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Formulation and assessment of a topical gel containing voriconazole for the management of fungal infections

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Abstract
The current research project was dedicated to the design, optimization, and comprehensive evaluation of a topical gel formulation containing voriconazole for the management of superficial fungal infections. Voriconazole, a potent broad-spectrum antifungal agent belonging to the imidazole class, is well-documented for its efficacy against a wide range of fungal pathogens. It is classified under the Biopharmaceutical Classification System (BCS) Class II, which denotes low aqueous solubility combined with high membrane permeability. Despite its favorable oral bioavailability (approximately 90%), systemic administration of voriconazole is often accompanied by dose-limiting toxicities, including hepatic dysfunction and renal impairment. These concerns have prompted the need for alternative drug delivery approaches. Thus, the present study sought to develop a topical drug delivery system capable of providing localized therapeutic action at the site of infection, while simultaneously minimizing systemic absorption and enhancing patient adherence to antifungal therapy

Keywords: Fungal infection, voriconazole, topical gel, optimization

Introduction
Fungal infections of the skin represent one of the most prevalent dermatological concerns in modern clinical practice. These infections, often caused by dermatophytes, yeasts, or molds, manifest in various forms such as athlete's foot, ringworm, or candidiasis. With increasing incidence due to factors like compromised immunity, poor hygiene, and tropical climates, effective treatment options have become a critical focus in dermatological therapeutics.
To address these conditions, clinicians have access to a wide spectrum of pharmaceutical formulations ranging from solid dosage forms (e.g., tablets, capsules) to semisolid (e.g., creams, ointments, gels) and liquid preparations. Among these, topical gels have garnered considerable attention and acceptance in both cosmetic and pharmaceutical domains due to their clarity, aesthetic appeal, and ease of application.
Topical drug delivery plays a pivotal role not only in treating dermatological disorders but also in facilitating local or systemic drug action through routes such as ophthalmic, rectal, vaginal, and transdermal. Among these, the skin offers a highly accessible and non-invasive route for local drug application. The topical drug delivery system enables the application of pharmacologically active substances directly onto the skin or mucous membranes, aiming to exert therapeutic effects either by restoring physiological functions or modifying pathological conditions.

Methodology
1. Preformulation Studies
Identification of Drug
Solubility: The solubility profile of voriconazole was determined to identify the most suitable solvent system for its formulation and analytical studies. An excess quantity of voriconazole was added to a series of selected aqueous and organic solvents to ensure saturation. These suspensions were placed in a thermostatically controlled water bath shaker and agitated continuously at 37 ± 2°C for a duration of 72 hours, which allowed sufficient time for the system to reach equilibrium solubility.
After equilibration, the mixtures were subjected to centrifugation at 3000 rpm for 15 minutes to separate the undissolved drug. The clear supernatant from each sample was then carefully collected and passed through a 0.45 µm membrane filter to eliminate any residual particulates. The filtrates were subsequently analyzed using a UV-Visible spectrophotometer at a predetermined wavelength of 255 nm, which corresponds to the maximum absorbance (λmax) of voriconazole. The solubility of the drug in each solvent system was then calculated based on the absorbance values obtained, using the calibration curve previously established.
Melting Point Determination
The melting point of voriconazole was assessed to verify its purity and thermal stability. The procedure was carried out using the sealed capillary tube method, wherein a small quantity of the drug was filled into a previously sealed capillary tube. The tube was then placed into a melting point apparatus, and the temperature was gradually increased. The temperature at which the drug completely melted was recorded. The test was repeated three times (in triplicate) to ensure reproducibility and consistency of the results. A sharp and narrow melting point range confirmed the high purity of the drug substance.
λmax Determination by UV Spectrophotometry
To determine the maximum wavelength of absorption (λmax) of voriconazole, an accurately weighed amount of the drug was dissolved in phosphate buffer solution (pH 6.4) to mimic physiological conditions. The resulting solution was filtered through a 0.45 µm membrane filter to remove any undissolved particulates. The clear filtrate was then

subjected to UV spectrophotometric scanning in the wavelength range of 200 to 800 nm using a calibrated UV-Visible spectrophotometer. The λmax was observed at 255 nm, and this value was cross-verified with literature values to confirm the identity and purity of the drug sample.

