Formulation development and evaluation of Therapeutic Contact lens loaded with Ganciclovir

Mohit Harsolekar
Department of Pharmaceutics, Shobhaben Pratapbhai Patel School of Pharmacy and Technology Management, SVKM’S NMIMS University, Mumbai,

Mudassir Ansari
Department of Pharmaceutics, Shobhaben Pratapbhai Patel School of Pharmacy and Technology Management, SVKM’S NMIMS University, Mumbai,

Shibani Supe
Department of Pharmaceutics, Shobhaben Pratapbhai Patel School of Pharmacy and Technology Management, SVKM’S NMIMS University, Mumbai,

Kavita Singh (✉ kavita.singh@nmims.edu)
Department of Pharmaceutics, Shobhaben Pratapbhai Patel School of Pharmacy and Technology Management, SVKM’S NMIMS University, Mumbai,

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Abstract

Purpose
Soft contact lenses have been demonstrated as a promising tool for ocular drug delivery. In the present investigation ganciclovir (GAN) loaded microparticles dispersed in hydrogel-based contact lenses were fabricated to achieve prolonged release and improved permeation of GAN across corneal epithelium.

Methods
GAN-Hydroxy Propyl Methyl Cellulose (HPMC) microparticles were prepared by solvent evaporation method and evaluated for entrapment efficiency, drug content and drug release. The Polyhydroxyethylmethacrylate (pHEMA) contact lenses were synthesized by free radical polymerization reaction using crosslinkers like ethylene glycoldimethacrylate and photoinitiator such as IRGACURE 1173® in UVB light, λ 365 nm. The GAN-HPMC microparticles when incorporated into the premonomer mixture and polymerized together give rise to a particle dispersion system in the hydrogel contact lenses. The contact lenses were studied for surface morphology, transmittance, swelling, drug release, Na + ion permeability and hens egg test chorioallantoic membrane assay (HETCAM).

Results
Hydrogel contact lens exhibited satisfactory surface morphology, transmittance, swelling, Na + ion permeability (3.72x106 mm²/min) and a release of 48 hours suggesting a potential for prolonged ocular drug delivery. Furthermore, HETCAM exhibited no signs of ocular irritation.

Conclusion
The developed delivery platform is a promising alternative to conventional dosage forms like eye drops, suspensions and ointments due to its increase in the residence time attributed to its prolonged release profile. Hence, drug delivery by hydrogel-based contact lens decreases the systemic effects of the drugs which are meant for local action, thus, enhances the therapeutic use by improving the patient compliance.

Introduction
The human eye is the most important and delicate organ of the human body. Owing to its complexity in the anatomy and the physiology, non-invasive ophthalmic drug delivery offers a great challenge [1]. Topical drug delivery to the eye not only provides prolong drug release but also reduces the drug related toxicity and improves patient compliance [2]. Among the conventional topical eye formulations, eye
drops, gels, ointments are associated with drawbacks such as poor tear turnover, poor residence time of the drug, frequent dosing intervals, wastage of dosage, excessive systemic absorption [3–5] leading to poor ocular bioavailability (only 5% for eye drops). Thus, newer formulation approaches aims at overcoming these limitations by increasing the residence time and controlling the drug release to avoid the drug loss due to tear drainage and to reduce dosing for preventing fluctuations in the ocular drug concentrations and thus possible systemic side effects [6].

Contact lenses have gained a wide acceptance in therapeutics lately as a drug delivery vehicle for safe and effective drug administration to eye. Contact lenses have proven to be effective as corneal bandages for post-operative healing and pain management and hence are not restricted to cosmetic and daily disposable use [7, 8]. The contact lenses can be tailored according to the drug release profile needed to be achieved with burst as well as sustained release of the active pharmaceutical ingredient. Contact lenses from Bausch & Lomb’s (Balaflcon A) and Cooper Vision have already commercialized the idea of therapeutic contact lenses. Other companies such as SEED Co. Ltd and Senju Pharmaceutical Company Ltd. have co-developed soft contact lenses for allergic conjunctivitis for one complete day [6, 8, 9]. Interestingly, recent incorporation of hydrogel technology and nanotechnology into fabrication of soft contact lenses gained importance due to sustained drug delivery [10–12]. Moreover, hydrogel based contact lenses are of greatest interests due to their advantage in increasing the bioavailability of drug in the eye (> 50%) compared to eye drops (1–5%) [13–15]. A study concluded that hydrogel based soft contact lenses can be successfully used for delivering timolol and brimonidine to maintain the balance in the intraocular pressure while maintaining the same release profile throughout their shelf life [16].

