



## Preparation and Evaluation of Ketoconazole Emulgel Using Isopropyl Myristate

Mrs. Begino Christophel. V<sup>1\*</sup>, Dr. V.S. Chandrasekaran<sup>2</sup>, Dr. M. Venkatesan<sup>3</sup>

<sup>1</sup>Student, Department of Pharmaceutics, JKKN College of Pharmacy, Kumarapalayam – 638 183, Tamil Nadu. India.

<sup>2</sup>Associate Professor, JKKN College of Pharmacy, Kumarapalayam – 638 183, Tamil Nadu. India.

<sup>3</sup>Principal, JKKN College of Pharmacy, Kumarapalayam – 638 183, Tamil Nadu. India.

Received: 27 December 2025

Revised: 10 January 2026

Accepted: 29 January 2026

### ABSTRACT

Ketoconazole is broad-spectrum anti-fungal drug, but due to its low aqueous solubility, its bioavailability is limited when used topically. The main objective of the current study was to formulate and characterize a microemulsion-based gel (microemulgel) loaded with ketoconazole to improve its solubilization, topical compatibility, and release characteristics for the treatment of cutaneous fungal infections. Microemulsion formulations were developed using pseudo-ternary phase diagrams with isopropyl myristate (IPM) as the oil component, Tween 80 and PEG 400 as the surfactant and co-surfactant, and water as the aqueous component. The optimized microemulsion was then formulated into a gel base using xanthan gum to improve topical applicability. The microemulsion formulation developed greatly improved the solubilization capacity of the hydrophobic ketoconazole, ensuring its uniform distribution in the formulation. The characterization studies showed a mean globule size of 146.9 nm with a polydispersity index of 0.210, which is an indication of the stability and homogeneity of the formulation. Among the batches analyzed, ME2 was found to be the optimized formulation based on physicochemical and in vitro analysis. The microemulgel exhibited a better release profile than the already available ketoconazole preparation in the market, and it was also established to be non-irritant, which justifies its application as a topical agent. In general, the findings indicate that the prepared ketoconazole microemulgel is an affordable, stable, and effective topical delivery system, which can reduce the needed dose and lead to the improved performance of the therapy. The gel preparation, which is made by microemulsion is an innovation that can be used to improve the topical antifungal therapy.

**Keywords:** Ketoconazole, Microemulgel, Isopropyl myristate, Topical drug delivery and Antifungal therapy.

### INTRODUCTION

Keratin fungus of the skin is a major health problem in the world with millions of cases reported to occur in different parts of the world.<sup>[1]</sup> Dermatophytes, yeasts, and molds are the most common causes of these infections resulting in such conditions as candidiasis, tinea infections, and seborrheic dermatitis.<sup>[2]</sup> The use of topical antifungal therapy is the treatment of choice of cutaneous fungus as it has a local effect, less systemic exposure, and enhances patient compliance.<sup>[3]</sup> Ketoconazole is a broad-spectrum imidazole derivative widely used in the treatment of the superficial mycoses, and is one of the available antifungal agents. Nevertheless, its low aqueous solubility and low skin penetration limit its therapeutic effectiveness in situations where conventional topical dosage forms are used.<sup>[4]</sup> Conventional topical preparations like creams, ointments, and gels do not necessarily lead to sufficient drug penetration into the deeper skin dermis and epidermis, which leads to poor antifungal efficacy and frequent dosage of such topical preparations.<sup>[5]</sup> As such, an increasing interest in the field of sophisticated drug delivery systems, which can enhance solubilization, stability, and penetration of poorly water-soluble drugs into the dermis, is emerging. Against this backdrop, microemulsion-based format of drug deliveries has attracted a lot of interests with respect to thermodynamic stability, large drug-loading capacity, and capability of increasing skin permeation. Microemulsions are transparent and isotropic systems, which consist of oil, co-surfactant, surfactant and aqueous phase and are organized into nanosized droplets that promote the diffusion of drugs throughout the stratum corneum easier.<sup>[6]</sup> Although these have benefits, conventional microemulsions have low viscosity and this restricts the direct use to the skin.<sup>[7]</sup> In order to address this weakness, addition of microemulsions to an adequate gel base leads to a microemulgel, which incorporates the penetration-enhancing qualities of microemulsions, with the rheological and patient-friendly attributes of gels. Microemulgels have an enhanced spreadability, increased time of residence on the application site, enhanced stability and high patient acceptability, and thus the best carriers in case of the antifungal topical therapy.<sup>[8]</sup> Isopropyl myristate (IPM) is extensively used as a topical oil phase in topical applications since the compound has good solubilizing abilities and skin penetrating properties.<sup>[9,10]</sup> Likewise, two non-ionic surfactant and co-surfactant with similar properties are Tween 80 and PEG 400, which is biocompatible with good ability to form stable microemulsion systems. Xanthan gum as a gelling agent also leads to



maintaining stability in the formulation and appropriate viscosity to be used topically.<sup>[11]</sup> In the current research, the effort was put in developing, optimizing, and assessing ketoconazole-loaded microemulgel in the presence of isopropyl myristate as an oil. The pseudo-ternary phase diagrams were used to determine the microemulsion area and formulation optimization. The ready formulations were compared based on physicochemical characteristics, the size of globules, the release of drugs, and their ability to produce irritation on the skin. This work was aimed at coming up with a cost-effective, stable, and efficient topical delivery system that would promote the therapeutic action of ketoconazole in the management of cutaneous fungal infections.

