RESEARCH PAPER

Physicochemical Characterization and Performance Evaluation of Polymeric Ocular Films for Ocular Delivery of Ciprofloxacin

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ABSTRACT
The present study focuses on the development and evaluation of polymeric ocular films for sustained delivery of ciprofloxacin hydrochloride to improve ocular bioavailability and therapeutic efficacy. The films were prepared using the solvent casting method employing polyvinyl alcohol (PVA) as the film-forming polymer and propylene glycol as plasticizer. The optimized formulation (F4) was systematically evaluated for physicochemical properties, mechanical strength, drug content uniformity, in vitro drug release, antimicrobial activity, and ocular safety.
F4 exhibited a clear, flexible, and uniform film with suitable thickness, excellent folding endurance, and high tensile strength. The surface pH was found to be close to physiological tear fluid, indicating good ocular compatibility. Drug content uniformity was high, ensuring consistent dosing. Swelling studies demonstrated moderate hydration behavior suitable for sustained release. In vitro drug release showed controlled release over 8 hours with a low initial burst effect and nearly complete drug release (99.5%). FTIR analysis confirmed compatibility between drug and excipients without any significant interaction. The antimicrobial study demonstrated effective activity against Staphylococcus aureus and Escherichia coli. Eye irritancy testing confirmed that the formulation is safe and non-irritating.
Overall, the optimized formulation (F4) demonstrated desirable characteristics for sustained ocular delivery of ciprofloxacin hydrochloride and holds potential for improving the management of bacterial ocular infections by enhancing drug residence time and reducing dosing frequency.

Keywords: Polymeric ocular film; Ciprofloxacin hydrochloride; Polyvinyl alcohol; Propylene glycol; Sustained drug delivery; Ophthalmic drug delivery; In vitro release; Antimicrobial activity; Solvent casting method.
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1. Introduction

The delivery of drugs to the eye is particularly difficult because of the multitude of eye protection systems such as a high rate of tear flow, frequent blinking and the presence of the nasolacrimal drainage (1,2). These serve to dramatically lower the amount of time the drug remains on the surface of the eye and elicits its response thereby leading to a poor bioavailability (<5% usually in case of normal eye drops). Outlined below are some drug delivery systems that offer prolonged contact with the eye (1,3).

Polymeric ocular films have been successfully used as an alternative ocular drug delivery system because they can be fashioned into thin, flexible matrices that are suitable for placement in the conjunctival sac (2,4). As the film comes in contact with tear fluid, it humidifies creating a controlled and sustained drug delivery system enhancing the effectiveness of the therapeutic agent and patient compliance (5,8).

The success of ocular films is largely dependent on the use of suitable components and their optimal concentrations. In this study, polyvinyl alcohol (PVA), a widely used film forming polymer was evaluated at concentration of 04 - 06 %w/v for formulation of polyvinyl alcohol ocular films (7,8). PVA having good film forming, transparent, water soluble and biocompatible nature was selected from the concentration range of 04 - 06 %w/v because of its ability to produce films with desirable mechanical strength and a good film uniformity without loss of flexibility (6,9,10).

Propylene glycol was added as a plasticiser (at 10–20% w/w of polymer) to increase the flexibility of the films (by reducing the brittleness) and to increase the mechanical stability of the films (6). Propylene glycol increases the mobility of the polymer chains by increasing the free volume, thus acting as a permeation enhancer as well as a plasticising agent (9,11).

Ciprofloxacin hydrochloride, a broad-spectrum fluoroquinolone antibiotic, was added at the concentration of 0.096% w/v, which is sufficiently effective in producing adequate antibacterial effects against common sight threatening ocular micro-organisms. The drug concentration used was based on maintaining a constant spread throughout the polymeric system and to can be held in the eye for long duration without irritating (8,13,14).
Use of distilled water as the solvent during the preparation of the casting solution produced a uniform solution of all the components (12).

➢ These ingredients were selected based on their optimal concentration aiming to produce:

- Sufficient mechanical strength and flexibility
- Uniform distribution of drug
- Controlled swelling/hydration properties
- Sustained release of drug with low initial burst
- Physiological compatibility with ocular tissue.

