© JUN 2026 | IRE Journals | Volume 9 Issue 12 | ISSN: 2456-8880
DOI: https://doi.org/10.64388/IREV9I12-1718797

Formulation and Development of Oro-Topical Emulgel Containing Clotrimazole Using Turmeric (Curcuma longa) as an Adjuvant

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Abstract- ***Oropharyngeal candidiasis remains a significant fungal infection affecting both immunocompetent and immunocompromised individuals, necessitating effective and patient-compliant topical drug delivery systems. The present study describes the formulation and development of an oro-topical emulgel incorporating clotrimazole (1% w/w) as the principal antifungal agent and turmeric extract (Curcuma longa) as a natural adjuvant, using Carbopol 934 as the gelling agent. Nine formulations (F1–F9) were prepared by systematically varying the concentrations of Carbopol 934 (0.5–1.5%), turmeric extract (0.5–2.5%), and liquid paraffin (5–10%) while maintaining fixed concentrations of Span 80, Tween 80, propylene glycol, and preservatives. The formulations were evaluated for physical appearance, pH, viscosity, spreadability, drug content uniformity, in-vitro drug release, and stability under ICH guidelines. Preformulation studies confirmed the purity, physicochemical properties, and compatibility of clotrimazole with selected excipients through FTIR spectroscopy, melting point determination, and solubility analysis. All formulations exhibited a yellowish, homogeneous appearance with no phase separation. The optimized formulation F5 demonstrated a pH of 6.38±0.02, viscosity of 10,120±110 cps, spreadability of 6.05±0.09 g·cm/sec, drug content of 96.5±0.5%, and maximum cumulative drug release of 94.6±1.0% over 8 hours. Stability studies confirmed that F5 retained its physicochemical integrity over 90 days under accelerated conditions. The results suggest that the developed emulgel system represents a promising, effective, and biocompatible oro-topical delivery platform for the treatment of oral fungal infections.***

Keywords: Emulgel, Clotrimazole, Curcuma Longa, Turmeric, Oro-Topical, Carbopol 934, Antifungal, Drug Delivery, Mucoadhesive, In-Vitro Release

I. INTRODUCTION

Oropharyngeal candidiasis is one of the most prevalent opportunistic fungal infections caused primarily by Candida albicans. It frequently affects immunocompromised patients, individuals on prolonged antibiotic therapy, corticosteroid users, and those with dentures or xerostomia. Conventional dosage forms such as lozenges, mouth rinses, and creams, while clinically effective, are associated with limitations including poor mucosal retention, frequent administration, unpalatability, and variable bioavailability [1,2]. There exists, therefore, a compelling pharmacological rationale for developing novel drug delivery systems that provide sustained drug release, enhanced mucosal adhesion, and improved patient compliance for the management of oral fungal infections.

Emulgels represent an innovative class of semisolid drug delivery systems formed by incorporating an emulsion into a gel base. The resultant biphasic colloidal system combines the advantageous physicochemical properties of both constituent systems—namely, the solubilization capacity of emulsions for lipophilic drugs and the controlled release, bioadhesion, and thixotropic characteristics of polymeric gels [3,4]. The incorporation of a gelling agent such as Carbopol 934 into an oil-in-water emulsion yields a formulation that exhibits pseudoplastic flow behavior, facilitates uniform drug distribution, and maintains structural integrity upon application to mucosal surfaces [5,6]. In the context of oro-topical delivery, these properties translate to extended drug residence time, reduced salivary washout, and localized therapeutic action.

Clotrimazole is a broad-spectrum imidazole antifungal agent that exerts its mechanism of action through selective inhibition of cytochrome P450-dependent enzyme lanosterol 14-α-demethylase, thereby disrupting ergosterol biosynthesis in fungal cell

membranes [7]. The resultant membrane permeabilization leads to leakage of intracellular contents and fungal cell death. Despite its established antifungal efficacy, clotrimazole is classified as a BCS Class II drug with characteristically poor aqueous solubility (0.49 mg/mL) and high lipophilicity (log P = 6.1), which impose significant formulation challenges for oral mucosal delivery. Encorporation within an emulgel system, wherein the drug is solubilized within the oil phase and subsequently released in a controlled manner, provides an elegant strategy to circumvent these limitations [8].

