

Herbal Formulation and Development of Ophthalmic in Situ Gel by Using *Strychnos Potatorum* Linn

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Abstract:

Ocular drug delivery presents a considerable challenge due to anatomical and physiological barriers of the eye, leading to low bioavailability and therapeutic efficacy of conventional dosage forms like eye drops. To address these limitations, in situ gel systems that undergo sol-to-gel transition upon exposure to ocular conditions have been developed. These systems enhance residence time and improve drug absorption. The present review explores the potential of herbal-based in situ gel formulations using *Strychnos potatorum* Linn., a medicinal plant traditionally used in the treatment of eye disorders. The seeds of this plant are rich in bioactive constituents including alkaloids, lignans, and polysaccharides, which exhibit antimicrobial, anti-inflammatory, and antioxidant properties. These characteristics make it a suitable candidate for ophthalmic drug delivery systems. The review further discusses the mechanisms of in situ gelation, primarily ion-activated gelling using seed polysaccharides, and provides insights into formulation strategies, sterilization methods, and critical evaluation parameters such as clarity, viscosity, gelling capacity, and drug release profile. Additionally, the study emphasizes the advantages of herbal ophthalmic systems, challenges in formulation standardization, and future prospects including the integration of nanotechnology. Overall, *Strychnos potatorum*-based in situ gel represents a promising natural therapeutic approach for sustained and effective ocular drug delivery.

Keywords — Ophthalmic in situ gel, *Strychnos potatorum* Linn., Herbal formulation, Ocular drug delivery, Polysaccharide gels, Mucoadhesion.

1. INTRODUCTION

Ophthalmic drug delivery presents unique challenges due to anatomical and physiological barriers such as blinking, tear turnover, nasolacrimal drainage, and limited corneal permeability. Conventional eye drops, though widely used, suffer from poor bioavailability (typically less than 5%), requiring frequent dosing. To overcome these limitations, in situ gelling systems have emerged as a promising alternative. These are liquid at room temperature and convert into gels upon contact with

ocular fluids due to pH, temperature, or ionic triggers. This transition prolongs the residence time of the drug on the ocular surface, enhancing therapeutic efficacy.

Incorporation of herbal bioactives into ophthalmic in situ gels offers dual benefits: the therapeutic effect of natural compounds and improved drug delivery performance. *Strychnos potatorum* Linn., a plant traditionally used in Indian medicine for treating eye diseases, has gained attention due to its gelling mucilage and antimicrobial properties. This review

explores the formulation and potential of ophthalmic in situ gels using *Strychnos potatorum*, offering a natural, effective, and patient-friendly approach to ocular therapy.

2. Botanical Description of *Strychnos potatorum* Linn.

Strychnos potatorum Linn., commonly known as “Nirmali,” “Clearing Nut,” or “Chilla,” is a medium-sized deciduous tree that belongs to the family **Loganiaceae**. It is indigenous to tropical regions of **India, Sri Lanka, and Myanmar**, and has held a longstanding position in traditional Indian systems of medicine, particularly **Ayurveda and Siddha**, due to its therapeutic and water-purifying properties.

2.1 Botanical Classification

The Botanical hierarchy of *Strychnos potatorum* is provided below:

Taxonomic Rank	Classification
Kingdom	Plantae
Order	Gentianales
Family	Loganiaceae
Genus	<i>Strychnos</i>
Species	<i>Strychnos potatorum</i> Linn.

Table 1: Botanical Classification of *Strychnos potatorum* Linn.



Figure 1: Image of *Strychnos potatorum* Tree

2.2 Morphological Features

- **Tree Height:** Ranges between 10 to 12 meters.
- **Leaves:** Simple, opposite, ovate-oblong, 4–10 cm in length; glossy and dark green.
- **Flowers:** Small, greenish-white, fragrant; appear in cymes during the summer season.
- **Fruits:** A drupe, ovoid to globose in shape, 1–2 cm in diameter, green when immature and yellowish when ripe.
- **Seeds:** Hard, disc-shaped, flattened, with a pale yellow to brown surface; highly mucilaginous when soaked in water.

2.3 Microscopic and Diagnostic Features

The **seed coat** contains abundant mucilage which swells upon contact with water, forming a viscous layer. Histological studies have revealed the presence of **parenchymatous cells** containing starch grains and mucilage, contributing to the seed’s swelling and gelation behavior.

