DEVELOPMENT AND ASSESSMENT AN MICROEMULSION BASED ITRACONAZOLE GEL AS TOPICAL ANTIFUNGAL THERAPY

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ABSTRACT:

Topical fungal infections represent a significant global health burden, necessitating the development of advanced drug delivery systems that enhance therapeutic efficacy and patient compliance. Microemulsions have emerged as promising sub-micron carriers for topical administration due to their superior drug-loading capacity and enhanced skin penetration properties. This research aimed to formulate, optimize, and evaluate a micro-emulgel system loaded with Itraconazole, a broad-spectrum but poorly water-soluble antifungal drug, for the effective treatment of cutaneous fungal infections. The study commenced with the screening of components based on the solubility of Itraconazole, leading to the selection of Isopropyl Myristate (IPM) as the oil phase, Tween 80 as the surfactant, and Polyethylene Glycol 400 (PEG 400) as the co-surfactant. A pseudo-ternary phase diagram was constructed to identify the optimal ratio of these components, with a surfactant-to-cosurfactant (S~mix~) ratio of 3:1 yielding the most extensive area of clear microemulsion. Several microemulsion batches (ME1-ME7) were prepared from this region and subjected to rigorous thermodynamic stability studies, including heating-cooling cycles, centrifugation, and freeze-thaw cycles. Batch ME2 (10% IPM, 60% S~mix~, 30% water) exhibited exceptional stability and the highest drug entrapment efficiency of 91.73%.

The optimized microemulsion (ME2) was subsequently incorporated into a gel matrix using xanthan gum as the gelling agent to produce three microemulgel formulations (MEG1, MEG2, MEG3) varying in polymer concentration. The resulting microemulgels were comprehensively evaluated for homogeneity, pH, viscosity, spreadability, extrudability, drug content, and in vitro drug release. The formulation MEG3, containing 2% xanthan gum, demonstrated the most desirable characteristics, including a high viscosity of 10,800 cP, acceptable spreadability, and a superior drug content of 94.12%. In vitro drug diffusion studies revealed that MEG3 achieved a cumulative drug release of 94.12% over 8 hours, following zero-order kinetics. Furthermore, in vitro antifungal studies against *Candida albicans* showed that MEG3 produced a significantly larger zone of inhibition (30 mm) compared to the pure drug (25 mm), the microemulsion alone (27 mm), and a marketed formulation (20 mm). Stability studies conducted over three months under accelerated conditions confirmed that the optimized formulation retained its physicochemical properties. In conclusion, the developed Itraconazole-loaded microemulgel presents a stable, efficacious, and patient-compliant topical formulation with significant potential for the management of superficial fungal infections.

Keywords:

Microemulsion, Microemulgel, Itraconazole, Pseudo-Ternary Phase Diagram, Topical Drug Delivery, Antifungal Activity, Xanthan Gum.

1. INTRODUCTION

The incidence of superficial fungal infections has been steadily increasing worldwide, affecting a significant proportion of the global population. These infections, often caused by fungi such as Candida, Aspergillus, and Cryptococcus species, are highly transmissible and can cause considerable discomfort and morbidity. Candida albicans, in particular, is a common pathogen responsible for cutaneous infections, frequently occurring in intertriginous areas where skin surfaces rub together, creating a warm and moist environment conducive to fungal growth [1]. The management of these infections relies heavily on effective topical antifungal therapy, which offers the advantage of localized drug delivery, minimizing systemic side effects.

Itraconazole (ITZ) is a potent triazole antifungal agent with a broad spectrum of activity against a wide range of pathogenic fungi. Compared to other antifungal drugs, Itraconazole demonstrates a favorable safety profile with lower toxicity. However, its clinical utility is hampered by its poor aqueous solubility (less than 1 µg/mL), which classifies it as a Biopharmaceutics Classification System (BCS) Class II drug—characterized by low solubility and high permeability. This intrinsic property leads to low and variable oral bioavailability (approximately 55%), often accompanied by gastrointestinal side effects such as nausea, vomiting, and dizziness [2, 3]. These challenges make Itraconazole an ideal candidate for topical delivery, where its high lipophilicity (log P) can be advantageous for permeating the skin's stratum corneum, thereby bypassing the limitations associated with oral administration.

