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Review Article

Nano-formulations: Recent Trends for Ocular Bioavailability Enhancement

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Abstract

Eye is a critical part of the body that is readily available and with damage having direct effects on the life of an individual. Delivery of ocular drugs always remain challenging for healthcare professionals and scientists all over the world due to the challenges that dynamic opthalamic environment provides. These challenges involves different barriers like corneal epithelium, corneal stroma, sclera and other bio-membranes (static barriers), choroidal or conjunctival blood flow, lymphatic clearance, tear turnover (dynamic barriers) and efflux pumps/enzymes(metabolic barriers).Ocular diseases include various diseases affecting different parts of the eye. The eye presents comprehensive perspectives and difficulties in the distribution of medicaments, primarily due to the exceptional ability inherent in this mechanism for drugs to enter the main circulatory system and also for eye barrier limitations. Even if conventional non-invasive and invasive treatments like eye drops, injectable preparations and implantable devices are available but these treatments either have bioavailability issues or serious adverse eye effects. Additionally, the new concept of nanoscience and nano-technology gives new a pathway for treating ocular disease. Different active molecules were engineered to communicate with nano-carriers to pass these eye barriers and interact closely with unique specific eye tissues. This study highlights the latest advances in nano-formulations for ophthalmic diagnosis and provides discussions in the mainstream of opthalamic diseases about the role of nano-formulations in nearby future.

Keywords: ocular diseases, nano-technology, static barrier, dynamic barrier, nano-carriers, bioavailability.

Introduction

A large proportion of the populations in the world suffer from eye diseases, while 39 million people are fully blind as per estimation report of World Health Organization (WHO). This number is expected to rise largely over the next 10–20 years[1]. By 2050, about 70 million adults are supposed to be affected by subsequent eye related problems which include degeneration problem and other eye related issues such as cataract and glaucoma in the anterior part. This concern is very significant since the visual pathway processes approximately 80 percent of the input information received externally transmitted to the brain[2]. Based on these figures and data, it can be claimed that as conventional formulations such as eye drops or eye ointments are patient-compliant and non-invasive way of drug administration, but still they are not of great benefit due to poor ocular bioavailability[3] (< 5%). At the other side, administering ocular drugs systemically requires very high dose to show desired therapeutic effects that could lead to possible toxicity[4]. So high need of research and investigation in the field of highly effective ocular drug delivery system remains same. It has focused our mind to some new novel drug delivery systems like nanoparticles, polymeric micelles, hydrogel and so on.

Anatomy of Human Eye and obstacles in the path of ocular drug delivery

Human eye is an organ, about 24 mm in size having globular shape, and consists of anterior and posterior segments, also known as front and back segments respectively[5] (Fig. 1). All sections have specific biological defenses shielding the eye from foreign objects. The anterior part is about 33% of the total eye part and is constitute of the aqueous humor, conjunctiva, cornea, iris, ciliary body and lens, with the remaining part is the posterior part consisting of choroid, neural retina, optic nerve, retinal pigment epithelium, sclera, and vitreous humor[6,7,8]. Numerous diseases encountered according to the section of eye elicited. Specific conditions such as vision loss and complications of diabetes affect the posterior part of the eye. Along these lines, eye treatment is a significant test since it must require the planning of various prescriptions with centered viewpoints to expel numerous hindrances present by the eye, for example, precorneal tissues, and to eliminate the reactions normally found in the items available in the current market.