## Materials and Methods

### Materials

The gift sample of ketoconazole was received at Dhamtec Pharm, Mumbai, India. Isopropyl myristate (IPM) was bought at BRM Chemicals. Oleic acid, castor oil, Tween 20, Tween 40, Tween 80, propylene glycol, PEG 200 and PEG 400 were purchased in Research Lab, Fine Chem Industries (Mumbai, India). The source of Xanthan gum was Pioneer Chemical Mart Pvt. Ltd. Double-distilled water was applied during the study. The rest of the chemicals and solvents used were of analytical grade.

### Methods

#### Formulation Design of Ketoconazole-Loaded Microemulsion

##### Selection of Oil

The oil stage is important in solubilizing lipophilic drugs and affected drug release and skin permeation. Ketoconazole (KT) is very lipophilic and thus needs an oil with a high solubilization capacity. KT solubility in various oils was assessed and isopropyl myristate (IPM) had better solubility than other oils that were tested. As well, IPM is a popular skin penetration enhancer that has low toxicity, high stability, and high compatibility with nonionic surfactants, which is why it is the right choice of oil phase.

##### Selection of Surfactant

Surfactants decrease the interfacial tension and enable stable suspension of microemulsions to form. The high hydrophilic-lipophilic balance (HLB) surfactants (HLB above 10) are preferred when developing the oil-in-water (O/W) microemulsion. Polysorbate 80 also known as tween 80 with an HLB value of about 15 was chosen because it is an effective emulsifier of IPM, is biocompatible, has minimal irritation potential, and has been reported to be used in topical microemulsion systems.

##### Selection of Co-surfactant

Co-surfactant is also needed to lower the interfacial free energy further and augment the plasticity of the interfacial movie. The different co-surfactants have been tested along with Tween 80 and PEG 400 has been chosen due to its synergistic activity, enhancement of oil solubilization and expansion of the micro emulsion area. The reason behind the Smix ratio of 3:1 (Tween 80:PEG 400) being selected was that it formed a clear, stable, and transparent microemulsion at a high drug-loading capacity.

##### Preparation of Ketoconazole-Loaded Microemulsion

According to the pseudo-ternary phase diagram research, the Smix ratio with the highest microemulsion area was chosen. Ketoconazole was dissolved in IPM and Smix mixture, and seven various formulations were made on the basis of this region. A magnetic stirrer (Remi, India) was used to stir the mixtures at room temperature, then, the solution of the water in the mixture was added dropwise up to the point at which a clear and transparent microemulsion was created. The formulations were stirred to achieve equilibrium further of 15-20 min and kept at room temperature. Table No:1 gives the composition of the formulations.



**Table No.1: FORMULATION DESIGN OF KT-LOADED MICROEMULSION**

Batch code	Oil (IPM)	Smix (3:1) (Tween80:PEG 400)	Water
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

### Formulation of Microemulsion-Based Gel

In the preparation of ketoconazole microemulgel, the optimized ketoconazole microemulsion was added to a hydrogel base. Xanthan gum has been used as the gelling agent. The necessary weight of xanthan gum was weighted precisely and mixed in the distilled water with constant stirring and left to soak thoroughly. Triethanolamine was dropwise put in the base of the system and this neutralized to give a clear gel, which was hydrated. Glycerin was also added to enhance the gel consistency with methyl paraben and propyl paraben being the preservatives. The resulting ketoconazole microemulsion was gently stirred into the transparent gel base to come up with the final ketoconazole microemulgel formulation.

**Table No.2: FORMULATION MICROEMULSION-BASED GEL**

S.NO	INGREDIENTS	ME1	ME2	ME3
1	Xanthan gum	1%	1.50%	2%
2	Microemulsion containing KT	1%	1%	1%
3	Methylparaben	0.02	0.02	0.02
4	Propylparaben	0.01	0.01	0.01
5	Triethanolamine	1 mL	1 mL	1 mL

### Evaluation of Emulgels

#### Physical Examination

The optimized emulgel is also visually analysed based on colour, homogeneity and consistency. The preparations were checked to make sure that there was no phase separation or grittiness.

#### pH Determination

The digital pH meter was calibrated and used to measure the pH of the emulgel formulations. The correct weight of emulgel 1 g was added to 100 mL of distilled water and the pH was measured at the room temperature. Each measurement was done thrice and the average was presented.

