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"HERBAL OPHTHALMIC DRUG DELIVERY: FROM MEDICINAL PLANTS TO ADVANCED FORMULATION STRATEGIES AND EMERGING THERAPEUTIC APPROACHES"

Sami Patel, Shraddha Sachin Gaikwad, Waghmode Madhuri Sundar., Jyoti Bhagwat Tapale,

Satish Balasaheb Gite

Ashvin College Of Pharmacy manchi hill

Abstract

Herbal medicines have long been investigated for their potential role in the management of various diseases because medicinal plants contain structurally diverse phytoconstituents with antioxidant, anti-inflammatory, antimicrobial and other biological activities. Their application in ophthalmic drug delivery has attracted increasing research interest because several ocular disorders involve oxidative stress, inflammation, microbial infection, tissue injury or cellular degeneration. However, topical ocular drug delivery is challenging because blinking, tear turnover, nasolacrimal drainage, corneal barriers and other physiological mechanisms rapidly remove administered formulations and restrict drug penetration into ocular tissues [7–10]. Consequently, conventional eye drops may provide limited ocular residence and bioavailability.

Medicinal plants and natural compounds including *Curcuma longa*, *Camellia sinensis*, *Plantago ovata*, *Emblica* species, *Ocimum* species, curcumin, quercetin and resveratrol have been investigated for different ophthalmic applications [11,15–21]. Nevertheless, biological activity demonstrated in an in-vitro or animal study should not be interpreted as established clinical efficacy. A systematic review of medicinal plants used for common ophthalmic disorders found substantial heterogeneity and limited-quality evidence, emphasizing the need for rigorous clinical research [11].

The development of herbal eye drops requires appropriate botanical authentication, extraction, standardization, formulation optimization, sterility assurance, microbial quality control, stability assessment and ocular safety evaluation [1–6,25,29,30]. Advanced delivery approaches such as in-situ gels, liposomes, nanoemulsions, polymeric nanoparticles and lipid-based nanocarriers are being investigated to improve solubility, stability, ocular residence and delivery of poorly soluble phytoconstituents [12–14,26–28].

This review discusses ocular barriers, medicinal plants and phytoconstituents, therapeutic potential, formulation strategies, evaluation parameters, safety, quality control, regulatory considerations, recent technological developments, challenges and future perspectives of herbal-based ophthalmic preparations.

Keywords:

Herbal eye drops; medicinal plants; ophthalmic drug delivery; phytoconstituents; ocular formulation; phytopharmaceuticals; ocular safety; nanotechnology; herbal medicines; ophthalmic preparations.

1. Introduction

The eye is a highly specialized organ responsible for vision and is protected by complex anatomical, physiological and biochemical mechanisms. Disorders affecting the ocular surface, cornea, lens, aqueous humor, retina and optic nerve can compromise visual function and, in severe cases, result in permanent visual impairment. Common ocular conditions include dry-eye disease, conjunctivitis, allergic eye disease, corneal injury, cataract, glaucoma, uveitis and retinal disorders [7–10].

Pharmacological treatment of ocular disorders may involve topical, systemic, periocular or intraocular administration. Topical administration in the form of eye drops is particularly useful for many anterior-segment disorders because it is non-invasive, convenient and generally suitable for self-administration. However, the ocular surface presents substantial barriers to effective drug delivery [7–10].

The precorneal tear film, blinking and nasolacrimal drainage can remove a large proportion of an instilled formulation before sufficient drug absorption occurs. The corneal epithelium, stroma and endothelium also impose physicochemical barriers to drug transport. These factors contribute to the generally low bioavailability of conventional topical ophthalmic preparations [7–10].

Medicinal plants contain numerous classes of secondary metabolites, including flavonoids, phenolic compounds, alkaloids, terpenoids, tannins, polysaccharides and other bioactive substances. Several plant-derived compounds have demonstrated antioxidant, anti-inflammatory, antimicrobial, anti-angiogenic or neuroprotective properties that may be relevant to ocular disorders [12–21].

However, herbal ophthalmic preparations require greater scientific scrutiny than a simple demonstration of traditional use. A plant extract may contain hundreds of chemical constituents, and its composition can vary according to species, geographic origin, cultivation conditions, harvesting, processing and extraction method. Therefore, authentication, standardization and quality control are fundamental requirements [4–6,29,30].

A systematic review published in 2023 identified a large body of literature concerning medicinal plants and eye disorders but found that only a small number of studies met the inclusion criteria and that the available evidence had substantial heterogeneity and publication-bias concerns [11]. Therefore, herbal eye drops should be considered an active area of research rather than a universally established replacement for conventional ophthalmic therapy.

2. Ocular Anatomy and Physiology

2.1 Structure of the eye

The eye consists of anterior and posterior anatomical compartments. The anterior segment includes the cornea, conjunctiva, anterior chamber, iris, ciliary body and lens. The posterior segment contains the vitreous body, retina, choroid and optic nerve.

The cornea is particularly important in topical ocular drug delivery because it forms a major physical and biochemical barrier between the formulation and intraocular tissues. It contains the epithelium, Bowman's layer, stroma, Descemet's membrane and endothelium. Differences in the lipid and aqueous characteristics of these layers influence the penetration of drug molecules [7–10].

