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Development And Evaluation Of Miconazole Nitrate Loaded Niosomal Suspension

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ABSTRACT

Niosomes, which are vesicular drug delivery vehicles made mostly of non-ionic surfactants, have a number of benefits over traditional formulations. Niosomes are a safer option than other nanoparticle-based carriers because of their improved stability, biodegradability, and decreased toxicity. These vesicles are very adaptable because they can contain both hydrophilic and lipophilic medications. They are especially useful in systemic applications like cancer therapy as well as topical and transdermal formulations like gels and creams because of their capacity to enhance drug penetration, maintain release, and target particular sites. The goal of this research is to maximize stability and integrity by optimizing the formulation of niosomes in the lab and testing various surfactant and cholesterol ratios. The study also attempts to evaluate the niosomal system's release behavior and drug loading efficiency. Thorough characterization methods, such as FTIR, TEM, SEM, and zeta potential analysis, are used to assess the physicochemical stability, morphology, and general performance of the prepared formulations.

Keywords: *Niosome, FTIR, SEM ,TEM, Miconazole, Transdermal delivery*

1. INTRODUCTION

Bypassing the gastrointestinal tract and hepatic first-pass metabolism, the transdermal drug delivery system provides a non-invasive way to deliver therapeutic agents straight into the systemic circulation. This method improves patient compliance, especially when applied in forms that are easy to use, like gels, patches, and creams. Transdermal systems offer a number of benefits over traditional routes, such as increased drug efficacy, targeted delivery, and fewer doses. Stabilizing medications that are susceptible to breakdown or metabolism in the digestive system is one of the main advantages of this route. Transdermal delivery reduces the possibility of systemic side effects like allergic reactions or sensitivities by avoiding the harsh environment of gastrointestinal fluids and liver metabolism. All things considered, this system guarantees consistent plasma drug levels, improves bioavailability.Another benefit of transdermal systems is site-specific drug delivery, which is especially helpful for localized treatments like cancer therapy. This focused strategy lowers systemic exposure while increasing drug efficacy. Transdermal patches and other formulations are easily removed in the event of adverse effects or dose dumping, adding an extra degree of safety. Their non-invasiveness greatly enhances patient comfort and compliance. Furthermore, transdermal delivery enables drug release modulation, which makes it appropriate for the creation of controlled-release formulations \[1]. The goal of this study is to formulate and evaluate a niosomal gel containing the antifungal drug miconazole sulfate. Niosomes are adaptable carriers that can be used for parenteral administration as well as topical applications. making them useful for a variety of drug delivery methods. Their potential as effective, reliable, and patient-friendly drug delivery systems is further supported by their capacity to encapsulate both hydrophilic and lipophilic medications.

1.1 Niosomes[4, 5]

Drug delivery systems have undergone significant change since the development of nanotechnology, mainly due to improvements in drug bioavailability and targeting effectiveness. Niosomal hybrid formulations, like emulgels and creams, have become a promising substitute for traditional dosage forms among the different nanocarrier approaches. Improved stability, biocompatibility, and the capacity to encapsulate both hydrophilic and lipophilic medications are just a few benefits that niosomes provide. Niosomes, in contrast to conventional systems, get around a lot of the drawbacks of conventional formulations, including low solubility, instability, and restricted bioavailability.Niosomes are self-assembled vesicles made of non-ionic surfactants that, in an aqueous environment, form bilayer membranes. Despite having a similar appearance to liposomes, they are fundamentally different. Niosomes are made of neutral surfactants, which makes them more stable, economical, and chemically inert than liposomes, which are usually made of negatively charged phospholipids. For a variety of biomedical applications, niosomes are frequently thought of as a better option than liposomes because of these characteristics.

Depending on the surfactant composition and preparation technique, niosomes can have unilamellar, bilayered, or multilamellar structural forms. A broad range of therapeutic agents, such as small molecule medications, proteins, peptides, vaccines, antibodies, and folic acid, can be encapsulated thanks to their bilayer structure. Lipophilic drugs integrate into the hydrophobic core, whereas hydrophilic drugs are typically trapped in the aqueous core.

The non-ionic surfactant, which is amphiphilic—having both hydrophilic and hydrophobic segments—is the primary element in niosomes that causes vesicle formation. In aqueous solutions, closed bilayer vesicles self-assemble due to this amphiphilicity. The type and length of the fatty acid chains involved are indicated by the numerical designation in the names of popular surfactants like Span and Tween.

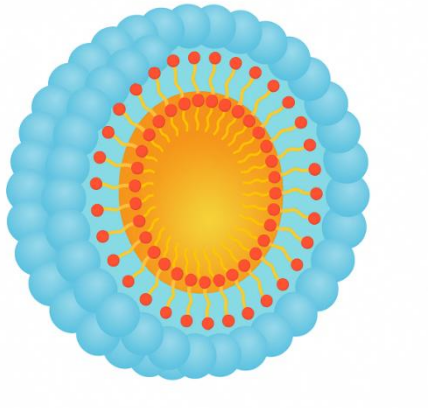

Fig 2.1

2. MATERIAL AND METHODS[6]

2.1 Materials

Miconazole Nitrate 98.35% (T), from Yarrow Chem Products, Ghatkopar (West), Mumbai- 400086 Maharashtra. Cholesterol, Span 60, Methanol, Chloroform and other chemicals from laboratory of Kailash institute of pharmacy and management, GIDA, Gorakhpur.

