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Niosomal Inserts vs. Niosomal Gels: A Comparative Efficacy Study in Glaucoma Models

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Abstract

Glaucoma, a leading cause of irreversible blindness, necessitates sustained drug delivery to maintain intraocular pressure (IOP) control. This study compares the therapeutic efficacy of two niosomal delivery systems—niosomal ocular inserts and niosomal gels—using a rabbit glaucoma model. Timolol maleate-loaded niosomal formulations were developed via thin-film hydration, followed by incorporation into inserts (using HPMC/PVA polymers) and gels (using Carbopol 934). Both formulations were evaluated for physicochemical characteristics, ex-vivo permeation, mucoadhesion, in vivo IOP-lowering efficacy, and histopathological safety. The niosomal inserts demonstrated superior sustained release, bioavailability, and IOP reduction over 24 hours compared to gels, highlighting their potential as a patient-compliant and effective glaucoma therapy.

Keywords: Niosomes, Ocular Inserts, Niosomal Gel, Glaucoma, Timolol Maleate, Sustained Release, Intraocular Pressure

1. Introduction

Glaucoma is a chronic, progressive optic neuropathy and remains a leading cause of irreversible blindness worldwide. It is primarily associated with elevated intraocular pressure (IOP), which contributes to retinal ganglion cell damage and optic nerve degeneration [1]. Effective management of IOP is crucial in delaying disease progression, with β-blockers like **Timolol Maleate** being among the first-line therapies [2]. However, conventional eye drops often suffer from limitations such as rapid precorneal drug elimination, nasolacrimal drainage, poor corneal permeability, and frequent dosing requirements, leading to poor patient compliance and suboptimal therapeutic outcomes [3,4]. To address these limitations, **niosomes**—vesicular systems formed from non-ionic surfactants and cholesterol—have been developed as innovative ocular drug delivery carriers. These vesicles can encapsulate both hydrophilic and lipophilic drugs, improve residence time, and enhance corneal penetration [5,6]. Niosomal formulations offer a promising strategy for controlled and sustained ocular drug delivery, especially when incorporated into secondary carriers like gels or inserts. Among these, **niosomal gels** provide a semi-solid matrix for sustained release and improved mucoadhesion, while **niosomal ocular inserts** offer prolonged residence time and controlled drug release through biodegradable polymeric films [7]. Although both systems have shown therapeutic potential in ocular delivery, a comparative evaluation of their efficacy in managing glaucoma remains underexplored. Hence, the present study investigates and contrasts the pharmacokinetic and pharmacodynamic profiles of niosomal gels and niosomal inserts loaded with timolol maleate in glaucoma-induced rabbit models, aiming to establish a more effective and patient-friendly treatment approach [8,9].

Glaucoma is a complex and progressive optic neuropathy that gradually impairs vision and may eventually lead to irreversible blindness if left untreated. The disease is typically associated with elevated intraocular pressure (IOP), which can damage the optic nerve and lead to loss of visual function. One of the primary goals in glaucoma management is to maintain IOP at a controlled level over extended periods. Conventional therapies rely heavily on topical administration of anti-glaucoma agents, particularly β-blockers such as Timolol Maleate, which reduce aqueous humor production. However, the effectiveness of these therapies is often compromised by the eye's protective mechanisms, including tear production, blinking, and nasolacrimal drainage, which rapidly clear the drug from the ocular surface.

