ADVANCE OCULAR DRUG DELIVERY SYSTEM

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Abstract :

Ocular medication delivery is the main issue facing pharmacologists and formulation scientists today. The most practical and patient-friendly drug delivery method, particularly for the treatment of disorders of the anterior segment, is topical eye drops. Various precorneal, dynamic, and static ocular barriers prevent medication delivery to the targeted ocular tissues. Additionally, target tissues do not retain therapeutic medication levels for an extended period of time. The development of innovative, secure, and patient-compliant medication formulations and drug delivery devices/techniques, which may overcome these obstacles and sustain drug levels in tissues, has increased over the past two decades in the field of ocular drug delivery research. Modulating traditional topical solutions with permeation and viscosity enhancers demonstrates gains in anterior segment medication delivery. Additionally, it involves creating traditional topical formulations including ointments, emulsions, and suspensions. Additionally, numerous nanoformulations for anterior segment ocular medication delivery have been established. The current analysis aims to summarise the advancements made in existing conventional formulations for ocular distribution, followed by recent developments in formulations based on nanotechnology. Also highlighted are recent advancements in various ocular drug delivery techniques using in situ gels, implants, contact lenses, and microneedles.

Keywords: biology and anatomy, Cornea, contact lenses, eye drops, liposomes, nanomicelles, ointments, retina, and suspensions are all examples of eye care products.

Introduction:

The architecture and physiology of the eye are distinctive, making it a complex organ. The anterior segment and posterior segment are the two primary components of the eye's anatomy (figure 1). About one-third of the eye's surface is taken up by the anterior segment, and the rest by the posterior section. The anterior section is made up of tissues such the cornea, conjunctiva, aqueous humour, iris, ciliary body, and lens. The sclera, choroid, retinal pigment epithelium, neural retina, optic nerve, and vitreous humour are all parts of the posterior segment of the eye. Several disorders that compromise eyesight can affect the eye's anterior and posterior segments. Among the illnesses that affect the anterior segment are glaucoma, allergic conjunctivitis, anterior uveitis, and cataract. While the two conditions that most frequently affect the posterior portion of the eye are age-related macular degeneration (AMD) and diabetic retinopathy.