Calibration Curve Preparation

A standard calibration curve of voriconazole was constructed to enable accurate quantitative analysis in subsequent drug content and release studies. Standard solutions were prepared in phosphate buffer (pH 6.4) over a concentration range of 0 to 30 µg/mL. The absorbance of each solution was measured at 255 nm using a UV-Visible spectrophotometer. A plot of absorbance versus concentration was constructed, which exhibited a linear relationship, indicating adherence to Beer-Lambert's law. The resulting regression equation and correlation coefficient (R^2) confirmed the reliability of the method for drug quantification.

FTIR Spectroscopy

Fourier Transform Infrared (FTIR) spectroscopy was performed to characterize the functional groups present in the voriconazole molecule and to assess its compatibility with excipients. The KBr pellet method was used for sample preparation, where the drug and potassium bromide were finely ground, mixed in appropriate ratios, and compressed into transparent pellets. The spectra were recorded over the range of 4000–400 cm^{-1} using a calibrated FTIR spectrometer. The resulting peaks were analyzed and compared with reference spectra to confirm the chemical structure and identity of the drug. This technique also aided in evaluating potential interactions when voriconazole was blended with formulation excipients in subsequent compatibility studies.

2. Preparation of Gel Base

HPMC was used as the gelling agent in different concentrations (0.5%, 1%, 1.5%, 2%, and 2.5% w/w). The polymer was dispersed in warm purified water with continuous stirring and allowed to hydrate overnight. Voriconazole (2 g) was dissolved and incorporated into the gel base. Glycerin (0.03% w/w) was added as a humectant. Methyl paraben (0.2% w/w) and propyl paraben (0.5% w/w) were added as preservatives. The pH was adjusted using triethanolamine and volume made up to 100 mL. The gel was homogenized until a smooth and uniform consistency was obtained.

Table 1: Optimized Gel Formulation Composition

Ingredient	Function	F1	F2	F3	F4	F5
Voriconazole	Active Ingredient	2.0 g	2.0 g	2.0 g	2.0 g	2.0 g
HPMC	Gelling Agent	0.5 g	1.0 g	1.5 g	2.0 g	2.5 g
Methyl Paraben	Preservative	0.2 g	0.2 g	0.2 g	0.2 g	0.2 g
Propyl Paraben	Preservative	0.5 g	0.5 g	0.5 g	0.5 g	0.5 g
Triethanolamine	pH Adjuster	q.s.	q.s.	q.s.	q.s.	q.s.
Glycerin	Humectant	0.03 g	0.03 g	0.03 g	0.03 g	0.03 g
Purified Water	Vehicle	q.s. to 100 mL for all formulations				

3. Characterization of Topical Gels

To ensure the quality, stability, and performance of the formulated voriconazole-loaded topical gels, a series of physicochemical evaluations were conducted. Each formulation was analyzed using standardized procedures under controlled laboratory conditions. The following parameters were assessed:

1. **pH Measurement:** The pH of each gel formulation was evaluated to ensure compatibility with skin, as deviations may cause irritation or affect drug stability. Precisely 1 gram of each gel sample was dispersed in 100 mL of freshly distilled water and allowed to equilibrate for 2 hours at room temperature. The pH of the resulting dispersion was measured using a calibrated digital pH meter. Each formulation was tested in triplicate to ensure reproducibility and statistical validity. The observed pH values were compared against the physiological skin pH range (approximately 4.5–6.5) to determine acceptability for topical application.

2. **Drug Content Determination:** The uniformity and accuracy of drug loading within the gel matrix were assessed by determining the drug content. For this, 1 gram of gel was accurately weighed and dissolved in 100 mL of phosphate buffer (pH 6.4). The solution was filtered through a 0.45 µm membrane filter to remove any undissolved excipients or polymeric residues. Suitable dilutions were then prepared from the stock solution, and the absorbance was measured at 255 nm using a UV-Visible spectrophotometer. The drug concentration was calculated using the linear regression equation obtained from the previously constructed calibration curve of voriconazole.