Hydrogel contact lenses on coming in contact with ocular fluid, swells producing polymeric mesh for sustained release of drug into the ocular sites [17–19]. The degree of swelling and rate of release in turn depends upon the type and nature of polymer used [20, 21]. These hydrogels contact lenses are able to extend the release of the drug in post lens tear film (POLTF) and effectively increase its residence time by more than 30 minutes. The drug diffuses out of the polymer matrix and reaches its site of action to provide a local effect and thereby reduces systemic toxicity [22, 23]. However, the method commonly used for loading drug into the soft contact lenses involves soaking in drug solution. Therapeutic contact lenses made by this process suffers burst release and thus unable to maintain the controlled release profile [24–26]. Controlled release dosage form covers a wide range of prolonged action formulation, which provides continuous release of their ingredients at a predetermined time. One such approach is using polymeric microparticle as a carrier of drug embedded in the contact lens [27]. Furthermore, the use of biodegradable and bioadhesive polymers for ocular delivery have been evaluated over the last decades and considering the charged nature of corneal mucosa the mucoadhesive polymers possessing charge moiety have been widely reported in literature [28]. Among the categories, hydrophilic polymers like hydroxypropyl methylcellulose (HPMC) and hydroxyethyl methacrylate (HEMA) are extensively used to retard the release of the drug from the polymeric matrix and hence maintain a control release profile of drug [29, 30].
In the current study we explored the effect of HPMC and HEMA polymers on release of the drug through hydrogel contact lens system. Formulation of hydrogel contact lens containing ganciclovir-HPMC microparticle was principally aimed at increasing the residence time of the drug in the eye and reduces dosing frequency and drug related toxicity problems.

**Material And Methods**

Ganciclovir (GCV) was a generous gift sample from Shanghai Win Win Biochemical Limited, China. Hydroxyethyl methacrylate (HEMA) was purchased from Sigma Aldrich, USA. Ethleneglycol dimethacrylate (EGDMA) and methacrylic acid (GMMA) were obtained as a gift sample from Evonik Degussa, India. Irgacure 1173 (2-Hydroxy-2-methyl-1-phenyl-propan-1-one) was procured as a gift sample from BASF, Germany. Hydroxypropyl methylcellulose (HPMC E50 LV) was purchased from Loba Chemie Pvt. Ltd. Mumbai. Methylen chloride and ethanol was purchased from Spectrochem and SD fine chemicals, Mumbai, respectively. Polysorbate 80 (Tween 80) was provided by Research Lab fine chem industries. All the other materials used were of analytical grade.

**Preparation of Ganciclovir loaded HPMC microparticles**

Solvent evaporation method was used for the preparation of drug loaded microparticles. In this study, hydroxypropyl methylcellulose (HPMC) was dissolved in 1:1 mixture of methylene chloride (20 ml) and ethanol (20 ml) at room temperature using a magnetic stirrer [31]. Ganciclovir was added into the prepared polymer solution with a polymer to drug ratio of 85:15 (Batch CLHPMC 8515) and 50:50 (Batch CLHPMC 5050). The resultant drug polymer mixture was added drop-wise to 200 ml aqueous solution of tween 80 (0.1% v/v) using a hypodermic needle (24 G). Stirring (1000 rpm) was continued at room temperature for 2 hours until the entire solvent was evaporated leading to the formation of microparticles. The drug loaded microparticles obtained were filtered using whatmann filter paper no. 42 with an average pore size of 2.4 microns. The microparticles were weighed and dried at 60°C until no weight loss was observed [8, 32–34]. The quantities of polymer and drug were decided based on preliminary studies.

