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Review Article

A Succinct Study in the Developments of Nano Ocular Delivery Techniques

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ABSTRACT

The study of materials physical, chemical, and biological characteristics at the nanoscale is referred to as nanoscience. Materials with at least one dimension in the nanoscale are used and constructed in nanotechnology [1]. Outstanding mechanical, electrical, optical magnetic and chemical properties are displayed by some nanoscale materials. Drugs and drug delivery systems can benefit from these qualities by having better physiochemical and biological properties [2-4]. Additionally, the use of nanotechnology in ocular disease diagnosis and treatment has advanced quickly. Polymer based systems, nanoparticles, and nanovescicles seem promise for controlled and extended drug release, which could result in improved therapeutic efficacy. Moreover, despite ongoing issues with the device's scalability and biocompatibility, micro and nanotechnology has the potential to revolutionize the treatment of ocular diseases. To validate these innovations in the therapeutic context of ophthalmology, more clinical research is required. However, over the past ten years, fundus lesions and ocular cancers have been included in the rapidly expanding field of nanomedicine in ophthalmology. By increasing the drugs solubility, stability and permeability and prolonging its residence duration, loading it into an ocular nano-level DDS (targeted drug delivery system) improves the drug's effectiveness. Notably, a thorough introduction is given to the latest developments in nano carrier DDS and their applications in the management of different ocular conditions. Lastly, more discussions are given to the present difficulties as well as potential future paths and viewpoints about the use of nanocarrier based DDS for ocular treatments.

INTRODUCTION

One of the most delicate organs, the eye has a number of defenses and barriers to keep the

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outside world out. For instance, this particular structure makes it difficult to treat ocular illness and distribute medications to various eye compartments, such as the blood aqueous barrier and blood retinal barrier. Problems like getting medications to less accessible areas of the eyes are common because of the many ocular barriers, which include the tear film barrier, corneal barrier, conjunctival barrier, scleral barrier, BRB (Blood-retinal barrier), BAB (Blood- aqueous barrier). Thus, developing novel ocular particle drug delivery (DDSs) with effects of prolonged release or increased permeability has emerged as a recent area of intense scientific interest. New medications must be studied using suitable delivery methods. Various nano carriers have been used by nanotechnology to create promising ocular drug delivery methods that interact with the ocular mucosa, enhance permeability, and lengthen the duration of drug retention in the eye. Many medications have poor therapeutic effects because of the eyes intricate drug delivery barrier, which lowers their bioavailability [5-7]. Liposomes, emulsions, micelles, dendrimers, and microspheres are the most common types of these particulate DDS [8,9]. The parameters influencing the administration of each route change because each component of the eye has a different barrier effect. To effectively distribute medications to various areas of the eye, the development of a unique ocular DDS has emerged as a key concern. In the past, glaucoma and other conditions affecting the surface of the eyes were the primary targets of nanomedicine. Drug efficacy is increased by loading the medication into an ocular nano level DDS, which also increases the drugs permeability, stability, and solubility while prolonging its half-life [10]

Various methods for treating eye diseases

Keratoconjunctivitis

Keratoconjunctivitis sicca often known as dry eye disease (DED), is a complex condition that affects both the ocular surface and tears. Surface inflammation and tear film osmolarity [12]. DED has complicated and multifaceted etiology. Aqueous deficient dry eye (ADDE) and evaporate dry eye (EDE) are the two primary categories into which it can be generally divided. While EDE is caused by excessive tear film evaporation and is frequently linked to meibomiam gland dysfunction (MGD), ADDE is defined by insufficient aqueous tear generation by the lacrimal gland [13]. Hormonal fluctuations, environmental factors, contact lens use, some medications, and systemic disorders such as Sjogrens syndrome are other contributing factors [14] . A variety of symptoms, including burning, stinging, a feeling of a foreign body or grit, and spells of clouded vision, are clinical indications of DED [15] . Artificial tears, lubricating eye drops, ointments, warm compresses, and lifestyle modifications like boosting humidity and reducing screen time are all examples of traditional therapies for dry eyes. [16] . The eye's special barriers, such as the tear film's h igh turnover and protective properties, make it dif ficult to deliver treatments for DED effectively si nce they quickly dilute and eliminate medications applied topically [17]While the corneal epithelium' s strong barrier restricts medication penetration a nd the disease's intricate pathophysiology makes efficient drug delivery more difficult by encourag ing inflammation and tear film instability, freque nt eye drop administration for DED is inconvenie nt and affects compliance [18,19] Numerous nanocarriers, including liposomes, dentrimers, and polymeric nanoparticles, have been investigated by researchers. (Figure. 1)

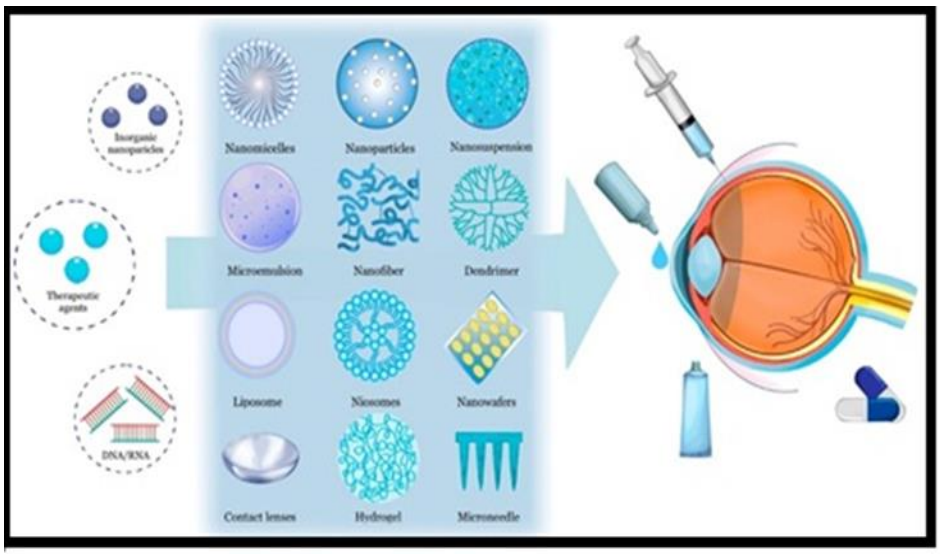

Fig 1. Diagram of nanotechnology-based ocular drug delivery systems. Adapted from Ref. [11]. Copyright 2023, Springer Nature (Creative Commons Attribution 4.0 International License).

