

Drug Eluting Therapeutic Contact Lens

Hitesh Gohel P.*, Ghadiyali Shahbaz, Viral Shah, Dr.U.M.Upadhyay

*Department of pharmaceuticals, sigma institute of pharmacy
vadodara, gujarat, india.*

Corresponding Author: lalohitesh@gmail.com

Subject: Pharmaceutics

Abstract:

Current ophthalmic drug delivery systems are insignificant as it gives low bioavailability and short time drug release, for example: eye drops, in which 95% of drug is lost due to absorption through the conjunctiva or through the tear drainage. Drug delivery through therapeutic contact lenses enhances the bioavailability of drug by controlled and extended release on the eye surface and enhances the residence time of drug in eye cavity. In this review focus has been made on developing drug eluting contact lens using two techniques like nanoparticle encapsulated therapeutic contact lens and molecularly imprinted therapeutic contact lens. Therapeutic contact lenses can prevent infections and unwanted reaction of eye tissues and can act as drug reservoir for treatment of several other ocular pathologies. The contact lenses prevent the drug from being lost to tear drainage by releasing the drug into tear layer on the contact lens, where it ultimately diffuses into the eye. Ex: hydro gel soft contact lens. Thus, this review will focus on potential of therapeutic lenses as effective dosage form for ophthalmic drug delivery system.

Keywords: *Therapeutic contact lens, ophthalmic drug delivery system, hydro gel soft contact lens*

Introduction:

Several eye diseases like cataract, age-related macular degeneration, diabetic retinopathy, glaucoma etc have reported to affect several millions of the world population. The intraocular and systemic therapy is not widely used due to their intrinsic limitations. The topical route is the most appropriate therapy for local and controlled delivery of bioactive and therapeutic molecules to the eye, as it offers higher patient compliance, better proximity to the infected site and avoids potential systemic side effects. Among the topical formulations, conventional topical eye drops is well accepted and represents ~70-90% of the marketed formulations. However, the success of topical therapy is limited by several issues such as low bioavailability (>1%), short residence time, low corneal permeability. Consequently, few products including contact lenses, have been launched in the market while many others are in pre-clinical and clinical stages. Contact lenses includes polymeric/ mucoadhesive formulations, hydrogels, in situ gelling systems etc. Contact lenses are particularly attractive for ODDS as these significantly increase the residence time (typically

days) of the drug in the eye, high degree of comfort and enhances the drug bioavailability considerably.

Basically several approaches have been used to incorporate drugs into contact lenses like “loading drugs into preformed lenses”, “ manufacturing the lens with the drugs entrapped inside”, “dissolving drug in the monomer solution and followed polymerization”, “nanoparticles encapsulated contact lens”, “ion exchange reaction with hydrogel functional groups” etc. These techniques increase the number of processing step and are tedious for fabrication. In nanoparticle encapsulated technique, encapsulation of the drug in nanoparticles or vesicles dispersed in the solution of the monomers which make up the lenses ensures that when the polymerization occurs, the particles remain trapped in the structure. And ,Colloidal particles are in charge of regulating the release of the drug. If the dimensions of the colloidal structures are adequate and are included in moderate proportions, the lenses will maintain optical transparency. This idea has been substantiated with the inclusion in acrylic hydrogel of microemulsions and liposomes carrying hydrophobic

drugs such as lidocaine. In polymerization; drug encapsulates nanoparticle of size less than 50 nm and p-HEMA hydrogel matrix polymerized by bulk, solution and free radical techniques in the presence of a cross-linker such as ethylene glycol-di-methacrylate (EGDMA). The particle-laden hydrogels were characterized by light transmission and electron microscopy studies. Release profiles of lidocaine, a model hydrophobic drug, were measured by UV-V spectrophotometer. Addition of drug-laden particles in the polymerizing medium results in particle dispersion in the hydrogel matrix.[1]

