RESEARCH PAPER

Formulation and Evaluation of Posaconazole-Loaded Niosomal Gel for Enhanced Topical Antifungal Therapy

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ABSTRACT

Therapeutic fungal infection is still a big challenge due to the limited aqueous solubility of most of the conventional antifungal formulations and insufficient penetration into the skin, poor retention at the infected site and frequent administration. The present study was directed towards the formulation and evaluation of Posaconazole loaded niosomal gel for enhanced topical antifungal drug delivery. The broad spectrum triazole antifungal drug posaconazole was chosen because of its activity against clinically relevant fungal organisms, but it suffers from lack of water solubility and limited topical availability, limiting the extent to which it can be used in conventional systems. The non-ionic surfactant and cholesterol were used as vesicle-forming agents and thin-film hydration technique was used for the preparation of niosomes. The optimized niosomal dispersion was added to a Carbopol gel base in order to improve its ease of application, skin residence and patient acceptability. Drug identity, linearity, compatibility and thermal stability were confirmed by preformulation studies such as UV spectrophotometry, FTIR and DSC. The appearance, pH, viscosity, spreadability, drug content, in-vitro diffusion, comparative release, antifungal activity, and stability of the prepared niosomal gel formulations were assessed. The pH, viscosity, spreadability and uniform drug content of the gel were found to be skin compatible. The optimized niosomal gel showed a sustained drug release for 12 hours with 98.95% cumulative drug release, which was higher than the conventional plain gel (64.20% cumulative drug release). The antifungal activity was also enhanced in the niosomal gel loaded with Posaconazole as compared to the pure drug and marketed formulation with larger zone of inhibition of 28 ± 0.4 mm for the Posaconazole niosomal gel versus 19 ± 0.5 mm for the pure drug and 23 ± 0.6 mm for the marketed formulation. The results of the stability observations showed no significant changes in the physical appearance or the performance parameters during storage. In conclusion, developed Posaconazole niosomal gel seems to be a promising topical drug delivery system that will help in increasing the antifungal efficacy, maintaining the release of the drug for longer duration, increasing the availability of the drug in the topical region and improve patient compliance.

Keywords: Posaconazole; niosomes; niosomal gel; topical drug delivery; antifungal therapy; thin-film hydration; sustained release; Carbopol gel

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INTRODUCTION

Mycoses, also known as fungal infections, are disease caused by pathogenic fungi which invade and multiply in host tissues[1]. Can involve the skin, hair and nails as superficial infections, or can become deeper, systemic infections in susceptible people[2]. Fungal infections have become more common due to various factors including immunosuppressive status, diabetes mellitus, organ transplantation, prolonged antibiotic use, corticosteroid therapy, poor hygiene and humid environmental conditions[3]. Superficial infections with fungi, such as tinea infections, cutaneous candidiasis, athlete's foot, ringworm, and onychomycosis, are common, and topical antifungal preparations are often used for their treatment[4]. These infections are generally not fatal but when the ability of the drug to penetrate into the affected tissue is low, they can be chronic and recurrent, uncomfortable and hard to get rid of[5]. There are certain formulation and pharmacological issues which limit the use of conventional antifungal therapy[6]. The majority of antifungal drugs have sub-optimal aqueous solubility, dissolution and local bioavailability. Topical creams and ointments may stay on the skin and not penetrate deep enough to provide adequate drug levels in the infected tissues. The low compliance rate may be further decreased because of the short time at the application sites and frequent dosage. Poor penetration and retention will

increase the likelihood of recurrence, length of therapy, and resistant fungal strains[7]. Some delivery restrictions may be overcome with systemic antifungal therapy, however, it can give undesirable side effects such as gastrointestinal upset, liver issues and drug interactions, especially when used over an extended period. Thus, there is an obvious requirement for improved, topical drug delivery systems that can increase penetration, provide a prolonged release and increase local antifungal activity with less systemic exposure[8-9]. Posaconazole is an antifungal drug from the second generation of broad-spectrum triazoles. It works by blocking lanosterol 14-alpha-demethylase, an enzyme in the fungal, lanosterol, 14-alpha-demethylase pathway which is dependent upon cytochrome P450. Ergosterol is a critical part of the fungal cell membrane and disrupting its synthesis leads to damage to the integrity of the membrane, increases permeability and inhibits fungal growth. Posaconazole is effective against various yeasts, molds and dermatophytes including Aspergillus species and Candida species. Although Posaconazole has a high antifungal activity, it belongs to BCS Class II and shows high lipophilicity and low aqueous solubility[10-11]. This property can hinder the dissolution of drugs and can also compromise the efficacy of conventional dosage forms, particularly in localized superficial fungal infections where maintained presence of the drug at the infection site is crucial[12]. Niosomes are non-ionic surfactant based vesicular system which self-assemble in the presence of cholesterol. They have a structure similar to liposomes and are more resistant to oxidative degradation and are generally more stable, economical and less likely to undergo oxidative degradation than liposomes[13]. Hydrophilic and lipophilic drugs can be entrapped in niosomes, which can protect any entrapped drug molecule, increase solubility, increase skin permeation and result in controlled release of the drug within the niosome. Cholesterol provides rigidity and stability to the bilayers of vesicles, while non-ionic surfactants facilitate vesicle formation and have effects on vesicle permeability, size and entrapment efficiency[14]. Niosomes are particularly useful for topical delivery due to their ability to increase the retention of the drug in the skin, decrease the systemic absorption and keep high concentrations at the infected site for a prolonged time. Here, the present work niosomes containing Posaconazole were prepared using the appropriate non-ionic surfactant and cholesterol by the thin-film hydration method. The particle size, PDI, zeta potential, EE, drug content and morphology of the prepared vesicles were investigated. The optimized niosomal dispersion was then further incorporated into a topical formulation of the gel matrix of Carbopol to obtain a patient-friendly topical formulation. Carbopol was chosen as it delivers appropriate gel consistency, spread ability and ease of use[15]. The physicochemical and performance characteristics such as appearance, pH, viscosity, spreadability, drug content, *in-vitro* diffusion, comparative release with plain gel, antifungal activity, and stability of the formulated niosomal gels were investigated. The objective of this study was to create a topical formulation of Posaconazole that could overcome the drawbacks of conventional formulations, such as inadequate drug penetration, sustained release, increased local antifungal activity and patient compliance[16-17].

MATERIALS AND METHODS

Materials

The active ingredient of a topical antifungal niosomal gel was posaconazole. The niosome was prepared using Span 60, Tween 80, and cholesterol, and the gel basis was prepared using Carbopol 940, triethanolamine, glycerine, and sodium benzoate. For extraction and analysis, methanol and other analytical-grade solvents were employed.

Preformulation Studies

The identification, purity, and appropriateness of Posaconazole for formulation development were confirmed using preformulation experiments. The organoleptic qualities of the medicine were assessed, including its look, colour, smell, and taste. The purity of Posaconazole was confirmed by determining its melting point using the capillary tube method. In order to choose appropriate excipients for the niosomal formulation, solubility tests were conducted in a range of surfactants, oils, and co-surfactants. Span 60 and Tween 80 were chosen for further formulation development because they demonstrated greater solubility of Posaconazole among the evaluated surfactants[18-19].