2.2 Preformulations[7, 8, 18]

2.2.1. Organoleptic Examination

Using our senses—such as sight, smell, taste, and touch—to assess a medication or formulation is known as organoleptic evaluation. It may seem easy, but it's actually a crucial first step in ensuring that a product feels, looks, and smells as it should. Unexpected changes in color, texture, or odor, for instance, could be an indication that something is amiss, such as contamination or the product beginning to degrade. Maintaining a consistent color scheme fosters user trust in addition to aesthetics. An odd odor could indicate a chemical shift or the growth of bacteria.

Property	Description
Odor	Odourless

Color	White to off-white
Description	Crystalline powder
Taste	Bitter (though usually masked in formulations)

Table 2.1 Organoleptic property

2.2.2 Analysis of Solubility[7,8,9]

Start by accurately weighing out 1 mg of Miconazole. Then, take five clean test tubes and add 10 mL of different solvents into each one—water, ethanol, methanol,chloroform and acetone. Add the weighed drug to each test tube individually. Once that's done, shake all the test tubes gently and allow them to stand at room temperature for a set period—typically around 24 hours. This helps the drug fully interact with each solvent. After the shaking period, filter the solutions to remove any undissolved particles. Then, take 1 mL of the clear filtrate from each test tube. These samples are then analyzed using a UV spectrophotometer, with the absorbance measured at a wavelength of 223 nm to determine solubility in each medium.

Solvents	**Solubility (mg/ml)**
Ethanol	0.72
Water	0.03
Acetone	0.34
Chloroform	0.12
Methanol	0.25

Table 2.2 Solubility of Miconazole

2.2.3 pH and pKa value of Miconazole[7,8,9]

- Ten milliliters of distilled water were used to dissolve one milligram of miconazole.
- Using common buffer solutions, set the digital pH meter to 4.0, 7.0, and 10.0.
- Note the Miconazole solution's pH level.

S.No	pH
1.	6.27
2.	6.52
3.	6.43
Mean ± S.D	6.41±0.15

Table 2.3 pH values

2.2.4. pKa of Miconazole[7,8,9]

Using pH and UV Absorbance Data

We have UV absorbance of ionized and unionized forms, we can calculate the ratio:
pH = pKa + log((A - AU)/(AI - A))
Where:
Absorbance of mixture(A) = 0.376
Absorbance of unionized form(AU) = 0.137

Absorbance of ionized form(AI) = 0.459

Putting the values in the equation

pH = pKa + log((A - AU)/(AI - A))

6.41 = pKa + log 2.39
6.41 = pKa + 0.3783

pKa = 6.09

2.2.5. Melting Point of Miconazole[7, 8, 9]

Miconazole's melting point can be determined by first packing a small amount of the powdered medication into a capillary tube with thin walls and sealing one end. Put this tube inside a device that measures melting points. Increase the temperature gradually while keeping a close eye on the sample. Keep track of the temperature at which the powder melts the most and the temperature at which it liquefies completely. The melting point range of miconazole is defined as the range between these two temperatures.

S.no	Temperature
1	162.7
2	161.4
3	161.5
Mean ± S.D	161.87±0.59°C

Table 2.4 Melting Point

2.2.6. Micrometrics[7, 8, 10]

2.2.6.1 True Density

The true density of a sample excludes the volume of the pores and voids within the powder sample.

$$\text{True Density} = \frac{\text{Weight of Powder}}{\text{True volume of Powder}}$$

Procedure to find True Density

- Weigh empty density bottle(pycnometer) with stopper as W1
- Fill completely density bottle with the solvent and place stopper
- Weigh the bottle with water as W2
- Remove water from the bottle
- Now transfer the Miconazole drug powder (approx. 1g) to the pycnometer bottle
- Now weigh the bottle containing powder as W3
- Now add water to fill this bottle completely and weighed as W4

Measures	Symbols	Weights
Pycnometer	W_1	24.758 g
Pycnometer with Water	W_2	50.638 g
Pycnometer with Powder	W_3	25.994 g
Pycnometer with Powder and Water	W_4	50.844 g

Table 2.5 Pycnometer observations

True density calculations

Water in gram would be, X = (W3-W1)

= 25.994−24.758

= 1.236g

Pycnometer weight with water content in powder (W5) = W4 – X

= 50.844 - 1.236

= 49.608

Weight of Powder displaced by Water = W2 – W5

= 50.638 - 49.608

= 1.030

The volume of water represents the actual volume of miconazole powder.

$$\text{True Density} = \frac{\text{Weight of Powder}}{\text{True volume of Powder}}$$

$$= \frac{1.236}{1.030} = 1.2\text{g/ml}$$

2.2.6.2 Bulk Density[7, 8, 10]

The bulk density value includes the volume of all of the pores within the powder sample.

$$\text{Bulk Density} = \frac{\text{Weight of Powder}}{\text{Bulk volume of Powder}}$$

Procedure for Bulk Density finding

- Weigh accurately 2 g of miconazole powder.
- Transfer this powder to measuring cylinder
- Note the bulk volume of powder

$$\text{Bulk Density} = \frac{\text{Weight of Powder}}{\text{Bulk volume of Powder}}$$

Parameter	Value
Weight of Miconazole Powder	2.00 g
Bulk Volume (Cylinder)	5.40 mL
Bulk Density	**0.370 g/mL**