2. Materials and Methods (Detailed Procedure)

2.1 Materials

a) Polyvinyl Alcohol (PVA):

PVA is a water-soluble synthetic polymer that is non-toxic, biocompatible, and has good film-forming properties (14). It can be crosslinked to improve its mechanical strength and regulate the rate of drug release. PVA finds extensive application in ocular drug delivery systems because it is capable of developing transparent and flexible films that are comfortable for the eye (15,16).

b) Polysorbate 80 (P80):

P80 is a nonionic surfactant employed in enhancing the solubility and stability of low water-soluble drugs such as Ciprofloxacin (16). It can further enhance the wetting characteristics of the ocular film and improve adhesion to the ocular surface. P80 enhances penetration of Ciprofloxacin through the corneal membrane, therefore enhancing drug bioavailability (17).

c) Propylene Glycol (PG):

Propylene Glycol is a humectant and stabilizer that is commonly added to ocular formulations to increase drug solubility and prolong retention on the ocular surface (20). It also works as a plasticizer, imparting flexibility to the film. PG thus controls the hydration and swelling behavior of ocular films, which is important for sustained drug release (15).

d) Ciprofloxacin Hydrochloride (Cip HCl):

The drug is a wide-spectrum antibiotic that can attack a number of infections of the eye (19). Unconventional eye drops have a relatively poor bioavailability in the ocular route. By loading Ciprofloxacin into the ocular films, one can achieve controlled and sustained release, thus minimizing the necessity of frequent administration (18).

Table.1: Ingredients

INGREDINTS	USES
Polyvinyl Alcohol (PVA)	Good Film Forming Properties
Polysorbate 80 (P80)	Non-ionic Surfactant
Propylene Glycol (PG	Humectant & Plasticizer
Ciprofloxacin Hydrochloride (Cip HCl)	API

2.2 Preparation of Polymeric Ocular Films

In combination of ciprofloxacin HCl and polymer the films were made using solvent casting. In distilled water heated and added PVA, and measured before use. The mixture was continually stirred, as the temperature slowly increased to 60-70 degrees C. It was deemed to be ready when the mixture became completely clear, and the flow became smooth. The mixture was then left stationary to cool back to room temperature (22,23,24).

2.2.1 Composition

The optimized formulation consisted of:

- Polyvinyl alcohol (PVA): 5.5% w/v
- Propylene glycol: 12% w/v (of polymer)
- Ciprofloxacin HCl: 0.096% w/v
- Polysorbate 80 (P80): 1.5% w/v
- Distilled water: quantity sufficient to 100 mL

2.2.2 Method of Preparation

Step 1: Preparation of Polymer Solution

In a controlled manner, sufficient amounts of poly (vinyl alcohol) were added to a volume of distilled water, and heated using gentle stirring to obtain a clear (and homogenous) solution, followed by allowing the solution to cool to room temperature (21,13).

Step 2: Drug Incorporation

In to the container accurately Ciprofloxacin HCl was added and a bit of distilled water to be dissolved. In the polymer mixture, the drug was seeped into drop by drop while continuous stirring so it was evenly dispersed into gel-like substance (24).

Step 3: Addition of Plasticizer

Mixed into this was propylene glycol to reduce the hardness of the polymer-drug mixture. This was also blended until it was very smooth, with no air bubbles trapped inside. A film made from this mixture would have better flexibility since the additive would work (25).

Step 4: Degassing

There was a pause as the mixture was left alone, allowing air bubbles trapped in the mixture to leave the mixture. This still period helped to disperse the pockets of gas, which had developed. The mixture took a few minutes of sitting still to eventually become perfectly clear, allowing the air gaps to slowly disperse while the entire contents sat on the counter. The stillness was just long enough to allow for everything to clear out again (22,25)

Step 5: Casting of Films

A portion of this liquid was transferred into a flat glass dish that had been placed vertically on the workbench. This was then carefully leveled by hand to ensure all of it spread out to create an equal shallow film across the surface, therefore creating an equal depth across from side to side (26).

Step 6: Drying

Film samples sat still in a calm setting, slowly losin g liquid as hours passed. Without hurry, hardened evenly because too much speed could spli t their surface or leave patches behind (24,28)

Step 7: Film Removal and Cutting

After the films were removed from the petri dish, they were gently removed, dried and cut into smaller 1 cm x 1 cm pieces for use as eye samples. Size was not as important as placement (27,28).

Step 8: Storage

Wrapped in tight containers, the ready-made films sat on shelves with drying crystals near by,

Moisture stayed away because of the setup inside e ach sealed unit (30).