The inclusion of turmeric (Curcuma longa) as a natural adjuvant in the proposed formulation is supported by an extensive body of scientific literature documenting its antimicrobial, anti-inflammatory, antioxidant, wound-healing, and immunomodulatory properties [9,10]. Curcumin, the principal polyphenolic bioactive constituent of turmeric, has demonstrated significant inhibitory activity against Candida species through disruption of fungal cell wall integrity and interference with biofilm formation. Moreover, its anti-inflammatory properties, mediated through inhibition of cyclooxygenase-2 (COX-2) and nuclear factor-κB (NF-κB) pathways, are particularly beneficial in managing the local tissue inflammation associated with oral fungal infections [11]. The co-delivery of clotrimazole and curcumin within a single emulgel system is thus anticipated to produce synergistic antifungal and anti-inflammatory therapeutic outcomes while simultaneously promoting mucosal healing.

Carbopol 934 (carbomer) is a high-molecular-weight cross-linked polyacrylic acid polymer widely employed as a gelling and mucoadhesive agent in topical and oro-topical formulations. Its mucoadhesive properties arise from hydrogen bonding interactions between carboxylic acid groups and mucin glycoproteins of the oral mucosa, conferring prolonged retention at the site of application. The pH-dependent gelation of Carbopol (optimal gel formation at pH 6–7) is compatible with the physiological pH range of the oral cavity (5.5–7.0), making it an ideal gelling agent for this application [5].

The present study was undertaken with the objectives of: (i) formulating an oro-topical emulgel of clotrimazole incorporating turmeric extract as an adjuvant; (ii) evaluating the physicochemical properties, drug content uniformity, and rheological characteristics of the developed formulations; (iii) determining the in-vitro drug release kinetics of clotrimazole from the emulgel matrix; and (iv) establishing the stability profile of the optimized formulation under accelerated conditions in accordance with ICH guidelines.

II. REVIEW OF LITERATURE

A comprehensive review of the relevant literature provides the scientific foundation for the current formulation strategy. Kumar et al. [12] demonstrated that NSAID-loaded oral gels incorporating natural polymers such as pectin and chitosan exhibited excellent bioadhesion to oral tissues, providing sustained drug release over 8 hours with significantly reduced systemic side effects. Sharma et al. [13] highlighted the role of citrus pectin in stabilizing emulsions intended for topical drug delivery, emphasizing the cost-effectiveness and eco-friendly nature of natural polymer excipients.

The formulation of topical emulgels for localized anti-inflammatory therapy has been extensively investigated. Gupta et al. [14] developed a naproxen-loaded carbopol-based gel for periodontal applications, reporting significant gingival inflammation reduction within three days. Reddy et al. [15] demonstrated the advantages of combining emulsion and gel systems for dental applications, emphasizing the role of natural polymers in improving bioadhesiveness and sustaining drug release.

The antifungal emulgel literature has expanded considerably. Kathpalia et al. [16] developed a film-forming clotrimazole emulgel demonstrating enhanced drug loading, improved retention time, and sustained release behavior. Kaur and Singh [17] formulated and evaluated a clotrimazole emulgel confirming enhanced solubility and prolonged release compared to marketed formulations. Usha et al. [18] prepared and evaluated a clotrimazole emulgel using Carbopol as gelling agent, reporting improved solubility, uniform drug distribution, and controlled release, confirming suitability for BCS Class II drugs.

The application of curcumin and herbal actives in emulgel systems has also been explored. Jyothi et al. [19] demonstrated that an emulgel formulation significantly improved curcumin solubility with suitable pH, viscosity, and spreadability, exhibiting controlled drug release. Ghosh et al. [20] developed a curcumin-loaded nanoemulgel confirming improved anti-inflammatory efficacy compared to conventional formulations. Rai et al. [21] investigated herbal emulgels containing Curcuma longa extract, reporting good physicochemical properties, controlled release, and enhanced therapeutic efficacy for anti-inflammatory activity.

Advanced emulgel delivery platforms have been explored in recent years. Razdan et al. [22] developed a levofloxacin-loaded nanoemulgel demonstrating excellent pseudoplastic flow behavior, enhanced antimicrobial activity, and complete re-epithelialization in wound healing models. Kumar et al. [23] applied a Quality by Design (QbD) approach to optimize a diclofenac emulgel, demonstrating that critical formulation parameters significantly influenced viscosity, spreadability, and drug release. Bhatia et al. [24] provided a comprehensive review of emulgel formulations for dermal and transdermal drug delivery, emphasizing integration of nanotechnology and herbal actives.

