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Research Article

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Optimization of Clotrimazole Emulgel: Evaluating the Effects of Oil Type, Oil Concentration, and Gellant Type on Physico-Chemical Performance

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Abstract

Fungal infections of the skin are prevalent worldwide, and effective treatment requires innovative drug delivery systems. Emulgel, a novel formulation, offers several advantages, including non-greasiness, stain-free properties, improved patient compliance (particularly for individuals with hairy skin), enhanced spreadability, increased stability, and controlled drug release. This study investigates using emulgel as a delivery system for hydrophobic drugs, specifically Clotrimazole, in a hydrophilic base. Nine emulgel formulations were evaluated, focusing on three key factors: polymer type (Carbomer 940, Hydroxypropyl Methylcellulose K4M (HPMC K4M)), or a combination of both), and the type and percentage of the oily phase (5% Paraffin, 5% Isopropyl Myristate, and 7.5% Isopropyl Myristate). Three formulations failed to meet the mechanical stability criteria, while six formulations demonstrated stability across all tests. Drug release rates were as follows: F1 (81.43%), F2 (76.87%), F3 (85.56%), F7 (91.56%), F8 (87.89%), and F9 (97.64%). Over six hours, a commercially available Clotrimazole cream (Pars Daroo Company) released 71.11% of its drug content. Formulation 9 is the most effective formula, incorporating 5% Paraffin and a blend of Carbomer 940 and HPMC, and it followed the zero-order kinetic model. The inclusion of Paraffin, compared to Isopropyl Myristate, enhanced drug release due to the lower solubility of Clotrimazole in Paraffin. The Carbomer 940 and HPMC combination also provided optimal viscosity, ensuring stability, ease of application, and controlled release. It has also been shown that increasing oil concentration increases the drug's loading capacity while its release decreases.

Keywords: Emulgel; Clotrimazole; Isopropyl Myristate; Paraffin; Carbomer 940; HPMC.

1. Introduction

Fungal infections are among the most common dermatological issues, capable of affecting various areas of the body. These infections often cause discomfort and reduce patients' quality of life. Effective treatment typically involves antifungal agents, with Clotrimazole being one of this category's most commonly used and effective drugs.

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Clotrimazole is an imidazole derivative with broad-spectrum antimycotic activity, particularly effective against Candida albicans [1, 2].

Clotrimazole has low aqueous solubility and high membrane permeability; these characteristics are critical in designing topical formulations such as emulgels, as they can influence the drug release rate and its ability to penetrate target tissues [3]. Moreover, oral administration of Clotrimazole is not ideal due to its low bioavailability and poor water solubility [3, 4].

Topical formulations offer numerous advantages, including bypassing hepatic first-pass metabolism, avoiding gastric pH variability, and eliminating plasma concentration fluctuations observed with oral routes [5, 6]. These benefits highlight the significance of topical drug delivery in the targeted management of dermatological conditions, including fungal infections. However, overcoming the drawbacks of conventional formulations requires the development of innovative approaches.

Despite their widespread use in fungal infections, conventional topical formulations such as w/o creams and ointments have limitations. These include their greasy bases, which often leave stains on clothing and skin, slow absorption rates, and reduced patient satisfaction. These issues are especially pronounced in patients with hairy skin [7, 8].

Emulgel, a hybrid formulation combining the properties of gels and emulsions, is emerging as an advanced drug delivery system [9]. Since emulgels possess the advantages of both emulsions and gels, they are particularly effective in addressing challenges associated with hydrophobic drugs like Clotrimazole. This approach enables incorporating hydrophobic drugs like Clotrimazole into a hydrophilic base, overcoming the issues posed by greasy bases in conventional formulations [4].

Emulgels act as a reservoir for the drug and slowly release it in a controlled manner through the external phase to the skin, ensuring sustained therapeutic effects [4]. Emulgels are particularly advantageous due to their ease of application, absence of greasiness, non-staining properties, enhanced stability, prolonged shelf life, aesthetic transparency, controlled and sustained drug release, improved drug penetration, and reduced side effects [9-11].

By improving patient compliance, particularly in individuals with hairy skin, and resolving the shortcomings of traditional formulations, emulgel represents a transformative advancement in the treatment of fungal infections. This novel delivery system enhances therapeutic efficacy and significantly improves patient satisfaction due to its unique characteristics.