Table 2.6 Bulk density Observations

2.2.6.3 Porosity[7, 8, 10]

Porosity (Ɛ) or void fraction is a measure of the void (i.e.) spaces in a material, and is a fraction of the volume of voids over the total volume

$$\text{Porosity } (\text{Ɛ}) = \frac{\text{Void volume}}{\text{Bulk volume}}$$

$$\text{True volume of powder} = \frac{\text{Weight of Powder}}{\text{True density}}$$

= 1.667 ml

$$= \frac{2\text{gm}}{1.2\text{g/ml}}$$

Bulk volume of powder = 5.4 ml

$$\text{Porosity } (\text{Ɛ}) = \frac{\text{Bulk volume} - \text{True volume}}{\text{Bulk volume}} \times 100$$

$$= \frac{5.4 - 1.667}{5.4} \times 100$$

= 69.13 %

2.2.7 Partition Coefficient (Log P) [7, 8, 9]

Procedure:

First, make the solution in a clean separating funnel by combining miconazole with equal parts distilled water and n-octanol. When the mixture is ready, shake it well for a predetermined period of time to aid in the drug's distribution between the two phases.Once the mixture has been shaken, leave it alone until the layers of octanol and water have fully separated. The drug has achieved equilibrium between the two solvents thanks to this separation. You can carry out additional analysis after the

layers are clearly separated, such as determining the partition coefficient by measuring the drug concentration in each layer.

Concentration Measurement: Use a UV spectrophotometer to determine the amount of miconazole present in each phase.

$$\textbf{Log P} = \textbf{Log}\ \frac{\textbf{Solute present in Octanol}}{\textbf{Solute present in Water}}$$

Observation	Solubility in Octanol (mg/mL)	Solubility in Water (µg/mL)	Log P
1	99.9997	2.51	5.62
2	99.9998	1.67	5.78
3	99.9999	0.79	6.18

Table 2.7 Solubility profile for partition coefficient

2.2.8. Thin layer Chromatography[7, 8, 11]

Procedure:

Get your solvent system ready first. A 7:3 methanol to chloroform ratio is employed for this process. After thoroughly mixing the solvents, pour them into a TLC chamber and let them saturate.Next, use a capillary tube or micropipette to carefully apply a spot close to the base of a clean TLC plate using a small volume of the miconazole solution. Make sure the spotted end of the TLC plate is slightly above the solvent level when you insert it upright into the chamber after the sample has dried. As the solvent moves upward and carries the sample with it, let the plate develop. Once the plate has developed, take it off and allow it to air dry. Depending on how visible the compound is, you can either expose the plate to iodine vapor or view it under a UV lamp to see the spot. Lastly, determine the Rf value by dividing the distance traveled by the solvent front by the distance moved by the spot. Based on its distinctive Rf value, this aids in locating and verifying the presence of miconazole.

$$R_f = \frac{\text{Distance travelled by solute}}{\text{Distance travelled by solvent}}$$

Parameter	Value
TLC Plate Reading	5.2 cm
Solvent Front	10.0 cm
Rf Value	0.52

Table 2.8 TLC plate solvent and solute front

2.2.9 UV Spectroscopy and calibration curve[12, 13]

Using an analytical balance, 10 mg of pure miconazole were precisely weighed to start the process. After the drug was weighed, it was put into a 10 mL volumetric flask and a tiny bit of methanol was added to help dissolve it. After being fully dissolved, methanol was added to bring the volume up to 10 mL, creating a standard stock solution with a 1000 µg/mL concentration.

A number of dilutions were made from this stock. 1 mL of the stock was pipetted into a sterile 10 mL volumetric flask, and the volume was adjusted with methanol to create a 100 µg/mL solution. Following a thorough mixing process, 1 mL of the 100 µg/mL solution was diluted to 10 µg/mL. Following extensive mixing, 1 mL of the 100 µg/mL solution was diluted with 10 mL of methanol to create a 10 µg/mL solution. From the 100 µg/mL solution, 1 mL, 2 mL, and 4 mL, 6 mL, and 8 mL, respectively, were transferred into separate 10 mL volumetric flasks, and each was filled to volume with methanol to create further dilutions of 10 µg/mL, 20 µg/mL, 40 µg/mL, 60 µg/mL, and 80 µg/mL. To guarantee consistent concentration, all solutions were thoroughly mixed. A UV-Visible spectrophotometer was used to scan the 100 µg/mL solution in order to find the λmax. It was discovered that 223 nm was the wavelength of maximum absorbance.Using methanol as the blank and quartz cuvettes, Every prepared dilution's absorbance was measured at the predetermined λmax. Every absorbance value was noted in order to prepare the calibration curve and conduct additional analysis.

Following the recording of the absorbance values for every prepared miconazole concentration, these values were plotted on a graph to create a calibration curve. The x-axis displayed the concentrations (in µg/mL), and the y-axis displayed the corresponding absorbance values.

Following the plotting of the data points, linear regression analysis was used to fit a straight line to the graph. This gave the line's equation, which is as follows: y = mx + c, where:

y stands for absorbance.
x is the solution's concentration,
The line's slope, m, represents the rate at which absorbance changes with concentration.
The y-intercept, or absorbance at zero concentration, is denoted by c.