Drug retention and release are improved by liposomes ability to interact with the lipid layer of the tear film due to their phospholipid bilayer structure, which encapsulates both hydrophilic and lipophilic medicines [20,21] . In order to improve formulations stability and possibly decrease tear evaporation, the liposomal Composition might be changed to match the lipid layer of the tear film [22] . This makes it easier for anti-inflammatory drugs like cyclosporine A to be released under control, which improves corneal penetration and prolongs the therapeutic effects [23]. In terms of drug solubility, ocular bioavailability, and anti-inflammatory activity, liposomal cyclosporine A formulations fared better than conventional formulations in the treatment of DED [24]. The effectiveness of liposomes in treating DED is further supported by their capacity to fuse with cell membranes and their innate tendency to be absorbed by local mononuclear phagocytic cells in inflammatory areas [20]. Because of their small size (usually less than 10nm), dendrimers, which are distinguished by their widely branched, tree like topologies, enable effective transcorneal penetration [25] . Mucoadhesive polymers, like hyaluronic acid, can be used to modify surfaces and increase their retention on the ocular surface. Dendrimers coupled with dexamethasone, for instance, have demonstrated improved efficacy and sustained drug release in the treatment of ocular inflammation [25]. Polymeric nanoparticles are made from biodegradable polymers, such as ploy (lactic-co-glycolic acid) (PLGA). Mucoadhesion and ocular surface retention can be enhanced by surface alterations using positively charged polymers, including chitosan [26] . However, PLGA delivery systems frequently experience early burst release, which calls for careful formulation modification [27]. For instance, PLGA nanoparticles loaded with cyclosporine A have demonstrated up to 24 hours of sustained drug release [28]. In DED, nanomicelles have been investigated for the delivery of lubricants and anti-inflammatory drugs, showing improved drug efficacy and retention [29]. For instance, hydrogels retain water, enhancing drug tissue interaction and extending drug retention, whereas nanofibers have a huge surface area [30].

Glaucoma

Increased intraocular pressure, or IOP, is typically the cause of several disorders. It is one of the main causes of vision loss, especially in those 60 years of age and beyond [31] . Ninety percent of cases of glaucoma are open-angle, which is characterized by a progressive rise in intraocular pressure (IOP) brought on by obstruction in the drainage canals. The optic nerve gradually deteriorates as a result. The fact that there are usually no symptoms in the early stages highlights how crucial routine eye exams are for prompt detection and treatment [31, 32]. In order to prevent irreparable vision loss, this kind of glaucoma is a emergency that requires prompt treatment [34]. The goal of traditional glaucoma therapies is to reduce intraocular pressure (IOP) by using drugs such carbonic anhydrase inhibitors, prostaglandin analogs, betablockers, and alpha agonists. Although these drugs can be useful, they frequently have adverse effects and need to be used for the rest of one's life, which can impact patient compliance and treatment outcomes overall [35] . Lowering intraocular pressure (IOP) is intended to protect the optic nerve but drug absorption and penetration are hampered by a number of obstacles. Medications transfer is restricted by the corneal epithelium, conjunctiva, sclera, and blood aqueous barrier [33,36,37] . Furthermore, common treatments like eyedrops and systemic medications may cause unintended adverse effects and frequently have adherence issues, especially in elderly patients [38.39] . Precise drug encapsulation and controlled release are made possible by dendrimers [40]. Drug solubility is enhanced and medications are shielded from enzymatic breakdown in the tear film by polymeric nanoparticles, such those derived from PLGA and chitosan [41,42] . Controlled medication release in response to changes in the pH of the eye or the makeup of tears [54]. For example, drug-loaded nanoparticles that contain glaucoma drugs such as latanoprost or timolol can lower intraocular pressure over time while lowering the frequency of doses, which improves patient adherence [44] . In order to improve retention duration and extend drug release certain nano-micelles are designed to be thermosensitive, which allows them to change from a liquid to a gel form. These characteristics are absent from conventional glaucoma treatment [45]. Hydrogels and nanofiber based drug delivery systems have also been developed as sustained release formulations for the treatment of glaucoma, in addition to these nanocarriers, maintaining effective IOP control without the need for frequent administration [46,47]. Moreover, hydrogels can be engineered to react to ocular stimuli, which, under some circumstances, can cause on-demand drug release [48] . By facilitating targeted drug delivery to particular ocular tissues, such as the ciliary body and trabecular meshwork, nanotechnology transforms the treatment of glaucoma, increasing therapeutic efficacy and reducing systemic side effects. The treatment of glaucoma and patient outcomes could be greatly enhanced by further advancement in this area [49] .