Determination of λmax and Calibration Curve

A UV-Visible spectrophotometer was used to find the λmax of Posaconazole. To get varied concentrations, a Posaconazole stock solution was made in methanol and then diluted further. Using methanol as a blank, the absorbance of every dilution was measured at the identified λmax. The x-axis represents concentration and the y-axis represents absorbance in a calibration curve. To estimate drug content, entrapment efficiency, and conduct in vitro drug release investigations, the calibration curve was utilised[20-21].

Drug–Excipient Compatibility Study

Fourier Transform Infrared Spectroscopy was used to study the drug-excipient compatibility. In order to determine potential drug-formulation interactions, FTIR spectra of both pure Posaconazole and its physical combination with chosen excipients were recorded. The physical mixture's peaks were compared to Posaconazole's distinctive peaks. Posaconazole was found to be well-tolerated by the excipients chosen since no discernible changes to the peaks, elimination of peaks, or formation of new peaks were noted[22-23].

Differential Scanning Calorimetry

The crystalline structure and thermal behaviour of Posaconazole were studied using differential scanning calorimetry (DSC). The presence of the distinctive endothermic peak was examined in the recorded and analysed thermogram of Posaconazole. The drug's purity and its formulation development were both aided by the DSC investigation. Posaconazole is a highly pure crystalline

substance, as seen by the strong endothermic peak at 170.2°C in the published study[24-25].

Preparation of Posaconazole-Loaded Niosomes

The thin film hydration approach was used to prepare niosomes laden with posaconazole. A round-bottom flask was used to dissolve accurately measured amounts of cholesterol, a non-ionic surfactant, and Posaconazole in an appropriate volatile organic solvent system. Using a rotary flask evaporator, the solvent was evaporated until a thin, dry layer formed on the inside wall of the flask. A niosomal dispersion was achieved by gently agitating the dry film while it was hydrated with an aqueous phase. In order to achieve homogenous niosomal vesicles and decrease vesicle size, the dispersion was subjected to further sonication. The effect of different surfactant types and surfactant-to-cholesterol ratios on vesicle formation, entrapment efficiency, and formulation stability were studied by preparing several formulation batches[26-27].

Evaluation of Posaconazole-Loaded Niosomes

Size of the vesicles, polydispersity index, zeta potential, shape, entrapment efficiency, drug content, and in vitro drug release were some of the criteria used to assess the niosomal formulations that were produced. Under controlled room temperature conditions, a Malvern Panalytical particle size analyser was used to assess particle size, PDI, and zeta potential. The stability, homogeneity, and distribution of vesicle sizes were evaluated using these criteria in the niosomal dispersion[28].

We used scanning electron microscopy to look at the optimised niosomal formulation's shape. The vesicles' surface structure, shape, and homogeneity were examined using scanning electron microscopy (SEM). It was noted that the produced niosomes did not aggregate and had a smooth surface in addition to their spherical shape[29].

By extracting the drug from the niosomal solution, we were able to measure the entrapment efficiency. Centrifuged at 3500 rpm for 20 minutes was a volume of the niosomal formulation that had been measured. After collecting the drug-free supernatant, it was appropriately diluted with methanol and examined using UV-Visible spectrophotometry at Posaconazole's λmax[30].

To find out how much drug was in the niosomal formulation, we transferred 1 millilitre of the dispersion into a volumetric flask with some methanol. The encapsulated medicine was released after 30 minutes of sonication, which disrupted the vesicles. Using methanol to adjust the volume, the mixture was spun in a centrifuge at 3500 rpm for 20 minutes. Spectrophotometric analysis was performed on the transparent supernatant at the λmax of Posaconazole, with methanol serving as a blank. We determined the drug content as a percentage of the total drug that was added[31].

Preparation of Posaconazole-Loaded Niosomal Gel

A Carbopol 940 gel foundation was used to integrate the optimised niosomal formulation of Posaconazole. Complete hydration of carbopol 940 was allowed after dispersal in distilled water. To achieve even mixing, the optimised niosomal suspension was gradually added to the hydrated polymer dispersion while swirling continuously. To achieve the desired gel consistency and neutralise the polymer dispersion, triethanolamine was added dropwise. A humectant called glycerine and a preservative called sodium benzoate were both added. By adjusting the Carbopol 940 concentration from 0.5% to 2%, four distinct gel compositions were created. Optimal niosomal dispersion (10 mL), triethanolamine (0.5%), sodium benzoate (0.1%), and glycerine were all components of each formulation[32].

Evaluation of Posaconazole-Loaded Niosomal Gel

The niosomal gel formulations that were made were tested for their in vitro diffusion, drug content, viscosity, homogeneity, pH, and physical appearance. Visual evaluations were carried out on the formulations to assess their colour, uniformity, grittiness, phase separation, and general look. A gel with a smooth, uniform and non-lumpy consistency was deemed appropriate for topical use[28].

A calibrated digital pH-meter was used to determine the pH of the gel formulations. A pH meter was calibrated prior to use with buffer solutions of pH 4.0 and 7.0. About 1 g of gel was dispersed in distilled water and allowed to equilibrate. The electrode was placed in the dispersion and the pH of dispersion was recorded. To reduce the risk of irritation the pH was kept within the range suitable for human skin[29].

We measured 100 milligrams of niosomal gel and transferred it to a volumetric flask with methanol to find out how much drug was in it. To fully remove Posaconazole from the gel matrix, the mixture was subjected to sonication. A UV-Visible spectrophotometer was used to analyse the solution at the λmax of Posaconazole after passing it through a 0.45 µm membrane filter. The percentage of drug content was used to express the drug concentration, which was determined using the calibration curve[30].

The glass plate method was used to determine the spreadability. One clean glass plate was used to place around 1 g of gel in the middle, and then another clean glass plate was used to cover it. After setting the plates aside for 5 minutes, a 500 g weight was added to them. Two measurements were taken in opposite directions to determine the spread gel's diameter, and the mean was reported. Thirdly, the spreadability was determined[31].

The gel compositions' viscosities were assessed with the help of a Brookfield viscometer equipped with an appropriate spindle. The rheological behaviour of the gels was assessed by taking measurements at various rotating speeds, such as 10, 20, 50, and 100 rpm. When loading the samples, great care was taken not to create air bubbles; measurements were conducted only after a consistent value had been achieved[32].

***In Vitro* Drug Release Study**

Utilising a Franz diffusion cell equipped with a dialysis membrane, the in vitro drug release investigation of niosomal gel filled with Posaconazole was done. The pH 7.4 phosphate buffer was added to the receptor compartment, which was then kept at 37 ± 0.5°C with constant magnetic

stirring. In the donor compartment, the dialysis membrane was evenly coated with about 1 g of gel. To maintain sink conditions, aliquots were removed from the receptor compartment and promptly replaced with an equal volume of new phosphate buffer at specified intervals of half an hour, one hour, two hours, three hours, four hours, six hours, eight hours and twelve hours. We used a UV-Visible spectrophotometer to examine the extracted samples at the λmax of Posaconazole, and we computed the cumulative percentage of drug release[33-34].

