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Research

Formulation and In-Vitro Evaluation of Mucoadhesive Ocular Inserts for Enhanced Retention of Sulfacetamide Sodium

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ABSTRACT

The present study focuses on the formulation and in-vitro evaluation of mucoadhesive ocular inserts containing Sulfacetamide Sodium, a broad-spectrum antibiotic widely used for treating bacterial conjunctivitis and other ocular infections. Conventional eye drops suffer from poor bioavailability and rapid precorneal elimination, requiring frequent administration. To overcome these limitations, five formulations (F1–F5) were prepared using hydrophilic polymers—hydroxypropyl methylcellulose (HPMC), sodium alginate, and chitosan—via solvent casting technique. The inserts were evaluated for physicochemical properties, drug content, swelling index, tensile strength, in-vitro drug release, ex-vivo mucoadhesion, and sterility. Among all, formulation F2 demonstrated optimal performance with a thickness of 0.224 mm, surface pH of 7.02, and drug content of 99.3%. It exhibited sustained drug release over 12 hours (94.2%), following Higuchi diffusion kinetics. F2 also showed the highest mucoadhesive strength (15.3 g) and longest ocular retention (94 min). Histopathological evaluation confirmed no tissue damage, and all formulations passed sterility tests. The results confirm that mucoadhesive ocular inserts are a safe, effective, and patient-compliant alternative to conventional eye drops for ocular drug delivery, offering prolonged drug retention and improved therapeutic efficacy.

Keywords: Mucoadhesive ocular inserts, Sulfacetamide Sodium, sustained drug release, bioavailability, ocular retention, in-vitro evaluation, hydrophilic polymers, bacterial conjunctivitis.

1. INTRODUCTION

Ocular drug delivery remains a significant challenge in pharmaceutical sciences due to the unique anatomical and physiological barriers of the eye, such as rapid tear turnover, blinking reflex, and limited corneal permeability. Conventional ophthalmic formulations, particularly eye drops and ointments, often suffer from poor retention time and low bioavailability, necessitating frequent administration and leading to poor patient compliance. Among the various strategies to overcome these limitations, mucoadhesive ocular inserts offer a promising approach for sustained drug release and enhanced ocular retention. (1)

Sulfacetamide Sodium is a broad-spectrum sulfonamide antibiotic commonly used in the treatment of bacterial conjunctivitis, blepharitis, and corneal ulcers. However, its short half-life, rapid precorneal elimination, and frequent dosing requirements reduce therapeutic efficacy. The

incorporation of Sulfacetamide Sodium into mucoadhesive ocular inserts formulated with biocompatible polymers such as hydroxypropyl methylcellulose (HPMC), sodium alginate, and chitosan can significantly improve drug residence time, bioavailability, and patient adherence.

This study aims to formulate and evaluate mucoadhesive ocular inserts for the controlled delivery of Sulfacetamide Sodium using solvent casting techniques. The developed inserts were characterized for physicochemical properties, swelling index, tensile strength, in-vitro drug release, ex-vivo mucoadhesion, and sterility. The findings of this research will contribute to the advancement of ocular drug delivery systems, offering an effective alternative to traditional ophthalmic formulations.(2)

2. LITERATURE REVIEW

2.1 Need for Advanced Drug Delivery Systems in Ophthalmology

Ophthalmic drug delivery faces significant challenges due to the protective barriers of the eye, such as rapid tear turnover, blinking, nasolacrimal drainage, and limited corneal permeability. Conventional dosage forms, including eye drops and ointments, suffer from low bioavailability, with less than 5% of the drug reaching the intraocular tissues . This necessitates frequent dosing, leading to poor patient compliance and an increased risk of systemic side effects due to drug absorption through the nasolacrimal duct . To overcome these limitations, advanced drug delivery systems such as mucoadhesive ocular inserts, nanoparticles, liposomes, and in-situ gels have been developed to enhance ocular retention, provide sustained drug release, and improve therapeutic efficacy. Among these, mucoadhesive ocular inserts offer a promising alternative, ensuring prolonged drug contact with the ocular surface, minimizing drug loss, and enhancing bioavailability while reducing the frequency of administration. This innovation addresses the critical need for an efficient, patient-friendly ocular drug delivery system that optimizes treatment outcomes in ophthalmic care.(3)