#### Viscosity Measurement

Brookfield synchro-electric viscometer (Model RVT) with a spindle D was used to measure the viscosity of the emulgel formulations. The samples of emulgel were placed into appropriate containers and spindle was placed vertically in the sample towards the bottom of the container. The rheological behavior of the formulations was tested by taking measurements of viscosity at the increasing shear rate of 0.5, 1, 2.5 and 5 rpm. Four rotational speeds were used and the forward dial readings and reverse dial readings were taken and the average value determined. The viscosity value was calculated by multiplying the mean dial value with the relevant factor given under Brookfield viscometer calibration chart.

#### Spreadability

Glass slide method was used to determine the spreadability of the emulgel formulations. The slide was a ground glass slide (20 cm long) firmly held against a flat surface, about 1 g of emulgel was put on the slide. A 500 g weight was then added on top and left to rest 5 min to eliminate entrained air and also to ensure a good uniform film of the emulgel was formed between the slides. A 50g



weight was then attached to the upper slide and the time taken to cover a distance of 7cm was measured. A reduced time meant that the emulgel was spreadable better.

### **Extrudability**

The extrudability was measured to measure how hard it was to extrude the emulgel out of a collapsible tube. This was placed in an aluminium collapsible tube and the weight added by piling a known weight on the formulation. The extrusion of the emulgel and area covered were measured and the extrudability was calculated.

### **Determination of $\lambda_{max}$ by UV-Visible Spectrophotometry**

The ketoconazole standard stock was made by dissolving 10 mg of the substance in 100 ml of methanol and incubating it with 15 min of sonication to transform the solution into a clear one. Methanol was added to the volume up to the mark to ensure the final concentration of 100  $\mu\text{g}/\text{mL}$ . Based on this stock solution, 1 mL was diluted in 10 mL with methanol to form a 10  $\mu\text{g}/\text{mL}$  solution that was scanned through 200-400 nm range with the use of the UV-visible spectrophotometer (Jasco V-630, Japan) to identify the  $\lambda_{max}$ .<sup>[12]</sup>

### **UV-Visible Spectrophotometric Analysis and Calibration Curve**

Ketoconazole plant extracts (100  $\mu\text{g}/\text{mL}$ ) were obtained in methanol and phosphate buffer (pH 5.5) separately. Concentrations of 2, 4, 6, 8 and 10  $\mu\text{g}/\text{mL}$  aliquots of the stock solution were prepared by adding methanol to the solution. A UV-visible spectrophotometer was used to measure the absorbance of every dilution at the  $\lambda_{max}$  (204 nm) of the experiment. Measurements were done three times each and a calibration curve was built to determine the linearity.

### **FTIR Spectroscopy**

Fourier Transform Infrared (FTIR) spectroscopy was used to assess the compatibility of the ketoconazole with the excipients that were chosen. The FTIR spectra of pure drug, excipients, and physical mixture at the individual level were taken. All the samples were combined with potassium bromide (KBr) in 1:100 ratio, pelletized and scanned between the 4000-400  $\text{cm}^{-1}$ . The spectra were matched with the view of determining any possible drug-excipient interactions.<sup>[13]</sup>

### **Determination of Percentage Drug Content**

The content of the drug was measured by weighing 1g of drug-loaded emulgel accurately and dissolving it in phosphate buffer solution (PBS, pH 5.5). A suitable filtration of the solution was done and appropriate dilutions were made. The ketoconazole was measured using UV-visible spectrophotometer (Shimadzu UV-1800) at a wavelength of 204 nm. Each of the measurements was in triplicate.

### **In-Vitro Drug Diffusion Release Study**

The diffusion profile of drugs in egg membrane diffusion cells was used to determine the diffusion studies of the ketoconazole microemulgel formulations in-vitro. The diffusion cell was mounted with the donor and the receptor compartments in between which the egg membrane was fixed. Phosphate buffer solution (PBS, pH 5.5) was poured in the receptor compartment and was used as a diffusion medium. A circulating water jacket was used to maintain the temperature of the receptor medium at  $37 \pm 1$  degC during the experiment and the medium stirred at all times to achieve a uniform distribution.

In the donor compartment, about 1 g of the emulgel formulation was put. To ensure that sink conditions were maintained, 1 mL samples were removed at a set time interval in the receptor compartment and replaced with 1 mL of fresh pre-warmed PBS. The withdrawn samples were then appropriately diluted and analyzed in a UV-visible spectrophotometer at the common wavelength  $\lambda_{max}$  and fresh receptor medium was used as a blank. The total ketoconazole that was emitted after every time was determined with the help of a previously constructed calibration curve.<sup>[14,15]</sup>

### **Skin Irritation Study**

As per the acceptable ethical standards, the irritation potential of the optimized emulgel formulation was tested by means of a standard irritation test on animal or human skin models. The formulation received an evaluation on erythema and edema and the outcome was compared with a control.