There are two significant hindrances in ocular drug delivery: blood–fluid and blood–retina obstruction. The blood–fluid hindrance is comprises of the ciliary body's non-pigmented epithelium, which principally contains the iris epithelium, the iris tube endothelium with close intersection, and the endothelium of Schlemm's channel. Tight cell junctions regulate active and paracellular transport[9,10,11]. The blood–retina barrier (BRB) is broken down into internal and external blood-retinal barriers. The previous is constituted of close junctions of retinal vascular endothelium. The last has epithelial monolayer of retinal pigment with close junctions[10,12]. These two components limit molecule's permeation to the intraocular space, resulting in inefficient treatment of intraocular tissues. Additionally, local delivery of medicament to the front eye segment is frequently restricted

by clearance mechanism of cornea and other precorneal factors, for instance, eye squinting, tear film, tear turnover, solution drainage and lacrimation[13]. Human tear film has a fast restore time of only 2–3 min. Thus, most of the drugs given through topical route are washed away in almost no time after instillation. If topically administered drug solution is having greater than 30 µL volume (maximum possible volume that eye can hold in the cul-de-sac), majority of the drugs get lost either by nasolacrimal waste or gravity-induced drainage[14].

Due to all these variables and eye obstructions, the adequacy of the complete medications is under 5%, proposing the helpless eye bioavailability[14,15].

To overcome the barriers faced by different ocular drug delivery drug systems and, concurrently, to improve the potency of the drugs, a few novel approaches were specially designed to evade such issues. Few of these are hydrogels, liposomes, emulsions, dendrimers, implants, nanoparticles, suspensions, nanomicelles and numerous others.

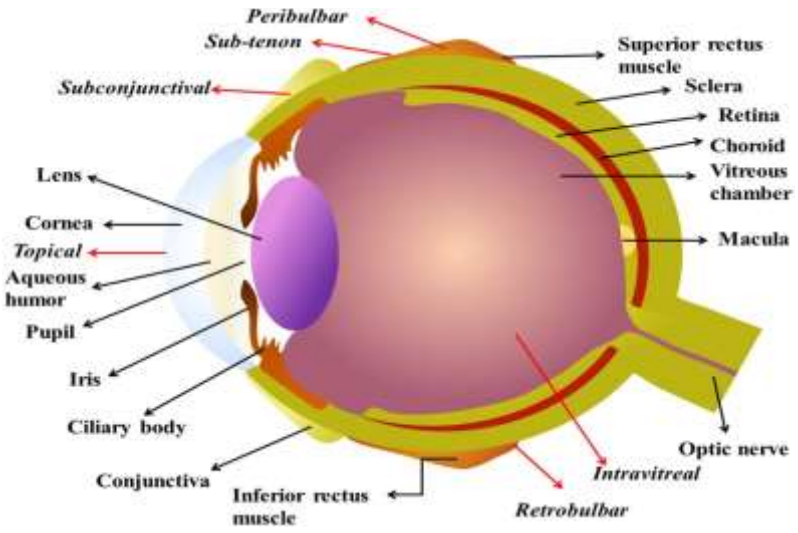

Figure 1: Anatomy of Eye and various routes of administration

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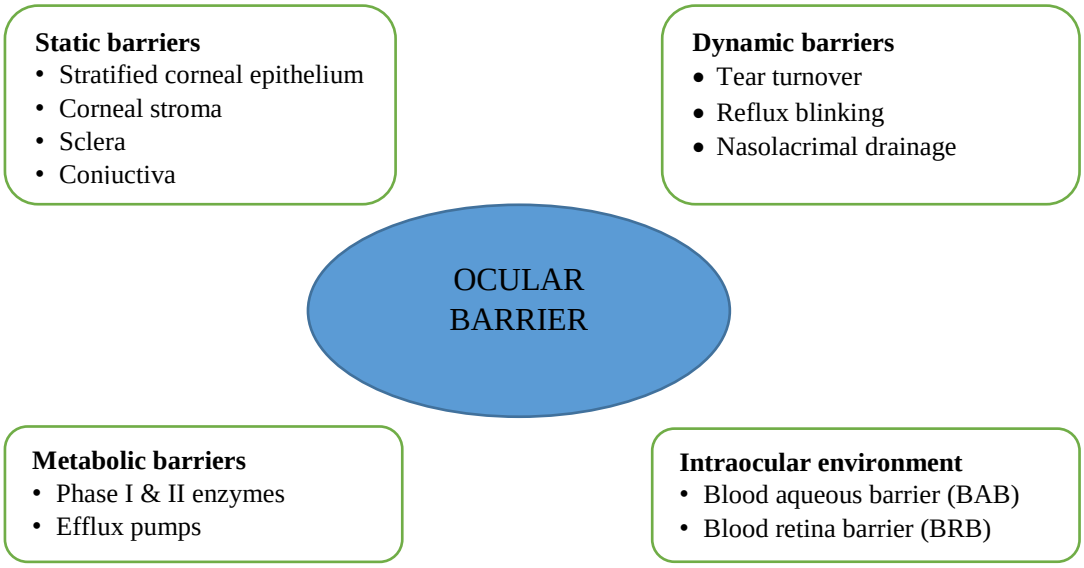