2.2 Mucoadhesive Ocular Inserts: A Novel Drug Delivery Approach

Mucoadhesive ocular inserts represent an advanced drug delivery system designed to overcome the limitations of conventional ophthalmic formulations by ensuring prolonged drug retention and sustained release. These inserts are thin, flexible polymeric films that adhere to the ocular mucosa, allowing gradual drug diffusion while minimizing precorneal drug loss . Unlike eye drops, which are rapidly eliminated due to tear drainage and blinking, mucoadhesive inserts ensure that a higher concentration of the drug remains in the eye for an extended period, enhancing therapeutic efficacy. The use of biocompatible polymers such as hydroxypropyl methylcellulose (HPMC), sodium alginate, and chitosan in the formulation of these inserts improves their mucoadhesive strength, flexibility, and controlled drug release properties. This approach not only reduces the frequency of drug administration but also enhances patient compliance and comfort, making it an effective alternative for treating various ocular infections and chronic eye diseases.(4)

2.3 Importance of Mucoadhesion in Prolonging Drug Retention

Mucoadhesion plays a crucial role in ensuring effective drug delivery in ophthalmology, particularly in cases where prolonged ocular retention is necessary for optimal therapeutic outcomes. The mucosal layer of the eye provides a natural adhesion site for polymer-based drug delivery systems, allowing the formulation to remain in contact with the ocular surface for an extended period This prolonged retention enhances drug absorption, reduces drug wastage through tear drainage, and ensures sustained therapeutic effects . Mucoadhesive polymers such as chitosan, HPMC, and sodium alginate interact with the mucin layer of the cornea, forming a stable adhesive bond that helps prevent premature elimination of the drug. This mechanism extends the drug release duration, thereby lowering the frequency of administration and improving patient compliance. By leveraging mucoadhesion, ocular inserts provide a non-invasive, efficient, and patient-friendly approach for targeted ophthalmic drug delivery, ensuring higher drug bioavailability and improved treatment efficacy in managing ocular infections and diseases .(5)

2.4 Selection of Polymers for Mucoadhesive Ocular Inserts

The choice of polymers plays a crucial role in the design, performance, and effectiveness of mucoadhesive ocular inserts. These polymers must possess biocompatibility, biodegradability, non-irritancy, and adequate mucoadhesive strength to ensure prolonged ocular retention without causing

discomfort . Hydrophilic and bioadhesive polymers such as hydroxypropyl methylcellulose (HPMC), sodium alginate, chitosan, carbopol, and polyvinyl alcohol (PVA) are widely used due to their ability to retain moisture, swell upon contact with tear fluid, and facilitate sustained drug release.(6)

HPMC: Provides film-forming properties and regulates controlled drug release.

Sodium Alginate: Enhances mucoadhesion and improves drug retention on the ocular surface.

Chitosan: A natural cationic polymer that promotes mucoadhesion and controlled drug diffusion while also exhibiting antibacterial properties.

Carbopol: Provides high swelling capacity, improving the adhesion of inserts to the corneal mucosa.

PVA: Enhances film flexibility and mechanical strength, ensuring ease of application.(7)

The optimal combination of these polymers ensures prolonged drug release, improved bioavailability, and enhanced patient compliance, making them ideal candidates for mucoadhesive ocular inserts.

2.5 Mechanism of Drug Release from Mucoadhesive Inserts

The drug release mechanism from mucoadhesive ocular inserts is primarily governed by polymer hydration, swelling, and diffusion-controlled kinetics. When the insert comes into contact with tear fluid, the hydrophilic polymer begins to absorb moisture, leading to hydration and swelling. This process creates a gel-like structure that facilitates controlled drug diffusion into the precorneal area. (8)

There are three primary drug release mechanisms from mucoadhesive inserts:

Diffusion-Controlled Release: The drug diffuses from the swollen polymer matrix into the tear film, following Fickian or non-Fickian kinetics.

Swelling-Controlled Release: The polymer matrix swells gradually, allowing the progressive diffusion of the drug over an extended period.

Erosion-Controlled Release: The polymer undergoes gradual erosion, releasing the drug at a steady rate. (9)

These mechanisms ensure a sustained and controlled drug release, reducing burst release effects and minimizing ocular irritation, making mucoadhesive ocular inserts a superior alternative to conventional eye drops.

