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Review Article

Visionary Nanomedicine: Transforming Ocular Therapy with Nanotechnology-Based Drug Delivery Systems

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ABSTRACT

In the realm of human anatomy, the eye is a critical organ distinguished by its intricate structure. The anterior segment and the posterior segment make up its two primary segments. Due to simplicity and convenience, the ocular route is one of the most used for administering medications to the eyes. It is challenging to effectively transport the medications to the eye due to a number of structural and physiological limitations attributed to the fact that a significant portion of the drug is rapidly eliminated with tear release; the bioavailability of topically applied ocular medicines is often less than 5%. For eye disorders, conventional drug delivery methods have a lower bioavailability and greater adverse effects, which makes the development of new, effective drug delivery methods necessary. Due to their flexibility, nanomaterials have been popular during the past few years as a solution to these problems. Various nanomaterials have been investigated over the past few years that are capable of breaking through a number of barriers in the anterior and posterior segments. As an alternative to conventional drug delivery systems, a number of nanotechnology-based ocular drug delivery systems, including nanoemulsion, nanosuspension, nanoparticles, niosomes, dendrimers, nanowafers, cubosomes, and liposomes, have been investigated. This in-depth review offers information on numerous eye illness, nanotechnology-based drug delivery systems, as well as a number of patents, current challenges and potential future applications. Additionally, various polymers used for the fabrication of ocular drug delivery systems have also been discussed.

INTRODUCTION

The eye is an important organ as our vision totally depends on it. Ocular diseases are a major public

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health challenge as it potentially impacts the quality of life and leads to vision impairment, if not properly treated causing blindness. As per the WHO Report 2019, approximately 2.2 billion people have visual impairment; this number can be reduced if treated properly. According to a survey conducted in 39 nations, 285 million people are visually impaired. Among them, 65% are older than 50, and 82% of the blind patients are older than 50 [1]. The complexity of the eye's anatomical structure and physiological barriers makes the treatment of various ocular disorders difficult. The delivery of therapeutic products into the anterior segment of the eye is difficult, due to a number of obstacles such as anatomy and physiology. In short, the anatomical barriers are divided into two types: static and dynamic. There are two types of static barriers: corneal epithelial and blood stromal barrier; whereas dynamic barriers consist of tears drainage, conjunctival blood and lymphoid flow. On the other hand, physiological barriers include blinking activities, tear film turnover and nasolacrimal drainage [2]. More than 70% of cases of blindness are due to anterior segment eye diseases (ASED), which include uncorrected refractive errors, cataracts, glaucoma, corneal opacity, and trachoma. ASED are among the seven most common conditions that impair vision [3]. Topical or periocular administration is used to treat anterior segment diseases such as blepharitis, conjunctivitis, scleritis, keratitis and dry eye syndrome. Delivering drugs to both the posterior and anterior segments of the eye, whether for conditions like glaucoma, endophthalmitis, or uveitis, presents a common challenge: achieving adequate bioavailability due to barriers in drug delivery. Nonetheless, despite the risk for complications, i.e. administration of an lntraocular solution could be preferred [4]. With the advancement in the field of nanoscience, a range of nanomaterials have been developed for ocular drug delivery systems. These nanomaterials possess promising characteristics and novel properties which makes them apt for the formulation of ocular drug delivery systems. Biopharmaceuticals are being exploited more and more by new nanotechnology and nanoscience techniques. Nanoscience is an interdisciplinary field that combines material science, physics, chemistry, and biology, whereas nanotechnology involves the design and fabrication of different materials in nanometer scale at least in one dimension [1]. Many innovative drug delivery systems have been designed with a view to improving bioavailability of the eye. These devices may also be able to penetrate the ocular barrier. Examples include mic, nanospheres, liposomes, dendrimers, water-soluble gels, nanometer emulsions and fluid suspensions,in situ gel etc [5].This comprehensive scientific review provides an extensive analysis of various ocular diseases, nanotechnology-driven drug delivery methodologies, and an array of associated patents, existing hurdles, and prospective future applications. Furthermore, the review delves into the examination of different polymers utilized in the development of ocular drug delivery systems.

1. Anatomy Of Eye:

The eye, from an anatomical point of view, can broadly be regarded as a series of overlapping layers of tissue. Eye's external structures consist of eyelashes, eyelids, muscles, attachment glands and conjunctiva. Three layers of tissue are laid out in concentric circles within the internal structure of the eye: The outer layers are made up of the sclera and cornea. The uvea is composed of a vascular layers in the middle, separated by irises,ciliary bones and choroids. The inner layer is the retina, which consists of nerve tissue. When scrutinizing an individual's ocular structures, one can readily discern several prominent components. Firstly, there is the visually conspicuous, darkened aperture known as the pupil. The pupil serves the vital function of

facilitating the entry of light into the eye, its apparent darkness stemming from the absorption properties of retinal pigments. Adjacent to this pivotal element is the iris, a circular muscular structure adorned with intricate pigmentation patterns, thereby defining an individual's eye color. Notably, the central opening within the iris corresponds to the pupil and plays a pivotal role in modulating the amount of incoming light, adapting to prevailing environmental conditions. The captivating diversity of eye colors, more accurately referred to as iris colors, emerges from the varying levels of eumelanin (responsible for brown and black pigments) and pheomelanin (responsible for red and yellow pigments) synthesized by melanocytes. [6-8].

2. Ocular Barriers:

In the light of this, a brief review is given of the introduction into the Ophthalmological literature of the concept of blood ocular barriers. Two fundamental blood-ocular barriers are posited: the blood-aqueous barrier and the blood-retinal barrier.

2.1.Blood Aqueous Barrier:

Blood-aqueous barriers are made up of the non-porous epithelium on the ciliary side of the body, the epithelium behind the iris (the posterior iris), the leaky endothelium on the iris (iris vessels with leaky junctions), and the schlemm's canal endothelium [9].

2.2.Blood Retinal Barrier:

Basically, the BRB is super tight and constricted, and it's a physical barrier that controls how ions, proteins, and water get in and out of your retina. It's made up of both the inner and outer BRB, with the inner one made up of tiny junctions between the cells that make up your retina, called retinal capillaries, and the outer one being made up of tiny connections between the cells made up of your retina's pigment epithelium. It's really important for keeping your eye like a special place, and it's also really important for your vision [10,11].