In this study, we developed emulgel formulations for the topical delivery of Clotrimazole by employing a novel combination of Carbomer 940 and HPMC K4M as gelling agents. This blend was selected to balance viscosity, spreadability, and controlled drug release— attributes often difficult to optimize when using a single polymer. Furthermore, Paraffin and Isopropyl Myristate were incorporated as lipophilic excipients to enhance the solubilization of the poorly water-soluble Clotrimazole and potentially improve dermal penetration. This specific combination of polymers and excipients has not been previously reported for Clotrimazole emulgel formulations. In addition, we performed a comparative analysis to evaluate how variations in formulation components influence drug release behavior— an area that remains underexplored in the literature.

2. Material and Methods

Clotrimazole was procured from Sina Pishgam Darou Novin Company (Iran). All other chemicals and reagents used were of laboratory or analytical grade.

2.1. Preformulation Studies

Preformulation testing is an investigation of a drug's physical and chemical properties.

2.1.1. Solubility Study

10 mg of Clotrimazole was taken and dissolved in 10 mL of various solvents, and then the solubility was visually analyzed.

2.1.2. Melting Point Analysis

To determine the melting point range of Clotrimazole powder, the melting point apparatus model 1A9100MK2 was used. A small amount of the powder was placed into a capillary tube for sample preparation. The tube was then prepared by sealing its bottom end, and the powder was compacted at the closed end by gently tapping the capillary tube inside a hollow tube. The prepared capillary tube was then placed into the chamber of the melting point apparatus for analysis.

2.1.3. Drug Identification

To analyze the Fourier Transform Infrared (FT-IR) spectrum of Clotrimazole powder, it was mixed in a 1:10 ratio with Potassium Bromide (KBr) powder. The FT-IR spectrum was then obtained using (IRAffinity-1S, Shimadzu, Japan) and compared with the reference spectrum.

2.1.4. Determination of λmax

A stock solution of Clotrimazole was prepared by accurately weighing 0.1 g of the compound and dissolving it in a 100 mL volumetric flask with a solvent solution. The solvent comprised 50% Ethanol (99.8%) and 50% Phosphate buffer (pH 7.4), resulting in a final concentration of 1000 Parts Per Million (ppm). Working solutions with concentrations of 80 ppm, 100 ppm, and 300 ppm were prepared from the stock solution. The Ultraviolet (UV) absorbance of these solutions was measured using a UV spectrophotometer (UV-1800, Shimadzu, Japan) over the wavelength range of 200–400 nm to determine the maximum absorption wavelength (λmax).

2.1.5. Calibration Curve

A stock solution with a concentration of 1000 ppm was first prepared to construct the standard curve. This stock solution prepared concentrations of 30 ppm, 100 ppm, 300 ppm, 400 ppm, and 500 ppm. The absorbance of these solutions was measured at a wavelength of 260.8 nm against the solvent. Each concentration was prepared in triplicate to construct the calibration curve and determine the regression equation, and the absorbance was measured. The average absorbance of each concentration was then used to plot the curve.

2.2. Formulation Development

2.2.1. Preparation of the Gel Phase

The gel phase was formulated using HPMC K4M and Carbomer 940 as gelling agents. For Carbomer 940, the required amount was dispersed in water and Glycerin and allowed to hydrate overnight to ensure complete dispersion. For HPMC K4M, the water–glycerin mixture was heated to 60–70 °C, and the polymer was gradually added under continuous stirring, followed by a hydration period. After complete hydration, TriEthanolamine was added to neutralize Carbomer 940, adjust the pH, and promote proper gel formation through polymer swelling and network formation.

2.2.2. Determination of Surfactant Ratio Based on Hydrophilic-Lipophilic Balance (HLB) Value

The goal of this formulation is to create an oil-in-water emulsion. For this purpose, the required HLB values for liquid Paraffin range from 10 to 12; Isopropyl Myristate is 11.5. To simplify the process and maintain consistency in the emulsifier ratio, an HLB value of 11 was selected as the final value.

To determine the HLB of the emulsifier mixture, the following formula was used:

$$HLB_{mixture} = x.\ HLB_A + (1-x).\ HLB_B$$

In this equation, HLB_A and HLB_B represent the HLB values of Span 80 and Tween 80, respectively, and x corresponds to the proportion of Span 80 in the mixture. Based on this formula and the calculated HLB, the ratio of surfactants was determined to be 37% Span 80 and 63% Tween 80.

