Formulation and Evaluation of Olopatadine Hydrochloride Opthalmic Solution

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DOI: https://doi.org/10.51584/IJRIAS.2026.11060285

Received: 03 July 2026; Accepted: 08 July 2026; Published: 18 July 2026

ABSTRACT

Olopatadine Hydrochloride is a selective histamine H1-receptor antagonist and mast cell stabilizer widely used in the treatment of allergic conjunctivitis. The present study aimed to formulate and evaluate a sterile ophthalmic solution of Olopatadine Hydrochloride with enhanced stability, safety, and patient compliance. The ophthalmic solution was prepared using suitable excipients, including buffering agents, tonicity adjusters, preservatives, and viscosity enhancers to achieve optimal physicochemical properties and ocular compatibility.

The formulated solution was evaluated for various quality control parameters such as appearance, pH, viscosity, drug content, sterility, isotonicity, clarity, and in-vitro drug release. Compatibility studies were conducted to ensure the stability of the drug with formulation components. The prepared formulation exhibited acceptable physicochemical characteristics with a pH suitable for ocular administration, adequate viscosity for prolonged ocular residence time, and uniform drug content. Sterility and isotonicity tests confirmed the safety of the formulation for ophthalmic use. In-vitro release studies demonstrated satisfactory drug release behavior, indicating effective availability of the drug at the site of action.

The results suggest that the formulated Olopatadine Hydrochloride ophthalmic solution meets the required pharmaceutical standards and possesses the potential to provide effective therapeutic management of allergic eye disorders. The study concludes that the developed formulation is stable, safe, and suitable for ocular delivery, offering improved patient comfort and compliance.

Keywords: Olopatadine Hydrochloride, Ophthalmic Solution, Allergic Conjunctivitis, Sterility, Ocular Drug Delivery, Formulation Development, In-vitro Evaluation.

INTRODUCTION

The eye is a highly sensitive organ that demands sterile, isotonic, and well-tolerated formulations for safe drug delivery. Ophthalmic solutions are sterile preparations meant for instillation into the conjunctival sac to treat various ocular diseases such as allergic conjunctivitis, inflammation, infection, and dryness.

Olopatadine Hydrochloride is an antihistaminic and mast cell stabilizer used for the treatment of allergic conjunctivitis. It selectively inhibits the H_1 receptor and prevents the release of inflammatory mediators such as histamine, stabilizing the conjunctival mast cells.

However, due to short precorneal residence time and tear turnover, conventional eye drops may have limited therapeutic efficacy. Hence, the formulation of an optimized ophthalmic solution of Olopatadine Hydrochloride with good stability, sterility, and prolonged therapeutic action is of great pharmaceutical interest.

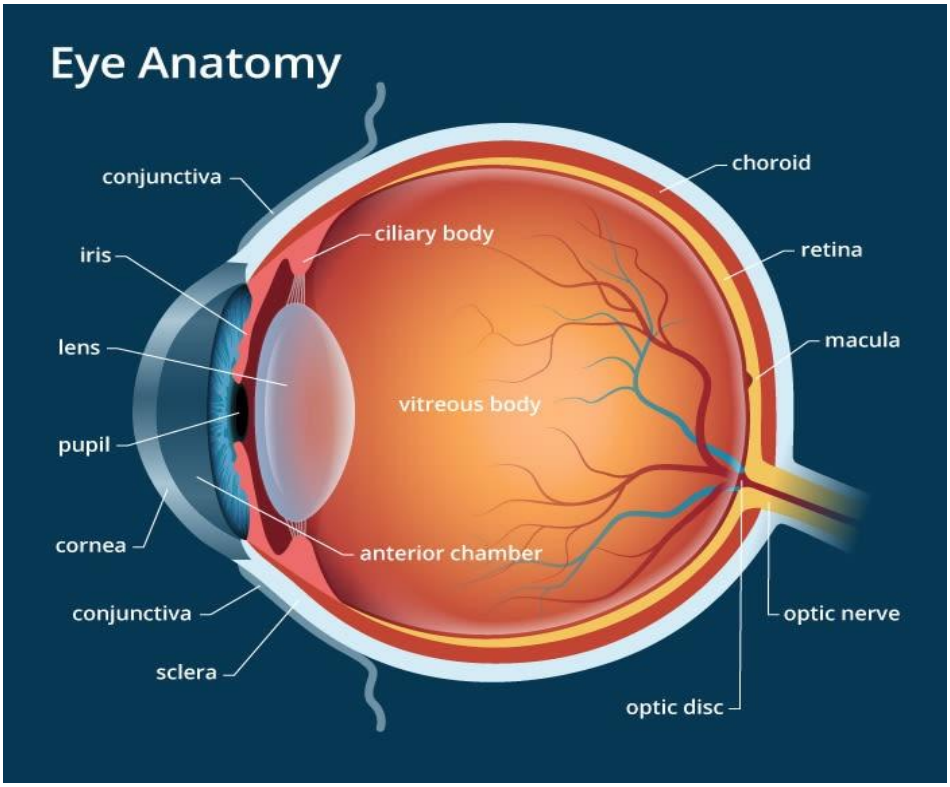
ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume XI Issue VI June 2026

Anatomy and Physiology of the Eye

1. Introduction

The human eye is a highly specialized sensory organ that allows vision by detecting light and converting it into electrical impulses that are interpreted by the brain. It functions like a **biological camera**, with structures that focus light onto the retina, adjust the amount of light entering, and transmit visual information through the optic nerve.