3. Ocular Disorders

3.1.Glaucoma:

The term "glaucoma" originates from the Greek word for "green" or "light gray". This group of disorders is characterized by their distinct pathophysiological and risk factors, as well as their various manifestations, treatment options, and prognosis. All of these disorders share one common characteristic: progressive degeneration in the optic nerve. This degeneration is characterized by the loss of visual neurons, the thinning of retinal nerve fibers, and the progressive erasure of the optic discs [12]. Glaucoma is a progressive disease of the optic neuropathies, in which retinal ganglionic cells are degenerated and the optic nerve head undergoes alterations. The loss of ganglionic cells is associated with an increase in intraocular pressure, although other factors may also contribute to the disease. The only effective treatment for glaucoma is to reduce intraocular pressure. Treatment is typically initiated with ocular hypoporosis drops, but other methods may be used to slow the progression of the disease, such as laser therapy and surgery [13].

3.2.Dry eye disease (DED):

Dry Eye Disease is a multifaceted condition of the tear system and the eye's surface that is characterized by symptoms of pain, visual disturbances, and instability of the tear system, with the potential for damage to the eye's surface. Additionally, it is characterized by an increase in the amount of osmolality in the tear system, as well as a decrease in ocular surface inflammation [14].Tear dysfunction happens when the LFU (Lacrimal Functional Unit) made up of the tear secreting glands (lacrimal gedgets, conjunctive goblet cockets, meibomian gedgets) and their nervous and immunological systems, is no longer capable of maintaining a stable preneuronal tear

layer [15]. There are a number of risk factors associated with dry eye disease, especially in the elderly, women who have gone through the menopause and those who suffer from autoimmune diseases. According to the NEI classification, dry eye disease is divided into two categories: aqueous-depleting and evaporative. Other risk factors associated with DED include: High altitude, Pterygium, Smoking, and Excessive consumption of multi-vitamins and caffeine [16].

3.3.Keratitis:

Keratitis consists of inflammation in the cornea, which is characterised by corneal edema, inflammatory cell infiltration and ciliary congestion. This is accompanied by infectious and noninfectious diseases that may be systemic or localised to the ocular surface. The majority of keratitis is caused by "microbial keratitis", which has been the primary cause of concern in developing countries [17].

3.3.1. Infectious Keratitis:

Infectious Keratitis is a type of corneal infection that is also referred to as Infectious Cornea Ulcer or Infectious Cornea Opacity. It can be divided into microbial and viral categories. Microbial keratitis refers to infections caused by bacteria, fungi, or parasites. Viral keratitis, on the other hand, is caused by herpes viruses [18].

3.3.2. Non infectious Keratitis:

Trichiasis, giant papillae, and a foreign body in the sulcus subtarsalis are examples of local causes ulcerative keratitis of the periphery, rheumatoid arthritis, granulomatosis with polyangiitis, polyarteritis nodosa, relapsing polychondritis, systemic lupus erythematosus, and others are collagen vascular diseases. Trigeminal nerve damage as a result of surgery or a tumor may cause neurotrophic corneal ulcers (post-herpetic zoster ophthalmicus).

3.4.Conjunctvitis:

Inflammation and swelling of the conjunctival tissue, engorgement of the blood vessels, ocular discharge, and pain are all symptoms of conjunctivitis. Conjunctivitis affects a large number of people globally and is one of the most common causes of office visits to general medical and ophthalmology clinics. Acute conjunctivitis is reported to be diagnosed by non-ophthalmologists such as internists, family practitioners, pediatricians, and nurse practitioners in more than 80% of cases [19]. Infectious and noninfectious causes of conjunctivitis can be distinguished. Bacteria and viruses are the most typical infectious causes. Noninfectious conjunctivitis includes inflammation brought on by immune-mediated illnesses and neoplastic processes, as well as allergic, toxic, and cicatricial conjunctivitis [20].

3.5.Cataract:

A cataract is an eye condition where the normally clear lens has become opaque, obstructing the passage of light. It is a slowly progressing illness that accounts for a sizable portion of global blindness. Infants, adults, and seniors can all develop this blinding disease, but older people are disproportionately affected. The severity can vary and it can be bilateral. If the cataract has advanced to the point where it is interfering with daily activities, surgery may be recommended, which is very effective. Treatment options include correction with refractive glasses only at earlier stages [21]. Finding the risk factors that cause cataract development could lead to the development of preventative measures. Only a small number of risk factors meet the requirements for a causal relationship, including smoking, which increases the risk of nuclear cataract, excessive UV-B exposure and diabetes, which raises the risk of cortical cataract, and steroidal therapy, diabetes, and ionizing radiation, which causes posterior subcapsular opacity [22].

4. Nanotechnology-Based Ocular Drug Delivery Systems

4.1.Nanoparticles:

Nanoparticles (NPs) are a diverse class of materials that include substances that are particulate and have at least one dimension that is less than 100 nm. These materials can be 0D, 1D, 2D, or 3D depending on the overall shape. Based on their characteristics, shapes, or sizes, they can be divided into various classes. Fullerenes, metal NPs, ceramic NPs, and polymeric NPs are some of the various groups. Nanoparticles (NPs) exhibit unique physical and chemical properties owing to their tiny size and extensive surface area. In contrast to conventional eye drops, nanoparticles (NPs) have been developed to overcome obstacles, boost drug penetration at the target region, and prolong drug levels by a few internals of medication administrations in lower doses.Through intravitreal injection and surface applications, NPs could target the cornea, retina, and choroid. The ocular system's obstacles were more easily overcome by the use of nanoparticles (NPs) with sizes ranging from 10 nm to 1000 nm [23]. Direct administration via either of these two routes has a number of issues with drug bioavailability, such as adverse effects and the need for numerous unpleasant treatments to reach therapeutic drug levels. Improved topical transit of big, inefficiently water-soluble compounds, like glucocorticoids or cyclosporine for immune-related, vision-threatening disorders, is one benefit of utilizing nanoparticles in this context [24]. The two main types of NPs used for drug delivery are organic and inorganic NPs. Polymer NPs, nanomicells, liposomes, quantum dots, nanoemulsions, and hybridized NPs are examples of organic NPs, while silica NPs, gold NPs, and carbon nanotubes are examples of inorganic NPsAdditionally, optical coherence tomography (OCT) can use NPs' strong stability and high light-scattering ability to enhance the early detection and diagnosis of eye diseases [25].

4.2.Niosomes:

Niosomes are amphiphilic, nonionic, bilayered, biodegradable, and non-immunogenic vesicles that are nanoscale in size [26].Drugs that are both hydrophilic and lipophilic can be contained by niosomes, which are bilayered, non-ionic surfactant vesicles. Chemically, niosomes are stable, and because they are non-ionic, their toxicity is low. They are chosen for ocular use over other vesicular formulations because of their many benefits [27]. Because of their high stability and permeability, hydrophobic and hydrophilic drugs have been delivered using liposomes, spherical vesicles made from biocompatible lipids that resemble cell membranes [25].