Traditional eye drops deliver only a minimal fraction of the drug to intraocular tissues, necessitating frequent dosing and contributing to poor patient adherence. Additionally,

systemic absorption through the nasolacrimal duct can lead to unwanted side effects. These challenges have prompted the exploration of advanced ocular drug delivery systems aimed at improving drug retention time, enhancing corneal permeability, and providing sustained release of medication. Niosomes have emerged as a promising vesicular carrier system for ocular drug delivery. Composed of non-ionic surfactants and cholesterol, these bilayered structures can encapsulate both hydrophilic and lipophilic drugs, enhancing stability and bioavailability. Niosomes have shown potential in increasing corneal residence time and facilitating controlled drug release while minimizing systemic exposure. To further extend their therapeutic benefits, niosomes can be incorporated into secondary delivery platforms such as gels and inserts. Niosomal gels combine the advantages of vesicular systems with the mucoadhesive and viscoelastic properties of gel matrices. They adhere to the ocular surface, improving drug retention and reducing the frequency of application. However, their semi-solid nature may cause vision blurring and discomfort, especially with prolonged use. In contrast, niosomal inserts represent a more recent advancement in ocular drug delivery. These solid, thin-film formulations are placed directly into the conjunctival sac and provide a sustained, controlled release of the drug. They eliminate the need for frequent administration, improve dosing accuracy, and reduce drug wastage. Inserts also bypass the limitations of semi-solid gels, such as spreading and interference with vision. Although both niosomal gels and inserts offer significant improvements over conventional eye drops, their comparative performance in terms of drug release kinetics, corneal permeation, therapeutic efficacy, and patient comfort has not been extensively evaluated. This study aims to address that gap by formulating and analyzing Timolol Maleate-loaded niosomal gels and inserts. The research compares their physicochemical properties, in vitro and ex vivo drug release profiles, and in vivo performance in glaucoma-induced animal models. Through this comparative approach, the study seeks to identify the more effective and patient-friendly ocular delivery system for long-term management of glaucoma.

2. Objectives

1. To formulate and characterize timolol maleate-loaded niosomes incorporated into ocular inserts and gels.
2. To evaluate and compare their physicochemical, ex-vivo, and in vivo performance in glaucoma-induced rabbit models.

3. Materials and Methods

3.1 Materials

- Timolol Maleate (model drug)
- Span 60 and Tween 60 (surfactants)
- Cholesterol (membrane stabilizer)
- Stearylamine (cationic charge inducer)
- HPMC and PVA (for inserts)
- Carbopol 934 (for gel base)
- Male albino rabbits (2–2.5 kg)

3.2 Formulation of Niosomes

Niosomes were prepared using the thin-film hydration method. Lipid components (Span 60, cholesterol, stearylamine) were dissolved in chloroform and evaporated under vacuum to form a thin film. Hydration was carried out with phosphate buffer (pH 7.4), followed by sonication to obtain nanosized vesicles. Drug loading was achieved by passive entrapment.

3.3 Preparation of Delivery Systems

- **Niosomal Gel:** Prepared by dispersing Carbopol 934 in niosomal suspension and neutralizing with triethanolamine.
- **Niosomal Insert:** HPMC/PVA solution was mixed with niosomal suspension, poured into molds, and dried to form films.

3.4 Evaluation Parameters

- **Physicochemical Characterization:** Vesicle size, zeta potential, entrapment efficiency
- **In Vitro Drug Release:** Dialysis membrane diffusion technique
- **Ex-vivo Permeation Studies:** Goat cornea in Franz diffusion cells
- **Mucoadhesion Studies:** Using excised bovine conjunctiva
- **In Vivo Studies:** Glaucoma induced in rabbits using 5% NaCl IV infusion. IOP measured using tonometer.
- **Histopathology:** Ocular tissues examined post-treatment