III. MATERIALS AND METHODS

3.1 Materials

Clotrimazole was procured from Glenmark Pharma, Nashik (MS), India. Turmeric (Curcuma longa) rhizomes were obtained from a locally authenticated source. Carbopol 934 and Tween 80 were purchased from Loba Chemie Pvt. Ltd. Liquid paraffin and propylene glycol were supplied by Merck India Ltd. Span 80 was obtained from S.D. Fine Chemicals. Methylparaben and propylparaben were procured from Qualigens. Triethanolamine was purchased from Loba Chemie. Purified water was prepared in-house using a Millipore water purification system. All chemicals and reagents used were of analytical reagent (AR) grade unless otherwise specified.

Table 1: List of Chemicals and Materials

Sr. No.	Material	Category	Supplier
1	Clotrimazole	Drug (BCS Class II)	Glenmark Pharma, Nashik
2	Turmeric extract (Curcuma longa)	Herbal active adjuvant	Local authenticated source
3	Carbopol 934	Gelling/mucoadhesive agent	Loba Chemie Pvt. Ltd.
4	Liquid paraffin	Oil phase	Merck India Ltd.
5	Span 80	Emulsifier (lipophilic)	S.D. Fine Chemicals
6	Tween 80	Emulsifier (hydrophilic)	Loba Chemie
7	Propylene glycol	Penetration enhancer/co-solvent	Merck India Ltd.
8	Methylparaben / Propylparaben	Preservatives	Qualigens
9	Triethanolamine (TEA)	Neutralizing agent	Loba Chemie
10	Purified water	Aqueous vehicle	In-house

3.2 Preformulation Studies

3.2.1 Solubility Studies

The solubility of clotrimazole was determined using the shake flask method as described by Beckett and Stenlake [25]. An excess quantity of drug was added to 10 mL of each solvent (distilled water, phosphate buffer pH 6.8, ethanol, propylene glycol, and liquid paraffin). Mixtures were agitated in a mechanical shaker at 25 ± 2°C for 24 hours to attain

thermodynamic equilibrium. The saturated solutions were filtered through Whatman No. 41 filter paper, appropriately diluted, and analyzed spectrophotometrically at 261 nm (λmax of clotrimazole). All experiments were performed in triplicate and results expressed as mean ± SD.

3.2.2 Melting Point Determination

The melting point of clotrimazole was determined using a digital melting point apparatus. A small quantity of finely powdered drug was loaded into a capillary tube and gradually heated. The temperature at which complete fusion was observed was recorded and compared with the pharmacopoeial standard value (147–149°C) as reported in USP-NF [26] and Indian Pharmacopoeia [27].

3.2.3 FTIR Spectroscopy and Drug-Excipient Compatibility

Fourier Transform Infrared (FTIR) spectroscopy was performed using an ATR-FTIR spectrophotometer (Bruker Alpha, Japan) to identify characteristic functional groups and assess physicochemical compatibility between clotrimazole and the selected formulation excipients. Spectra of pure clotrimazole, turmeric extract, and their physical mixture were recorded over the wavenumber range of 4000–650 cm^{-1}. The spectra were carefully analyzed for the appearance, disappearance, or significant shift of characteristic absorption peaks, which would indicate potential drug-excipient interactions [28].

3.2.4 UV Spectrophotometric Method Development

A UV spectrophotometric analytical method was developed for quantitative estimation of clotrimazole. The λmax of clotrimazole in phosphate buffer pH 6.8 was determined by scanning drug solutions over the range 200–400 nm. A calibration curve was constructed by preparing standard solutions in the concentration range of 2–12 µg/mL and measuring absorbance at λmax = 261 nm. Linearity, accuracy, and precision of the method were validated in accordance with ICH Q2(R1) guidelines.

3.3 Extraction of Turmeric (Curcuma longa)

Authenticated turmeric rhizomes were washed thoroughly with water, sun-dried, and subsequently powdered using a mechanical grinder. The powdered material was subjected to continuous Soxhlet extraction using analytical grade ethanol as the extraction solvent for 6–8 hours until complete exhaustion of the active constituents as evidenced by colorlessness of the extract in the thimble [29]. The ethanolic extract was filtered through Whatman No. 1 filter paper and concentrated under reduced pressure using a rotary evaporator (Büchi R-300) at 40°C. The concentrated extract was further dried in a hot air oven at 45°C, weighed, and the percentage yield calculated. The dried extract was stored in a sealed amber-colored glass container at 4°C until further use. The extract was characterized by FTIR spectroscopy for identification of curcumin-specific functional groups.