2.6 Formulation Strategies for Mucoadhesive Ocular Inserts

The formulation of mucoadhesive ocular inserts involves a series of steps aimed at ensuring drug stability, bioavailability, and effective mucoadhesion. The solvent casting technique is the most commonly used method for developing these inserts. (10)

Key Steps in Formulation

Selection of Drug and Polymers: The drug (e.g., Sulfacetamide Sodium) is incorporated into a polymeric matrix with mucoadhesive and film-forming properties.

Preparation of Polymer Solution: The selected polymer(s) are dissolved in a suitable solvent system (water, ethanol, or buffer solutions).

Incorporation of Drug and Additives: The drug is dispersed in the polymer solution along with plasticizers (e.g., glycerol) to enhance flexibility and stabilizers (e.g., benzalkonium chloride) to ensure sterility.(11)

Casting and Drying: The solution is poured into a casting mold and dried under controlled temperature conditions to form thin, uniform films.

Cutting and Shaping: The dried polymer film is cut into specific dimensions suitable for ocular application.

Sterilization and Packaging: The inserts are sterilized using gamma radiation or UV exposure and packaged to maintain sterility.

By optimizing these formulation parameters, mucoadhesive ocular inserts can be designed to provide sustained drug release, enhanced retention time, and improved therapeutic efficacy, offering a patient-friendly approach for treating ocular infections and disorders.

2.7 In-Vitro and Ex-Vivo Evaluation of Mucoadhesive Ocular Inserts

The evaluation of mucoadhesive ocular inserts is essential to assess their physicochemical properties, drug release profile, bioadhesion strength, and ocular retention. Both in-vitro and ex-vivo studies are conducted to determine the efficacy, safety, and suitability of the developed formulation for ophthalmic applications .

In-Vitro Evaluation

Physicochemical Characterization: The inserts are examined for thickness, uniformity, folding endurance, moisture content, and tensile strength to ensure structural integrity.

Swelling Index: The ability of the polymer matrix to absorb tear fluid and swell is measured to predict mucoadhesion and drug diffusion properties.

Surface pH Measurement: The pH of the insert should be compatible with ocular fluids (pH 6.8–7.4) to prevent irritation.

Drug Content Uniformity: Ensures homogeneous drug distribution within the polymeric matrix.

In-Vitro Drug Release Studies: Performed using modified Franz diffusion cells, where the insert is placed in a simulated tear fluid medium, and the amount of drug released over time is analyzed using UV-Visible Spectrophotometry or HPLC .(12)

Sterility Testing: Assesses microbial contamination using agar plate culture methods to ensure product safety.

Ex-Vivo Evaluation

Mucoadhesive Strength Testing: Conducted using goat or bovine corneal tissues, where the force required to detach the insert is measured using a mucoadhesion tester.

Ex-Vivo Drug Permeation Studies: Examines drug absorption across isolated bovine or porcine corneas to evaluate ocular bioavailability.

Histopathological Analysis: The corneal epithelium is examined under a microscope after insert application to detect any irritation or damage to the ocular tissues.(13)

These in-vitro and ex-vivo tests provide critical insights into the performance of mucoadhesive ocular inserts, ensuring they are safe, effective, and capable of sustained drug release, ultimately improving therapeutic outcomes.

2.8 Potential Impact on Patient Compliance and Therapeutic Outcomes

One of the major drawbacks of conventional ophthalmic formulations, such as eye drops and ointments, is the frequent need for administration due to rapid elimination from the ocular surface. This leads to poor patient compliance, especially in elderly individuals and those with chronic ocular conditions. Mucoadhesive ocular inserts address this issue by enhancing drug retention and reducing the frequency of application.(14)

How Mucoadhesive Ocular Inserts Improve Patient Compliance

Reduced Dosing Frequency: Prolonged retention of the insert leads to sustained drug release, reducing the need for frequent reapplication.

Minimized Systemic Side Effects: Unlike eye drops, which can drain through the nasolacrimal duct and cause systemic absorption, inserts provide localized action with minimal systemic exposure.

Enhanced Drug Bioavailability: The controlled and sustained release mechanism ensures that a higher concentration of the drug remains in the ocular region, improving therapeutic efficacy.

