# EMERGING DEVELOPMENTS IN OCULAR DRUG DELIVERY SYSTEMS

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**Abstract**

The eye is a particularly safe organ due to its structure and function. A successful treatment for eye illnesses, especially those affecting the retina and optic nerve, has been viewed as an enormous challenge. Scientists have been pushed to develop novel modes of administration such periocular channels due to the limitations of topical and intravitreal routes. Ocular medication delivery systems typically face difficulties with ocular barriers and active drug bioavailability. Microneedle, iontophoresis, dendrimers, and other applications of nanotechnology have showed promise in the treatment of ocular disorders. The development of novel delivery systems would benefit substantially from an improved knowledge of the causes, symptoms, and treatment of ocular illnesses. Future research and development efforts will focus heavily on creating non-invasive sustained medication release for treating both anterior and posterior segment eye problems.

**Keywords:** Ocular delivery systems, Periocular channels, Intravitreal routes, Novel delivery systems and Nanotechnology.

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## INTRODUCTION

A system, vehicle, or dosage form developed for instilling, administering, or delivering medicine to the eye against any affliction or disorder predominantly affecting vision is referred to as an ocular drug delivery system. One of the trickiest challenges for pharmaceutical chemists has been perfecting ocular medicine delivery. The human's eye is a highly immune organ to foreign particles because of its structure, physiology, and biochemistry. For treating ocular diseases that threaten vision, the use of traditional methods such suspensions, ointments and eye drops cannot be regarded as optimum. How strange that eye drops make up more than 90% of the commercially available ophthalmic formulations. These formulas primarily focus on the eye's frontal region. The rear of the eye is not reached by topical ocular treatments. Intravenous high dosage regimens, intravitreal injections, implants, and periocular injections are all viable therapeutic alternatives for the posterior segment (retina, vitreous, and choroid). Significant emphasis is currently being focused on the topic of medicine distribution to the back of the eye[1].

The formulator faces a huge hurdle in getting through the eye's protective barriers without enduring long-term tissue damage. The advancement of improved, Ocular delivery systems continues to have excellent therapeutic efficacy thanks to more sensitive diagnostic methods and cutting-edge therapeutic compo-nents[2]. Distribution and elimination of the medication depend on the drug's physicochemical properties, which in turn depend on the architecture and physiology of the eye. Therefore, the creation of an efficient drug delivery system requires an in-depth understanding of both the drug molecule and the constraints imposed by the ocular route of administration. The many diverse tissues that make up the eye make it difficult to design efficient ocular delivery methods. Therefore, the pharmacological substances must be dispersed to numerous places across the entire ocular globe[3].

### 1. Contact lens

As an innovative drug delivery technology, soft drug-loaded contact lenses outperform conventional eye drops in terms of drug absorption through the corneal epithelium. Increasing the drug's bioavailability requires increasing the drug's contact time on eye. Antifungal drugs can now be delivered through a variety of soft contact lenses for up to 21 days. For instance, timolol maleate, dorzolamide HCl, and vitamin E (additive)-filled contact lenses are employed to accomplish sustained pharmaceutical release. Contact lenses, being so close to the cornea, have the highest drug absorption compared to other non-invasive ophthalmic treatments[4].

**Fig – 1:** Contact lens

Various drug releasing contact lenses have been developed, they are yet to get US FDA- approval.[4] The primary challenge this treatment faces is proving itself to be safer and more effective than current eye drops. Corneal toxicity can be observed if contact lens are used for an extended period of time. Analysis of some parameters, such as resistance to microbes, diffusion of oxygen, continuous and effective drug release, is still needed for successful commercialization[5].

| Ocular drug | Classification | Condition | Results |
|---|---|---|---|
| Acetazolamide | Anti-glaucoma | *In vitro* | Drug release in 48h |
| Ciprofloxacin | Antibiotic | *In vitro* | Drug release in 7 days |
| Dexamethasone | Steroid | *In vitro* | Inhibited by Staphylococcus epidermidis Biofilms |
| Dorzolamide | Anti-glaucoma | *In vitro* | Sustained release |
| Ethoxzolamide | Anti-glaucoma | *Ex vivo* | No cytotoxicity |
| Timolol | Anti-glaucoma | *In vivo* | Ocular bioavailability in tear film ↑ |
| Ketotifen fumarate | Anti-histamine | *In vivo* | Ocular bioavailability in tear film ↑ |
| Gentamicin | Antibiotic | *In vivo* | Ocular bioavailability in tear film ↑ |
| Hyaluronic acid | Corneal healing aid | *In vitro* | Sustained release |
| Levofloxacin | Antimicrobial | *In vitro* | Sustained release |
| Nanosilver | Antimicrobial | *In vitro* | Antimicrobial activity |
| Puerarin | Antioxidant | *In vivo* | Ocular bioavailability in tear film ↑ |