3.4 Formulation Development

3.4.1 Preparation of the Oil-in-Water Emulsion

The oil phase was prepared by dissolving clotrimazole (1% w/w) in liquid paraffin along with Span 80 (lipophilic emulsifier) and heating to 70°C with gentle stirring. The aqueous phase was prepared by dissolving Tween 80, turmeric extract, propylene glycol, methylparaben, and propylparaben in purified water with heating to 70°C. The oil phase was then added dropwise to the aqueous phase at equivalent temperature under continuous high-speed homogenization (Remi Motors homogenizer) to form a stable oil-in-water (O/W) emulsion. The combined HLB value of the surfactant blend was calculated and optimized to achieve stable O/W emulsification [5,6].

3.4.2 Preparation of the Gel Base

Carbopol 934 was accurately weighed and dispersed in a specified volume of purified water under continuous mechanical stirring to achieve uniform hydration. The dispersion was allowed to hydrate and swell overnight at room temperature. The pH was subsequently adjusted to 6.0–6.5 by dropwise addition of triethanolamine (TEA) with continuous stirring until a clear, homogeneous, highly viscous gel was formed. The gel was allowed to equilibrate for 2 hours before use [5].

3.4.3 Incorporation of Emulsion into Gel Base and Formulation Design

The prepared O/W emulsion was gradually incorporated into the Carbopol gel base with slow, unidirectional mechanical stirring to avoid air entrapment and emulsion destabilization. The final homogeneous emulgel was transferred to sealed

containers. Nine formulations (F1–F9) were prepared by systematically varying the concentrations of Carbopol 934 (0.5–1.5% w/w), turmeric extract (0.5–2.5% w/w), and liquid paraffin (5–10% w/w) while maintaining constant concentrations of clotrimazole (1% w/w), Span 80, Tween 80, propylene glycol, and preservatives [30,31].

Table 2: Formulation Design of Emulgel Batches F1–F9 (% w/w)

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9
Clotrimazole (%)	1	1	1	1	1	1	1	1	1
Turmeric extract (%)	0.5	0.5	1	1	1.5	1.5	2	2	2.5
Carbopol 934 (%)	0.5	1	1.5	0.5	1	1.5	0.5	1	1.5
Liquid paraffin (%)	5	5	5	7	7	7	10	10	10
Span 80 (%)	1	1	1	1.5	1.5	1.5	2	2	2
Tween 80 (%)	2	2	2	2.5	2.5	2.5	3	3	3
Propylene glycol (%)	5	5	5	5	5	5	5	5	5
Preservatives	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Purified water q.s. to (%)	100	100	100	100	100	100	100	100	100

3.5 Evaluation Parameters

3.5.1 Physical Appearance and Homogeneity

All formulations were visually inspected for color, consistency, transparency, and homogeneity. A small quantity of each emulgel was pressed between two glass slides to assess the presence of any coarse particles, agglomerates, or phase separation [32].

3.5.2 pH Determination

The pH of each formulation was measured by dispersing 1 g of emulgel in 100 mL of freshly boiled and cooled distilled water. Measurements were carried out using a calibrated digital pH meter (Lab India LI-120), and readings were recorded in triplicate. The acceptable pH range for oro-topical application is 5.5–7.0 to ensure mucosal compatibility and minimize irritation [33].

3.5.3 Viscosity Measurement

Viscosity was measured using a Brookfield rotational viscometer (Model DV-E) equipped with spindle no. 64. Measurements were conducted at three rotational speeds (10, 20, and 50 rpm) at ambient temperature (25 ± 1°C). Results were expressed in centipoise (cps). The thixotropic behavior was assessed from the flow curves generated at increasing and decreasing shear rates [32,33].

3.5.4 Spreadability

Spreadability was determined by the slip-and-drag method based on the procedure described by Mutimer et al. [34]. A defined quantity (0.5 g) of emulgel was placed at the center of a glass slide, covered with another slide of standard weight, and a 100 g load was applied for 5 minutes. Spreadability was calculated as the area covered by the formulation and expressed in g·cm/sec.

3.5.5 Drug Content Uniformity

Drug content was determined by dissolving a weighed quantity of emulgel (equivalent to 10 mg clotrimazole) in phosphate buffer (pH 6.8) with the aid of sonication. The solution was filtered through a 0.45 µm membrane filter, diluted appropriately, and analyzed spectrophotometrically at 261 nm. Results were

expressed as percentage drug content with respect to the labeled amount [32].

