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# REVIEW ON NANOTECHNOLOGY BASED ON OCULAR DRUG DELIVERY SYSTEM

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## ➢ ABSTRACT

Ocular drug delivery faces significant challenges due to the eye's complex anatomy and physiological barriers. Conventional eyedrops have limited bioavailability, leading to reduced efficacy and increased systemic side effects. Recent innovations aim to overcome these hurdles.

This review discusses.

1. Novel drug delivery systems: nanoparticles, liposomes, microneedles, and implants.
2. Sustained release technologies: contact lenses, ocular inserts, and biodegradablepolymers.
3. Targeted delivery approaches: prodrugs, gene therapy, and stem cell-based therapies.
4. Anterior and posterior segment targeting strategies.
5. Challenges, regulatory considerations, and future directions.

Recent studies demonstrate improved therapeutic outcomes for glaucoma, age-related macular degeneration, and diabetic retinopathy. Translating these innovations into clinical practice requires addressing scalability, biocompatibility, and cost-effectiveness.

**KEYWORDS**: ocular drug delivery, nanoparticles, sustained release, targeted therapy.

## ➢ INTRODUCTION

The eye is an extremely delicate organ that possesses a complex physiology. It consists of both anterior and posterior segments. In most cases, the quality of life is greatly impacted by visual impairment caused by different diseases. Cataract is the leading cause of blindness worldwide. Approximately 40–60% of vision loss worldwide arises as a complication of cataracts.[1] Ocular disposition and elimination of a therapeutic agent rely on its

physicochemical properties, along with the pertinent ocular anatomy and physiology. To create a successful drug delivery system, one must possess a comprehensive understanding of both the drug molecule and the specific limitations associated with administering it through the ocular route.[2] Ocular formulations are designed for application on the anterior surface of the eye via the topical route, intraocularly, periocularly (subtenon or juxtascleral), or in combination with ocular devices. Ocular dosage forms may come in liquid, semi- solid, solid, or mixed formats. Liquid dosage includes drops, suspension, and emulsion. Eye drops account for over 95% of the ocular products available in the market.[3] Smooth Version: Achieving efficient ocular absorption requires suitable corneal penetration and effective precorneal residence time to achieve and maintain a sufficient drug concentration with minimal active therapeutic ingredient. Nanosystem are advanced technologies designed to overcome ocular obstacles, protect the drug from the biological environment, prolong drug residence time, and enhance corneal permeation across biological barriers.[4]

The characterization of the developed nanosystems is crucial to verify their capacity to perform the intended function. Various methods for characterization exist, including assessing visual characteristics, stability, size, zeta potential, potential interactions, pH assessment, and other essential ex vivo and in vivo evaluations.[5]

## ➢ ANATOMY OF THE EYE

The human eye is made up of front and back chambers. The forefront The segment consists of tear film, cornea, pupil, lens, and ciliary structure. The posterior segment consists of con conjunctiva, sclera, choroid, retina, vitreous body, and optic nerve. The formation and amount of tears are regulated by glands of the orbit and secretions from epithelial tissue. Cornea is the forefront segment of the eye that transmits and directs light into the sight. It is categorized into epithelium, stroma, and endothelium. The epithelium consists of five to seven layers of tightly connected linked cells. Stroma is a dense layer that is water-based. It seems like your message may have been cut off. Please provide the complete text that you'd like me to paraphrase, and I'll be happy to assist. The endothelium maintains the clarity of the cornea.[6] Iris refers to the colored part of the eye that regulates the amount of light entering the eye. The opening at the dark center The part at the center of the iris is known as the pupil. The student transforms. its dimensions based on the light that is present. The lens is clear. section that directs the light onto the retina. The ciliary body is composed of pigmented and non-pigmented ciliary epithelium, a stroma, and ciliary muscles. Capillaries of the ciliary

body enable interaction between the anterior and posterior segments. The vitreous humor is a clear, gel-like, avascular connective tissue located between the eye lens and the retina. It consists of 99.9% water, hyaluronic acid, ions, and collagen.[7] It seems that your input text is incomplete. Could you please provide the full text you would like paraphrased The conjunctiva is a thin, clear membrane that lines the interior. the eyelids protect the front part of the sclera. It is a mucous membrane made up of three layers, an external epithelium, a connective tissue containing nerves, lymphatic and blood vessels, along with a submucosa layer connected to the sclera.[8]