**Fig - 2:** List-Drugs as contact lens

## 2. Cul-de-sac Implants

The bulbar and palpebral conjunctiva meet at the upper/lower eyelid intersection, forming the cul-de-sac of the eye[6]. The anterior portion of the eye can be medicated using cul-de-sac implants like Lacrisert (Bausch & Lomb) and Ocusert (Akorn). In terms of risk and safety, episcleral and conjunctival implantations are preferable to other implant placement methods[7]. A hydroxypropyl cellulose implant called Lacrisert is put into the low part(cul-de-sac). This implant can be used for moderate and severe dry eye condition[8]. Because it decreased recurrent corneal erosions, corneal sensitivity, and keratitis exposure, lacriset is a truly excellent treatment for conjunctival hyperemia[9]. The tear film can be maintained with the help of Lacrisert since it releases cellulose. The implant helps keep the eye's surface moist and protected. However, lacrisert can cause some unease. It results in eye discomfort, hypersensitivity, hyperemia, and foreign body sensation. [10].

## 3. Punctal plugs

To prevent tear leakage, biocompatible implants called punctal plugs are placed into the tear ducts[11]. These lacrimal plugs, which have sizes ranging from 2 to 5 mm, are also termed to as occludes. Punctum plugs can deliver regulated medicine release to the eye's anterior portion without causing any harm and without surgery.Such ocular inserts can be made out of both biodegradable and non-biodegradable materials[12]. Nonbiodegradable punctal plug delivery systems (PPDS) are designed to offer controlled medication release for up to 180 days and are made of silicone, polycaprolactam, and hydroxyethyl methacrylate. The inlay is taken out after this time frame[13].Recently, a thermosensitive hydrophobic acrylic polymer was used to create a PPDS (SmartPlug, Medennium Inc.) for the treatment of dry eye illness[14]. After being inserted into the eye, the thermosensitive PPDS is altered, going from a stiff solid to a soft gel-like form[15].

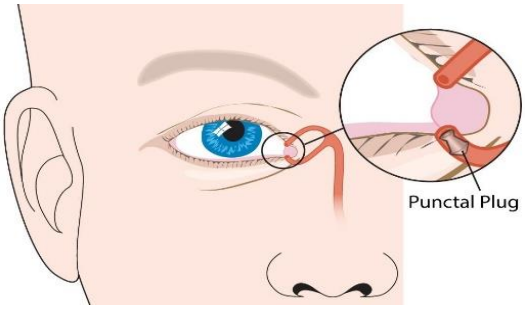


**Fig - 3:** Punctal Plug

## 4. Subconjunctival/ Episcleral Implants

Into the anterior segment of the eye Ocular implants can be inserted for a prolonged period to control the drug delivery. To specify the regions, into the episcleral regions, subconjunctival, aqueous humor, and these implants can be surgically inserted[16]. In contrast to conventional eye drops, these implants offer site-specific medication administration and good patient compliance. Making an insertion on the conjunctiva allows the implant to be placed during the surgery. The aqueous humour and the area where the conjunctiva and sclera meet are two more places where some of the other implants can be placed.[17]. Example- Surodex- It is a rod shaped bio-degradable insert[18].

Cataract surgery patients who experience postoperative inflammation may find relief from an anterior ocular segment injection of Surodex[19]. This Surodex offers extended dosing intervals of 7–9 days. In order to keep the drug dexamethasone contained, it makes use of polymers such poly lactide-co-glycolide (PLGA) and hydroxypropyl methyl cellulose[20]. One investigation found that after 7 days of drug release using Surodex, peak concentrations of the medicine were lower than those after topical therapy with dexamethasone eye drops[21].