Cataract

One of the main causes of blindness and visual impairment in the world is cataracts. Vision is diminished as a result of clouding of the eyes natural lens [50] . Aggregation of proteins within the lens is often the cause of this disorder, and it can be impacted by aging, trauma, radiation exposure, and other medical problems such as diabetes [51] . Blurred vision, glare and bright light problems, color fading, and night vision problems are the main signs of cataracts [52,53] .\ Over time, these symptoms may worsen and significantly impair the affected persons daily activities and quality of life. Nowadays, surgically removing the clouded lens and replacing it with an artificial intraocular lens (IOL) is the standard treatments of cataract [54] . Even though cataract surgery is

usually safe and successful, it can sometimes have side effects including posterior capsule opacification (PCO), which may call for additional care [55]. To treat cataracts, for example, liposomal drug delivery methods encapsulate antioxidants such as N acetyl carnosine, which are then sent to the lens to reduce protein aggregation and oxidative stress [56]. By encapsulating anti cataract drugs, transporting them straight to the eye, improving medication absorption, and focusing on the afflicted lens area, polymeric nanoparticles made of PLGA treat cataracts [57]. Because they can increase bioavailability, improve corneal permeability, and boost the effectiveness of low soluble and low permeable medications like curcumin, nanoemulsions have showed promise in the treatment of cataract illness [58]. Research is still ongoing on the use of nanotechnology in ophthalmology to treat cataracts. Nanoparticles may transform cataract care in the future by offering a successful and non-invasive substitute for surgery [56,59].

Diabetic retinopathy

A common consequence of diabetes that affects the retinal blood vessels and can cause blindness or visual impairment is diabetic retinopathy. [60]. From mild non proliferative retinopathy, when new blood vessels cover the surface of the retina, this illness progresses in stages [61]. The symptoms of diabetic retinopathy when it progresses, blindness or severe vision loss may result [62]. For people with diabetes, routine eye exams are essential since early stages of diabetic retinopathy frequently show no symptoms [63]. Vitrectomy is a surgical operation that removes blood from the centre of the eye. [64]Even if these treatments are beneficial, they have drawbacks. Anti VEGF injections need to be administered frequently and have the potential to cause infection and elevated intraocular pressure, laser photocoagulation can result in peripheral vision loss and night vision issues, and vitrectomy is an invasive procedure that carries the risk of retinal detachment and cataracts.[65-67] . Therapeutic dosages are guaranteed to reach the intended locations within the retina due to their efficient blood retinal barrier crossing [68] A paradigm shift in the treatment of this crippling condition has been ushered in by the use of nanotechnology in diabetic retinopathy drug delivery, which not only improves treatment precision and efficacy but also significantly increases patient adherence and overall quality of life [69].

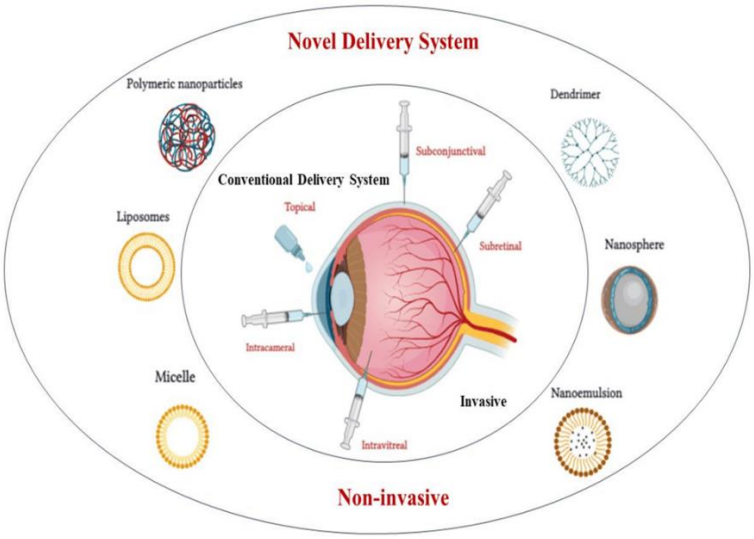

Fig. 2 Various Nano drug delivery system (taken from Rajan et al. Cureus 15(8): e66476. DOI 10.7759/cureus.66476 (Ref 104)

Nanotechnology in eye disease (FIGURE.2)

Nanoenzymes

Nanozymes are microscopic organisms with catalytic characteristics similar to those of enzymes that have the stability to transform substrates into products. Because eye therapy avoids systemic distribution, these qualities are important in nanomedicine [70] . Age related macular degeneration (AMD), cataracts, diabetic retinopathy, and glaucoma can all be effectively treated with nanoenzyme-based drug delivery systems in ophthalmology [70,71] .

By reducing reactive oxygen species (ROS), nanoenzymes may reduce oxidative stress in diseases like AMD or diabetic retinopathy and protect retinal cells from harm.

Nanoenzymes biodegrade into nontoxic byproducts after medication administration, ensuring safe ocular clearance and few side effects. This method improves the safety and effectiveness of medications for eye conditions by enabling precise, targeted treatment [70-72]

Nanoemulsion

Transparent, inert and stable mixes of water and oil that are uniformly distributed and held together by surface active agents and co surfactants using an interfacial fluid are known as nanoemulsions [73] .

Nanoemulsions range in size from 20 to 500nm [74] Because of their longer shelf life, higher rate of bioavailability, and transparency at a larger droplet volume fraction, nano emulsions designed for ocular drug administration have a promising future in pharmaceutical products [75] .

They are developed by dispersing a liquid, usually oil, into another liquid, water, using low energy processes like phase inversion or high energy methods like high pressure homogenization and ultrasonication.

Because of their small droplet size and exceptional kinetic stability, nanoemulsions prevent droplet separation or coalescence over time [74].Surfactant is one of the primary excipients used in the creation of nanoemulsions. Nanoemulsions improve the transport and digestion of active substances due to their small size and high surface area to volume ratio.In the field of drug delivery, for instance, they can facilitate the passage of pharmaceuticals across biological membranes, hence boosting the bioavailability of medications that have low water solubility [76].

There are therapeutic advantages to creating brimonidine tartarate nanoemulsions with biocompatible lipids. The stability of the produced nano emulsion is verified using a zeta sizer. The nano preparation is examined using a transmission electron microscope to evaluate its morphological and physical properties [77]. Drug delivery via nano emulsions is being investigated for conditions like glaucoma, dry eye syndrome, and ocular infections. Antioxidants from nano emulsions can shield the eyes from inflammation and oxidative damage. This can aid in the treatment of conditions such as degenerative eye diseases and age-related macular degeneration (Table.1) [77-80] (104)

Nanosuspension

Colloidal dispersion of submicron sized medication particles stabilized by polymers, surfactants, or both are known as nanosuspensions [81]. Because of their adaptability, these systems have drawn interest in the delivery of drugs to the eyes [82] .