4.3.Nanowafers:

A tiny, transparent disc called a nanowafer can be applied to the surface of the eye with the tip of a finger and can withstand repeated blinking without moving. It has a variety of drug-filled nanoreservoir arrays from which the drug will be released under strict control for a few hours to days. Due to the nanowafer's slow drug release, the drug spends more time on the ocular surface before being absorbed into the surrounding ocular tissue. The nanowafer will dissolve and disappear at the conclusion of the predetermined time for drug release [28]. Dexamethasone-loaded nanowafers (Dex-NW) were created to increase convenience and effectiveness for dry eye patients. The Dex-NW nanowafers, which feature 500 nm square reservoirs filled with dexamethasone, were made using carboxymethyl cellulose [26].

4.4.Nanosuspension:

Nanosuspensions are colloidal dispersions of drug particles that are nanoscale in size and are stabilized by surfactants. Poorly water-soluble drugs without any matrix material are suspended in dispersion as nanosuspensions [29].

Recently, a high pressure homogenization process has made it possible to mill drug micro-particle suspensions. The increase in saturation solubility and subsequent increase in the compound's rate of dissolution are two outstanding characteristics of the nanosuspension [30]. By keeping the active pharmaceutical ingredients (API) in a crystalline state and enabling them with increased drug loading during formulation development, nanosuspensions can resolve such specific drug delivery problems related to them. Due to the reduced use of harmful non-aqueous solvents and extreme pH, accommodating large drug amounts with minimal dose volume has additional benefits in parenteral and ophthalmic drug delivery systems. Additional benefits include improved stability, prolonged drug release, increased effectiveness via tissue targeting, reduced first pass metabolism, and deep lung deposition [31].

4.5. Nanoemulsion:

Nanoemulsions are transparent, kinetically stable formulations with inner-phase droplets that are typically between 20 and 200 nm in size (some authors raise this upper limit to 500 nm). Ophthalmic o/w nanoemulsions are made up of two immiscible phases of the nanoemulsion—an immiscible phase of oil and an immiscible phase of water—as well as a carefully chosen mixture of surfactants and cosurfactants that allows for the reduction of surface tension at the interphase [32]. Due to their ability to reduce interfacial tension and produce small particle sizes as a result of their role in the formation of stable preparations as a result of the repellent electrostatic interaction and steric hindrance, the surfactant and cosurfactant molecules play an effective role in the formation of nanoemulsions [33]. Due to their capacity to increase drug bioavailability, NEs are extensively researched as a cost-effective formulation and non-invasive method. Ophthalmic NEs also have the following benefits: Compared to gels or ointments, the drug has (i) a longer pre-corneal retention time, (ii) high penetration ability, (iii) improved ocular bioavailability, (iv) improved drop drainage through the cornea, and reproducible amounts in the eye,(v) ocular formulations are retained in the conjunctival sac for a longer period of time due to the interface of lipid present in NEs to the lipid layer of tear film, (vi) By electrostatically interacting with the anionic surface of the corneal mucin when using cationic NEs, it is possible to extend the drug's residence time and, as a result, increase the bioavailability of the drug in the eye. The interaction of the mucin's surface with the cationic NEs lengthens their time in the pre-corneal site [34].

4.6. Nanomicelles:

Nanomicelles are self-assembling colloidal dispersions with a hydrophobic core and a hydrophilic shell, typically with particle sizes between 10 and 100 nm. Nanomicelles exhibit some distinctive or novel characteristics due to their size, solubility, customized surface, or exposure to the environment. This multifunctionality makes nanomicelles essential for use in biomedical applications as well as numerous other fields. The process of targeted drug delivery uses nanomicelles, allowing for deeper tissue penetration and greater drug bioavailability [35]. Reverse micelles are amphiphilic copolymer self-assemblies in a non-aqueous medium, whereas regular micelles are amphiphilic copolymer self-assemblies in an aqueous medium. Block copolymers, such as core (laur)-polyethylene glycol (core [laur]PEG), are used to create monomolecular micelles. One molecule of these polymers contains a number of hydrophilic and hydrophobic regions, allowing it to self-assemble into a micelle [36]. In contrast to reverse nanomicelles, which are used to encapsulate and deliver hydrophilic drugs, positive micelles are used to encapsulate,

solubilize, and deliver hydrophobic drugs. Nanomicelles are thought to be safe substitutes for intraocular drug delivery because of their distinctive chemical structure, which can solubilize drugs internally, reduce side effects, improve drug stability, and have a sustained release effect [37].

4.7.Dendrimers:

Dendrimers are nanostructured polymers with a "tree-like" structure that have potential for ocular drug delivery. Due to their range of nanosizes, capacity to display multiple surface groups that allow for targeting, ease of preparation, and functionalization, they are desirable systems for drug delivery. Ongoing research into creating better ocular dendrimeric systems may not only improve drug delivery to the ocular surface but may also enable noninvasive delivery of therapeutic agents to intraocular tissues like the retina or choroid [38]. Dendrimers are promising new scaffolds for drug delivery because of their special qualities, which include their high degree of branching, multivalency, globular architecture, and well-defined molecular weight. The design and synthesis of biocompatible dendrimers, as well as their use in the development of vaccines, antimicrobials, and antivirals, as well as drug delivery, have all been the subject of increased research over the past ten years [39]. Both divergent and convergent methods can be used to prepare dendrimers. These two construction ideas are fundamentally different from one another. Dendrimer expands from a multipurpose core molecule using the divergent techniques. The core molecule interacts with monomer molecules that have one reactive group and two dormant groups to produce the first generation dendrimer. The divergent synthesis's flaws led to the development of the convergent methods. The dendrimer is built in stages using the convergent approach, working inwardly from the end groups. When the expanding dendrons, or branched polymeric arms, reach a sufficient size, they are joined to the multipurpose core molecule [40].

4.8. Cubosomes:

Cubosomes are special structures made of self-assembled amphiphilic lipid molecules dispersed in aqueous media as a liquid crystalline phase with cubic crystallographic symmetry. Due to the presence of two continuous water channels separated by a twisted lipid bilayer, they are distinguished by having a large surface area. They range in size from 100 to 500 nm and have a structure resembling honeycomb (cavernous) structures [41]. Cubosomes are reversibly polarized bicontinuous cubic phases with distinctive physicochemical properties. Because they can deliver a wide variety of hydrophobic, hydrophilic, and amphiphilic medications with improved bioavailability and loading potential, these special systems are a study area of interest. They are frequently used in chemotherapy, oral, transdermal, ocular, and other drug delivery methods [42].