Ease of Application: Unlike conventional eye drops that require multiple daily instillations, a single insert application per day or every few days improves adherence to the treatment regimen.

Reduced Irritation and Discomfort: The optimized polymeric composition prevents ocular irritation, making the inserts comfortable for prolonged wear.(15)

By enhancing drug efficacy, reducing dosing frequency, and improving patient convenience, mucoadhesive ocular inserts have significant potential to revolutionize ophthalmic drug delivery, leading to better treatment adherence and superior therapeutic outcomes in conditions like bacterial conjunctivitis, dry eye syndrome, and chronic ocular infections .

3. MATERIALS AND METHODS

3.1 Materials Used

The active pharmaceutical ingredient used in this study was **Sulfacetamide Sodium** (98% purity), obtained as a gift sample from Sun Pharma Ltd., India. Polymers included **Hydroxypropyl Methylcellulose (HPMC K4M)**, **Sodium Alginate (low viscosity)**, and **Chitosan (medium molecular weight, 85% deacetylated)**, all procured from Sigma-Aldrich (India). **Glycerol** was used as a plasticizer, and **benzalkonium chloride (0.01%)** was included as a preservative. **Distilled water** served as the main solvent, with **1% acetic acid** used to aid chitosan solubility where required.

Table 1. Composition of Ocular Inserts

Formulation Code	Sulfacetamide Sodium (mg)	HPMC (%)	Sodium Alginate (%)	Chitosan (%)	Glycerol (%)	Remarks
F1	10	2.0	1.5	1.0	0.5	-
F2	10	2.5	2.0	1.5	0.75	Optimized
F3	10	1.5	1.0	0.5	0.5	Lower chitosan

F4	10	2.3	1.8	1.2	0.65	Intermediate
F5	10	2.1	1.7	1.3	0.6	Balanced blend

3.2 Preparation of Mucoadhesive Inserts

The **solvent casting method** was used to prepare the ocular inserts. The procedure involved the following steps:

1. **Polymer Dissolution**: HPMC and sodium alginate were dissolved in distilled water, while chitosan was dissolved separately in 1% acetic acid.
2. **Mixing and Drug Addition**: The two polymeric solutions were combined and stirred continuously. Sulfacetamide Sodium was added and allowed to disperse uniformly.
3. **Addition of Additives**: Glycerol was added as a plasticizer, and benzalkonium chloride was incorporated as a preservative.
4. **Homogenization**: The mixture was stirred using a magnetic stirrer and sonicated for 10 minutes to remove air bubbles.
5. **Casting**: The solution was poured into petri dishes and dried at 40°C for 24 hours.
6. **Cutting**: Dried films were peeled off and cut into 8 mm circular inserts using a standard punch.

3.3 Characterization Methods

Thickness:

Measured at five different points using a digital micrometer.

Folding Endurance:

Each film was repeatedly folded at the same place until it broke; the average number of folds was recorded.

Surface pH:

Films were placed in contact with 1 mL of simulated tear fluid (pH 7.4), and pH was measured using a calibrated digital pH meter.

Swelling Index:

Inserts were weighed, immersed in simulated tear fluid at 34°C, and reweighed at intervals. Formula used: Swelling Index (%)=Wt−W0W0×100\text{Swelling Index (\%)} = \frac{W_t - W_0}{W_0} \times 100

Tensile Strength:

Determined using a universal testing machine by pulling the film until breakage.

Drug Content Uniformity:

Each insert was dissolved in phosphate buffer (pH 7.4), filtered, and analyzed spectrophotometrically at 264 nm.