The conjunctiva covers much of the exposed ocular surface and participates in lubrication, protection and immune defense. It also contains blood and lymphatic vessels that can contribute to drug clearance following topical administration [7,9].

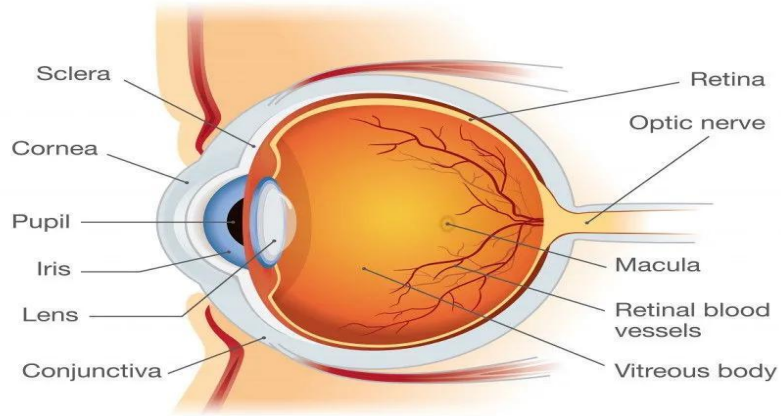


Figure 1. Anatomical barriers influencing topical ophthalmic drug delivery.

2.2 Tear film

The tear film provides lubrication, maintains optical quality and contributes to defense against environmental microorganisms. It also participates in the rapid dilution and clearance of topically administered formulations. Consequently, although the tear film is essential for ocular health, it represents an important challenge for drug delivery [8–10].

2.3 Corneal barrier

The corneal epithelium contains tight junctions and represents an important barrier to drug permeation. Hydrophilic and hydrophobic properties of the drug therefore influence its ability to cross the cornea. The stroma presents a different physicochemical environment from the epithelium, creating a requirement for an appropriate balance of drug properties for efficient transcorneal transport [7–10].

2.4 Ocular barriers

The major barriers include:

- Tear film
- Corneal epithelium
- Corneal stroma
- Corneal endothelium
- Blood–aqueous barrier
- Blood–retinal barrier
- Conjunctival and episcleral clearance mechanisms
- Ocular metabolic and transport processes [8,9]

These barriers are physiologically protective but make it difficult to achieve therapeutic concentrations at deeper ocular sites.

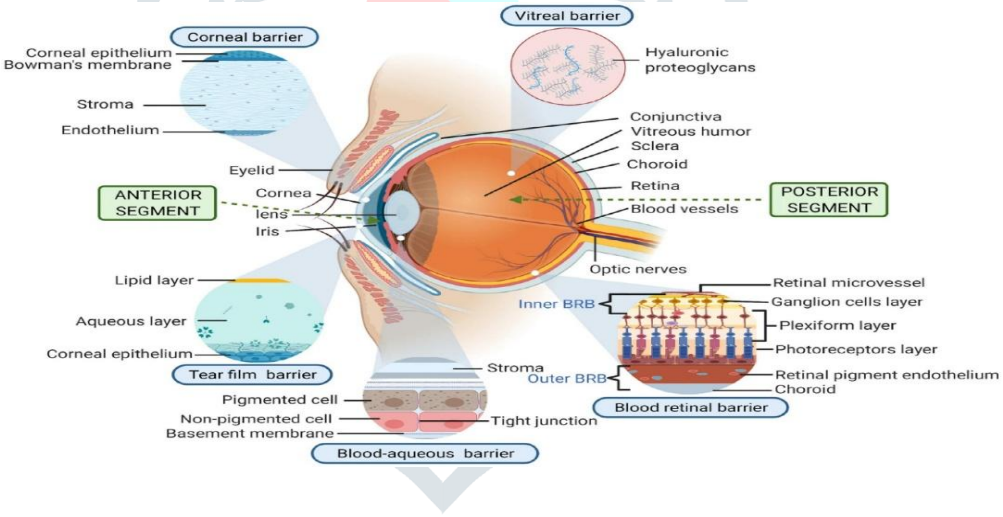


Fig2.Physiological barriers affecting the ocular bioavailability of topical administration formulations.

3. Ocular Drug Delivery and Its Challenges

3.1 Topical ocular delivery

Topical eye drops remain an important route for anterior-segment drug delivery. Their advantages include ease of administration, non-invasive dosing and relatively simple manufacturing. More than 95% of marketed ophthalmic products have historically been liquid preparations, although gels, ointments, inserts and other advanced dosage forms are also used [8].

3.2 Precorneal drug loss

After administration, the formulation mixes with tears and may be removed through blinking, reflex lacrimation and nasolacrimal drainage. Excess volume may also overflow from the ocular surface. These processes shorten residence time and reduce the quantity of active substance available for absorption [8–10].

3.3 Corneal penetration

The drug must cross several corneal layers before reaching many anterior-segment tissues. Tight epithelial junctions and the physicochemical characteristics of the corneal layers can restrict penetration [7–10].