Table 1: Nanocarriers used in ophthalmology (taken from Rajan et al. Cureus 17(8): e66476. DOI 10.7759/cureus.66476 (Ref 104)

Nanocarriers	Size	Description	Marketed preparations
Solid lipid nanoparticles	10 to 500 nm	They are non-toxic carriers and maintain long-term stability and prevent lipophilic drug decomposition. They easily modify the surface for targeted delivery of drugs.	Natacyn
Polymeric nanoparticles	<400 nm	Target-specific delivery of drugs. They increase treatment efficacy by avoiding nonspecific distribution and reaching the correct ocular tissues. Drug degradation can be prevented. They enhance the absorption of drugs by boosting intracellular penetration.	Timoptic
Liposomes	0.08 to 10.00 µm	Water-soluble as well as fat-soluble drugs can be encapsulated. They are non-toxic and biocompatible. Corneal permeability can be improved.	Lipoquin
Niosomes	10 to 1000 nm	Drug delivery to ocular tissues with targeted distribution and controlled release, hence improving the drug's bioavailability. They are less toxic, biodegradable, biocompatible, and mucoadhesive.	Cyclopentol
Nanosuspensions	10 to 1000 nm	They enhance the bioavailability of ophthalmic medicines by improving their ability to dissolve. They also increase the duration of drug release and prolong the residency time in the cul-de-sac because it can make drugs that are poorly soluble in water more soluble in lacrimal fluid.	Rimoflo T Eye Drops, ILEVRO (Nepafenac ophthalmic suspension)
Nanostructured lipid carriers	50 to 1000 nm	They are biocompatible and stable and prevent the release of drugs when they are stored. They increase the drug's bioavailability to the ocular tissue.	Tetrandrine
Nanoemulsion	100 nm	They are clear and thermodynamically stable. They prolong the drug's release and increase its solubility, which lower the frequency of the dose. Corneal permeability is increased.	Cationorm ophthalmic emulsion, Durezol (difluprednate ophthalmic suspension)
Dendrimers	5 to 20 nm	Delivering lipophilic and hydrophilic drugs is feasible. They increases the solubility of the drugs and demonstrate significant drug loading and sustained release.	PAMAM (G1.5-4.0), PAMAM core micelle

They are appropriate for treating a variety of ocular disorders since they can be delivered via topical, intravitreal, and periocular injections, among other ways. Furthermore, the medicine can be released gradually by nanosuspensions, which lessens the need for frequent administration and increases patient compliance [83] . By improving the solubility and bioavailability of hydrophobic medication, nanosuspensions solve this issue and produce better therapeutic results [84] . Moreover,

nanosuspensions are safe for ocular applications since the inclusion of biocompatible stablizers reduces the possibility of toxicity and irritation [85] .There are several uses for nanosuspensions in ocular medication delivery. For example, anti-inflammatory medication distribution and effectiveness have enhanced by the use of nanosuspensions.When used to treat uveitis, Indomethacin nanosuspensions have demonstrated improved anti-inflammatory benefits [86] . When it comes to treating eye infections, the administration of antibiotics using nanosuspensions can increase their efficacy. Research has shown that ciprofloxacin in nanosuspensions have better antibacterial activity than traditional formulations [87] . The use of nanosuspensions to deliver antifungal medicines is also being investigated . It has been demonstrated that amphotericin B nanosuspensions enhance medication penetration and effectiveness in the treatment of fungal keratitis [88. As evidenced by brinzolamide nanosuspensions, which have outperformed conventional eye drops in their ability to lower intraocular pressure, nanosuspensions can improve drug delivery for anti-glaucoma drugs [89] .Drugs that target ocular neovascularization are also delivered using nano suspensions. Triamcinolone acetonide nanosuspensions have demonstrated efficacy in mitigating neovascularization in diabetic retinopathy and AMD models [90] .

Nanocrystalline

Drug nanocrystals are pure drug particles that range in size from 10-1000nm. They can be stabilized using polymeric stabilizers or surfactants. The purpose of this size reduction technique is to increase the solubility of medications [91,92]

The Ostwald -Freundlich equation, the Kelvin equation, and the Noyes-Whitney equation are among the several hypotheses put out to support the idea of enhanced solubility [93] .

When administering hydrophobic medications to the eye, this technique is particularly helpful [92]

Nanomicelles

Micelles are highly structured supra molecular structures that are produces whom amphiphilic molecules self assemble in aquatic environments. Micelles can take many different shapes, including spherical, cylindrical, and starshaped, and they range in 10-1000nm. Surfactant, poly ionic complex, and polymeric micelles are the three main categories into which the current research on nano micelles for oral drug delivery (ODD) Can be divided [94,95] In most of these systems, polyethylene glycol is the primary hydrophilic component [96] . Hydrophobic medications can be encapsulated in the center of nano micelles to prevent disintegration. Their surface characteristics can be altered to target certain tissues, assuring sustained drug release and fewer systemic adverse effects, and their small size facilitates greater penetration through the corneal barrier. [96] .

Nanowafers

Using a fingertip, the nano wafer -a tiny, clear circular disc, is gently applied to the eyes surface. It stays stable even when blinking continuously. The drug loaded arrays of nano reservoirs in the device are released in a controlled fashion over a period of hours to days. In a mouse model of ocular burn, this study demonstrates that the application of this drug delivery technique enchances the efficacy of treatment for corneal neovascularization [97,98] E beem lithography is used in the fabrication process to create arrays of wells on the silicon wafer that have a diameter and depth of 500nm. Polyvinylpyrrolidone (PVP),

carboxymethylcellulose (CMC), and polyvinyl alcohol (PVA) nano wafers are manufactured in this study, along with PVA nanowafers loaded with doxycycline, suitinib, axitinib and sorafenib [98-102] .