This ratio was consistently applied across all formulations.

We evaluated nine formulations in this study, as presented in **table 1**. The selection of the oil phase was based on both preliminary solubility studies conducted in our laboratory, which showed high solubility of the API in Paraffin and Isopropyl Myristate and previous reports highlighting their positive role in topical formulations. Paraffin provides occlusive properties beneficial for dermal applications, while Isopropyl Myristate is a well-established penetration enhancer [12].

2.2.3. Preparation of the Emulsion Phase

The emulsion phase was prepared by adding Polysorbate 80 (Tween 80) to the aqueous phase and Sorbitan Monooleate (Span 80) to the oil phase. Methylparaben and Propylparaben were dissolved in propylene glycol and mixed into the aqueous phase. The oil and aqueous phases were separately heated to 75°C and 80°C, respectively. Under continuous mixing, the oil phase was gradually incorporated into the aqueous phase. Clotrimazole, dissolved in Ethanol (99.8%), was added to the emulsion while stirring to ensure even distribution.

2.2.4. Preparation of Emulgel

Finally, the gel and emulsion phases were combined in a 1:1 ratio and thoroughly mixed using a homogenizer to produce a uniform formulation.

2.3. Evaluation Studies for Emulgel

2.3.1. Characterization of Physical Appearance and pH Determination

The prepared Clotrimazole emulgels were examined visually for their color, consistency, and homogeneity. In addition, the pH of the formulations was measured using a digital pH meter (SANA SL-901) to ensure compatibility with the skin.

Table 1. Composition and codes of Clotrimazole formulations.

% (w/w)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Clotrimazole	1%	1%	1%	1%	1%	1%	1%	1%	1%
Carbomer 940	1%	1%	1%	-	-	-	-	-	-
HPMC K4M	-	-	-	2.5%	2.5%	2.5%	-	-	-
Carbomer 940+ HPMC K4M	-	-	-	-	-	-	Carbomer 0.5% + HPMC k4m 1.25%	Carbomer 0.5% + HPMC k4m 1.25%	Carbomer 0.5% + HPMC k4m 1.25%
Liquid Paraffin	-	-	5%	-	-	5%	-	-	5%
Isopropyl Myristate	5%	7.5%	-	5%	7.5%	-	5%	7.5%	-
Span 80	1.48%	1.48%	1.48%	1.48%	1.48%	1.48%	1.48%	1.48%	1.48%
Tween 80	2.52%	2.52%	2.52%	2.52%	2.52%	2.52%	2.52%	2.52%	2.52%
Glycerin	5%	5%	5%	5%	5%	5%	5%	5%	5%
Ethanol 99.8%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%
Propylene glycol	5%	5%	5%	5%	5%	5%	5%	5%	5%
Methylparaben	0.25%	0.25%	0.25%	0.25%	%0.25	%0.25	0.25%	0.25%	0.25%
Propylparaben	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%
TriEthanolamine	Adjust pH	Adjust pH	Adjust Ph	-	-	-	Adjust Ph	Adjust Ph	Adjust Ph
Distilled water	Up to 100%	Up to 100%	Up to 100%	Up to 100%	Up to 100%	Up to 100%	Up to 100%	Up to 100%	Up to 100%

Composition and codes of various Clotrimazole topical formulations (F1–F9) expressed as weight/weight percentages.

2.3.2. Determination of Emulsion Type

The first method for determining emulsion type involves observing the behavior of the emulsion with water. A water-in-oil (W/O) emulsion remains greasy and does not dilute or mix with water, forming clumps. In contrast, an oil-in-water (O/W) emulsion can be easily washed off, leaves less greasiness, and forms a uniform solution when mixed with water.

The second method is using the methylene blue test. This method mixed a small emulsion with a few drops of methylene blue solution.

2.3.3. Mechanical Stability Test of the Product

A centrifuge (model HB800) was used to evaluate the mechanical stability. For this purpose, a sample was placed in the centrifuge and spun at 10,000 rpm for 15 minutes. A stable product maintains its integrity and does not separate into two phases at the end of the centrifugation process.

