation was produced in these most modern methods of cyclopentolate delivery. In comparison to the Timolol solution, the

niosomal formulation coated the (chitosan or carbopol) Timolol maleate significantly reduced the effect on IOP in rabbits [68].

Conclusion

For researchers in the field, developing effective treatments for eye conditions is a hard undertaking. They inject collagen shields, disposable contact lenses, ocular films, and other formulations using a novel ophthalmic delivery technique. The ocular delivery mechanisms in question include the Combining medication delivery systems is a more recent approach that aims to enhance the therapeutic impact or therapeutic response of an effective drug. The target tissue should effectively contain the medication in these ideal systems. This time frame had a minimal systemic impact. Any comfortable ophthalmic drug delivery system should be designed with patient acceptance in mind. Sustained drug release, larger-scale manufacturing, and stability all need significant improvements. In these, ocserts' ocular medicine delivery technology offers numerous benefits, including improved patient lowering the dosage frequency increases compliance. They offer controlled and sustained drug administration, lower the dosage, and lessen the drug's side effects. These combinations of the drug delivery system may provide a fresh direction for enhancing a system's ineffective therapeutic response.

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