Nanogels

Nanoscale particles made of crosslinked polymer networks that rapidly enlarge upon solvent absorption are reffered to as "nanogels" Originally, a bifunctional system consisting of a polyionic polymer and a nonionic polymer, more precisely, cross-linked polyethyleneimine (PEI) and poly(ethylene glycol)() (PEG), known as PEG-cl-PEI- was referred to as "nanogel" (NanoGel^{TM}) [103] .

Niosomes

Niosomes were added to gels to enhance the anti-glaucoma effects of latanoprost. More than 88% of the medication was encapsulated due to the non-specific interactions between latanoprost and the surfactant

CONCLUSION:

Drug delivery methods based on nanotechnology are becoming more and more common in biomaterial science and clinical pharmacology, especially in the treatment of eye conditions. By increasing drug permeability, stability, and targeted release, these nanocarriers increase medication bioavailability and decrease the frequency of dose.
These nanocarriers have shown increased therape utic efficacy, sustained and regulated release, targ eted distribution, and higher drug bioavailability.
With continuous research centered on customized medicine, multifunctional nanocarriers,Minimally invasive delivery techniques, combination therapies, and regenerative medicine , the future of nanotechnological developments in ophthalmology is bright. These technologies have the potential to revolutionize ocular drug delivery as they develop further, offering more individualized, efficient, and patient friendly therapies for a variety of eye conditions.These various models have produced uneven and perhaps contradictory toxicity or safety results.Because of their intricacy, nanocarrier materials may provide financial difficulties that limit their scalability and affordability. Numerous upscaling techniques might occasionally result in unanticipated modifications to the characteristics of nanoparticles.To overcome this obstacle, more creative research is needed to improve nanocarrier penetration and accomplish targeted delivery. Although nanocarriers show promise for ocular drug delivery, a comprehensive assessment is necessary to comprehend their benefits and drawbacks. This assessment should cover up capabilities, and regulatory considerations In summary ophthalmology's adoption of nanotechnology marks a substantial advancement in treating unmet needs and enhancing patient outcomes. To fully utilize nanotechnology in ocular drug delivery and eventually improve the vision and quality of life for millions of people worldwide, more research, creativity, and cooperation will be needed

Conflicts of interest: There are no conflicts of interest.

REFERENCE

1. Raghava S, Goel G, Kompella UB. Ophthalmic applications of nanotechnology. In: Tombran-Tink J, Barnstable CJ, editors. Ocular transporters in ophthalmic diseases and drug delivery. Humana Press; 2008. p. 415–35. https:// doi. org/ 10. 1007/ 978-1- 59745- 375-2_ 22. Print ISBN: 978-158829-958-1, Online ISBN: 978-1-59745-375-2.

2. Amrite AC, Kompella UB. Nanoparticles for ocular drug delivery. Nanoparticle technology for drug delivery. CRC Press 2006; 343. https:// doi. org/ 10. 1201/ 97808 493745 55. ch11
3. Kompella UB, Amrite AC, Ravi RP, Durazo SA. Nanomedicines for back of the eye drug delivery, gene delivery, and imaging. Prog Retin Eye Res. 2013; 36:172.
4. Ahmadkhani L, Mostafavi E, Ghasemali S, Baghban R, PazokiToroudi H, Davaran S, et al. Development and characterization of a novel conductive polyaniline-g-polystyrene/Fe3O4 nanocomposite for the treatment of cancer. Artif Cells Nanomed Biotechnol. 2019; 47:873.
5. Adelli GR, Bhagav P, Taskar P, et al. Development ofa Δ9-tetrahydrocannabinol amino acid-dicarboxylate prodrug withimproved ocular bioavailability. Invest Ophthalmol Vis Sci. 2017; 58:2167. doi:10.1167/iovs.16-207573.
6. Weinreb RN, Robinson MR, Dibas M, Stamer WD. Matrix metallo-proteinases and glaucoma treatment. J Ocul Pharmacol Ther. 2020 ; 36:208. doi:10.1089/jop.2019.01464.
7. DeSantis L. Preclinical Overview of Brinzolamide. Surv Ophthalmol. 2000; 44: S119
8. Mehta M, Deeksha SN, Vyas M, et al. Interactions with the macro-phages: an emerging targeted approach using novel drug deliverysystems in respiratory diseases. Chem Biol Interact. 2019; 304:10 . doi:10.1016/j.cbi.2019.02.0216.
9. Drescher S, van Hoogevest P. The phospholipid research center: cur-rent research in phospholipids and their use in drug delivery. Pharmaceutics. 2020 ; 1:12.
10. Bozzuto G, Molinari A. Liposomes as nanomedical devices. Int J Nanomedicine. 2015 ; 975.
11. Li, S.; Chen, L.; Fu, Y. Nanotechnology-based ocular drug delivery systems: Recent advances and future prospects. J. Nanobiotechnol. 2023 ; 21: 232.
12. Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo CK, et al. TFOS DEWS II definition and classification report. Ocul Surf. 2017; 15(3):276.
13. Group DEW. The definition and classification of dry eye disease: report of the definition and classification subcommittee of the international dry eye workshop. Ocul Surf. 2007 ; 5:75.
14. Stern ME, Beuerman RW, Fox RI, Gao J, Mircheff AK, Pflugfelder SC. The pathology of dry eye: the interaction between the ocular surface and lacrimal glands. Cornea. 1998;17(6):584.
15. Miljanović B, Dana R, Sullivan DA, Schaumberg DA. Impact of dry eye syndrome on vision-related quality of life. Am J Ophthalmol. 2007;143(3):409–15.
16. Lemp MA, Foulks GN. The definition and classification of dry eye disease. Ocul Surf. 2007;5(2):75–92.
17. Shin YJ, Hyon JY, Choi WS, Yi K, Chung ES, Chung TY, et al. Chemical injury-induced corneal opacity and neovascularization reduced by rapamycin via TGF-β1/ERK pathways regulation. Invest Ophthalmol Vis Sci. 2013 ; 54(7):4452.
18. Yuan X, Marcano DC, Shin CS, Hua X, Isenhart LC, Pflugfelder SC, et al. Ocular drug delivery nanowafer with enhanced therapeutic efficacy. ACS Nano. 2015 ; 9(2):1749.
19. Ludwig A. The use of mucoadhesive polymers in ocular drug delivery. Adv Drug Deliv Rev. 2005 ; 57(11):1595.
20. van Alem CMA, Metselaar JM, van Kooten C, Rotmans JI. Recent advances in liposomal-based anti-inflammatory therapy. Pharmaceutics. 2021; 13(7):1004.

