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Review Article

A Review On Novel Drug Delivery Systems Used For Delivering Of Drugs Into Ophthalmic Region

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ABSTRACT

Eye is a very sensitive organ, the dosage forms to be administered are very peculiar. Design of ophthalmic drug delivery systems is a major challenge, as they are to be made to pass various ocular barriers and improve drug bioavailability for a prolong period of time. Conventional delivery systems are employed for administration of drug into the ocular region and find difficult to pass through the barriers of the eye, low bioavailability and potential drug side effects, hence the novel drug delivery systems are developed for effective release of drug and prolong release and more retention time of drug in the ophthalmic region. These novel drug delivery systems offer manifold advantages over conventional systems as they increase the efficiency of drug delivery by improving the release profile and also reduce drug toxicity. Development of novel therapeutic agents continue to provide ocular delivery systems with high therapeutic efficacy. Need to develop ocular drug delivery systems that provide controlled release for the treatment of chronic diseases in order to reduce dosing frequency. The current article gives a quality of information about novel drug delivery system employed in the delivery of drug to optical region.

INTRODUCTION

The human eye is an extremely delicate organ, often prone to irritation, dryness and various diseases, such as glaucoma, cataracts, keratoconus, age-related macular degeneration, and many others [1]. The eye is a complex organ with a unique anatomy and physiology. The structure of eye can be divided into two main parts: Anterior segment and Posterior segment. Anterior segment of the eye occupies approximately one-third while the remaining portion is occupied by the posterior segment. Tissues such as cornea, conjunctiva, aqueous humour, iris, ciliary body and lens make up the anterior portion. Back of the eye or posterior segment of the eye includes sclera, choroid, retinal pigment epithelium, neural retina,

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optic nerve and vitreous humour. The anterior and posterior segment of eye is affected by various vision threatening diseases. Diseases affecting anterior segment include, but not limited to glaucoma, allergic conjunctivitis, anterior uveitis and cataract. While, age-related macular degeneration (AMD) and diabetic retinopathy are the most prevalent diseases affecting posterior segment of the eye [2]. Topical drug delivery is the most widely preferred route of drug administration to treat ophthalmic diseases such as keratitis, conjunctivitis, dry eye disease, glaucoma, uveitis etc., now a days, there are multifarious forms of traditional ophthalmic drugs, and approximately 90% of drugs are administered in the form of eye drops. Owing to the complicated structure of eye, lipophilicity of corneal epithelium, defines mechanisms, bonding of drug with proteins contained in tears, enzymolysis, and metabolism, traditional ophthalmic drugs have disadvantages such as low bioavailability and potential drug side effects. In addition, many patients (especially elderly patients) have difficulties in correctly instilling the eye drops, which can reduce the efficiency of the drug and even lead to potential contamination of a chronically used bottle. All these factors limit their development [3-4]. Ocular diseases can be broadly classified into anterior and posterior segment diseases. Anterior segment diseases that can cause serious vision impairment or discomfort include corneal neovascularization (CNZ), glaucoma, bacterial/fungal keratitis, uveitis, herpes simplex keratitis, blepharitis and dry eye syndrome. Additionally, diseases that originate in the posterior segment of the eye lead to permanent loss of vision, if left untreated, and account for the majority of blindness, such as in age-related macular degeneration (AMD), diabetic retinopathy, diabetic macular edema, cytomegalovirus retinitis, and other Chori retinal diseases [3]. To overcome the ocular drug delivery barriers and improve ocular bioavailability, various conventional and novel drug delivery systems have been developed such as emulsion, ointments, suspensions, aqueous gels, Nano micelles, nanoparticles, liposomes, dendrimers, implants, contact lenses, nanosuspensions, microneedles, and in situ thermosensitive gels for the earlier mention ocular diseases [2]. The current review gives a brief description of novel drug delivery systems used for ophthalmic drug delivery such as Contact lens, Iontophoresis, Microneedles, Micelles, Dendrimers, Noisome, Microemulsions, Implants, Microspheres and In-situ gels etc,

1. Contact lens:

Contact lenses loaded with drugs are certainly among the most innovative delivery systems proposed to improve corneal permeation and the bioavailability of ophthalmic drugs. Nowadays, conventional hydrogel-based soft contact lenses are the most proposed ones for therapeutic purposes [1]. Drug-loaded contact lenses, as new drug delivery tools that use different techniques to load ophthalmic drugs into contact lenses, have attracted considerable attention. Particularly, drug-loaded contact lenses can overcome the problem of incorrectly instilling eyedrops, and also can continuously release drugs from lens to tear film, prolong drug retention time on the ocular surface and improve bioavailability. In the past few years, the development of drug-loaded contact lenses has progressed rapidly, and the contact lens-based drug delivery systems have been proved to play an important role in preventing of keratitis, glaucoma, dry eye, colour blindness, corneal injury, keratoconus, ocular scar, retinopathy, and other ophthalmic diseases [4]. Contact lenses can be prepared by molecular imprinting, polymer nanoparticles, liposomes and super critical fluid technology.