Comparative Study with Conventional Gel

Under the same experimental settings, the normal Posaconazole gel and the optimised Posaconazole-loaded niosomal gel were compared. The physical characteristics, viscosity, spreadability, drug content, and in vitro drug release profile were all taken into account throughout the comparison. This study aimed to assess if the niosomal vesicular system provided better topical distribution performance compared to the traditional gel formulation[35].

Antifungal Activity Study

This study compared the antifungal efficacy of the optimised niosomal gel containing Posaconazole to that of the pure medication and a commercially available formulation. To evaluate the effectiveness of the antifungal, the zone of inhibition was measured in millimetres. The findings that were uploaded demonstrated that the niosomal gel containing Posaconazole had better antifungal activity than the pure drug and the commercial formulation. This is likely because the niosomal gel method allowed for better penetration and prolonged release of the drug[36].

Stability Study

Optimal Posaconazole-loaded niosomal gel stability experiments were conducted for a duration of three months. At regular intervals, the formulation's visual appeal, pH, viscosity, medication content, and in vitro drug release were assessed. Confirming the optimised formulation's appropriateness for topical application and learning about its physical and chemical stability during storage were the goals of the stability study[36].

RESULTS AND DISCUSSION

It was focused on Posaconazole-loaded niosomal gel for topical antifungal therapy. The results obtained from preformulation studies, spectrophotometric analysis, compatibility testing, niosome characterization, gel evaluation, in vitro diffusion, comparative release, antifungal activity, and stability studies are discussed below.

Organoleptic Properties and Melting Point

The organoleptic evaluation showed that Posaconazole was a white to off-white, odourless, bitter, crystalline powder (Table 1). These observations complied with the reported official characteristics of Posaconazole, authorizing uniqueness & suitability of sample. Results showed a melting point between 168 and 172 degrees Celsius, which is in agreement with the previously reported range of 170 to 173 degrees Celsius (Table 2). This proved that the medicine utilised in the formulation was genuine and of high purity

Table 1. Organoleptic properties of Posaconazole

Test	Observation	Inference
Appearance	Crystalline powder	Complies with USP
Colour	White to off-white	Complies with USP
Odour	Odourless	Complies with USP
Taste	Bitter	Complies with USP

Table 2. Melting point of Posaconazole

Method Used	Started to Melt	Completely Melted	Reported MP
Capillary tube method	168 ± 1°C	172 ± 1°C	170-173°C

Solubility Study

In order to choose appropriate excipients for the niosomal formulation, a solubility analysis was conducted (Table 3). Span 60 exhibited the surfactant with the maximum solubility, measuring 0.3826 ± 0.00182 mg/mL, while Tween 80 came in second with 0.3684 ± 0.00210 mg/mL. Span 60 and Tween 80 were thus decided to be appropriate for niosome preparation. Table 4 shows that out of all the co-surfactants, propylene glycol had the highest solubility at 0.2468 ± 0.00155 mg/mL, followed by oleic acid with 0.5284 ± 0.00230 mg/mL, which had the highest solubility among oils. Because of their high solubility, certain excipients may be effective.

Table 3. Solubility of Posaconazole in selected surfactants

Surfactant	Solubility (mg/mL)
Tween 20	0.0824 ± 0.00120
Tween 40	0.0118 ± 0.00042
Tween 60	0.0265 ± 0.00058
Tween 80	0.3684 ± 0.00210
Span 80	0.0312 ± 0.00046
Span 60	0.3826 ± 0.00182

Table 4. Solubility of Posaconazole in co-surfactants and oils

Excipient	Type	Solubility (mg/mL)
Propylene glycol	Co-surfactant	0.2468 ± 0.00155
PEG 400	Co-surfactant	0.1842 ± 0.00126
PEG 600	Co-surfactant	0.0624 ± 0.00102
Oleic acid	Oil	0.5284 ± 0.00230
Coconut oil	Oil	0.1762 ± 0.00154
Castor oil	Oil	0.1685 ± 0.00138
Orange oil	Oil	0.4268 ± 0.00172

Spectrophotometric Analysis

Figure 1 shows that the highest absorbance of Posaconazole in methanol was measured at 262 nm using UV-visible spectrophotometric scanning. Figure 2 shows that the analytical method followed Beer-Lambert law within the defined concentration range, as indicated by the linear connection between concentration and absorbance in the calibration curve. This means the drug content, entrapment efficiency, and in vitro release analysis could all be accommodated by the calibration curve.