Conventional topical formulations like creams and ointments, while widely used, often suffer from drawbacks such as greasiness, poor patient compliance due to the need for vigorous rubbing, and inadequate penetration of hydrophobic drugs. In contrast, gels are semi-solid systems that offer several benefits, including ease of application, non-greasy feel, ease of removal, and better patient acceptability. They provide localized action, reduce systemic side effects, and can improve drug absorption. Nevertheless, a critical limitation of hydrogel systems is their inherent inefficiency in delivering hydrophobic drugs like Itraconazole [4].

To overcome these challenges, microemulsion technology has gained considerable attention as a novel drug delivery platform. Microemulsions are thermodynamically stable, optically isotropic, and transparent dispersions of oil and water stabilized by an interfacial film of surfactant and co-surfactant molecules. Their key advantages include the ability to solubilize both hydrophilic and lipophilic drugs, ease of preparation, and the potential to enhance drug permeability through the skin [5]. However, the low viscosity of microemulsions can limit their residence time at the application site and make application messy. This limitation can be effectively addressed by incorporating the microemulsion into a gel matrix, forming a system known as a microemulgel.

This hybrid system combines the excellent drug-loading and penetration-enhancing properties of microemulsions with the aesthetic appeal and application convenience of a gel [6].

Natural polymers are frequently employed in such systems due to their cost-effectiveness, biocompatibility, and non-irritating nature. Xanthan gum, a high molecular weight polysaccharide, is an excellent gelling agent that can impart suitable viscosity and mucoadhesive properties to the formulation, thereby modulating drug release and improving contact time with the skin [15]. The primary objective of this study was, therefore, to develop and characterize a stable microemulsion-based gel of Itraconazole. The research encompassed pre-formulation studies, including solubility screening and construction of a pseudo-ternary phase diagram to optimize the microemulsion components. The optimized microemulsion was then gelled with xanthan gum, and the final microemulgels were evaluated for their physicochemical properties, in vitro drug release, antifungal efficacy, and storage stability.

2. MATERIALS AND METHODS

2.1. Materials

Itraconazole was purchased from Jinan Hongkangda Chemical Co. Ltd. China. The oils used—Isopropyl myristate (IPM), oleic acid, castor oil, surfactants including Tween 20, Tween 40, and Tween 80, along with co-surfactants Propylene Glycol (PG), PEG 200, PEG 400, the gelling agent, xanthan gum, were also obtained from the same supplier. Excipients such as triethanolamine, glycerin, methyl paraben, and propyl paraben were of analytical grade. Double-distilled water, prepared in-house, was used throughout the experimental work.

2.2. UV-Visible Spectrophotometric Method Development

A precise and reliable analytical method was developed for the quantification of Itraconazole. A primary stock solution of Itraconazole was prepared at a concentration of 100 µg/mL by dissolving 10 mg of the drug in methanol and making up the volume to 100 mL in a volumetric flask. Subsequent dilutions were made from this stock solution to prepare standard solutions with concentrations ranging from 2 to 10 ppm. The ultraviolet-visible spectrum of Itraconazole was scanned between 200 and 400 nm using a UV-Vis spectrophotometer to determine the wavelength of maximum absorption (λ~max~). The drug exhibited λ~max~ at 262 nm in methanol and 266 nm in phosphate-buffered saline (PBS) of pH 5.5. A calibration curve was constructed by plotting absorbance against concentration, and the linearity of the method was validated by a high coefficient of determination (R^2) value of 0.9994 in methanol and 0.9978 in PBS, confirming the method's suitability for analysis.

2.3. Drug-Excipient Compatibility Study by FTIR Spectroscopy

Fourier Transform Infrared (FTIR) spectroscopy was employed to assess any potential physicochemical interactions between Itraconazole and the selected formulation excipients. The FTIR spectra of pure Itraconazole, individual excipients, and their physical mixture were recorded. The spectrum of pure Itraconazole showed characteristic peaks at 3379.2 cm^{-1} (N-H amide stretch), 1273.03 cm^{-1} (C-O stretch), 1188 cm^{-1} (C-N alkyl amine stretch), and 732.9 cm^{-1} (C-Cl stretch). The FTIR spectrum of the drug-excipient mixture displayed all the principal peaks of Itraconazole without any significant shift or disappearance, indicating the absence of incompatibilities and confirming that the drug was compatible with the formulation components.