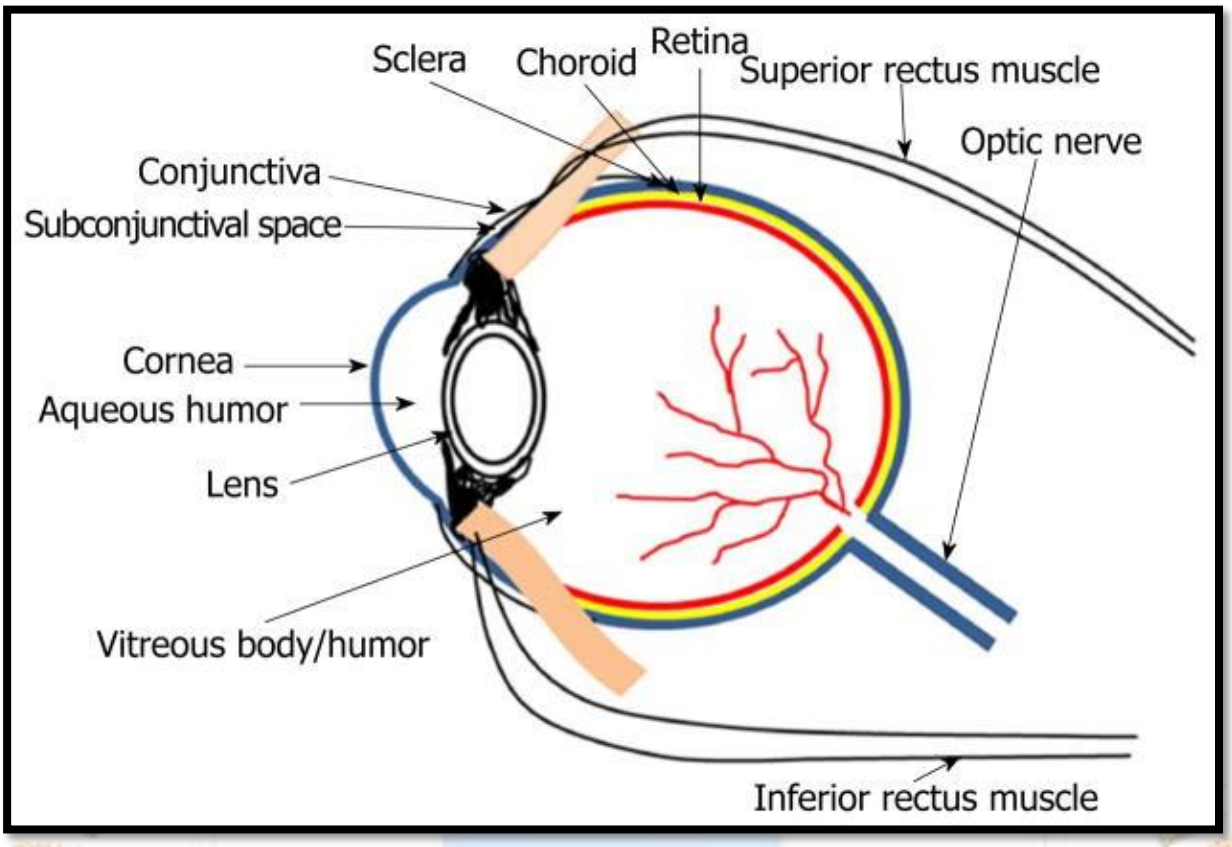


Figure 1 shows the eye's structure.

The most popular non-invasive drug delivery method for treating illnesses of the anterior segment is topical instillation. 90% of the commercially available ophthalmic formulations are in conventional dose forms like eye drops. The cause might be related to patient compliance and convenience of administration.[1] However, topical drop delivery results in very limited ocular absorption. Deeper ocular medication absorption is hampered by a variety of anatomical and physiological restrictions, including tear turnover, nasolachrymal drainage, reflex blinking, and ocular static and dynamic barriers [3]. Therefore, only 5% of the dose administered topically reaches the deeper eye structures.[4]. Due to the aforementioned barriers, it is also challenging to establish therapeutic medication concentration into posterior segment ocular tissues after topical eye drop application. Different methods of delivery, including intravitreal injections, periocular injections, and systemic administration, are available for delivering the medication to the posterior segment ocular tissues. However, systemic administration is not a viable strategy due to the tiny volume of the eye in comparison to the rest of the body and the presence of blood retinal barriers. The most popular and frequently advised method of administering medication to treat posterior ocular disorders is intravitreal injection. However, the recurring requirement for intravitreal injections can have a number of adverse effects, including endophthalmitis, haemorrhage, retinal detachment, and poor patient tolerance [5]. As an alternative method of delivering drugs to the posterior ocular tissues, transscleral drug delivery with periocular administration has developed. Although transscleral distribution is relatively simple, less invasive, and patient-friendly, ocular static and dynamic obstacles impair drug penetration. Ocular barriers to transscleral drug administration include both static and dynamic barriers, such as the lymphatic flow in the conjunctiva and episclera and the blood flow in the conjunctiva and choroid [6,7]. Static barriers include the sclera, choroid, and retinal pigment epithelium (RPE).

System for Convenient Drug Delivery to the Eye

A popular and patient-friendly drug delivery method is topical drop instillation into the lower precorneal region. Only 20% (or about 7 L) of the instilled dose is kept in the precorneal pocket after being applied topically, as most of it is lost to reflux blinking. The drug's concentration in the precorneal region serves as a catalyst for its passive diffusion through the cornea. However, greater corneal penetration with longer drug cornea contact time are necessary for effective ocular drug administration with eye drops. Improvements in precorneal residence duration and corneal penetration have been made in a number of ways. Iontophoresis, prodrugs, ion-pair forming substances, and cyclodextrins are used to enhance corneal permeability [9–13]. There is a large selection of ophthalmic products on the market, and about 70% of prescriptions call for traditional eye drops. High patient acceptability, drug product efficacy, stability, and cost effectiveness may all play a role in the reasoning.

liquid/solution eye drops for topical use

The most practical, secure, immediately effective, patient-compliant, and non-invasive method of administering ocular medications is via topical drops. Following topical drop instillation, an eye drop solution delivers a pulse of drug penetration, after which its concentration rapidly falls. Drug concentration drop kinetics may roughly follow a first order. Therefore, various additives such as viscosity enhancers, permeation enhancers, and cyclodextrins may be added to topical eye drops in order to improve medication contact time, penetration, and ocular bioavailability. By increasing formulation viscosity, viscosity enhancers increase precorneal residence duration and bioavailability after topical drop delivery. Examples of viscosity enhancers include polyalcohol, sodium carboxy methyl cellulose, hydroxypropyl methyl cellulose, hydroxymethyl cellulose, and hydroxyethyl cellulose. By altering the integrity of the cornea, permeation enhancers increase corneal uptake. Bile salts, surface active agents, preservatives, and other additives were investigated as potential permeation enhancers. Examples of permeation enhancers studied for enhancing ocular transport include cremophor EL, sodium taurocholate, ethylenediaminetetraacetic acid sodium salt, polyoxyethylene glycol ethers (lauryl, stearyl, and oleyl), and benzalkonium chloride[17–19]. Ocular medication bioavailability is increased by adding permeation enhancers to solutions, however few investigations have found that permeation enhancers have a local toxicity[20]. As a result, research is ongoing to alter the effect of permeation enhancers and assess their safety with regard to corneal tissues. According to Hornof et al. [21], polycarbophil-cysteine as an excipient did not compromise the integrity of the corneal tissue, indicating that it would be safe for ocular formulations. In an aqueous solution, cyclodextrins serve as carriers for hydrophobic medicinal molecules. This facilitates the delivery of medications to biological membrane surfaces. A biological membrane that is highly lipophilic has a substantially lower affinity for hydrophilic cyclodextrins. Cyclodextrins stay in aqueous solution as a result, and the biological membrane absorbs the hydrophobic medication. A concentration of cyclodextrins in eye drops of less than 15% was shown to produce the best bioavailability [22]. Cholkar et al. recently examined and provided a detailed description of other cyclodextrin uses in eye drop formulation.