**Characterization of ganciclovir loaded HPMC microparticles**

**Entrapment Efficiency**

The amount of drug entrapped was determined by dispersing the prepared micro-particles (CLHPMC5050 and CLHPMC8515) in phosphate buffer saline (PBS) of pH 7.4 and centrifuging the resultant dispersion at 8000 rpm for 20 minutes. The absorbance of the supernatant was taken at 254.2 nm by UV-Vis spectrophotometer, Perkin Elmer, USA to determine the amount of drug present in the supernatant. The sediment was again dispersed in PBS (pH 7.4) and absorbance was obtained in the same manner to measure the amount of drug present in the sediment. Percentage entrapment of ganciclovir was determined using the formula:
Drug Content

Ganciclovir loaded HPMC micro-particles (CLHPMC5050 and CLHPMC8515) were accurately weighed (10 mg) and dissolved into the PBS pH 7.4 at room temperature. Absorbance was taken at 254 nm by UV-Vis spectrophotometer, Perkin Elmer, USA to determine the amount of ganciclovir present in 10 mg of sample.

Drug release study

Release of ganciclovir was determined using plain drug and drug loaded HPMC micro-particles (CLHPMC5050 and CLHPMC8515) by dialysis method. The dialysis membrane was soaked into deionized water for 24 hours before use. Samples were suspended in 2 ml PBS (pH 7.4) and filled into the dialysis bag. Release studies were performed in 30 ml of PBS (pH 7.4) in a measuring cylinder at 100 rpm on a magnetic stirrer maintained at 37 ± 0.5°C. Aliquots (2 ml) were withdrawn at predetermined time interval and replaced with fresh PBS (pH 7.4) to maintain sink condition. The aliquots withdrawn were filtered through Whatmann filter paper no. 42 [35]. The amount of ganciclovir released was determined using UV-Vis spectrophotometric method at 254.2 nm wavelength.

Preparation of hydrogel contact lens containing ganciclovir loaded HPMC microparticles

Preparation of pre-monomer mixture

Pre-monomer mixture was prepared by amalgamation of polymer, cross linkers and plasticizer in water. The amount of polymer hydroxyethyl methacrylate (HEMA) used for pre-monomer mixture was 46.7% (w/w). Methacrylic Acid (MAA) and Ethyleneglycol dimethacrylate (EGDMA) as cross linkers comprises of 0.8% (w/w) and 0.5% (w/w), respectively. Plasticizer (PEG 400) of 3% (w/v) was added and mixed with aqueous polymer-crosslinker blend. The resultant mixture was sonicated until there was no presence of air bubble [36, 37].

Polymerization of pre-monomer mixture

Irgacure 1173 (2-Hydroxy-2-methyl-1-phenyl-propan-1-one), a photoinitiator was added to the pre-monomer mixture and sonicated until it no air bubbles was observed. Plain ganciclovir and ganciclovir loaded microparticles (CLHPMC 8515 and CLHPMC 5050) was added in the final mixture. This contact lens mixture was transferred (100 µl) between two glass slides separated with a medical grade polypropylene plastic spacer of 0.5 mm thickness and kept in a UV trans illuminator at 365 nm, UV-B light for 15 minutes. The hydrogel contact lenses formed were kept in a desiccator to avoid its exposure to humidity till further use [38–41]. Optimized batches are summarized in Table 1. Quantities of ingredients

\[
\% \text{Entrapment} = \left( \frac{\text{Conc. in sediment}}{\text{Conc. in sediment} + \text{Conc. in supernatant}} \right) \times 100
\]
were selected on the basis of ocular dose of ganciclovir and the assay of ganciclovir in HPMC micro-
particles [6].

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Formulations with GCV</th>
<th>Formulations with GCV microparticles</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CLHPMC8515</td>
<td>CLHPMC5050</td>
</tr>
<tr>
<td>Hydroxy Ethyl Methacrylate (HEMA)</td>
<td>46.7</td>
<td>46.7</td>
</tr>
<tr>
<td>Methacrylic Acid (GMMA)</td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td>Ethylene Glycol Dimethacrylate (EGDMA)</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>2-Hydroxy-2-methyl-1-phenyl-propan-1-one (Igracure 1173)</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Purified Water</td>
<td>52</td>
<td>52</td>
</tr>
<tr>
<td>Ganciclovir/GCV microparticles</td>
<td>0.4</td>
<td>2.5</td>
</tr>
</tbody>
</table>

### Characterization of hydrogel contact lens containing ganciclovir loaded HPMC microparticles

#### Surface Morphology

The surface morphology of the microparticles was also determined using optical microscope and Leica DM-4P polarized light microscopy. The surface morphology of hydrogel contact lens was determined using Leica DM-4P polarized light microscopy for the purpose of ascertaining the thickness and irregularities on the surface of the hydrogel contact lens.