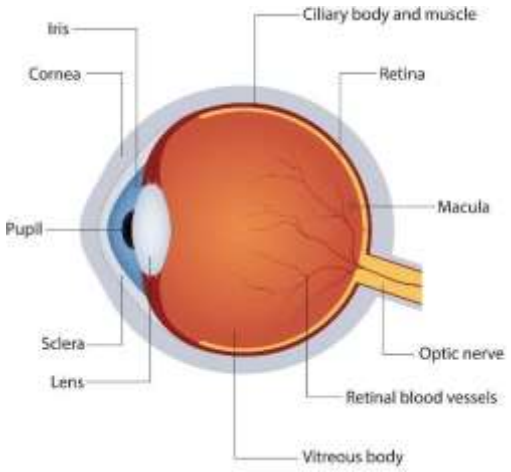



**Fig 1: Anatomy of the human eye.[9]**

➢ **Route of drug administration**

**Topical route of administration**

In contrast to systemic administration, it offers benefits such as (1) being relatively non-invasive, (2) reducing systemic side effects of the medication, and (3) the relative simplicity of patient administration.[10] Nevertheless, because of the distinct physiological and anatomical Due to the anatomical design of the eye, the administration of drugs within the eye is restricted, and bioavailability typically is below 5%[11] Elevated substance frequent applications and continuous administration are typically required to enhance the effectiveness of medication delivery via the local path, which could result in suboptimal patient adherence and various adverse effects[12] There are two primary approaches to enhance ocular bioavailability following local application.

(a) enhance the pre-corneal retention duration, and (b) improve the permeability capability of corneal, scleral,or conjunctival medications.[13]

**Intracameral Injections**

Intracameral injections consist of administering an antibiotic via injection. straight into the front part of the eyeball or in the aqueous chamber. It is typically performed after cataract surgery to prevent endophthalmitis caused by an infection of the eye that may arise following cataract surgery. Recently, the application Indication for intracameral injection as a therapy for glaucoma. utilizing hydrogel modified with vinyl sulfone and thiol groups were released.[14]

**Intravitreal injections**

Intravitreal injection is a method for administering medication into the vit tissue that is adjacent to the retina located at the rear of the eye. A novel method for treating glaucoma involves a single intravitreal administration of vitamin E/poly-lactic-co-glycolic acid microspheres encapsulating glial cell line derived neurotrophic element. This method offered an extended release for a duration of 6 months. Comparable outcomes were achieved following intravitreal. injection ofdexamethasone dimer implants without polymers.[15]

**Retrobulbar injection**

The retrobulbar pathway entails inserting a needle through the eyelid and orbital tissue to administer the medication behind the globe into the space behind the eyeball. Intraocular injection Amphotericin B demonstrated greater antifungal effectiveness than IV injection.[16] Retrobulbar administration of triamcinolone is employed to treat macular swelling occurred due to blockageof the retinal vein.[17]

**Irrigating solution**

They are preparations created in sterileconditions without the addition of preservatives. They are utilized as balanced salts. by surgeons to remove blood, cellular debris, and sustain the correct amount of eye hydration.[18]

**Subconjunctival injection**

Subconjunctival delivery is a low-invasivemethod. and efficient pathway to transport drugs to the front or posterior eye chamber, steering clear of the cornea and blood water barriers, possible negative impacts and initial pass metabolism of certain systemic substances.[19]

**Juxtascleral Injections**

Juxtascleral injections are employed for the treatment of certain complaints from the back

section that cannot be addressed through traditional topical approach. It is utilized for the management of cystoid macular edema, injury, and diabetes- related conditions It seems that the text you provided. is incomplete and lacks context. Please provide the complete text you would like paraphrased, and I'll be happy to help! A novel method for treating AMD includes juxtascleral injections of anecortave cortisone that demonstrated prosought liberation for 6 months within the choroid and retina.[20]