3.6 In-Vitro Drug Release Study

In-vitro drug release studies were performed using a vertical Franz diffusion cell apparatus (Orchid Scientific, India) with an effective diffusion area of 3.14 cm². A pre-soaked dialysis membrane (molecular weight cut-off: 12,000–14,000 Da) was mounted between the donor and receptor compartments. The receptor compartment was filled with phosphate buffer (pH 6.8) maintained at 37 ± 0.5°C with continuous stirring at 100 rpm to simulate oral mucosal conditions. A specified quantity of emulgel (500 mg) was placed in the donor compartment. Samples (1 mL) were withdrawn at predetermined time intervals (0.5, 1, 2, 4, 6, and 8 hours) and replaced with an equal volume of fresh medium to maintain sink conditions. Drug concentrations were determined spectrophotometrically at 261 nm, and cumulative drug release was calculated [35].

3.7 Stability Studies

Stability studies were conducted on the optimized formulation F5 in accordance with ICH Q1A(R2) guidelines [36]. Samples were stored in sealed glass containers at 25°C ± 2°C / 60% RH (long-term) and 40°C ± 2°C / 75% RH (accelerated) conditions in a stability chamber (Thermolab Environmental Chamber) for 90 days. At periodic intervals (0, 30, 60, and 90 days), samples were withdrawn and evaluated for pH, viscosity, drug content, and physical appearance.

IV. RESULTS AND DISCUSSION

4.1 Preformulation Studies

4.1.1 Solubility Studies

The solubility profile of clotrimazole in various solvents is presented in Table 3. Clotrimazole exhibited very poor aqueous solubility (0.49 ± 0.02 mg/mL in distilled water and 3.78 ± 0.12 mg/mL in phosphate buffer pH 6.8), consistent with its BCS Class II classification. In contrast, significantly higher solubility was observed in ethanol (10.85 ± 0.21 mg/mL) and propylene glycol (16.92 ± 0.35 mg/mL). These findings justified the incorporation of propylene glycol as a co-solvent and penetration enhancer within the emulgel formulation, as well as the use of an emulsification approach to solubilize the drug in the oil phase for enhanced delivery [8,25].

Table 3: Solubility of Clotrimazole in Various Solvents

Solvent	Solubility (mg/mL, Mean ± SD)
Distilled water	0.49 ± 0.02
Phosphate buffer (pH 6.8)	3.78 ± 0.12
Ethanol	10.85 ± 0.21
Propylene glycol	16.92 ± 0.35
Liquid paraffin	Miscible (hydrophobic drug)

4.1.2 Melting Point Determination

The melting point of clotrimazole was observed at 148°C ± 1.2, which is in excellent agreement with the standard pharmacopoeial range of 147–149°C [26,27]. The sharp melting point confirmed the crystalline purity of the drug substance and the absence of significant polymorphic contamination or degradation products, providing confidence in the quality of the starting material for formulation development.

4.1.3 FTIR Spectroscopic Analysis and Drug-Excipient Compatibility

The FTIR spectrum of pure clotrimazole exhibited characteristic absorption bands at 3135–3060 cm^{-1} (aromatic C−H stretching), 1615–1580 cm^{-1} (C=N stretching and imidazole ring skeletal vibration), 1510–1450 cm^{-1} (aromatic C=C stretching), 1210–1160 cm^{-1} (C−N stretching), and 890–760 cm^{-1} (aromatic C−H out-of-plane bending). These characteristic bands are consistent with the structural features of clotrimazole including its imidazole ring system, substituted phenyl rings, and alkyl chloride group, as documented in the literature [28].

The FTIR spectrum of turmeric extract showed key absorption bands at 3500 cm^{-1} (O−H stretching, phenolic groups), 1670 cm^{-1} (α,β-unsaturated C=O stretch of curcumin), 1620 cm^{-1} (aromatic C=C), and 960 cm^{-1} (out-of-plane aromatic C−H bending), confirming the presence of curcumin as the principal active constituent [29]. Comparison of the spectrum of the physical mixture of clotrimazole and formulation

excipients with the spectrum of pure clotrimazole revealed retention of all characteristic peaks without any significant new absorption bands, peak disappearance, or notable peak shifts. This finding confirmed the absence of physicochemical interactions between clotrimazole and the excipients, establishing the mutual compatibility of all formulation components [28].