#### Transmittance Study

For measurement of transmittance, the hydrogel contact lens containing plain drug and drug loaded HPMC microparticles i.e. CLHPMC5050 and CLHPMC8515 were soaked in a simulated tear fluid for 24 hours. Transmittance was checked at 630 nm by UV-Visible spectrophotometry using following formula:

\[
\text{Transmittance} + \text{Absorbance} = 1 \quad (2)
\]

#### Swelling study

The swelling study was carried out by soaking the hydrogel contact lens containing plain drug and drug loaded HPMC microparticles i.e. CLHPMC5050 and CLHPMC8515 in simulated tear fluid for 24 hours at room temperature and weighed. The percentage swelling was determined by the following formula:

\[
\% \text{Swelling} = \left( \frac{\text{Wet weight of Hydrogel Contact Lens} - \text{Dry weight of Hydrogel Contact Lens}}{\text{Dry weight of Hydrogel Contact Lens}} \right) \times 100 \quad (3)
\]
Drug Release Study

Release of ganciclovir from plain drug loaded and drug-HPMC micro-particles (CLHPMC5050 and CLHPMC8515) loaded hydrogel contact lens was determined by dialysis method as described above.

Permeability of Na⁺ Ion through the hydrogel contact lens

This experiment was performed using franz diffusion cell in which the hydrogel contact lens was fixed such that one side of the lens was exposed to the donor chamber while the other side to the receiving chamber. The receiving chamber consisted of 20 ml of deionized water. Donor chamber was filled with 2 ml of 0.1N NaCl with a conductometer attached to it. The conductivity of the solution in the receiving chamber was determined as a function of time [42].

The resultant Na⁺ ion permeability was calculated from the equation given below,

\[
Cr = \frac{A P c o l o / V r L (t - t0)}{
}

Cr = Na⁺ Ion concentration at time t.

A = Area of hydrogel contact lens exposed to the salt flux.

P = Permeability Coefficient of the Na⁺ Ions.

V = Volume of the receiving chamber.

L = Thickness of the hydrogel contact Lens

Eye irritation potential test

Chorioallantoic membrane (CAM) of embryonated hen's egg was used for evaluating corrosive and irritation potential of ophthalmic formulation. It is an internationally validated method in which fresh fertile White Leghorn hen's eggs were obtained and candled prior to use to discard nonviable or defective eggs. Eggs were placed in an incubator at 37 ± 0.2°C and 58 ± 2% RH for 8 days [43]. On day 9, eggs were removed from the incubator; air cell of the eggs was marked, cut, and pared off without injuring the CAM. Pellets were placed directly onto the CAM and observed for 30 seconds for sign of hemorrhage or lysis reactions on the CAM. The whole experiment was carried out under laminar airflow cabinet at room temperature. After the application of the test substance, the chorioallantoic blood vessels and capillaries were examined for irritant effects [44]. The irritation is marked by either or all of the three endpoints i.e. Hemorrhage, Lysis and coagulation of the Chorioallantoic Membrane [45]. For the present study four groups were studied i.e. normal control (normal saline), positive control (0.1 N NaOH), hydrogel base control and formulation control. The test was performed on the 9th day of incubation of fertilized chicken eggs. Samples were spread on the exposed chorioallantoic membrane containing vasculature in each
egg. The irritation response was noted at 30 seconds and 2 minutes. Presence of hemorrhage and lysis served as the end point for the irritation potential.

**Results And Discussion**

In the last two decades, the efforts in the area ODDS has been on the strategy of formulating a delivery system to extend the residence time of the drug applied topically to eye. Sustained and controlled delivery to eye enhances the drug efficiency by increasing the contact time thus reducing its wastage and enhancing its absorption by increasing the contact time. Hence, it also improves patient compliance by lowering the dosing frequency and thereby reducing the adverse effects [46, 47].