3.4 Posterior-segment delivery

Topical eye drops are particularly limited for delivery to the retina and other posterior-segment tissues. Anatomical barriers, including the blood–retinal barrier, make non-invasive delivery to the posterior segment difficult [9].

3.5 Strategies for improving ocular bioavailability

Several pharmaceutical strategies have been developed:

1. Increasing formulation viscosity.
2. Incorporating mucoadhesive polymers.
3. Developing in-situ gelling systems.
4. Improving solubility.
5. Using lipid-based delivery systems.
6. Developing nanoemulsions.
7. Using nanoparticles or nanomicelles.
8. Developing sustained-release systems [8,10,13,26–28].

These approaches are particularly relevant to herbal compounds because many phytoconstituents have poor water solubility or limited chemical stability.

4. Medicinal Plants Used or Investigated in Ophthalmic Therapy

4.1 *Curcuma longa* L.

Curcuma longa contains curcuminoids, particularly curcumin. Curcumin is a polyphenolic compound investigated extensively for antioxidant, anti-inflammatory, antimicrobial, anti-angiogenic and neuroprotective activities. Research has examined its possible role in anterior- and posterior-segment ocular disorders [16,17].

A major pharmaceutical limitation of curcumin is its poor aqueous solubility and limited bioavailability. These characteristics make it a suitable candidate for investigation using advanced ophthalmic delivery systems such as nanoparticles, transferosomes, proniosomal systems and cyclodextrin-based formulations [14,17].

4.2 *Camellia sinensis*

Green tea contains catechins, including epigallocatechin gallate (EGCG), epicatechin and related polyphenols. A 2024 review summarized research involving green tea in ocular-surface diseases, cataract, glaucoma, uveitis and retinal disorders. Reported mechanisms include antioxidant, anti-inflammatory, antimicrobial, anti-angiogenic and aldose-reductase-related effects [18].

The available evidence remains predominantly experimental or preclinical for many indications, and further controlled clinical research is necessary.

4.3 *Plantago ovata*

Plantago ovata contains mucilage rich in polysaccharides. Unlike a plant extract used primarily as a pharmacologically active ingredient, *P. ovata* mucilage has also been investigated as a natural lubricant or polymeric material in ocular formulations.

A randomized, double-blind clinical trial involving 60 patients with dry-eye symptoms investigated *P. ovata* mucilage eye drops. The study reported improvement in OSDI scores and no serious adverse events during the study period, although not every tear-film parameter showed a significant between-group difference [21].

4.4 *Emblica officinalis* / *Phyllanthus emblica*

Phyllanthus emblica contains polyphenolic and tannin-related constituents and is widely recognized for antioxidant potential. Such activity provides a rationale for investigating it in conditions involving oxidative stress. However, a demonstrated antioxidant effect does not by itself establish clinical efficacy of an ophthalmic preparation.

4.5 *Ocimum* species

Ocimum species contain phenolic compounds, flavonoids and volatile constituents such as eugenol in some species. Their antioxidant and antimicrobial properties have resulted in research interest in ocular formulations.

4.6 Polyherbal formulations

Polyherbal preparations combine extracts or constituents from multiple plants. An example reported in the scientific literature is Ophthacare, a polyherbal eye-drop preparation investigated experimentally and clinically [22,23].

The 2001 clinical study was an open prospective multicentre trial and reported improvement in several studied ophthalmic conditions. Because of the study design and age of the evidence, the results should be interpreted as preliminary clinical evidence rather than definitive proof of efficacy [22].

5. Important Phytoconstituents

5.1 Flavonoids

Flavonoids are widely distributed plant secondary metabolites. Quercetin is an extensively investigated flavonoid with antioxidant, anti-inflammatory and other biological activities. Research has examined its potential relevance to ocular-surface disorders, corneal inflammation and neovascularization [20].

Importantly, biological activity of quercetin does not mean that a quercetin-containing eye drop is an approved treatment for these conditions.

5.2 Curcuminoids

Curcumin is the most extensively studied curcuminoid. Its pharmacological activities include antioxidant and anti-inflammatory effects, while experimental studies have investigated anti-angiogenic and neuroprotective mechanisms [16,17].

5.3 Catechins

Green-tea catechins have antioxidant and anti-inflammatory properties and have been investigated in several ocular disease models [18].

5.4 Resveratrol

Resveratrol is a polyphenolic stilbene found in grapes and several other plant sources. Experimental literature has investigated its effects on oxidative stress, inflammation, mitochondrial function, apoptosis and angiogenesis in ocular disease models [19].

A 2022 review examined its potential relevance to glaucoma, cataract, diabetic retinopathy and macular degeneration, while also recognizing that the clinical evidence remains incomplete [19].

5.5 Tannins and other polyphenols

Tannins and polyphenolic compounds may contribute antioxidant or antimicrobial properties. However, their concentrations can vary considerably between plant materials and extraction processes. Therefore, their presence should be accompanied by appropriate analytical characterization.