Figure 2: Major obstructions in ocular drug delivery

Various Approaches for Ocular Drug Delivery

Topical Route: Administration of medicament through topical route is the most favoured delivery route to the anterior part of the eye because of its simplicity and is less expensive. However, administration of drug through topical application to the anterior portion is substantially restricted due to corneal surface clearance mechanisms, which include tearing, dilution of drug by tears, and tear turnover[14]. Moreover, topically directed medications are typically absorbed by two ways: i. corneal course i.e. from cornea to intraocular tissues via aqueous humor or through the non-corneal course i.e from conjunctiva through sclera to choroid/RPE)[14], which limits the quantity of drug that is eventually retained in the ocular tissues. Regardless of these clearance mechanisms and eye barriers, under 5 % of the general directed medication enters the aqueous humor[16].

Eye drops

Drop instillation conducted via topical route to target the required amount of drug into the lower precorneal eye portion is a well-known way of administering drug with patient's compliance. Nevertheless, because of refluxing phenomena occurring during eye squinting, only about 20 percent of the given drug dose is remain into the precorneal part of the eye. The passage of medicament via corneal tissues is primarily

influenced by the amount of drug reached in the pre-corneal sites. However, to ensure good medication administration via eye drops, a long residence period in the corneal tissue and and a high corneal permeability coefficient are required[8,17].

Emulsion

Emulsion formulations are found to improve both solubility and bioavailability of the entrapped drugs. The key mechanism for yielding this effective system depends on two emulsion types i.e. oil-in-water (O/W type) and water-in-oil (W/O type). The oil in water type, rather than water in oil type is favoured for medication delivery to ocular tissues. This is just due to the desirable features as decreased irritation in the tissues and improved eye tolerance to this selected oil in water type emulsion[18,19,20]. A few existing examples of emulsion based medicines are RestasisTM, Refresh Endura® and AzaSite®[21,22,23]. A wide range of research studies have been able to highlight the benefits associated with such formulations like more retention time in pre-corneal tissues, the improved corneal permeability, the capacity to control the drug release rate and thus, improved BA of the drug[24,25].

Ointments

Ointments are also there in the class of topically given formulations and serve as carrier for delivering drugs. As the composition of ointments depends upon the ratio of its ingredients, their normal melting points are very much same to ocular temperature (34^0C). But for a given reason, what type of hydrocarbon should we use? This basic detail creates a substantial variability in product's biocompatibility as the product should be accepted by the human system to avoid more natural side responses and also to guarantee the efficacy of the products aimed at improving the availability of medicament and maintaining the drug delivery pattern[26,27,28,29].

Suspensions

Suspensions may be defined as liquid dosage form in which drug/ medicament is dispersed uniformly in the dispersion medium (solvent usually water) with the aid of suspending agent or suspension with saturated character to obtain final solution. This type of dosage form would also be sufficient because it is non- invasive method of application. Pre-corneal tissue takes the solute particles which makes suspension, enhancing the drug's contact time and also increases the time duration for which drug remains in therapeutically active form. The key parameter of such formulations is the particle size that constitutes the formulation since it will directly affects the drug's efficacy[30,31]. It was found in animal model (rabbit), using the TobraDex® formulation, that both drugs i.e. tobramycin and dexamethasone exhibited high concentration values. Overall, greater the size of the particles, longer the remaining time would be, and the slower will be drug dissolution rate. It is expected on the account of this that the particles of appropriate size can achieve excellent drug's activity[32]. A few drugs are available worldwide for the treatment of infectious diseases.