2.4 Ethnobotanical Relevance

Traditionally, the seeds are used to **clarify turbid water** due to their **coagulant and antimicrobial properties**, making them highly valuable in rural communities for potable water treatment. In Ayurveda, seeds are used for:

- Treating **conjunctivitis, eye irritation, and chronic ophthalmic conditions**
- Managing **urinary disorders, headaches, and skin diseases**
- Their **cooling, astringent, and demulcent** actions

2.5 Pharmaceutical Significance

The **mucilage** extracted from *S. potatorum* seeds serves as a **natural polymer** with high **gel-forming potential**, making it suitable for **ion-activated in situ gel formulations**. Its **biodegradable and non-**

toxic nature, combined with **good ocular tolerability**, supports its application in ophthalmic drug delivery systems.

3. Phytochemical Constituents of *Strychnos potatorum* Linn.

Strychnos potatorum Linn., a medicinally significant plant in traditional Indian systems of medicine, owes its pharmacological and excipient potential largely to its diverse and complex phytochemical profile. The seeds, which are the primary part used in ophthalmic formulations, are known to be rich in mucilage and numerous secondary metabolites. These constituents not only exhibit therapeutic benefits but also contribute significantly to the **gelling, bioadhesive, and film-forming properties** required in ophthalmic in situ gel systems.

3.1 Major Classes of Phytochemicals

The following classes of compounds have been isolated and characterized from the seeds and other parts of *S. potatorum*:

3.1.1 Alkaloids

Alkaloids are nitrogen-containing compounds known for their pronounced physiological activities. The principal alkaloid found in *S. potatorum* is **diaboline**, a mild central nervous system depressant. Other minor alkaloids may also be present in trace amounts. Although the alkaloid content is lower compared to other *Strychnos* species (e.g., *Strychnos nux-vomica*), these compounds exhibit **anti-inflammatory** and **antioxidant** effects, which support their use in ocular formulations to reduce irritation and inflammation.

3.1.2 Lignans

Lignans, including **potatorine**, are phenolic compounds that serve as **antioxidants and mild antimicrobial agents**. Their role in scavenging free radicals can help protect delicate ocular tissues from

oxidative stress, especially in chronic inflammatory eye conditions.

3.1.3 Mucilage and Polysaccharides

The **mucilage** present in *S. potatorum* seeds constitutes the most pharmaceutically important class of constituents. Composed of **complex polysaccharides**, it hydrates upon contact with aqueous environments to form a **viscous gel**, which is key for **in situ gel formation**. The mucilage enhances **ocular retention**, acts as a **sustained release matrix**, and provides **lubrication** to the ocular surface.

Key roles of mucilage in ophthalmic delivery:

- Ion-sensitive gelation (triggered by Na⁺, Ca²⁺ ions in tears)
- Bioadhesive to the corneal epithelium
- Prolongs drug contact time
- Minimizes drug drainage and increases absorption

3.1.4 Glycosides

Although present in smaller quantities, **glycosides** contribute to **anti-inflammatory** and **mild diuretic** effects. These compounds may assist in reducing mild ocular swelling and irritation when incorporated into eye drop formulations.

3.1.5 Steroids and Triterpenoids

Phytosterols isolated from the seeds may provide **membrane-stabilizing** effects, reducing cellular permeability and leakage under stress conditions. Triterpenoids offer **anti-inflammatory** and **wound healing** properties, beneficial for ocular applications, especially in post-surgical or infected eyes.

3.1.6 Saponins

Strychnos potatorum contains low concentrations of saponins, which are known for their **surface-active properties**. These compounds may help improve drug solubility and **enhance permeability** across the corneal membrane. They also possess **antimicrobial** actions that help maintain sterility in ocular formulations.

3.1.7 Tannins

The presence of **hydrolysable tannins** provides **astringent** and **antimicrobial** effects. In eye care, tannins contribute to **tissue contraction**, reducing irritation and redness. Their protein-binding ability may also create a protective layer over inflamed ocular tissues.

Class of Compound	Main Example(s)	Pharmaceutical Role in Eye Gels
Alkaloids	Diaboline	Mild CNS depressant, anti-inflammatory
Lignans	Potatorine	Antioxidant, antimicrobial
Mucilage	Polysaccharide complex	Gelling agent, bioadhesive, sustained release matrix
Glycosides	Strychnoside (possible)	Anti-inflammatory, ocular comfort
Steroids	Phytosterols	Membrane stabilization, healing
Saponins	-	Solubility enhancer, antimicrobial
Tannins	Hydrolysable tannins	Astringent, antimicrobial, reduces redness

Table 2: Key Phytoconstituents of *Strychnos potatorum* and Their Roles in Ophthalmic Use.

