Review Article

Drug delivery through soft contact lenses: An introduction

Abstract

Current ophthalmic drug delivery systems are insufficient, specifically eye drops, which allow approximately 95% of the drug contained in the drops to be lost due to absorption through the conjunctiva or through the tear drainage. The use of soft contact lenses has been proposed as a method to deliver drugs to the eye in an efficient manner. The contact lenses restrict the drug from being lost to tear drainage by releasing the drug into two tear layers on either side of the contact lens, where it ultimately diffuses into the eye. By using loaded soft contact lenses, continuous drug release for extended period is possible. This paper focuses on the different methods of drug loading used throughout a polymer hydrogel.

Key words:
Contact lens, drugs, drug delivery, nanoparticles, hydrogel

Introduction

Ocular drug delivery has remained as one of the most challenging tasks for pharmaceutical scientists. The unique structure of the eye [Figure 1] restricts the entry of drug molecules at the required site of action. Currently, most of the eye medications or ophthalmic drugs are applied directly to the eye in the form of eye drops, suspensions and ointments.[1] However, more than 90% of the marketed ophthalmic formulations are in the form of eye drops. These formulations mainly target the anterior segment eye diseases[2] and cannot be considered optimal for the treatment of vision threatening ocular diseases. Most of the topically applied drugs are washed off from the eye by various mechanisms (lacrimation, tear dilution and tear turnover), resulting in low ocular bioavailability of drugs. Moreover, human cornea which comprises epithelium, substantia propria and endothelium also restricts the ocular entry of drug molecules.[3] As a result of these limiting factors, less than 5% of the administered drug enters into the eye. Alternative approaches like incorporation of permeation enhancers/cyclodextrins and increasing the viscosity of solutions have not provided any significant improvement so far. Recently, many drug efflux pumps have been identified and significant enhancements in ocular drug absorption have been achieved following their inhibition or evasion. However, prolonged use of such inhibitors may result in undesirable effects.[4]

In recent times, increased attention is being paid to the development of soft contact lenses (especially acrylate and silicone hydrogel based) with the ability to carry drugs for sustained release in the precorneal area to enhance their bioavailability, and thus, to improve the efficiency of treatments. This administration method requires smaller dosages with the consequence that systemic absorption can be minimized. An additional objective of such development is to simplify administration of drugs and improve compliance of therapeutic regimes.[5] Although the possibility of concurrently addressing the correction of an eyesight problem with pharmacological treatment of an ocular pathology is clearly attractive, if it is to be used only as a sustained release system, neutral lenses could be utilized. In any case, it is necessary to improve the drug in sufficient amounts and for it to be released at the specified rate. The difficulty of designing contact lenses with these two characteristics remained an obstacle for many years, but new approaches have been identified and optimized

Access this article online	
Website: http://www.cysonline.org	Quick Response Code
DOI: 10.4103/2229-5186.79342	

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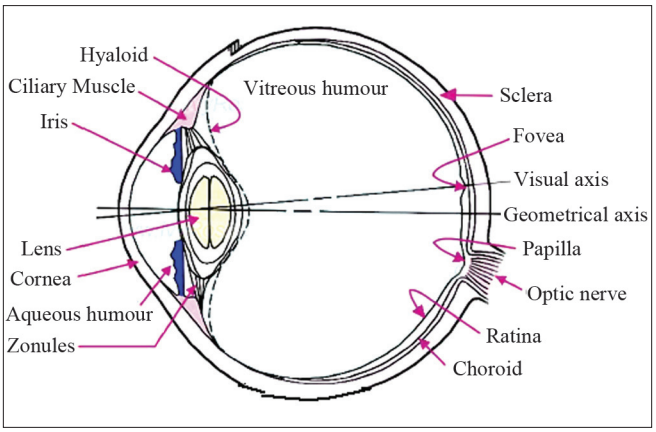

Figure 1: Schematic diagram of the structure of human eye

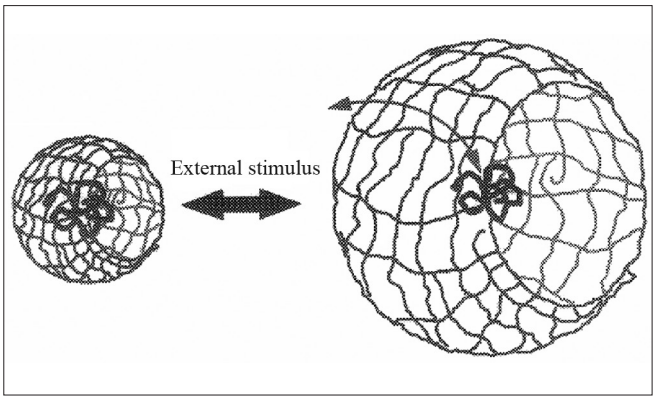

Figure 2: Three-dimensional structure of hydrogel before and after swelling in aqueous medium

recently which open up interesting prospects to include medicated contact lenses into mainstream practice.