3. Evaluation Parameters

3.1 Introduction to Evaluation Parameters

Most times, how well eye films made from polymers work ties back to their physical and chemical traits along with how they respond inside the body. Checking each batch carefully helps confirm it won't harm users while still doing its job right in the eye (32). Look at things like thinness, even texture, firmness when handled, acidity level on contact, medicine amount present, how much water gets pulled in, and the pace drugs come out - these shape how comfortable someone feels, how much medicine reaches the target, plus whether treatment hits the mark. Though small, every detail shifts real world results (16,31).

A close look at the adjusted mix (F4) began with routine testing procedures meant to check how well it works for long-term eye treatment delivery. Each step followed established lab routines without deviation, focusing on real performance under typical conditions. Testing didn't assume success - measurements came straight from repeated trials. The method stayed steady throughout, matching known benchmarks for similar systems. Results emerged directly from timed release patterns observed during monitoring sessions (28,32)

3.2 Evaluation Parameters and Methods

3.2.1 Appearance

Films showed no flaws when held up to light over d ark or bright surfaces. One could see straight throu gh them without spotting haze, specks, or ripples. T heir even tint suggested ingredients had spread well during mixing. Not a single ripple broke the surfac e - no trapped pockets of air, no grainy patches forming inside (14,18,27).

3.2.2 Thickness

Three locations on the film were measured with a digital micrometer screw gauge to determine the thickness. The average thickness was then calculated to verify that the thickness was the same to promote consistent drug content and release (31,33).

3.2.3 Folding Endurance

The folding endurance was performed by folding a small strip of film until it broke at the same point over and over again. The number of folds before breaking indicates the flexibility and mechanical durability of the film (32,33).

3.2.4 Tensile Strength

The tensile strength of the film was determined using a tensile testing machine by pulling on the film until it broke. This measurement is indicative of the mechanical strength and overall structural integrity of the film (33,34).

3.2.5 Surface pH

The surface pH of the film was estimated by swelling of the film in distilled water for 30 minutes. Then measured the pH by digital pH meter, this will give an idea of physiological pH of tear fluid and prevent irritation of eyes (35).

3.2.6 Drug Content Uniformity

Each film sample was weighed and dissolved in phosphate buffer (pH 7.4) and filter and then analyse by UV-visible spectrophotometer at 276 nm. This will also ensure homogeneous distribution of drug throughout the film (29,36).

3.2.7 Swelling Index

Each film was weighted before and after swelling in simulated tear fluid and calculated as swelling index Swelling Index=W2W1W1100This was used to characterize the hydration potential and bio adhesive strength of the film.

Swelling Index = $W2-W1/W1\times100$

This parameter indicates the hydration capacity and bio adhesion potential of the film (28, 37).

3.2.8 In Vitro Drug Release

In vitro drug release study was carried out using the Franz diffusion cell apparatus, the receptor compartment was filled with phosphate buffer (pH 7.4) at 37 0.5C. Samples were withdrawn after specified interval of time and analysed by UV visible spectrophotometer (38).

3.2.9 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectra of the film was obtained using KBr pellet method over a range of 4000-400 cm-1 for to see any interaction between drug and polymers (38,39).

3.2.10 Antimicrobial Activity

The antimicrobial activity was determined using agar diffusion method against common ocular microbes like Staphylococcus aureus and Escherichia coli. The zone of inhibition was then determined for the evaluation (22,34,40).

3.2.11 Eye Irritancy Test

The eye irritancy of formulation was determined on animal models using Draize test by instilling film in conjunctival sac and then eye was checked for signs of redness, swelling, watering etc. At different intervals up to 24 hr (38,41).

4. Result

Using the solvent casting technique, polymeric ocular films (F1-F4) were created and tested for their physical and mechanical properties. The optimised formulation of the ocular films (F4: PVA + Propylene Glycol) (indicated as having superior characteristics across almost all aspects assessed) appears to make it most advantageous for long-term delivery of drugs to the eyes.

4.1 Characterization of ocular film-

The prepared ocular films were evaluated for their physical, mechanical, and drug-related properties. Among all formulations, F4 (PVA + propylene glycol) showed the best overall performance for ocular use.

The appearance of the films varied with formulation. F4 was clear, transparent, and flexible, while other films showed opacity, brittleness, or slight stickiness. The clarity and flexibility of F4 indicate good polymer mixing and proper plasticizer action, which is important for patient comfort (42,43,44).