## Stability Studies

The optimized microemulsion-based gel formulation was allowed to undergo stability studies over a three-month time duration in various storage conditions. According to ICH guidelines, the formulations were stored in  $25 \pm 2^\circ\text{C}/60 \pm 5\% \text{RH}$  and  $40 \pm 2^\circ\text{C}/75 \pm 5\% \text{RH}$ . The formulations were tested in terms of color, grittiness, spreadability, pH and drug content at the end of 1, 2 and 3 months to determine their physical and chemical stability.<sup>[16]</sup>

## RESULTS AND DISCUSSION:

### Pre-formulation Studies of Ketoconazole

#### Organoleptic Properties

Ketoconazole was also tested regarding its organoleptic properties such as color, odor, appearance, and pH. The substance was found to be white, odorless, and crystalline with a neutral pH (7), which is associated with a description of pure ketoconazole. These properties show the lack of visible impurities and prove the possibility of further formulation work.

#### Melting Point

The capillary method took the melting point as  $148.6^\circ\text{C}$  which is within the range of reported  $148\text{--}152^\circ\text{C}$ . This establishes whether the drug is pure or not.

#### UV Spectroscopic Identification

Analysis in methanol using a UV spectroscopic had a maximum absorbance ( $\lambda_{\text{max}}$ ) of 204 nm, with the same reported values of ketoconazole. This peak of absorption was further analyzed quantitatively utilizing this characteristic absorption peak.

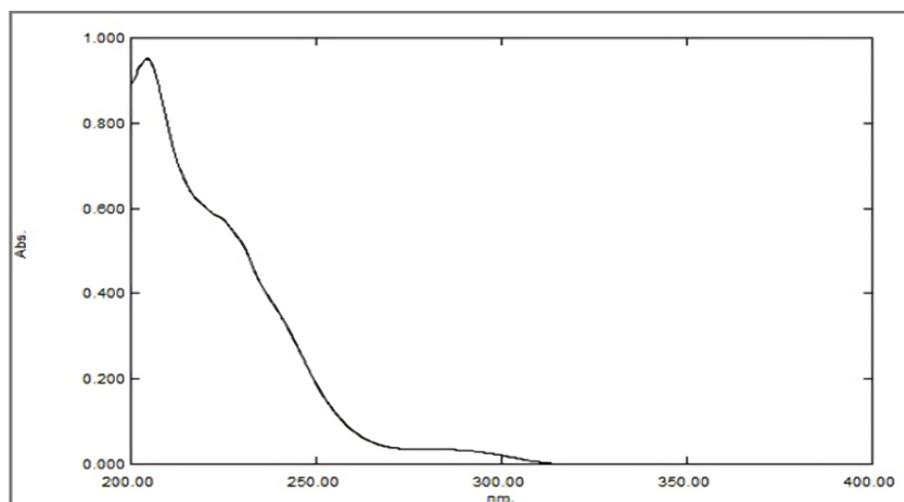


Figure No.1:  $\lambda_{\text{max}}$  Scan of Ketoconazole

#### Calibration Curve of Ketoconazole

In a range of 10-50  $\mu\text{g/mL}$ , a calibration curve was developed in methanol at a wavelength of 204 nm. The plot was well linear in terms of correlation coefficient  $R^2 = 0.9955$  thus this value proved Beer-Lamberts law adherence within this range.



Table No.3: Calibration Data of Ketoconazole

S.No	Concentration (µg/mL)	Absorbance
1	0	0
2	10	0.093
3	20	0.189
4	30	0.29
5	40	0.427
6	50	0.501

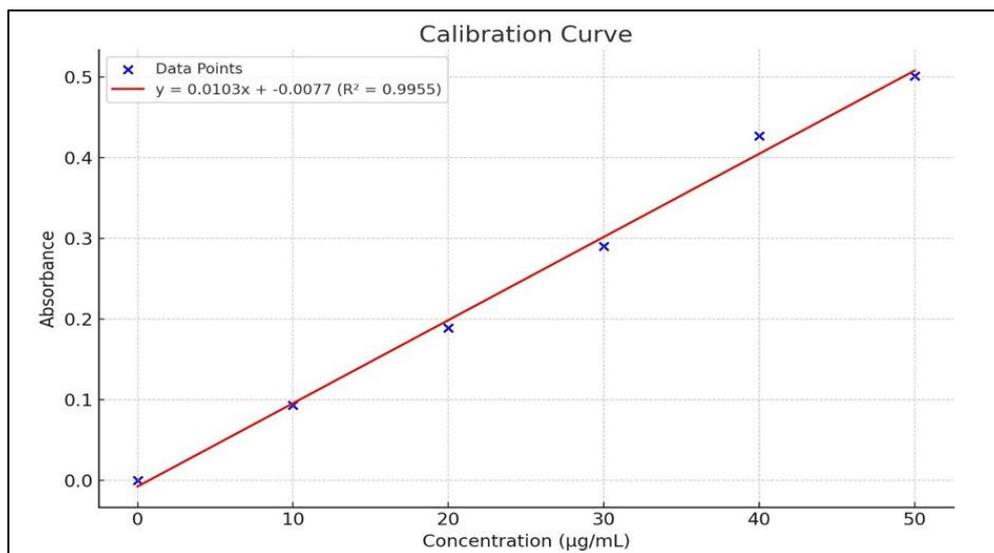


Figure No.2: Standard curve for Ketoconazole

### Solubility Studies

The solubility screening was used to determine the appropriate ingredients to use in the microemulsion product of ketoconazole. Of all the tested oils, ketoconazole had the best solubility in isopropyl myristate (IPM) (60.21 ± 1.76 mg/mL), then oleic acid and the lowest solubility was recorded in olive oil; hence, IPM was chosen as the oil phase because it was the most solubilizing agent. With the example of surfactants, Tween 80 exhibited the best solubility of the drug, with the use of co-surfactants, PEG 400 was found to be highly solubilizing than PEG 200 and propylene glycol. The choice of Tween 80 and PEG 400 to develop microemulsions was based on the findings, because these two substances have greater solubilization capability and can ensure better drug loading and lower the chances of drug precipitation in the final formulation.