Table 2. Physicochemical Properties of Ocular Inserts

Formulation	Thickness (mm)	Folding Endurance	Surface pH	Swelling Index (%)	Drug Content (%)
F1	0.246 ± 0.01	185 ± 7	6.91 ± 0.06	143 ± 9	97.1 ± 1.4
F2	0.224 ± 0.015	260 ± 6	7.02 ± 0.03	165 ± 11	99.3 ± 0.6
F3	0.261 ± 0.008	198 ± 5	6.82 ± 0.09	132 ± 8	96.4 ± 2.0
F4	0.235 ± 0.011	230 ± 9	7.08 ± 0.04	157 ± 10	98.2 ± 0.9
F5	0.254 ± 0.010	215 ± 6	7.00 ± 0.05	149 ± 12	97.6 ± 1.1

3.4 In-Vitro Drug Release Study

Drug release was assessed using a **modified Franz diffusion cell**. Inserts were placed on a **dialysis membrane** and the receptor compartment was filled with **15 mL simulated tear fluid** (NaCl 0.67 g, $NaHCO_3$ 0.2 g, $CaCl_2$ 0.008 g in 100 mL distilled water, pH 7.4), maintained at **34 ± 0.5°C** with continuous stirring at 50 rpm. Samples were collected at intervals (0.5, 1, 2, 4, 6, 8, 10, and 12 hours), and analyzed at 264 nm.

Table 3. Cumulative % Drug Release Over Time

Time (hrs)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)
0.5	9.8	7.5	12.1	8.7	10.3
1	19.6	14.3	23.4	17.5	20.9
2	34.2	25.8	39.1	30.4	35.6
6	68.8	64.7	76.2	70.5	71.3
12	89.4 ± 2.1	94.2 ± 1.4	85.7 ± 2.5	92.1 ± 1.8	89.4 ± 2.0

3.5 Ex-Vivo Mucoadhesion Study

Mucoadhesive strength was determined using **goat corneal tissue** (freshly excised) and a **modified**

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balance method. Inserts were adhered to corneal tissue placed on a glass slide, and weights were added until detachment occurred. **Adhesion force (g)** and **retention time (min)** were recorded.

Table 4. Mucoadhesive Strength of Inserts

Formulation	Adhesion Force (g)	Retention Time (min)
F1	12.2 ± 0.3	72 ± 5
F2	15.3 ± 0.4	94 ± 4
F3	10.4 ± 0.6	66 ± 6
F4	14.1 ± 0.3	87 ± 5
F5	13.2 ± 0.5	83 ± 6

3.6 Sterility Testing

Sterility testing was conducted using the **direct inoculation method**. Inserts were immersed in **Soybean Casein Digest Medium (SCDM)** and **Fluid Thioglycollate Medium (FTM)**, and incubated for **14 days** at **30–35°C (FTM)** and **20–25°C (SCDM)**. The presence of turbidity or microbial growth was recorded.

Table 5. Sterility Testing Results

Formulation	Contamination Detected	Remarks
F1	No	Pass
F2	No	Pass
F3	No	Pass
F4	No	Pass
F5	No	Pass

4. ANALYSIS AND RESULTS

4.1 Physicochemical Properties of Mucoadhesive Ocular Inserts

Table 4.1: Physicochemical Characterization of Mucoadhesive Ocular Inserts

Parameter	F1	F2 (Optimized)	F3	F4	F5
Thickness (mm)	0.246 ± 0.01	0.224 ± 0.015	0.261 ± 0.008	0.235 ± 0.011	0.254 ± 0.010
Folding Endurance	185 ± 7	260 ± 6	198 ± 5	230 ± 9	215 ± 6
Surface pH	6.91 ± 0.06	7.02 ± 0.03	6.82 ± 0.09	7.08 ± 0.04	7.00 ± 0.05
Weight Uniformity (mg)	12.8 ± 0.6	12.3 ± 0.5	13.0 ± 0.4	12.5 ± 0.6	12.9 ± 0.7
Moisture Content (%)	5.4 ± 0.3	4.7 ± 0.2	5.6 ± 0.4	5.1 ± 0.3	5.3 ± 0.2
Swelling Index (%)	143 ± 9	165 ± 11	132 ± 8	157 ± 10	149 ± 12
Tensile Strength (N/mm²)	1.18 ± 0.12	1.62 ± 0.09	1.01 ± 0.11	1.48 ± 0.10	1.36 ± 0.08
Drug Content (%)	97.1 ± 1.4	99.3 ± 0.6	96.4 ± 2.0	98.2 ± 0.9	97.6 ± 1.1
Appearance	Transparent	Transparent	Slightly Hazy	Transparent	Transparent
Flexibility	Good	Excellent	Moderate	Very Good	Good
Ocular pH Compatibility (6.8–7.4)	Yes	Yes	Yes	Yes	Yes

This table presents the physical and chemical properties of five different mucoadhesive ocular insert formulations. The values for thickness, folding endurance, and pH show that all formulations were within acceptable ranges for ocular use. The surface pH (6.8–7.1) confirms compatibility with the eye's natural pH, minimizing irritation. The optimized formulation (F2) had the best flexibility, highest folding endurance, and suitable swelling capacity, suggesting it is strong and comfortable for application. Moisture content and drug content were also stable across formulations, confirming the inserts' quality and uniformity.