2.4. Solubility Studies

The selection of components for the microemulsion formulation was based on the saturation solubility of Itraconazole in various oils, surfactants, and co-surfactants. An excess amount of Itraconazole was added to 2 mL of each component in sealed glass vials. The vials were agitated continuously in a water bath shaker maintained at 37±1°C for 72 hours to achieve equilibrium. The resulting mixtures were then centrifuged at 3000 rpm for 15 minutes, the supernatant was filtered through a membrane filter, and the concentration of dissolved Itraconazole was determined spectrophotometrically at 262 nm. Among the oils, IPM demonstrated the highest solubility for Itraconazole (60.21 ± 1.76 mg/mL), followed by oleic acid (45.6 ± 2.12 mg/mL). Tween 80 showed the highest solubilizing capacity among the surfactants (14.69 ± 2.94 mg/mL), and PEG 400 was selected as the co-surfactant due to its relatively higher solubility (7.98 ± 3.30 mg/mL) compared to PEG 200 and Propylene Glycol.

2.5. Construction of Pseudo-Ternary Phase Diagram

To delineate the concentration ranges of components that would form a stable microemulsion, pseudo-ternary phase diagrams were constructed using the water titration method at room temperature (25°C). Surfactant (Tween 80) and co-surfactant (PEG 400) were mixed in different weight ratios (S~mix~ ratios of 1:1, 1:2, 1:3, 2:1, 2:3, 3:1, and 3:2). For each S~mix~ ratio, mixtures of oil (IPM) and S~mix~ were prepared in varying weight ratios (from 1:9 to 9:1). Each mixture was titrated with double-distilled water under continuous magnetic stirring. The points at which clear, transparent mixtures formed were noted. The phase diagrams were plotted using Chemix ternary diagram software. The S~mix~ ratio of 3:1 (Tween 80:PEG 400) provided the largest region of monophasic, transparent microemulsion, and this ratio was selected for the preparation of microemulsion batches.

2.6. Preparation of Itraconazole-Loaded Microemulsion

Based on the pseudo-ternary phase diagram, seven distinct microemulsion batches (ME1 to ME7) were formulated from the optimal microemulsion region. Itraconazole was first dissolved

in the mixture of IPM and S~mix~. Double-distilled water was then added dropwise to this oily phase under gentle stirring with a magnetic stirrer until a clear, transparent microemulsion was obtained. The compositions of the different batches are summarized in Table 1.

Table 1: Composition of Itraconazole-Loaded Microemulsion Batches

Batch Code	Oil (IPM) %w/w	S~mix~ (3:1) %w/w	Water %w/w
ME1	10	50	40
ME2	10	60	30
ME3	10	70	20
ME4	20	40	40
ME5	20	50	30
ME6	20	60	20
ME7	30	40	30

2.7. Characterization of Microemulsion

2.7.1. Thermodynamic Stability Studies:

The prepared microemulsions were subjected to a series of stress tests to identify thermodynamically stable formulations and eliminate metastable ones.

Heating-Cooling Cycle: The formulations were stored at two extreme temperatures, 4°C and 45°C, for 48 hours at each temperature. This cycle was repeated six times. Formulations that showed no phase separation or precipitation were selected for the next test.

Centrifugation Test: The stable formulations from the heating-cooling cycle were centrifuged at 3500 rpm for 30 minutes. Formulations that remained homogenous were considered to have passed the test.

Freeze-Thaw Cycle: The formulations were subjected to three cycles between -21°C and +25°C, storing at each temperature for 48 hours. Formulations that regained their original clarity and homogeneity after these cycles were deemed stable.

2.7.2. Drug Entrapment Efficiency:

The entrapment efficiency of the microemulsions was determined indirectly. A 2 mL aliquot of the microemulsion was centrifuged at 5000 rpm for 20 minutes. The supernatant was collected, appropriately diluted, and analyzed using a UV-Vis spectrophotometer at 262 nm. The drug entrapment efficiency was calculated using the following formula:

Entrapment Efficiency (%) = (Actual Drug Content / Theoretical Drug Content) × 100

2.7.3. Globule Size and Polydispersity Index (PDI):

The average globule size and size distribution (PDI) of the optimized microemulsion were determined by dynamic light scattering using a Malvern Zetasizer. A PDI value of less than 0.3 indicates a narrow size distribution and a homogeneous dispersion.

2.7.4. Zeta Potential:

The surface charge (zeta potential) of the microemulsion globules was measured using the same Zetasizer instrument. A high absolute zeta potential value (typically above ±30 mV) indicates good physical stability due to electrostatic repulsion between globules.