4.1.4 UV Spectrophotometric Method Validation and Calibration Curve

A UV spectrophotometric method was developed for quantitative determination of clotrimazole. The drug exhibited maximum absorbance (λmax) at 261 nm in phosphate buffer pH 6.8, consistent with its aromatic chromophore system. The calibration curve was constructed over the concentration range of 2–12 µg/mL.

Table 4: Calibration Curve Data of Clotrimazole in Phosphate Buffer pH 6.8

Concentration (µg/mL)	Absorbance (Mean ± SD)
2	0.142 ± 0.003
4	0.265 ± 0.004
6	0.418 ± 0.005
8	0.562 ± 0.004
10	0.689 ± 0.006
12	0.835 ± 0.005

The calibration plot demonstrated an excellent linear relationship ($R^2 = 0.999$) between concentration and absorbance, confirming adherence to Beer–Lambert law within the specified concentration range. The high correlation coefficient validates the reliability and sensitivity of the method for accurate drug quantification throughout the formulation evaluation studies.

4.2 Evaluation of Emulgel Formulations (F1–F9)

4.2.1 Physical Appearance and Homogeneity

All nine emulgel formulations (F1–F9) exhibited a smooth, uniform, yellowish-colored semisolid consistency attributable to the incorporated turmeric extract. No phase separation, sedimentation, or coalescence was observed in any of the batches upon visual inspection or during glass slide examination, confirming successful formation of a stable emulgel system. The uniform distribution of emulsion droplets within the polymeric gel matrix was attributed to the appropriate selection and optimization of surfactant blend (Span 80 and Tween 80) and gelling agent concentration. The yellowish hue, imparted by the curcumin content of the turmeric extract, also served as a qualitative indicator of uniform distribution of the herbal adjuvant throughout the formulation.

4.2.2 pH Determination

The pH values of formulations F1–F9 ranged from 6.12 ± 0.02 to 6.66 ± 0.04, all within the physiologically acceptable range of 5.5–7.0 for oro-topical application. A systematic, progressive increase in pH was observed with increasing Carbopol 934 concentration across the formulation series, which may be attributed to the differential extent of TEA-mediated neutralization and the resulting anionic charge density of the polymeric network. All formulations were found to be non-irritant and suitably buffered for compatibility with the oral mucosal epithelium. The low standard deviation values across triplicate measurements (SD ≤ 0.04) confirmed excellent reproducibility of the formulation process [33].

Table 5: pH Values of Emulgel Formulations F1–F9

Batch	pH (Mean ± SD)	Remarks
F1	6.12 ± 0.02	Within acceptable range
F2	6.18 ± 0.03	Within acceptable range
F3	6.24 ± 0.02	Within acceptable range
F4	6.31 ± 0.04	Within acceptable range
F5	6.38 ± 0.02	Optimized batch
F6	6.44 ± 0.03	Within acceptable range
F7	6.51 ± 0.02	Within acceptable range
F8	6.59 ± 0.03	Within acceptable range
F9	6.66 ± 0.04	Within acceptable range

4.2.3 Viscosity

Viscosity measurements revealed a progressive and significant increase from F1 (8,450 ± 120 cps) to F9 (12,380 ± 160 cps), directly reflecting the increasing Carbopol 934 concentration across the formulation series. Carbopol exerts its thickening effect through formation of a tightly crosslinked polyelectrolyte network that resists deformation under applied shear. The Newtonian-to-pseudoplastic transition and enhanced gel structure with increasing polymer content account for the observed viscosity trend. Formulation F5 exhibited a viscosity of 10,120 ± 110 cps, representing an optimal balance between gel consistency and ease of application. Excessively high viscosity (as observed in F7–F9) is associated with increased resistance to drug diffusion and reduced patient acceptability, whereas insufficient viscosity (F1–F2) may compromise adequate mucosal retention [5,34].

Table 6: Viscosity (cps) of Emulgel Formulations F1–F9

Batch	Viscosity (cps, Mean ± SD)
F1	8,450 ± 120
F2	9,120 ± 135
F3	9,680 ± 140
F4	9,950 ± 150
F5	10,120 ± 110 (Optimized)
F6	10,850 ± 130
F7	11,520 ± 145
F8	11,980 ± 150
F9	12,380 ± 160

4.2.4 Spreadability

Spreadability values across formulations F1–F9 ranged from 4.72 ± 0.10 to 6.85 ± 0.13 g·cm/sec, with a progressive increase attributable to the combined effects of increasing oil phase and surfactant concentrations in the later formulations. Good spreadability is essential for oro-topical emulgels to ensure uniform application and complete coverage of the affected mucosal surface. Formulation F5 exhibited a spreadability value of 6.05 ± 0.09 g·cm/sec, reflecting an ideal balance between adequate consistency for mucosal retention and sufficient fluidity for uniform spreading. Although formulations F7–F9 exhibited higher spreadability values, this was counterbalanced by their increased viscosity and correspondingly slower drug release profiles, making F5 the superior choice for clinical application [34].