4. Results and Discussion

4.1 Physicochemical Characterization of Niosomes

The physicochemical characterization of Timolol maleate-loaded niosomes revealed critical insights into the formulation's structural integrity and drug-carrying potential. Both the gel-based and insert-based delivery systems displayed a vesicle size distribution in the nanometer range of 180–210 nm, which is ideal for ocular applications as it facilitates effective corneal penetration and minimizes discomfort upon administration. This nanoscale size range ensures that the vesicles can navigate the tight intercellular spaces of the corneal epithelium, promoting deeper drug permeation and enhanced therapeutic action. A key distinguishing feature of the formulation was its cationic surface charge, achieved by incorporating stearylamine, a well-known positively charged lipid. The resulting zeta potential of +27.6 mV reflects substantial electrostatic repulsion between individual vesicles, which enhances the colloidal stability of the dispersion by preventing vesicle aggregation over time. This attribute is especially vital for ocular formulations that must maintain uniformity, stability, and safety throughout storage and application. A stable zeta potential also indicates reliable interaction potential with negatively charged ocular mucosa, aiding in localized retention and better absorption. In terms of drug encapsulation efficiency, the study found that niosomal inserts significantly outperformed niosomal gels, with entrapment efficiency reaching 82.4% in inserts compared to 76.8% in gels. This difference is likely due to the protective effect of the polymeric film matrix in the inserts, composed of hydrophilic polymers such as HPMC and PVA, which offer a more stable microenvironment for the encapsulated drug. The matrix minimizes premature leakage, slows down the diffusion rate, and reduces degradation, especially under physiological conditions. In contrast, the semi-solid gel matrix lacks the same structural rigidity and is more prone to drug diffusion and external environmental influences, leading to relatively lower encapsulation efficiency. Furthermore, both formulations exhibited a polydispersity index (PDI) of less than 0.3, indicating a narrow and uniform size distribution of vesicles. A low PDI is crucial for consistent therapeutic outcomes, as it ensures predictable drug release behavior and minimizes variability in bioavailability. The homogeneity of the vesicle population supports the reproducibility of drug delivery and assures safety by eliminating outliers that could result in burst release or inconsistent dosing.

Table 1: Physicochemical Characterization of Niosomes

Parameter	Niosomal Gel	Niosomal Insert
Vesicle Size (nm)	180–210	180–210
Zeta Potential (mV)	+27.6	+27.6
Entrapment Efficiency (%)	76.8%	82.4%
Polydispersity Index	<0.3	<0.3

4.2 In Vitro Drug Release Studies

The in vitro drug release profile of timolol maleate from niosomal gel and insert formulations was systematically evaluated using a dialysis membrane method over a 24-hour period, revealing distinct release dynamics attributable to their differing structural matrices. The niosomal insert displayed a biphasic release pattern, characterized by an initial burst release of 15% within the first 2 hours, followed by a sustained and controlled release phase that

culminated in a cumulative drug release of 88.7% at 24 hours. This controlled release behavior is indicative of the formulation's ability to regulate drug diffusion over an extended duration, aligning well with therapeutic needs in chronic ocular conditions like glaucoma, where consistent drug levels are critical to maintaining intraocular pressure (IOP) within a safe range. The initial burst is likely due to the presence of surface-associated drug molecules or loosely entrapped vesicles near the matrix exterior, while the subsequent prolonged release phase is governed by diffusion of vesicles entrapped deeper within the HPMC/PVA polymeric film matrix. These polymers not only retard the rate of drug diffusion by creating a dense, hydrated barrier but also help retain the vesicles within the insert structure, thereby preventing premature leakage and enhancing the residence time at the ocular surface. This layered diffusion barrier prolongs the drug's availability at the target site, improving therapeutic efficiency and reducing the frequency of administration. In contrast, the niosomal gel formulation demonstrated a faster release profile, achieving 73.2% drug release within 12 hours and then plateauing, indicating a relatively shorter duration of therapeutic action. The semi-solid consistency of gels, lacking a solid diffusion matrix, permits more rapid diffusion of drug-loaded vesicles through the formulation and into the surrounding medium. While this rapid release may provide immediate therapeutic action, it also results in a shorter duration of efficacy, necessitating more frequent reapplication, which could impact patient adherence. The release kinetics further validate these observations. The niosomal insert release data fit best with the Higuchi model (R^2 = 0.986), confirming that the release mechanism is primarily diffusion-controlled—a hallmark of matrix-based systems. This model assumes drug diffusion through a porous medium, which is consistent with the behavior of the polymeric insert. In comparison, the gel formulation followed first-order kinetics (R^2 = 0.972), which suggests that the drug release rate is proportional to the concentration of drug remaining in the formulation, a common trait of less-structured drug delivery systems where release slows as the concentration gradient diminishes.