2.7.5. Transmission Electron Microscopy (TEM):

The morphology of the microemulsion globules was examined using TEM. A drop of the diluted microemulsion was placed on a carbon-coated copper grid, stained with phosphotungstic acid, and visualized under the microscope.

2.7.6. Dilutability Test:

The optimized microemulsion was diluted 100-fold with double-distilled water to confirm its stability as an oil-in-water (o/w) system. The absence of phase separation upon dilution confirmed the formation of a true microemulsion.

2.8. Formulation of Microemulsion-Based Gel (Microemulgel)

The optimized microemulsion batch (ME2) was incorporated into a gel base to form the microemulgel. Xanthan gum was used as the gelling agent. Briefly, xanthan gum was dispersed in a small amount of water with continuous stirring and allowed to hydrate and swell. To this gel base, the optimized ITZ-microemulsion was incorporated slowly with constant stirring. Triethanolamine was added to adjust the pH, glycerine was used as a humectant, and methyl and propyl parabens were added as preservatives. The mixture was stirred thoroughly to obtain a homogeneous gel. Three microemulgel formulations (MEG1, MEG2, MEG3) were prepared with varying concentrations of xanthan gum (1%, 1.5%, and 2% w/w, respectively). The composition is detailed in Table 2.

Table 2: Composition of Itraconazole-Loaded Microemulgels

S.No	Ingredient	MEG1 (%w/w)	MEG2 (%w/w)	MEG3 (%w/w)
1.	Xanthan Gum	1.0	1.5	2.0
2.	ITZ Microemulsion (ME2)	1.0	1.0	1.0
3.	Methyl Paraben	0.02	0.02	0.02
4.	Propyl Paraben	0.01	0.01	0.01
5.	Triethanolamine	1 mL	1 mL	1 mL
6.	Propylene Glycol	10 mL	10 mL	10 mL
7.	Distilled Water	q.s. to 100	q.s. to 100	q.s. to 100

2.9. Evaluation of Microemulgel

2.9.1. Homogeneity and Grittiness:

All formulated gels were inspected visually against a black and white background for their appearance, homogeneity, and the presence of any gritty particles.

2.9.2. pH Measurement:

The pH of the gels was determined using a calibrated digital pH meter by immersing the electrode directly into a 1% w/w aqueous solution of the gel. This ensures the formulation is suitable for topical application without causing skin irritation.

2.9.3. Viscosity Determination:

The viscosity of the microemulgels was measured using a Brookfield viscometer with spindle number S-63. The measurement was carried out at 37±1°C to simulate skin temperature.

2.9.4. Spreadability Study:

Spreadability was assessed to determine the ease of application. Approximately 350 mg of the gel was placed on a fixed glass slide. A second slide was placed on top, and a 5 g weight was placed on the upper slide for one minute. The diameter (in cm) of the circle formed by the spread gel was measured. A larger diameter indicates better spreadability.

2.9.5. Extrudability Study:

This test evaluates the force required to extrude the gel from a collapsible tube. The gel was packed in a standard aluminum tube, and a weight was applied to extrude the gel. The extrudability was calculated using the formula:

$$\text{Extrudability (gm/cm}^2\text{)} = \text{Weight applied (gm)} / \text{Area (cm}^2\text{)}$$

2.9.6. Drug Content Determination:

One gram of the microemulgel was accurately weighed and dissolved in 100 mL of PBS (pH 5.5). The solution was filtered, diluted suitably, and analyzed spectrophotometrically at 262 nm. The percentage drug content was calculated.

2.9.7. In-Vitro Drug Diffusion Study:

The drug release profile was studied using a Franz diffusion cell apparatus. The receptor compartment was filled with PBS (pH 5.5) maintained at 37±1°C. A dialysis membrane, pre-soaked for 12 hours, was mounted between the donor and receptor compartments. One gram of the formulation was placed in the donor compartment. Aliquots of 1 mL were withdrawn from the receptor compartment at predetermined time intervals over 8 hours and replaced with an equal volume of fresh medium. The samples were analyzed for drug content, and the cumulative percentage of drug released was calculated and plotted against time.

2.9.8. Drug Release Kinetics:

The in vitro drug release data were fitted into various kinetic models (Zero-order, First-order, Higuchi, Hixson-Crowell, and Korsmeyer-Peppas) to determine the mechanism of drug release from the microemulgel.