Viscosity enhancers and cyclodextrins among these methods have precorneal loss as a drawback. Due to the great sensitivity of ocular tissues, caution should be given when choosing penetration enhancers. As a result, other traditional formulation approaches using inert carrier systems for the administration of medicines to the eye are developed. To increase a drug's solubility, precorneal residence duration, and ocular bioavailability, conventional ocular formulations such emulsions, suspensions, and ointments are created. These traditional formulations continue to have a significant role in today's nanotechnology-based world and continue to dominate the market. The negative

effects of these formulations, however, include ocular irritation, redness, inflammation, visual impairment, and stability problems [24]. Research is currently being done to enhance the in vivo efficacy of these carrier systems and to lessen their negative effects [25]. There have been several attempts to use conventional formulations to deliver medications to the posterior ocular structures. The following sections make an effort to summarise recent initiatives to enhance the in vivo performance of standard ocular formulations and lessen their negative effects.

Emulsions:

The solubility and bioavailability of pharmaceuticals can be enhanced via an emulsion-based formulation strategy. Oil in water (o/w) and water in oil (w/o) emulsion systems are the two forms of emulsions that are commercially used as carriers for active medicinal ingredients [26]. O/w emulsion is a popular and well-liked drug delivery method for use in the eye over w/o systems. Less irritability and improved ocular tolerance of o/w emulsion are some of the causes. Examples of ocular emulsions that are now marketed in the United States include Restasise, Refresh Endura (a non-medicated emulsion for eye lubrication), and AzaSite. Emulsions' usefulness in raising precorneal residence duration, drug corneal penetration, providing sustained drug release, and consequently enhancing ocular bioavailability has been shown in a number of investigations [27]. Tajika et al. recently shown enhanced anti-inflammatory activity of 0.05% [3H] difluprednate, a prednisolone derivative, using emulsion as the vehicle. The results showed that, following single and numerous topical drop instillations, emulsion may deliver drug to anterior ocular tissues in the rabbit eye, with little drug reaching posterior tissues. The cornea had the most radioactivity, followed by the iris-ciliary body, retina, choroid, conjunctiva, sclera, aqueous humour, lens, and vitreous humour in experiments using single and multiple topical drop instillations. Tmax after a single drop of medication was 0.5 hours for the cornea, conjunctiva, lens, iris-ciliary body, aqueous, and vitreous humour while it was 1 hours for the retina and choroid. The amount of medication in systemic circulation was quite little. Tmax for the lens and retina-choroid were 8 and 0.5 hours, respectively, after repeated dosage instillation. A total dose of about 99.5% of the radioactivity was eliminated in urine and faeces after 168 hours. This study supports difluprednate emulsion as a viable treatment option for inflammations of the anterior eye. To exhibit higher ocular performance and absorption, azithromycin was investigated as a carrier system in emulsions with fatty additions such soyabean lecithin and stearylamine[29]. The parameters of tear elimination were compared between azithromycin solution and emulsion at dosages of 3, 5, and 10 mg/mL azithromycin. In vivo tests via topical drop delivery were carried out on rabbits. Emulsion was found to improve the chemical stability and precorneal residence time of azithromycin in addition to acting as a vehicle for the drug and slowing drug release. Furthermore, emulsion formulation increased azithromycin's chemical stability (t1/2) at pH 5.0. Derivatizing active pharmaceutical ingredients (API) and increasing their ocular bioavailability using an emulsion as a carrier system is a similar unique method. This tactic might lessen ocular irritation and enhance API's effectiveness. Shen et al worked to increase the flurbiprofen's emulsion biocompatibility in an effort to test this theory. This study's emulsion was made using castor oil, tween-80, and the flurbiprofen derivative flurbiprofen axetil [30]. Four distinct emulsions were created and labelled as F1, F2, F3, and F4, with various amounts of tween 80 (0.08 wt%-4 wt%) and castor oil (0.1 wt%-2.5 wt%). Male New Zealand albino rabbits used in the in vivo trials were topical drop instillations. The F2 emulsion (castor oil to tween 80 wt% ratio of 0.5:0.4) was found to be superior to other emulsion formulations and solution in aqueous humour pharmacokinetic investigations. Compared to 0.03% flurbiprofen sodium eye drops, the F2 emulsion translocated high drug quantities into aqueous humour after topical drop application (Figure 2).