3. **Spreadability:** Spreadability is a crucial attribute influencing the ease of application and uniformity of distribution of gel over the skin surface. The spreadability of each formulation was evaluated by the slip and drag method. In this procedure, a fixed amount of gel was placed between two pre-weighed glass slides. A known weight was placed on the upper slide to compress the sample, and the time taken (in seconds) for the slides to slip apart under the influence of the applied weight was recorded. A lower detachment time indicated superior spreadability and ease of application.

4. **Viscosity Measurement:** Viscosity plays a pivotal role in determining the stability, flow characteristics, and patient acceptability of gel formulations. The rheological behavior of the prepared gels was assessed using a Brookfield viscometer. The measurements were carried out at varying spindle speeds of 0.3, 0.6, and 1.5 revolutions per minute (rpm). The corresponding dial

readings at each speed were recorded to evaluate the flow consistency and shear-thinning behavior of the formulations.

5. **Extrudability:** Test Extrudability is indicative of the ease with which the gel can be squeezed out from a collapsible tube, a common packaging format. For this study, the gel samples were filled into standard aluminum or plastic collapsible tubes. The force (in grams) required to extrude a 0.5 cm ribbon of gel within 10 seconds was recorded using a standardized apparatus. A lower force requirement implied better extrudability and user convenience during application.

6. **In *Vitro* Drug Release Study:** The drug release behavior of voriconazole from the gel matrix was investigated using a dialysis membrane technique to simulate percutaneous diffusion. A known quantity of gel (5 mL) was placed in contact with a pre-soaked dialysis membrane. The setup was immersed in 100 mL of phosphate buffer (pH 6.4) maintained at 37 ± 0.5°C and stirred continuously at 100 rpm using a magnetic stirrer. At predetermined time intervals, 1 mL samples were withdrawn from the receptor compartment and replaced with an equal volume of fresh buffer to maintain sink conditions. The drug concentration in each sample was analyzed spectrophotometrically at 255 nm.

7. **In *Vitro* Antifungal Activity:** The antifungal efficacy of the developed formulations was evaluated against Candida albicans using the agar cup diffusion method. A fungal suspension containing approximately 1×10^6 spores/mL was prepared and uniformly mixed with molten Sabouraud Dextrose Agar. The mixture was poured into sterile Petri dishes and allowed to solidify. Wells (1 cm diameter) were then bored into the solidified agar and filled with 0.5 g of each test formulation. The plates were incubated at 25 ± 1°C for 72 hours. Following incubation, the diameter of the zone of inhibition was measured in millimeters, and the mean value of three replicates was recorded to determine antifungal potency.

8. **Stability Studies:** Stability testing was conducted to evaluate the physical integrity of the gel formulations under varying temperature conditions. Each formulation was subjected to a freeze-thaw cycle, which included storage at 4°C, 25°C, and 40°C for one month at each temperature. Following these stress conditions, the gels were examined for any signs of phase separation, syneresis (liquid separation), changes in consistency, or color. These observations helped determine the shelf-life stability and robustness of the formulations under real-time.

Results and Discussion

Table 2: The solubility of voriconazole.

S. No.	Solvents	Solubility (mg/ml)
1	Water	0.75
2	Dichloro methane	1.6
3	Phosphate buffer saline (pH 6.4)	1.17
4	Chloroform	22
5	Acetone	20
6	Ethanol	20