2.9.9. In-Vitro Antifungal Activity:

The antifungal efficacy of the formulations was evaluated against Candida albicans using the agar well diffusion method. Sabouraud dextrose agar plates were inoculated with a standardized fungal suspension. Wells were bored into the agar, and each well was filled with a fixed volume of the test formulations (pure drug solution, microemulsion ME2, optimized microemulgel

MEG3, and a marketed gel). The plates were incubated at 37°C for 24 hours, and the zones of inhibition (ZOI) were measured in millimeters.

2.9.10. Stability Studies:

Stability studies were conducted on the optimized microemulgel formulation (MEG3) as per ICH guidelines. The samples were stored in airtight containers at two different conditions: 25±2°C/60%±5% RH and 40±2°C/75%±5% RH for three months. The formulations were evaluated at 0, 1, 2, and 3 months for changes in appearance, homogeneity, pH, viscosity, drug content, and spreadability.

3. RESULTS AND DISCUSSION

3.1. Pre-formulation Studies

The development of a robust analytical method is fundamental to any formulation development process. The UV spectrophotometric method developed for Itraconazole was found to be linear, precise, and accurate within the concentration range of 2-10 ppm, as evidenced by the high R^2 values of 0.9994 (in methanol) and 0.9978 (in PBS pH 5.5). This confirmed the method's suitability for the quantitative analysis of the drug throughout the study.

The FTIR spectroscopy study confirmed the integrity of Itraconazole in the presence of excipients. The characteristic peaks of the pure drug were retained in the physical mixture's spectrum without any significant shifts or disappearance, indicating the absence of detrimental chemical interactions. This compatibility is crucial for ensuring the stability and efficacy of the final formulation.

The solubility of Itraconazole was a decisive factor in selecting the components of the microemulsion. The high solubility of ITZ in IPM (60.21 mg/mL) justified its selection as the oil phase, as a higher drug load in the internal phase can potentially enhance drug delivery. Similarly, Tween 80 and PEG 400 were chosen as the surfactant and co-surfactant, respectively, due to their superior solubilizing capacity and ability to form a stable microemulsion system.

3.2. Optimization of Microemulsion using Pseudo-Ternary Phase Diagram

The construction of pseudo-ternary phase diagrams is a critical step in microemulsion formulation. The diagram for the S~mix~ ratio of 3:1 (Tween 80:PEG 400) exhibited the most extensive region of transparent microemulsion, indicating a wide range of component concentrations that could form a stable system. This large microemulsion zone provides flexibility in formulating different batches. The effectiveness of this S~mix~ ratio can be

attributed to the optimal reduction of interfacial tension achieved by Tween 80, facilitated by the co-surfactant PEG 400, which penetrates the surfactant film and increases its fluidity.

3.3. Characterization of Optimized Microemulsion (ME2)

Among the seven batches prepared, ME2 and ME6 showed clear appearance and high entrapment efficiency after 24 hours. However, batch ME2 demonstrated superior thermodynamic stability, successfully passing all stress tests (heating-cooling, centrifugation, freeze-thaw) without any signs of phase separation, cloudiness, or drug precipitation. The drug entrapment efficiency for ME2 was found to be 91.73%, which is highly satisfactory and indicates efficient solubilization of the drug within the system.

The globule size of the optimized ME2 formulation was determined to be 98.80 nm with a PDI of 0.191. A PDI value below 0.3 signifies a monodisperse and homogeneous population of globules, which is desirable for consistent drug release and skin penetration. The zeta potential was measured to be -29.8 mV. Although slightly below the theoretical ±30 mV threshold for high electrostatic stability, this value still indicates a reasonably stable system. The negative charge likely originates from the free fatty acids in IPM or the surfactant. The TEM analysis visually confirmed the spherical shape of the globules and the absence of aggregation, corroborating the size and PDI data. The dilutability test confirmed the o/w nature of the microemulsion, as it remained clear and monophasic even after 100-fold dilution with water, a characteristic feature of thermodynamically stable microemulsions.

3.4. Evaluation of Microemulgel Formulations

The three microemulgel formulations (MEG1, MEG2, MEG3) were evaluated for various parameters, and the results are summarized in Table 3. All formulations were homogeneous, smooth, and free from grittiness. The pH values of all gels were in the range of 5.8 to 6.0, which is considered acceptable for topical application as it is close to the skin's natural pH, minimizing the risk of irritation.