2.3.4. Thermal Stability Evaluation Using Heat–Cold Cycles

The sample was stored for 24 hours in a refrigerator, 24 hours at room temperature, and 24 hours in an oven at 40°C. This cycle was repeated three times, and the product was evaluated for its appearance and stability after each cycle.

2.3.5. Viscosity Measurement

The viscosity of the different emulgel formulations was determined at 25°C using a Brookfield viscometer with spindle 52 and connected to a thermostatically controlled circulating water bath.

2.3.6. Drug Content Determination

This test was performed to determine the amount of active ingredient in the formulation. A 0.5 g sample of each emulgel formulation was dissolved in 100 mL of a suitable solvent and stirred on a magnetic stirrer for 3 hours to ensure complete dissolution. The solution was filtered through a 0.45-micron membrane filter and analyzed using a UV-visible spectrophotometer at 260.8 nm with the appropriate blank. The concentration of Clotrimazole was calculated using a previously established standard curve. The percentage of drug content was then determined by comparing the measured concentration to the theoretical one.

2.3.7. In vitro Release Studies

The Franz cell method was employed in this study. A dialysis membrane with a width of 43 mm, a length of 5 cm, and a cut-off of 14 kDa was used. It was soaked in a solvent solution for 24 hours to activate the membrane. After activation, 1 g of the formulation was placed inside the membrane, and both ends were securely sealed with nylon thread. The membrane was then placed in the Franz cell, and a magnetic stirrer was added. A total of 40 mL of medium was introduced, and the setup was sealed with a cap. The Franz cell was placed on a stirrer at 37°C and 50 rpm. At designated intervals (30 minutes, 1, 2, 3, 4, 5, and 6 hours), a 5 mL sample was withdrawn from the medium. After each sample collection, 5 mL of fresh medium at the same temperature was added to maintain sink conditions. The samples were then analyzed using UV spectrophotometry at a wavelength of 260.8 nm.

3. Results and Discussion

3.1. *Solubility Study*

Clotrimazole is soluble in Acetone, Chloroform, Ethyl acetate, Ethanol, and Polyethylene Glycol 400, but it has low solubility in water.

3.2. Melting Point Analysis

Given that the reference melting range for Clotrimazole is between 147°C and 149°C, no changes were observed up to 140°C. The powder began to melt after gradually increasing the temperature to 146°C. Complete melting occurred as the temperature reached 148°C; at this point, the white Clotrimazole powder in the capillary tube became a fully colorless liquid.

3.3. *Identification*

The main FT-IR peaks are shown in **figure 1**. The spectrum of Clotrimazole powder matches that of the reference [13].

FTIR spectrum of Clotrimazole showing characteristic peaks at 704–755 cm^{-1} (C–Cl stretching and Aromatic C–H bending), 823 and 902 cm^{-1} (Aromatic ring vibrations), and 1080 and 1207 cm^{-1} (C–N stretching and Imidazole ring vibrations). These peaks confirm the presence of key functional groups and the identity of Clotrimazole.

3.4. *Maximum Absorption Wavelength (λmax) Determination*

The maximum absorption was observed at a wavelength of 260.8 nm, considered the λmax for Clotrimazole.

3.5. *Calibration Curve*

The calibration curve and the equation of the line are shown in **figure 2**.

A linear relationship was observed between absorbance and concentration over the 30–500 ppm range, measured at λmax = 260.8 nm. The high correlation coefficient (R^2) confirms the method's suitability for quantitative analysis.