The curve's linearity verifies that, within the tested range, absorbance and concentration obey Beer-Lambert's law. Any unknown sample's miconazole concentration can be precisely determined using this calibration equation by measuring its absorbance and entering the result into the formula. Likewise it used for the detemination of solubility of miconazole in different solvents as well as in partition coefficient, it also had helped in determining the drug entrapment % in the niosomes.

S no.	Concentration(ug/ml)	Absorbance at 223
1	20	0.128
2	40	0.243
3	60	0.372
4	80	0.476
5	100	0.602

Table 2.9 UV Absorbance

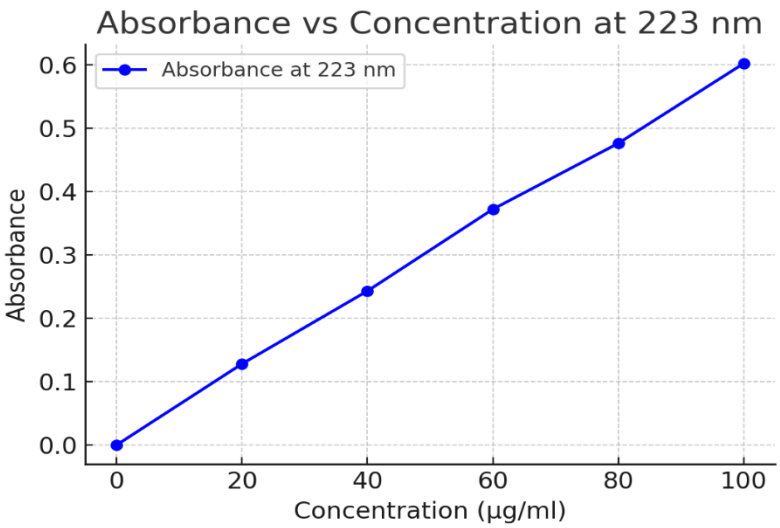

Fig 2.1 UV Absorbance of Miconazole

Use Two Points to Calculate the Slope

Using points (20, 0.128) and (40, 0.243):

Slope (m) = $(y_2 - y_1) / (x_2 - x_1)$

= (0.243- 0.128) / (40 - 20)

= 0.00575

Find the Y-intercept (c)

Using the point (20, 0.128) and slope m = 0.00575:

y = mx + c

0.128 = 0.00575 × 20 + b

b = 0.013

Final Equation of the Line

y = 0.00576 x + 0.013

R^2 = 0.9994

2.3 Formulation[7, 8, 14]

2.3.1 Thin Film Hydration Method[14]

A precise amount of a chosen non-ionic surfactant and cholesterol were precisely weighed in order to start the formulation process. Following that, both substances were dissolved in a 2:1 volume ratio of methanol and chloroform in an organic solvent mixture. A flask with a round bottom was used for this dissolution. When incorporating a lipophilic drug, such as miconazole, the drug was added straight to this lipid phase while the solvent was being mixed. After dissolution, the mixture was subjected to vacuum-induced rotary evaporation. Throughout this step, the temperature was carefully kept between 40°C and 60°C. A thin, consistent lipid layer developed on the inside of the round-bottom flask as the solvents evaporated. The homogeneity and consistency necessary for effective vesicle formation were ensured through the use of controlled evaporation. The next stage of the procedure was the hydration of the dry lipid film. The flask was filled with an aqueous phase, usually a pH 7.4 phosphate buffer solution. The temperature at which hydration was performed was higher than the surfactant's phase transition temperature, which is roughly 60°C. After that, the flask was slowly turned to help the lipid film swell and separate from the flask wall. This made it easier for multilamellar niosomal vesicles to form. After 30 to 60 minutes of hydration, a milky suspension was produced, signifying that the vesicles had successfully formed. The milky niosomal dispersion was sonicated in order to increase the suspension's homogeneity and decrease its particle size

Fig 2.2 Thin film Hydration

Ingredient	Amount (mg)	Purpose
Miconazole nitrate	285 mg	Active drug (to achieve 200 mg at ~70% EE)
Span 60	300 mg	Non-ionic surfactant (vesicle former)
Cholesterol	150 mg	Membrane stabilizer
Chloroform:Methanol (2:1)	q.s. (10 mL)	Organic solvents for lipid dissolution
Phosphate buffer (pH 7.4)	q.s. (10 mL)	Aqueous phase for hydration

Table 2.10 Composition chart of Niosome

Since the entrapment efficiency of nisome is approximated at 70%, the drug will actually released of 200mg rather than 285 mg

After preparing niosomes by thin-film hydration, used probe sonication or extrusion to reduce vesicle size.

Formulation Procedure[14]

Prepare Niosomes:

1. Dissolve miconazole, cholesterol, and Span 60 in chloroform:methanol.
2. Form thin film via rotary evaporation.
3. Hydrate with phosphate buffer.
4. Sonicate to reduce size.