Understanding the anatomy and physiology of the eye is essential for developing safe and effective ophthalmic formulations, such as eye drops, since every component plays a role in drug absorption, distribution, and elimination.



2. Gross Anatomy of the Eye

The human eye is a roughly **spherical structure** (about 24 mm in diameter) situated in the **bony orbit** of the skull. It is protected by the **eyelids, eyelashes, and lacrimal apparatus**.

Main parts of the eye:

1. **Outer Fibrous Coat** – Cornea and Sclera
2. **Middle Vascular Coat (Uveal Tract)** – Iris, Ciliary Body, and Choroid
3. **Inner Nervous Coat** – Retina

3. External Protective Structures

a. Eyelids

- Protect the eyes from injury, dust, and excessive light.
- Spread the tear film evenly over the eye surface during blinking.

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b. Conjunctiva

- A thin, transparent mucous membrane covering the inner surface of the eyelids and the anterior sclera.
- Secretes mucus and tears, maintaining ocular surface moisture.
- Plays an important role in immune defense and is the common site for **allergic conjunctivitis.**

c. Lacrimal Apparatus

- Includes **lacrimal glands, ducts,** and **nasolacrimal drainage system**.
- Produces **tear fluid** containing water, electrolytes, lysozyme, and mucin.
- Tears lubricate the eye, provide oxygen to the cornea, and have antibacterial properties.

4. Layers of the Eyeball

A. Fibrous Layer

1. **Cornea**
   - Transparent, avascular, and dome-shaped front part.
   - Major refractive surface of the eye (about 70% of total focusing power).
   - Composed of five layers:
     - Epithelium
     - Bowman’s membrane
     - Stroma
     - Descemet’s membrane
     - Endothelium
   - The corneal epithelium acts as a **barrier to drug penetration** due to tight junctions.
2. **Sclera**
   - The white, opaque part of the eye that provides protection and structural support.
   - Made up of dense connective tissue and is continuous with the cornea anteriorly and dura mater posteriorly.

B. Vascular Layer (Uveal Tract)

1. **Iris**
   - The colored part of the eye that controls the size of the **pupil**, regulating light entry.
   - Contains two sets of muscles:
     - **Sphincter pupillae** (constricts pupil)
     - **Dilator pupillae** (dilates pupil)

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2. **Ciliary Body**

- Contains the **ciliary muscles** (responsible for accommodation) and **ciliary processes** that secrete aqueous humor.
- Plays an important role in maintaining **intraocular pressure (IOP)**.

3. **Choroid**

- Highly vascular layer that supplies nutrients and oxygen to the retina and outer eye structures.

C. Nervous Layer (Retina)

- Innermost layer containing **photoreceptor cells** (rods and cones).
- **Rods** – sensitive to dim light (night vision).
- **Cones** – responsible for color and daylight vision.
- Converts light stimuli into **nerve impulses**, which are transmitted via the **optic nerve** to the visual cortex in the brain.

5. Optical Structures

a. Lens

- Transparent, biconvex structure located behind the iris.
- Focuses light rays onto the retina by changing its curvature (accommodation).
- Composed mainly of proteins called **crystallins.**
- Becomes opaque in cataract.

b. Aqueous Humor

- A clear, watery fluid produced by the ciliary body.
- Circulates through the **anterior and posterior chambers**, maintaining intraocular pressure and providing nutrients to the cornea and lens.
- Drains through the **canal of Schlemm.**

c. Vitreous Humor

- A transparent, gel-like material filling the posterior segment of the eyeball.
- Helps maintain the shape of the eye and supports the retina.

6. Chambers of the Eye

Chamber	**Location**	**Contents**	**Function**
Anterior Chamber	Between cornea and iris	Aqueous humor	Maintains IOP
Posterior Chamber	Between iris and lens	Aqueous humor	Nourishes lens and cornea
Vitreous Chamber	Behind lens to retina	Vitreous humor	Maintains shape and optical clarity

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7. Physiology of Vision

1. **Refraction of Light:**
   - Light rays pass through cornea → aqueous humor → lens → vitreous humor → retina.
   - Cornea and lens together focus the image on the retina.
2. **Accommodation:**
   - The ability of the lens to change shape (curvature) to focus on near or distant objects.
3. **Pupillary Reflex:**
   - Iris muscles adjust pupil size to control light intensity reaching the retina.
4. **Phototransduction:**
   - Conversion of light energy into electrical impulses by photoreceptor cells (rods and cones).
5. **Transmission of Impulses:**
   - Signals travel through **optic nerve → optic chiasma → optic tract → visual cortex** for image interpretation.

8. Blood Supply and Innervation

- **Arterial Supply:** Ophthalmic artery (branch of internal carotid artery)
- **Venous Drainage:** Ophthalmic veins → cavernous sinus
- **Nerve Supply:**
  - Optic nerve (II) – vision
  - Oculomotor (III), Trochlear (IV), Abducens (VI) – eye movements
  - Trigeminal (V1) – corneal sensation
  - Sympathetic and parasympathetic fibers – pupil control, tear secretion

9. Ocular Barriers to Drug Absorption

For formulation scientists, understanding ocular barriers is crucial. The major barriers are:

- **Tear film** – rapid drainage of instilled drug.
- **Corneal epithelium** – lipophilic barrier to hydrophilic drugs.
- **Conjunctival absorption and nasolacrimal drainage** – systemic absorption reduces ocular bioavailability.
- **Blood-aqueous and blood-retinal barriers** – limit penetration of drugs into intraocular tissues.