6. Therapeutic Potential of Herbal Eye Drops

6.1 Dry-eye disease

Dry-eye disease involves abnormalities in tear-film homeostasis and ocular-surface inflammation. Plant-derived polymers and phytoconstituents may provide potential supportive approaches through lubrication, antioxidant activity or modulation of inflammatory processes.

The clinical study of *P. ovata* mucilage provides one example of a plant-derived ocular formulation evaluated using a randomized controlled design [21]. Aloe-containing ocular formulations have also been investigated for ocular-surface disease.

Nevertheless, individual herbal products should not be generalized from one plant or formulation to another.

6.2 Antioxidant activity

Oxidative stress contributes to the pathogenesis of several ocular conditions. Polyphenolic compounds such as curcumin, quercetin and resveratrol can influence oxidative pathways and have therefore attracted ophthalmic research interest [16–20].

6.3 Anti-inflammatory activity

Inflammation participates in dry eye, corneal disease, uveitis and several retinal disorders. Curcumin and other polyphenols have been investigated for their effects on inflammatory signaling pathways [16,17].

6.4 Antimicrobial activity

Some plant extracts demonstrate antimicrobial activity against bacteria or fungi in laboratory models. For example, experimental research on a polyherbal Ophthacare preparation reported antibacterial and antifungal activity against selected microorganisms [23].

However, **in-vitro antimicrobial activity should not be interpreted as proof that an herbal eye drop can treat ocular infection in humans**. Clinical efficacy, appropriate dosing, ocular toxicity and sterility of the final product must be established separately.

6.5 Corneal wound healing

Oxidative stress and inflammation influence corneal injury and repair. Certain phytoconstituents have been investigated for their potential effects on cellular protection and inflammatory pathways. Curcumin and quercetin are examples of compounds receiving experimental attention [16,20].

6.6 Glaucoma

Curcumin, quercetin and resveratrol have been investigated for antioxidant and neuroprotective effects relevant to glaucoma. However, these experimental findings should not be interpreted as evidence that herbal eye drops can replace established intraocular-pressure-lowering medicines [16,19,20].

6.7 Cataract

Oxidative damage is one of the mechanisms involved in cataract development. Natural polyphenols such as resveratrol and curcumin have therefore been investigated experimentally for protective effects [16,19].

6.8 Retinal diseases

Natural compounds have been investigated in diabetic retinopathy, age-related macular degeneration and other retinal disorders. However, topical eye drops face substantial barriers to reaching posterior-segment tissues, so the route and delivery system are critical considerations [9,12,14].

7. Formulation Strategies for Herbal Eye Drops

7.1 Authentication of plant material

Correct identification of the plant is the first requirement for reproducible herbal formulation. Authentication may involve:

- Botanical identification
- Macroscopic examination
- Microscopic examination
- Voucher specimen documentation
- Chemical fingerprinting
- Molecular authentication when necessary [4–6,29,30]

Misidentification or adulteration can result in ineffective or potentially harmful products.

7.2 Extraction

Common extraction approaches include:

- Maceration
- Percolation
- Infusion
- Decoction
- Soxhlet extraction
- Hydroalcoholic extraction
- Other validated modern extraction methods

The extraction solvent, temperature, duration and plant-to-solvent ratio influence the chemical profile of the resulting extract.

7.3 Standardization

Standardization aims to achieve consistent quality between batches. It may involve:

- Identification of marker compounds

- Assay of selected constituents
- Chromatographic fingerprinting
- Physicochemical parameters
- Contaminant testing
- Microbial quality testing [4–6,29,30]

WHO guidance emphasizes that the quality of herbal medicinal products depends strongly on the quality and control of their starting materials and manufacturing processes [3–6].

7.4 Selection of vehicle

Purified water is frequently used for aqueous ophthalmic preparations, but the choice depends on the physicochemical properties of the active constituents. Poorly water-soluble phytoconstituents may require solubilization, complexation, emulsification or incorporation into a suitable carrier.

7.5 pH

The pH of the formulation should be selected by considering ocular tolerability, chemical stability, solubility and compatibility with the active constituents and excipients.

7.6 Tonicity

Ophthalmic formulations should have suitable osmotic properties to minimize discomfort. Tonicity can be adjusted using suitable pharmaceutical excipients when required.

7.7 Viscosity

Viscosity enhancers can prolong residence time on the ocular surface. However, excessive viscosity can cause blurred vision and discomfort. Therefore, an optimum balance is required [8,10].

7.8 Preservatives

Preservatives may be used in multidose aqueous formulations to control microbial growth. However, preservative selection requires careful consideration because some preservatives can adversely affect the ocular surface during repeated exposure [24,25].

7.9 Sterilization

Sterility is a critical requirement for applicable ophthalmic preparations. The selected sterilization method must achieve the required microbiological quality without unacceptable degradation of the herbal active constituents.

8. Types of Herbal Ophthalmic Formulations

8.1 Conventional aqueous eye drops

These are the simplest ophthalmic dosage forms and may be suitable for appropriately standardized water-soluble extracts.

Their principal limitation is short ocular residence time.