If contact lenses made of these materials are placed on the eye, the drug will diffuse from the particles, travel through the lens matrix, and enter the post lens tear film, and the thin tear film is trapped between the cornea and the lens, which are shown in fig. 1 and 2

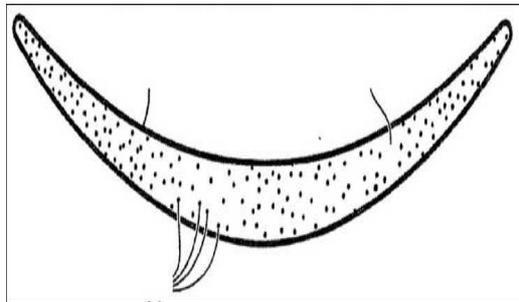


Fig1. Schematic diagram of the novel particle-laden soft contact lens

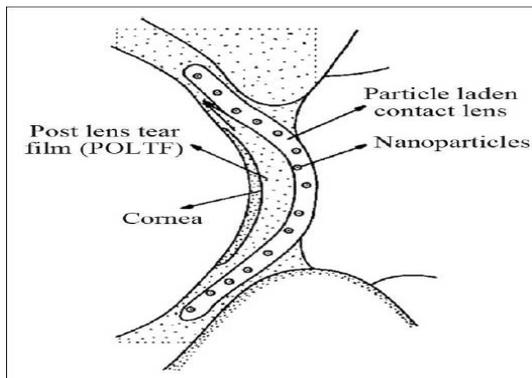
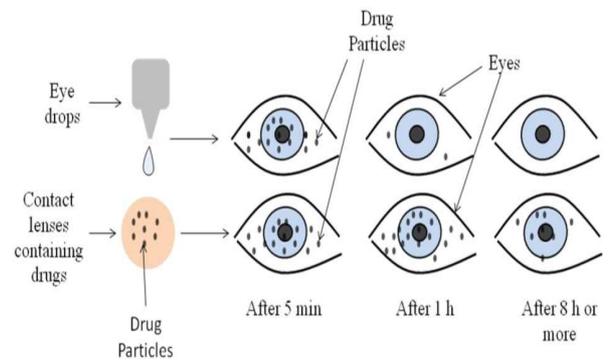


Fig.2 Schematic diagram of the novel particle-laden soft contact lens inserted in the eye

In the presence of a lens, drug molecules would have a much longer residence time than drops. The longer residence time would presumably result in higher drug flux through the cornea and reduce the drug absorption into the blood stream through the conjunctiva or the nasolachrimal duct. In addition, due to the slow diffusion of the drug molecules through the particles and the lens matrix, drug-laden contact lenses can provide continuous drug release for extended periods. By using drug-eluting lenses, there is enhanced localized absorption and decreased potential for systemic toxicity.[2,3]

Fig. 3 Schematic representation of drug release time for contact lenses and conventional topical formulation:



Methods:

(1) Nanoparticle encapsulation:

Encapsulation of the drug in Nano metric particles or vesicles is made by drug dispersed in the solution of the monomers which make up the lenses so that, when the polymerization occurs, said particles remain trapped in the structure. Colloidal particles are in charge of regulating the release of the drug. If the dimensions of the colloidal structures are adequate and are included in moderate proportions, the lenses will maintain optical transparency. This idea has been substantiated with the inclusion in acrylic hydrogel of micro emulsions and liposomes carrying hydrophobic drugs such as lidocaine. The resulting systems release about 25% of the dosage within 24 hours and control the release of the remaining fraction for over one week in an efficient manner. However, this interesting approach has a couple of drawbacks:

- i) A low degree of stability of colloidal structures during sterilization, and
- ii) Premature release of a significant portion of the dosage in the lens conservation liquid, which requires

their storage in a medium which does not allow said release.