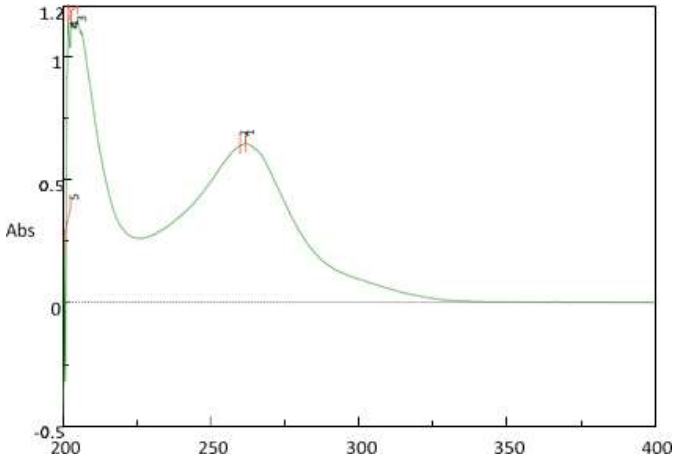

Figure 1. Absorbance spectra of Posaconazole

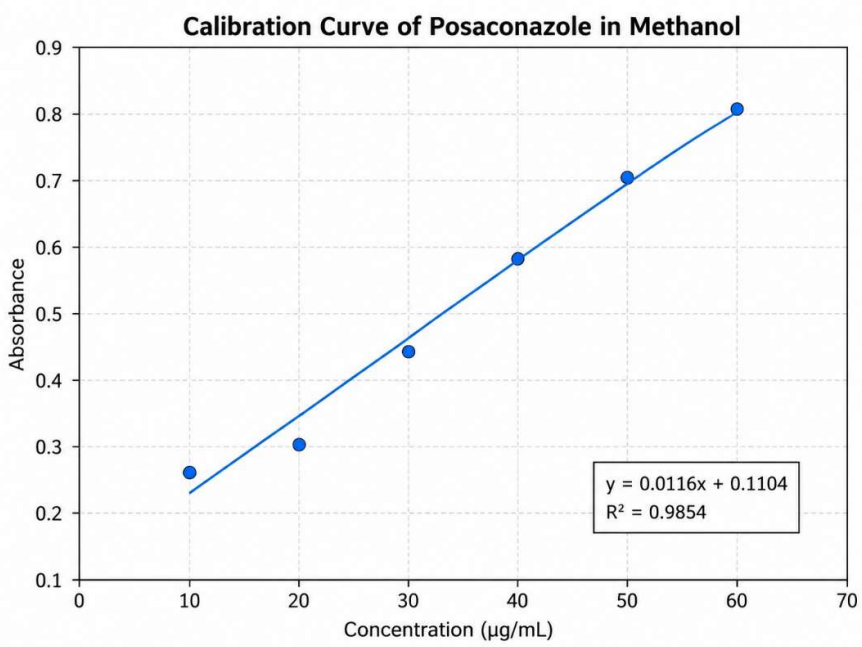

Figure 2. Calibration curve of Posaconazole in Methanol

Drug-Excipient Compatibility Studies

FTIR Analysis

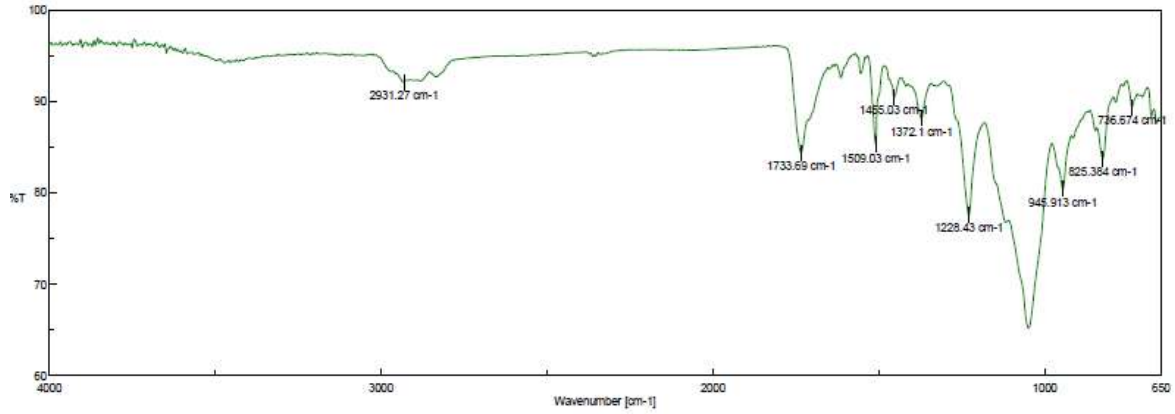

Figure 3. FTIR Spectrum of Posaconazole

Figure 3 shows the FTIR spectrum of Posaconazole, which confirmed the existence of key functional groups in the medication structure. The spectrum displayed distinctive absorption peaks. O-H stretching, which occurs within the typical range of 3200-3600 cm^{-1}, caused a large peak to be seen at 3448 cm^{-1}. While aliphatic C-H stretching was validated by peaks at 2926 cm^{-1} and 2854 cm^{-1}, aromatic =C-H stretching was shown by the peak at 3062 cm^{-1}. An absorption band at 1596 cm^{-1} was seen, which was determined to be the C=N stretching of the azole ring. This confirmed that the azole functional group was present. The observation of aromatic C=C stretching at 1508 cm^{-1} and 1456 cm^{-1} provides further evidence that the molecule contains aromatic rings. A peak at 1275 cm^{-1} was indicative of C-O stretching, and a band at 1158 cm^{-1} showed C-N stretching. The aromatic C-H bending was responsible for the band at 834 cm^{-1}, while the band at 1028 cm^{-1} was determined to be C-O-C stretching. Also, the presence of C–Cl stretching was corroborated by the band at 582 cm^{-1}. In general, the peaks observed for FTIR were in the reported standard range, thus confirming the identity and purity of Posaconazole.

DSC Analysis

The DSC thermogram of Posaconazole revealed a steep endothermic peak at 170.2°C which is the melting point of the drug (Figure 4). There was a sharp peak in the spectrum, which was indicative of the crystal nature and purity of the drug. No other thermal event or major shift was observed, indicating that the drug was thermally stable and can be considered for further formulation development.

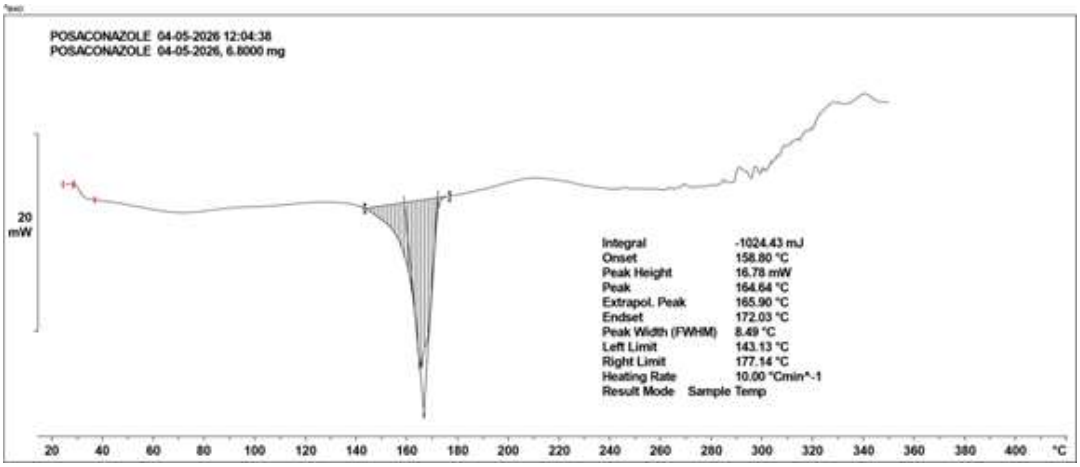

Figure 4. Differential Scanning Calorimetry

Characterization of Posaconazole-Loaded Niosomes

Niosomes were prepared using thin film hydration method with different proportions of Span 60 and cholesterol and their loading with posaconazole was achieved. The prepared niosomes were tested for vesicle size, polydispersity index, zeta potential, drug content and morpho-form (Table 5). The

outcome revealed the formation of nanosized vesicles which are appropriate for topical drug delivery.

Table 5. Characterization of niosomal formulations

Formulation	Particle Size (nm)	PDI	Zeta Potential (mV)
F1	514.8	0.2987	-5.372
F2	390.2	0.3000	-4.467
F3	275.0	0.368	-2.066
F4	178.5	0.312	-26.27
F5	295.0	0.276	-25.90
F6	416.1	0.4587	-28.71

The particle size of the formulations varied from 178.5 nm to 514.8 nm. The formulation F4 had the smallest vesicle size (178.5 nm) and PDI (0.312) which is considered as acceptable particle size distribution (Figure 5). The zeta potential values for formulations F4, F5 and F6 were more negative as compared to the previous formulations indicating enhanced electrostatic stability and reduced aggregation tendency (Figure 6). The optimized vesicle size and zeta potential substantiated the suitability of niosomal system for topical application.