Formualtion Table of Nisomal Suspension

Formulation	Miconazole (mg)	Span 60 (mg)	Cholesterol (mg)	Span:Cholesterol Ratio
F1	285	300	150	2:1
F2	285	300	100	3:1
F3	285	300	200	3:2
F4	285	300	300	1:1

Table 2.11 Formulation Table

2.4.0 Physicochemical Characterization of Niosomal Formulation[14, 15]

2.4.1. Zeta Potential[14, 15,]

When evaluating the physical stability of niosomal suspensions containing miconazole, zeta potential is essential. It acts as a gauge of the vesicles' surface charge, which has a direct impact on their interactions, especially when it comes to repulsion or aggregation. There is more electrostatic repulsion between vesicles when their absolute zeta potential values are higher (either positive or negative). Over time, this repulsion promotes a more stable suspension by drastically lowering the possibility of particle clumping or fusion. The measured zeta potential in the formulation of miconazole-loaded niosomes is significantly influenced by the ratio of Span 60 to cholesterol. Span 60 aids in the vesicles' structural development, In contrast, cholesterol stabilizes membrane rigidity and may indirectly affect surface charge. By changing the concentration of these elements, the membrane's properties are changed, which results in changes to the surface charge and, ultimately, the zeta potential.Maintaining a consistent and stable colloidal system requires finding the ideal ratio between Span 60 and cholesterol. By keeping the vesicles evenly distributed, an ideal formulation lowers the chance of sedimentation or aggregation while being stored. Therefore, zeta potential serves as a predictor of long-term physical stability in niosomal drug delivery systems in addition to reflecting vesicle behavior at the microscopic level.

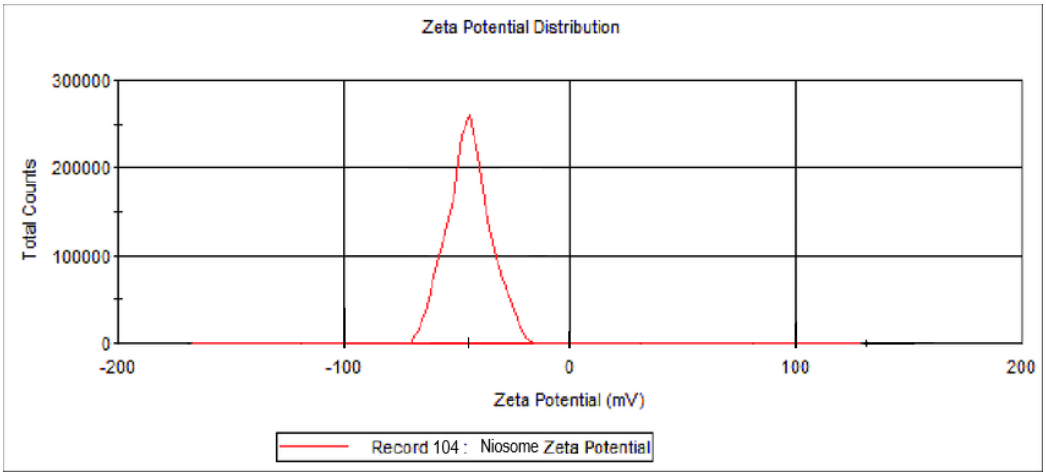

Fig 2.3 Zeta Potential of Niosome

Peak No.	Zeta Potential (mV)	Area (%)	St Dev (mV)
Peak 1	≈ -44.0	100.0	~3– 4
Peak 2	0.00	0.0	0.00
Peak 3	0.00	0.0	0.00

2.4.2 Encapsulation Efficiency of Niosome[14, 15, 20]

To extract the unentrapped (free) drug from the vesicles, the prepared niosomal suspension is first centrifuged at a high speed (usually 10,000–15,000 rpm for 30–60 minutes). For analysis, the clear supernatant—which contains the free drug—is meticulously gathered. The remaining pellet, which contains vesicles loaded with drugs, is either sonicated or treated with a mild detergent. The encapsulated medication is released into the solution when this breaks down the vesicle membranes. The drug concentration in the supernatant (free drug) and lysed vesicle solution (total drug) is then measured using a UV-Visible spectrophotometer (at the determined λmax, e.g., 223 nm for miconazole) or High-Performance Liquid Chromatography (HPLC) for greater accuracy.

Batch Code	Cholesterol (mg)	Span 60 (mg)	Miconazole (mg)	Chloroform:Methanol (2:1)	Phosphate Buffer (pH 7.4)	Entrapment Efficiency (%)
F1 (− −)	50	100	285	15 mL	15 mL	85%
F2 (− +)	50	200	285	15 mL	15 mL	76%
F3 (+ −)	150	100	285	15 mL	15 mL	68%
F4 (+ +)	150	200	285	15 mL	15 mL	72%

Table 2.13 Encapsulation Efficiency

2.4.3 Morphological Evidences (SEM and TEM) [14, 15, 19]

Miconazole-loaded niosomal suspensions can be effectively characterized using scanning electron microscopy (SEM), which provides comprehensive information on the size, shape, and surface morphology of the particles. The high-resolution imagery provided by this method allows for a detailed analysis of the vesicle's structure, integrity, and homogeneity—parameters crucial for assessing the formulation's effectiveness. The final morphology of the vesicles is greatly impacted by variations in the concentration of formulation ingredients like cholesterol and Span 60. The size distribution, level of smoothness, and general shape of the vesicles are determined by these components. SEM images, for example, can show whether particles have a smooth, spherical surface or show indications of irregularities and aggregation. SEM makes it possible to verify that vesicle formation has taken place as planned by visualizing these characteristics. Early on in the formulation's development, any physical irregularities or inconsistencies can also be found. The method also helps identify the most stable and effective composition for drug delivery by comparing different batches or formulations.