### Pseudo-Ternary Phase Diagram

IPM (oil), Tween 80 (surfactant), PEG 400 (co-surfactant) and water were used to construct pseudo ternary phase diagrams. The Smix ratios tested 3:1 (Tween 80:PEG 400) formed the biggest transparent microemulsion area, which signifies the highest emulsification efficiency and area.

Table No.4: Effect of Smix Ratio on Microemulsion Region

Smix Ratio	Microemulsion Region	Relative Size
1:1	Small	Least
1:2	Moderate	Small
1:3	Moderate	Medium
2:1	Moderate	Medium
2:3	Moderate	Medium
3:1	Largest	Highest

Thus, Smix (3:1) was selected for formulation optimization.

### Drug–Excipient Compatibility (FTIR)

The FTIR spectroscopy was determined as the drug-excipient compatibility of ketoconazole. The chemical structure of ketoconazole was confirmed by the spectrum of pure ketoconazole which revealed characteristic peaks in C=O stretching (1643-1698 cm<sup>-1</sup>), aromatic C=C stretching (1584-1512 cm<sup>-1</sup>), C-N stretching (1222-1033 cm<sup>-1</sup>), C-Cl stretching (817-790 cm<sup>-1</sup>) and =C H stretching at 3119 cm<sup>-1</sup>. These unique peaks were maintained in the FTIR spectrum of the physical mixture of ketoconazole and the chosen excipients and there was neither any significant shift, disappearance, or creation of new peaks. This shows that chemical reactions do not occur and proves that ketoconazole is compatible with isopropyl myristate (IPM), Tween 80, as well as PEG 400, to be used in formulation development.