(2) Molecular imprinting:

The utilization of the molecular imprinting technique is an important progress in this work. The procedure consists in synthesizing the contact lens in the presence of the drug molecules which act as a mould causing monomers to arrange themselves according to their affinity. The spatial arrangement of monomers becomes permanent when the polymerization process is completed. In this way, specific receptors are created in the structure of the lens having the most adequate size and chemical groups for capturing the drug with the highest affinity. The limited number of functional monomers available and the reduced physical stability of the receptors (derived from the flexibility of the lenses) are important for the application of this technique. However, with a careful optimization of the composition and the synthesis procedures, it has been possible to develop contact lenses with improved bearing capacity and controlled delivery which provide levels of norfloxacin exceeding the MIC of numerous bacteria or which enhance considerably the ocular bioavailability of timololol in animal models. Ease of use and low cost of manufacturing processes have made soft contact lenses very attractive as controlled release systems for ocular drugs[4]. Although more research is required, particularly in vivo trials, before we see medicated contact lenses in the market, said recent developments allow us to forecast that in a not too distant future they will become a very useful instrument for prolonging the permanence of drugs in the pre-corneal area, reducing their systemic absorption and improving compliance of dosage regimes.

(3) Particle-laden soft contact lenses

Particle-laden hydrogels are promising approach for ocular drug delivery and are expected to deliver the drugs at therapeutic levels for a period of time. It involves liposomes-laden, surfactant laden, biomimetic hydrogels and drug polymer films coated with hydrogels. It may be possible to use this system for both therapeutic drug delivery to eyes and the provision of lubricants to eye problems prevalent in extended lens wear. Typically, they are transparent and provide controlled drug delivery. Gulsen and Chauhan encapsulated the ophthalmic drug formulations in nanoparticles and dispersed these drug-laden particles in the lens material, such as p-HEMA hydrogels[5]. This drug-laden p-HEMA hydrogels were synthesized by free radical solution

polymerization of the monomers in presence of nanoparticles and were found to control the drug release for few days. Similarly, to reduce drug loss and side effects, it is proposed to encapsulate the ophthalmic drug formulations in liposomes and disperse the drug-laden liposomes in the lens material. Upon insertion into eye, the liposome-laden lens is likely to release the drug between air and lens and/or between cornea and lens, thus provides drug delivery for extended periods of time. In another study, dimyristoyl phosphatidylcholine liposomes are dispersed in p-HEMA hydrogel contact lenses and the results indicate the prepared lenses are transparent and exhibited controlled release (~8 days). Further, the delivery rates can be modified by controlling particle size and drug loading. Alternatively, drug delivery from contact lenses can be controlled by formulating microencapsulation[8]. Gulsen embedded micro emulsion drops in p-HEMA hydrogels, stabilized with a silica shell, which were found to be transparent and provided controlled release for >8 days. Kapoor and Chauhan have developed surfactant-laden p-HEMA contact lenses of cyclosporine A for the controlled release using various Brij surfactants and evaluated the influence of chain length and unsaturated groups on drug release. The results indicate that surfactant-laden p-HEMA gels are potential for extended release of cyclosporine A, and possess suitable mechanical and optical properties for contact lens applications[11,13]. All these studies points to the fact that particle-laden hydrogels could be considered as one of the most promising approaches for the successful delivery of ODDS.[6,7]

Factors Affecting Drug Delivery:

- (1) Transparency Of The Lens:
- (2) Oxygen Permeability:
- (3) Glass Transition Temperature:
- (4) Wettability:
- (5) Water Content:
- (6) Drug Loading In Preformed Lenses:

1) Transparency of the lens:

Transparency of the formulated contact lens is a key factor affecting the drug delivery, and cannot be compromised due to the incorporation of drug particles or additives. The novel approaches have enabled to formulate and incorporate materials in contact lenses which demonstrated good transparency[14]. For instance, contact lenses formulated with advanced techniques such as molecular imprinting and supercritical solvent

approaches, loaded liposomes and microemulsions, exhibited good transparency.