Because of these barriers, **only 1–5%** of an eye drop dose typically reaches intraocular tissues.

Overview of Eye Allergies (Allergic Conjunctivitis)

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1. Introduction

Eye allergies, also known as **allergic conjunctivitis**, are **inflammatory disorders of the conjunctiva** induced by exposure to allergens such as pollen, dust mites, pet dander, mold, and other environmental agents. These allergens trigger an **immune-mediated hypersensitivity reaction,** leading to symptoms like itching, redness, tearing, and swelling of the eyelids.

Unlike infectious conjunctivitis, eye allergies are **non-contagious** and are primarily due to the **overreaction of the immune system** to harmless environmental substances. The condition can be **seasonal, perennial, or chronic**, depending on the allergen exposure pattern.

2. Definition

Allergic conjunctivitis is defined as an **immunologically mediated inflammation** of the conjunctival mucous membrane characterized by itching, redness, watery discharge, and chemosis (swelling of the conjunctiva) caused by exposure to allergens.

3. Epidemiology

- Eye allergies are **one of the most common ocular surface disorders**, affecting up to **20–30% of the global population.**
- It is frequently associated with other atopic conditions such as **allergic rhinitis, asthma, and eczema.**
- **Children and young adults** are more commonly affected, with symptoms often worsening during **spring and summer.**
- Increasing air pollution, climate change, and urbanization have contributed to a rise in allergic eye diseases.

4. Anatomy Involved in Eye Allergy

- The **conjunctiva,** a thin mucous membrane covering the sclera and inner eyelids, contains **mast cells, lymphocytes, and blood vessels**, making it highly reactive to allergens.
- The **lacrimal glands** and **Meibomian glands** contribute to the tear film, which plays a role in distributing allergens and inflammatory mediators.
- **Mast cells** are key effector cells that release histamine and other mediators during allergic reactions.

5. Etiology (Causes of Eye Allergies)

Eye allergies result from exposure to allergens that interact with **IgE-sensitized mast cells** in the conjunctiva. Common causes include:

Type	**Examples**
Outdoor allergens	Pollen (grass, trees, weeds)
Indoor allergens	House dust mites, pet dander, molds
Chemical irritants	Perfumes, smoke, cosmetics
Contact lens solutions	Preservatives, cleaning agents
Drugs	Topical ophthalmic medications (e.g., preservatives like benzalkonium chloride)

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6. Pathophysiology (Mechanism of Eye Allergy)

Eye allergies primarily involve a **Type I hypersensitivity reaction** (immediate, IgE-mediated).

Stepwise Mechanism:

1. **Sensitization Phase**
   - On first exposure, allergens are recognized by antigen-presenting cells (APCs) in the conjunctiva.
   - APCs activate **T-helper 2 (Th2)** lymphocytes, which stimulate **B cells** to produce **IgE antibodies** specific to the allergen.
   - IgE binds to **mast cells**, sensitizing them.
2. **Re-exposure Phase**
   - Upon re-exposure, the allergen binds to IgE on mast cells → **mast cell degranulation.**
   - This releases **histamine, tryptase, prostaglandins**, and **leukotrienes.**
3. **Clinical Effects**
   - Histamine causes **vasodilation, itching, tearing,** and **redness**.
   - Late-phase reaction involves **eosinophils** and **neutrophils**, leading to chronic inflammation and tissue damage.

7. Classification of Eye Allergies

Eye allergies are broadly divided into **acute** and **chronic** forms depending on duration and severity.

Type	**Description**	**Common Symptoms**
Seasonal Allergic Conjunctivitis (SAC)	Occurs during specific seasons (spring/summer); triggered by pollen.	Itching, redness, watery discharge
Perennial Allergic Conjunctivitis (PAC)	Occurs year-round due to indoor allergens like dust mites, animal dander.	Mild but persistent itching and tearing
Vernal Keratoconjunctivitis (VKC)	Severe, chronic condition in children and young males, often in hot climates.	Thick mucus, photophobia, cobblestone papillae
Atopic Keratoconjunctivitis (AKC)	Chronic bilateral inflammation in adults with atopic dermatitis.	Redness, thick discharge, corneal involvement
Giant Papillary Conjunctivitis (GPC)	Caused by contact lenses or prosthetic eye irritation.	Large papillae under eyelid, discomfort, lens intolerance
Contact Allergy	Reaction to cosmetics, drugs, or preservatives.	Swelling, itching, eyelid dermatitis

8. Signs and Symptoms

Typical symptoms include:

- **Intense itching** (most common hallmark symptom**)**

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- **Redness and irritation**
- **Watery or mucous discharge**
- **Swollen eyelids (chemosis)**
- **Photophobia (light sensitivity)**
- **Foreign body sensation**
- **Burning and tearing**

Symptoms are often **bilateral,** although one eye may be more affected initially.