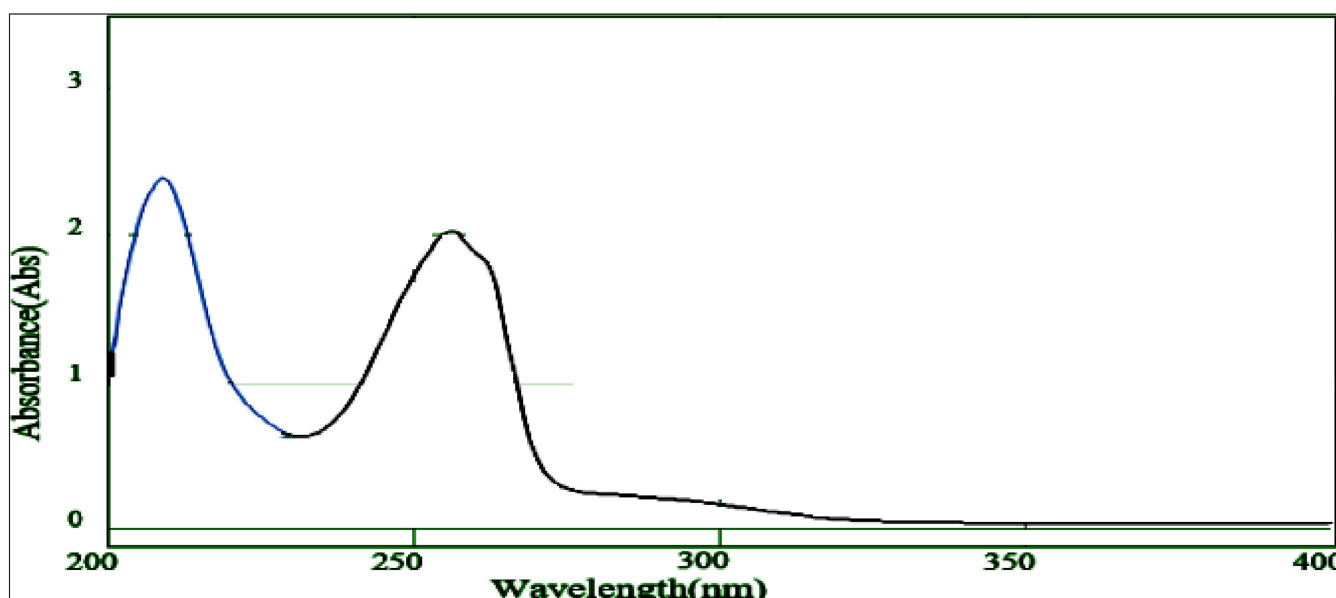

Fig 1: Lambda Max determination of Voriconazole

Table 3: Calibration curve

Sr.no.	Concentration (µg/ml)	Absorbance at 255nm
1	0	0
2	10	0.228
3	20	0.424
4	30	0.621
5	40	0.823
6	50	0.999