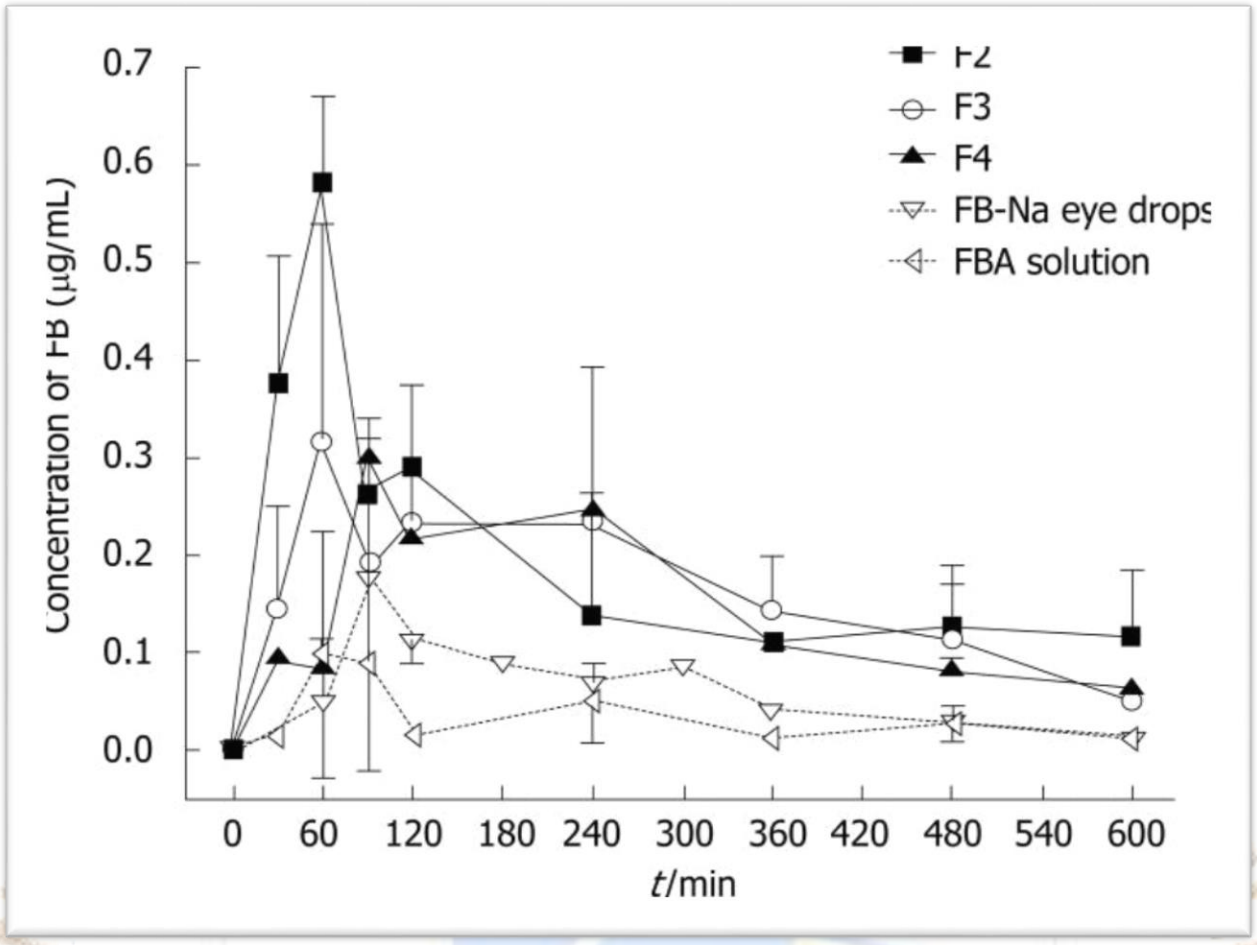


Figure 2 shows flurbiprofen concentration-time profiles in rabbits following administration of flurbiprofen axetil emulsion F2-F4, FB-Na eye drops, and flurbiprofen axetil-oil solution.

Suspensions:

Another category of non-invasive ocular topical drop medication carrier systems are suspensions. Suspension is the dispersion of finely divided insoluble API in an appropriate suspending and dispersing agent-containing aqueous solution. In other words, API is dissolved in a saturated solution in the carrier solvent system. Drug contact time and duration of effect are increased in comparison to drug solution thanks to suspension particles' retention in the precorneal pocket. The length of the drug's activity in suspension depends on the particle size. The medication absorbed into the ocular tissues from the precorneal pocket is replenished by smaller size particles. However, bigger particle size aids in the retention of particles for a longer period of time and slows medication dissolution [32]. So it stands to reason that the best drug activity would arise from the ideal particle size. To treat bacterial infections of the eyes, several suspension formulations are sold internationally. One of the commercial products that is frequently suggested for patients who are responding to steroid therapy is TobraDex suspension. TobraDex is a medication that combines the steroids dexamethasone (0.1%) and the antibiotic tobramycin (0.3%). High viscosity is this commercial product's main flaw. Recently, Scoper et al tried to make TobraDex less viscous while also enhancing its in vivo pharmacokinetics and bactericidal efficacy. The goal of creating this formulation was to enhance the qualities of suspension formulation, including quality, tear film dynamics, and tissue permeability. The new suspension (TobraDex ST) contains dexamethasone (0.05%) and tobramycin (0.3%). Studies on suspension settling revealed that the new formulation had very little settling over 24 hours (3%), compared to commercially available Tobra-Dex (66%). In comparison to Tobra-Dex, rabbits treated with TobraDex ST had greater tissues concentrations of dexamethasone and tobramycin, according to ocular distribution tests.