8.2 Suspensions

Suspensions may be useful for poorly soluble constituents. Important quality attributes include:

- Particle size
- Sedimentation
- Redispersibility
- Uniformity of dose
- Physical stability

8.3 Emulsions

Emulsions may improve the delivery of lipophilic phytoconstituents. Droplet size, interfacial properties, physical stability and ocular tolerability are important considerations.

8.4 Ophthalmic gels

Gels can increase residence time compared with conventional aqueous drops. However, excessive viscosity can negatively affect visual comfort.

8.5 In-situ gels

In-situ gelling systems are administered in a liquid state and undergo sol-to-gel transformation after exposure to ocular conditions. The transition may be triggered by temperature, pH or ions [26,27].

A 2024 systematic review identified substantial research activity in ocular in-situ gels, while newer 2026 literature continues to investigate thermosensitive systems and polymers [26,27].

8.6 Liposomes

Liposomes are vesicular carriers capable of incorporating compounds with different physicochemical characteristics. They can potentially protect active constituents and modify their release and interaction with ocular tissues [28].

8.7 Nanoparticles and nanoemulsions

Nanoparticles and nanoemulsions are being investigated to address poor solubility, instability and limited ocular retention of plant-derived compounds [12–14].

9. Excipients Used in Herbal Eye Drops

Excipient category	Main function
Purified water	Vehicle
Buffer	pH control
Sodium chloride or suitable tonicity agent	Osmotic adjustment
HPMC/cellulose derivatives	Viscosity enhancement
Carbomer	Viscosity and mucoadhesion
Poloxamers	Thermosensitive systems/solubilization
Cyclodextrins	Solubility enhancement
EDTA	Chelation and formulation support
Preservatives	Microbial control
Antioxidants	Protection against oxidative degradation

Table No 1. Excipients Used In Herbal Eye Drop

Excipients should not be selected only because they are commonly used. Each excipient should be assessed for concentration, compatibility, ocular tolerability, stability and suitability for the intended dosage form.

10. Evaluation Parameters of Herbal Eye Drops

10.1 Appearance

The formulation should be examined for colour, clarity, homogeneity and visible particulate matter.

10.2 pH

A calibrated pH meter should be used. The pH should remain within the selected formulation specification during stability studies.

10.3 Viscosity

Viscosity should be measured using a suitable viscometer. The result provides information about administration characteristics and expected ocular residence.

10.4 Osmolality

Osmolality should be determined using a validated method and assessed in relation to ocular tolerability.

10.5 Marker-compound assay

For a standardized herbal formulation, one or more suitable marker compounds may be quantified using validated analytical techniques such as HPLC or HPTLC [6,29,30].

10.6 Particle size

Particle-size determination is important for suspensions, nanoemulsions, nanoparticles and other dispersed systems.

10.7 Sterility

Ophthalmic products that are required to be sterile must comply with applicable sterility requirements. In India, Schedule FF of the Drugs Rules contains specific standards for ophthalmic preparations, including sterility provisions for ophthalmic solutions and suspensions subject to the stated pharmacopoeial exceptions [1].

10.8 Microbial quality

Raw materials and finished products should be evaluated according to the applicable pharmacopoeial and regulatory requirements.

10.9 Antimicrobial testing

Antimicrobial assays can be used during research to investigate the biological activity of extracts. However, these tests are not substitutes for sterility testing of an ophthalmic dosage form.

10.10 Antioxidant assays

DPPH, ABTS and other laboratory methods may provide preliminary information about antioxidant capacity. Such assays should not be presented as evidence of clinical efficacy.

10.11 Ocular irritation and cytotoxicity

Research formulations should undergo appropriate ocular-safety assessment using scientifically justified and ethically acceptable methods.

10.12 Stability testing

Important stability parameters include:

- Appearance
- pH
- Viscosity
- Marker-compound content
- Microbial quality

- Particle size
- Phase separation
- Container compatibility

11. Safety and Toxicological Considerations

11.1 "Natural" does not mean automatically safe

The assumption that all herbal substances are inherently safe is scientifically inappropriate. The Ministry of AYUSH itself recognizes the importance of pharmacovigilance for traditional medicines and notes that adverse effects may become apparent only after wider or prolonged use [24-related regulatory context].

11.2 Ocular irritation

A plant extract may contain constituents capable of irritating the conjunctiva or cornea. Therefore, safety must be established for the **final formulation**, not simply inferred from the historical use of the plant.

11.3 Corneal toxicity

Concentrated extracts, unsuitable solvents, penetration enhancers or preservatives may damage ocular tissues. Safety assessment should therefore consider both active constituents and excipients.

11.4 Allergic reactions

Plant proteins, volatile constituents and other compounds can potentially produce hypersensitivity reactions.

11.5 Microbial contamination

Raw herbal materials may contain microorganisms or environmental contaminants. WHO quality-control guidance emphasizes appropriate testing for microbial contamination and other contaminants [4,5].

11.6 Preservative toxicity

Benzalkonium chloride is one of the most extensively studied ophthalmic preservatives. Experimental and clinical literature has raised concerns regarding ocular-surface toxicity, particularly with repeated exposure [24,25].

Therefore, preservative-free packaging or alternative preservation strategies may be considered when scientifically and commercially appropriate.