4. Mechanism of In Situ Gelation

In situ gelation represents a sophisticated strategy in drug delivery systems, particularly in ophthalmology, where the precorneal residence time of conventional eye drops is severely limited due to blinking, tear turnover, and nasolacrimal drainage. In situ gels are administered as low-viscosity solutions that transform into gels upon exposure to specific physiological conditions in the eye, enabling prolonged retention, controlled drug release, and improved therapeutic efficacy.

Among the various stimuli-responsive systems, *Strychnos potatorum* Linn. mucilage has shown remarkable potential for **ion-sensitive gelation**, making it highly suitable for ophthalmic in situ gel formulations.

4.1 Types of In Situ Gelation Mechanisms

In situ gels are broadly classified based on the environmental stimuli that trigger the sol-gel transition:

- **pH-sensitive gelation**
- **Thermo-sensitive gelation**
- **Ion-sensitive gelation**

These mechanisms depend on the polymer's physicochemical characteristics and the formulation's compatibility with ocular conditions.

4.1.1 pH-Sensitive Gelation

Certain polymers, such as **Carbopol 940**, remain in solution at acidic pH but undergo gelation when exposed to the slightly alkaline pH of the tear fluid (approximately 7.4). In this system, the sol-to-gel transition occurs due to ionization of functional groups, increasing viscosity and network formation.

4.1.2 Thermo-Sensitive Gelation

These formulations remain in a liquid state at room temperature and gel upon exposure to the ocular surface temperature (~34–35°C). **Poloxamers (e.g., Poloxamer 407)** are classic examples that exhibit reversible gelation at physiological temperatures due to micellar aggregation and network formation.

4.1.3 Ion-Sensitive Gelation (Applicable to *Strychnos potatorum*)

The mucilage of *Strychnos potatorum* exhibits **ion-sensitive gelation**, wherein the presence of mono- and divalent ions (e.g., Na⁺, Ca²⁺) in the lacrimal fluid induces cross-linking of polymer chains, resulting in gel formation. This transition is **instantaneous and reversible**, making it ideal for ophthalmic use.

The mucilaginous polysaccharides contain **hydroxyl and carboxyl groups**, which interact with cations in tears, forming ionic bridges and 3D gel networks. The gelling process is also influenced by polymer concentration, ionic strength, and tear volume.

4.2 Role of *Strychnos potatorum* Mucilage in Gelation

- The **hydrophilic** nature of the mucilage facilitates hydration and swelling in the aqueous tear environment.
- The **anionic character** of polysaccharides promotes **ionic interactions** with tear electrolytes, such as Ca²⁺ and Mg²⁺.
- The **molecular weight** and chain flexibility contribute to robust 3D gel matrix formation.

These properties allow the formulation to **transition from a low-viscosity drop to a viscous gel** in the conjunctival cul-de-sac within seconds, extending the residence time and reducing the need for frequent instillation.

Table 3: Comparison of In Situ Gelation Mechanisms and Key Polymers

4.3 Benefits of Ion-Sensitive In Situ Gelation in Ocular Delivery

Mechanism	Triggering Factor	Common Polymers	Characteristics
pH-sensitive	Tear pH (~7.4)	Carbopol, Polyacrylic acid	Sharp sol-gel transition, good for buffering
Thermo-sensitive	Ocular temperature (~34°C)	Poloxamer 407, Pluronic F127	Easy administration, gel at body temperature
Ion-sensitive	Tear ions (Na ⁺ , Ca ²⁺ , Mg ²⁺)	Gellan gum, Sodium alginate, <i>S. potatorum</i> mucilage	Natural gelation, stable viscosity, biocompatible

- **Immediate gelation** upon contact with tear fluid
- **Enhanced precorneal residence time**
- **Sustained drug release** for prolonged therapeutic effect
- **Better patient compliance** due to reduced frequency
- **Natural polymer compatibility**, reducing toxicological risks

4.4 Limitations and Mitigation

Although ion-sensitive gels offer numerous advantages, some challenges remain:

- **Variability in tear composition** can affect gelation time.
- **Potential ocular irritation** from high mucilage concentrations.
- **Sterilization challenges** due to polymer instability at high temperatures.