4.8.1. Types of Cubosomes:

Depending on the formulation technique, cubosome precursors can be divided into liquid and powdered forms. By combining monoolein with a hydrotropic solvent, such as ethanol, cubosomes can form on their own. Particles can form through the nucleation process and grow through the crystallization and precipitation processes. Powdered cubosomes can also be created using dehydrated surface-active agents combined with a suitable polymer, in addition to the liquid cubosome precursors. Powdered cubosomes can be created by spray-drying after liquid droplet particles have been encapsulated in emulsion and dispersion [43].Figure 1 show different Nano based systems for Ocular drug Delivery System.

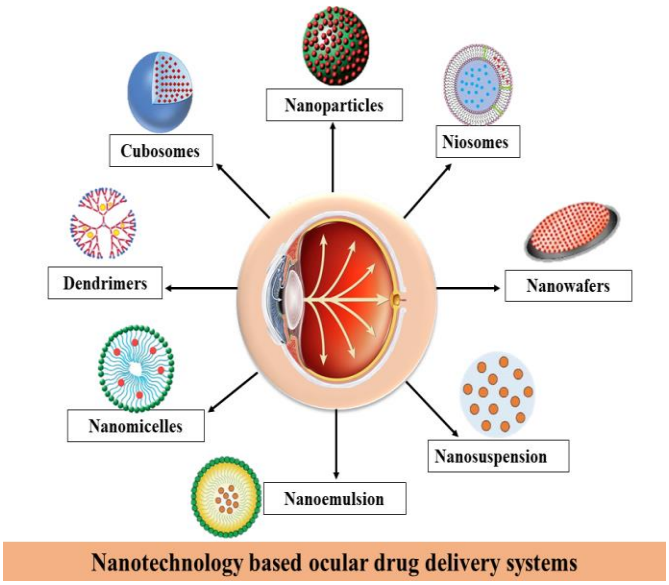

Figure: 1 Different Nano based systems for Ocular drug Delivery System

Table 1 summarizes various nanotechnology based ocular drug delivery systems. Figure 1 illustrates the various types of nanotechnology-based formulations available for ocular drug delivery.

Table 1: Nanotechnology based ocular drug delivery systems [44-83]

Formulation	Drug	Excipients	Formulation method	Targeted disease	Reference
Nanoparticles	Bimatoprost	Glyceryl monostearate, poloxamer 407	Solvent evaporation/ultrasonication	Glaucoma	Satyanarayana SD *et al* 2023
	Loteprednol	Xyline, hematoxylin	Hot emulsification and ultrasonication	Inflammation and allergy	Uner B *et al* 2023
	Difluprednate	Tween 80, poly lactic co glycolic acid	Encapsulation	Uveitis	Kaviarasi B *et al* 2023
	Ciprofloxacin	Chitosan, sodium tripolyphosphate	Ionic gelation	Ocular infections	Jalal RR *et al* 2023
	Dexamethasone	Tween 20, dimethyl sulfoxide	Nanoprecipitation	Dry eye syndrome	Kantaria T *et al* 2023
Liposomes	Timolol & brimonidine	HPMC	Thin layer hydration	Glaucoma	Bigdeli A *et al* 2023
	Acetazolamide	Span 60, span 40	Reverse phase evaporation and thin film hydration	Glaucoma	Guinedi AS *et al* 2005
	Tacrolimus	Sodium dodecyl sulfate, phosphate buffer	Thin layer hydration	Dry eye disease	Chen X *et al* 2022

	Tropicamide	Phospholipon 90, stearylamine	Conventional lipid dispersion method	Mydriasis	Nagarsenker MS *et al* 1999
	Distamycin A	Phosphatidyl choline and cholesterol	Reverse phase evaporation method	Ocular HSV infections	Chetoni P *et al* 2015
Nanosuspensions	Itraconazole	Poloxamer-188	Nanoprecipitation	Ocular infections	Ahuja M *et al* 2015
	Moxifloxacin	PLGA	Solvent evaporation	Ocular infections	Mudgil M *et al* 2013
	Voriconazole	Eudragit RS 100, Pharmasolve	Quassi-emulsion solvent diffusion	Fungal keratitis	Qin T *et al* 2021
	Travoprost	Tween 80, isopropyl alcohol	Aqueous titration (emulsification)	Glaucoma	Xu B *et al* 2020
	Acyclovir	Eudragit RS 100	Quassi-emulsion solvent diffusion	Ocular infections	Dandagi P *et al* 2009
Nanoemulsions	Celecoxib	Gellan gum	Ionotropic gelation	Glaucoma	Salimi A 2017
	Dorzolamide	Tween 80, isopropyl myristate	Water titration	Glaucoma	Ammar HO *et al* 2009
	Cyclosporin A	Chitosan, oleic acid, tween 20	Aqueous titration (emulsification)	Dry eye disease	Akhter S *et al* 2016
	Tacrolimus	Gellan gum, aluminium chloride	Ionotropic gelation	Dry eye disease	Modi D *et al* 2021
	Triamcinolone acetonide	Tween 20, gellan gum	Homogenization and ultrasonification	Ocular inflammation	Tatke A *et al* 2018
Micelles	Cyclosporine	PEG, Nile red	Self-assembling	Dry eye syndrome and uveitis	Ghezzi M *et al* 2022
	Dexamethasone	PCL-PEG-PCL	Film hydration method	Uveitis	Alami-Milani M *et al* 2018
	Resveratrol	PBS	Film dispersion method	Ocular diseases	Li M *et al* 2020
	Ciprofloxacin	Pluronic F127	Solvent evaporation	Ocular infections	Taha EI *et al* 2014
	Diclofenac	mPEG-PCL	Simple solvent diffusion	Ocular inflammations	Li X *et al* 2012
Niosomes	Prednisolone	Span 60	Thin film hydration and ether injection	Ocular infections	Gaafar PM *et al* 2014
	Azithromycin	Tween 60, span 60	Thin film hydration	Bacterial conjunctivitis	Eid HM *et al* 2021
	Brimonidine tartarate	Span 60, Tween 80	Coacervation phase separation method	Glaucoma	Emad Eldeeb A *et al* 2019