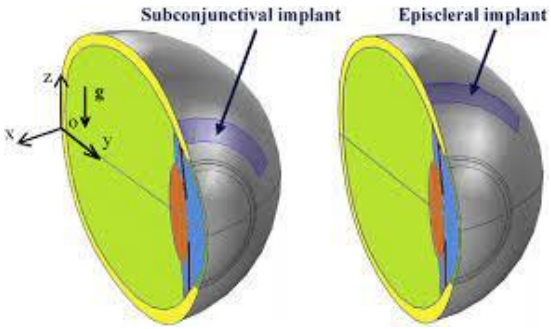


**Fig - 4:** Subconjunctival & Episcleral Implants

## 5. Ocular iontophoresis

The successful delivery of active medications across the ocular barriers with the least amount of electric charge is called optical iontophoresis. Iontophoresis enhances the distribution of ocular medications by using electroporation, electro-phoresis, and electro-osmosis, which produce structural changes in ocular tissue and the creation of pores[22]. In comparison to invasive procedures needing surgical interventions, iontophoresis is a non-invasive treatment with benefits. For anterior and posterior ocular diseases, respectively, this drug permeation technique can be used via the trans-corneal and trans-scleral pathways. Trans-corneal iontophoresis is effective in treating corneal ulcers, dry eye syndrome, ocular inflammation, keratitis, and uveitis[23]. Obstacles like the lens diaphragm and the iris-ciliary prevent

trans-corneal iontophoresis from reaching the posterior segment effectively[24].

Drugs can be delivered directly to the retina via the trans-scleral channel without having to first overcome the anterior segment's many challenges. The effectiveness of iontophoresis-mediated drug delivery is affected by many parameters, including as the charge density of the targeted molecule, the electric current used, the duration of the therapeutic application, the type of medicine being given, and the placement of the electrode[25]. Compared to injections and topical drops, iontophoresis has some advantages over these other methods of delivering medications to the eye. When compared to topical eye drops, it can yield better bioavailability and lower clearance[26].Patient compliance with iontophoresis treatment is typically higher than it is with ocular injections. Nonetheless, some of the individuals who had ocular iontophoresis screening felt some pain and burning[27].

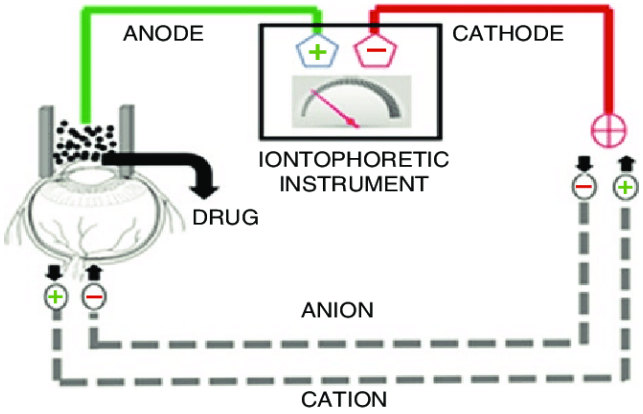


**Fig - 5:** Ocular Iontophoresis

**Novel Ocular Drug Delivery Systems**

Colloidal carriers have been widely used in medication delivery science. It offers a more focused targeting as well as a sustained release of particles at the targeted location. It can be quite interesting to employ nanotechnology to cure various ailments that affect both the eye's anterior and posterior parts. To develop an effective ocular medicine delivery system, one must have a firm grasp on the physiological and biochemical factors at play in both healthy and sick conditions.