Innovative Ocular Drug Delivery Methods:

Ocular medication delivery using nanotechnology

For the treatment of eye problems, numerous strategies have been used in recent years. One of the strategies now being studied for both anterior and posterior segment drug delivery is nanotechnology-based ophthalmic formulations. Systems based on nanotechnology that have the right particle size can be created to guarantee reduced irritancy, sufficient bioavailability, and compatibility with ocular tissue. For ocular medication administration, a number of nanocarriers have been created, including nanoparticles, nanosuspensions, liposomes, nanomicelles, and dendrimers (Figure 3).

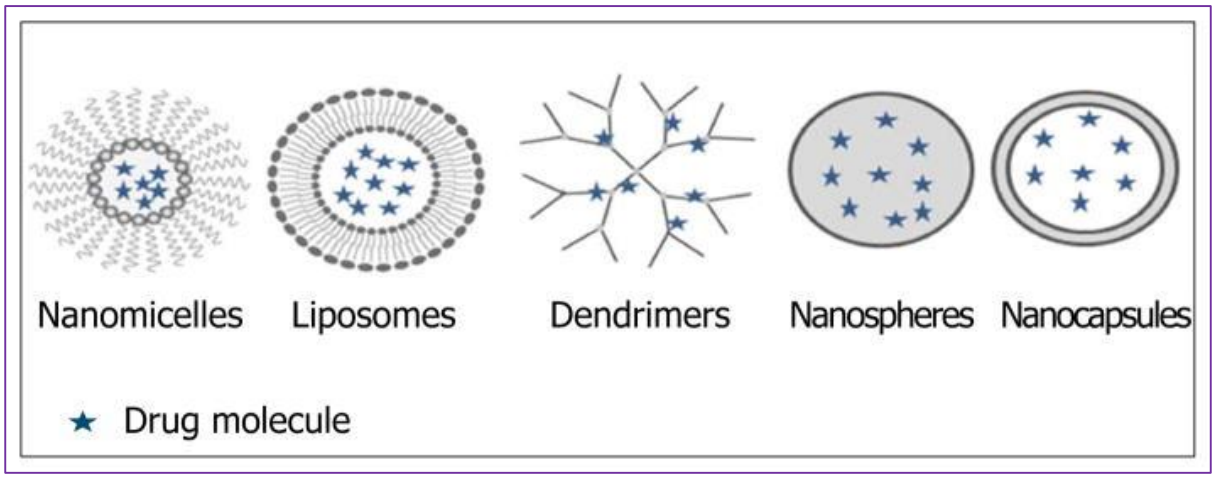


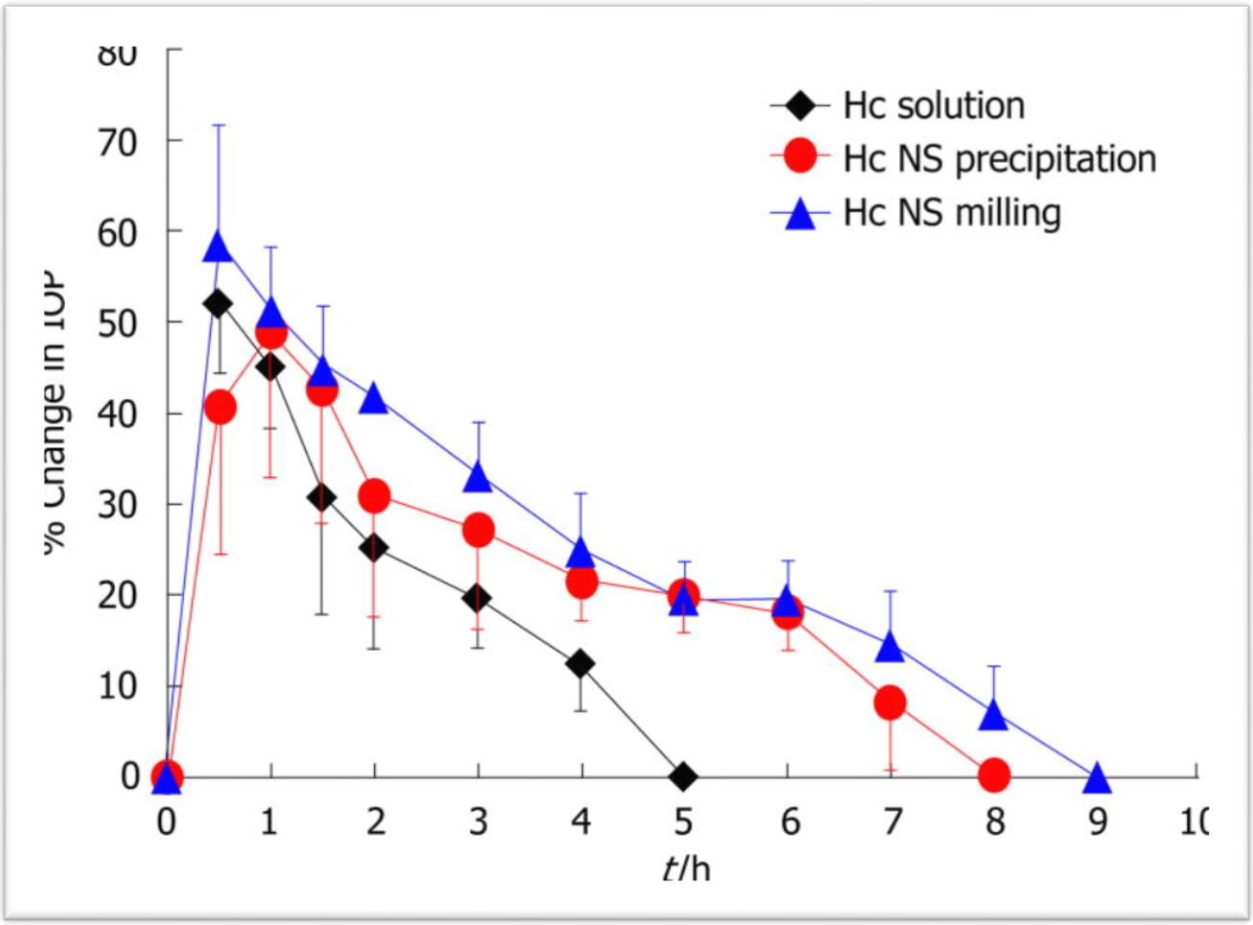
Figure 3 shows ocular medication delivery using nanocarriers.Nanomicelles

The most popular carrier methods for creating therapeutic medicines in clear aqueous solutions are nanomicelles. Typically, amphiphilic compounds are used to create these nanomicelles. These compounds could be polymeric or surfactant-based. Cholkar et al. has studied the topic of ocular barriers and the use of nanomicelles-based technology for ocular medication administration in great detail. The development of ocular medication delivery technology based on nanomicellar formulations is currently receiving a lot of attention. They have a high drug encapsulation capacity, are simple to prepare, are tiny, and produce an aqueous solution thanks to their hydrophilic nanomicellar corona. Additionally, micellar formulation can improve the therapeutic medications' bioavailability in ocular tissues, implying greater therapeutic results. Numerous proof-of-concept experiments have so far been carried out to examine the viability of