These limitations can be addressed through:

- Optimization of mucilage concentration
- Blending with compatible polymers (e.g., HPMC, sodium alginate)
- Use of membrane filtration for sterilization

5. Formulation Approach

The development of an ophthalmic **in situ gel using *Strychnos potatorum* mucilage** involves a strategic formulation methodology that integrates both pharmaceutical sciences and herbal excipient optimization. The primary goal is to ensure that the formulation remains a **low-viscosity liquid before instillation**, then undergoes **ion-sensitive gelation** upon contact with tear fluid, ensuring **prolonged ocular retention** and **sustained drug release**.

The formulation process comprises several critical stages, including **mucilage extraction, polymer selection, drug incorporation, adjustment of physicochemical parameters, and sterilization and packaging**. Each stage must be meticulously optimized to maintain the **sterility, bioadhesiveness, clarity, and therapeutic efficacy** of the final product.

5.1 Extraction and Purification of *Strychnos potatorum* Mucilage

The mucilage, which serves as the natural gelling polymer, is obtained from the seeds of *Strychnos potatorum* through the following steps:

1. **Seed Cleaning and Soaking:** Mature, dried seeds are cleaned to remove surface debris and soaked in distilled water for 24 hours to allow mucilage hydration and swelling.
2. **Mechanical Agitation:** The hydrated seeds are subjected to mechanical agitation or gentle crushing to release the mucilage.

3. **Filtration:** The mixture is filtered through muslin cloth or a fine mesh to separate the mucilaginous extract from the seed residue.
4. **Precipitation (Optional):** Ethanol or acetone may be added to the extract to precipitate polysaccharides and increase purity.
5. **Drying:** The purified mucilage is dried under vacuum or in a tray dryer at low temperature to preserve its gelling properties.
6. **Pulverization and Sieving:** The dried material is powdered and passed through a suitable mesh (e.g., #80) for uniformity.

This mucilage is then stored in an airtight container until use.

5.2 Selection of Additional Polymers and Excipients

To enhance the formulation properties, additional polymers are commonly included. These may serve to modify viscosity, enhance mucoadhesion, or adjust gel strength.

- **Hydroxypropyl Methylcellulose (HPMC):** Improves viscosity and forms a stable film over the cornea.
- **Carbopol 940:** Enhances pH-sensitive gelling, often blended with natural polymers for synergistic effects.
- **Sodium Alginate:** Another ion-sensitive polymer that supports controlled gelation with divalent cations.

Other essential excipients include:

- **Buffers** (e.g., borate, phosphate): To maintain ocular-compatible pH (~7.0–7.4)
- **Tonicity Adjusters** (e.g., NaCl): To ensure isotonicity with tear fluid
- **Preservatives** (e.g., benzalkonium chloride): When multi-dose vials are used (optional in single-dose sterile units)
- **Solubilizers** (e.g., propylene glycol): For poorly water-soluble drugs

5.3 Drug Incorporation

The selected active pharmaceutical ingredient (API), such as **ciprofloxacin**, **timolol maleate**, or **diclofenac sodium**, is added to the polymeric dispersion under constant stirring to ensure uniform distribution.

Key considerations include:

- **Drug solubility:** Adjusted using cosolvents if necessary
- **Compatibility:** Preformulation studies to ensure no interaction with mucilage or other excipients
- **Concentration:** Optimized based on therapeutic dose and ocular retention kinetics

5.4 Preparation of In Situ Gel Formulation

The formulation is prepared using the following protocol:

1. **Polymer Dispersion:** The extracted *Strychnos potatorum* mucilage is dispersed in sterile water and hydrated with continuous stirring.
2. **Incorporation of Co-Polymers:** Secondary polymers such as HPMC or Carbopol are added and allowed to dissolve.
3. **Drug Addition:** The API is added and dissolved under mild heating if needed.
4. **Adjustment of pH and Tonicity:** The solution is adjusted to a physiological pH (7.0–7.4) and isotonic conditions.
5. **Filtration:** The entire mixture is passed through 0.22 μm membrane filters to ensure particulate removal and sterilization.

5.5 Sterilization

Sterility is a mandatory requirement for ophthalmic preparations.

- **Thermolabile Components:** Formulations containing heat-sensitive drugs or mucilage are sterilized using **membrane filtration** followed by aseptic filling.
- **Thermostable Formulations:** Can be sterilized using **autoclaving** at 121°C for 15 minutes, provided that the mucilage retains its gelling properties post-processing.

5.6 Packaging

The final sterile gel formulation is filled into **sterile low-density polyethylene (LDPE) containers** or **single-dose vials** using aseptic filling machines under laminar air flow conditions. The containers are sealed and labeled appropriately.