21. Wang TZ, Liu XX, Wang SY, Liu Y, Pan XY, Wang JJ, et al. Engineering advanced drug delivery systems for dry eye: a review. Bioengineering. 2023; 10(1):53.
22. Garrigue JS, Amrane M, Faure MO, Holopainen JM, Tong L. Relevance of lipid-based products in the management of dry eye disease. J Ocul Pharmacol Ther. 2017 ; 33(9):647.
23. López-Machado A, Díaz-Garrido N, Cano A, Espina M, Badia J, Baldomà L, et al. Development of lactoferrin-loaded liposomes for the management of dry eye disease and ocular inflammation. Pharmaceutics. 2021 ; 13(10):1698.
24. Huang L, Gao H, Wang Z, Zhong Y, Hao L, Du Z. Combination nanotherapeutics for dry eye disease treatment in a rabbit model. Int J Nanomedicine. 2021; 26(16):3613.
25. Dhull A, Yu C, Wilmoth AH, Chen M, Sharma A, Yiu S. Dendrimers in corneal drug delivery: recent developments and translational opportunities. Pharmaceutics. 2023 ; 15(6):1591.
26. Burhan AM, Klahan B, Cummins W, Andrés-Guerrero V, Byrne ME, O'Reilly NJ, et al. Posterior segment ophthalmic drug delivery: role of muco-adhesion with a special focus on chitosan. Pharmaceutics. 2021 ; 13(10):1685.
27. Yoo J, Won YY. Phenomenology of the initial burst release of drugs from PLGA microparticles. ACS Biomater Sci Eng. 2020 ; 6(11):6053.
28. Li S, Chen L, Fu Y. Nanotechnology-based ocular drug delivery systems: recent advances and future prospects. J Nanobiotechnol. 2023; 21(1):232.
29. Kattar A, Quelle-Regaldie A, Sánchez L, Concheiro A, Alvarez-Lorenzo C. Formulation and characterization of epalrestat-loaded polysorbate 60 cationic niosomes for ocular delivery. Pharmaceutics. 2023 ; 15(4):1247.
30. Rizvi SAA, Saleh AM. Applications of nanoparticle systems in drug delivery technology. Saudi Pharm J SPJ Off Publ .Saudi Pharm Soc. 2018 ; 26(1):64.
31. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. Ophthalmology. 2014 ; 121(11):2081.
32. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. JAMA. 2014; 311(18):1901–11.
33. Santra R, Munshi S. Emerging glaucoma therapeutics. Int J Basic Clin Pharmacol. 2015; 4(4):606.
34. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmol. 2002 ; 86(2):238.
35. Casson RJ, Chidlow G, Wood JP, Crowston JG, Goldberg I. Definition of glaucoma: clinical and experimental concepts. Clin Exp Ophthalmol. 2012 ; 40(4):341.
36. Ahmed I, Patton TF. Importance of the noncorneal absorption route in topical ophthalmic drug delivery. Invest Ophthalmol Vis Sci. 1985 ; 26(4):584.
37. Burstein NL, Anderson JA. Corneal penetration and ocular bioavailability of drugs. J Ocul Pharmacol. 1985 ; 1(3):309 .
38. Shell JW. Ophthalmic drug delivery systems. Surv Ophthalmol. 1984; 29(2):117.
39. Kass MA, Heuer DK, Higginbotham EJ, Johnson CA, Keltner JL, Miller JP, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch