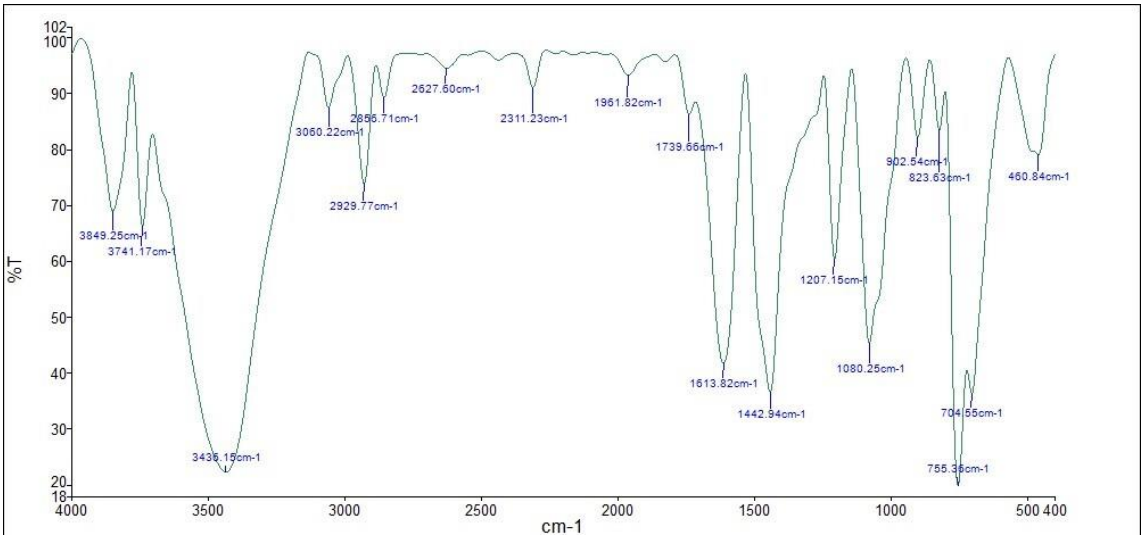

Figure 1. FTIR spectrum of Clotrimazole drug

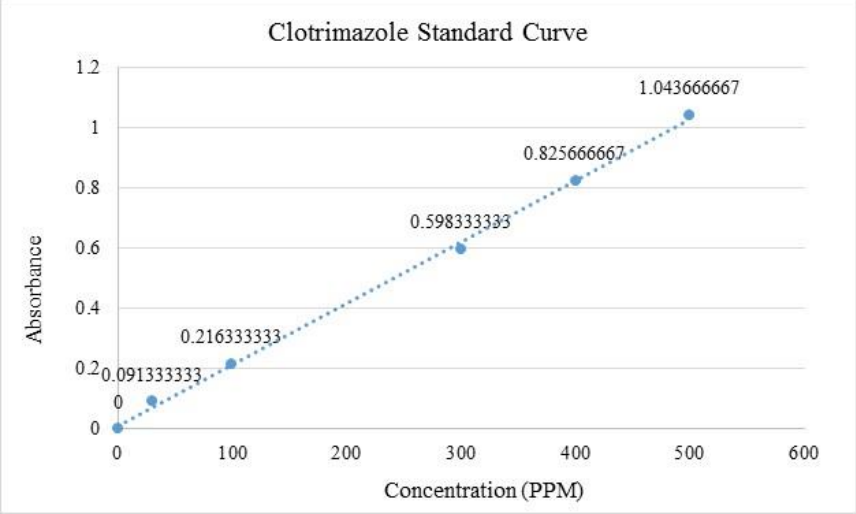

Figure 2. Calibration curve of Clotrimazole in solvent solution (50% Ethanol (99.8%) and 50% Phosphate buffer, pH 7.4).

3.6. Physical Appearance and pH

None of the formulations exhibited any unpleasant odor; all were homogeneous and uniform. The pH of all formulations ranged from 6.1 to 6.4.

3.7. Emulsion Type

It was observed that all emulgel formulations were easily washed off with water, indicating that the emulsions were of the O/W type. In the second method, where methylene blue was used, a blue color was observed in all formulations, further confirming that the emulsion type in the emulgels was o/w.

3.8. Mechanical Stability

Formulations 1, 2, 3, 7, 8, and 9 were completely stable, whereas formulations 4, 5, and 6 were separated into two phases and excluded from the study.

3.9. Thermal Stability Evaluation Using Heat–Cold Cycles

Formulations 1, 2, 3, 7, 8, and 9 were stable.

3.10. Viscosity Measurement

The viscosity values of the Clotrimazole emulgel formulations are presented in **table 2**. The viscosity of Clotrimazole emulgel formulations was measured at 25°C using a Brookfield viscometer (spindle 52).

Table 2. Viscosity of emulgel formulations.

Formulation Code	Viscosity (cp)
1	4835 ± 0.13
2	4565 ± 0.17
3	4352 ± 0.16
7	4075 ± 0.17
8	3865 ± 0.11
9	4135 ± 0.15

3.11. Drug Content

The drug content of the Clotrimazole emulgel formulations is presented in **table 3**.
The drug content ranged from 96% to 99%.

Table 3. Drug content of emulgel formulations.