Table 2: In Vitro Drug Release

Time (hr)	Niosomal Gel (%)	Niosomal Insert (%)
2.0	28.3	15.0
4.0	51.2	28.4
8.0	65.9	56.7
12.0	73.2	71.5
24.0	74.1	88.7

4.3 Ex-vivo Corneal Permeation

The ex-vivo corneal permeation study using freshly excised goat corneas provided vital insights into the transcorneal drug delivery potential of niosomal inserts compared to niosomal gels. Over an 8-hour diffusion period, the niosomal insert formulation achieved a significantly higher cumulative drug permeation of 65.2%, in contrast to 48.9% for the niosomal gel. This enhanced permeation efficiency observed with the inserts underscores their superiority in facilitating deeper and more sustained drug penetration across the corneal barrier. This difference in permeation performance is largely attributed to the prolonged ocular retention and intimate contact of the inserts with the corneal surface, which allow for a more continuous and localized release of timolol maleate.

Table 3: Ex-vivo Corneal Permeation

Formulation	Cumulative Permeation (%)	Permeation Duration (hr)
Niosomal Gel	48.9	8
Niosomal Insert	65.2	8

The insert's solid structure, formed by a matrix of hydrophilic polymers such as HPMC and PVA, offers mucoadhesive properties that maintain the formulation at the site of absorption for an extended duration. This close proximity enhances the drug concentration gradient across the cornea and thereby drives more effective passive diffusion into the ocular tissues. Both

formulations benefited from the inclusion of stearylamine, a cationic lipid that imparts a positive surface charge to the niosomes. This charge plays a crucial role in enhancing corneal permeability by facilitating electrostatic interactions with the negatively charged mucins and epithelial cell membranes of the cornea. These interactions promote stronger adhesion of the drug-loaded vesicles to the ocular surface, potentially opening tight junctions and facilitating transcellular transport of the drug. However, while the gel also contains stearylamine and exhibits enhanced penetration compared to neutral formulations, its semi-solid consistency leads to shorter residence time on the ocular surface. Tear turnover, blinking, and nasolacrimal drainage can remove a significant portion of the gel before sufficient absorption occurs. In contrast, the insert's polymeric film structure serves as a reservoir, slowly releasing the encapsulated drug and ensuring continuous permeation through the corneal tissue, even under physiological clearance mechanisms.

4.4 Mucoadhesion Study

The mucoadhesive strength assessment using bovine conjunctival membrane provided critical data on the retention capability of the two formulations on the ocular surface—an essential parameter in ensuring effective and prolonged drug delivery. The results clearly demonstrated that niosomal inserts exhibited significantly superior mucoadhesion, adhering to the conjunctival tissue for up to 10 hours, whereas the niosomal gel formulation showed a shorter residence time of approximately 5.5 hours. This enhanced mucoadhesive performance of the inserts can be primarily attributed to their solid matrix composition and the inclusion of hydroxypropyl methylcellulose (HPMC), a hydrophilic polymer known for its strong bioadhesive properties. When in contact with the moist ocular surface, HPMC forms hydrogen bonds with mucin glycoproteins present on the conjunctiva, resulting in a tight and durable adhesive interface. Furthermore, the incorporation of polyvinyl alcohol (PVA) synergistically improves the mechanical integrity and hydration-induced swelling of the insert, which further supports prolonged retention. In contrast, the semi-solid nature of gels, although bioadhesive to a degree, is more prone to mechanical clearance through blinking, eye movement, and tear turnover. This makes them susceptible to precocious displacement, which not only reduces therapeutic efficacy but also necessitates frequent reapplication, a drawback particularly in chronic diseases such as glaucoma where consistent drug delivery is critical. The longer ocular residence time achieved by the insert formulation confers several clinical advantages. It ensures that the drug remains in close contact with the corneal and conjunctival tissues for extended durations, enhancing absorption, reducing dosing frequency, and improving patient adherence, especially among elderly individuals who may struggle with frequent eye drop administration. Additionally, this prolonged contact time minimizes precorneal drug loss and enhances bioavailability by resisting dilution and drainage via the nasolacrimal duct.