Table 1: Novel contact lens used in ophthalmic diseases.

Sr. No	Novel contact lens	Ophthalmic disease
1	Soft hydrogel lens	Keratitis
2	Bandage contact lenses	Corneal wound healing
3	Silicon hydrogel lenses	Dry eye disease
4	Scleral contact lens	Keratoconus and myopia
5	True eye Goldin lens	Ocular cytosis
6	X chrome lenses	Color vision deficiency
7	galaklens	Glaucoma

2. IONTOPHOROSIS:

Iontophoresis refers to the non-invasive application of a low-amplitude electrical current to enhance delivery of charged drug molecules across biological membranes, such as the skin, joints, nails, and eye structures. Iontophoresis allows controlled drug delivery, with the amount of drug delivered being directly proportional and controlled by the applied current (milliamperes), the duration of application (min) and the surface area contacted. Further, depending on whether continuous or pulsatile delivery is used, the current profile during iontophoresis can be customized to produce the desired drug penetration kinetics. Drug penetration and molecular transport during iontophoresis are accomplished primarily through electro repulsion and electro-osmosis. Electro repulsion is the primary mechanism for electro transport of ionized substances and refers to the ordered movement of ions in the presence of an electric field. In contrast, electro-osmosis is the motion of liquid in the anode-cathode direction induced by an electric potential applied across a negatively charged membrane and plays a greater role in the iontophoresis of drugs with high molecular weight. The first report of ocular iontophoresis was a 1908 publication by Wirtz, who reported on the iontophoresis assisted topical delivery of zinc salts for the treatment of corneal ulcers. Subsequent studies examined iontophoresis mediated drug delivery to or across the sclera and the cornea. Applications of the technology included ocular delivery of small molecules (antibiotics), macromolecules (oligonucleotides, small interfering ribonucleic acid), and nanocarriers. Importantly, preclinical studies showed that iontophoresis employing low-current densities is safe and does not induce pathological structural changes in the cornea. Ocular iontophoresis has also been explored as a delivery mode for iodide to treat dry eye, and for 6-hydroxydopamine to treat glaucoma, but these applications did not advance into clinical practice. Iontophoresis has only more recently become accepted by the clinical community as a promising technique for facilitating ocular delivery [6].

Mechanism of iontophoresis

Iontophoresis is a non-invasive approach which drives the penetration of pharmacological molecules across anatomic barriers using a small electric current. This technique has been used in a broad spectrum of pharmacological experiments and clinical conditions. Generally, the iontophoresis uses two types of voltage supply-direct current and alternating current. The most commonly used method is direct current iontophoresis. The crux of iontophoresis is to take advantage of electrical field to prompt the drugs penetration through media, cell membranes, or tissues, respectively. The amount of delivered therapeutic molecules is about 10–2000 times greater than conventional forms. This method has been used in dentistry, ophthalmology, otorhinolaryngology, and dermatology. The central tenet of iontophoresis is built on the basic electrical principle in which oppositely charged ions attract and same charged ions repel. In ophthalmic practice, iontophoresis enhances drug penetration across biological membranes via Direct-field effect, electroosmosis and electro permeabilization.

Direct-field effect

The direct-field effect, also called the Nernst-Planck effect, is based on the principle of ion movement caused by an applied electrical potential gradient. The ionized substances are attracted by direct-field effect to anode or the cathode depend on the charge. The direct-field effect, is the largest contributor to flux enhancement for small ions, but not the only one.

Electroosmosis

Also called the Electroosmotic flow, is the bulk fluid flow which occurs when a voltage difference is imposed across a charge membrane. The motion of the solvent can enhance the transport of ionic and neutral drugs. Electroosmosis is a dominant mechanism for the enhanced transport of large monovalent ionic during iontophoresis.