Topical injections

The most common form of drug administration, among the many topical injections, is to inject a drug solution or suspension into the vitreal cavity. The injection is given by using 27-or 30-gauge needle. This administration route is called intravitreal injection. Normally, vitreal cavity can hold liquid of 20–100 µL volume comfortably[33]. These types of injection results in high concentration of drugs locally in vitreal cavity and retina and ultimately act as successful administration route for treating eye diseases mainly posterior segment[34]. Despite this, due to the gel-like structure of the vitreous, the drug distribution pattern is diverse. Distribution pattern of molecules depends significantly on drug's molecular weight and the vitreous pathophysiological state[35,36,37]. Small molecules are stated to be able to spread rapidly in the vitreous cavity, while molecules with high molecular weight (greater than 40kDa) or globular molecules having molecular weight greater than 70kDa show a longer residing time. Also, intravitreal injection is an invasive procedure that must cross all the ocular layers and results in number of adverse effects like cataract, retinal detachment, endophthalmitis, inflammation of iris, uveitis, and intraocular hemorrhage. The occurrence of such complications is increased by repeated injections.

Systemic administration:

Intravenous injections and oral dosage are two approved systemic ways of drug administration to the ocular sites. Since the eye choroid has vascular choroid plexus, medications can quickly penetrate the choroid via blood capillaries. Nonetheless, the outer blood– retinal barrier regulates the drug's entry from the choroid into the retina. Most drugs are inhibited by close junctions of RPE cells and only minute quantity of administered drugs (1%-2%) can reach to retina and vitreous cavity[12,38]. Therefore, the delivery of drugs by systemic administration into the deep interior of the eye always remains a difficult task.

All these topical and systemic drug administration routes have numerous limitations which restricts ocular bioavailability. There are many reasons behind this such as clearance phenomena of the corneal surface, including lacrimation, dilution and tear turnover, low corneal tissues retention time and most drugs hampered by tight junctions of RPE cells and only minute quantity of administered drugs (1%-2%) can reach the retina and vitreous cavity when administered intravenously or given topically. So for ocular disorders, an effective drug delivery method that can overcome these restrictions should be available and that offer complete ocular bioavailability alongwith patient compliance.

Design considerations for nanomaterials for ocular delivery

The size of particles affects drug's effectivity in terms of absorption, circulation, adhesion, degradation, clearance[39-43]. The effect of particles within the body has been reported as:

≥ 2 µm trapped within liver cells;

≥ 300-400 nm captured and excreted by macrophages;

≥ 200 nm absorbed in the spleen;

≥ 100 nm escape from the blood vessels through the endothelial lining.

Thus, the activity of nanoparticles within tissues is controlled by their size. In the eye region, size range nanoparticles 10 to 1000 nm enabled the improved topical movement of large size, poorly soluble molecules through the eye system barriers[44]. Superficial barriers obstruct the access to precise target site by individual and systemic drugs. Drug-loaded nanoparticles show longer retention time for eye drops, increase the drug's ability to penetrate deeper ocular layers and aqueous humor thereby minimizing pre-corneal drug loss resulting due to rapid lachrymal fluid turnover and reduced toxicity[45,46]. Techniques were designed for transformation of nanoparticles from lipophilic to hydrophilic and down-regulation eye irritation. Nanoparticles preparation has been discovered to be effective in the prolonged delivery of ophthalmic drugs[47,48].

Table 1: Criteria for the selection of optimal formulation parameters

Parameter	Preferences
Drug/API	Preferentially lipophilic. (Non-ionizable lipophilic-corneal epithelium Ionizable lipophilic- aqueous humor)
Carrier type	On the basis of drug molecule to be encapsulated (Should have high loading capacity)
Carrier size	small as much as possible for easy uptake and movement
Osmolarity	Isotonic with lachrymal fluid.
pH	Close to physiological pH.