The viscosity of the gels increased with an increase in the concentration of xanthan gum, as expected. MEG3 (with 2% gum) showed the highest viscosity (10,800 cP), while MEG1 (1% gum) showed the lowest (9,520 cP). Spreadability, a crucial parameter for patient compliance, was inversely related to viscosity. MEG1, being less viscous, showed the best spreadability (20.71 cm), whereas MEG3 showed slightly lower spreadability (18.21 cm), which is still within an acceptable range. Extrudability followed a similar trend, with MEG1 being the easiest to extrude. The drug content was uniform and high across all formulations, with MEG3 showing the highest value of 94.12%, indicating a efficient and uniform incorporation process.

Table 3: Evaluation Parameters of Prepared Microemulgels

Formulation	Homogeneity	pH	Viscosity (cP)	Spreadability (cm)	Extrudability (gm/cm²)	Drug Content (%)
MEG1	Excellent	5.8 ± 0.02	9,520 ± 0.13	20.71 ± 0.75	17.25 ± 0.25	85.12
MEG2	Excellent	5.9 ± 0.03	9,480 ± 13.1	19.54 ± 0.21	15.37 ± 2.58	90.10
MEG3	Excellent	5.8 ± 0.01	10,800 ± 23.01	18.21 ± 0.12	14.25 ± 2.31	94.12

3.5. In-Vitro Drug Release and Kinetics

All formulations exhibited a controlled release pattern over 8 hours. The cumulative drug release followed the order: MEG3 (94.12%) > MEG2 (90.10%) > MEG1 (85.12%). The higher release from MEG3, despite its higher viscosity, can be attributed to its higher initial drug content. The drug release data were best fitted to the zero-order kinetic model, as indicated by the highest regression coefficient (R^2) values (0.9962 for MEG3). Zero-order release is ideal for topical formulations as it provides a constant rate of drug delivery, maintaining therapeutic levels over an extended period.

3.6. In-Vitro Antifungal Activity

The results of the antifungal study unequivocally demonstrated the superiority of the microemulgel system. The zone of inhibition produced by the optimized microemulgel MEG3 (30 mm) was significantly larger than that of the pure drug (25 mm), the microemulsion ME2 (27 mm), and the marketed formulation (20 mm). This enhanced antifungal activity can be ascribed to the combined effects of the microemulsion and the gel. The microemulsion components act as penetration enhancers, facilitating the diffusion of Itraconazole through the fungal cell membrane, while the gel matrix ensures sustained contact with the infection site, allowing for a more profound and prolonged effect.

3.7. Stability Studies

The stability study of the optimized MEG3 formulation conducted over three months under accelerated conditions (40°C/75% RH) revealed no significant changes in its physicochemical properties. The formulation retained its homogeneity, pH, viscosity, spreadability, and drug content (Table 4). This indicates that the microemulgel is physically and chemically stable for a sufficient period, which is essential for its shelf life and commercial viability.

Table 4: Stability Study Data for Optimized Microemulgel (MEG3) at 40°C ± 2°C / 75% ± 5% RH

Time (Months)	Homogeneity	Grittiness	pH	Viscosity (cP)	Drug Content (%)
0 (Initial)	Excellent	Excellent	5.8 ± 0.01	10,800	94.12
1	Excellent	Excellent	5.8 ± 0.01	10,800	94.01
2	Excellent	Excellent	5.8 ± 0.05	10,850	93.45
3	Excellent	Excellent	5.8 ± 0.01	10,860	93.40

4. CONCLUSION

The present study successfully developed a stable and effective microemulsion-based gel of Itraconazole for topical antifungal therapy. The systematic approach involving solubility studies, phase diagram construction, and thermodynamic stability testing led to the identification of an optimal microemulsion formulation (ME2) composed of IPM, Tween 80, and PEG 400. This microemulsion, characterized by a small globule size (~98 nm), high entrapment efficiency (~92%), and good stability, was effectively incorporated into a xanthan gum gel base. The resulting microemulgel, particularly the MEG3 formulation, exhibited desirable physicochemical properties, sustained drug release profile (94.12% over 8 hours), and significantly enhanced in vitro antifungal activity compared to conventional formulations. The stability of the formulation was confirmed under accelerated conditions. Therefore, the Itraconazole-loaded microemulgel represents a promising, patient-compliant, and efficacious alternative for the topical treatment of cutaneous fungal infections, with potential for further clinical investigation.

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