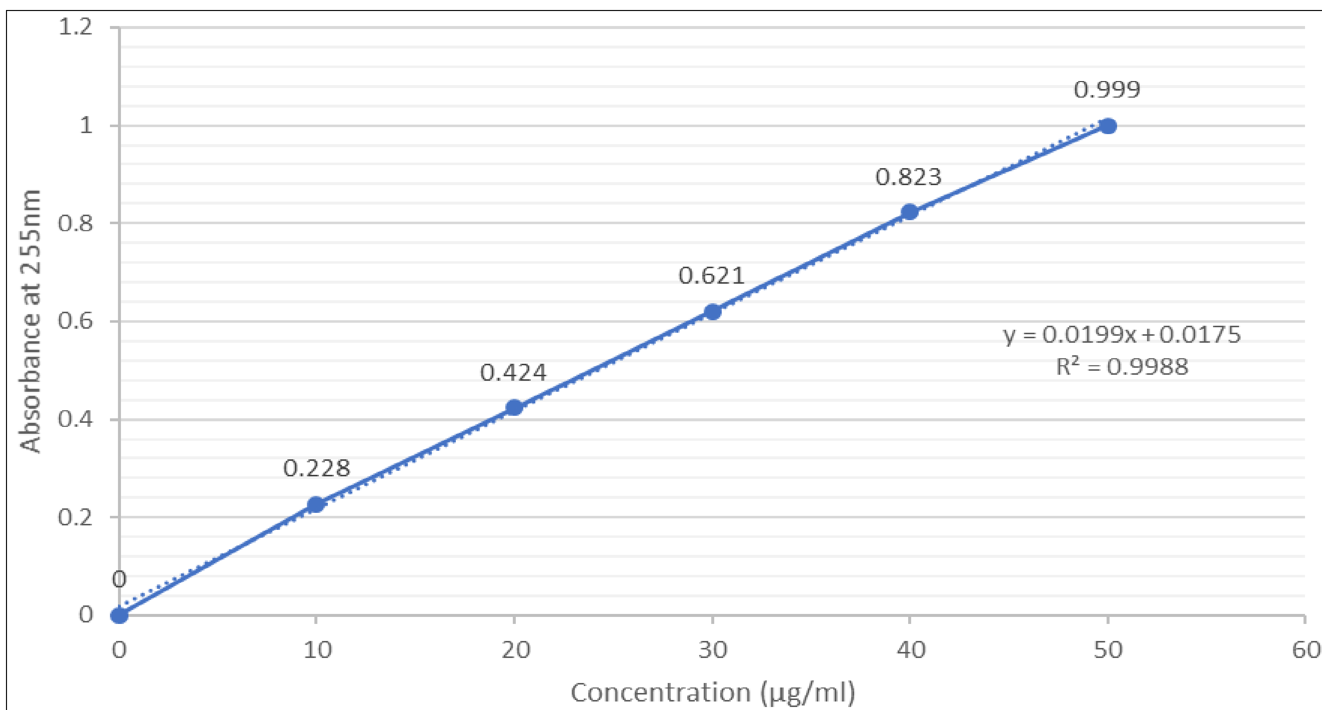

Fig 2: calibration curve of voriconazole

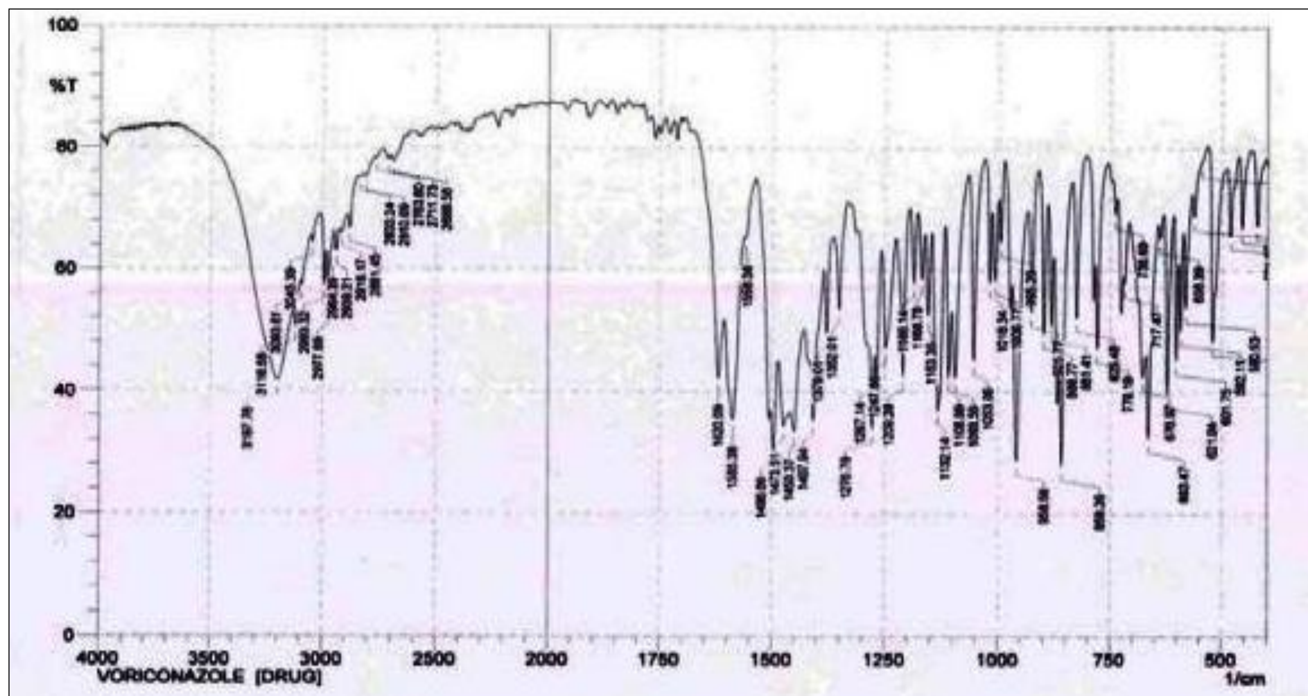

Fig 3: FTIR spectra of voriconazole

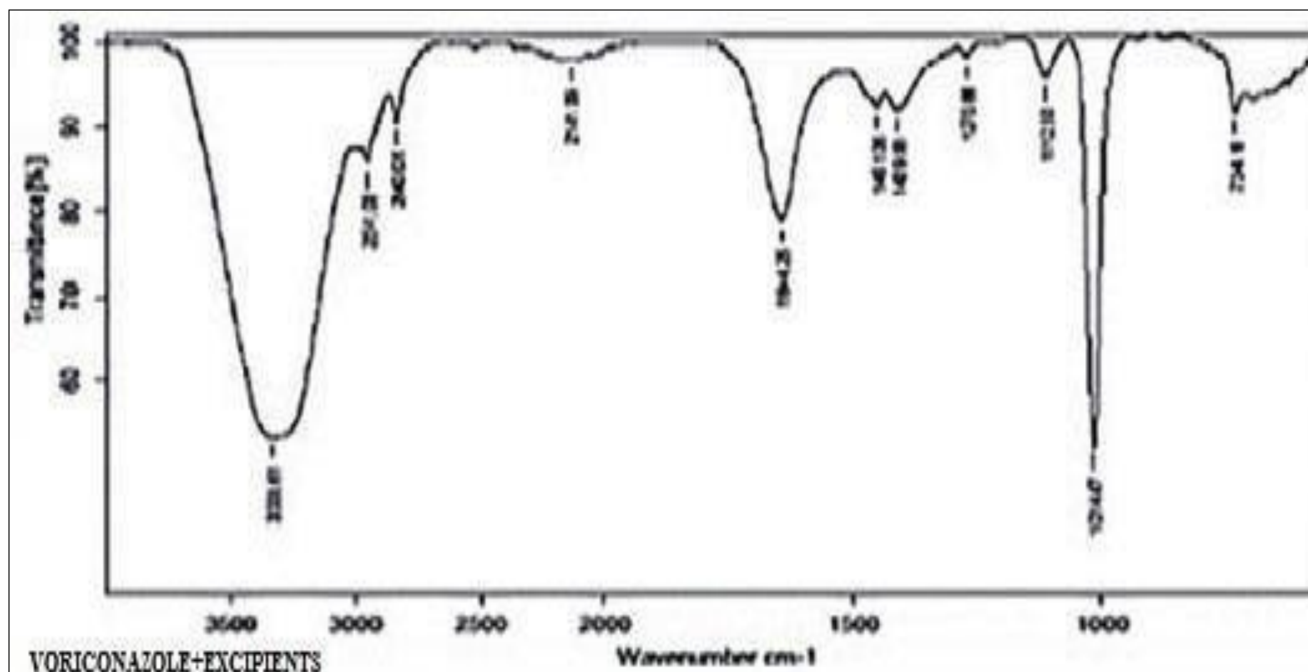

Fig 4: FTIR spectra of voriconazole and excipients blend

Table 4: Drug content of optimized gel formulation after 1-month stability studies

Formulation	**Drug Content**	
	30±2ºC at 65±5 RH	40±2ºC at 75±5 RH
F1	96.5	75

Table 7: In *vitro* diffusion study of optimized gel formulation after 1-month stability