11.7 Batch-to-batch variation

Variation can occur because of:

- Species differences
- Geographic origin
- Soil
- Climate
- Harvesting time
- Plant part
- Drying conditions
- Extraction method
- Storage conditions

This is one of the main reasons why herbal ophthalmic products require strong standardization programs [4–6,29,30].

12. Recent Advances in Herbal Ophthalmic Drug Delivery

12.1 Nanotechnology

Nanotechnology is being investigated to improve the delivery of phytoconstituents with poor solubility, limited stability or inadequate ocular penetration.

A 2025 review specifically identified liposomes, polymeric nanoparticles, lipid nanoparticles, nanoemulsions, in-situ gels, nanofibers and other systems as emerging approaches for herbal ocular delivery [12].

12.2 Nanoemulsions

Nanoemulsions can improve the dispersion of poorly water-soluble compounds and may facilitate interaction with the ocular surface. Their development requires optimization of droplet size, surfactant system, stability and ocular tolerability.

12.3 Liposomes

Liposomes can encapsulate hydrophilic or lipophilic molecules and may modify drug release and tissue interaction. Their use with natural compounds is being investigated as part of advanced ocular delivery research [12,14,28].

12.4 Polymeric nanoparticles

Polymeric nanoparticles may protect phytoconstituents from degradation and allow controlled release. Their surface characteristics can also be modified to influence ocular residence.

12.5 In-situ gels

In-situ gels are particularly attractive because the formulation can be administered as a drop and subsequently form a gel on the ocular surface. The objective is to extend residence time and potentially reduce the frequency of administration [26,27].

12.6 Combination systems

Combining nanoparticles with in-situ gels or other delivery systems may provide multiple advantages, such as improved retention, protection of the active compound and controlled release [14,26].

12.7 Advanced analytical and computational approaches Modern quality-control research is increasingly incorporating chromatographic fingerprints, multivariate analysis and machine-learning approaches to address the complexity of herbal products [29,30].

13. Mechanisms of Action of Herbal Phytoconstituents

13.1 Antioxidant action

Reactive oxygen species can contribute to cellular injury and oxidative damage. Natural polyphenols may act through direct antioxidant mechanisms and/or modulation of cellular antioxidant pathways.

Curcumin, quercetin and resveratrol have been investigated extensively in this context [16,19,20].

13.2 Anti-inflammatory action

Inflammatory signaling contributes to several ocular conditions. Curcumin and other polyphenols have been investigated for their ability to modulate inflammatory mediators and signaling pathways [16,17].

13.3 Anti-angiogenic activity

Abnormal angiogenesis is involved in several ocular diseases. Certain natural compounds have demonstrated anti-angiogenic effects in experimental models [16,19].

13.4 Neuroprotective effects

Oxidative stress, inflammation and mitochondrial dysfunction may contribute to neuronal injury. Resveratrol and curcumin have been investigated for potential neuroprotective effects in ocular disease models [17,19].

13.5 Antimicrobial effects

Plant-derived constituents can act against microorganisms through different mechanisms, including interference with membranes or microbial enzymes. Nevertheless, antimicrobial activity must be evaluated in the context of the final ophthalmic formulation.

14. Quality Control and Standardization

Quality control is particularly important for herbal ophthalmic products because the product combines a complex botanical material with the stringent requirements of ophthalmic dosage forms.

14.1 Botanical authentication: The identity of the plant should be confirmed using validated pharmacognostic and/or analytical procedures.

14.2 Physicochemical standardization

Depending on the material, parameters may include:

- Moisture content
- Ash values
- Extractive values
- Foreign matter
- Particle characteristics

14.3 Phytochemical standardization

Marker compounds can be quantified to establish batch consistency. However, one marker may not adequately represent a chemically complex extract. WHO guidance therefore supports scientifically justified approaches for selecting marker substances [6].

14.4 Chromatographic fingerprinting

HPLC, HPTLC and other chromatographic methods can provide qualitative and quantitative information. Fingerprinting can help detect changes in the overall chemical profile.

14.5 Contaminant control

Herbal raw materials may require assessment for:

- Microorganisms
- Aflatoxins
- Heavy metals
- Pesticide residues
- Adulterants
- Other relevant contaminants [4,5].

14.6 Good Manufacturing Practices

WHO has published specific GMP guidance for herbal medicines, emphasizing control of raw materials, manufacturing operations, documentation, quality control and personnel [3].

For Ayurvedic, Siddha and Unani medicines in India, Schedule T of the Drugs and Cosmetics Rules establishes GMP requirements, including authenticity and quality of raw materials, manufacturing controls and quality-control measures [2].

15. Regulatory Considerations

15.1 Indian regulatory framework

In India, the regulatory pathway depends on the legal classification of the product.

For conventional drugs and ophthalmic preparations regulated under the Drugs and Cosmetics Act and Rules, CDSCO provides the Drugs Rules and applicable standards. Schedule FF specifically addresses standards for ophthalmic preparations [1].

The Indian Pharmacopoeia is the official book of standards for drugs manufactured or marketed in India. The Indian Pharmacopoeia Commission states that IP standards are authoritative and are used by regulatory authorities for quality assurance [2].