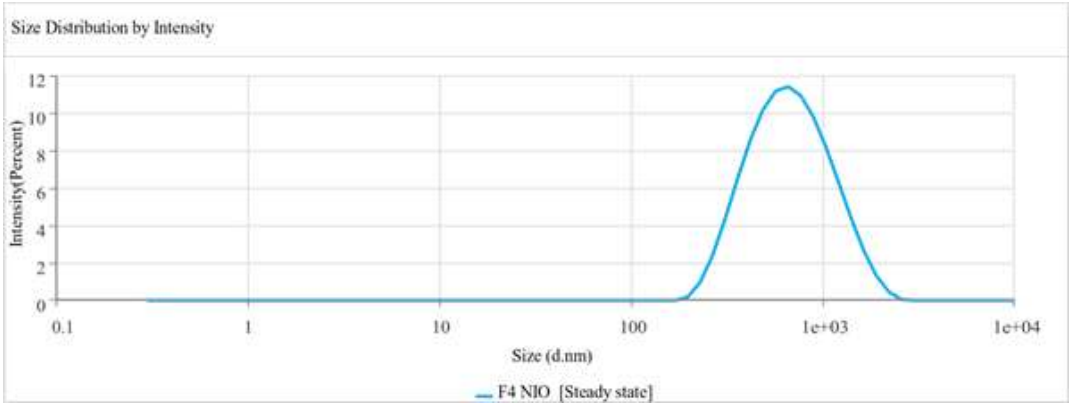

Figure 5. Particle size [nm] F4

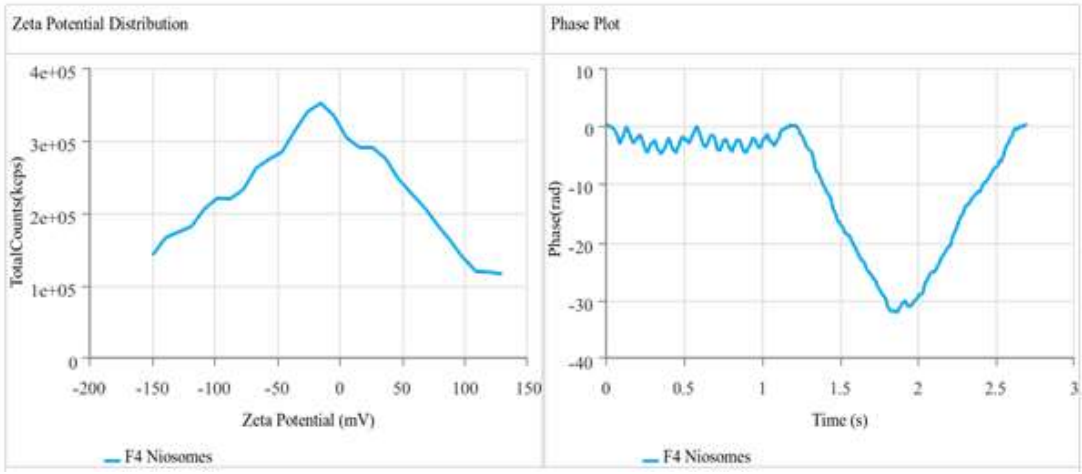

Figure 6. Zeta potential Batch No.F4

Table 6. Entrapment efficiency and drug content of niosomes

Formulation	Entrapment Efficiency (%)	Drug Content (%)
N1/F1	68.4	81.4 ± 1.3
N2/F2	72.8	84.8 ± 1.2
N3/F3	78.6	88.6 ± 1.4
N4/F4	82.9	91.2 ± 1.3
N5/F5	86.7	93.5 ± 1.1

N6/F6	81.3	89.7 ± 1.5

The entrapment efficiency of the prepared niosomes were between 68.4% and 86.7% (Table 6). The highest entrapment efficiency was observed in N5/F5, which may be due to the optimized surfactant-to-cholesterol ratio. Cholesterol makes the bilayer more rigid and less permeable to the drug leakage from vesicles. The amount of drug content was also the highest (93.5 ± 1.1%) in F5, suggesting efficient incorporation and uniform distribution of Posaconazole in the vesicular system.

SEM Analysis

The optimized niosomal vesicles were spherical to nearly spherical and with smooth and uniform surfaces as revealed by SEM (Figure 7). There was no obvious aggregation or irregularity, which validated the successful formation of vesicles and physical stability of the optimized formulation.

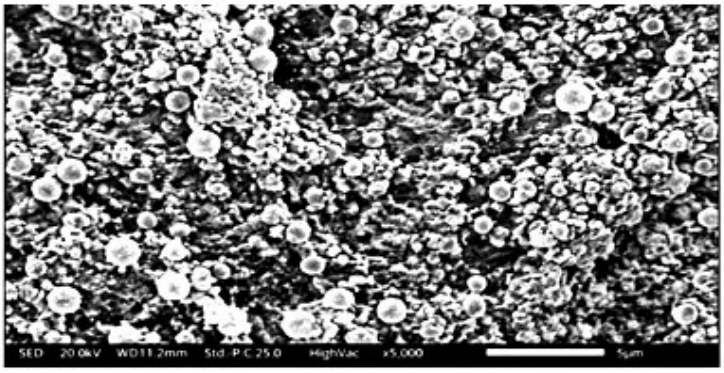

Figure 7. Scanning Electron Microscopy

Evaluation of Posaconazole-Loaded Niosomal Gel

The optimized niosomal formulation was then incorporated into a Carbopol 940 gel base to get a topical niosomal gel. The pre-made gel formulations were tested for pH, viscosity, spreadability, content of drug and in vitro diffusion. The formulations were free of grittiness and phase separation and were smooth and homogeneous, showing good physical acceptability for topical application.

Table 7. pH of niosomal gel formulations

Formulation	pH
G1	5.46 ± 0.02
G2	6.66 ± 0.015
G3	6.74 ± 0.02
G4	6.85 ± 0.015

The pH of the gel formulations ranged from 5.46 ± 0.02 to 6.85 ± 0.015 (Table 7). This range is thought to be appropriate for topical use and is likely to cause less skin irritation. The results revealed that the prepared niosomal gels were pH compatible with the skin pH and suitable for topical antifungal application.

Table 8. Viscosity of niosomal gel formulations

RPM	F2 (cP)	F3 (cP)	F4 (cP)	F5 (cP)
10	4280 ± 35	4525 ± 42	4810 ± 38	5095 ± 45
20	4015 ± 30	4268 ± 36	4552 ± 34	4820 ± 40
50	3728 ± 28	3954 ± 30	4216 ± 32	4485 ± 35
100	3415 ± 25	3628 ± 28	3885 ± 30	4126 ± 32

The viscosity values have decreased with the increase in shear rate, showing a pseudoplastic behaviour. This property is desirable when designing topical gels, because the formulation is stable within the container, but upon application spreads well. The viscosity of F5 was higher than other formulations which could increase residence time on the skin surface and lead to more sustained drug diffusion (Table 8).

Table 9. Spreadability of niosomal gel formulations

Formulation	Initial Diameter (cm)	Final Spread Diameter (cm)	Weight (g)	Time (min)	Observation
F2	2.0	5.6 ± 0.12	500	5	Good
F3	2.0	5.9 ± 0.08	500	5	Very good

F4	2.0	6.1 ± 0.10	500	5	Excellent
F5	2.0	6.4 ± 0.09	500	5	Excellent

The spreadability was found to be greater from F2 to F5 which meant that it was easier to apply. The highest spreading diameter was observed in F5 with 6.4 ± 0.09 cm without requiring much effort for spreading (Table 9). A good spreadability will ensure the drug is evenly distributed over the affected area, and may enhance patient compliance.

Table 10. Drug content of niosomal gel formulations

Formulation	Drug Content (%)
F2	91.84 ± 0.24
F3	93.62 ± 0.20
F4	95.48 ± 0.18
F5	97.16 ± 0.15

The drug content of niosomal gel formulations was found between 91.84 ± 0.24% and 97.16 ± 0.15% (Table 10). The high drug content values were indicative of an even distribution of Posaconazole in the gel matrix. The drug content of F5 was highest, which implied its highest stability in vesicles and incorporation of drug in gel system.