Film thickness ranged from 70 ± 5 µm to 90 ± 8 µm. F4 showed slightly higher thickness, which helps in better strength and controlled drug release without affecting comfort in the eye.

Surface pH of all films was close to eye tear pH. F4 had pH 7.4 ± 0.1, which is ideal and reduces the risk of eye irritation.

Drug content was uniform in all films. F4 showed the highest drug content (99.0 ± 0.8%), meaning good drug distribution and accurate dosing.

Swelling study showed that F4 had moderate swelling (165%), which is good for drug release and maintaining film shape.

Overall, F4 showed the best balance of strength, flexibility, safety, and drug release, making it the most suitable formulation for sustained ocular delivery of ciprofloxacin HCl.

Table.2: Characterization of film

Parameter	F1 (HPMC E15)	F2 (Poloxamer P407)	F3 (PVA + Glycerol)	F4 (PVA + Propylene Glycol)
Appearance	Slightly opaque	Light yellow, brittle	Clear, slightly tacky	Clear, highly flexible
Thickness (µm)	75 ± 5	70 ± 5	80 ± 5	90 ± 8
Folding Endurance	20 ± 5	25 ± 5	30 ± 5	≤ 35
Tensile Strength (Kg/mm²)	2.3 ± 0.3	2.6 ± 0.3	3.6 ± 0.4	4.1 ± 0.5
Surface pH	7.2 ± 0.1	6.8 ± 0.2	7.3 ± 0.1	7.4 ± 0.1
Drug Content (%)	97.4 ± 1.1	96.8 ± 1.3	98.1 ± 0.9	99.0 ± 0.8
Swelling Index (%)	150	185	160	165

Fig.1: Appearance

4.2 *Tensile strength & Folding Endurance-*

Tensile strength was improved in F4. It showed the highest folding endurance (≤ 35 folds) and tensile strength (4.1 ± 0.5 Kg/mm²), indicating strong and flexible films that can withstand handling and blinking.

Fig.2: DOE of film (Tensile strength)

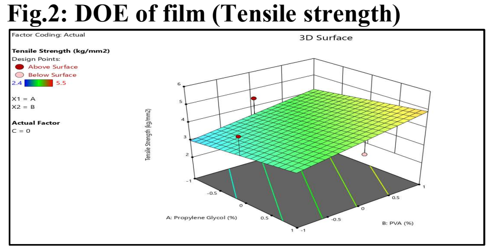
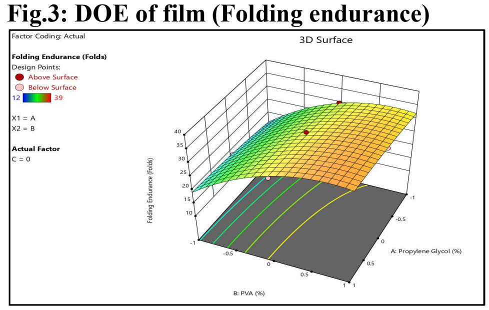


Fig.3: DOE of film (Folding endurance)



4.2 In- Vitro Release study

In vitro release of ciprofloxacin HCl from ocular films was studied using a Franz diffusion cell and presented in Figure (7). A notable difference was observed in the pattern of release depending upon the polymer-plasticizer combination of each formulation (43,45).

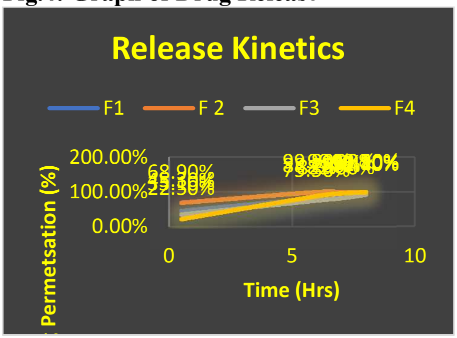
The formulation F2 had showed fast release rate with remarkable burst effect, which means less control over drug diffusion. F1 also exhibited fast release profile. Formulation F3 had showed moderate control over the release. Formulation F4 exhibited most sustained and controlled release profile with least burst effect and nearly 100% drug release at 8hrs (44,46).