Electro-permeabilization is the alteration of a tissue barrier under the influence of an electric field that can increase the permeability of the tissue during and after iontophoresis. The porosity of a membrane and the properties of the transport pathways in the membrane can be altered by the electric field. For neutral molecule, the electroosmotic flow is the major mechanism. Siva Ram Kiran found that the transport enhancement by iontophoresis was predominantly caused by the electrophoresis and/or electro-osmosis. [7].

Factors affecting iontophoresis:

Several factors can affect the efficiency of iontophoresis, such as the density, duration of stimulation, concentration of drug, pH value and permeability of tissue. In iontophoresis, the current density and duration of stimulation are closely related to the total amount of drugs. The current density is proportional to the electric field intensity. The electric field force on the drug ions would increase in parallel with the augment of current density. Thus, more ions are delivered within a fixed period of time. Moreover, the longer the stimulation time is, the more drug ions would be delivered. Although iontophoresis has the advantage of enhancing the bioavailability of drugs, we should pay attention to the toxic damage that caused by high current density and the long length of iontophoretic duration. Clinical trials have verified that an electric current with the density of 20mA/cm2 for 5 min would be harmless to the corneal tissue. Previous study also shows that an electric current with the density of 5.0 mA/cm2 for 10 min would not cause any intraocular complications in transscleral iontophoresis. However, the higher electric current (with the densities of 100–Y0mA/cm2) would cause retina and choroid burns, haemorrhagic necrosis, edema and infiltrations in the subjects. These unwanted damages may be closely correlated with the area of application site, the length of iontophoretic duration, and the intensity of applied current. Additionally, if the concentration of drug is small, drug concentration and tissue permeability are positively correlated with the amount of drug (md) passing through the epithelium [7].

3. MICRONEEDLES:

Microneedles, which are patches containing an array of micron-scale needles (<1 mm), have the potential to meet this need. These platforms can enable localized drug delivery to the eye while enhancing penetration of drug molecules through key ocular barriers, thereby improving overall therapeutic outcomes [3]. Among the various novel drug delivery systems, injectable formulations have the most impactful application as they can deliver the right amount of drug in the desired area of the eye. Conventional hypodermic needles are used for giving therapy through intraocular injections. There are various routes through which these intraocular injections are given namely, subconjunctival, periocular, intravitreal (IVT), intracorneal etc. Considering this, some of the disadvantages associated with intraocular injections are invasive nature, frequent application of injections leads to non-compliance

and also less bioavailability Microneedles (MNs) are devices made up of polymer or metal having dimensions in the range of few micrometres to 200 μm. MNs have micro sized projections which makes them minimal invasive in nature. These MNs are able to not only overcome the disadvantages associated with the presently used conventional delivery systems but also are able to cross the ocular barriers to specifically target the drugs at the needed site of action. MNs as a technique is efficient enough for expediting percutaneous drug delivery. Other than the promising role MNs have shown in eye treatment they are also useful in percutaneous delivery across the oral mucosal and GIT etc. These microns sized needle have easy insertion on to the eye for various types of applications. As compatibility Microneedles (MNs) as an alternate novel delivery system facilitate drug delivery to various ocular diseases with promising approaches in healthcare. Advances in pharmaceutical technology have made MNs provide localized, effective, less invasive and targeted drug delivery in the eye. The purpose of this review is to provide an insight to efficacious therapeutic applications the MNs can bring in various ocular diseases. In reality, using MNs for drug delivery to the eye is a fairly new concept since very little research has been carried out in this field. To date, in enhancing ocular drug delivery using MNs, only three of the above five strategies of MN application have been investigated namely coated, soluble and hollow MNs. Primarily these three modes of MN application allow instant delivery and retrieval of the MNs (or its baseplate), which imitate the administration of conventional hypodermic needles to the eye. Literature indicates the use of either single solid or hollow MNs for ocular delivery of drug molecules of various molecular weights including sustain release nanoparticles, microparticles or depot forming gels where the MNs were fabricated using silicon, stainless steel or glass [8].