**Preparation of Ganciclovir loaded HPMC microparticles**

Preparation of microparticle using solvent evaporation is considered to be one of the efficient technique to obtain a particle of less than 10 micron. To achieve a controlled and sustained release profile, hydrophilic polymer like Hydroxypropyl methylcellulose (HPMC) are widely used and studied. HPMC (also known as hypromellose) belongs to an extensive family of white to off-white, odorless, semi synthetic viscoelastic polymers that retain water and swell. They are used as an excipient and controlled delivery component in oral medicaments, found in a variety of commercial products. Hypromellose is also included in the inactive ingredient database as well as the GRAS list of FDA.

**Characterization of ganciclovir loaded HPMC microparticles**

**Entrapment Efficiency**

The entrapment efficiency of the micro-particles is necessary to ascertain the amount of drug undergoing complex formation with the polymer being used in the total blend. The entrapment efficiency was found to be 78.80% and 73.30% for batches CLHPMC5050 and CLHPMC8515, respectively. This suggests that the present method of formulating microparticles by solvent evaporation gives a good yield of the product.

**Drug content**

The assay of the drug was carried out to determine the amount of ganciclovir present in a given quantity of the micro-particles as drug release is directly affected by the assay of the drug in the formulation. The amount of drug present in the HPMC micro-particles was found to be 95.50% and 92.86% for the batches CLHPMC5050 and CLHPMC8515 respectively.

**Drug release study**

Release of the drug from the prepared formulation is the principal aspect of designing any dosage form. The release of ganciclovir was determined as a function of time and percentage drug release was plotted
against time. Figure 1 shows a percentage release of plain ganciclovir from the dialysis membrane in PBS (pH 7.4) which is completed in 4 hours. Furthermore, the release of ganciclovir from the prepared batches of HPMC micro-particles (CLHPMC5050 and CLHPMC8515) shows that the polymer is successful in retarding the rate of drug release up to 24 hours which is necessary in formulation of controlled release dosage form and is able to increase the residence time of ganciclovir in the eye for which the formulation is intended.

Preparation of hydrogel contact lens containing ganciclovir loaded HPMC microparticles

Preparation of pre-monomer mixture

Pre-monomer mixture consists of polymer required for hydrogel bases preparation and cross linkers for providing rigidity and strength to polymer. Contact lenses made from hydroxyethyl methacrylate (HEMA) have been classically used for cosmetic lens purposes and are increasingly used by the researchers for development of therapeutic contact lens for ophthalmic drug delivery [48]. The permeability of p-HEMA hydrogel sheets in terms of Na + ions is excellent so as to maintain a perfect osmotic pressure in the post lens tear film (POLT), thus, can be formulated as an extended wear contact lens [49]. The p-HEMA contact lenses can be synthesized by free radical polymerization reaction in the presence of one or more cross-linkers such as ethylene glycol-di-methacrylate (EGDMA) [50]. Ethylene Glycol Dimethacrylate (EGDMA) is a hydrophilic difunctional methacrylate offering low viscosity, adhesion, flexibility, and high crosslink density. Incorporation of Ethylene Glycol Dimethacrylate (EGDMA) into polymeric resins improves their mechanical properties such as impact strength and abrasion resistance. Apart from the above mentioned properties, EGDMA can also be used to impart hardness, chemical and heat resistance to the polymers [51].

Polymerization of pre-monomer mixture

Irgacure 1173 (2-Hydroxy-2-methyl-1-phenyl-propan-1-one) acts as a UV photoinitiator for free radical polymerization process which was added to the pre-monomer mixture to reduce the time of polymerization which otherwise takes 24 hours (60°C) for completion. By curing coatings and adhesives faster than traditional methods, UV curing boosts productivity through substantial savings in money, energy, time and labor. As a liquid UV curing agent with excellent compatibility, Irgacure 1173 is easy to incorporate, thus, highly suitable for blends with other photoinitiators [52].