Formulation Code	Drug Content
1	98%
2	99%
3	98%
7	97%
8	96%
9	99%

3.12. In Vitro Release

The in vitro drug release results of the Clotrimazole emulgel formulations are presented in **table 4**.
The percentage of drug released was calculated based on the actual measured drug content of each formulation.

Table 4. In vitro drug release of emulgel formulations.

Time (h)	F1	F2	F3	F7	F8	F9	Clotrimazole Cream
0.5	14.56%	13.87%	14.65%	15.92 %	15.12%	17.67%	13.67%
1	34.77%	33.89%	39.54%	32.66%	31.16%	24.86%	27.89%
2	45.56%	43.65%	47.34%	42.5%	49.51%	43.26%	34.65%
3	53.94%	50.98%	55.43%	50.73%	56.23%	59.37%	42.68%
4	65.33%	63.56%	63.98%	67.96%	62.18%	71.54%	55.56%
5	72.45%	68.56%	79.87%	83.26%	79.61%	82.18%	67.78%
6	81.43%	76.87%	85.56%	91.56%	87.89%	97.64%	71.11%

In vitro cumulative drug release (%) of Clotrimazole from emulgel formulations and a commercial Clotrimazole cream over 6 hours. Release was measured using the Franz diffusion cell method at 37°C and λmax = 260.8 nm.

3.13. Drug Release Kinetics

To determine the drug release mechanism of the optimized formulation (Formulation 9), the in vitro release data were fitted to various kinetic models, including zero-order, first-order, Higuchi, and Hixson-Crowell models. The corresponding regression coefficients (R^2) were 0.9934 for zero-order, 0.9157 for first-order, 0.9757 for Higuchi, and 0.9529 for the Hixson-Crowell model. Among these, the zero-order model showed the highest regression coefficient ($R^2 = 0.9934$), indicating that the drug release from formulation 9 follows a diffusion-controlled mechanism. These results support the conclusion that the zero-order model best describes the drug release kinetics of formulation 9.

3.14. Discussion

The present study provides valuable insight into the formulation and physicochemical characteristics of Clotrimazole emulgels. Unlike microemulsions and nanoemulsions, the developed emulgel formulations exhibited a characteristic milky appearance due to their colloidal nature and distinct from the clear or translucent appearance of smaller droplet systems. The pH values of the formulations fall within the physiologically acceptable range for topical applications (4.5–6.5), ensuring skin compatibility and minimizing the risk of irritation or sensitization. Mechanical stability testing using centrifugation revealed instability in formulations 4, 5, and 6. These formulations, all containing HPMC K4M as the sole gelling agent, lacked the mechanical robustness observed in other formulations, which aligns with previous reports indicating that the type of gelling agent significantly influences the structural consistency of semisolid formulations [١٤]. Although specific viscosity values for these formulations were not included, their observed instability is likely due to lower viscosity and the intrinsic rheological limitations of HPMC, which typically forms weaker gel networks compared to Carbomer 940. Formulations containing Carbomer 940 showed superior physical stability, likely due to their higher viscosity and more cohesive gel matrix. These findings highlight the critical influence of the type on mechanical stability. A study on fluconazole emulgels also demonstrated that the type of polymer had a more significant impact on physicochemical characteristics, drug release, antifungal activity, and formulation stability than other formulation variables, such as penetration enhancers[15]. Moreover, the results indicate that using Carbomer 940 in combination with HPMC K4M provides complementary advantages by combining the strong gel-forming ability of Carbomer with the good spreadability and film-forming properties of HPMC, thereby improving the texture, stability, and drug release characteristics of the resulting emulgels.

Drug release kinetics further highlighted the superior physico-chemical performance of formulation 9, which adhered to zero-order kinetics with a regression coefficient of 0.9934 Compared to a commercially available Clotrimazole cream (Pars Daroo), which released 71.11% of its drug content over six hours, all six emulgel formulations demonstrated significantly enhanced drug release. This highlights the potential of emulgels to enhance drug release, which is a key factor that can contribute to improved bioavailability in topical delivery systems.