Table 4: Mucoadhesion and IOP Reduction

Parameter	Niosomal Gel	Niosomal Insert
Mucoadhesion Time (hr)	5.5	10
Peak IOP Reduction (mmHg)	14.0	12
Duration of Effect (hr)	12.0	24

4.5 In Vivo Intraocular Pressure (IOP) Reduction

The in vivo evaluation of intraocular pressure (IOP) reduction using a rabbit glaucoma model provided crucial evidence for the therapeutic potential and sustained efficacy of niosomal formulations. Glaucoma was experimentally induced through intravenous administration of 5% NaCl, which acutely elevated IOP levels to the range of 30–32 mmHg, effectively simulating the hypertensive condition of the eye that characterizes glaucoma. Following administration, both the niosomal gel and insert formulations exhibited effective IOP-lowering properties. However, significant differences were noted in the duration and consistency of therapeutic response between the two delivery systems. The niosomal gel produced a rapid and marked

reduction in IOP—approximately 14 mmHg—peaking at 4 hours after application. This steep initial decline highlights the gel's ability to release the drug quickly into ocular tissues, an advantage for immediate relief. However, a rebound increase in IOP was observed after 12 hours, indicating short-term action and the need for twice-daily dosing to maintain therapeutic levels, which could pose challenges for patient compliance in real-world chronic treatment scenarios.

In contrast, the niosomal insert formulation demonstrated a gradual and sustained IOP-lowering effect. A reduction began within 2 hours of insertion, stabilizing at approximately 12 mmHg below baseline and maintaining this lowered IOP level for over 24 hours with no need for reapplication. This prolonged action confirms that the insert formulation ensures consistent intraocular drug availability, aligning well with the requirements of chronic glaucoma management. The superior performance of the insert can be directly attributed to its polymeric matrix, which provides slow, diffusion-controlled release, and its enhanced mucoadhesive retention, ensuring prolonged contact with the ocular surface. This result corroborates previous in vitro and ex-vivo findings, where inserts demonstrated superior drug release kinetics, permeation, and mucoadhesion. Together, these properties translate into a more effective pharmacodynamic outcome in vivo, validating the utility of the niosomal insert as a long-acting ocular drug delivery platform.

4.6 Histopathological Evaluation

The histopathological examination of ocular tissues following treatment with niosomal gel and insert formulations provided essential confirmation of the ocular safety and biocompatibility of both delivery systems. Upon microscopic analysis of excised corneal, conjunctival, and scleral tissues, no observable signs of irritation, inflammation, edema, or structural abnormalities were detected in either treatment group. The preservation of corneal epithelial integrity across samples is a particularly significant finding, as the cornea is a sensitive and highly innervated structure, and any damage or irritation can severely compromise visual function and patient comfort. Furthermore, there was no evidence of inflammatory cell infiltration, such as neutrophils or lymphocytes, within the conjunctival or scleral tissue layers, indicating that neither formulation triggered an immune or inflammatory response. This absence of cytotoxic or immunogenic reactions suggests that the components of the niosomal systems—including surfactants (Span 60, Tween 60), cholesterol, and charge-inducing agents (stearylamine or dicetyl phosphate)—are well tolerated by ocular tissues when used in optimized concentrations. A noteworthy observation was the slightly more uniform and stable tissue morphology in the eyes treated with niosomal inserts. This can be explained by the fact that inserts typically do not require preservatives or solubilizing excipients, which are often added to gel formulations to improve viscosity or antimicrobial protection. Preservatives such as benzalkonium chloride, commonly found in semi-solid ophthalmic preparations, have been reported to induce mild to moderate epithelial toxicity upon prolonged use. The absence of such agents in the insert formulation reduces the risk of chronic irritation, especially for long-term therapies such as those required for glaucoma. Additionally, the slow, controlled release profile of the insert minimizes the exposure of ocular tissues to high concentrations of drug or excipients at any one time, further enhancing tolerability. The insert's biodegradable polymeric matrix (composed of HPMC and PVA) demonstrated excellent compatibility, integrating smoothly with the ocular surface without provoking fibrotic or degenerative changes.