	Doxycycline hyclate	Span 20, Tween 60	Thin film hydration and reverse phase evaporation method	Ocular infections	Gugleva V *et al* 2019
	Tacrolimus	Hyaluronic acid	Solvent evaporation	Ocular surgery	Zeng W *et al* 2016
Dendrimers	Pilocarpine nitrate and tropicamide	PAMAM	Chemical synthesis	Ocular infections	Vandamme TF *et al* 2005
	Puerarin	PAMAM	Solvent evaporation	Cataract and ocular hypertension	Yao W *et al* 2010
	Brimonidine tartarate	polyaminoamine	Electrospinning	glaucoma	Lancina III MG *et al* 2017
	Acetazolamide	carbosilane	chemical synthesis	glaucoma	Bravo-Osuna I *et al* 2016
Cubosomes	Beclomethasone dipropionate	CMC, Glyceryl monooleate	Top down technique	Uveitis	Gaballa SA *et al* 2020
	Flurbiprofen	Poloxamer 407, glyceryl monooleate	Hot and high pressure homogenization	Conjunctivitis	Han S *et al* 2010
	Timolol maleate	Poloxamer 407, glyceryl monooleate	Homogenization	Glaucoma	Huang J *et al* 2017
	Ciprofloxacin	Chitosan, poloxamer	Sonication	conjunctivitis	Alharbi WS *et al* 2020
	Natamycin	Span 80, poloxamer 407	Probe sonication	Fungal keratitis	KAZI M *et al* 2020
Nanowafers	Dexamethasone	Sodium CMC	Modified hydrogel template	Dry eye disease	Coursey TG *et al* 2015

5. Patents On Nanotechology-Based Drug Delivery Systems

Various patents have been granted over years for various nanotechnology-based ocular dru delivery systems. These patents have been summarized in Table 2.

Table 2: Patents on nanotechnology based ocular drug delivery systems

Patent no.	Formulation	Indication	Year
US8414904B2	Nanoemulsion	General ocular drugs.	2013
US8153156 B2	Nanoparticles	Substitute of vitreous humor	2012
US8273366	Nanoemulsion via contact lens	Anti- inflammatory, Antiinfective, Glaucoma	2012
US8097270	Nanoparticles	Antimicrobial, glaucoma	2012
US8298568	Nanoemulsion	Uveitis	2012
US20110008421	Liposome	Posterior ocular segments disease	2011
WO2010144194	Nanomicelles	Posterior ocular segments disease	2010
US7732404	Nanoemulsion	Dry eye treatment	2010

US 20090074828A1	Nanoparticles	Age-Related Macular Degeneration, Choroidal Neovascularization	2009
US20090092665	Nanomicelles	Dry eye syndrome (DES), Sjogren's syndrome, uveitis, conjunctivitis (pink eye)	2009

6. Ocular Nanoformulations Under Clinical Trials

Various nanotechnology-based ocular drug delivery systems under clinical trials have beensummarized in the table 3. The information of these clinical trials have been accessed from https://www.clinicaltrials.gov/

Table 3: Undergoing clinical trials

Formulation	Phase	Study Purpose	Study design	Clinical trial identifier
Liposome (latanoprost)	II	Glaucoma	Open labeled, multi-center, randomized, active controlled	NCT02466399
Liposome (sirolimus)	I	Dry eye disease	Randomized, parallel	NCT04115800
Liposome (latanoprost)	I, II	Ocular hypertension	Single group assignment	NCT01987323
Liposome (mitoxantrone hydrochloride)	II	Neuromyelitis optical spectrum disorder	Multi-center, randomized, double blind	NCT05551598
Liposome (phospholipid)	NA	Dry eye disease	Randomized, crossover	NCT02420834
Nanomicelle (cyclosporine)	III	Dry eye disease	Single group, open label	NCT02845674
Nanoparticle (dexamethasone)	II	Inflammation	Randomized, double masked	NCT04130802
Nanoparticle (urea)	II	Cataract	Randomized, parallel	NCT03001466
Nanoparticle (dexamethasone)	II	Diabetic macular edema	Randomized, parallel	NCT05343156
Nanoparticle (urea)	II	Cataract	Randomized	NCT03001466
Nanoemulsion (Brimonidine tartarate)	III	Dry eye disease	Randomized, double masked	NCT03785340
Nanoemulsion (Clobetasol propionate)	III	Inflammation	Randomized, multi-center	NCT05724446

7. Current Challenges and Future Prospects

Drug delivery to the eye possesses significant challenges because of numerous barriers present in the ocular region, especially in the posterior segment of the eye. Conventional drug delivery systems are effective in treating ocular disorders, but the major shortcomings are poor permeability, insufficient bioavailability, and improper distribution. To overcome these challenges, various novel drug delivery systems have been formulated that significantly improve the efficacy of conventional systems. These novel drug delivery systems include niosomes, nanoparticles, liposomes, cubosomes, nanowafers, and many more. Gene therapy and other formulations such as exosomes have also been developed to enhance drug delivery. Although novel approaches are efficient in delivering the drug to the target area, a few problems still exist. The complexity of production technology and processes remain on top, which hinders the clinical translation of nanotechnology-based ocular drug delivery systems. Stability and safety both are major concerns in the case of nanocarriers. The lack of comprehensive in-vivo studies on human eyes is also a major reason why nanocarriers are not completely translated into clinical care. Despite numerous advantages, these systems require high technical knowledge and machinery and possess higher costs for production, which are the major reasons for their commercial production. Addressing these challenges is required for the successful implementation of novel drug delivery systems in clinical practice. The applications of these systems in ocular drug delivery are undeniable, but the challenges need to be addressed. Novel non-invasive ocular systems should be developed to overcome ocular barriers. More studies need to be conducted on animal models and human eyes to ensure the safety and efficacy of ODDS in clinical practice.

It can be concluded that nanocarriers have a bright future in the treatment of ocular disorders, and will continue to be used in clinical practice.

CONCLUSION

Nanomaterials have emerged as a promising strategy for the treatment of ocular diseases, as they have unique tunable and programmable properties which allow optimization of the efficacy of ocular drug delivery while minimizing toxicity. The involvement of nanotechnology-based ocular drug delivery systems has brought numerous advancements over conventional treatments. Several ocular barriers are major hindrances in effective ocular delivery to the target region, relentless efforts have been directed toward the development of novel nanotechnology-based formulations in the hope of clinical translation of the strategy from the bench to the bedside. A multidisciplinary approach including pharmacology, ophthalmology, biomaterial science and pharmaceutical science will bring these unique nanosystems in the clinical treatment of severe sight-threatening ocular diseases.