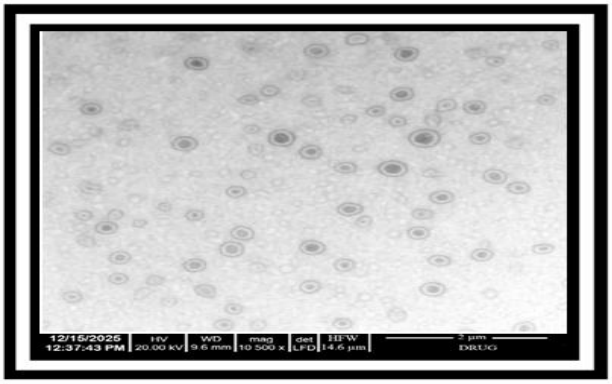

Fig 2.4 SEM of Niosome

Miconazole-loaded niosomes can be seen in great detail using Transmission Electron Microscopy (TEM), which also provides important information about the size, shape, and surface characteristics of the particles. This method aids in determining how vesicle morphology is affected by Span 60 and cholesterol levels. A successful and repeatable formulation is indicated by the observation of uniformly spherical and smooth vesicles. Additionally, structural irregularities like deformation, aggregation, or fusion are revealed by TEM, which can direct required formulation modifications. Batch-to-batch consistency in morphology indicates carefully regulated preparation conditions, which promote formulation stability. Furthermore, TEM makes it possible to correlate drug release behavior with vesicle structure, which improves our comprehension of delivery performance. Its high-resolution imaging greatly aids in the creation of a stable, dependable, and efficient drug delivery platform while also confirming the integrity of the niosomal system.