In Vitro Diffusion Study

In vitro diffusion study was carried out for 12 hours in Franz diffusion cell. The release of the drug from the niosomal gel formulations was in the form of sustained and controlled release profile (Table 11). An early morning release was noted and was followed by release throughout the study period. This biphasic release can be explained by the surface associated drug release and the slow diffusion of the entrapped drug from the niosomal vesicles.

Table 11. *In vitro* diffusion study of niosomal gel formulations

Time (h)	F2 (%)	F3 (%)	F4 (%)	F5 (%)
0	0	0	0	0
1	16.80	13.60	10.90	8.80
2	27.50	23.20	19.40	16.60
3	39.20	33.80	28.60	24.80
5	53.60	47.50	41.90	36.80
6	64.20	58.10	52.40	47.60
8	79.80	73.20	67.40	61.50
10	91.40	86.30	81.20	75.80
12	98.90	98.10	97.20	98.42

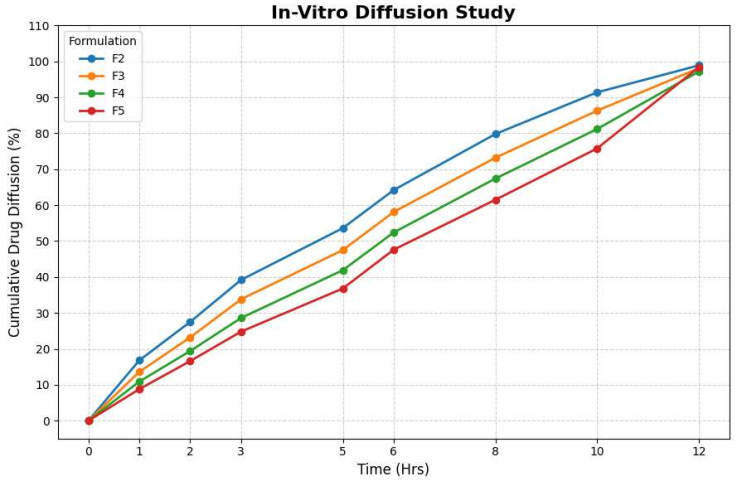

Figure 8. *In Vitro* Diffusion Study

The drug release was quicker in F2 during the first hours, which is likely due to less viscosity and less diffusional resistance (Figure 8). F5 exhibited a controlled release showing a 47.60% release at 6 hrs and 98.42% at 12 hrs, which suggests that the drug released is controlled with better diffusion. Vesicle rigidity, cholesterol concentration

and gel viscosity can affect the release behaviour. The optimization formulation was designed to give sufficient release and a long duration of drug in the topical antifungal treatment.

Comparative Study with Conventional Gel

The optimized niosomes in gel exhibited higher extent of drug release compared to the plain gel. The optimized niosomal gel released 98.95% drug at the 12th hour while the conventional gel released 64.20% drug (Table 12 & Figure 9)). The improved release of niosomal gel is probably attributed to the improvement of the solubilisation of Posaconazole, an increase of surface area of the vesicles and diffusion-through improvement of the hydrated gel matrix. Conventional gel drug release was slower and incomplete due to the poor solubility parameter and passive diffusion of the drug.

Table 12. Comparative drug release of optimized niosomal gel and conventional gel

Time (h)	Optimized Niosomal Gel F4 (%)	Conventional Plain Gel (%)
0	0	0
1	10.90	6.20
2	19.40	11.50
3	28.60	17.40
5	41.90	28.60
6	51.12	35.20
7	63.25	42.60
8	76.56	48.80
9	86.21	53.40
10	94.63	57.20
11	96.50	60.10
12	98.95	64.20

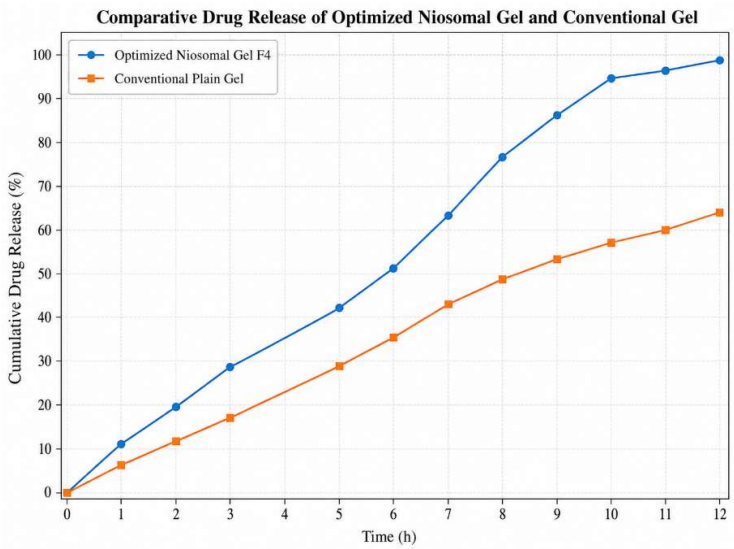

Figure 9. Comparative drug release of optimized niosomal gel and conventional gel

Antifungal Activity

The study on the activity of Posaconazole showed that the Posaconazole-loaded niosomal gel was really good at fighting against Candida albicans and Aspergillus niger. It was better than the Posaconazole and the Posaconazole that you can buy in stores.

If we look at the results in Figure 10 and Table 13 we can see that the special niosomal gel with Posaconazole in it was the best at stopping the growth of these fungi. It had a zone of inhibition of 28 millimeters. The pure Posaconazole was not as good it only had a zone of inhibition of 19 millimeters. The Posaconazole that you can buy in stores was a little better but still not as good as the niosomal gel it had a zone of inhibition of 23 millimeters.

This means that the niosomal gel with Posaconazole in it is really good at fighting against these fungi. The reason it is so good is that it helps Posaconazole to dissolve it helps Posaconazole to get into the fungal cells better and it releases Posaconazole slowly over time.

So the results of the study show that the niosomal gel with Posaconazole in it is better at stopping the growth of Candida albicans and Aspergillus niger, than the Posaconazole and the Posaconazole that you can buy in stores. The Posaconazole-loaded niosomal gel is more effective because it has Posaconazole in it and it works well.