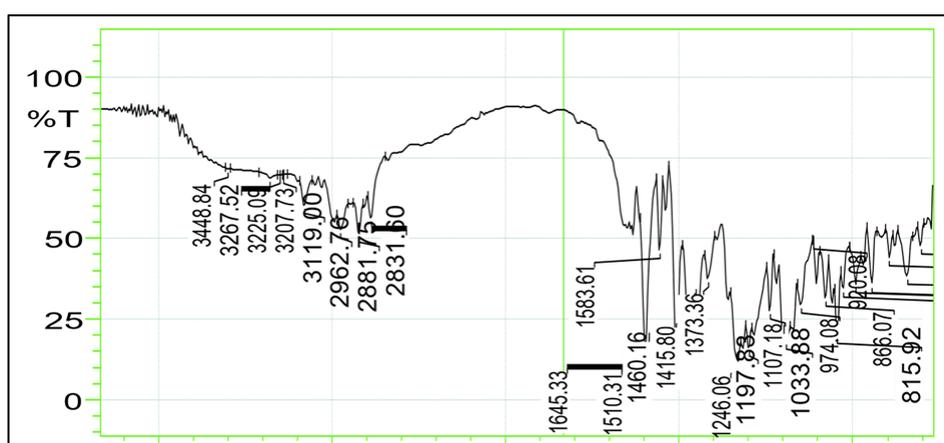


Figure No.3: FTIR Image Of Pure Ketoconazole

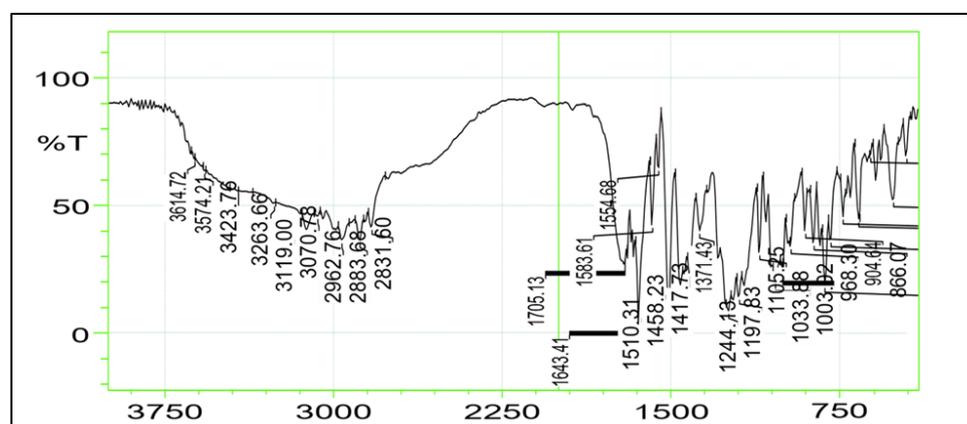


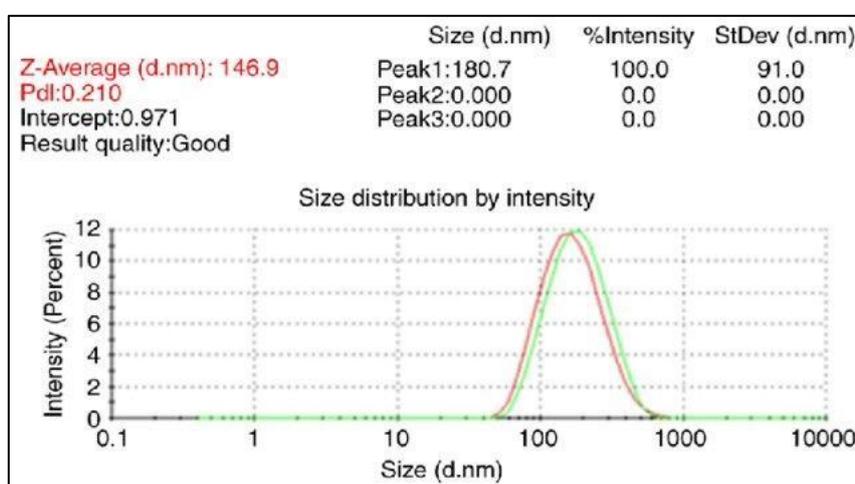
Figure No.4: FTIR Image Of Physical Mixture Ketoconazole

### Evaluation of Microemulsion

Thermodynamic stability, entrapment efficiency, and size distribution of the globules in the prepared batches of the microemulsions were assessed to determine the optimized microemulsion formulation. Out of the seven batches, ME2 and ME6 showed good stability during heating cooling cycles, centrifugation and freeze thaw experiments although ME2 showed better stability which did not appear in any of the stress conditions as ME2 neither showed any phase separation nor any instability. The efficiency of the entrapment of the formulations ranged between 73.82% and 91.73% with the maximum values of 91.73 and 90.31 of ME2 and ME6 respectively as well as the good appearance of the formulations, suggesting that the drug is incorporated effectively within the microemulsions system. Moreover, the optimized batch ME2 had a mean globule size of 146.9 nm and polydispersity index (PDI) of 0.210 indicating a strong homogeneity and narrow droplet size distribution. This nano-sized globules and low PDI value are all indications that a stable and uniform microemulsion was formed to achieve improved topical drug delivery.

**Table No.5: Evaluation of Microemulsion Batches**

Batch Code	Heating–Cooling Cycle	Centrifugation Test	Freeze–Thaw Cycle	Appearance After 24 h	Entrapment Efficiency (%)
ME1	✓	×	×	Hazy	84.65
ME2	✓	✓	✓	Clear	91.73
ME3	✓	×	×	Hazy	78.4
ME4	×	×	×	Hazy	82.41
ME5	✓	×	×	Hazy	87.18
ME6	✓	✓	×	Clear	90.31
ME7	×	×	×	Hazy	73.82



**Figure No.5: Globule Size and PDI**

### Evaluation Parameters of Microemulsion Gel

#### 1. Physical Appearance

The emulgel preparations were all noted to be viscous, creamy preparations due to their smooth homogeneous texture as well as a glossy appearance. Each formulation was tested in the white and black background, and discoloration was not observed or phase separation. Topical application was also evaluated to check consistency which was to spread evenly and have a good feel on the skin.

#### 2. pH Determination

The pH of the made emulgel preparations was determined by a calibrated pH meter. The pH of all formulation was between 5.7-6.1, which is deemed to be ideal in topical application and reduces the chances of skin irritation.

#### 3. Rheological Study

Brookfield DV-E viscometer was used to measure the viscosity of the emulgel formulations. The values of viscosity were found to be between 9520 and 10,800 cps, which implies a sufficient consistency to be used topically. It was found out that with increasing concentration of the gelling agent, it increased in viscosity and this indicated that the formulations could be controlled rheologically.



#### 4. Spreadability

The emulgel formulations were observed to have a spreadability of between 18.21-20.71, which was good spreading behavior. MEG2 had a relatively low spreadability compared to the tested formulations, which can result in a better localized retention and targeted site of application therapy.

#### 5. Drug Content Determination

The drug content of the emulgel formulations was measured using a UV-visible spectrophotometer and the wavelength measured between the wavelengths of 200 to 400 nm. The drug content was between 85.12-94.12 percent showing that the drugs were evenly distributed in the formulations. MEG2 showed the most content to drugs than MEG1 and MEG3.

#### 6. Dilutability Test

The microemulsion batch ME2 that was optimized was diluted with distilled water in a 1:100 proportion and visually analyzed in terms of clarity and phase separation. There was no observed phase separation and this proved the oil-in-water (O/W) character of the microemulsion system.