Abbreviations

DED: Dry eye disease
ODDS: Ocular drug delivery system
ASED: Anterior Segment Eye Diseases
BRB: Blood retinal barrier
LFU:Lacrimal Functional Unit
OCT: Optical Coherence Tomography
NE: Nanoemulsion
NP: Nanoparticles

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Conflict Of Interest

Nil

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Nil

REFERENCES

1. Weng Y, Liu J, Jin S, Guo W, Liang X, Hu Z. Nanotechnology-based strategies for treatment of ocular disease. Acta pharmaceutica sinica B. 2017 May 1;7(3):281-91.
2. Khiev D, Mohamed ZA, Vichare R, Paulson R, Bhatia S, Mohapatra S, Lobo GP, Valapala M, Kerur N, Passaglia CL, Mohapatra SS. Emerging nano-formulations and nanomedicines applications for ocular drug delivery. Nanomaterials. 2021 Jan 12;11(1):173.
3. Onugwu AL, Nwagwu CS, Onugwu OS, Echezona AC, Agbo CP, Ihim SA, Emeh P, Nnamani PO, Attama AA, Khutoryanskiy VV. Nanotechnology based drug delivery systems for the treatment of anterior segment eye diseases. Journal of Controlled Release. 2023 Feb 1; 354:465-88.
4. Dubald M, Bourgeois S, Andrieu V, Fessi H. Ophthalmic drug delivery systems for antibiotherapy—A review. Pharmaceutics. 2018 Jan 13;10(1):10.
5. Jaiswal P, Mishra A, Kesharwani D, Paul SD. Overview on Ocular Drug Delivery through Colloidal Nano-Suspension. Research Journal of Pharmacy and Technology. 2023 Mar 1;16(3):1533-9.
6. Kaplan HJ. Anatomy and function of the eye. Immune Response and the Eye. 2007;92:4-10.
7. Snell RS, Lemp MA. Clinical anatomy of the eye. John Wiley & Sons; 2013 Apr 9.
8. Senior KR, editor. The eye: the physiology of human perception. The Rosen Publishing Group, Inc; 2010 Aug 15.
9. Cunha-Vaz J. The blood-ocular barriers. Survey of ophthalmology. 1979 Mar 1;23(5):279-96.
10. Cunha-Vaz J, Bernardes R, Lobo C. Blood-retinal barrier. European journal of ophthalmology. 2011 Nov;21(6_suppl):3-9.
11. Occhiutto ML, Freitas FR, Maranhao RC, Costa VP. Breakdown of the blood-ocular barrier as a strategy for the systemic use of nanosystems. Pharmaceutics. 2012 May 14;4(2):252-75.
12. Schuster AK, Erb C, Hoffmann EM, Dietlein T, Pfeiffer N. The diagnosis and treatment of glaucoma. Deutsches Ärzteblatt International. 2020 Mar;117(13):225.
13. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. Jama. 2014 May 14;311(18):1901-11.
14. Messmer EM. The pathophysiology, diagnosis, and treatment of dry eye disease. Deutsches Ärzteblatt International. 2015 Jan;112(5):71.
15. Stern ME, Schaumburg CS, Pflugfelder SC. Dry eye as a mucosal autoimmune disease. International reviews of immunology. 2013 Jan 13;32(1):19-41.
16. Kuo YK, Lin IC, Chien LN, Lin TY, How YT, Chen KH, Dusting GJ, Tseng CL. Dry eye disease: a review of epidemiology in Taiwan, and its clinical treatment and merits. Journal of Clinical Medicine. 2019 Aug 15;8(8):1227.
17. Singh P, Gupta A, Tripathy K. Keratitis. [Updated 2023 Feb 22]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559014/
18. Cabrera-Aguas M, Khoo P, Watson SL. Infectious keratitis: A review. Clinical & Experimental Ophthalmology. 2022 Jul;50(5):543-62.
19. Azari AA, Barney NP. Conjunctivitis: a systematic review of diagnosis and treatment. Jama. 2013 Oct 23;310(16):1721-30.
20. Azari AA, Arabi A. Conjunctivitis: a systematic review. Journal of ophthalmic & vision research. 2020 Jul;15(3):372.

21. Nizami AA, Gulani AC. Cataract. [Updated 2022 Jul 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539699/
22. Robman L, Taylor H. External factors in the development of cataract. Eye. 2005 Oct;19(10):1074-82.
23. Zhou HY, Hao JL, Wang S, Zheng Y, Zhang WS. Nanoparticles in the ocular drug delivery. International journal of ophthalmology. 2013;6(3):390.
24. Diebold Y, Calonge M. Applications of nanoparticles in ophthalmology. Progress in retinal and eye research. 2010 Nov 1;29(6):596-609.
25. Yang C, Yang J, Lu A, Gong J, Yang Y, Lin X, Li M, Xu H. Nanoparticles in ocular applications and their potential toxicity. Frontiers in Molecular Biosciences. 2022 Jul 15; 9:931759.
26. Bachu RD, Chowdhury P, Al-Saedi ZH, Karla PK, Boddu SH. Ocular drug delivery barriers—role of nanocarriers in the treatment of anterior segment ocular diseases. Pharmaceutics. 2018 Feb 27;10(1):28.
27. Bhattacharjee A, Das PJ, Adhikari P, Marbaniang D, Pal P, Ray S, Mazumder B. Novel drug delivery systems for ocular therapy: With special reference to liposomal ocular delivery. European journal of ophthalmology. 2019 Jan;29(1):113-26.
28. Yuan X, Marcano DC, Shin CS, Hua X, Isenhart LC, Pflugfelder SC, Acharya G. Ocular drug delivery nanowafer with enhanced therapeutic efficacy. ACS nano. 2015 Feb 24;9(2):1749-58.
29. Patel VR, Agrawal YK. Nanosuspension: An approach to enhance solubility of drugs. Journal of advanced pharmaceutical technology & research. 2011 Apr;2(2):81.
30. Kassem MA, Rahman AA, Ghorab MM, Ahmed MB, Khalil RM. Nanosuspension as an ophthalmic delivery system for certain glucocorticoid drugs. International journal of pharmaceutics. 2007 Aug 1;340(1-2):126-33.
31. Jacob S, Nair AB, Shah J. Emerging role of nanosuspensions in drug delivery systems. Biomaterials research. 2020 Dec;24:1-6.
32. Gawin-Mikołajewicz A, Nartowski KP, Dyba AJ, Gołkowska AM, Malec K, Karolewicz B. Ophthalmic nanoemulsions: From composition to technological processes and quality control. Molecular Pharmaceutics. 2021 Sep 17;18(10):3719-40.
33. Dhahir RK, Al-Nima AM, Fadia AB. Nanoemulsions as ophthalmic drug delivery systems. Turkish Journal of Pharmaceutical Sciences. 2021 Oct;18(5):652.
34. Fernandes AR, Sanchez-Lopez E, Santos TD, Garcia ML, Silva AM, Souto EB. Development and characterization of nanoemulsions for ophthalmic applications: Role of cationic surfactants. Materials. 2021 Dec 8;14(24):7541.
35. Bose A, Roy Burman D, Sikdar B, Patra P. Nanomicelles: Types, properties and applications in drug delivery. IET nanobiotechnology. 2021 Feb;15(1):19-27.
36. Trivedi R, Kompella UB. Nanomicellar formulations for sustained drug delivery: strategies and underlying principles. Nanomedicine. 2010 Apr;5(3):485-505.
37. Li S, Chen L, Fu Y. Nanotechnology-based ocular drug delivery systems: recent advances and future prospects. Journal of Nanobiotechnology. 2023 Dec;21(1):1-39.
38. Yavuz B, Bozdağ Pehlivan S, Ünlü N. Dendrimeric systems and their applications in ocular drug delivery. The Scientific World Journal. 2013 Oct;2013.