using nanomicelles for ocular medication delivery. For example, Civiale et al. [44] created dexamethasone-loaded nanomicelles for anterior segment distribution using copolymers of polyhydroxyethylaspartamide [PHEAC(16)] and pegylated PHEAC(16). With aqueous humour sampling, in vivo dexamethasone concentration time patterns in rabbits were examined and determined. According to the findings, PHEA micelles with dexamethasone loaded on them have a better ocular bioavailability than dexamethasone solution. Dexamethasone micellar formulation had a 40% greater area under the curve than control suspension. The results indicate that topical ocular administration of small compounds using nanomicellar formulations is a feasible alternative. Nanomicelles have also been used by researchers to transport genes to the eye. In a study, Liaw et al [45] attempted to administer topical drops to the cornea in order to deliver genes. Micelles were created using the copolymer poly (ethylene oxide)-

poly (propylene oxide)-poly (ethylene oxide) (PEO-PPO-PEO) as a means of delivering genes. In rabbit and mouse ocular tissues, this polymeric method effectively transported plasmid DNA carrying the LacZ gene. The results were encouraging and suggested a potential use for copolymers in DNA transfer. Additional research was done to deliver two cornea-specific promoters, keratin 12 (K12) and keratocan, using the copolymer. The amount of transgene expression was measured using -Gal activity. In both mouse and rabbit corneas, significant increased levels were measured after six doses of pK12-Lac Z-PM eye drops administered three times per day. Endocytosis and particle size dependent paracellular transport of polymeric micelles were the likely transfection mechanisms [46].