**Table No.6: Evaluation of Ketoconazole Emulgel Formulations**

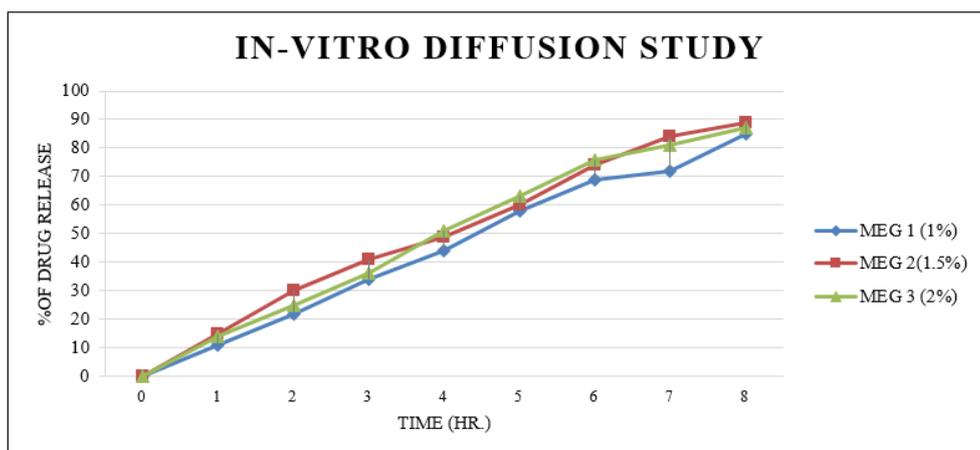
S.No	Parameter	MEG1	MEG2	MEG3
1	Physical Appearance	Smooth, homogeneous, glossy	Smooth, homogeneous, glossy	Smooth, homogeneous, glossy
2	pH ( $\pm$ SD, n=3)	6.1 $\pm$ 0.10	5.9 $\pm$ 0.15	5.7 $\pm$ 0.35
3	Viscosity (cps $\pm$ SD, n=3)	9520 $\pm$ 0.13	9480 $\pm$ 13.1	10800 $\pm$ 23.01
4	Spreadability (g·cm/sec $\pm$ SD)	18.21 $\pm$ 0.12	20.71 $\pm$ 0.75	19.54 $\pm$ 0.21
5	Drug Content (%)	85.12	94.12	90.12
6	Dilutability (ME2)	—	No phase separation (o/w)	—

#### In-Vitro Diffusion Study

The ketoconazole microemulgel formulations that were prepared were investigated in the in-vitro test that is a drug release examination using an egg membrane diffusion cell apparatus. Phosphate buffer (pH 5.5) was used as the diffusion medium to expose the study to release conditions over a period of 8 hours. The cumulative data of drug release indicated the release rate as MEG2, MEG3 and MEG1 respectively. MEG2 had the best drug release among all other formulations and this could be explained by the fact that it had an optimized microemulsion formulation, reduced globule size and enhanced drug solubilization. Each of the formulations exhibited a regulated and prolonged drug release profile throughout the study period, which showed their applicability in the topical treatment of antifungal therapy.

**Table No.7: IN-VITRO DIFFUSION STUDY**

Time (hr.)	MEG 1 (1%)	MEG 2(1.5%)	MEG 3 (2%)
0	0	0	0
1	11	15	14
2	22	30	25
3	34	41	36
4	44	49	51
5	58	60	63
6	69	74	76
7	72	84	81
8	85	89	87



### Thermodynamic Stability of Microemulsion Batches

Stress tests with regard to thermodynamic stability of the prepared microemulsion batches were done to test the strength of these batches in stress conditions. According to visual inspection with a phase separation when storing, ME2 and ME6 were determined to be stable formulations as compared to other batches (ME1, ME3, ME4, ME5, and ME7). These chosen batches were also subjected to heating cooling, centrifugation and freeze-thaw tests. The ME2 was the most stable of them, and it was able to survive all stress conditions without any phase separation or instability. As such, ME2 was deemed to be the most stable and viable batch to be further formulated to emulgel.

### Stability Study Results

The microemulsion gel formulation MEG2 that was optimized was stable both physically and chemically during the three months period of stability study. Homogeneity and grittiness were not altered, which means that there were no signs of poor physical integrity of the formulation. The pH did not change (~5.8), which ensured that it could be used topically. There was a slight rise in viscosity, which did not influence spreadability or appearance. There was also little change in the content of the drug as it was found to be above 93 meaning that it was so chemically stable at the tested conditions.