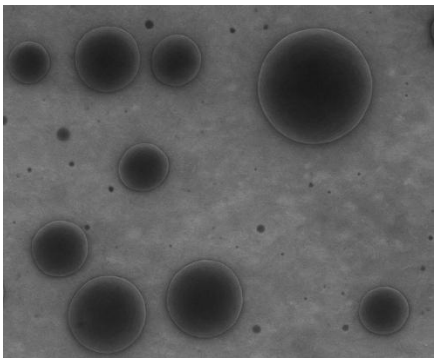

Fig 2.5 TEM of Niosome

2.4.4 Fourier Transform Infrared Spectroscopy (FTIR) [11, 12, 14, 15,]

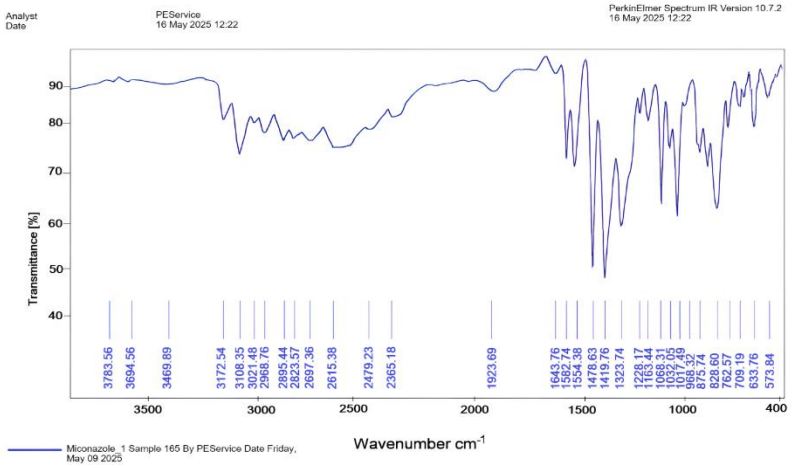

Fig 2.6 FTIR of Miconazole

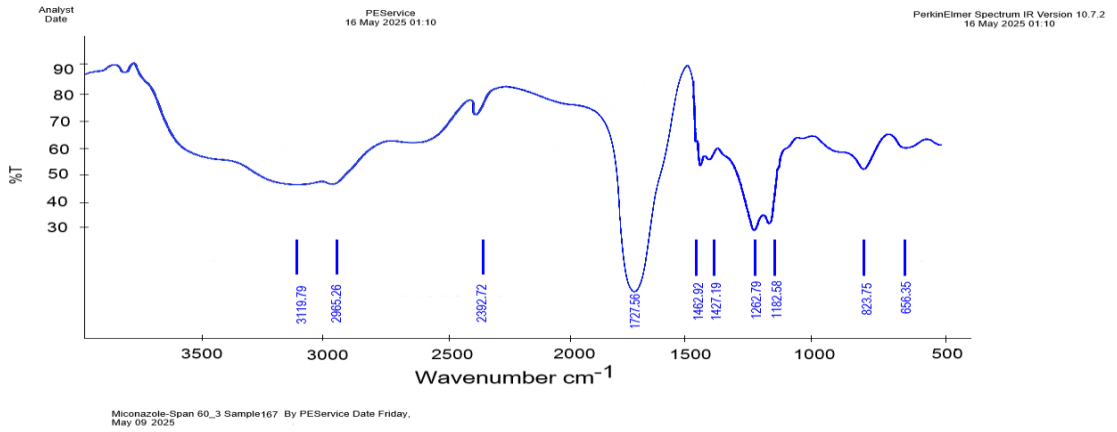

Fig 2.7 FTIR of Miconazole + Span 60

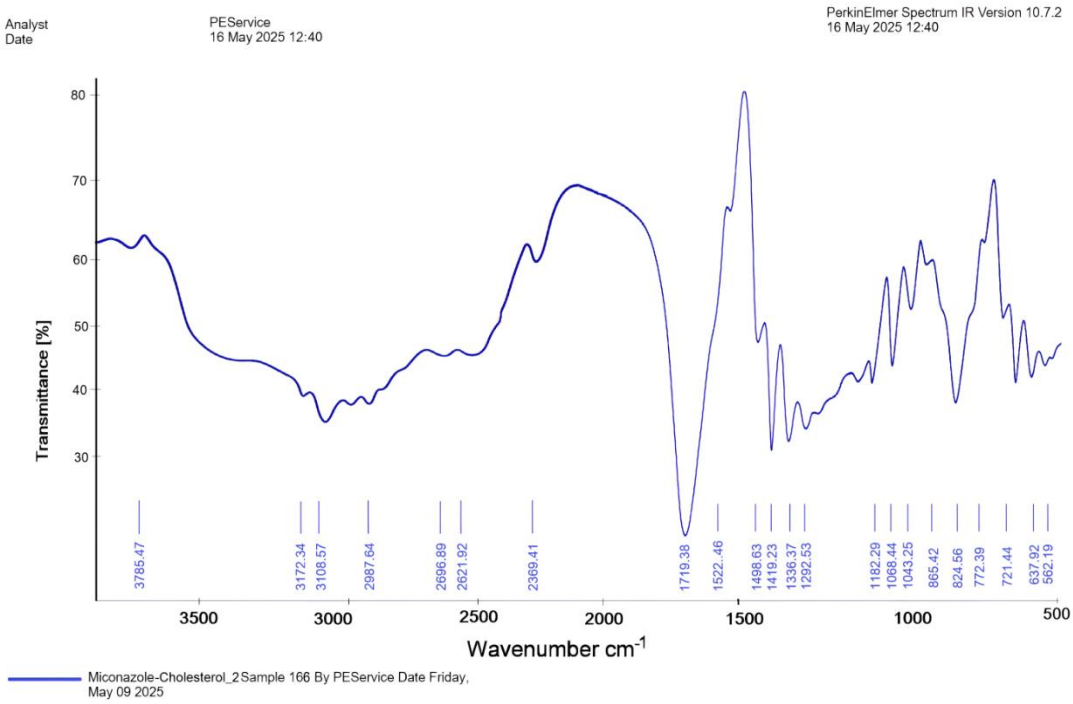

Fig 2.8 FTIR of Miconazole + Cholestrol

2.4.5 pH determination[14, 15, 16]

A niosomal suspension's pH has a significant impact on the formulation's overall performance, vesicle integrity, and drug stability. Acid/base solutions or buffering agents are frequently used to maintain or raise the pH to a desired level.Phosphate buffer (pH 7.4) is frequently used to simulate physiological conditions for miconazole-loaded niosomes.

Formulation	Surfactant:Cholesterol Ratio	Hydration Buffer pH	Measured Suspension pH
F1	2:1	7.4	6.82
F2	3:1	7.4	7.15

F3	3:2	7.4	7.38
F4	1:1	7.4	7.42

Table 2.14 pH of Niosomal Suspension

2.4.6 In vitro drug Release[4, 14, 16, 18]

S.No.	Time	FS1	FS2	FS3	FS4
1	0	0.0	0.0	0.0	0.0
2	1	8.1	11.7	9.1	10.8
3	2	12.4	17.8	16.2	21.9
4	3	20.3	25.9	21.9	29.5
5	4	32.4	37.8	29.1	43.5
6	5	40.9	46.4	41.4	50.3
7	6	54.4	60.8	48.0	61.5
8	7	60.8	69.4	57.9	69.7
9	8	67.6	82.7	63.5	81.3