9. Diagnosis

Diagnosis is usually clinical, based on history and symptoms, but may include:

Test	**Purpose**
Slit-lamp examination	To examine conjunctiva and cornea
Tear cytology	Detects eosinophils and mast cells
Skin prick or patch test	Identifies specific allergens
Serum IgE levels	Indicates systemic allergic response

10. Management and Treatment

The treatment aims to **relieve symptoms, prevent recurrence,** and **minimize allergen exposure.**

A. Non-pharmacological Measures

- Avoid allergen exposure (use air filters, sunglasses).
- Apply **cold compresses** to reduce swelling and itching.
- Maintain **ocular hygiene** and avoid rubbing eyes.

B. Pharmacological Therapy

Drug Class	**Example**	**Mechanism of Action**
Antihistamines	Olopatadine HCl, Levocabastine, Ketotifen	Block histamine (H_1) receptors
Mast Cell Stabilizers	Sodium Cromoglycate, Nedocromil	Prevent mast cell degranulation
Dual-acting Agents	Olopatadine, Azelastine	Antihistamine + Mast cell stabilizer
Corticosteroids	Loteprednol, Fluorometholone	Reduce severe inflammation
NSAIDs	Ketorolac Tromethamine	Reduce pain and redness
Artificial Tears	Hydroxypropyl methylcellulose	Dilute allergens and provide soothing effect

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RESULT AND DISCUSSION

Preformulation studies

Characterization of Olopatadine Hydrochloride

Physical Appearance

Olopatadine Hydrochloride was observed as a **white to off-white crystalline powder**, odorless and free-flowing in nature. The drug was found to be a white to off-white crystalline powder with no visible impurities.

Solubility Profile

Solvent	Solubility	Parts Required for 1 Part Solute	Symbol
Water	Freely soluble	1–10 parts	++++
0.1 N HCl	Freely soluble	1–10 parts	++++
Methanol	Soluble	10–30 parts	+++
Ethanol	Slightly soluble	100–1000 parts	++
Chloroform	Practically insoluble	>10,000 parts	−

Olopatadine Hydrochloride was found to be freely soluble in water and 0.1 N HCl and suitable for ophthalmic formulation development.

PH of Drug Solution

A 1% w/v solution of Olopatadine Hydrochloride was prepared in distilled water and analyzed using a calibrated pH meter.

Parameter	Result
pH of Drug Solution	4.8 ± 0.1

The pH of the Olopatadine Hydrochloride solution was found to be **4.8 ± 0.1**.

Melting Point Determination

 Olopatadine Hydrochloride was finely powdered and dried, if necessary.

 A clean, dry capillary tube sealed at one end was taken.

 The powdered drug was filled into the capillary tube to a height of about **2–3 mm** by gently tapping the tube on a hard surface.

 The capillary tube containing the sample was attached to a thermometer or placed in the capillary holder of the melting point apparatus.

 The capillary tube was inserted into the melting point apparatus.

 The temperature was increased gradually at a controlled rate (approximately **1–2°C per minute**) near the expected melting range.

 The temperature at which the drug started to melt and the temperature at which it completely melted were recorded.

 The melting point was determined and compared with the reported literature value.The melting point was determined using a digital melting point apparatus.

Parameter	**Result**
Melting Point	248–252°C

The melting point of Olopatadine Hydrochloride was found to be **248–252°C**, which complies with reported literature values.

Compatibility with Excipients (FTIR Study)

The FTIR spectra of pure Olopatadine Hydrochloride and its physical mixture with Benzalkonium Chloride, Sodium Chloride, HPMC, and Sodium Phosphate Buffer were recorded using the KBr pellet method in the range of **4000–400 cm^{-1}**. The spectra were compared to identify any possible drug–excipient interactions.

The characteristic peaks of Olopatadine Hydrochloride were observed in both the pure drug and drug–excipient physical mixtures.

Wavenumber (cm-1)	**Olopatadine HCl**	**Physical Mixture**
4000	98	98
3600	95	95
3405	72	73
3000	92	92
2500	95	95
1715	60	61
1602	65	66
1500	82	82
1258	55	56
1108	70	71
1000	78	78
800	88	88
400	95	95