2) Oxygen permeability:

Human eye does not receive adequate blood flow to supply the eye with enough oxygen, or to remove enough carbon dioxide. It mainly relies on its exposure to the air for oxygen supply. Hence, the prepared lenses should allow free transfer of oxygen to the eyes and any low oxygen transfer eventually causes severe side effects. The lens permeability (Dk) is the product of the diffusivity (D) and the oxygen partition coefficient (k), and it is typically expressed in units of 10^{-11} ($\text{cm}^2/\text{s} \cdot \text{mlO}_2/(\text{mlmmHg})$) or 10^{11} $\text{mlO}_2 \text{ cm}/(\text{s cm}^2 \text{ mmHg})$, which is also referred as barrer or Fatt. The oxygen permeability is an intrinsic property of a material to transport oxygen through its bulk and is independent of thickness. The oxygen transmissibility refers (below equation) to the oxygen transport capacity of a specific contact lens with thickness t , and it generally expressed in units of 10^{-9} $\text{cm mlO}_2/(\text{s ml mmHg})$ or 10^{-9} $\text{mlO}_2/(\text{s cm}^2 \text{ mmHg})$.

$$DK/T$$

Seeking to improve soft contact lens permeability scientist started to make hydrogels from silicone based polymers like polydimethylsiloxane (PDMS). The silicone hydrogel contact lens, also known as siloxane lens, show impressive permeability (PDMS has a Dk of 600 barrer), while retaining the comfort, wettability and biofilm resistance of non-silicon based hydrogels. However, in order to avoid hypoxia, an extended wearable contact lens must provide at least minimum oxygen transmissibility (Dk/t) of 87 barrer, which may not be easy to attain with traditional hydrophilic contact lens. Recently, one report suggested the minimum value of Dk/t to avoid hypoxia as 125 barrer. The reported values of Dk of various commercial contact lenses are given in Table 1. With an approximate average thickness of 80 μm , these commercial siliconehydrogel contact lenses can provide sufficient oxygen transmissibility to be used as extended wear. Various researchers have used these extended wear contact lenses for ophthalmic drug delivery with no effect on the oxygen permeability of the lens [9,10].

3) Glass transition temperature:

The Tg (Glass transition temperature) of contact lenses is not expected to alter during the drug loading process or due to incorporation of additives. Several studies indicate that the contact lenses manufactured by various approaches have not shown any

significant effect on Tg. Further, the alteration in Tg on addition of βCD was found to be insignificant, which suggests that the grafted βCD has little or no effect on the degree of cross-linking of the hydrogels or the stiffness of the network. Costa et al also found that the Tg of contact lenses was not affected after the impregnation process and drug release. Yanez et al reported no alteration in the Tg values of the SCLs (Soft contact lenses) with successive supercritical fluid processing steps. Thus, most of the methods used for the fabrication of contact lenses have good feasibility of loading the drugs with no change in Tg [15].

4) Wettability:

Hydrophobic polymers will repel the water that makes up a majority of the tear surface. This disrupts the tear flow and results in the deposition of an albumin film on the lens, which eventually reduces the effectiveness of the contact and can cause infection and/or irritation. Therefore, if a contact lens surface is highly hydrophobic it needs to be made hydrophilic. Doping the polymer or treating the surface of the polymer can do this change in the morphology of the surface. However, wettability of soft contact lenses affects their physiological compatibility and the stability of the pre-lens lacrimal fluid and can be measured by contact angle measurements. For instance, wettability of pHEMA was slightly increased when copolymerized with high proportions of glycidyl methacrylate (GMA), but slightly decreased when $\beta\text{-CD}$ was attached [4,15]. However, contact lenses using $\beta\text{-CD}$ -loading can be used for extended drug delivery. On the other hand, no significant effect on the contact angle was measured when timolol maleate and acetazolamide was impregnated using supercritical solvent impregnation technique. The theoretical contact angles above 90° indicates non-wetting of the lens surface. There are reports in the literature which suggests that supercritical fluid based contact lenses keep their wettability properties after processing. In addition to wettability and content, the comfort of soft contact lens also depends on the viscoelasticity of the network and on its sliding over the eye surface and the lids. All these results indicate that several processing techniques could be used for the loading of drugs in contact lenses without producing much effect on the wettability. Further one should be aware that contact lens should be highly hydrophilic and must resist the deposition of a biofilm on the lens, in the case of extended wear.