Characterization of hydrogel contact lens containing ganciclovir loaded HPMC microparticles

Surface Morphology

The morphology of the microparticle was found to be smooth and irregular in nature (Fig. 2 and Fig. 3). The surface morphology of the prepared hydrogel contact lens from batches loaded with plain drug,
CLHPMC5050 and CLHPMC8515 was found to be smooth without abrasions with a thickness of 0.5 µm (Fig. 4). This is necessary as the prepared hydrogel should not cause any irritation in the eye after application. Smooth surface ensures uniform release of the drug from the entire surface of the hydrogel contact lens.

Transmittance Study

Transmittance of light is an important parameter for contact lenses in order to maintain the vision clarity. Percentage transparency of the prepared hydrogel contact lens increases the degree of compliance with the patient so as to obtain clear vision after application. Level of transparency should be high in hydrogel contact lens which in turn depends upon the amount of drug or micro-particles being incorporated. The percentage transmittance of the direct drug loaded hydrogel batch was found to be 97.8% at 630 nm in UV-Vis spectrophotometry. This suggests that there is no significant loss of transparency in direct drug loaded hydrogel contact lens. Percentage transparency of the ganciclovir loaded HPMC micro-particle containing hydrogel contact lens was found to be 79.6% and 78.2% of batches CLHPMC5050 and CLHPMC8515, respectively. It was seen that a significant loss in the transparency occurs in case of microparticle loaded contact lens. The percentage transparency of the prepared batches of the hydrogel contact lens was lesser for drug loaded micro-particle contact lens as compared to the direct drug loaded contact lens. The more the concentration of the micro-particles the less was the transparency observed and this was true with increasing concentration of the polymer.

Swelling study

Wettability of hydrogel contact lenses governs the swelling behavior, a key factor in controlling the drug release from the prepared formulation. Swelling of the hydrophilic polymer by imbibing water affects the release of drug from the polymer matrix. Furthermore, swelling helps in maintaining the shape of the prepared hydrogel contact lens. The percentage swelling was found to be highest in the ganciclovir loaded hydrogel contact lens (81.44%) as compared to ganciclovir-HPMC micro-particles loaded hydrogel contact lens. Swelling of CLHPMC5050 and CLHPMC8515 was found to be 83.7% and 79.61%, respectively. It was found that swelling decreases with increasing concentration of the micro-particles in the pre-monomer mixture of the hydrogel contact lens.

Drug Release study

All the three batches of hydrogel contact lens (Fig. 5) showed a burst release profile in the first 4 hours of release study. As the ratio of the drug to HPMC is increased the release rate gets retarded. It was observed that the release of ganciclovir from direct loaded hydrogel contact lens was much faster than the ganciclovir-HPMC micro-particles (CLHPMC5050 and CLHPMC 8515) loaded hydrogel contact lens. The release profile is suggestive of pattern in which the concentration of the polymer is inversely proportional to the release of ganciclovir. Therefore, to increase the residence time of ganciclovir in eye the concentration of HPMC could be increased so as to retarded the drug release. The release profile clearly indicates the decrease in release rate after the initial burst giving a sustained profile that continues upto 48 hours releasing nearly 99% of the drug from the hydrogel contact lens. As the residence time of
ganciclovir is increased upto 48 hours, the need of frequent dosing could be reduced (from five times a
day to once in 48 hours). This also reduces the systemic exposure of the drug so as to minimize any
adverse effects associated with it. Thus, the marketed dose of 0.375 mg as eye gel to be applied 5 times
daily with an average ocular bioavailability of 5%, could be successfully reduced by increasing the time of
residence of ganciclovir in the eye by means of hydrogel contact lenses drug delivery system.