Table 7.1 FTIR Spectrum Of Olopatadine Hcl+ Physical Mixture Of Excipients

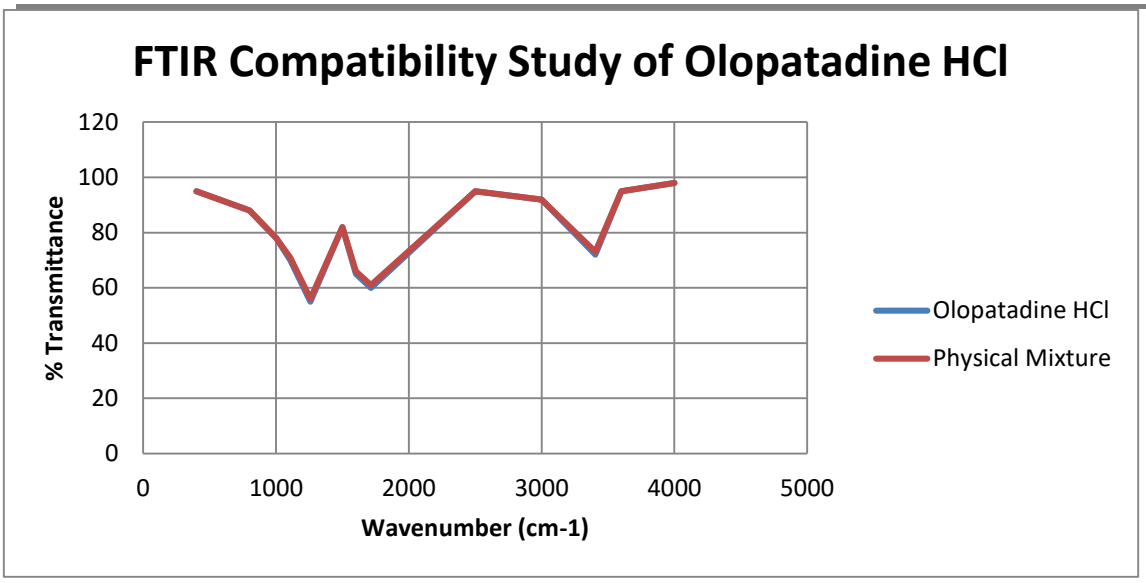

Figure 7.1 FTIR Spectrum of Olopatadine HCl+ physical mixture of excipients

FTIR Spectral Analysis

Functional Group	Pure Drug (cm^{-1})	Physical Mixture (cm^{-1})	Observation
O–H Stretching	3405	3402	No significant shift
C=O Stretching	1715	1713	No significant shift
Aromatic C=C Stretching	1602	1600	No significant shift
C–N Stretching	1258	1256	No significant shift
C–O Stretching	1108	1106	No significant shift

Table 7.2 FTIR Spectral Analysis

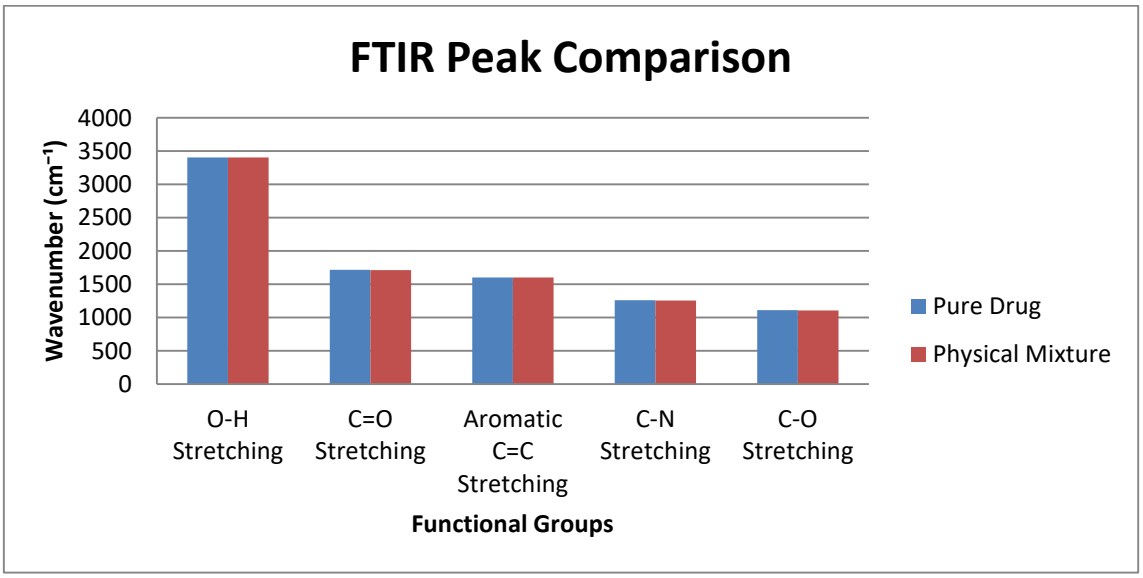

Figure 7.2 FTIR Peak Comparison

No significant shift or disappearance of characteristic peaks was observed, indicating compatibility between Olopatadine Hydrochloride and the selected excipients.

Compatibility with Excipients (DSC Study)

Sample	Endothermic Peak (°C)	Observation
Pure Olopatadine HCl	250.4	Sharp melting peak observed
Olopatadine HCl + Benzalkonium Chloride + Sodium Chloride + HPMC + Sodium Phosphate Buffer	249.8	Peak retained with negligible shift

Table 7.3 Compatibility with Excipients (DSC Study)

The characteristic melting endothermic peak of **Olopatadine Hydrochloride** was observed at **250.4°C.** In the physical mixture containing **Benzalkonium Chloride, Sodium Chloride, HPMC, and Sodium Phosphate Buffer,** the peak appeared at **249.8°C** with only a minor shift. This indicates the absence of significant drug–excipient interaction and confirms compatibility of the drug with the selected excipients.