Ideal ocular drug delivery system

An optimal opthalamic drug delivery system should have main characteristics, including:

(1) A programmed and continuous-drug release profile for preserving drug's therapeutic concentration for desired time period to minimize the frequent administration;

(2) Specific site targeting and long residing period in the targeted tissues to enhance therapeutic effectiveness and to minimize side effects;

(3) patient-compliance drug delivery routes which reduces side effects directly resulting from various drug delivery routes.

Currently, nano-carriers found to be the most effective promising tool for meeting the all requirements of an ideal eye delivery system. Nano based formulations have high degree of diffusivity across the bio-membranes like the corneal epithelium because of their very small size. A series of research investigations showed that the nanomaterials given through topical route has improved the drug's permeability to the cornea[49-52]. Similarly, nano-material show improved interaction with the corneal surface's outer mucus membrane due to their high surface-volume ratio, increasing the retention time of the drug. Continuous advancements in the improved nano carrier based delivery systems results in enhancement of the drug delivery to the eye surface along with new pathways for successful delivery of drugs to intraocular tissues using noninvasive methods.

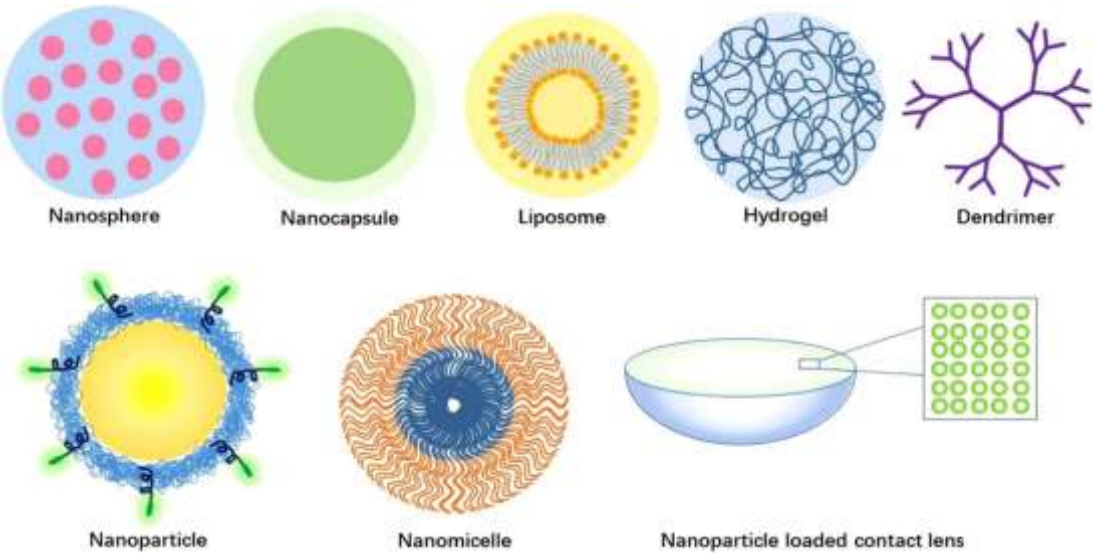

Figure 3: Nano carriers as ocular drug delivery system

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Nano-Enhanced Contact Lens

Usually, the contact lens drug delivery system is formulated by dipping commercial products in a drug solution which allows drug retention in the hydrogel matrix. Afterwards, the drug substance is released on the surface of cornea as the lens is applied in the eye. When applied on the eye surface, they get attach to the wet surface of the eye mainly due to occurring of surface tension phenomena. The aim of using such type of drug delivery system is to extend the time that drug spend on the corneal surface as compared to current usage which ultimately leads to increase the corneal absorption of these drugs. A basic diffusion mechanism controls the drug release from the lens, which usually occurs in the first few hours of drug discharge[53]. Consequently, some studies have centered on using some more elements in the contact lens to regulate the drug release rate. Also, the contact lens with nanomaterial-filled hydrogel was investigated to achieve controlled drug-release rate[54-57]. Phan *et al*. for example integrated the poly (D,L-lactide)-b-dextran nanoparticles into the contact lens materials and investigated that overall drug absorption by the lens and the release time were improved[58]. Nonetheless, still some obstacles faced by nanomaterial-loaded contact lens. The major drawback is that the margin of therapeutic window get increased with this controlled release mechanism which results in the patient noncompliance as they have to wear lens for long time duration. Two different formulations were designed to address these limitations, consisting of a contact