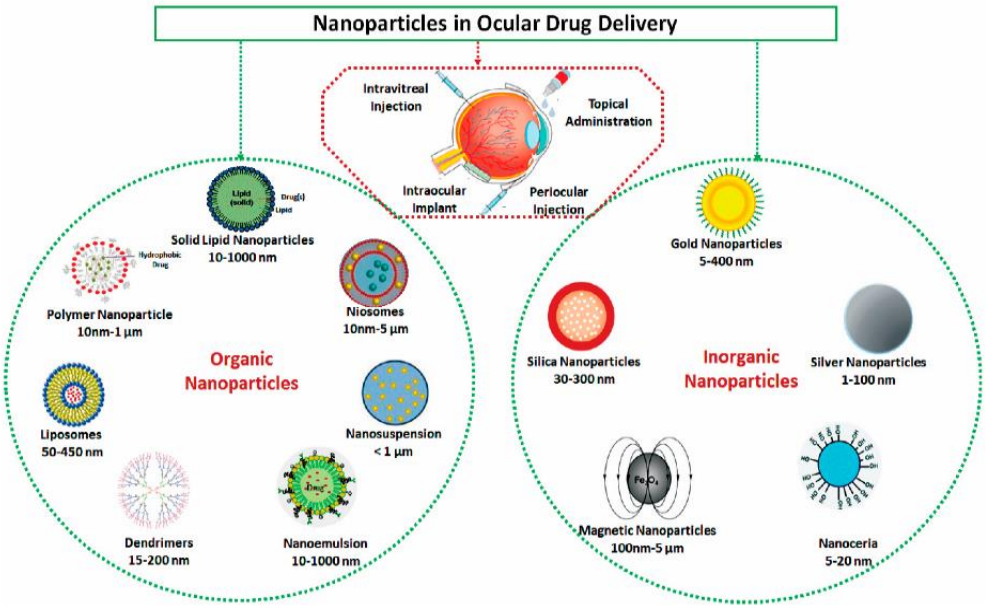


**Fig - 6:** Different Types of Nanoparticles In Ocular Drug Delivery

The active ingredient in the ideal remedy would be targeted especially at various disorders like eye tumours, choroid neovascularization, and diabetic retinopathy. The absence of a lymphatic system in the retina causes its angiogenesis to mirror that of a solid tumour and to have enhanced permeability and retention (EPR) effects. By deploying goods based on nanotechnology, drug delivery is able to

accomplish the following three main objectives:
(1) Promotes better drug permeability.
(2) Regulates the drug's release.
(3) Is a drug target.
Micro/nanoparticles, nanoemulsions, nanosuspensions, and liposomes have been the primary focus of study. The best drug delivery has also been achieved in the last ten years using niosomes, cyclodextrins and dendrimers,. Drugs can be encapsulated in these colloidal carriers to dramatically improve penetration across the membrane and halt ocular enzyme breakdown. Implants made of nonbiodegradable polymers that need to be surgically removed after a certain amount of time could be replaced by such biodegradable carriers. Complications from surgery, including as astigmatism, vitreous haemorrhage, and noncompliance on the part of the patient, might occasionally occur[28].

## 1. Microemulsions

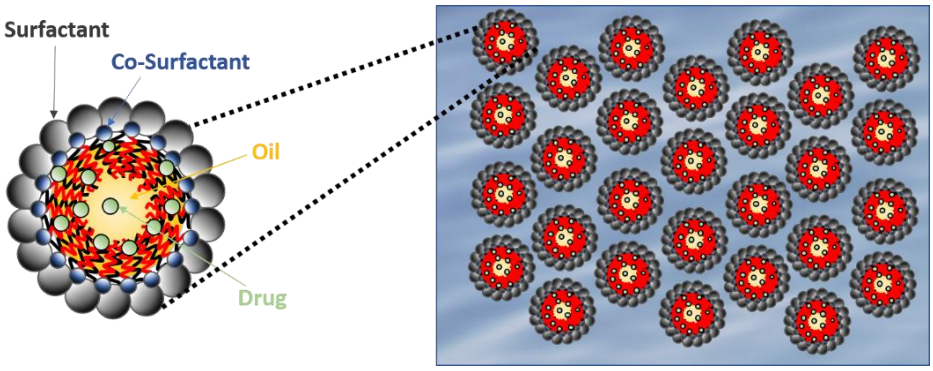


**Fig – 7:** Microemulsion Particles

Microemulsions are formed by combining surfactants and co-surfactants to lower interfacial tension[29]. Microemulsions are often differentiated by their increased thermodynamic stability, small droplet size (100 nm), and translucent appearance. The many advancements and difficulties occurring in the field are carefully covered in a review on the use of microemulsions in ocular medication administration[30]. It is crucial to choose the right organic phase, aqueous phase, and surfactant/co-surfactant systems since they can have an impact on the system's stability.
The solubility of the medication molecule, such as indomethacin or chloramphenicol, is significantly improved as a result of the optimization of these components[31]. Microemulsion technologies have been employed to improve ocular permeability in addition to solubility. Using lecithin, propylene glycol, PEG 200, and isopropyl myristate, we were able to create a non-irritating oil-in-water solution containing pilocarpine in a rabbit animal model. The frequency of medication treatment is reduced by the extended drug release that is typically provided by these formulations[32]. The microemulsion-based method for pilocarpine reduces the frequency of delivery from four times daily to twice daily compared to regular eye drops. This resulted from the enhancement of penetration provided by the surfactant-co-surfactant combination[33].

## 2. Nanosuspensions

This can be described as a weakly water-soluble medication dispersed in a suitable dispersion media that has been stabilised by surfactants. Inert polymeric resins are frequent colloidal carriers in nano suspension products. They help make medicines more soluble and hence more absorbable by the body. They are also preferred since they do not irritate the skin like microemulsions can. Myosis, which can occur following extracapsular cataract surgery, can be prevented with the use of flurbiprofen encased in the polymer resins eudragit RS 100® and RL 100®. Nanoparticles' surface charge aids in their capacity to bind to the cornea[34]. Methylprednisolone acetate (MPA) was encapsulated in a copolymer of ethyl acrylate, methyl acrylate, and chlorotrimethylammoethacrylate, and its anti-inflammatory effects were studied[35] using rabbits with endotoxin-induced uveitis (EIU). Nanosuspensions were found to be more effective than micro suspensions in decreasing inflammation in animal studies.