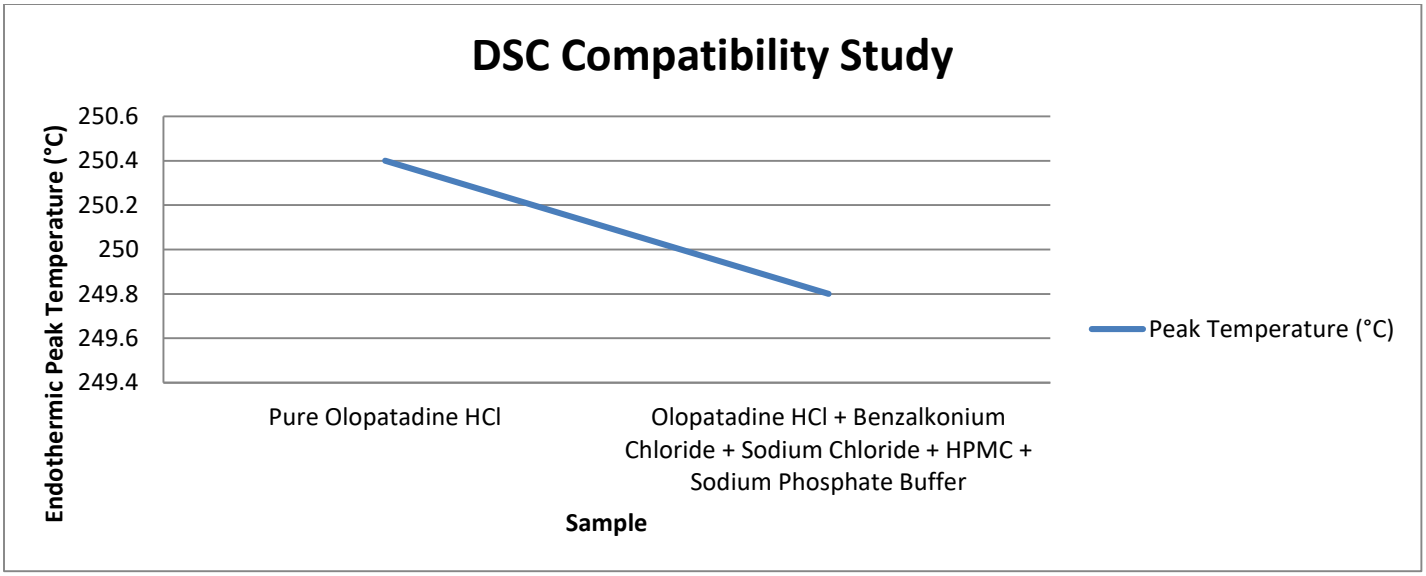

Figure 7.3 DSC Compatibility Study

Formulation Development

Formulation of Olapatadine hcl Ophthalmic solution by aseptic technique.

Ingredients (% w/v)	F1	F2	F3	F4	F5	F6
Olopatadine HCl	0.10	0.10	0.10	0.10	0.10	0.10
Benzalkonium Chloride	0.01	0.01	0.01	0.01	0.01	0.01
Sodium Chloride	0.60	0.70	0.80	0.90	1.00	1.10
HPMC	0.20	0.30	0.40	0.50	0.60	0.70
Sodium Phosphate Buffer	0.20	0.20	0.20	0.20	0.20	0.20
Purified Water	q.s. to 100 mL	q.s. to 100 mL	q.s. to 100 mL	q.s. to 100 mL	q.s. to 100 mL	q.s. to 100 mL

Table 7.4 Formulation Batches of Olopatadine Hydrochloride Ophthalmic Solution

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Optimization of formulation composition

Batch	pH	Viscosity (cP)	Drug Content (%)	Observation
F1	6.5	12	98.2	Low viscosity
F2	6.6	16	98.8	Acceptable
F3	6.7	20	99.4	Good
F4	6.8	24	99.8	Optimized
F5	6.8	30	99.5	High viscosity
F6	6.9	36	99.1	Very high viscosity

Table 7.5 Optimization of formulation composition

Formulation F4 was selected as the optimized batch because it exhibited:

- Acceptable pH (6.8)
- Suitable viscosity for ocular retention
- Maximum drug content (99.8%)
- Good clarity and stability
- Desired drug release profile

Sterilization and Packaging of Optimized Batch (F4)

The optimized formulation batch (**F4**) of Olopatadine Hydrochloride Ophthalmic Solution was subjected to sterilization and packaging under aseptic conditions.

1. The optimized batch (F4) was prepared and transferred to a sterile filtration assembly.
2. The formulation was sterilized by passing through a 0.22 μm membrane filter under laminar airflow conditions.
3. The sterile filtrate was collected in a sterile receiving vessel.
4. The filtered solution was visually inspected for clarity and absence of particulate matter.
5. The sterile ophthalmic solution was aseptically filled into pre-sterilized ophthalmic containers.
6. The containers were immediately sealed with sterile dropper caps to maintain sterility.
7. Filled containers were inspected for leakage, fill volume uniformity, and container integrity.
8. The containers were labeled with formulation code (F4), batch number, manufacturing date, expiry date, and storage conditions.
9. The packaged containers were stored for further evaluation and stability studies.

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S. No.	Parameter	Observation	Result
1	Formulation Code	F4	Optimized Batch
2	Filtration through 0.22 µm Membrane Filter	Filtration completed successfully	Passed
3	Appearance after Filtration	Clear and transparent solution	Passed
4	Presence of Particulate Matter	No visible particles observed	Passed
5	Sterility of Filtered Solution	No microbial growth detected	Sterile
6	Filling into Ophthalmic Containers	Uniform filling achieved	Passed
7	Container Integrity	No cracks or defects observed	Passed
8	Leakage Test	No leakage detected	Passed
9	Sealing Efficiency	Containers properly sealed	Passed
10	Labeling Compliance	All required information provided	Complied
11	Packaging Quality	Suitable for storage and handling	Accepted

Table 7.6 Sterilization and Packaging of Optimized Batch (F4)

The optimized batch **F4** was successfully sterilized using a **0.22 µm membrane filtration technique** and aseptically packaged into sterile ophthalmic containers. The formulation remained **clear, sterile, free from particulate matter, leak-proof, and properly labeled,** confirming its suitability for ophthalmic administration.