Time (Min)	**%Drug Release**	
	30±2º C at 65±5 RH	**40±2ºC at 75±5 RH**
0	0	0
30	21	14.49
60	43	33.85
90	50.88	47.55
120	57.46	51.85
150	63.20	59.55
180	72.25	63.36
210	79.60	73.04
240	85.59	81.1
270	97.81	92.60

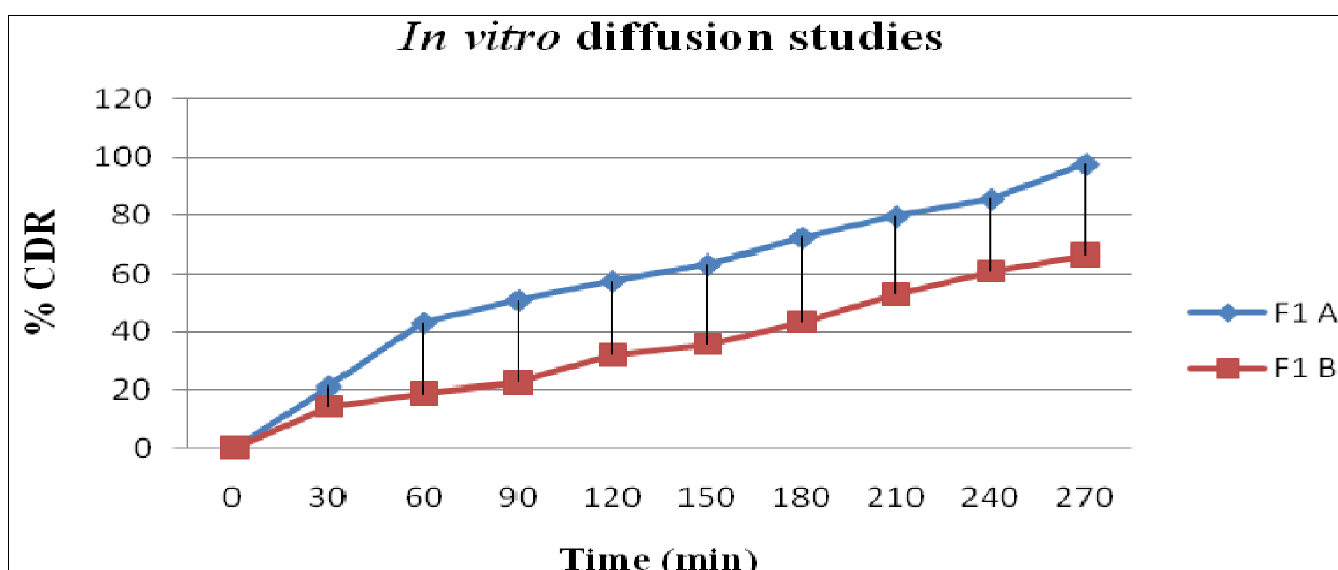

Fig 5: In *vitro* diffusion studies after 1-month stability studies

Conclusion

Formulation F1 was identified as the optimized topical gel formulation based on its comprehensive performance across all key evaluation parameters, including pharmaceutical quality, physicochemical stability, diffusion efficiency, dermatological safety, and antifungal efficacy. The formulation exhibited desirable rheological properties, consistent drug release, non-irritant behavior upon application, and pronounced inhibitory activity against Candida albicans. These attributes collectively underscore its suitability for localized antifungal therapy.

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References

1. Singh MP, Nagori BP, Shaw NR, Tiwari M, Jhanwar B. Formulation development & evaluation of topical gel formulations using different gelling agents and its comparison with marketed gel formulation. International Journal of Pharmaceutical Erudition,2013:3(3):1-0.
2. James WD, Elston D, Berger T. Andrew's diseases of the skin E-book: clinical dermatology. Elsevier Health Sciences, 2011.
3. Dayan N. Pathways for skin penetration. Cosmetics and toiletries,2005:120(6):67-76.
4. Clark AH. Gels gelling. Physical chemistry of foods,1992:7:263-305.
5. Yamauchi A. Gels. Introduction. In Gels handbook. Academic Press, 2001, 4-12.