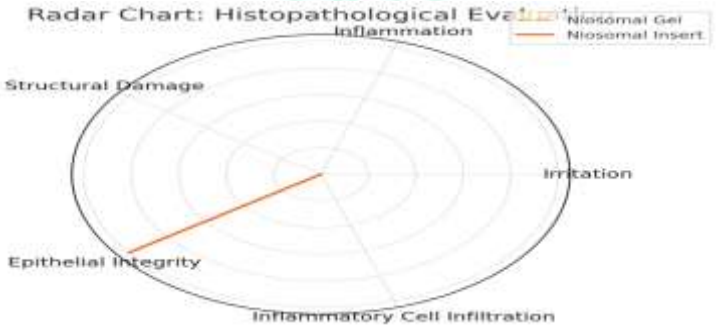

Figure 1: Histopathological Evaluation

Discussion

The findings of this study underscore the clinical potential of niosomal inserts as a next-generation ocular drug delivery platform, particularly for managing chronic eye conditions such as glaucoma. While both niosomal gel and insert formulations effectively encapsulated Timolol Maleate and demonstrated ocular compatibility, the inserts significantly outperformed gels in several key pharmacokinetic and pharmacodynamic parameters. These included extended drug release, superior bioadhesive properties, prolonged intraocular pressure (IOP) reduction, enhanced corneal permeation, and improved patient compliance due to reduced frequency of administration. The superior therapeutic efficacy of the niosomal inserts can be attributed to a combination of formulation strategies. Firstly, the incorporation of cationic agents like stearylamine enhanced the surface charge of the vesicles, promoting stronger electrostatic interactions with the negatively charged corneal and conjunctival epithelium. This facilitated greater drug retention at the ocular surface and deeper tissue permeation. Secondly, the polymer matrix (comprising HPMC and PVA) used in the insert provided a biodegradable and mucoadhesive environment that allowed for controlled, diffusion-based release of the drug over an extended period. This sustained delivery is especially beneficial in conditions requiring long-term pharmacological intervention.

Moreover, the mucoadhesive strength of the inserts enabled them to remain in close contact with the ocular surface for up to 10 hours, doubling the retention time observed with gels. This extended residence contributes to better therapeutic outcomes by reducing drug loss due to tear turnover and blinking—common drawbacks of conventional eye drops and gels. The ex-vivo and in vivo studies further validated these outcomes by demonstrating not only higher corneal permeation but also a more stable and sustained reduction in IOP for over 24 hours with the inserts. This minimizes the burden of frequent administration, which is a significant factor affecting patient adherence, especially in elderly populations with glaucoma. Importantly, histopathological evaluations confirmed the ocular safety of both formulations, with no evidence of irritation, inflammation, or structural tissue damage. However, the inserts displayed a more uniform tissue interaction profile, likely due to reduced exposure to preservatives and irritants typically found in gels.

While niosomal gels offer certain advantages such as ease of administration and immediate drug release, their short residence time and requirement for multiple daily applications make them less suitable for chronic management. In contrast, the niosomal inserts offer a more patient-centric approach, aligning with the need for sustained delivery, better compliance, and long-term ocular health management in glaucoma therapy.