4. MICELLES:

Nano micelles are core- shell nanocarriers formed by spontaneous assembly of amphophilic copolymers with hydrophobic groups as the core and hydrophilic groups as the outer shell Usually the particle size range from 10 to 100 nm and can be divided into 3 categories: polymers, surfactants, and multi-ion composite nano micelles. Positive micelles are generally formed when the hydrophobic moiety forms cluster within the core and hydrophilic moiety is aligned out words to increase contact with water [9]. They may be spherical, cylindrical or star shaped. They could entrap both hydrophilic and lipophilic drugs. They have simple preparation techniques reduced toxicity increased bioavailability increased stability and enhanced permeation. Ying fang et.al developed nano micelles of pipecuroniums using poly ethylene glycol and poly (e- caprolactone) as co-polymer. Terreni et. al used hyaluronic acid to sustain release of cyclosporine. For instance, civil et. al developed dexamethasone loaded nano micelles by employing co polymers of Poly Hydroxy Ethyl Aspartame [PHEAC] and Pegylated [PHEAC] for anterior segment delivery. In-vivo dexamethasone concentration time profile was studied and determined in rabbits with aqueous humour sampling resulted showed that dexamethasone loaded PHEA micelles have higher ocular bioavailability relative to dexamethasone suspensions. As the most significant parameter of micelles, the CMC determines the minimum concentration for micelle structure formation. When the polymer concentration is below the CMC, the polymer chains are freely dispersed in the solution as monomers. When the polymer concentration is higher than the CMC, a large number of polymeric micelles can be self-assembled. In the water-based environment inside the body, the drug might be

rapidly released once the polymer concentration drops below the CMC, which means that a lower CMC is ideal. Similar to surfactants, polymeric micelles are self-assembly structures formed spontaneously by amphiphilic segments in water.10 When the concentration of block or graft copolymers in water reaches a certain level, microphase separation in the hydrophobic and hydrophilic segments of polymers will occur. As a result, the typical core–shell micelles with hydrophobic segment inward and hydrophilic segment outward will be formed automatically.

5. DENDRIMERS:

Dendrimers are the characterized as nanosized, highly branched, start shaped polymeric system. The branched polymeric systems are available in different molecular weights with terminal end amine, hydroxyl or carboxyl functional groups. Dendrimers are being employed as carrier systems in drug delivery, selection of molecular weight size, surface charge, functional group are critical to deliver drug poly amido amine (PAMAM) dendrimers are widely employed in ocular drug delivery [10]. They show increased residence time, prolonged activity, improved bio availability, targeted delivery and anti- microbial property They are suitable for both hydrophilic and lipophilic drugs. They could transfer medication to both segments of eye. Lavinia et.al developed brimonidine tartrate loaded dendrimers using methoxy polyethylene glycol [11]. They high capacity for drug encapsulation and conjugation and functionalization of drug groups. As dimer sodium is a poly anionic dendrimer with antiviral activity. Increased branching of dendrimers permits incorporation of a greater variety of drugs, both hydrophilic & hydrophobic. As dimer sodium (SPL7013) is a polyanionic dendrimers with antiviral activity. Romanowski et al. evaluated ocular tolerance and anti-adenovirus potency of topical SPL7013 in the rabbit eye model with adenovirus (HAdV5) ocular infections [12].

6. NIOSOMES:

They are vesicles and formed from the hydrated mixture of cholesterol, change inducing substance and non- ionic surfactants. As an alternative to liposomes, Noisome are vesicles made up of non-ionic surfactant that are biodegradable, comparatively nontoxic. These Noisome are more stable, and less expensive Noisome can entrapped both hydrophilic and lipophilic drugs. Either in an aqueous layer are lipid based vesicular membrane. It has potential to prolong the circulation of the entrapped drug. It could be very useful for more effectively targeting the drug for treating ocular disease and other microbial disease [13]. Noisome can be small uni-lamellar vesicles, (MLC) multi unilamellar vesicles and (LUV) large unilamellar vesicles. They can be formulated by things film hydration, Hand shaking, Ether Injection, Reverse phase evaporation, sonication, micro fluidization and transmembrane pH gradient. Noisome properties depending on the method of production and composition of bilayer the alternative and various difficult task faced by pharma scientist to develop ocular dosage forms because of significant and pharmacokinetically specific environment that exist in the eye. It may challenge is to get around the shielding barrier of the eye without affecting any permanent tissue damage. The majority of existing ocular drug delivery system provides enhance drug permeation, improved bio availability and control the release of the drug [14]

Composition of Noisome:

It comprises of two essential components like cholesterol and non-ionic surfactants. Cholesterol provides firmness and appropriate shape. The surfactants take part in a very important function in the formation of Niosomes. Surfactants of nonionic groups like spans have different grades as span 20, span 40, span 60, span 80 and span 85. Similarly, the surfactant of Tweens also has different grades such as Tween 20, Tween 40,

Tween 60 and tween 80. Moreover, the surfactant Brij also has variety of grades such as brij 30, brij 35, brij 52, brij 58, brij 72 and brij 76. These surfactants are generally used for the preparation of Niosomes [15].