15.2 Ophthalmic sterility requirement

Schedule FF of the Drugs Rules specifies that ophthalmic solutions and suspensions should be sterile when dispensed or sold in the unopened manufacturer's container, subject to the stated pharmacopoeial exception. It also specifies requirements concerning preservatives, foreign matter, containers, droppers and labelling [1].

Therefore, a research formulation described as an “herbal eye drop” should **not** be presented as legally marketable merely because it contains medicinal plants.

15.3 AYUSH medicines

If a product is intended to be an Ayurvedic, Siddha or Unani medicine, the applicable AYUSH regulatory provisions must be followed. Ministry of AYUSH documentation states that licensing and enforcement for ASU medicines are handled by the relevant State/UT Licensing Authorities and that manufacturers must comply with applicable safety, effectiveness, GMP and pharmacopoeial requirements [2].

Schedule T provides GMP requirements for Ayurvedic, Siddha and Unani medicines, including authentication and quality of raw materials and adequate quality-control measures [2].

15.4 Regulatory claims

Claims should correspond to the evidence and approved product category. A formulation should not be described as “FDA approved,” “CDSCO approved,” “AYUSH approved” or “clinically proven” unless the specific product and claim have actually received the relevant authorization.

15.5 Pharmacovigilance: The Ministry of AYUSH has established a pharmacovigilance program for Ayurveda, Siddha, Unani and Homoeopathy medicines to support detection, assessment and prevention of adverse effects and to monitor misleading advertisements [2].

16. Marketed and Investigational Herbal Ophthalmic Products

Scientific literature contains reports of polyherbal ophthalmic formulations. One example is Ophthacare, which was investigated in an open prospective multicentre clinical trial involving different ophthalmic conditions [22].

An experimental study of the same product reported anti-inflammatory, antioxidant, antibacterial and antifungal activities [23].

These publications demonstrate that polyherbal ophthalmic formulations have been investigated scientifically. However, the existence of a published study does not establish that every similar herbal eye drop is legally approved or clinically effective.

The *Plantago ovata* mucilage study provides another useful example because it employed a randomized, double-blind, placebo-controlled clinical design and evaluated symptoms and tear-film parameters [21].

For a review article, it is preferable to classify evidence into:

1. Traditional use.
2. In-vitro evidence.
3. Animal/preclinical evidence.
4. Human observational evidence.
5. Controlled clinical evidence.
6. Regulatory authorization.

This classification prevents overstatement of therapeutic claims.

17. Challenges and Limitations

17.1 Variability of botanical materials

Plant chemistry varies according to genetics, geography, climate and cultivation.

17.2 Standardization difficulties

A complex extract cannot always be adequately represented by a single chemical marker [29,30].

17.3 Poor solubility

Several phytoconstituents, particularly curcumin, have low aqueous solubility [16,17].

17.4 Short ocular residence

Conventional eye drops are rapidly removed from the ocular surface [7–10].

17.5 Sterility

The need for sterile ophthalmic manufacturing makes herbal formulations more technically demanding than many oral herbal products.

17.6 Stability

Plant constituents may undergo oxidation, hydrolysis, photodegradation or other chemical changes.

17.7 Limited clinical evidence

The 2023 systematic review of medicinal plants for ophthalmic disorders identified a substantial evidence gap and high heterogeneity among the available studies [11].

17.8 Regulatory complexity

A herbal ophthalmic preparation may involve overlapping considerations concerning botanical quality, pharmaceutical quality, ophthalmic sterility, clinical evidence and the applicable national regulatory pathway.

17.9 Scale-up

A formulation that performs well at laboratory scale may encounter problems during:

- Sterile filtration
- Filling
- Container closure
- Storage
- Scale-up mixing
- Batch reproducibility
- Stability testing

18. Future Perspectives

18.1 Standardized phytopharmaceuticals

Future development should focus on chemically characterized and reproducible herbal preparations rather than poorly defined crude extracts.

18.2 Nanotechnology-based delivery

Nanoparticles, nanoemulsions, liposomes and related systems may help address poor solubility, stability and ocular retention [12–14].

18.3 Long-acting formulations

In-situ gels and sustained-release systems may reduce the need for repeated administration [26,27].

18.4 Advanced quality control

Chromatographic fingerprints, chemometrics and machine-learning approaches may improve authentication and batch consistency [29,30].

18.5 Advanced ocular models

Three-dimensional corneal models, cell-based systems and ex-vivo ocular models may provide more informative platforms for studying ocular safety and drug delivery.

18.6 Clinical trials

Future clinical studies should use:

- Standardized formulations
- Defined phytochemical profiles
- Appropriate control groups
- Adequate sample sizes
- Validated clinical endpoints
- Appropriate safety monitoring
- Sufficient follow-up

18.7 Sustainable development: Medicinal-plant sourcing should also consider authentication, sustainable cultivation, environmental impact and traceability.