Ophthalmol Chic Ill 1960. 2002;120(6):701–13

40. Occhiutto ML, Maranhão RC, Costa VP, Konstas AG. Nanotechnology for medical and surgical glaucoma therapy-a review. Adv Ther. 2020; 37(1):155.
41. Watcharadulyarat N, Rattanatayarom M, Ruangsawasdi N, Patikarnmonthon N. PEG–PLGA nanoparticles for encapsulating ciprofloxacin. Sci Rep. 2023; 13(1):266.
42. Pei K, Georgi M, Hill D, Lam CFJ, Wei W, Cordeiro MF. Review: neuroprotective nanocarriers in glaucoma. Pharmaceuticals. 2024;17(9):1190.
43. Guo X, Zuo X, Zhou Z, Gu Y, Zheng H, Wang X, et al. PLGA-based micro/nanoparticles: an overview of their applications in respiratory diseases. Int J Mol Sci. 2023; 24(5):4333.
44. Zhang J, Sun H, Gao C, Wang Y, Cheng X, Yang Y, et al. Development of a chitosan-modified PLGA nanoparticle vaccine for protection against Escherichia coli K1 caused meningitis in mice. J Nanobiotechnology. 2021 ; 19(1):69.
45. Liu LC, Chen YH, Lu DW. Overview of recent advances in nano-based ocular drug delivery. Int J Mol Sci. (2023)24(20):15352.
46. Mungenast L, Nieminen R, Gaiser C, Faia-Torres AB, Rühe J, Suter-Dick L. Electrospun decellularized extracellular matrix scaffolds promote the regeneration of injured neurons. Biomater Biosyst. 2023 ; 18(11):100081.
47. J H, M Y, Gh Y, G K. Cell-electrospinning and its application for tissue engineering. Int J Mol Sci. 2019; [cited 2024 Oct 14]; 20(24). https:// pubmed. ncbi. nlm. nih. gov/ 31835 356/
48. Lambuk L, Suhaimi NAA, Sadikan MZ, Jafri AJA, Ahmad S, Nasir NAA, et al. Nanoparticles for the treatment of glaucoma-associated neuroinflammation. Eye Vis. 2022 ; 9(1):26.
49. Qin M, Yu-Wai-Man C. Glaucoma: novel antifibrotic therapeutics for the trabecular meshwork. Eur J Pharmacol. 2023 ; 5(954):175882.
50. Yang B, Li G, Liu J, Li X, Zhang S, Sun F, et al. Nanotechnology for age-related macular degeneration. Pharmaceutics.(2021 ;13(12):2035.
51. Steinmetz JD, Bourne RRA, Briant PS, Flaxman SR, Taylor HRB, Jonas JB, et al. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the right to sight: an analysis for the global burden of disease study. Lancet Glob Health. 2021; 9(2):144.
52. Asbell PA, Dualan I, Mindel J, Brocks D, Ahmad M, Epstein S. Age-related cataract. Lancet Lond Engl. 2005; 365(9459):599.
53. Kessel L, Erngaard D, Flesner P, Andresen J, Tendal B, Hjortdal J. Cataract surgery and age-related macular degeneration. An evidencebased update. Acta Ophthalmol (Copenh). 2015; 93(7):593.
54. Prokofyeva E, Wegener A, Zrenner E. Cataract prevalence and prevention in Europe: a literature review. Acta Ophthalmol (Copenh). 2013;91(5):395.
55. Lamoureux EL, Fenwick E, Pesudovs K, Tan D. The impact of cataract surgery on quality of life. Curr Opin Ophthalmol. 2011 ; 22(1):19.
56. Apple DJ, Solomon KD, Tetz MR, Assia EI, Holland EY, Legler UF, et al. Posterior capsule opacification. Surv Ophthalmol. 1992 ; 37(2):73.
57. Cetinel S, Montemagno C. Nanotechnology for the prevention and treatment of cataract. Asia-Pac J Ophthalmol Phila Pa. 2015; 4(6):381.
58. Krishnaswami V, Kandasamy R, Alagarsamy S, Palanisamy R, Natesan S. Biological macromolecules for ophthalmic drug delivery

to treat ocular diseases. Int J Biol Macromol. 2018 ; 15(110):7.
59. Chen Y, Ye Z, Chen H, Li Z. Breaking barriers: nanomedicine-based drug delivery for cataract treatment. Int J Nanomedicine. 2024 ; 6(19):4021.
60. Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. Lancet Lond Engl. 2010; 376 (9735): 124.
61. Yau JWY, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. Diab Care. 2012 ; 35(3):556.
62. Wilkinson CP, Ferris FL, Klein RE, Lee PP, Agardh CD, Davis M, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology. 2003 ; 110(9):1677.
63. American Diabetes Association. 10. Microvascular complications and foot care: standards of medical care in diabetes-2018. Diab Care. 2018; 41: 105
64. Stewart MW. Anti-VEGF therapy for diabetic macular edema. Curr Diab Rep. 2014; 14(8):510.
65. Garg S, Davis RM. Diabetic retinopathy screening update. Clin Diab. 2009;27(4):140.
66. Virgili G, Parravano M, Evans JR, Gordon I, Lucenteforte E. Anti-vascular endothelial growth factor for diabetic macular oedema: a network meta-analysis. Cochrane Database Syst Rev.2017 ; 6(6):CD007419.
67. Bhagat N, Grigorian RA, Tutela A, Zarbin MA. Diabetic macular edema: pathogenesis and treatment. Surv Ophthalmol. 2009; 54(1):1.
68. Xu Q, Kambhampati SP, Kannan RM. Nanotechnology approaches for ocular drug delivery. Middle East Afr J Ophthalmol. 2013 ; 20(1):26.
69. Wang Z, Zhang N, Lin P, Xing Y, Yang N. Recent advances in the treatment and delivery system of diabetic retinopathy. Front Endocrinol. 2024. https:// doi. org/ 10. 3389/ fendo. 2024. 13478 64/ full.
70. Wong KY, Wong MS, Liu J. Nanozymes for treating ocular diseases. Adv Healthc Mater. 2024. 13:e2401309.
71. Chen Z, Li Z, Tang N, Huang Y, Li S, Xu W, et al. Engineering ultra-small cerium-based metal-organic frameworks nanozymes for efficient antioxidative treatment of dry eye disease. Adv Funct Mater. 2024 ; 34(6):2307569.
72. Xue B, Lu Y, Wang S, Xiao Q, Luo X, Wang Y, et al. The emerging role of nanozymes in ocular antioxidant therapy. Nano Today. 2024 ; 58:102448.
73. Bodkhe AA, Bedi RS, Upadhayay A, Kale MK. Ophthalmic microemulsion: formulation design and process optimization. Res J Pharm Technol. 2018 ; 11(12):5474–82.
74. Siekmann B, Westesen K. Submicron-sized parenteral carrier systems based on solid lipids. Pharm Pharmacol Lett. 1992 ; 1(3):123.
75. Choradiya BR, Patil SB. A comprehensive review on nanoemulsion as an ophthalmic drug delivery system. J Mol Liq. 2021; 339:116751.
76. Troy DB, Beringer P. Remington: the science and practice of pharmacy. Lippincott Williams & Wilkins; 2006 ; 2452.
77. Ali Y, Lehmussaari K. Industrial perspective in ocular drug delivery. Adv Drug Deliv Rev. 2006;58(11):1258–68.
78. Vandamme TF. Microemulsions as ocular drug delivery systems: recent developments and future challenges. Prog Retin Eye Res. 2002; 21(1):15.
79. Siekmann B, Westesen K. Submicron-sized parenteral carrier systems based on solid

lipids. Pharm Pharmacol Lett. 1992;1(3):123–.