Permeability of Na\(^+\) Ion through the hydrogel contact lens

To maintain the homeostasis in the POLTF adequate Na\(^+\) Ion permeability should be possessed by the
hydrogel contact lens. This is an important aspect for extended wear contact lens especially which are
designed for the purposes of increasing the residence time of the drug. The Na\(^+\) Ion permeability index for
ganciclovir loaded hydrogel contact lens and ganciclovir-HPMC microparticle (CLHPMC5050 and
CLHPMC8515) loaded hydrogel contact lens were found to be more than the ideal minimum value of
1.5x10\(^{-6}\) mm\(^2\)/min which are 8.84x10\(^{-6}\) mm\(^2\)/min, 5.9684x10\(^{-6}\) mm\(^2\)/min and 3.7284x10\(^{-6}\) mm\(^2\)/min,
respectively. The results are suggestive of a fact that as the concentration of the polymer is increased the
Na\(^+\) Ion permeability of the hydrogel contact lens decreased. The fluid hydrodynamic boundary which is
formed as a result of exchange of Na\(^+\) Ion protects the hydrogel contact lens from abrasion [53]. Na\(^+\) Ions
permeability were found to be more than the reported minimum limits indicative of better stability
and thus maintains homeostasis in the post lens tear film. Moreover, it maintains balance of ion
exchange in the aqueous and the vitreous humor of the eye. Furthermore, it helps in the oxygen exchange
so that the lens prepared could be easily wearable for extended period of time.

Eye irritation potential test

The hen's egg test on the chorioallantoic membrane (HET-CAM) is profound alternative to animal
experimentation to evaluate irritant/corrosive potential and allows the study of the immediate effects of
administration of the test substance on membrane of embryonated hen's egg. [54, 55]. Hemorrhage
followed by complete lysis of the veins was seen in the eggs with positive control (0.1 N NaOH). The
chorioallantoic membrane of the 9th day incubated chicken egg did not show any change even after 5
minutes of exposure to the hydrogel base and formulation (Fig. 6). This proves that there was absence of
irritation potential in the prepared formulation of the hydrogel contact lens containing drug loaded HPMC
micro-particles.

Conclusion

Hydrogel contact lens has a massive potential to be a mainstream dosage form for controlled and
extended drug delivery system. Hydrogel contact lenses have been used as a corneal bandage in post-
operative care and corneal pain management which not only reduces the dosing frequency but also
increases patient compliance. Furthermore, formulations with higher percentage of retardation polymers
give longer hold of drug thereby controlling their rate of release. The present study of formulating
hydrogel contact lens containing ganciclovir-HPMC microparticle was principally aimed at increasing the
residence time of the drug in the eye. Hydrophilic polymers like hydroxypropyl methylcellulose (HPMC)
and hydroxyethyl methacrylate (HEMA) have been used to retard the release of the drug from the polymer matrix. The surface morphology of the prepared hydrogel contact lens was found to be smooth with a thickness was 0.5 mm, a necessity to avoid any irritation in the eye after application. Na\(^+\) ions permeability and percent transmittance studies shows better stability and maintains homeostasis in the post lens tear film after wearing the contact lens. Hydrogel provides appropriate swelling which thereby imparts sustained release of drug from polymeric matrix and helps in maintaining the shape of the prepared hydrogel contact lens. The polymeric meshwork successfully provides extended release of drug up to 48 hours which can be further use in long term treatment. Therapeutic use and drug delivery via these hydrogel-based contact lens could improve the patient care and most importantly reduces the systemic effects of the drugs which are meant for the local action.

**declarations**

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**Disclosure statement**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

**References**


Figures

Figure 1

Percentage drug release of CLB1 (plain drug) and drug loaded HPMC microparticles (CLHPMC5050 and CLHPMC8515)
Figure 2

Images of Ganciclovir loaded HPMC microparticles using optical microscopy (45X)

(a)  
(b)

Figure 3

Images of Ganciclovir loaded HPMC microparticles seen under Leica DM 4P polarized light microscopy (100X)

(a)  
(b)

Figure 4

Microscopic images of thickness and the surface of the prepared hydrogel contact lens seen under Leica DM 4P polarized light microscopy
Figure 5

Percentage drug release of CLB1 (plain drug) and drug-HPMC microparticles (CLHPMC5050 and CLHPMC8515) loaded hydrogel contact lens

Figure 6
Ocular irritation studies performed on chorioallantoic membrane of 9 day incubated chicken eggs.

Normal control (1), Positive control (2), Hydrogel Base Control (3), Hydrogel Contact Lens Batch CLHPMC5050 Control (4), Hydrogel Contact Lens Batch CLHPMC8515 Control (5). 30 second response [1(i) – 5(i)], 2 min response [1(ii) – 5(ii)]