6. Evaluation Parameters

Evaluation of an ophthalmic in situ gel formulation is a critical aspect of the development process. The formulation must comply with pharmaceutical standards for **sterility, clarity, viscosity, pH, drug content, gelation behavior, and release kinetics** to ensure efficacy, safety, and patient acceptability. A series of **physicochemical, microbiological, and pharmacotechnical tests** are employed to assess the suitability of the formulation for ophthalmic use.

These evaluations are carried out as per the **Indian Pharmacopoeia (IP)**, **United States Pharmacopoeia (USP)**, and **ICH guidelines**, ensuring that the product meets international quality benchmarks.

6.1 Clarity and Appearance

The formulation should be a **clear, colorless to pale yellow liquid** before administration and should **gel rapidly upon contact with tear fluid**. Any presence of **particulates, turbidity, or sedimentation** is considered unacceptable.

- **Method:** Visual inspection against a black and white background.

- **Acceptance Criteria:** Optically clear, free from suspended particles.

6.2 pH Measurement

The pH of the ophthalmic gel must be **compatible with the natural tear fluid**, which ranges from **6.5 to 7.4**, to avoid ocular irritation or discomfort.

- **Instrument:** Calibrated digital pH meter.
- **Acceptance Criteria:** 6.8–7.4 for optimal patient comfort and drug stability.

6.3 Viscosity

Viscosity directly impacts the **retention time** and **ease of instillation**. Before administration, the gel should exhibit **low viscosity** for dropwise application, which increases significantly upon gelation in the eye.

- **Instrument:** Brookfield Viscometer (spindle no. 64, 20 rpm at 25°C).
- **Desired Range:**
 - Before gelation: 20–100 cps
 - After gelation: 100–300 cps

This dual-behavior ensures easy application with extended residence time.

6.4 Gelation Capacity

The formulation must rapidly gel upon contact with **tear fluid ions** (especially Ca^{2+} and Na^+), forming a stable and soft gel.

- **Method:** Simulated Tear Fluid (STF) method.
- **Procedure:** 100 μL of formulation is added to 2 mL STF; time for gel formation is recorded.
- **Acceptance Criteria:** Instantaneous to <30 seconds for gel formation and stability for at least 6 hours.

6.5 Drug Content Uniformity

This parameter ensures that the formulation consistently delivers the **labeled amount of active drug**, vital for achieving therapeutic efficacy.

- **Method:** UV–Vis spectrophotometry or HPLC.
- **Procedure:** Dilution of a known quantity followed by absorbance measurement at the drug's λ_{max} .
- **Acceptance Criteria:** 95%–105% of the labeled claim.

6.6 In Vitro Drug Release

This test simulates how the drug will be released over time from the gel matrix once instilled in the eye. It is crucial for determining the **release kinetics** (zero-order, first-order, Higuchi model, etc.).

- **Apparatus:** Franz diffusion cell or dialysis membrane method.
- **Medium:** Simulated Tear Fluid (STF) or phosphate buffer saline (PBS), pH 7.4.
- **Sampling:** At predetermined intervals (e.g., 0, 1, 2, 4, 6, 8, 12 hrs).
- **Acceptance Criteria:** Sustained release over 8–12 hours, matching kinetic model (e.g., Higuchi).

6.7 Sterility Testing

Sterility is an essential requirement for ophthalmic formulations. The test ensures that the product is **free from viable microbial contaminants**.

- **Method:** Membrane filtration method or direct inoculation as per IP/USP.
- **Incubation Media:**
 - Soybean Casein Digest Medium (for bacteria)
 - Fluid Thioglycolate Medium (for anaerobes)

- **Incubation:** 14 days under specified conditions.
- **Acceptance Criteria:** No microbial growth observed.
- **Parameters Monitored:** pH, viscosity, drug content, gelation, and sterility.

6.8 Ocular Irritancy Test

This test determines the **ocular safety** of the formulation, confirming that it does not cause **redness, itching, excessive lacrimation, or other signs of irritation**.

- **Model:** Draize test in rabbits (ethical clearance required) or in vitro models like HET-CAM (Hen's Egg Test – Chorioallantoic Membrane).
- **Observation Period:** 24–72 hours.
- **Acceptance Criteria:** Non-irritant or mild irritation only (depending on the model).

6.9 Spreadability and Droplet Formation

Ease of administration is assessed by examining the **droplet formation ability** and **spreadability** on the corneal surface.

- **Method:** Drop formation using ophthalmic dropper; droplet weight is recorded.
- **Acceptance Criteria:** Uniform drops of consistent volume (~30–50 μL), good spreading on corneal surface models.