Table No.8: Stability Study of Optimized Microemulsion Gel Formulation (MEG2)

S.No	Time Interval (Months)	Zero Month	After 1 Month	After 2 Months	After 3 Months
1	Homogeneity	+++	+++	+++	+++
2	Grittiness	+++	+++	+++	+++
3	pH	5.8 ± 0.01	5.8 ± 0.01	5.8 ± 0.05	5.8 ± 0.01
4	Viscosity (cP)	10,800	10,800	10,850	10,860
5	Drug Content (%)	94.12	94.01	93.95	93.9

### Summary and Conclusion

The current research was able to formulate and test a gel (microemulgel) containing ketoconazole loaded into microemulsions as a topical delivery system to be used in the management of fungal infections on the skin. Pseudo-ternary phase diagrams were systematically used to optimize microemulsion formulations and the short-listed formulations were then integrated into a gel base to enhance topical applicability and patient acceptability. The optimum microemulgel was prepared with the following components; the oil phase, which was isopropyl myristate (IPM), the surfactant-co-surfactant system, which comprised Tween 80 and PEG 400, the aqueous phase which was water, and the gelling component, which was xanthan gum.

The microemulsion system developed was effective in improving the solubilization of the hydrophobic ketoconazole to achieve the uniformity of drug in the formulation. The research of characterization showed a mean globule diameter of 146.9 nm and a polydispersity index of 0.210 which showed the stability and the homogeneity of the system. ME2 was found to be the optimized formulation among the tested batches, which was determined by the reasonability of physicochemical properties, drug content homogeneity, and in-vitro performance.



The optimized microemulgel had a better in-vitro drug release profile over the commercial ketoconazole formulation, which demonstrated better diffusion of the drug as well as availability of drug at the administration site. Also, the formulation was identified to be non-irritant, which proves its topical utility. The improved solubilization and release property indicates that the microemulgel can be used to reduce dosage, thus, increasing cost-effectiveness and reducing the side effects that might occur. In general, the results of the current research prove the developed ketoconazole microemulgel to be a stable, safe, and effective topical delivery system. The gel method of microemulsion is a possible solution to enhancing the therapeutic effectiveness of ketoconazole, and alternative to a traditional topical antifungal preparation.

#### REFERENCES:

1. Fitzpatrick JE. Superficial fungal skin diseases. *Military Dermatology*. 1917;41(2):423.
2. Wollina U, Nenoff P, Verma S, Hipler UC. Fungal infections. In *Roxburgh's Common Skin Diseases 2022* Apr 18 (pp. 81-90). CRC Press.
3. Kyle AA, Dahl MV. Topical therapy for fungal infections. *American journal of clinical dermatology*. 2004 Dec;5(6):443-51.
4. Raab W. The treatment of mycosis with imidazole derivatives. Springer Science & Business Media; 2012 Dec 6.
5. Kaur IP, Kakkar S. Topical delivery of antifungal agents. *Expert opinion on drug delivery*. 2010 Nov 1;7(11):1303-27.
6. Patravale VB, Date AA. Microemulsions: pharmaceutical applications. *Microemulsions: Background, New Concepts, Applications, Perspectives*. 2009 Oct 24:259-301.
7. Souto EB, Cano A, Martins-Gomes C, Coutinho TE, Zielińska A, Silva AM. Microemulsions and nanoemulsions in skin drug delivery. *Bioengineering*. 2022 Apr 5;9(4):158.
8. Garg A, Sharma GS, Goyal AK, Ghosh G, Si SC, Rath G. Recent advances in topical carriers of anti-fungal agents. *Heliyon*. 2020 Aug 1;6(8).
9. Nining N, Amalia A, Maharani N, Adawiyah SR. Effect of Isopropyl Myristate and Oleic Acid as the Penetration Enhancer on Transdermal Patch: Characteristics and In-Vitro Diffusion. *Egyptian Journal of Chemistry*. 2023 Dec 1;66(12):251-9.
10. Jin X, Imran M, Mohammed Y. Topical semisolid products—understanding the impact of metamorphosis on skin penetration and physicochemical properties. *Pharmaceutics*. 2022 Nov 17;14(11):2487.
11. C Vadlamudi H, Narendran H, Nagaswaram T, Yaga G, Thanniru J, R Yalavarthi P. Microemulsions based transdermal drug delivery systems. *Current Drug Discovery Technologies*. 2014 Sep 1;11(3):169-80.
12. Naveed S, Jaweed L. UV spectrophotometric assay of Ketoconazole oral formulations. *American Journal of Life Sciences*. 2014;2(5):108-11.
13. Bunaciu AA, Hoang VD, Aboul-Enein HY. Fourier transform infrared spectroscopy used in drug excipients compatibility studies. *Applied Spectroscopy Reviews*. 2025 May 28;60(5):385-403.
14. Reddy EP, Raghavamma ST, Nadendla RR. Formulation and Evaluation of Ketoconazole Microemulgel with Mixture of Penetration Enhancers.
15. Pranali S, Charushila S, Sayali C, Namrata M. Design and characterisation of emulgel of an antifungal drug. *Journal of pharmaceutical sciences and research*. 2019 Jun 1;11(6):2357-61.
16. Guidance D. Guidance for industry. Center for Biologics Evaluation and Research (CBER). 1996 Apr.

How to cite this article:

Mrs. Begino Christophel. V et al. *Ijppr.Human*, 2026; Vol. 32 (2): 178-188.

Conflict of Interest Statement: All authors have nothing else to disclose.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.