19. Conclusion

Herbal-based ophthalmic formulations represent an important research area at the intersection of pharmacognosy, phytochemistry, pharmacology, pharmaceutics and ocular drug-delivery science. Medicinal plants and natural compounds such as curcumin, quercetin, catechins and resveratrol possess biological activities that may be relevant to oxidative stress, inflammation, microbial activity and cellular protection [16–20].

Nevertheless, the therapeutic potential of a medicinal plant should not be confused with established clinical efficacy. Current evidence varies substantially among plants and formulations, and systematic evidence indicates considerable gaps in the clinical literature [11].

The successful development of herbal eye drops requires correct botanical authentication, standardized extraction, reproducible phytochemical characterization, appropriate excipient selection, physicochemical evaluation, sterility assurance, microbial control, stability testing and ocular-safety assessment [3–6,29,30].

Advanced systems such as nanoparticles, nanoemulsions, liposomes and in-situ gels may overcome some limitations of conventional formulations by improving solubility, stability, residence time and controlled delivery [12–14,26–28]. However, these technologies also introduce additional challenges related to toxicity, scale-up, characterization and regulatory acceptance.

For India, particular attention must be given to the distinction between conventional ophthalmic drugs and products regulated under the AYUSH framework. Applicable requirements of the Drugs and Cosmetics Act and Rules, Schedule FF, Indian Pharmacopoeia and relevant AYUSH provisions should be followed according to the classification of the product [1,2].

Overall, the future of herbal ophthalmic therapy depends on combining **traditional medicinal knowledge with rigorous pharmaceutical science, modern analytical techniques, validated safety assessment and high-quality clinical evidence**. Herbal eye drops should therefore be viewed as a promising research field requiring systematic validation rather than as automatically safe or clinically established alternatives to conventional ophthalmic medicines.

Table No.2. Common ocular disorders and major drug-delivery challenges

Ocular Conidition	**Major Pathological Factors**	**Relevant Herbal Research Area**
Dry-eye disease	Tear-film instability, inflammation, oxidative stress	Lubricating, antioxidant and anti-inflammatory systems
Conjunctivitis	Infection/inflammation/allergy	Antimicrobial and anti-inflammatory plants
Corneal injury	Inflammation, oxidative stress, tissue damage	Wound-healing and antioxidant compounds
Glaucoma	Elevated IOP, retinal ganglion-cell injury	Neuroprotective/antioxidant compounds

Cataract	Lens protein alteration, oxidative stress	Antioxidant phytoconstituents
Retinal disorders	Oxidative stress, inflammation, angiogenesis	Polyphenols and advanced delivery systems

Table No.2. Common ocular disorders and major drug-delivery challenges

Table No.3. Important medicinal plants and phytoconstituents

Sr.No	Plant	Constituents	Potential activity	Evidence Category
1.	*Curcuma longa*	Curcuminoids	Antioxidant, anti-inflammatory	Preclinical/review
2.	*Camellia sinensis*	Catechins, EGCG	Antioxidant, anti-inflammatory	Manly Preclinical
3.	*Plantago ovata*	Mucilage polysaccharides	Lubricating/tear-film support	Clinical evidence
4.	*Phyllanthus emblica*	Polyphenols, tannins	Antioxidant	Experimental
5.	*Ocimum* spp.	Phenolics, flavonoids, volatile constituents	Antioxidant/antimicrobial	Experimental
6.	Grapes/other sources	Resveratrol	Antioxidant/neuroprotective	Mainly preclinical

Table No.3. Important medicinal plants and phytoconstituents

Table No.4. Excipients And Their Functions

Sr.No	Excipients	Function
1.	Sodium Cloride	Tonicity Adjustment
2.	Buffer	pH control
3.	HPMC	Viscosity Enhansement
4.	Carbomer	Viscosity/Mucoadhesion
5.	Cyclodextrin	Solubility Enhansement
6.	Poloxamer	Thrmosensitive Delivery
7.	EDTA	Chelation
8.	Preservative	Microbial Control

Table No.4. Excipients And Their Function

Table No.5. Evalution Parameter

Sr.No	Parameter	Purpose
1.	Apperance	Physical Quality
2.	PH	Compatibility/Stability
3.	Viscosity	Recidence Characteristics
4.	Osmolality	Ocular Comfort
5.	Marker Assay	Standardization
6.	Particle Size	Dispence/Nano System
7.	Sterility	Pateint Safety
8.	Microbial Quality	Contmination control
9.	Irritation	Occular Tolaribility
10.	Stability	Shelf-life

Table No.5. Evalution Parameter

Table No.6. Advanced herbal ocular delivery System

Sr.No	System	Potential Advantages	Major Limitations
1.	In-situ gel	Increase residence time	Gelstin/viscosity optimization
2.	Liposome	Encapsulation of different compound	Physical Stability
3.	Nnoemulsion	Useful for poorly soluble comound	Surfactant/tolaribility consideration
4.	Polymeric Nanoparticles	Controlled Delivery	Mnufacturing complexity
5.	Lipid Nanoparticel	Protection and Controlled release	Scale up and characterization
6.	Nanoparticle loaded gel	Combined retention and controlled release	More complex formulation

Table No.6. Advanced herbal ocular delivery System

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