6.10 Stability Studies

Formulations are subjected to **accelerated and real-time stability testing** to ensure **chemical, physical, and microbiological stability** throughout the shelf-life.

- **Conditions:**
 - Accelerated: $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$ / 75% RH $\pm$ 5% for 6 months

Parameter	Purpose	Acceptance Criteria
Clarity	Visual transparency	Clear, particle-free
pH	Compatibility with tears	6.8–7.4
Viscosity	Ease of instillation and retention	20–100 cps (sol), 100–300 cps (gel)
Gelation Time	Onset of gelling	<30 seconds
Drug Content	Dose accuracy	95–105%
In Vitro Release	Release profile and kinetics	Sustained 8–12 hrs
Sterility	Microbial safety	No microbial growth
Ocular Irritancy	Patient safety	Non-irritant
Spreadability	Ease of ocular application	Uniform droplet, good spreadability
Stability	Shelf-life prediction	No significant changes post storage

Table 4: Summary of Evaluation Parameters for Ophthalmic In Situ Gel.

7. Advantages of Strychnos potatorum In Situ Gel

- Natural, biodegradable gelling agent
- Enhanced ocular retention time
- Controlled and sustained drug release
- Reduced dosing frequency and better patient compliance
- Antimicrobial and anti-inflammatory effects of plant components

- Minimal risk of systemic absorption and side effects
- Eco-friendly and economically viable
- Development of preservative-free formulations for sensitive eyes.

8. Recent Studies and Applications

- **Singh et al. (2021)** formulated a ciprofloxacin in situ gel using *S. potatorum* mucilage and observed significant antimicrobial activity against *S. aureus* and *E. coli*.
- **Ramesh et al. (2020)** incorporated diclofenac into a *S. potatorum*-based in situ gel, showing effective anti-inflammatory activity in rabbit eye models.
- **Chaudhary et al. (2019)** demonstrated sustained drug release for over 10 hours with improved patient tolerability.

Applications are expanding in:

- Bacterial conjunctivitis
- Post-surgical eye care
- Glaucoma treatment
- Anti-allergic formulations

9. Challenges and Future Prospects

Challenges:

- Standardization of mucilage content and quality
- Long-term physical and microbial stability
- Regulatory hurdles for herbal ophthalmic products
- Batch-to-batch variability in herbal extracts

Future Directions:

- Incorporation of nanocarriers in *S. potatorum* gel base
- Combination therapies with herbal and allopathic drugs
- Clinical trials to validate safety and efficacy

10. CONCLUSIONS

The development of ophthalmic in situ gels represents a significant advancement in the field of ocular drug delivery, offering improved patient compliance, prolonged retention time, and sustained drug release. Among the various natural polymers investigated, *Strychnos potatorum* Linn. has emerged as a promising excipient due to its favorable physicochemical characteristics, including its high mucilage content, ion-sensitive gelation capability, and inherent antimicrobial and anti-inflammatory properties.

This review has highlighted the comprehensive botanical profile of *S. potatorum*, its phytochemical richness, and the relevance of its mucilage in achieving desirable in situ gelation behavior upon exposure to tear fluid. The formulation strategies using *S. potatorum* incorporate conventional and ion-sensitive gelling agents to ensure effective drug incorporation, stability, and ocular compatibility. Furthermore, the evaluation parameters such as clarity, pH, viscosity, drug content, gelation capacity, sterility, and in vitro release kinetics have demonstrated the scientific validity and pharmaceutical acceptability of these formulations.

Recent preclinical studies have reinforced the therapeutic advantages of using *S. potatorum*-based gels, including enhanced corneal penetration, reduced dosing frequency, and minimal ocular irritation, which collectively contribute to better treatment outcomes. Despite certain challenges like standardization, scalability, and regulatory acceptance of herbal excipients, the future of such biopolymer-based drug delivery systems remains promising. Innovations in nanotechnology, hybrid gel systems, and clinical validation are expected to

further accelerate the adoption of these formulations in mainstream ophthalmic therapy.

In conclusion, the incorporation of *Strychnos potatorum* mucilage into in situ gel formulations not only leverages the therapeutic potential of natural compounds but also aligns with the growing preference for safer, biodegradable, and patient-friendly drug delivery platforms. Continued interdisciplinary research and clinical collaboration will be instrumental in translating these promising formulations from laboratory to clinical application, ultimately advancing the field of herbal pharmaceuticals and ocular therapeutics.

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