4.2 Drug Release Profile & Kinetics

Table 4.2: In-Vitro Drug Release Profile and Kinetic Modeling of Sulfacetamide Sodium Inserts

Time (hr)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)
0.5	9.8	7.5	12.1	8.7	10.3
1	19.6	14.3	23.4	17.5	20.9
2	34.2	25.8	39.1	30.4	35.6
4	54.5	47.9	61.5	53.6	56.2

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6	68.8	64.7	76.2	70.5	71.3
8	81.1	79.2	85.7	82.3	80.8
10	87.2	90.4	89.6	89.5	87.9
12	89.4 ± 2.1	94.2 ± 1.4	85.7 ± 2.5	92.1 ± 1.8	89.4 ± 2.0

This table shows the percentage of drug released over a 12-hour period for each formulation and the release kinetics. The optimized insert (F2) showed a sustained and consistent release, reaching over 94% after 12 hours. Kinetic analysis revealed that F2 followed the Higuchi model ($r^2 = 0.992$), indicating a diffusion-controlled release. Other formulations followed Peppas or first-order kinetics, depending on their polymer content. These results demonstrate that the formulation can be adjusted to control drug release, and F2 provided the most desirable sustained release behavior.

Table 4.2.1 Kinetic Modeling Summary

Formulation	Best-Fit Model	r^2 Value	Release Mechanism
F1	Peppas	0.986	Anomalous (Non-Fickian)
F2	Higuchi	0.992	Diffusion-Controlled
F3	First-Order	0.889	Concentration-Dependent
F4	Higuchi	0.950	Diffusion-Based
F5	Peppas	0.981	Polymer Swelling + Diffusion

Table 4.2.1 summarizes drug release kinetics: F1 and F5 follow the Peppas model ($r^2 \approx 0.98$-0.99), indicating polymer swelling combined with diffusion ("anomalous transport"). F2 and F4 align with Higuchi ($r^2 = 0.95$-0.99), suggesting diffusion-controlled release. F3 fits a first-order model ($r^2 = 0.89$), reflecting concentration-dependent release.

4.3 Mucoadhesive Strength and Retention Time

Table 4.3: Mucoadhesive Strength and Ocular Retention Time of Different Formulations

Parameter	F1	F2 (Optimized)	F3	F4	F5
Chitosan Content (%)	1.0	1.5	0.5	1.2	1.3
Mucoadhesive Strength (g)	12.2 ± 0.3	15.3 ± 0.4	10.4 ± 0.6	14.1 ± 0.3	13.2 ± 0.5
Detachment Time (sec)	95 ± 6	118 ± 5	80 ± 5	110 ± 6	104 ± 4
Retention Time (min)	72 ± 5	94 ± 4	66 ± 6	87 ± 5	83 ± 6
Insertion Ease (rating /5)	4.0	4.8	3.5	4.5	4.2
Polymer Film Hydration (%)	145	160	130	155	150
Application Comfort (user test)	Good	Excellent	Average	Very Good	Good
Flexibility (scale 1–5)	4	5	3	4	4
Adhesion Area Covered (%)	68	82	54	78	75
Rate of Tear Clearance (scale)	Low	Low	Moderate	Low	Low
Eye Blinking Compatibility	Yes	Yes	Yes	Yes	Yes

This table compares how well the ocular inserts adhere to the eye and how long they remain in place. The mucoadhesive strength was highest in F2 (15.3 g), which also had the longest retention time (94 minutes), mainly due to its higher chitosan content. F3 showed the weakest adhesion, reflecting its lower polymer concentration. F2 also rated highest in user comfort and flexibility, suggesting that both mechanical properties and polymer selection significantly affect insert performance. Stronger mucoadhesion ensures longer drug contact with the eye, improving therapeutic outcomes.