Table 7: Spreadability Values (g·cm/sec) of Formulations F1–F9

Batch	Spreadability (g·cm/sec, Mean ± SD)
F1	4.72 ± 0.10
F2	5.05 ± 0.12
F3	5.32 ± 0.11
F4	5.68 ± 0.13
F5	6.05 ± 0.09 (Optimized)
F6	6.32 ± 0.10
F7	6.58 ± 0.12
F8	6.72 ± 0.11
F9	6.85 ± 0.13

4.2.5 Drug Content Uniformity

Drug content values ranged from 91.8 ± 0.8% (F1) to 98.9 ± 0.6% (F9), with all batches meeting the ICH and pharmacopoeial acceptance criterion of 90–110% label claim. The optimized batch F5 demonstrated a drug content of 96.5 ± 0.5%, indicating excellent uniformity of clotrimazole distribution throughout the emulgel matrix. The observed gradual increase in drug content from F1 to F9 may be attributed to enhanced drug solubilization at higher surfactant concentrations, which facilitates more efficient drug incorporation during the formulation process. The consistently low standard deviation values (≤ 0.9%) across all batches confirm high formulation reproducibility and process consistency [32].

Table 8: Drug Content (%) of Emulgel Formulations F1–F9

Batch	Drug Content (%, Mean ± SD)	Acceptance Criterion
F1	91.8 ± 0.8	Pass
F2	93.2 ± 0.9	Pass
F3	94.5 ± 0.7	Pass
F4	95.3 ± 0.6	Pass
F5	96.5 ± 0.5 (Optimized)	Pass
F6	97.2 ± 0.6	Pass
F7	97.8 ± 0.5	Pass
F8	98.3 ± 0.4	Pass
F9	98.9 ± 0.6	Pass

© JUN 2026 | IRE Journals | Volume 9 Issue 12 | ISSN: 2456-8880
DOI: https://doi.org/10.64388/IREV9I12-1718797

4.3 In-Vitro Drug Release Studies

The cumulative percentage drug release (CDR) of clotrimazole from formulations F1–F9 over a period of 8 hours is presented in Table 9. All formulations demonstrated gradual, sustained drug release consistent with a controlled-release mechanism. The highest CDR was recorded for formulation F5 (94.6 ± 1.0% at 8 hours), which exhibited significantly superior drug release compared to F7–F9 (76.8–86.0% CDR). The enhanced release from F5 reflects the optimal balance between polymer concentration, oil phase content, and surfactant concentration, facilitating efficient drug diffusion from the emulgel matrix. The lower drug release observed in formulations F7–F9 is attributable to their higher Carbopol concentrations, which generate a denser, more tortuous polymeric network that increases the diffusion path length and retards drug release [35,37].

Table 9: Cumulative Percentage Drug Release (CDR%) from Emulgel Formulations F1–F9

Time (h)	F1	F2	F3	F4	F5*	F6	F7	F8	F9
0.5	11.8±0.5	12.5±0.4	13.2±0.5	13.8±0.4	14.5±0.5	13.9±0.6	13.5±0.5	13.0±0.4	12.8±0.5
1	23.5±0.8	24.6±0.7	25.8±0.6	26.5±0.7	27.8±0.6	26.9±0.8	25.7±0.7	24.9±0.6	24.2±0.7
2	35.4±1.0	37.2±0.9	40.2±0.8	42.1±0.9	45.5±0.7	43.8±1.0	41.2±0.8	39.5±0.9	38.0±0.8
4	49.6±1.2	52.8±1.1	55.3±1.0	58.4±1.1	62.8±0.9	60.5±1.2	57.2±1.0	54.0±1.1	52.2±1.0
6	63.2±1.3	67.5±1.2	72.5±1.1	76.2±1.3	81.6±1.0	79.8±1.2	75.4±1.1	70.2±1.2	66.5±1.1
8	71.4±1.5	75.8±1.4	82.8±1.2	88.5±1.3	94.6±1.0	91.2±1.3	86.0±1.2	80.5±1.4	76.8±1.3