The use of Piroxicam in eudragit RS 100 was also seen in related studies. Significantly greater anti-inflammatory benefits were seen in in vivo trials on rabbits compared to micro suspensions. The three glucocorticoids (hydrocortisone, prednisolone, and dexamethasone) were prepared as nanosuspensions using distinct approaches[36]. An in vivo trial using rabbits demonstrated that the delivery of

glucocorticoids to the eye was much improved by the use of nanosuspensions. The effectiveness of these nanosuspensions was increased with time, and they also result in prolonged drug release. Additionally, nano- suspensions provide formulation stability[37] for the drug. Examples include cloricromene (AD6) nanosuspensions prepared using eudragit RS100 and RL100. The bioavailability and stability of the medication were dramatically increased by ocular administration of the AD6-loaded eudragit retarded nanoparticle slurry[38].

## 3. Nanoparticles

Polymers, phospholipids, lipids, and metals that have a diameter of less than 1 m are commonly referred to as nanoparticles[39]. Recent studies have shown that nanoparticles are delivered to RPE cells in a largely undamaged state following intravitreal injection of dispersion[40]. This shift has been linked to the activation of retinal microglial cells and the bursting of the internal limiting membrane (ILM)[41]. The ILM's permeability and anchoring mechanism are both modified by this moderate transitory mechanism are both modified by this moderate transitory mechanism in the inflammatory phase. These discoveries are essential for the disorders that affect the eye's posterior portion[42].

The distribution and uptake of nanoparticles are influenced by their size. The kinetics of fluorescein nanospheres (2000, 200, and 50 nm) were studied after they were injected intravitreally into rabbits. The vitreous cavity and trabecular meshwork were discovered to only contain particles of a greater dimension[43], but the retinal cells were found to include nanospheres smaller than 200nm.The right formulation can only be achieved by carefully considering numerous formulation characteristics. The interaction of the drug's surface charge with the polymer's has greatly altered the drug's ability to be released from the polymer. Polybutyl cyanoacrylate nanospheres[44] were discovered to release progesterone in a dose-dependent manner due to surface charge interaction between the drug and polymer.

Drugs can be delivered topically by Tobramycin has been made into a solid lipid nanoparticle system. For much longer than an aqueous solution of the same drug, a particulate system can persist on the corneal surface and conjunctival sac. Compared to the time it takes for a comparable dose of eye drops to take effect, in vivo research shows that the medicine is released steadily over the period of 6 hours. Nanoparticles of varying sizes (20 and 200 nm) were injected periocularly into Sprague Dawley rats and studied for their effects on ocular placement and dispersion[45]. Their studies showed that the sclera rarely transferred particles smaller than 20 nm and that there was no detectable particle transfer between the choroid, the RPE, and the sclera. Because the 20 nm particles can only be eliminated by the periocular circulation (blood and lymphatic), this was thought to be the reason for the low penetration. After intraocular injection, the ideal nanoparticulate formulation for treating illnesses of the posterior segment would have little clearance by the blood and lymphatic circulation. Researchers looked into the effectiveness of various naturally occurring polymers as nanoparticle carriers. Albumin nanoparticles may successfully encapsulate both positively charged (GCV) and negatively charged (oligonucleotides (ODNs)) molecules[46].

Example 1: The bioavailability of chitosan-coated indomethacin poly (epsilon-caprolactone) nano-particles in the eyes was increased by a factor of two. Coating poly(epsilon-caprolactone) nano-particles with polyethylene glycol enhanced their permeability through the cornea[47].

## 4. Microspheres

Microspheres can prolong the release of ODNs after intravitreal injection[48]. Since microspheres are unable to enter cells, the "Trojan" delivery mechanism was devised as an alternative[49]. Polymeric microspheres were designed for this type of delivery method in order to control the release of nanosized anti-TGF-2 phosphorothioate ODNs complexes[50]. For bleb survival following trabeculectomy, this "Tro-jan" injection was significantly superior to the microsphere or control alone[51]. Moreover, Macugen® was delivered transsclerally, trapped in microspheres, and then examined[52]. According to an in vitro release research, macugen (2 μg/day) can be released throughout the sclera for up to 20 days[53]. It was demonstrated that encapsulation had no impact on biological activity through the inhibition of endothelial cell growth[54,55].