There are tens of millions of people suffering from other ocular diseases such as age-related macular degeneration, dry eye, allergies, inflammation and glaucoma. There are three objectives to develop medicated contact lenses for slow and sustained release of entrapped drugs to the site of action in the eye in a time-dependent manner. First is a "comfort lens" which enables one to wear contact lenses for a long period because of dry eyes. Incorporating anti-dry eye formulations in contact lenses with extended release on the order of a day could improve the tolerance for contact lenses. Second is a contact lens for patients, providing an easier means to maintain treatment compliance. Third are "bandage lenses" for applications such as corneal wound healing, viral corneal erosion and management of postoperative complications. These lenses would incorporate antimicrobial or anti-inflammatory drugs for insertion and removal by a physician, with extended drug release over a 1–30 day treatment period.

Method of Drug Delivery through Contact Lenses

Soft contact lens has been used for the delivery of drugs to the eye since 1965.[6] From a structural point of view, soft contact lenses are made of hydrogel (a three-dimensional polymer network) capable of absorbing requisite volume of aqueous medium [Figure 2]. When submerged in a concentrated solution of a drug, the aqueous phase can absorb small amounts of the drug or take it into the polymer mesh by means of non-specific absorption. The improved ocular bioavailability of drugs can be obtained when wearing drug-impregnated conventional soft contact lenses. As a result of this, the amount of drug which is diffused toward the corneal surface is five times higher than that released toward the external lachrymal fluid. Accordingly, the cornea remains in contact with high concentrations of the drug for longer periods of time and drug penetration is more efficient.[7]

A number of studies[7-11] delved into the ability of contact lenses to enhance the penetration of topically applied therapeutic agents. In the present article, emphasis has been given on various methods for the drug delivery through use of contact lenses in the following subheadings.

1. One of the conventional approaches is to soak the lenses in the drug solution and thereafter insert the lenses into the eyes of the patient. The contact lenses may be solid or may have the cavity for receiving the drug solution. Conventional hydrogel soft contact lenses (Poly 2-hydroxyethyl methacrylate) have the ability to absorb some drugs and release them into the post-lens lachrymal fluid, minimizing clearance and sorption through the conjunctiva. Their drug reservoir ability strongly depends on the water content and thickness of the lens, the molecular weight of the drug, the concentration of the drug loading solution and the time the lens remains in it. This approach produces unsatisfactory results because the drug release rate drops quickly over time.[12]
2. Chemical functionalization[5,13-15] of the hydrogels allows for coordination or physical bonds with the drug molecules, mainly through the application of molecular molding or imprinting. This procedure aims at adapt–interact mechanism directly with the polymer chains. For instance, researchers have developed contact lenses based on 2-hydroxyehtylmethacrylate (HEMA) and ionic comonomers exhibiting an affinity with certain antiallergic agents such as azulene or naphazoline in order to promote their charge and control the release by means of an ion exchange mechanism. The main drawback of these materials is neutralization of ionic groups because it involves important changes in the volume which can deteriorate the properties of lenses such as light transmittance by means of protein or lipid deposition.
3. The utilization of the molecular imprinting technique[5] is an important progress in this line of work. The procedure consists in synthesizing the contact lens in the presence of the drug molecules which act as a mold

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 which has appropriate 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 hurdles for the application of this technique.

4. Encapsulation of the drug in nanoparticles[7,16] or vesicles dispersed in the solution of the monomers which make up the lenses ensures that when the polymerization occurs, the 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 microemulsions and liposomes carrying hydrophobic drugs such as lidocaine. *In situ* polymerization; drug encapsulates nanoparticle of size less than 50 nm[7,16] 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).[17] 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–Vis spectrophotometer. Addition of drug-laden particles in the polymerizing medium results in particle dispersion in the hydrogel matrix. If contact lenses made of this material are placed on the eye, the drug will diffuse from the particles, travel through the lens matrix, and enter the post lens tear film (POLTF), and the thin tear film is trapped between the cornea and the lens, which are shown in Figures 3 and 4.

In the presence of a lens, drug molecules would have a much longer residence time in the POLTF than the residence time of approximately 2–5 minutes which is the case with topical application of drugs as drops.[18,19] 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.