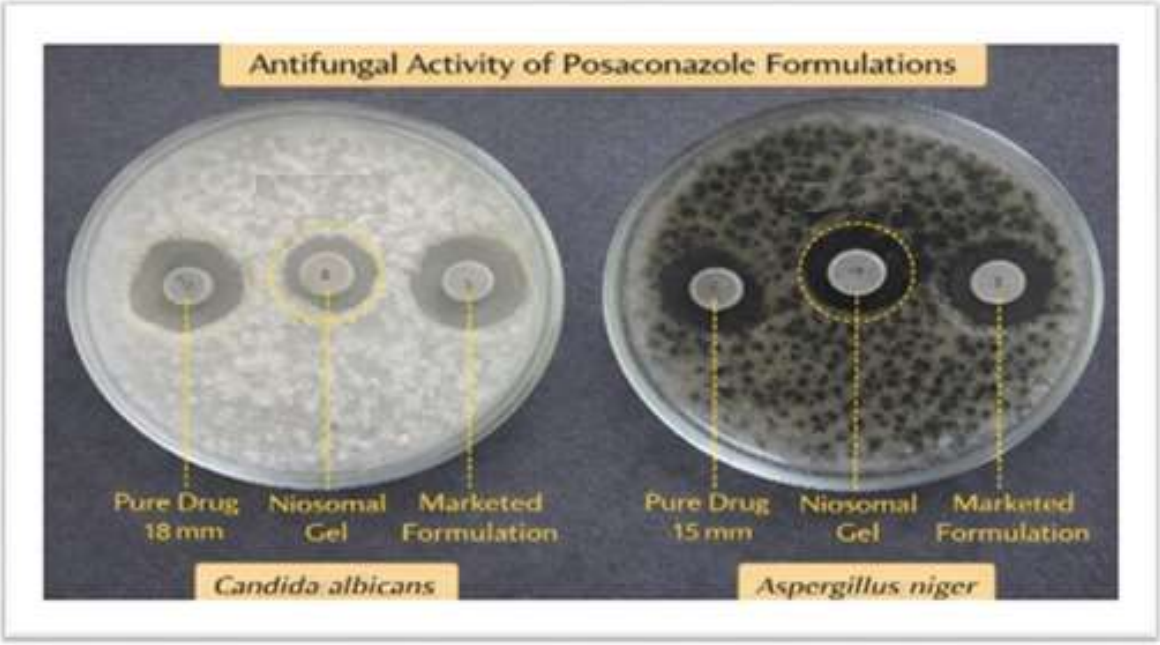

Figure 10. Antifungal activity of formulations

Table 13. Antifungal activity of formulations

Formulation	Zone of Inhibition (mm)
Pure drug	19 ± 0.5
Posaconazole-loaded niosomal gel	28 ± 0.4
Marketed formulation	23 ± 0.6

Stability Study

The Posaconazole-loaded niosomal gel was tested for stability over three months in hot and humid conditions, which is 40 degrees Celsius and 75 percent relative humidity. The Posaconazole-loaded niosomal gel was checked every now and then to see if it looked okay if the pH was right if it was thick or thin if it spread easily if it still had the amount of Posaconazole in it and if the parts were still mixed together. The Posaconazole-loaded niosomal gel did not change color it was still the same it did not get thicker or thinner it did not get grainy it did not turn into liquid. The parts did not separate. The only small changes were in how thick or thin the Posaconazole-loaded niosomal gel was and how easily it spread. The amount of Posaconazole in the Posaconazole-loaded niosomal gel did not decrease much. These results showed that the Posaconazole-loaded niosomal gel stayed stable when it was stored in these conditions.

CONCLUSION

This study was successful in making and testing a Posaconazole-loaded niosomal gel that can be used on the skin to fight fungus. Using niosomes was an idea because it helped to fix the problems with Posaconazole, which is that it does not dissolve well it does not go deep into the skin and it does not stay on the skin for a long time. Before making the Posaconazole-loaded niosomal gel the ingredients were tested to make sure they were good to use. The tests showed that the Posaconazole and the other ingredients were compatible and that the Posaconazole-loaded niosomal gel was stable. The Posaconazole-loaded niosomal gel had the characteristics for use on the skin, such as the right pH it was not too thick or too thin it spread easily and the Posaconazole was distributed evenly. The test that showed how the Posaconazole was released from the Posaconazole-loaded niosomal gel over time showed that it was released slowly and steadily over 12 hours. The Posaconazole-loaded niosomal gel released Posaconazole than the regular gel. The test that showed how well the Posaconazole-loaded niosomal gel fought fungus showed that it was better than the Posaconazole and the Posaconazole that is sold in stores. The Posaconazole-loaded niosomal gel stayed stable when it was stored. Overall the Posaconazole-loaded niosomal gel is a way to deliver Posaconazole to the skin because it makes more Posaconazole available, to the skin it releases the Posaconazole over a long time it fights fungus better and it may not need to be applied as often. More tests are needed to see if the Posaconazole-loaded niosomal gel is safe to use on the skin and if it can be made in quantities.

REFERENCES

1. Courtney R, Pai S, Laughlin M, Lim J, Batra V. Pharmacokinetics, safety, and tolerability of oral posaconazole administered in single and multiple

doses in healthy adults. Antimicrobial agents and chemotherapy. 2003 Sep;47(9):2788-95. https://doi.org/10.1128/aac.47.9.2788-2795.2003
2. Walsh TJ, Raad I, Patterson TF, et al. Treatment of invasive aspergillosis with posaconazole. Clin Infect Dis. 2007;44(1):2-12. https://doi.org/10.1086/508774
3. Ullmann AJ, Cornely OA, Donnelly JP, et al. ESCMID guideline for diagnosis and management of Candida diseases. Clin Microbiol Infect. 2012;18 Suppl 7:19-37. https://doi.org/10.1111/1469-0691.12039
4. Logan A, Wolfe A, Williamson JC. Antifungal resistance and the role of new therapeutic agents. Current Infectious Disease Reports. 2022 Sep;24(9):105-16. https://doi.org/10.1007/s11908-022-00782-5
5. Chen L, Krekels EH, Verweij PE, Buil JB, Knibbe CA, Brüggemann RJ. Pharmacokinetics and pharmacodynamics of posaconazole. Drugs. 2020 Apr 22;80(7):671. https://doi.org/10.1007/s40265-020-01306-y
6. Mosallam S, Albash R, Abdelbari MA. Advanced vesicular systems for antifungal drug delivery. AAPS PharmSciTech. 2022 Jul 28;23(6):206. https://doi.org/10.1208/s12249-022-02357-y
7. Ahmed S, Mehana D, Attia H, El-Ashmoony MM. Terpene-enhanced olaminogel for superior vaginal permeation: robust assessment through in vitro, microbiological, ex vivo, and in vivo evaluations. Naunyn-Schmiedeberg's Archives of Pharmacology. 2026 Mar;399(6):8003-20. https://doi.org/10.1007/s00210-025-04838-w
8. Uchegbu IF, Florence AT. Non-ionic surfactant vesicles (niosomes): physical and pharmaceutical chemistry. Adv Colloid Interface Sci. 1995;58(1):1-55. https://doi.org/10.1016/0001-8686(95)00242-I
9. Baillie AJ, Florence AT, Hume LR, Muirhead GT, Rogerson A. The preparation and properties of niosomes. J Pharm Pharmacol. 1985;37(12):863-868. https://doi.org/10.1111/j.2042-7158.1985.tb04990.x
10. Batur E, Özdemir S, Durgun ME, Özsoy Y. Vesicular drug delivery systems: promising approaches in ocular drug delivery. Pharmaceuticals. 2024 Apr 16;17(4):511. https://doi.org/10.3390/ph17040511
11. Moghassemi S, Hadjizadeh A. Nano-niosomes as nanoscale drug delivery systems. J Control Release. 2014;185:22-36. https://doi.org/10.1016/j.jconrel.2014.04.015
12. Pirojiya H, Dudhat K. Niosomes: a revolution in sustainable and targeted drug delivery-green synthesis, precision medicine, and beyond. Regenerative Engineering and Translational Medicine. 2025 Jun;11(2):379-415. 379–415 (2025). https://doi.org/10.1007/s40883-024-00373-x
13. Mawazi SM, Ge Y, Widodo RT. Niosome preparation techniques and structure—An illustrated review. Pharmaceutics. 2025 Jan 6;17(1):67. https://doi.org/10.3390/pharmaceutics17010067
14. Kumar M, Mandal UK, Mahmood S. Dermatological formulations. InDosage forms, formulation developments and regulations 2024 Jan 1 (pp. 613-642). Academic Press. https://doi.org/10.1016/B978-0-323-91817-6.00021-8
15. Benson HAE, Watkinson AC. Transdermal and topical drug delivery: principles and practice. Hoboken: Wiley; 2012. https://doi.org/10.1002/9781118140505.ch18
16. Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy. 4th ed. New Delhi: CBS Publishers; 2013.
17. Allen LV, Popovich NG, Ansel HC. Ansel's pharmaceutical dosage forms and drug delivery systems. 10th ed. Philadelphia: Wolters Kluwer; 2014.
18. Kakkar S, Kaur IP. Spanlastics: a novel nanovesicular carrier system for enhanced dermal delivery of antifungal drugs. Int J Pharm. 2011;413(1-2):202-210. https://doi.org/10.1016/j.ijpharm.2011.04.027
19. Bhaskar R, Ola M, Tikhe R, Madwe V, Pawar A, Khade S, Shinde S. Current and Emerging Formulations in Topical Antifungal Therapy: A Comparative Overview. Journal of Drug Delivery & Therapeutics. 2025 May 1;15(5). 10.22270/jddt.v15i5.7127
20. Kaur CD, Saraf S. Topical vesicular formulations of ketoconazole for enhanced antifungal activity. Int J Drug Deliv. 2011;3:1-10. https://doi.org/10.1111/j.1473-2165.2011.00586.x
21. Verma S, Utreja P. Vesicular nanocarrier based treatment of skin fungal infections: Potential and emerging trends in nanoscale pharmacotherapy. Asian journal of pharmaceutical sciences. 2019 Mar 1;14(2):117-29. https://doi.org/10.1016/j.ajps.2018.05.007.
22. Gupta M, Vaidya B, Mishra N, Vyas SP. Effect of surfactants on the characteristics of fluconazole niosomes for enhanced cutaneous delivery. Artificial cells, blood substitutes, and biotechnology. 2011 Dec 1;39(6):376-84. https://doi.org/10.3109/10731199.2011.611476
23. Kaur M, Singh K, Jain SK. Luliconazole vesicular based gel formulations for its enhanced topical delivery. Journal of Liposome Research. 2020 Oct