7. MICRO EMULSIONS:

Microemulsions have colloidal dispersions composed of specific properties with different patches, including aqueous phase, oil phase& co surfactant & surfactant. Their droplets size ranges from 10 to 100 nm based on the type and amount of surfactant in the formulation. Microemulsions can be divided into three categories o/w, w/o and bi-continuous structure. Microemulsions are the most potential submicron drug carriers especially for poorly water- soluble drugs. At the same time, microemulsions are thermodynamically stable, inexpensive and relatively simple to produce [16]. Various researches have demonstrated the efficiency of microemulsions in delivering multiple drugs to different issues of the eye. Interestingly, some researchers have found that the methylglyoxal (MGO) concentration in Manuka honey is quite high and can effectively manage bacterial over load. The term micro emulsion was coined by hoar and Schulman in 1943.Pharmaceutically, micro emulsions are colloidal nano dispersion of o/w or w/o types stabilized by a surfactant film. The solubilization theory considers microemulsions as swollen micellar systems, in which water or oil is solubilizes the reverse micelles structures to form one phase system. The three main theories of ME formation are briefly discussed here: interfacial or mixed film theory, solubilization theory, and thermodynamic theory. According to the thermodynamic theory of stabilization, ME forms spontaneously because of the low value of interfacial tension on account of the diffusion of surfactant in the interfacial layer and to the major entropy contribution that depends on the mixing of one phase in the other in the form of numerous small droplets. In the mixed film theory, the interfacial film is considered to demonstrate dissimilar behavior towards the aqueous and oily segment of the interface. The solubilization theory considers ME as swollen micellar systems, in which water or oil is solubilized the reverse micelle structures to form one-phase system. However, despite of all the theories of ME formation, the reduction of the interfacial free energy to a very low value is of prime importance in the ME formation [16].

8. IMPLANTS:

Intraocular implants are specifically designed to provide localized controlled drug release over a extended period. These devices help in circumventing multiple intraocular injections and associated complications. Though implantation is invasive procedure, these devices are gaining interest due to their associated advantages. such as sustained drug release, local drug release to diseased ocular tissues in therapeutic levels, reduced side effects and ability to circumvent blood retina barrier. Several implantable devices have been developed for ocular drug delivery especially for the treatment of chronic vitreotinal diseases. Ocular implants are available as biodegradable and non-biodegradable drug releasing devices [17].

Biodegradable implants:

The implants containing biodegradable polymers can be either matricial (monolithic) or reservoir systems. In the former, the drug can also be released by diffusion through the matrix pore. In reservoir systems, the membrane generally degrades slower than in drug diffusion. A wide variety of natural and synthetic biodegradable polymers have been investigated for the development of implants. Natural polymers, such as bovine serum albumin, human serum albumin, collagen, and gelatin have been studied drug delivery. However, the use of these polymers is limited due to their higher cost and

questionable purity. Synthetic polymers such as poly(amides), poly (amino- acids), poly(alkyl-α-cyanoacrylates), poly(esters), poly (orthoesters), poly(urethanes), and poly(acrylamides) have been increasingly used to deliver drugs as they are devoid of most of the problems associated with natural polymers [18].

Non-biodegradable implants:

Non-biodegradable polymeric implants can be presented in the form of matrix (monolithic) or reservoir systems. In the matrix system, the drug is dispersed, homogeneously, inside the polymeric matrix or adsorbed onto the surface. Slow diffusion of the drug through the matrix provides its controlled or sustained release. In the reservoir-type system, the drug is surrounded by a permeable non-degradable membrane whose thickness and permeability properties can control the diffusion of the drug into the body. The release kinetics of the drug from this system suggest that if the concentration of the drug within the reservoir is in constant equilibrium with the inner surface of the enclosed membrane, the driving force for diffusional release of the agent is constant, and zero order release kinetics of the drug from the delivery system is achieved. The drug-release rate is determined by different factors, such as the release area, the thickness of the polymeric membrane, the implant form, as well as drug solubility18. The polymers most employed in the preparation of these implants include: silicon, polyvinyl alcohol (PVA) and ethylene vinyl acetate (EVA) [19].