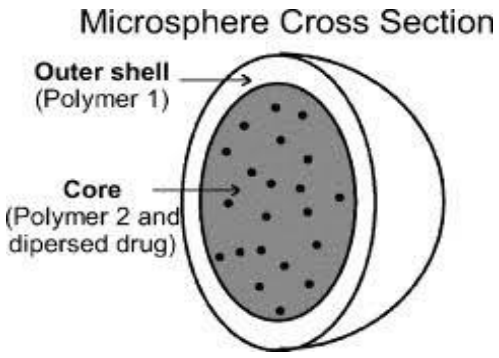


**Fig - 8:** Microsphere Particles

## 5. Liposomes

Many medicinal substances have been delivered to the eye using liposomes, lipid vesicles having an aqueous core. Reversed phase evaporation was employed to make ganciclovir (GCV)-containing liposomes, and a rabbit model was used for the in vivo pharmacokinetic testing. Both the liposomal formulation containing GCV and the GCV solution's permeability were investigated. The transcorneal permeability was 3.9 times higher and the AUC was 1.7 times higher than the solution[56]. After liposomal formulation, the sclera, cornea, and vitreous humour showed a more dramatic dispersion of ocular tissue. Liposomal formulation of the vasoactive intestinal peptide (VIP) was used (VIP-Lip)[57].The concentration of VIP in ocular fluid was roughly 15 times higher after intravitreal injection than it was when VIP solution was administered alone. Consider the liposomal formulation of the antibiotic ciprofloxacin (CPFX). Lecithin & alpha-L-dipalmithoyl-phosphatidylcholine were used to make multilamellar vesicles, which were then used to make liposomes containing CPFX[58]. For topical distribution, acetazolamide was enclosed in a liposomal formulation[59].Multilamellar vesicles and reversed-phase evaporation (REVs) were used to create liposomes (MLVs). Different phos-phatidylcholine and cholesterol molar ratios were used when producing MLVs, and this increased the entrapment efficiency compared to REV[60]. Entrapment effectiveness was improved when lipid and charge-inducing compounds like cholesterol and stearylamine were present in higher amounts. For liposomes and selective formulation, in vivo intraocular pressure was examined. MLVs outperformed REV-prepared liposomes in terms of effectiveness length[61].

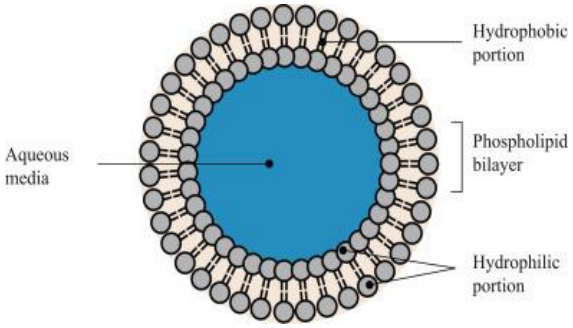


**Fig – 9:** Liposome Particle

## 6. Niosomes

The non-ionic niosomes, bilayered structural vesicles that can enclose both the substances-hydrophilic and lipophillic. Niosomal formulation was recently created as a method of cyclopentolate delivery. The drug's bioavailability in the eye was much improved because its release was not pH dependant. Discomes are a new type of delivery mechanism that has been created. These huge structures, which range in size from 12 to 16 m, were created by adding the nonionic surfactant Solutan C24 to niosomes. Niosomes and discomes were successful in encasing timolol maleate. The discomes have a higher in vivo bioavailability than niosomes[62].

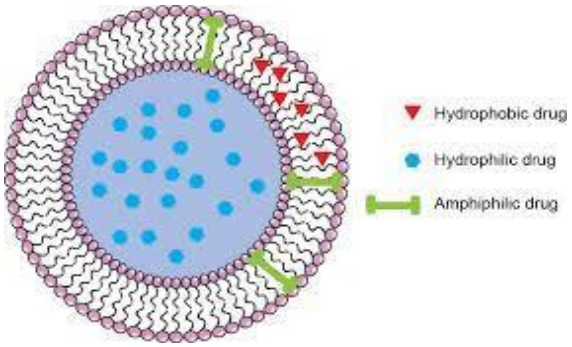


**Fig - 10**: Niosome Particle

## 7. Dendrimers

Macromolecules known as dendrimers are composed of several branches arranged around a central core[63]. They are a good substitute drug delivery system for the eye due to their nanoscale, ease of fabrication, functionalization, and capacity to link many surface groups. In the past, bioadhesive polymers containing poly (acrylic) acids were developed to lengthen residence time and reduce administration frequency[64]. The creation of a veil that causes vision loss and fuzzy vision are two of these systems' major downsides[65].