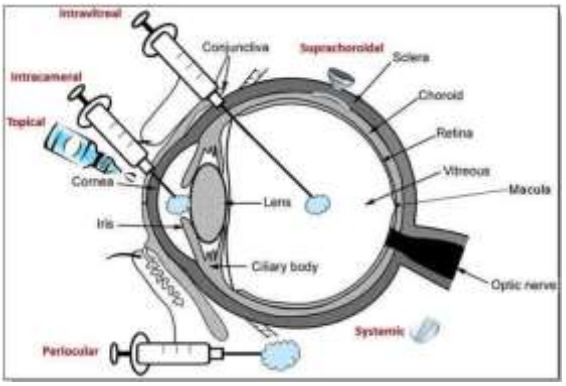
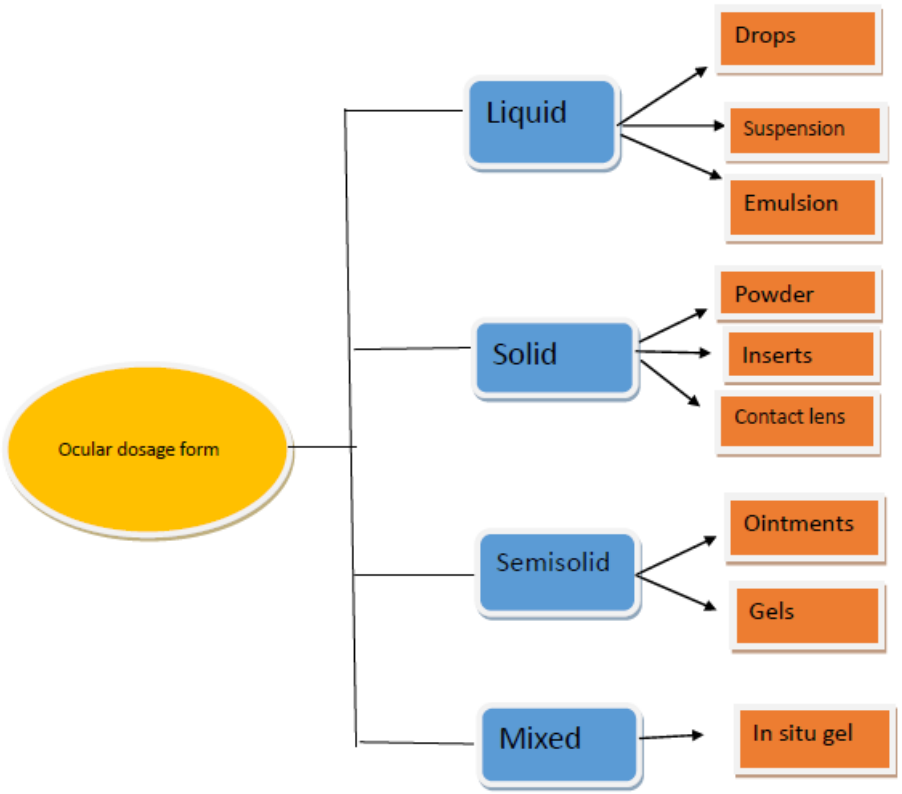



**Fig 2: Different route of drugadministration.**[21]

- **Classification of ocular dosage form**[22]



➢ **Nanotechnology based on ocular drugdelivery**

**Liposomes**

They are spherical nanocarriers composed of one or several concentric lipid layers bilayer structures. They were able to transport lipophilic medications within thelipid region, while the interior could capture hydrophilic medications.

Modifying the method of formation and their makeup could change their surface electrical charge, responsiveness to ions or pH levels, or temperature modifications and the resulting particle size[23] It appears that your request was cut off.

Could you please provide the complete text you would like me to paraphrase? Neural epithelium carries a negative charge; hence, a positively Charged liposomes are expected to exhibit strong adhesion and extended retention. tion duration, and improved absorption. These results will diminish the gap between doses and enhance patient contentment[24] Zhang and Wang developed a liposomal system made up of phosphatidylcholine, cholesterol, α-tocopherol, and chitosan. The resulting formula demonstrated a high percentageof entrapment, continuous effort, and improved effectiveness.[25]

**Nanomicelles**

Nanomicelles are nanocarriers structured as core–shell formations created by unplanned organization of amphiphilic copolymers with hydrophobic components at the center and hydrophilic components as the external layer.[26] Typically, the size of the particles varies ranging from 10 to 100 nm and can be classified into three categories. Categories: polymers, surfactants, and multi-ion composites nanomicelles[27] Moreover, nonpolar interactions, Hydrogen bonds, electrostatic attractions, and similar forces are the factors influencing the creation of polymer micelles[28] Positive micelles are typically created when the hydrophobic moiety creates clusters inside the core and the hydrophilic moiety is oriented outward to enhance interaction with liquid. Similarly, when the reverse configuration takes place, The aggregates are known as reverse micelles.[29] The distinct chemical structure of nanomicelles can internally solubilize drugs, minimizing side effects. tions, enhance the reliability of medications, and maintain a prolonged release effect, considered safe options for ocular medication administration.[30,31]

**Microemulsions**

Microemulsions represent the most promising submicron medication. carriers, particularly for

drugs that are poorly soluble in water. At the At the same time, microemulsions are stable from a thermodynamic perspective. affordable, cost-effective, and comparatively easy to manufacture.[32] Numerous studies have shown the effectiveness of microemulsions in transporting various medications to different problems related to the eye. For example, Mahran and colleagues utilized oleic acid, Cremophor EL, along with propylene glycol, to create microemulsion preparations infused with TA for the treatment of uveitis. Various diagramas de fases pseudoternarios también fueron conconstructed using the water titration approach, and the formulation made up of oil, surfactant-co- surfactant (1:1), and water (15:35:50% w/w, respectively) were found to be most effective (total drug release in 24 hours). uveitis-induced rabbit model, the created TA-loaded Microemulsion noticeably decreased inflammation symptoms, protein levels, and inflammatory cells in relation to suspensions available for commercial sale[33] Additionally, Santonocito et al. employed a new microemulsion system (NaMESys) to administer sorafenib to the retina NaMESys containing 0.3% sorafenib (NaMESys-SOR) exhibits strong cytocompatibility and tolerance. capability. It can also lessen pro- inflammatory and proangiogenic agents in a strong model of proliferation retinal disease. In addition, NaMESys-SOR notably suppressed the mRNA expression of tumor necrosis factor alpha (20.7%) and iNOS (87.3%) in rats with retinal ischemia– reperfusion in contrast to the experimental group. Additionally, NaMESys-SOR also monitors effectively suppressed 54% of the new blood vessel formation lesions in mice exhibiting laser- induced CNV. Los hallazgos indican que NaMESys eye drops could efficiently administer different medications. toward the retina.[34]