Nanosuspensions

Nanosuspensions are colloidal dispersions of medication particles that are submicron in size and are stabilised by one or more polymers or surfactants. It has shown promise as a method of delivering hydrophobic medications. It offers various benefits for ocular distribution, including sterilisation, ease in formulating eye drops, less discomfort, increased precorneal residence time, and improved ocular bioavailability of medications that are insoluble in tear fluid[68]. Prednisolone, dexamethasone, and hydrocortisone are among the many glucocorticoids that are frequently advised for the treatment of inflammatory diseases affecting the tissues of the anterior portion of the eye. By formulating as nanosuspensions, efforts have been undertaken to increase the ocular bioavailability of glucocorticoids. For instance, Kassem et al. examined the ocular bioavailability of several glucocorticoids from nanosuspensions, solutions, and microcrystalline suspensions (prednisolone, dexamethasone, and hydrocortisone). Ali et al. compared the ocular bioavailability of hydrocortisone (Hc) nanosuspensions made by the precipitation and milling process with that of HC solution in rabbits following topical instillation in another investigation. In comparison to HC solution (15.86 2.7 g/mL), nanosuspensions made using the precipitation and milling methods had considerably higher AUC (0-9 h) values of 28.06 4.08 and 30.95 2.2 g/mL, respectively. For the nanosuspensions, a sustained pharmacological effect that was measured by changes in intraocular pressure was maintained for up to 9 hours, as opposed to 5 hours for the drug solution.



Intraocular pressure changes in rabbits' eyes after receiving nanosuspensions made by milling and precipitation as well as a hydrocortisone solution.

Dendrimers

Dendrimers are classified as star-shaped, nanoscale, highly branching polymeric structures. These branched polymeric systems come in a variety of molecular weights and have functional groups at the terminal ends of amine, hydroxyl, or carboxyl. Targeting moieties may be conjugated using the terminal functional group [91]. Dendrimers are used in medicine delivery as carrier systems. To distribute medications, it is essential to choose the right molecular weight, size, surface charge, molecule shape, and functional group. Dendrimers' highly branching structure enables for the inclusion of a wide variety of medicines, both hydrophilic and hydrophobic. Using these branched polymeric structures for ocular drug delivery, some encouraging results have been reported [4,92,93]. Ocular medication administration frequently makes use of poly (amidoamine) (PAMAM) dendrimers [92] Vandamme et al. showed how PAMAM dendrimers might be used to transport tropicamide and pilocarpine nitrate to the eyes for miotic and mydriatic activities. This study looked at the rabbit eye's mean ocular residence time for fluorescein in saline and PAMAM solutions. Fluorescein was employed as a reference bioadhesive polymer in a 0.2% w/v Carbopol solution. In comparison to saline, the mean ocular residence time was substantially longer with PAMAM solutions and 0.2% w/v Carbopol solution. Therefore, using dendrimers could be an additional alternative for lengthening the time an eye stays open during treatment, improving ocular bioavailability, and producing superior therapeutic results. For instance, PAMAM dendrimers showed increased miotic and mydriatic activity in albino rabbits when co-administered with pilocarpine nitrate and tropicamide [94]. Conjugates of modified PAMAM dendrimers with glucosamine (DG) and glucosamine 6-sulfate (DGS) to perform immunomodulatory and anti-angiogenic actions, respectively, were created to prevent the formation of scar tissue after glaucoma

filtration surgery. In a rabbit model of glaucoma filtration surgery, the subconjunctival administration of these modified conjugates resulted in a considerable reduction of pro-inflammatory and pro-angiogenic responses, which in turn resulted in lessened scar tissue formation. The experiment's findings suggested that the ocular administration of DG and DGS would be efficient and secure in clinical practise in preventing the formation of scar tissue following glaucoma filtration surgery [95].

methods for in-situ gelling

In-situ hydrogels are polymeric solutions that, in response to external stimuli, go through a sol-gel phase transition to create viscoelastic gel. Gelation can be brought on by variations in temperature, pH, and ions, as well as by UV radiation. Research has mostly concentrated on creating thermosensitive gels for ocular administration that react to temperature changes. Poloxamers, multiblock copolymers consisting of polycaprolactone, polyethylene glycol, poly(lactide), poly(glycolide), poly(N-isopropylacrylamide), and chitosan are among the thermogelling polymers that have been described for ocular administration. Due to aggregation or packing, these thermosensitive polymers form temperature-dependent micellar aggregates that gelify with a subsequent temperature increase. These polymers are combined with pharmaceuticals in the solution state for drug delivery, and the resulting solution can be ingested to create an in situ gel depot at physiological temperature. These thermosensitive gels showed encouraging results for improving both anterior and posterior segment ocular bioavailability. Dexamethasone acetate (DXA) can be delivered to the eyes using a thermosensitive gel formed of the triblock polymer PLGA-PEG-PLGA (poly-(DL-lactic acid co-glycolic acid)-polyethylene glycol-poly-(DL-lactic acid co-glycolic acid). The formulation was applied topically to the rabbit eye and was either 0.1% w/v DXA solution or 0.1% w/v DXA in 20% PLGA-PEG-PLGA in situ gel forming solution. Following topical application, the PLGA-PEG-PLGA solution (125.2 g/mL) substantially had a larger Cmax of DXA in the anterior chamber combined with higher AUC values than the eye drop (17.6 2.18 ng/mL). PLGA-PEG-PLGA in situ gel increased Cmax and AUC by around 7.00 and 7.98 fold as compared to solution eye drops. These findings indicate PLGA-PEG-PLGA thermosensitive gel forming solution's potential for improving ocular bioavailability.