5) Water content

The permeability of the lens is proportional to the amount of water in the lens. As the percent weight of water increases in the lens, the permeability increases linearly. The ability of lenses to absorb large amounts of water also makes them highly hydrophilic. These attributes give soft contact lenses the ability to achieve greater permeability and could be used for extended wear without disturbing the eye. However, achieving greater permeability is a complex issue as increase in water content will eventually lose the polymer strength. This can lead to tearing or scratching of the lens. A softer lens also offers the cornea less protection. Lenses with higher water content absorb more water soluble drug compounds and release it later into the tear film than do low water content lenses. Nevertheless, there is no correlation exist between the amount of drug release and the water content of the lens for hydrophobic drug as shown by Kim et al. The plausible reason is that the hydrophobic drugs will partition into the silicone rich phases, and the partition coefficient of drug in the gels will be influenced by the silicone composition [18].

Drug delivery through commercially available soft contact lenses:

The drug release rate on commercially available soft contact lenses (silicone hydrogel and acrylate hydrogel) has also been reported for topical extended release of ciprofloxacin hydrochloride. Silicone hydrogel materials tested were balafilcon A (PureVision, Bausch and Lomb), comfilcon A (Biofinity, CooperVision), galyfilcon A (Acuvue Advance, Johnson and Johnson), lotrafilcon A (Night and Day, CIBA Vision), lotrafilcon B (O₂ Optix, CIBA Vision) and senofilcon A (Acuvue Oasys, Johnson and Johnson). Conventional lens materials were alphafilcon A (SofLens 66, Bausch and Lomb), etafilcon A (Acuvue2, Johnson and Johnson) and polymacon (SofLens 38, Bausch and Lomb). Of the silicone hydrogel materials, balafilcon A released the highest amount of drug and appears to be the most encouraging for high delivery levels.

ADVANTAGES:

- ❖ Several benefits including,
- ❖ Increased ocular bioavailability,
- ❖ Prolonged residence time,
- ❖ Improved patient compliance,
- ❖ Higher efficiency and
- ❖ Low side effects compared to conventional dosage forms.

- ❖ Ease of application,
- ❖ Convenient for long term therapy due to their excellent biocompatibility,
- ❖ Provides continuous drug delivery,
- ❖ Unproductive systemic absorption, higher patient compliance etc.

DISADVANTAGE:

- ❖ A capital disadvantage of lens resides in their 'solidity', i.e., in the fact that they are felt by the (often oversensitive) patients as an extraneous body in the eye. This may constitute a formidable physical and psychological barrier to user acceptance and compliance[19].
- ❖ The occasional inadvertent loss during sleep or while rubbing the eyes.

CONCLUSION:

Progress in the field of contact lenses drug delivery has been established recently with controlled loading and sustained release. Different techniques have been used for increasing the drug load and controlled release. Each technique may have some pros and cons with little effect on mechanical and optical properties of the lens. Various lens materials and their requirement for ophthalmic use, also have effect on the drug loading. Experimental works demonstrated that the contact lenses exhibit greater drug loading with adequate mechanical and optical properties. The type of the contact lenses and the technique of drug loading are found to affect the residence time of the drug. In comparison with topical alternatives, contact lenses provide an increased residence time at the surface of the eye for efficacious therapy.

Cite this article"

Hitesh Gohel , Ghadiyali Shahbaz "Drug Eluting Therapeutic Contact Lens" Int. J. of Pharm. Res. & All. Sci.2012; Volume 1, Issue 4,1-6
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