lens filled with drug-loaded nanoparticles and a contact lens printed on a molecular level. The first approach utilizes the micelles or liposomes to absorb the drug and then distribute the systems into the material that makes up the contact lens. One of the other study invented contact lens to deliver the drug lidocaine filled with nanoparticles. Such products designed by dispersing microemulsion drops containing lidocaine or liposomes in poly-2-hydroxyethyl methacrylate (p-HEMA) hydrogels. The findings shown that the drug from such nano-systems was released for 8 days approximately and lenses filled with nanoparticles were suitable for prolonged eye delivery[59].

Dendrimers

Dendrimers have a nano-sized multi-branched network of polymers having star shape structure. Dendrimers are available with many changes about the chain terminals with several functional groups present. These are available in variety of molecular weights and variability. Their combination with selective molecules according to the desired milieu also comes with the ability to wear on complex chemical groups. Poly(amidoamine) (PAMAM) based dendrimers are mostly used for ocular administration. To assure this, a research was conducted by Vandamme and collaborators in which they showed that pilocarpine nitrate and tropicamide as PAMAM dendrimers were effective in opthalamic miotic and mydriatic effects[60]. In addition, to avoid the wound tissue due to surgery for glaucoma filtration, immunomodulation, and angiogenesis blockage, newly prepared compounds showed decrease in developing scar tissue. These novel compounds were derived from PAMAM glucosamine(GA) and glucosamine 6-sulphate (GAS) dendrimers. This conducted study has shown a positive impact on the evasion of damaged tissue formation[60,61].

Microemulsions

These are thermodynamically stable liquid preparations in which water as well as oil are dispersed by a mixture of surfactant and co-surfactant to overcome the interfacial tension. Such structures have high thermodynamic stability, very small droplet size (~100 nm) and looks like simple clear liquid[62]. A selection of water phase, an oil phase, and surfactant/co-surfactant mixture are the critical parameters which can influence the stability of microemulsion. Optimization of these critical parameters results in substantial improvement in drug molecule solubility[63]. Besides solubility, microemulsion systems has also demonstrated increased corneal permeation. An O/W system prepared by using lecithin, PG, PEG 200 as surfactant/co-surfactants, and isopropyl myristate as oil phase and by incorporating pilocarpine drug is found to be non-irritating to the eye[64]. These formulations also provide sustained release of drugs which reduces the dosing frequency of drug. In the case of pilocarpine, this system founds to reduce the drug administration frequency when compared with conventional eye drops. This is due to the reason that the mixture of surfactant-co-surfactant improved permeation. Another M/E system of pilocarpine hydrochloride[65] has been found to results in higher viscosity which increases the residing period of formulation in the cornea resulting in improved drug effectiveness when get converted in different forms like liquid crystalline and coarse emulsion.

Nanoparticles

The nanoparticulated system is useful in preventing repeated administration and continued release, if the incorporated drug has poor solubility or susceptible to degradation. Flurbiprofen-charged PLGA based nanoparticles including Poloxamer 188 showed significantly boost nanoparticles stability[66]. Also, the nanoparticles based formulation showed no any type of discomfort and toxic effects when tested in rabbit's eye following topical instillation. Several scholars have also studied that permeation of drugs through cornea get enhanced when we use nanoparticles based formulations[66-68]. A nanoparticle have the capability to transform and retain drugs in unionized form in the pre-cornea and conjunctiva and increases the drug passage rate through various ocular membranes and deep into intraocular tissues.