9. MICROSPHERS:

In ocular drug delivery system, there is a main problem of rapid and extensive elimination of conventional eye drops from the eye. The main region of drug loss includes lachrymal drainage and drug dilution by tears. A number of factors, namely rapid tear turnover and the resulting eye to form viscoelastic changes response to environmental changes lately release the drug precorneal loss, induction of tear flows due to irritation caused by the drug preparations, as well as the relatively large volume of administered eye drop (-50 versus -7 of corneal tear film) lead to high lacrimal damaged to the resulting elimination rate. In micro or nanoparticles contain the drug either dissolved in the polymer, matrix in form of a solid dispersion. The drug may be adsorbed to the particle surface it is important note that the particle size for ophthalmic application should not exceed loom because with large sizes a scratching feeling might occur. The high amount of drug that is drained nose or into gut. Especially gut is very efficient absorption organ of the body this leads to expensive. System systemic absorption may result in unwanted side effects. They avoid the discomfort that is combined with application of viscous or sticky preparations such as ointments. The lateral preparations lead to a total blurring of vision if they are be of properly utilized. The large number of producing methods exist for microspheres, microcapsules and nanoparticles. The optical method they may be used for the preparation depends mainly on the drug to be used [20]. Microspheres can be prepared by denaturation or cross-linking of macromolecules in emulsion form, interfacial polymerization, formation in an aerosol phase, desolvation, aggregation by pH adjustment and heat treatment and formation of nanoparticles via microemulsions

10. IN SITU GEL's:

Ophthalmic in-situ gelling is comprising of environmentally sensitive polymers that will be altered structurally with the small changes in specific conditions like pH, temperature and ionic strength in the environment [21]. In-situ forming gels are liquid during instillation into the eye and then undergoes rapid gelation in the cul-de-sac of

slowly under physiological conditions consequently, the extended and the drug is

released in a sustained manner which leads to enhanced bioavailability, minimized systemic absorption and reduce the frequency dosing and it is easy to administration, and deliverance of accurate dose have been exhibited by in-situ gelling system. In situ gel forming system are drug delivery system that are in the solution from before administered undergo gelatin in situ, to form a gel triggered by external stimulus such as temperature. They can release sustained are control manner novel concept was of producing in situ gel was suggested for the first time in the early 1980s. Gelatin occur via cross linking of polymer chain that can be achieve by the covalent bond formation (chemical cross linking). In situ gel farming system can be described as low viscosity solution that undergo phase transition in the conjunctival cul-de-sac to form viscoelastic gels due to conformational changes of polymers in response of physiological environment [20]. Use of biodegradable and water-soluble polymers for the in situ gel formulations can make them more acceptable and excellent drug delivery systems. Moreover, in situ gels have ease of commercialization which adds advantage from industrial point of view.

Advantages:

- Less blurred vision as compared ointment.
- Sustained prolonged drug release and maintaining relatively constant plasma profile.
- Reduced frequency of application hence improved patient compliance and comfort.
- Its production is less complex and thus lower the investment manufacturing cost

Sr.No	Route of drug delivery	Drugs	Polymers	Marketed products
1.	Contact lens	Pirfenidone	Polymethyl cellulose	ACUVUE Vita Unisex contact lens
2.	Iontophoresis	Opioids, steroids.	-	Iontopatch, Iontophoresis galvanic cell
3.	Microneedles	Lidocaine, pilocarpine.	Maltose 60, CMC 43,64	Daytona MT &
4.	Micelles	BCS-II drugs	Polyethylene	Dry eye relief
5.	Dendrimers	Poly-amidoamine	PAMAM, PPI dendrimer	Uvia gel
6.	Niosome	Pilocarpine HCl	PVA, ethyl alcohol	Noisome
7.	Microemulsions	Chloramphenicol	Poloxamer	Cationorum cyclosporin ophthal &Latoprost
8.	Implants	triamcinolone	Poly vinyl alcohol	Acrolab aqueous drainage implant
9.	Microspheres	Pilocarpine hydrocartisone	Poly lactic acid	Careprost
10.	In-situ gels	Poloxomer with chitsan	Gellangum, pectin.	Lumigan

CONCLUSION

Novel drug delivery system has been widely used these days to deliver the drugs into different regions of the eye, and in ophthalmic portion the novel delivery made it easy to deliver the drugs and to pertain for a longer period of time. Also, patients are widely accepting these novel techniques due to their wide range of application

and prolong drug release. Application in development of novel strategies of ophthalmic drug delivery has been significant for their effective release of drug and prolong the drug retention time in the eye region. Contact lens and Iontophoresis are widely developing these days and researches are being for their effective action. Microneedles and micro emulsions and Insitu gels are being developed these days for their application inside the eye for increased therapeutic efficiency of the drug. This article gives a quality of information about the novel techniques used to deliver of drugs into eye with more therapeutic efficiency and retain drug for longer period of time.

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