Table.3: In Vitro Drug Release Profile of Ocular Films

Formulation	Initial Burst (30 min)	Drug Release (6 hrs)	Total Release (8 hrs)

F1	45.3%	82.0%	95.1%
F2	68.9%	99.8%	>99.9% (7 h)
F3	35.1%	75.5%	92.4%
F4	22.5%	88.2%	99.5%

Fig.4: Graph of Drug Release



4.3 FTIR

FTIR studies were carried out for the drug and excipients to establish the structure and functional groups. Spectra were obtained within the range 4000-600 cm. The results of spectra showed distinct peaks which identify each component and indicates its purity.

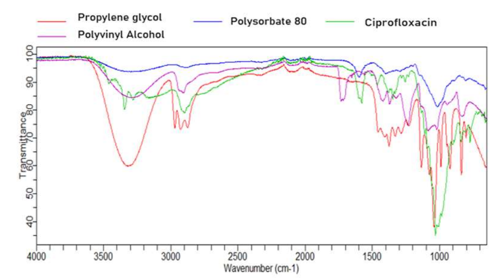
From FTIR spectra of Ciprofloxacin peaks at 1705cm (C=O stretch) and 1623cm (quinolone ring) appeared to identify structure. From FTIR spectra of PVA a broadband appears between 3200-3400cm (O-H stretch) due to hydrogen bonding between molecules. From FTIR spectra of propylene glycol a peak at 3319cm (O-H stretch) appears and C-O stretch peak at 1036cm was observed. From FTIR spectra of polysorbate 80 an ester C=O stretch at 1735cm appeared.

Thus, all materials can be said to be pure and structurally sound prior to incorporation into formulation. These spectra will also serve as reference for checking for interaction of drug with the polymer in final formulation (47,48).

Table.4: FTIR Peaks of Drug and Excipients

Component	Wavenumber (cm^{-1})	Functional Group
Propylene Glycol	3319	O–H stretching
	2970	C–H stretching
	1036	C–O stretching
Polysorbate 80	1735	Ester C=O
	2858	C–H stretching
	1105	C–O–C stretching
Ciprofloxacin	1705	Carbonyl group
	1623	Quinolone ring
	1270	C–F stretching
Polyvinyl Alcohol	3200–3400	O–H stretching
	2910	C–H stretching
	1095	C–O stretching

Fig.5: Spectra of Ingredients for Ocular film



4.4 Antimicrobial efficacy

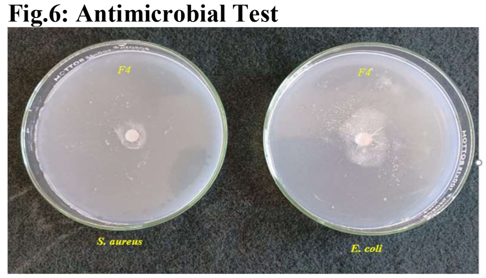
Agar diffusion assay for antimicrobial activity: The ciprofloxacin-loaded ocular film was tested against the standard ocular pathogens like Staphylococcus aureus and Escherichia coli by using Agar Diffusion method. The formulation was placed on the seeded agar plates and incubated at 37 C for 24h. The inhibition zone was recorded (40,50).

The clear and measurable zone of inhibition was obtained for both the organisms with F4 as clearly seen from the results which indicates that F4 has got good antimicrobial activity. This is due to the slow and sustained release of the drug from the polymeric matrices (11,50).

Table.5: Antimicrobial Activity of Optimized Ocular Film (F4)

Test Organism	Zone of Inhibition (mm)
Staphylococcus aureus	4.8 ± 0.4
Escherichia coli	4.2 ± 0.3

Fig.6: Antimicrobial Test



4.5 Eye irritancy Test-

The eye irritation study was performed to assess the ocular safety of the optimum formulation (F4) with Draize test method. The tests were conducted on healthy albino rabbits and guinea pigs. A sample piece of ocular film was dropped into the lower conjunctival sac of one eye, and the other eye served as control.

Eyes were examined at regular time intervals during the 24-hour period and there was no damage or irritation noticed.