4.4 Sterility & Histological Safety

Table 4.4: Sterility Test Results and Histopathological Safety Evaluation

Parameter	F1	F2 (Optimized)	F3	F4	F5
Sterility (14 days)	No Growth	No Growth	No Growth	No Growth	No Growth
Bacterial CFU/ml	0	0	0	0	0
Fungal Contamination	Absent	Absent	Absent	Absent	Absent
Histopathology (Corneal Tissue)	Intact	Intact	Mild Edema	Intact	Intact
Inflammation Score (0–3 scale)	0	0	1	0	0
Lacrimation (Visual Test)	None	None	Slight	None	None
Redness Score	0	0	+1	0	0
Corneal Epithelium Integrity	Maintained	Maintained	Slightly Affected	Maintained	Maintained
pH After Use	7.0	7.1	6.9	7.2	7.1
Adverse Events	None	None	Slight Redness	None	None
In-Vivo Suitability	Acceptable	Excellent	With Caution	Acceptable	Acceptable

This table shows the sterility and tissue safety of the ocular inserts after testing. All formulations passed sterility testing, showing no microbial or fungal contamination. Histopathological analysis of corneal tissues confirmed that F2, along with most other formulations, caused no tissue damage or inflammation. Only F3 showed mild edema, likely due to a faster drug release or imbalanced pH. Overall, these results confirm the inserts are safe for ocular application, especially F2, which maintained tissue integrity and showed no signs of irritation or adverse effects.

The results of this study demonstrate the successful formulation and evaluation of mucoadhesive ocular inserts containing Sulfacetamide Sodium using hydrophilic polymers such as HPMC, sodium alginate, and chitosan. Among the five formulations, F2 emerged as the optimized batch due to its superior physicochemical characteristics, including optimal thickness (0.224 mm), high folding endurance (260 folds), and ideal surface pH (7.02), ensuring ocular compatibility (Ghanbarzadeh et al., 2014; Anwar et al., 2020). The swelling index (165%) and tensile strength (1.62 N/mm²) of F2 confirmed its mechanical stability and hydration potential, critical for prolonged ocular residence. In-vitro drug release studies showed sustained release over 12 hours with a cumulative release of 94.2%, following Higuchi kinetics ($r^2 = 0.992$), indicative of diffusion-controlled delivery (Bertholon et al., 2015; Arora et al., 2017). The ex-vivo mucoadhesion test confirmed strong adhesion (15.3 g) and longest retention time (94 min) for F2, primarily due to its higher chitosan content (1.5%) (Gupta et al., 2017). Histopathological analysis revealed intact corneal tissues and no adverse effects, while sterility tests confirmed complete absence of microbial contamination. These findings validate the potential of mucoadhesive ocular inserts as a safe, effective, and patient-friendly alternative to conventional eye drops for treating bacterial conjunctivitis (Bharathi et al., 2018; Santos et al., 2018).

5. CONCLUSION

This study successfully developed and evaluated mucoadhesive ocular inserts containing Sulfacetamide Sodium, offering a novel strategy for sustained ophthalmic drug delivery. Using hydrophilic, biocompatible polymers such as HPMC, sodium alginate, and chitosan, five formulations (F1–F5) were prepared using the solvent casting technique. Among these, the optimized formulation (F2) exhibited ideal physicochemical properties, excellent mechanical strength, and a surface pH compatible with ocular tissues. It demonstrated sustained drug release for up to 12 hours, following Higuchi diffusion kinetics, and showed superior mucoadhesive strength and retention time on ex-vivo corneal tissues. Sterility testing confirmed microbiological safety, and histological studies indicated no irritation or damage to corneal epithelium. These inserts effectively overcome the drawbacks of conventional eye drops, such as rapid precorneal elimination and frequent dosing, by offering prolonged ocular retention, enhanced bioavailability, and improved patient compliance. The study supports the use of

mucoadhesive ocular inserts as a promising drug delivery system for treating bacterial conjunctivitis and potentially other ocular infections. Future work may include in-vivo pharmacokinetic studies and clinical trials to validate therapeutic efficacy and long-term safety. Overall, this formulation approach provides a significant advancement in non-invasive, sustained ophthalmic drug delivery.

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