In addition, particles coated with inorganic material such as medications filled with gold nanoparticles have also demonstrated an improved pharmacological effect in treating corneal epithelial wounds[69]. Nanoparticles are preferred to be layered with mucoadhesive agents such as PEG, chitosan-hyaluronic acid, or occasionally thermosensitive gels to overcome the complex barrier, i.e. precorneal elimination. Poly (dl-lactic-co-glycolic) acid (PLGA), non-mucoadhesive anionic biocompatible polymer is also used in nanoparticles based ocular formulations as its small particle size provides high degree of retention in the ocular region[70]. PLGA based nanoparticles/nanospheres demonstrated improved residence time in the cornea, increased permeation alongwith improved drug's encapsulating efficiency. Lipophilic and hydrophilic drugs found to be capable of being loaded onto nanoparticles using various emulsion techniques. In addition, nanoparticles were integrated in thermosensitive gels such as PLGA-PEG-PLGA, efforts were made to remove the disadvantage of sudden burst release in nanoparticles' drug release pattern[71]. Indomethacin NPs made from chitosan-coated poly (epsilon-caprolactone) resulted in improved eye bioavailability. Increased permeation through the corneal surface was also investigated, when nanoparticles made up of poly (epsilon-caprolactone) were coated with PEG[72].

Polymeric micelles

These are core–shell shaped nanoparticles formed with the self-assembled amphiphilic copolymers. Polymeric micelles were extensively studied in the field of drug delivery since they present number of benefits. They can be manufactured in aqueous media by simple self-assembly, usually by using the techniques such as nanoprecipitation, emulsion, or dialysis. The shell structure of polymeric micelles allow encapsulation of lipophilic drug molecules in its core. Since the inner lipophilic core is protected by the water soluble layer, the blood circulation considerably prolongs the stability and the drug's biological half-life. In addition, biodegradable and biocompatible polymers are chosen for micellar carriers formulation that prevent occurrence of any toxic effects by the carriers in the body system. Because of these benefits, polymeric micelles are considered by the researchers in the drug delivery sector over last few years including ocular drug delivery system[73-75].

Many researchers have used drug carriers with polylactide (PLA) or poly(lactide-co-glycolide) (PLGA) to improve the drug delivery rate. PLGA copolymers form microparticles or nanoparticles by simple self-assembly process in an aqueous medium and can be employed for drug entrapment. The problem with these PLGA based carriers is their susceptibility towards hydrolytic degradation when comes in contact with water, which eventually reduces the carrier-drug complex quality. Most scientists have tried to investigate hydrophilic chain copolymers like polyethylene glycol (PEG) or polyethylene oxide (PEO), to improve nanoparticles life by protecting the susceptible cores from degradation when comes in contact with aqueous medium. In one test, as regards the capacity to permeate and distribute drugs through the eye membrane, the effect of PEG as well as chitosan surface modified polymeric micelles was studied and analyzed. In various studies, PEG-based polymeric micelles were found to

be safe in both intracorneal and through intravitreal injections and are effective in enhancing bioavailability of the drug supplied[72].

Hydrogels

These are water-soluble network of polymers capable of absorbing more than 20 percent of their water weight and have three dimensional structures. Despite their special properties, hydrogels are studied on large scale in healthcare field. The physical and chemical properties of hydrogels can be changed easily by selecting the right polymers as hydrogels can be made from any type of hydrophilic polymer. Hydrogels are found to be effective for regulated and sustained drug delivery mechanism because their matrix structure can be modified to regulate the drug diffusion through the matrix by adjusting the cross-linking or using any external stimuli like pH or temperature. Because of having desirable properties, chitosan containing nanomaterials have been studied for various medicinal applications[76]. Chitosan's mucoadhesive properties are very significant in the administering ocular drug through topical route, as this prolongs retention time within mucin layer and thus enhances duration of drug action. *In vitro* drug-release study proved that the nanoparticles have prolonged drug release mechanism, and the drug release rate depends on the concentration of chitosan polymer in the hydrogel matrix. More recent research has focused on the in vivo effect on drug bioavailability and activity in the eye using in situ gelation features of hydrogel material. Pluronic F127 found to be very effective in producing hydrogel network systems. Because of its sensitive temperature, Pluronic F127 has been studied as an *in situ* gelling agent for ocular delivery by various groups[77,78]. Its transition temperature of sol-gel was less than normal body temperature. This property of Pluronic F127 was used to prepare a liquid solution in which drugs are incorporated at low temperatures. After administration, the solution undergoes sol-gel transition and a matrix get formed out of which the drug get released by diffusion mechanism.