39. Gillies ER, Frechet JM. Dendrimers and dendritic polymers in drug delivery. Drug discovery today. 2005 Jan 1;10(1):35-43.
40. Klajnert B, Bryszewska M. Dendrimers: properties and applications. Acta biochimica polonica. 2001;48(1):199-208.
41. Teba HE, Khalil IA, El Sorogy HM. Novel cubosome based system for ocular delivery of acetazolamide. Drug Delivery. 2021 Jan 1;28(1):2177-86.
42. Sivadasan D, Sultan MH, Alqahtani SS, Javed S. Cubosomes in Drug Delivery—A Comprehensive Review on Its Structural Components, Preparation Techniques and Therapeutic Applications. Biomedicines. 2023 Apr 7;11(4):1114.
43. Umar H, Wahab HA, Gazzali AM, Tahir H, Ahmad W. Cubosomes: Design, Development, and Tumor-Targeted Drug Delivery Applications. Polymers. 2022 Jul 31;14(15):3118.
44. Satyanarayana SD, Abu Lila AS, Moin A, Moglad EH, Khafagy ES, Alotaibi HF, Obaidullah AJ, Charyulu RN. Ocular Delivery of Bimatoprost-Loaded Solid Lipid Nanoparticles for Effective Management of Glaucoma. Pharmaceuticals. 2023 Jul 13;16(7):1001.
45. Uner B, Ozdemir S, Yildirim E, Yaba A, Tas C, Uner M, Ozsoy Y. Loteprednol loaded nanoformulations for corneal delivery: Ex-vivo permeation study, ocular safety assessment and stability studies. Journal of Drug Delivery Science and Technology. 2023 Mar 1;81:104252.
46. Kaviarasi B, Rajana N, Pooja YS, Rajalakshmi AN, Singh SB, Mehra NK. Investigating the effectiveness of Difluprednate-Loaded core-shell lipid-polymeric hybrid nanoparticles for ocular delivery. International Journal of Pharmaceutics. 2023 Jun 10;640:123006.
47. Jalal RR, Ways TM, Elella MH, Hassan DA, Khutoryanskiy VV. Preparation of mucoadhesive methacrylated chitosan nanoparticles for delivery of ciprofloxacin. International Journal of Biological Macromolecules. 2023 Jul 1;242:124980.
48. Kantaria T, Kantaria T, Heiduschka P, Eter N, Tugushi D, Katsarava R. Dexamethasone-Loaded Pseudo-Protein Nanoparticles for Ocular Drug Delivery: Evaluation of Drug Encapsulation Efficiency and Drug Release. Journal of Nanotechnology. 2023 May 8;2023.
49. Bigdeli A, Makhmalzadeh BS, Feghhi M, SoleimaniBiatiani E. Cationic liposomes as promising vehicles for timolol/brimonidine combination ocular delivery in glaucoma: formulation development and in vitro/in vivo evaluation. Drug Delivery and Translational Research. 2023 Apr;13(4):1035-47.
50. Guinedi AS, Mortada ND, Mansour S, Hathout RM. Preparation and evaluation of reverse-phase evaporation and multilamellar niosomes as ophthalmic carriers of acetazolamide. International journal of pharmaceutics. 2005 Dec 8;306(1-2):71-82.
51. Chen X, Wu J, Lin X, Wu X, Yu X, Wang B, Xu W. Tacrolimus loaded cationic liposomes for dry eye treatment. Frontiers in Pharmacology. 2022 Feb 4;13:838168.
52. Nagarsenker MS, Londhe VY, Nadkarni GD. Preparation and evaluation of liposomal formulations of tropicamide for ocular delivery. International journal of pharmaceutics. 1999 Nov 10;190(1):63-71.
53. Chetoni P, Monti D, Tampucci S, Matteoli B, Ceccherini-Nelli L, Subissi A, Burgalassi S. Liposomes as a potential ocular delivery system of distamycin A. International journal of pharmaceutics. 2015 Aug 15;492(1-2):120-6.
54. Ahuja M, Verma P, Bhatia M. Preparation and evaluation of chitosan–itraconazole co-