Dendrimers are liquid or semi-solid polymers with surface groups that include amine, carboxylic, and hydroxyl that keep getting bigger as the generation number grows[66]. PAMAM, poly (amidoamine) dendrimers, have been employed extensively in the administration of medications. This system of branching polymers has a distinctive design and is capable of encasing both hydrophilic and lipophilic medicines[67]. When designing a delivery system, it is important to consider the molecular weight and size of the dendrimer, as well as the choice of functional group on the surface (hydroxyl, carboxylate, amine)[68].

A few instances include

1. Dendrimers with carboxylate and hydroxyl surface groups, as DG1.5 and DG4.0 (OH), were implanted to increase the bioavailability of pilocarpine and tropicamide, respectively. The formulation has been shown to increase the longevity of glaucoma filtration surgery in a rabbit model of scar tissue formation[69].
2. Dendrimers were used to successfully

administer anti-VEGF ODN in a rat model of CNV treatment. The effects of PANAMs were studied to see if pilocarpine nitrate and a small amount of tropicamide could be released in a laboratory setting[69].

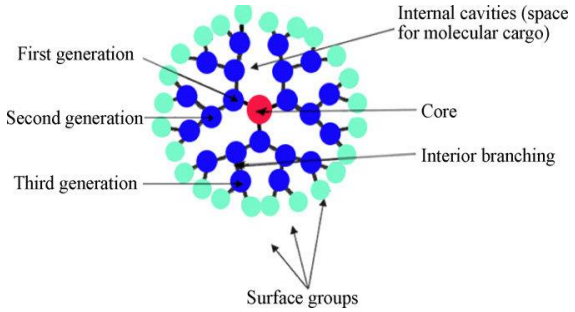


**Fig - 11:** Dendrimer Particle

## 8. Cyclodextrins

When combined with a number of guest molecules, cyclic oligosaccharides called cyclodextrins (CDs) can create inclusion complexes. Drugs that are hydrophobic can have their water solubility increased through CD complexation without having their chemical makeup or natural ability to penetrate biological membranes altered. Low water solubility molecules have been supplied as CD complexes[70]. It has been demonstrated that these complexes enhance the corneal penetration of medications like dexa-methasone, cyclosporine, and others. Drugs that are weakly water soluble can have their ocular bioavailability greatly increased via CD complexation.

In some circumstances, these inclusion complexes can also give the medications in the formulation water stability[71,72]. Similar techniques were used to create inclusion complexes using rhEGF suspended in poloxamer gel. The drug's AUC has increased significantly as a result of this formulation. This strategy also benefits the medicine by making it more stable[73]. Drug complexes like dexamethasone acetate, dexamethasone, and pilocarpine that were combined with HP—CD had a greater bioavailability than regular eye drops. When compared to more traditional permeability enhancers like benzalkonium chloride, this complexation method does not disturb the biological membrane[74].Moreover, since the free drug is not available due to inclusion, this method can successfully administer irritant-containing pharmaceuticals. Since CD molecules are neutral by nature, it was discovered that HP— CD (up to 45%) does not irritate both human and animal eyes[75,76].

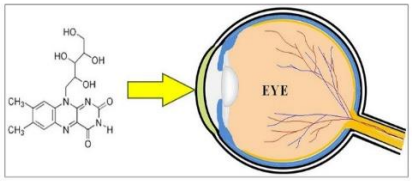


**Fig - 12:** Cyclodextrin particle to eye

## 9. Microneedle

To the topical approach's alternative, researchers have recently tried using microneedles to administer drugs to the posterior section. In the sclera of human cadavers, sulforhodamine diffusion was shown to be of comparable size. Coated solid metal microneedles for medication delivery have been tested *in-vitro* and *in-vivo*. Amazing *in-vitro* sclera encroachment and quick coating solution spread after insertion were demonstrated by the microneedle. It was discovered that the drug level in vivo was much higher than the level that was seen after topical medication administration. Pilocarpine was successfully delivered using this method of drug delivery as well. The inventors assert that their coated microneedle can successfully deliver medication with the least amount of invasion across the cornea and sclera[77].