Liposomes

In order to achieve targeted drug delivery, liposomes functions very much same to the nano-particles. Liposomes are constituted of one or more dense spherical sac which consists of a bilayer of lipids divided by phospholipid enclosing aqueous compartments. These can confined both hydrophilic and lipophilic drugs, this ability helps liposomes to act as an effective opthalamic drug delivery device as it helps to protect the drug moiety from any enzymatic degradation in the eye and in the lachrymal fluid. The amphiphilic existence of corneal membranes can act as an obstruction for the activity of the drug. This should provide a compromise between its lipophilic and hydrophilicity for a dosage form to cross the cornea. Strong biocompatibility and amphiphatic nature of liposomal formulation can address this problem. Liposomes can adhere to the corneal surface and are advantageous for large molecular weight, poorly soluble and poorly absorbed drugs[79]. Ganciclovir in its liposomal formulation showed 10 folds of higher drug concentrations in the ocular tissues as compared to simple solution[80]. Modification of liposomal surface charge by incorporation of positively charged lipids or addition of mucoadhesive agent can confer improved precorneal residence time. The addition of Didodecyl dimethylammonium bromide, stearylamine, and N-[1-(2, 3-dioleoyloxy) propyl]-N, N, N-trimethylammonium can provide positive charge to liposomes[80-82]. Addition of these cationic lipids have found to decrease elimination rate of drug through lachrymal flow as the viscosity get increased and being positively charged get associated to cornea as it has mucin coating which is negatively charged.

Advantages of Nanotechnology based ocular drug delivery

Few years back, it was thought that nano-formulations would not meet with clinical reality, but soon this turns out to be misconception, as the FDA approved nano-formulations against numerous human diseases for clinical purpose. For example, in 2002, FDA approved the Restasis®,a anionic nano-emulsion with zero preservatives for the delivering 0.05% Cyclosporin. This formulation was first ocular nano-based formulation prepared in early 2000. This nano-emulsion is used in dry eye condition. As eye is one of the most sensitive organ of human body and ability of eye to protect itself with number of layers, it becomes very difficult for drugs to cross all these barriers so that drug can reach to the target site which ultimately lead to drug loss and hence low bioavailability. Nano-formulations prove to overcome all these limitations. Nano-formulations will mitigate the loss of drugs caused by quick turnover of tear fluids. The size of nanoparticles carrying the active drug moiety can also be changed as per the need (which obstructs the required drug passage to move through ocular system). In addition, nano-formulations often pose less of toxicity hazard, which is one of the best benefits in ocular treatment.

Conclusion

The recent nano-formulation technologies and developments result in major advances in the ocular treatment. This nanotechnology is certainly an emerging technology, and it helps to overcome all the constraints encountered by other modes of drug delivery. Because of its flexibility, the formulation can be modified to administer the medication via different routes like oral, parenteral, and other mucosal routes and is approved for human use by the regulatory agencies. With the advent of nanotechnology, the ocular drug delivery field has made significant strides forward. A number of research have looked into using several forms of nanomaterials as hydrogels, dendrimers, liposomes, polymeric micelles, niosomes as drug carriers to increase the bioavailability of ocular drugs. Administration of nanomaterials related drugs showed extended drug release which ultimately increases the duration of action, thus reducing the frequent administration when given topically.

Increasing number of animal based studies and human studies and increasing literature for utilising nano-formulations in ocular therapy suggest that the nano formulations and nano-delivery settings centered on nanotechnology may result in modification in eye disorder management.

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