Implants

Intraocular implants are created especially to deliver regulated localised drug release over time. These tools aid in avoiding repeated intraocular injections and their accompanying risks. Implants are typically inserted intravitreally for drug delivery to posterior ocular tissues by making an incision through minor surgery at the pars plana, which is situated posterior to the lens and anterior to the retina. Despite the fact that implantation is an invasive procedure, interest in these devices is growing because of the benefits they offer, including prolonged drug release, local drug release to sick ocular tissues at therapeutic levels, fewer side effects, and the capacity to cross the blood-retinal barrier. The delivery of drugs into the eye has been made possible by a number of implanted devices, particularly for the treatment of persistent vitreoretinal disorders. Both biodegradable and non-biodegradable drug-releasing technologies are available for ocular implants. Non-biodegradable implants provide nearly zero order release kinetics, which provides long-lasting release. Non-biodegradable implants are made using polymers like polyvinyl alcohol (PVA), ethylene vinyl acetate (EVA), and polysulfone capillary fibre (PCF). Two examples of commercially available non-biodegradable implants are Vitrasert and Retisert.

The Food and Drug Administration (FDA) has approved Vitrasert, a controlled-release intraocular implant of ganciclovir, for the treatment of CMV retinitis associated with acquired immune deficiency syndrome. It is manufactured by Bausch and Lomb Inc. in Rochester, New York, USA. It consists of a 4.5 mg ganciclovir pill enclosed in PVA/EVA that releases the medication gradually over a lengthy period of 5-8 mo.

The gadget offers reduced cost long-term sustained release without systemic toxicity. The FDA has approved Retisert (Bauschnd Lomb Inc., Rochester, NY, USA) for the treatment of chronic uveitis that affects the eye's posterior portion. It is the first silicone laminated PVA implant to be commercialised. For up to three years, fluocinolone acetonide is released continuously. The implant had successfully reduced uveitis recurrences, regulated inflammation, and enhanced visual acuity. Cataracts and a higher IOP are related side effects. With these non-biodegradable implants, long-term medication release may be possible, although there are some drawbacks. Given that these devices must be surgically implanted and removed after drug depletion, the treatment is costly and suffers from patient non-compliance. Additionally, their applications are restricted by negative side effects such endophthalmitis, pseudoendophthalmitis, vitreous haze and haemorrhage, cataract development, and retinal detachment. Biodegradable implants are a different class of ocular implant. Due to their biocompatibility and sustained drug release qualities, these implants are receiving a lot of attention and are being explored extensively. These implants have a notable benefit over non-biodegradable implants in that they can be removed without surgery due to their biodegradable nature. For the creation of biodegradable implants, polylactic acid (PLA), polyglycolic acid (PGA), polycaprolactones (PCL), and PLGA are most frequently employed polymers.

Conclusion

For many years, ocular scientists have faced a significant barrier in delivering drugs to specific eye tissues. Different carrier systems for ocular delivery were first introduced as a result of specific limitations connected with topical drop administration of pharmacological solutions in standard formulations. Massive efforts are being made in ocular research to create novel medicine delivery methods that are secure and acceptable to patients. Researchers are working very hard right now to enhance the in vivo performance of traditional formulations. On the other hand, ocular scientists are becoming extremely interested in the development of nanotechnology, novel techniques, gadgets, and their applications in medication administration. Drug delivery methods include invasive, non-invasive, and minimally invasive methods. Drug molecules are enclosed in nanosized carrier systems or devices. Numerous carrier systems based on nanotechnology are being created and extensively researched, including nanoparticles, liposomes, nanomicelles, nanosuspensions, and dendrimers. Only a few number of them are produced commercially on a large scale and are used in medicine. Nanotechnology helps patients' bodies by reducing side effects and eyesight loss brought on by medications. Additionally, these nanocarriers and devices prolong drug release, increase targeted specificity, and aid in lowering dose frequency. However, after non-invasive medication administration, it is still necessary to build a carrier system that can reach targeted ocular tissue, including tissues in the back of the eye. With the current pace of ocular research, it is anticipated that a topical drop formulation will be developed that maintains a long precorneal residence time, prevents the tissue accumulation of non-specific drugs, and delivers therapeutic drug levels to the targeted ocular tissue (both anterior and posterior). This drug delivery method may soon take the place of invasive methods like intravitreal and periocular injections for administering medication to the back of the eye.

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