Evaluation of Formulated Olopatadine Hydrochloride Ophthalmic Solution (F1–F6)

A. Physical Evaluation

Batch	Appearance	Color	Clarity	Particulate Matter
F1	Clear Solution	Colorless	Clear	Absent
F2	Clear Solution	Colorless	Clear	Absent
F3	Clear Solution	Colorless	Clear	Absent
F4	Clear Solution	Colorless	Clear	Absent
F5	Clear Solution	Colorless	Clear	Absent
F6	Clear Solution	Colorless	Clear	Absent

B. Physicochemical Evaluation

Batch	pH	Viscosity (cP)	Refractive Index	Surface Tension (dynes/cm)	Osmolarity (mOsm/L)
F1	6.5 ± 0.02	12 ± 0.3	1.334	43.2 ± 0.5	275 ± 2

F2	6.6 ± 0.03	16 ± 0.4	1.335	42.8 ± 0.4	282 ± 3
F3	6.7 ± 0.02	20 ± 0.5	1.336	42.3 ± 0.3	288 ± 2
F4	6.8 ± 0.01	24 ± 0.4	1.336	41.8 ± 0.2	295 ± 2
F5	6.8 ± 0.03	30 ± 0.6	1.337	41.4 ± 0.4	302 ± 3
F6	6.9 ± 0.02	36 ± 0.5	1.338	40.9 ± 0.3	308 ± 2

C. Drug Content Analysis

Batch	**Drug Content (%)**
F1	98.2 ± 0.4
F2	98.8 ± 0.3
F3	99.4 ± 0.2
F4	99.8 ± 0.2
F5	99.5 ± 0.3
F6	99.1 ± 0.4

D. Sterility Testing

Batch	**Sterility Observation**	**Result**
F1	No microbial growth	Sterile
F2	No microbial growth	Sterile
F3	No microbial growth	Sterile
F4	No microbial growth	Sterile
F5	No microbial growth	Sterile
F6	No microbial growth	Sterile

E. In-Vitro Drug Release Study

Cumulative Drug Release (%)

Time (hr)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
1	25.4	23.8	22.5	21.2	20.0	18.8
2	42.8	40.9	39.4	37.8	35.9	34.2
4	61.3	59.5	57.8	56.2	54.4	52.8
6	78.6	76.9	75.4	73.8	72.2	70.6
8	91.4	90.2	89.3	88.5	87.2	86.0

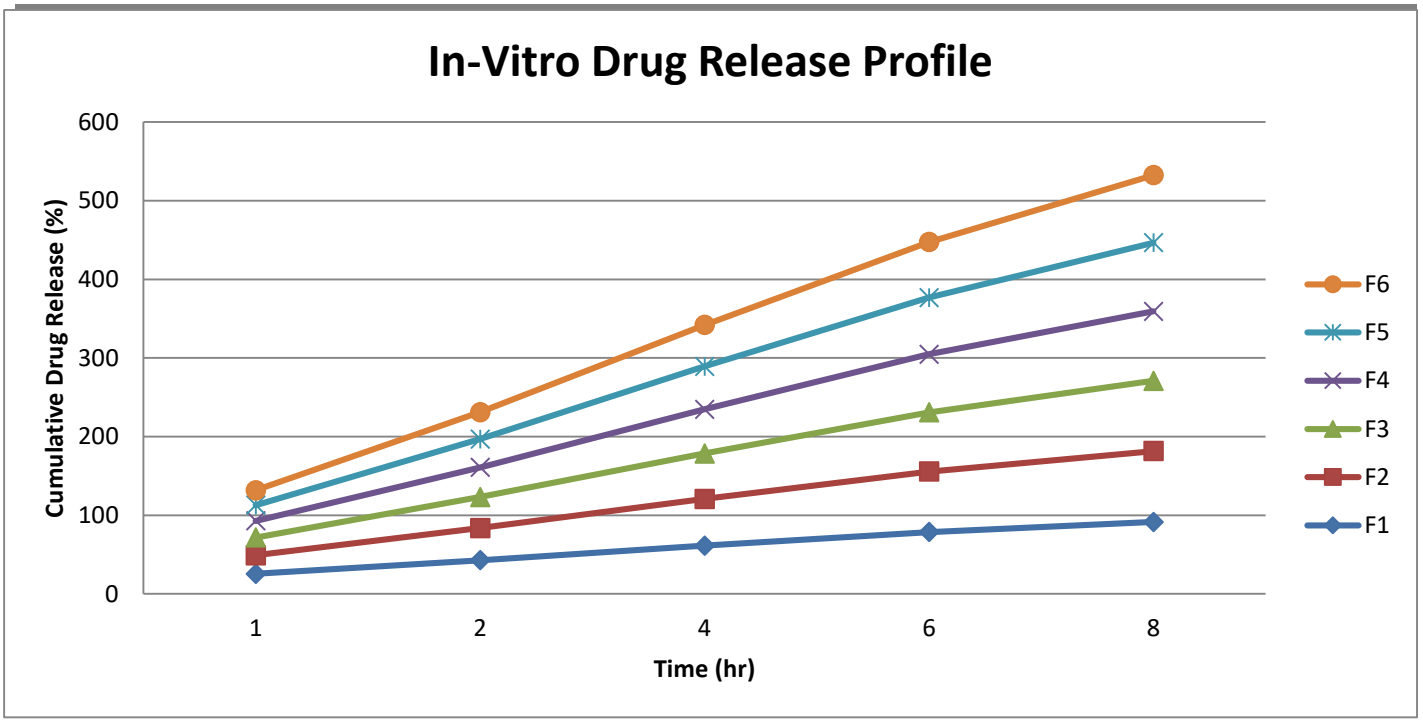

Figure 7.4 In-Vitro Drug Release Profile

Summary of Optimized Batch Selection

Batch	**Overall Performance**
F1	Low viscosity
F2	Acceptable
F3	Good
F4	**Optimized Batch**
F5	High viscosity
F6	Very high viscosity