Table.6: Eye Irritancy Observations

Parameter	Observation
Redness	None
Swelling	None
Watering	Very mild (initial)
Irritation	None

Fig.7: Guniea Pig Eye Test

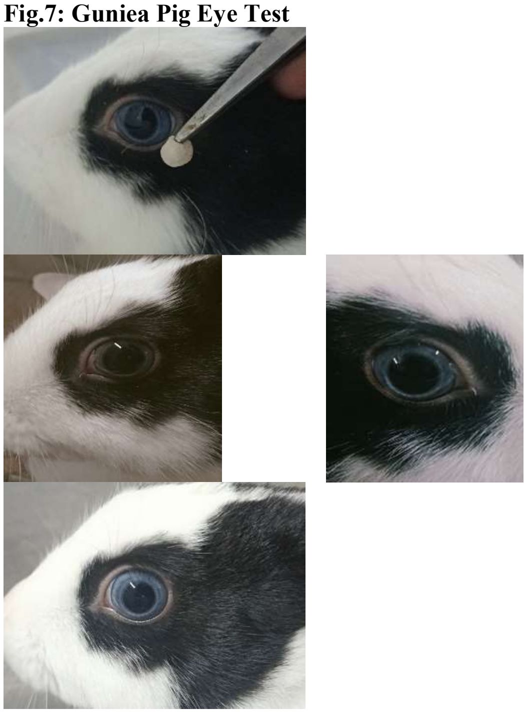


Fig.8: Rabbit Eye Test

5. Discussion

The current study aimed to develop an ocular film system for the controlled delivery of ciprofloxacin hydrochloride using polyvinyl alcohol (PVA) as a film forming polymer along with propylene glycol as plasticizer. Out of all the formulations F4 had superior physiochemical, mechanical and biological profiles than all other formulations and hence deemed fit for ocular drug delivery (52).

Enhanced clarity and increased pliability of F4 shows the favorable interaction of PVA with propylene glycol as a plasticizer which decreased the intermolecular hydrogen bonding between PVA chains and increased chain mobility hence providing a good homogenous film. Properties like flexibility, clarity, uniformity and easy moldability are very critical for ocular films to improve comfort, ease of handling and to reduce foreign body sensation.

In the mechanical studies, it was found that F4 has maximum tensile strength and maximum folding endurance compared to all other formulations. This may be because; a strong and flexible polymeric matrix is formed which resists all the stress during administration and also during blinking of eye. The mechanical properties are well balanced between PVA and propylene glycol to facilitate enough elasticity to withstand mechanical stresses without disrupting the film (38,51).

Surface pH of all the formulations were within the physiological limit for tear fluid and F4 was the closest to neutral pH which is essential for no ocular irritation. Eye irritation studies conducted, showed no irritation to the eye in which no signs of redness and inflammation were noted, hence it proves to be very safe for ocular drug delivery.

F4 showed good drug content and this is because the drug is well dispersed throughout the polymer matrix, which results in better dose consistency. In case of F4 the swelling nature was moderate which shows sufficient wetting with tear fluid, leading to an increased drug diffusion.

FTIR spectrum indicates no interaction between ciprofloxacin and PVA/propylene glycol in the formulations. This shows that there are no chemical reactions between the drug and the excipients, and the drug release is mainly through diffusion (50,52,53).

Antimicrobial studies showed good antibacterial activity against S. Aureus and E.coli thus suggesting that the ciprofloxacin activity remained intact. Slow release of the drug from the film for a long duration will ensure sustained action against bacterial infections (55,56).

Thus, the PVA-propylene glycol-based ocular film offers a good compromise between mechanical strength, flexibility, drug delivery, biodegradability and suitability for ocular use, and F4 formulation appeared to be the most potential candidate for subsequent studies.

6. Conclusion

The formulation and evaluation of polymeric ocular film for sustained release of ciprofloxacin hydrochloride has been successful. Among all the formulations prepared and characterized, the optimal formulation (F4) contained both polyvinyl alcohol and propylene glycol and showed excellent overall profile (56).

The optimized formulation (F4) has clear appearance, possesses good flexibility and adequate mechanical strength and also having the surface pH near to that of the tear fluid, thereby it has good ocular compatibility. F4 possessed high drug content uniformity, moderate swelling behaviour in different media and thus leads to controlled drug release.

The drug release from this film was observed to be a controlled sustained release, within 8 hrs of release time; there was less burst release effect of ciprofloxacin hydrochloride, which causes more drug release at the ocular surface. The FTIR study shows that there was no interaction between drug and excipients and thus the drug remained stable in the formulation. The antimicrobial study clearly shows that formulation possesses activity against both Gram-positive and Gram-negative bacteria. The eye irritancy study of the formulated film shows the safe and non-irritating nature (54,55).

Overall, it was found that formulation F4 is a stable, safe, efficient ophthalmic drug delivery system that has good prospects to be used in the treatment of bacterial eye infections by increasing the ocular residence time and thus decreasing the dosing frequency.

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