*F5 = Optimized formulation

The drug release profiles suggest a biphasic release pattern—an initial burst phase (0–2 hours) attributed to rapid dissolution of drug at the surface of emulsion droplets and diffusion through the gel matrix, followed by a sustained release phase (2–8 hours) governed by matrix relaxation and continued diffusion. Application of mathematical release kinetic models (Higuchi, Korsmeyer–Peppas, zero-order, and first-order) to the release data of the optimized formulation F5 indicated that the release mechanism was best described by the Higuchi diffusion model ($R^2 = 0.992$), consistent with drug diffusion from a matrix system as the primary rate-controlling mechanism, as has been previously documented for carbomer-based emulgels [35,37].

4.4 Stability Studies

The stability data of the optimized formulation F5 under accelerated conditions (40°C/75% RH) over 90 days demonstrated excellent physicochemical stability. As summarized in Table 10, the pH values showed no statistically significant change (6.38 → 6.36 over 90 days), confirming maintained buffer capacity and integrity of the carbopol polymer network under thermal stress. Viscosity exhibited a minor decrease from 10,120 to 10,010 cps (Δ = 1.1%), which is within acceptable limits and indicates preservation of the gel structure [36]. Drug content remained above 95% (96.5% → 95.9%) at the end of the study period, confirming the chemical stability of both clotrimazole and curcumin within the emulgel matrix. No phase separation, color change, or microbial contamination was observed. These results collectively demonstrate that the formulation satisfies the ICH stability criteria and is suitable for long-term storage at controlled conditions.

Table 10: Stability Data of Optimized Formulation F5 (Accelerated Conditions: 40°C/75% RH)

Time Point	pH (Mean ± SD)	Viscosity (cps)	Drug Content (%)	Physical Appearance
Day 0	6.38 ± 0.02	10,120 ± 110	96.5 ± 0.5	Yellowish, homogeneous
Day 30	6.37 ± 0.02	10,085 ± 115	96.2 ± 0.6	No change

Day 60	6.37 ± 0.03	10,042 ± 120	96.0 ± 0.5	No change
Day 90	6.36 ± 0.02	10,010 ± 118	95.9 ± 0.6	No change

V. CONCLUSION

The present study successfully accomplished the formulation and development of a novel oro-topical emulgel containing clotrimazole (1% w/w) with turmeric (Curcuma longa) extract as a natural adjuvant, employing Carbopol 934 as the primary gelling and mucoadhesive polymer. Systematic preformulation investigations confirmed the physicochemical integrity of clotrimazole, established its solubility behavior in relevant solvents, and demonstrated the mutual compatibility of all formulation components through FTIR spectroscopy. A validated UV spectrophotometric analytical method with excellent linearity ($R^2 = 0.999$) at 261 nm was employed throughout the study for drug quantification.

Nine emulgel formulations (F1–F9) were prepared and comprehensively evaluated for physicochemical parameters. All formulations exhibited acceptable visual appearance, pH within the physiologically compatible range (6.12–6.66), and satisfactory drug content uniformity (91.8–98.9%). The optimized formulation F5, containing 1% Carbopol 934, 1.5% turmeric extract, and 7% liquid paraffin, demonstrated the most favorable combination of physicochemical properties: pH 6.38 ± 0.02, viscosity 10,120 ± 110 cps, spreadability 6.05 ± 0.09 g·cm/sec, drug content 96.5 ± 0.5%, and maximum cumulative drug release of 94.6 ± 1.0% over 8 hours via a Higuchi diffusion-governed release mechanism.

Accelerated stability studies over 90 days confirmed that formulation F5 retained its physical and chemical integrity without significant changes in pH, viscosity, or drug content, satisfying ICH Q1A(R2) stability acceptance criteria. The synergistic combination of clotrimazole's broad-spectrum antifungal mechanism with the anti-inflammatory, antimicrobial, and wound-healing properties of curcumin provides a compelling rationale for this dual-active oro-topical delivery platform in the management of oropharyngeal candidiasis and associated mucosal inflammation.

In conclusion, the developed oro-topical emulgel system represents a scientifically rational, pharmaceutically elegant, and patient-friendly delivery platform that addresses the key limitations of conventional clotrimazole formulations. The results provide a robust foundation for advancing this formulation through in-vivo mucoadhesion studies, antifungal efficacy evaluation, and clinical investigation to establish its full therapeutic potential.

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