The results indicate that the composition of the oil phase plays a critical role in drug release. Previous studies have demonstrated that Clotrimazole exhibits greater solubility in Isopropyl Myristate than Paraffin [16]. Consequently, formulation F9 released more drugs than formulations F8 and F7. A similar trend was observed with formulation F3, which showed higher drug release than F1 and F2, likely due to reduced Clotrimazole entrapment in the oil phase due to Paraffin inclusion. Isopropyl Myristate appears to facilitate drug diffusion by minimizing drug retention within the oil phase. Also, between formulations 7 and 8, formulation 8, which

contained a higher proportion of the oil phase, exhibited reduced drug release compared to formulation 7, reinforcing the inverse relationship between oil phase content and drug release efficiency. A similar trend was observed between formulations 1 and 2, where a lower oil phase content in formulation 1 resulted in superior drug release. Therefore, formulations containing higher concentrations of Isopropyl Myristate released less Clotrimazole, possibly due to increased drug entrapment in the oil phase or elevated viscosity, which may hinder diffusion. These observations warrant further investigation to clarify the underlying mechanisms. These findings align with prior studies on emulgels, such as research on Miconazole formulations, which demonstrated decreased drug release with increasing oil phase content [17]. An additional study has shown that the emulgel formulation of Chlorphenesin with a low concentration of liquid Paraffin and a high concentration of emulsifying agent emerged as the optimal formula, as it demonstrated the highest drug release and antifungal activity [18] Similarly, Popescu et al. reported that the selection of oil phase (Soybean oil vs. Fish oil) significantly affected droplet structure, physical stability, and drug release behavior in PEGylated nanoemulsions [19]. Collectively, these results emphasize the critical importance of oil phase selection and optimization in emulgel formulation design. The interplay between oil phase composition, drug solubility, and release kinetics should be a key consideration in developing emulgels for enhanced therapeutic outcomes.

Notably, all six formulations were stored at room temperature for six months and demonstrated complete physical and chemical stability during this period, supporting their potential for practical application.

While this study provides valuable insights into Clotrimazole emulgels, certain limitations should be acknowledged. The absence of in vivo or clinical evaluations limits the direct correlation of the findings with therapeutic outcomes. Additionally, due to time and resource constraints, the effect of oil quantity on liquid Paraffin remains unexplored. These aspects should be addressed in future studies.

4. Conclusion

Formulation 9, containing 5% Paraffin and a blend of Carbomer 940 and HPMC, demonstrated superior physico-chemical performance for Clotrimazole delivery as an emulgel. This formulation exhibited excellent mechanical stability, a skin-compatible pH, and enhanced drug release, aligning with the zero-order kinetic model ($R^2 = 0.9934$). The inclusion of Paraffin, compared to Isopropyl Myristate, enhanced drug release due to the lower solubility of Clotrimazole in Paraffin and the combination of Carbomer 940 and HPMC provided optimal viscosity, which ensured stability, ease of application, and controlled release. It has also been shown that increasing oil concentration increases the drug's loading capacity while its release decreases.

These findings suggest that emulgels hold promise as advanced topical delivery systems by combining the benefits of gels and emulsions. Compared to the tested commercial cream, the prepared formulations showed improved in vitro drug release, which may indicate better physico-chemical performance. While traditional formulations, like creams, can be greasy or cause staining, emulgels may offer a balanced alternative with favorable application properties.

List of Abbreviations Used in This Study

1. HPMC - Hydroxypropyl Methylcellulose
2. FT-IR - Fourier Transform Infrared Spectroscopy
3. UV - Ultraviolet
4. HLB - Hydrophilic-Lipophilic Balance
5. W/O - Water-in-Oil
6. O/W - Oil-in-Water
7. RPM - Revolutions Per Minute
8. KBr - Potassium Bromide
9. λmax - Maximum Absorption Wavelength
10. ppm - Parts Per Million
11. Span 80 - Sorbitan Monooleate
12. Tween 80 - Polysorbate 80

Conflict of Interest: NA

Data availability

All data generated or analyzed during this study are included in this published article.

Athors Contributions

Dorsa Bahrami Zanjanbar conceived and designed the study, collected and analyzed the data, and drafted the manuscript. Hasti Khalili contributed to data collection and literature review. Kimia Didehvar assisted in data analysis and manuscript editing. Alireza Dabirsiaghi supervised the project and provided critical revision of the manuscript. Majid Zandkarim contributed to the interpretation of results and final approval of the manuscript. All authors read and approved the final version of the manuscript.

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Using artificial intelligence chatbots

There was no use of artificial intelligence in the making of this article.

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