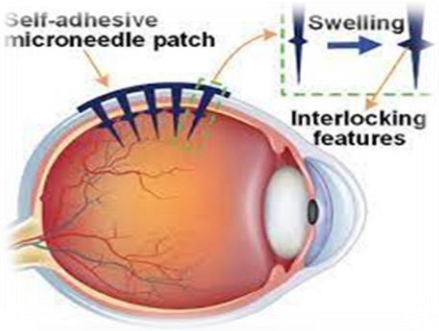


**Fig – 13:** Microneedle patch instilled on the eye

## 10.Gene delivery

Nucleic acids can now be delivered to a particular spot within the eye via a variety of approaches[78]. For researchers in ocular delivery field, designing a delivery system for antisense ODN (Oligo dextro nucleoside), siRNAs, aptamers is a profound task because ocular tissues like the retina and cornea have complex structures that are high in molecular mass, surface charge, size, and bioavailability of the medication. Recent FDA approvals include an aptamer for treating "wet" AMD, an ODN for treating Cytomegalovirus in AIDS patients (Vitravene®), and an injectable form of pegaptanib (Macugen®)[79]. Since they can overcome viral

vector drawbacks like immunogenicity, safety, and probable brain persistence, non-viral vectors have become widely accepted in gene delivery[80]. The existing system's inability to attain better transfection efficiency is a significant problem[81]. Three basic delivery methods are used in nonviral gene therapy: chemical approaches, physical vectorization of the genetic material, and "naked" DNA. There has been a significant effort to transfer naked DNA topically, intracamerally, intracorneally, subconjunctivally, intravitreally, and subretinally[82].

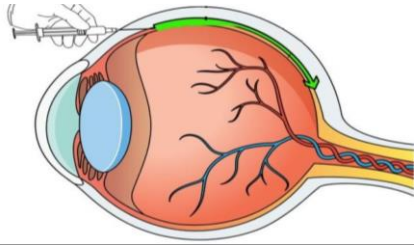

**Fig – 14:** Delivering of gene to the eye

**11.Hydrogel systems**

They are hydrophilic, three-dimensional polymeric networks that can absorb huge volumes of water or biological fluids.A hydrogel composition can greatly lengthen residence time. The pH and temperature can be changed to produce gelation. The most common type of polymer, poloxamers, have a hydrophobic portion in the middle surrounded by a hydrophilic portion. While being commonly used to extend the residency period, they have a number of significant drawbacks, including poor in built strength, immediate breakage, and non-biodegradability. Many initiatives have been launched to solve this issue. The essential gelling temperature was altered using oligomerization. For cellulose derivatives like HPMC, the interaction of hydrophobic components at higher temperatures results in gelation. In comparison to poloxamer407, the pilocarpine formulation has demonstrated improved miotic responsiveness at lower xyloglucan concentrations. Artificial latexes like Pseudo latexes made by adding water to pre-existing polymers provide the therapeutic molecule that is sensitive to aqueous media with physical stability of gel. A specific type of gel procedure known as Atrigel involves dissolving a polymer with the suitable carrier. Both polymer and carrier are equally biocompatible and degradable. Water in the adjacent tissue precipitates a polymer when a material is injected into the subcutaneous area, which takes the drug immediately and withdraw it under control. The method can be used, according to the product's creators, for a wide range of compounds, including proteins and peptides. The system's main characteristics included targeted drug delivery, compatibility with a wide range of compounds, the ability to accomplish regulated release, and biocompatibility. Eligard®, a medicine that is currently on the market, uses a similar approach to treat prostate cancer[83].

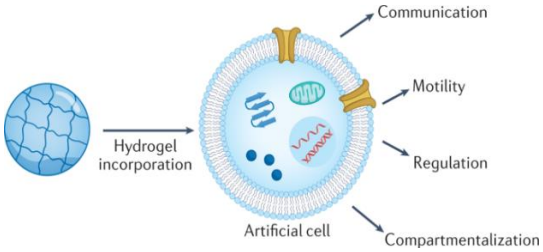


**Fig – 15:** Hydrogel particle

## 7. CONCLUSION

An ideal treatment plan would keep drug levels at an important level for prolong period of time even after single application. Periocular drug administration may be able to circumvent several of these limitations and provide sustained medication doses in conditions affecting both segments of the eye. Following their periocular delivery, colloidal carriers may replace the present therapy in a significant way. In recent years, researchers have concentrated on developing a multidisciplinary water-soluble method, such as microneedles and iontophoresis. For a variety of disorders, continued improvement in gene delivery seems to be quite promising. In the future, both groups will place a lot of attention on achieving non-invasive sustained medication release. A greater understanding of the nuances associated to all the aspects discussed will significantly speed up further advancement in the field. Technology transfer and mass production of novel ocular medication delivery like nanomicelles, nanoparticles present significant challenges. In the near future, nanotechnologies may be able to replace conventional ophthalmic drugs, but concurrent efforts in both novel product development and product scale-up are needed.

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