1;30(4):388-406. https://doi.org/10.1080/08982104.2019.1682602

24. Mostafa M, Al Fatease A, Alany RG, Abdelkader H. Recent Advances of Ocular Drug Delivery Systems: Prominence of Ocular Implants for Chronic Eye Diseases. Pharmaceutics 2023; 15: 1746. doi. org/10.3390/pharmaceutics15061746 Academic Editors: Francisco Javier Otero-Espinar and Blanca Arango-Gonzalez Received. 2023 May;16. hps://doi.org/10.3390/ pharmaceutics15061746
25. Chatur VM, Dhole SN, Kulkarni NS, Rudrapal M. Development and characterization of antifungal niosomal gel of luliconazole: In vitro and ex vivo approaches. Chemical Physics Impact. 2025 Jun 1;10:100801. https://doi.org/10.1016/j.chphi.2024.100801
26. Khamkat P, Mohapatra S, Mukherjee S, Dutta G, Singh S. Design and Assessment of Posaconazole-Loaded Transfersomal Gel for Antifungal Efficacy Against Candida Albicans and Aspergillus Niger. Journal of Pharmaceutical Innovation. 2026 Apr;21(2):105. https://doi.org/10.1007/s12247-025-10317-9.
27. Izhar MP, Hafeez A, Kushwaha P, Simrah. Drug delivery through niosomes: a comprehensive review with therapeutic applications. Journal of Cluster Science. 2023 Sep;34(5):2257-73. https://doi.org/10.1007/s10876-023-02423-w
28. Nagpal M, Kaur M. Nanomaterials for skin antifungal therapy: An updated review. Journal of Applied Pharmaceutical Science. 2021 Feb 11;11(1):015-25. https://dx.doi.org/10.7324/JAPS.2021.11s102
29. Witika BA, Mweetwa LL, Tshiamo KO, Edler K, Matafwali SK, Ntemi PV, Chikukwa MT, Makoni PA. Vesicular drug delivery for the treatment of topical disorders: current and future perspectives. Journal of Pharmacy and Pharmacology. 2021 Nov 1;73(11):1427-41. https://doi.org/10.1093/jpp/rgab082
30. Hashem SM, Gad MK, Anwar HM, Saleh NM, Shamma RN, Elsherif NI. Itraconazole-loaded ufasomes: evaluation, characterization, and anti-fungal activity against Candida albicans. Pharmaceutics. 2022 Dec 21;15(1):26. https://doi.org/10.3390/pharmaceutics15010026
31. Fatima I, Rasul A, Shah S, Saadullah M, Islam N, Khames A, Salawi A, Ahmed MM, Almoshari Y, Abbas G, Abourehab MA. Novasomes as nano-vesicular carriers to enhance topical delivery of fluconazole: a new approach to treat fungal infections. Molecules. 2022 May 4;27(9):2936. https://doi.org/10.3390/molecules27092936.
32. Rukari T, Pingale P, Upasani C. Vesicular drug delivery systems for the fungal infections' treatment through topical application-a systemic review. J Curr Sci Technol. 2023 Jul 24;13(2):500-16. https://doi.org/10.59796/jcst.V13N2.2023.1856.
33. Abdelkader H, El-Wahab AA, El-Gendy AO, Abou-Taleb HA. Formulation and optimization of lipid-and Poloxamer-tagged niosomes for dermal delivery of terbinafine: preparation, evaluation, and in vitro antifungal activity. Pharmaceutical Development and Technology. 2023 Oct 21;28(9):803-10. https://doi.org/10.1080/10837450.2023.2255889
34. Phatak KM, Yawalkar AN, Sole SS, Vavia PR. Overcoming corneal barriers: Posaconazole loaded cationic surfactant vesicles for enhanced ocular permeability and anti-fungal efficacy. Asian Journal of Pharmaceutical Sciences. 2025 Aug 17:101087. https://doi.org/10.1016/j.ajps.2025.101087
35. Morteza-Semnani K, Saeedi M, Akbari J, Hedayati S, Hashemi SM, Rahimnia SM, Babaei A, Ghazanfari M, Haghani I, Hedayati MT. Green formulation, characterization, antifungal and biological safety evaluation of terbinafine HCl niosomes and niosomal gels manufactured by eco-friendly green method. Journal of Biomaterials Science, Polymer Edition. 2022 Nov 23;33(18):2325-52. https://doi.org/10.1080/09205063.2022.2103626
36. Kaoud RM, Khalid AA, Ghazi YA, Talip AM. Formulation, In-Vitro Characterization, And Antifungal Efficacy of Itraconazole Topical Niosomal Gel: Development and Microbiological Evaluation. Palestinian Medical and Pharmaceutical Journal (Pal. Med. Pharm. J.). 2024 Dec 13;10(5):345-50. https://doi.org/10.59049/2790-0231.10.4.2418