precipitated nanosuspension for ocular delivery. Journal of Experimental Nanoscience. 2015 Feb 11;10(3):209-21.
55. Mudgil M, Pawar PK. Preparation and in vitro/ex vivo evaluation of moxifloxacin-loaded PLGA nanosuspensions for ophthalmic application. Scientia pharmaceutica. 2013 Jun;81(2):591-606.
56. Qin T, Dai Z, Xu X, Zhang Z, You X, Sun H, Liu M, Zhu H. Nanosuspension as an efficient carrier for improved ocular permeation of voriconazole. Current Pharmaceutical Biotechnology. 2021 Jan 1;22(2):245-53.
57. Xu B, Liu T. Travoprost loaded microemulsion soaked contact lenses: Improved drug uptake, release kinetics and physical properties. Journal of Drug Delivery Science and Technology. 2020 Jun 1;57:101792.
58. Dandagi P, KERUR S, Mastiholimath V, Gadad A, Kulkarni A. Polymeric ocular nanosuspension for controlled release of acyclovir: in vitro release and ocular distribution. 2009
59. Salimi A. Preparation and evaluation of celecoxib nanoemulsion for ocular drug delivery. Asian Journal of Pharmaceutics (AJP). 2017 Oct 11;11(03).
60. Ammar HO, Salama HA, Ghorab M, Mahmoud AA. Nanoemulsion as a potential ophthalmic delivery system for dorzolamide hydrochloride. Aaps Pharmscitech. 2009 Sep;10:808-19.
61. Akhter S, Anwar M, Siddiqui MA, Ahmad I, Ahmad J, Ahmad MZ, Bhatnagar A, Ahmad FJ. Improving the topical ocular pharmacokinetics of an immunosuppressant agent with mucoadhesive nanoemulsions: Formulation development, in-vitro and in-vivo studies. Colloids and Surfaces B: Biointerfaces. 2016 Dec 1;148:19-29.
62. Modi D, Mohammad, Warsi MH, Garg V, Bhatia M, Kesharwani P, Jain GK. Formulation development, optimization, and in vitro assessment of thermoresponsive ophthalmic pluronic F127-chitosan in situ tacrolimus gel. Journal of Biomaterials Science, Polymer Edition. 2021 Sep 2;32(13):1678-702.
63. Tatke A, Dudhipala N, Janga KY, Balguri SP, Avula B, Jablonski MM, Majumdar S. In situ gel of triamcinolone acetonide-loaded solid lipid nanoparticles for improved topical ocular delivery: Tear kinetics and ocular disposition studies. Nanomaterials. 2018 Dec 27;9(1):33.
64. Ghezzi M, Ferraboschi I, Delledonne A, Pescina S, Padula C, Santi P, Sissa C, Terenziani F, Nicoli S. Cyclosporine-loaded micelles for ocular delivery: Investigating the penetration mechanisms. Journal of Controlled Release. 2022 Sep 1;349:744-55.
65. Alami-Milani M, Zakeri-Milani P, Valizadeh H, Salehi R, Jelvehgari M. Preparation and evaluation of PCL-PEG-PCL micelles as potential nanocarriers for ocular delivery of dexamethasone. Iranian journal of basic medical sciences. 2018 Feb;21(2):153.
66. Li M, Zhang L, Li R, Yan M. New resveratrol micelle formulation for ocular delivery: Characterization and in vitro/in vivo evaluation. Drug Development and Industrial Pharmacy. 2020 Dec 1;46(12):1960-70.
67. Taha EI, Badran MM, El-Anazi MH, Bayomi MA, El-Bagory IM. Role of Pluronic F127 micelles in enhancing ocular delivery of ciprofloxacin. Journal of Molecular Liquids. 2014 Nov 1;199:251-6.
68. Li X, Zhang Z, Li J, Sun S, Weng Y, Chen H. Diclofenac/biodegradable polymer micelles for ocular applications. Nanoscale. 2012;4(15):4667-73.
69. Gaafar PM, Abdallah OY, Farid RM, Abdelkader H. Preparation, characterization and evaluation of novel elastic nano-sized niosomes (ethoniosomes) for ocular delivery

of prednisolone. Journal of liposome research. 2014 Sep 1;24(3):204-15.

70. Eid HM, Naguib IA, Alsantali RI, Alsalahat I, Hegazy AM. Novel chitosan-coated niosomal formulation for improved management of bacterial conjunctivitis: a highly permeable and efficient ocular nanocarrier for azithromycin. Journal of Pharmaceutical Sciences. 2021 Aug 1;110(8):3027-36.
71. Emad Eldeeb A, Salah S, Ghorab M. Proniosomal gel-derived niosomes: an approach to sustain and improve the ocular delivery of brimonidine tartrate; formulation, in-vitro characterization, and in-vivo pharmacodynamic study. Drug delivery. 2019 Jan 1;26(1):509-21.
72. Gugleva V, Titeva S, Rangelov S, Momekova D. Design and in vitro evaluation of doxycycline hyclate niosomes as a potential ocular delivery system. International journal of pharmaceutics. 2019 Aug 15;567:118431.
73. Zeng W, Li Q, Wan T, Liu C, Pan W, Wu Z, Zhang G, Pan J, Qin M, Lin Y, Wu C. Hyaluronic acid-coated niosomes facilitate tacrolimus ocular delivery: Mucoadhesion, precorneal retention, aqueous humor pharmacokinetics, and transcorneal permeability. Colloids and Surfaces B: Biointerfaces. 2016 May 1;141:28-35.
74. Vandamme TF, Brobeck L. Poly (amidoamine) dendrimers as ophthalmic vehicles for ocular delivery of pilocarpine nitrate and tropicamide. Journal of controlled release. 2005 Jan 20;102(1):23-38.
75. Yao W, Sun K, Mu H, Liang N, Liu Y, Yao C, Liang R, Wang A. Preparation and characterization of puerarin–dendrimer complexes as an ocular drug delivery system. Drug development and industrial pharmacy. 2010 Sep 1;36(9):1027-35.
76. Lancina III MG, Singh S, Kompella UB, Husain S, Yang H. Fast dissolving dendrimer nanofiber mats as alternative to eye drops for more efficient antiglaucoma drug delivery. ACS biomaterials science & engineering. 2017 Aug 14;3(8):1861-8.
77. Bravo-Osuna I, Vicario-de-la-Torre M, Andrés-Guerrero V, Sánchez-Nieves J, Guzmán-Navarro M, De La Mata FJ, Gómez R, de las Heras B, Argueso P, Ponchel G, Herrero-Vanrell R. Novel water-soluble mucoadhesive carbosilane dendrimers for ocular administration. Molecular pharmaceutics. 2016 Sep 6;13(9):2966-76.
78. Gaballa SA, El Garhy OH, Moharram H, Abdelkader H. Preparation and evaluation of cubosomes/cubosomal gels for ocular delivery of beclomethasone dipropionate for management of uveitis. Pharmaceutical Research. 2020 Oct;37:1-23.
79. Han S, Shen JQ, Gan Y, Geng HM, Zhang XX, Zhu CL, Gan L. Novel vehicle based on cubosomes for ophthalmic delivery of flurbiprofen with low irritancy and high bioavailability. Acta Pharmacologica Sinica. 2010 Aug;31(8):990-8.
80. Huang J, Peng T, Li Y, Zhan Z, Zeng Y, Huang Y, Pan X, Wu CY, Wu C. Ocular cubosome drug delivery system for timolol maleate: preparation, characterization, cytotoxicity, ex vivo, and in vivo evaluation. Aaps Pharmscitech. 2017 Nov;18:2919-26.
81. Alharbi WS, Hosny KM. Development and optimization of ocular in situ gels loaded with ciprofloxacin cubic liquid crystalline nanoparticles. Journal of Drug Delivery Science and Technology. 2020 Jun 1; 57:101710.
82. KAZI M, DHAKNE R, DEHGHAN MH. Ocular delivery of natamycin based on monoolein/span 80/poloxamer 407 nanocarriers for the effectual treatment of fungal keratitis. Journal of Research in Pharmacy. 2020 Mar 1;24(2).

83. Coursey TG, Henriksson JT, Marcano DC, Shin CS, Isenhart LC, Ahmed F, De Paiva CS, Pflugfelder SC, Acharya G. Dexamethasone nanowafer as an effective therapy for dry eye disease. Journal of Controlled Release. 2015 Sep 10;213:168-74.

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