**Niosomes**

Niosomes are nanocarriers with bilayer structure made of self-assembled non- ionic surfactants. They can break down naturally, encompass both hydrophilic and lipophilic medications and non- immunogenic. They might extend the release of the drug and improve its permeability and effectiveness[35,36] Elmotasem and Awad created a niosomal system made up of span 60, cholesterol, and poloxamer. 407, methylcellulose hydroxypropyl, cyclodextrin, and chitosan.

The resulting formula demonstrated significant drug entrapment, improved corneal permeability, and effectiveness.[37]

**Nanosuspensions**

They are colloidal nanocarriers made up of lipophilic or semi-lipophilic medications,

dispersed in a medium solution and stabilized through the use of surfactants or polymers[38] The most frequently utilized mucoadhesive substances in Nanosuspensions consist of Eudragit® polymers. Pignatello and others. created a nanosuspension of cloricromene made up of Eudragit® RS and RL 100 along with Tween 80. The outcome formula demonstrated improved stability, cornealretention duration, and diffusion.[39]

**Polymeric Nanoparticles**

Polymeric nanoparticles can be classified based on their framework and technique for preparation into nanospheres and nanocapsules. Nanospheres are tiny solid spheres comcomposed of a compact polymer network. They possess a matrix. type material with a large surface area.

The medication might be absorbed on thesurface or enclosed within the particle.

Nonetheless, nanocapsules consist of a tiny liquid core surrounded by a membrane made of polymers. The medication might be absorbed onto thecapsule exterior or enclosed within the liquid center.[40]

**Nanostructured Lipid Carriers**

They are regarded as a second generation of lipid nanoparticles,consisting of approximately 30% liquid lipids, but the finished forMula is firm, lacking any crystalline formation.[41] Pai and Vavia developed nanostructured lipid carriers loaded with etoposide by employing various solid and liquid lipids, glyceryl stearyl citrate, and chitosan. The resulting formula demonstrated ongoing and enhanced activity.[42]

**Nanocrystals**

The medication consists primarily of nanocrystal structures, being surrounded and supported by various excipients. They possess minimal particle dimensions, straightforward creation methods, excellent mucoadhesion characteristics, and enhanced bioavailability.[43]

Tuomela et al. developed nanocrystals containing brinzolamide utilizing poloxamer F68/F127, polysorbate 80, and hydroxypropyl methylcellulose. The completed formula showed instant dissolution. and enhanced effectiveness.[44]

**Dendrimers**

They are 3D structures that are highly branched and resemble stars or trees. framework, made up of repeating molecules surrounding a main center[43] They demonstrated prolonged

residence duration, prodesired action, enhanced bioavailability, directed delivery, and properties that combat microorganisms. They might shift medical-Connections to both parts of the eye.[4]

**Cubosomes**

They are cubic liquid crystalline nanocarriers that are bicontinuous. created through the emulsification of lipids in water with the assistance of stabilizing agent. They are stable, capture significant quantities of drugs because of their extensive surface area, simple to produce, biodegradable, and fairly safe. El Deep et al. developed cubosomes loaded with brimonidine tartrate using glyceryl monooleate and poloxamer 407. The resulting formula showed prolonged release, enhanced permeation, and increased bioavailability.[45]

**Bilosomes**

Bilosomes are nanocarriers with two layers that include bile salts. They possess significant drug entrapment and small particle size, acknowledged zeta potential, recognized safety, improved corneal pervasion, and engagement. Abdelbary et al. created bilosomes loaded with terconazole using cholesterol, span 60, and an edge activator. The resulting formula demonstrated excellent entrapment, boosted penetration and increased effectiveness.[46]

**Olaminosomes**

Olaminosomes primarily consist of oleic acid and oleylamine, and surface-active agent. Oleic acid is a naturally occurring unsaturated free fatty acid. Oleic acid is non-toxic, environmentally friendly, and compatible with biological systems.

Therefore, oleic Acid is frequently utilized in the formulation of ocular nanocarrier.[47]

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