Among all six formulations, **Batch F4** showed optimum pH, suitable viscosity, highest drug content, acceptable osmolarity, satisfactory sterility, and controlled drug release profile. Therefore, **F4 was selected as the optimized formulation of Olopatadine Hydrochloride Ophthalmic Solution.**

Stability Studies of Optimized Batch (F4)

Stability Study Conditions

The optimized formulation (**Batch F4**) was subjected to stability studies as per ICH guidelines.

Study Type	**Storage Condition**	**Duration**
Short-Term Stability Study	25 ± 2°C / 60 ± 5% RH	3 Months
Accelerated Stability Study	40 ± 2°C / 75 ± 5% RH	3 Months

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume XI Issue VI June 2026

Time Interval	pH	Drug Content (%)	Clarity	Sterility	Cumulative Drug Release at 8 hr (%)
Initial	6.80 ± 0.01	99.80 ± 0.20	Clear and Transparent	Sterile	88.5
1 Month	6.79 ± 0.02	99.52 ± 0.18	Clear and Transparent	Sterile	88.2
2 Months	6.78 ± 0.02	99.21 ± 0.22	Clear and Transparent	Sterile	87.9
3 Months	6.77 ± 0.03	98.94 ± 0.25	Clear and Transparent	Sterile	87.7

Overall Stability Study Result

Parameter	Observation After 3 Months
pH	Within acceptable range
Drug Content	>98%
Clarity	No change
Sterility	Maintained
Drug Release Profile	No significant variation

The optimized batch (**F4**) of Olopatadine Hydrochloride Ophthalmic Solution remained physically, chemically, and microbiologically stable under both short-term and accelerated storage conditions. No significant changes were observed in pH, drug content, clarity, sterility, or drug release profile. Therefore, the formulation was found to be stable and suitable for ophthalmic administration.

Comparison of Optimized Formulation (F4) with Official Standards and Marketed Product

Parameter	Official Standards (IP/USP)	Marketed Product (Olopatadine Eye Drops)	Optimized Batch (F4)
Appearance	Clear, colorless solution	Clear, colorless solution	Clear, colorless solution
Clarity	Free from visible particles	Clear	Clear
pH	6.0 – 7.5	6.8 ± 0.02	6.8 ± 0.01
Drug Content (%)	90 – 110%	99.2 ± 0.3	99.8 ± 0.2
Viscosity (cP)	Suitable for ophthalmic use	22 ± 0.5	24 ± 0.4
Osmolarity (mOsm/L)	280 – 320	292 ± 3	295 ± 2
Sterility	Must be sterile	Sterile	Sterile
Particulate Matter	Absent	Absent	Absent
Drug Release at 8 hr (%)	—	87.5 ± 0.5	88.5 ± 0.4
Stability (3 Months)	No significant change	Stable	Stable

The optimized formulation (**F4**) complied with all official pharmacopoeial requirements for ophthalmic preparations. The formulation showed comparable or slightly better performance than the marketed Olopatadine Hydrochloride ophthalmic solution in terms of **drug content, viscosity, osmolarity, and drug release profile.** Therefore, the developed formulation was considered suitable for ophthalmic administration and comparable to the marketed product.

CONCLUSION

The present study successfully achieved the formulation and evaluation of **Olopatadine Hydrochloride Ophthalmic Solution** intended for the management of allergic conjunctivitis. The preformulation studies established the favorable physicochemical characteristics of the drug and confirmed its compatibility with the selected excipients. FTIR and DSC studies demonstrated the absence of any significant drug-excipient interactions, ensuring the stability and integrity of the formulation.

Six different formulations were prepared and systematically evaluated. Among them, formulation **F4** emerged as the optimized batch due to its balanced physicochemical properties, including suitable pH, optimum viscosity, high drug content, acceptable osmolarity, excellent clarity, sterility, and controlled drug release behavior. The formulation provided prolonged drug release while maintaining patient comfort and ocular compatibility.

The optimized formulation was successfully sterilized and packaged under aseptic conditions, meeting all pharmaceutical quality requirements for ophthalmic preparations. Stability studies further confirmed that the formulation remained stable under recommended storage conditions without significant deterioration in quality attributes.

Comparison with the marketed ophthalmic product showed that the developed formulation complied with official pharmacopoeial standards and exhibited comparable or improved performance characteristics. Therefore, the developed **Olopatadine Hydrochloride Ophthalmic Solution (F4)** can be considered a safe, effective, stable, and reliable ophthalmic dosage form.

Compliance with ethical standards:

Acknowledgments: The authors appreciate very one that contributed to the successof this research.

Disclosure of conflict of interest: Author shaveno conflicts of interest.

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