Researchers also encapsulate proteins that are involved in wound healing (e.g. growth factors) in nanoparticles and then cross-link into hydrogel poly-HEMA by UV curing.[20] They use both inorganic transparent nanoparticles and biopolymer nanoparticles. The protein releases through a

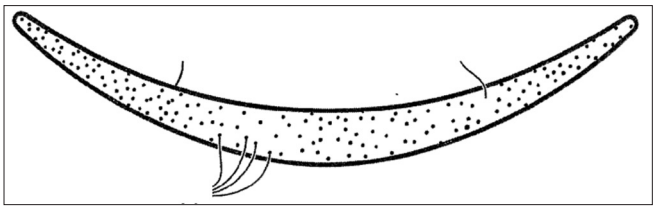

Figure 3: Schematic diagram of the novel particle-laden soft contact lens

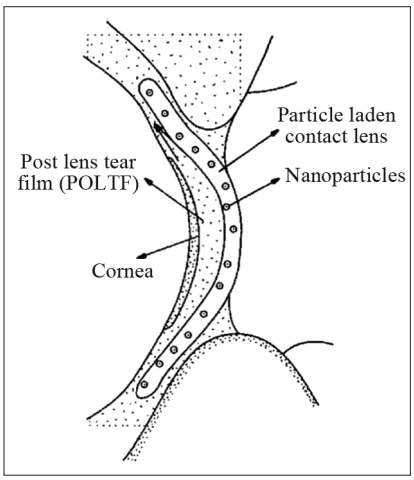

Figure 4: Schematic diagram of the novel particle-laden soft contact lens inserted in the eye

diffusion-based mechanism and is monitored for 25 days.[20] It has been shown that hydrophilic proteins can be encapsulated in different types of nanoparticles, and it is expected that nanoparticle-laden contact lenses would be considered as new mechanism of protein (growth factor) drug delivery. There is potential for broad application of this technology. By using drug-eluting lenses, there is enhanced localized absorption and decreased potential for systemic toxicity.

In an interesting study, contact lenses were made by coating poly (lactic-co-glycolic acid) (PLGA) films containing test compounds with poly (hydroxyethyl methacrylate) (poly-HEMA) by ultraviolet light polymerization. The films containing encapsulated fluorescein or ciprofloxacin were characterized by scanning electron microscopy. Release studies were conducted in phosphate buffered saline at 37°C with continuous shaking. Ciprofloxacin eluted from the contact lens was studied in an antimicrobial assay to verify antimicrobial effectiveness. This study revealed that hydrogel lens containing a polymer film and medicine is capable of releasing medication that prevents bacterial growth. The rate of drug release can be controlled by altering the properties of the polymer film and the lens by infusion process.[21] The Eyenovations team developed a patented process for contact lens which delivers high doses of medication for up to 100 days and has a plan to develop commercial lenses using materials approved by the Food and Drug Administration (FDA), which deliver drugs for up to 30 days for single use.[22]

Benefits of Drug Delivery through Contact Lenses

The use of soft contact lenses for therapeutic drug delivery may correct three inherent deficiencies seen with the typical administration of eye drops into the eye: (i) the contact time of drug with the precorneal tear film may be longer; (ii) compliance as compared to frequent and complicated dosage regimens may be improved; and (iii) less systematic toxicity may be expected because of the total amount of drug administered compared to multidrops. The slower drug release rates with drug encapsulated nanoparticle loaded contact lenses lead to more complete ocular absorption and less systemic absorption. On the basis of above discussion, we can conclude that

- controlled therapy of eye diseases such as glaucoma and dry eyes can be achieved through medicated contact lens;
- fabrication of lenses for vision correction, eye color modification or treatment of diabetic eye diseases can be done; and
- they can be used in artificial cornea and corneal wound healing.

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. Study revealed that majority of the conventional soft lenses released their drug within the first 10–15 minutes.

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 (O_2 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.[23]

Conclusions

Ease of use and low cost of manufacturing processes have made soft contact lenses a very attractive carrier as controlled drug release systems for ocular disease treatment, although more research is still required, particularly *in vivo* trials, before we see efficient medicated contact lenses in the market. Recent developments have paved the way for prolonging the permanence of drugs in the precorneal area, reducing their systemic absorption and improving compliance of dosage regimes. Therefore, we propose soft contact lenses as a new vehicle for ophthalmic drug delivery in an efficient and time-dependent manner for correcting eye diseases.

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How to cite this article: Jha G, Kumar A. Drug delivery through soft contact lenses: An introduction. Chron Young Sci 2011;2:3-6.

Source of Support: Nil, **Conflict of Interest:** None declared