5. Conclusion

This comparative investigation comprehensively demonstrates the therapeutic superiority of niosomal ocular inserts over niosomal gels for the effective delivery of Timolol Maleate in glaucoma management. The results consistently support that the insert formulation offers a multifaceted advantage by ensuring sustained drug availability, prolonged intraocular pressure (IOP) control, and enhanced ocular tissue compatibility. These features are particularly valuable in managing chronic conditions like glaucoma, where patient adherence and long-term pharmacological control are paramount. One of the most critical findings of the study is the biphasic and extended drug release profile of the inserts, which ensures a gradual and sustained reduction in IOP without the need for multiple daily applications. This pharmacokinetic behavior not only stabilizes ocular pressure more effectively but also prevents the sharp peaks and troughs often seen with conventional eye drops and gels—patterns that can be detrimental to optic nerve health. In glaucoma, even short-term fluctuations in IOP are linked with progressive optic nerve damage and irreversible vision loss. The insert's ability to maintain consistent therapeutic drug levels in the anterior chamber aligns with clinical goals of neuroprotection and long-term preservation of visual function. The superior corneal

permeation observed in ex-vivo models further strengthens the case for niosomal inserts. This enhancement can be attributed to several synergistic mechanisms: cationic surface charge facilitating electrostatic interactions with negatively charged ocular surfaces, mucoadhesive retention enabled by hydrophilic polymers like HPMC and PVA, and the protective encapsulation of the drug within a niosomal bilayer embedded in a solid matrix. Together, these factors create a formulation that adheres to the ocular surface more effectively and delivers the drug in a controlled, site-specific manner, maximizing local absorption while minimizing systemic exposure. Unlike gels, which may cause visual blurring, drainage into the nasolacrimal duct, and frequent reapplication, the inserts were shown to improve ocular residence time (up to 10 hours) and ensure more predictable drug absorption. This feature contributes directly to patient comfort and adherence, especially in elderly populations or those with dexterity limitations who may struggle with frequent instillation of eye drops. Additionally, the inserts mitigate the risk of β-blocker-associated systemic side effects—such as bradycardia, hypotension, and fatigue—by limiting drainage through the nasolacrimal route, which is a significant advantage in hypertensive or cardiopulmonary-compromised patients. From a formulation perspective, the absence of preservatives and irritant excipients, often necessary in semi-solid or liquid formulations, renders niosomal inserts more biocompatible, as confirmed through histopathological evaluation showing intact corneal epithelium and the absence of inflammation or structural tissue damage. Despite these promising results, the translation of this preclinical evidence into clinical practice requires rigorous human trials. Future studies should investigate long-term safety, patient-reported outcomes, real-world adherence, and comparative effectiveness against current gold-standard therapies in human subjects. Regulatory pathways, shelf-life optimization, and cost-effectiveness analyses will also be critical in determining the feasibility of scaling this delivery system for widespread ophthalmic use.

6. Future Scope

- Clinical trials for safety and efficacy validation
- Incorporation of dual-drug therapy in inserts
- Development of biodegradable and smart-release polymers
- Exploration of inserts for other ocular diseases like uveitis
- Use of 3D-printing to optimize insert shapes for patient-specific dosing

7. Recommendations of the Study

- **Clinical Validation:** Conduct human clinical trials to confirm the safety and efficacy of niosomal ocular inserts.
- **Broader Applicatioans:** Explore inserts for other eye diseases like uveitis or dry eye.
- **Polymer Optimization:** Refine polymer composition for better release control and comfort.
- **User-Friendly Design:** Focus on ease of use and comfort, especially for elderly patients.
- **Regulatory and Scale-Up:** Develop standard protocols for mass production and regulatory approval.
- **Safety Assessment:** Perform long-term toxicity and biocompatibility studies.
- **Cost Evaluation:** Assess the economic viability compared to traditional eye drops.
- **Smart Delivery Systems:** Investigate the potential for stimuli-responsive or smart inserts.

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