80. Oliverio GW, Spinella R, Postorino EI, Inferrera L, Aragona E, Aragona P. Safety and tolerability of an eye drop based on 0.6% povidone iodine nanoemulsion in dry eye patients. J Ocul Pharmacol Ther. 2021;37(2):90–6.
81. Müller RH, Jacobs C, Kayser O. Nanosuspensions as particulate drug formulations in therapy. Rationale for development and what we can expect for the future. Adv Drug Deliv Rev. 2001 ; 47(1):3.
82. Kesisoglou F, Panmai S, Wu Y. Nanosizing: oral formulation development and biopharmaceutical evaluation. Adv Drug Deliv Rev. 2007 ; 59(7):631.
83. Merisko-Liversidge E, Liversidge GG. Nanosizing for oral and parenteral drug delivery: a perspective on formulating poorly-water soluble compounds using wet media milling technology. Adv Drug Deliv Rev. 2011 ; 63(6):427.
84. Patravale VB, Date AA, Kulkarni RM. Nanosuspensions: a promising drug delivery strategy. J Pharm Pharmacol. 2004 ; 56(7):827.
85. Shegokar R, Müller RH. Nanocrystals: industrially feasible multifunctional formulation technology for poorly soluble actives. Int J Pharm. 2010 ; 399(1–2):129.
86. Das S, Suresh PK. Nanosuspension: a new vehicle for the improvement of the delivery of drugs to the ocular surface. Application to amphotericin B. Nanomed Nanotechnol Biol Med. 2011; 7(2):242.
87. Alhajj N, O'Reilly NJ, Cathcart H. Development and characterization of a spray-dried inhalable ciprofloxacin-quercetin co-amorphous system. Int J Pharm. 2022 ; 25(618):121657.
88. Agnihotri SM, Vavia PR. Diclofenac-loaded biopolymeric nanosuspensions for ophthalmic application. Nanomed Nanotechnol Biol Med. 2009;5(1):90.
89. Bagul US, Nazirkar MV, Mane AK, Khot SV, Tagalpallewar AA, Kokare CR. Fabrication of architectonic nanosponges for intraocular delivery of Brinzolamide: an insight into QbD driven optimization, in vitro characterization, and pharmacodynamics. Int J Pharm. 2024; 5(650):123746.
90. Gao L, Liu G, Ma J, Wang X, Zhou L, Li X. Drug nanocrystals: In vivo performances. J Control Release Off J Control Release Soc. 2012; 160(3):418.
91. Malkani A, Date AA, Hegde D. Celecoxib nanosuspension: single-step fabrication using a modified nanoprecipitation method and in vivo evaluation. Drug Deliv Transl Res. 2014; 4(4):365.
92. Shelar DB, Pawar SK, Vavia PR. Fabrication of isradipine nanosuspension by anti-solvent microprecipitation-high-pressure homogenization method for enhancing dissolution rate and oral bioavailability. Drug Deliv Transl Res. 2013 ; 3(5):384.
93. Junyaprasert VB, Morakul B. Nanocrystals for enhancement of oral bioavailability of poorly water-soluble drugs. Asian J Pharm Sci . 2015 ; 10(1):13.
94. Felt O, Furrer P, Mayer JM, Plazonnet B, Buri P, Gurny R. Topical use of chitosan in ophthalmology: tolerance assessment and evaluation of precorneal retention. Int J Pharm. 1999 ; 180(2):185 .
95. Vaishya RD, Khurana V, Patel S, Mitra AK. Controlled ocular drug delivery with nanomicelles. WIREs Nanomed Nanobiotechnol. 2014 ; 6(5):422.
96. Mandal A, Bisht R, Rupenthal ID, Mitra AK. Polymeric micelles for ocular drug delivery: from structural frameworks to recent

preclinical studies. J Control Release Off J Control Release Soc. 2017 ; 28(248):96.

97. Shin YJ, Hyon JY, Choi WS, Yi K, Chung ES, Chung TY, et al. Chemical injury-induced corneal opacity and neovascularization reduced by rapamycin via TGF-β1/ERK pathways regulation. Invest Ophthalmol Vis Sci. 2013;54(7):4452
98. Yuan X, Marcano DC, Shin CS, Hua X, Isenhart LC, Pflugfelder SC, et al. Ocular drug delivery nanowafer with enhanced therapeutic efficacy. ACS Nano. 2015 ; 9(2):1749.
99. Ludwig A. The use of mucoadhesive polymers in ocular drug delivery. Adv Drug Deliv Rev. 2005 ; 57(11):1595
100. Aragona P, Spinella R, Rania L, Postorino E, Sommario MS, Roszkowska AM, et al. Safety and efficacy of 0.1% clobetasone butyrate eyedrops in the treatment of dry eye in sjögren syndrome. Eur J Ophthalmol. 2013 ; 23(3):368.
101. Acharya G, Shin CS, McDermott M, Mishra H, Park H, Kwon IC, et al. The hydrogel template method for fabrication of homogeneous nano/microparticles. J Controlled Release. 2010; 141(3):314.
102. Acharya G, Shin CS, Vedantham K, McDermott M, Rish T, Hansen K, et al. A study of drug release from homogeneous PLGA microstructures. J Controlled Release. 2010 ; 146(2):201.
103. Brannigan RP, Khutoryanskiy VV. Synthesis and evaluation of mucoadhesive acryloyl-quaternized PDMAEMA nanogels for ocular drug delivery. Colloids Surf B Biointerfaces. 2017; 1(155):538.
104. Praiseth Bellston Rajan , Jebastin Koilpillai and Damodharan Narayanasamy, Advancing Ocular Medication Delivery with Nano-Engineered Solutions: A Comprehensive Review of Innovations, Obstacles, and Clinical Impact, Cureus ., 17(8) (2024) e66476. DOI 10.7759/cureus.66476.

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