Table 2.15 In vitro commulative release

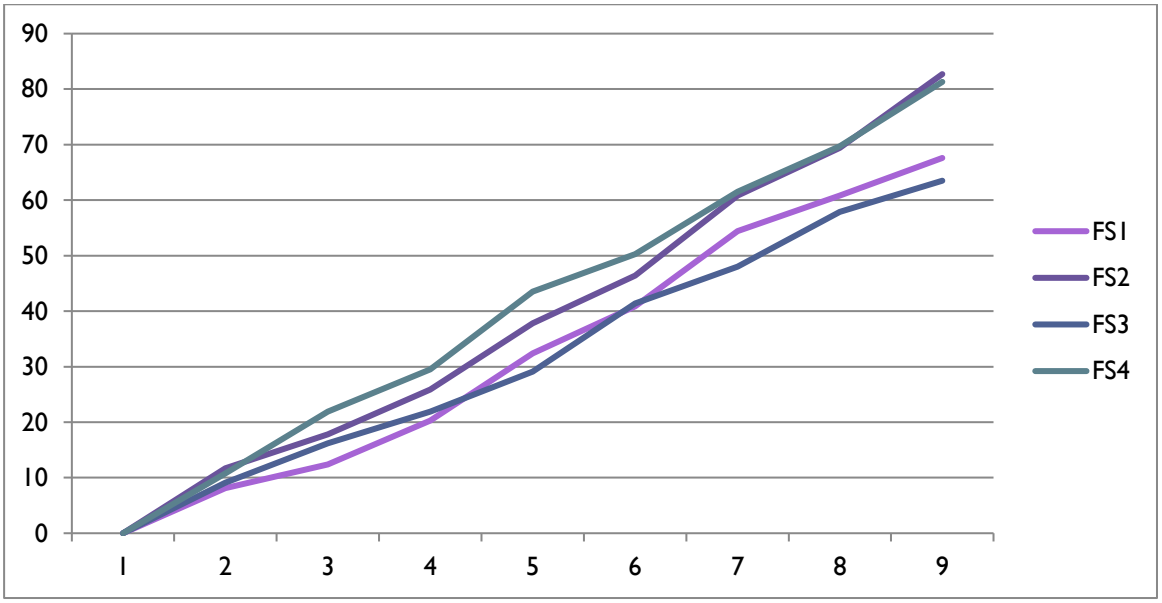

Fig2.9Commulative release graph

2.4.9 Stability studies[14, 15]

2.4.9.1 pH stability Study[14, 15, 16]

Time (Months)	Temp. Condition	FS1 (pH)	FS2 (pH)	FS3 (pH)	FS4 (pH)
0	All	6.85	6.92	6.88	6.90
1	Refrigerated	6.84	6.91	6.86	6.89
	Room Temp	6.81	6.87	6.85	6.87
	Accelerated	6.75	6.82	6.80	6.83
2	Refrigerated	6.83	6.90	6.84	6.88
	Room Temp	6.78	6.85	6.82	6.85
	Accelerated	6.69	6.78	6.75	6.79

Table 2.16 pH of Stability check

2.4.9.2 In vitro release of F1 formulation[4, 14, 16, 18]

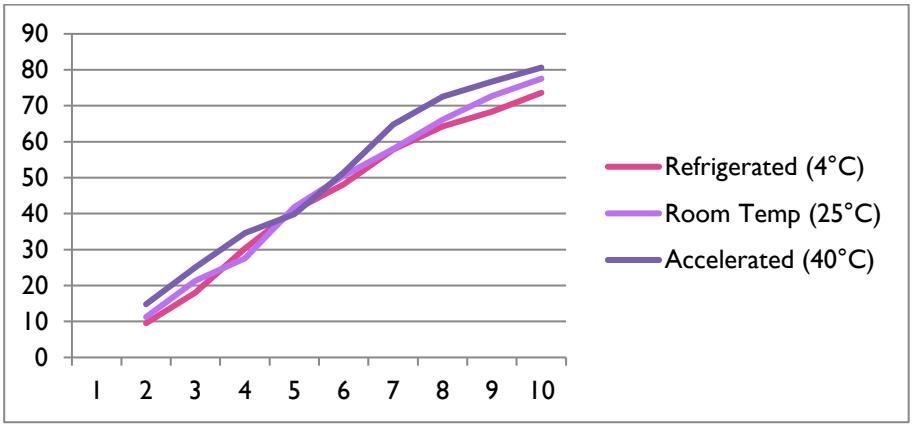

Fig 2.10 in vitro release for stability check

2.4.10 Zeta potential for stability[11, 12, 14]

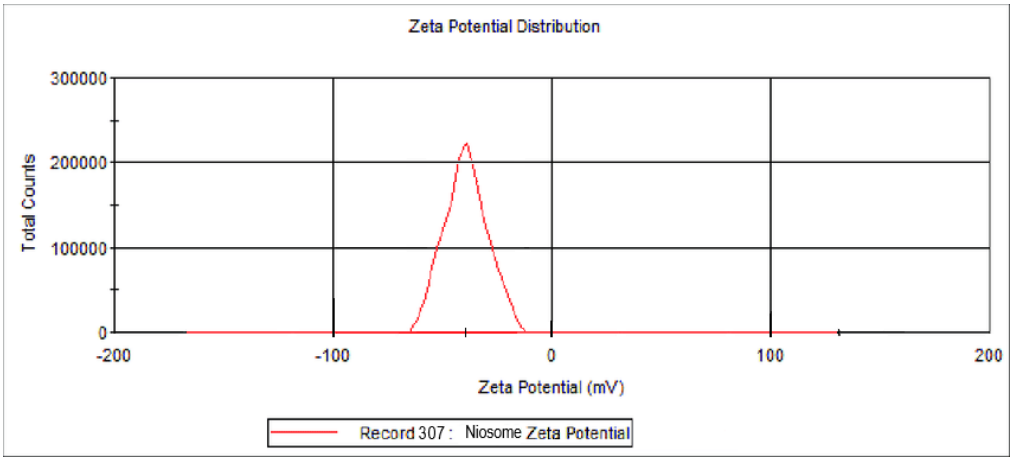

Fig 2.11 Zeta Potential for stability after a month

Peak No.	Zeta Potential (mV)	Area (%)	St Dev (mV)
Peak 1	≈ -39.0	100.0	~3– 5
Peak 2	0.00	0.0	0.00
Peak 3	0.00	0.0	0.00

Table 2.17 Zeta potential of stability check

3. RESULTS

The thin-film hydration technique was successfully used in this study to formulate miconazole-loaded niosomes, which were then assessed using a number of preformulation and characterization parameters.

Miconazole is an odorless, bitter-tasting, white to off-white crystalline powder, according to an organoleptic analysis. The drug's purity was confirmed when the melting point was determined to be 161.87 ± 0.59 °C. Its lipophilic nature was demonstrated by the solubility analysis, which showed that it was most soluble in ethanol (0.72 mg/mL) and least soluble in water (0.03 mg/mL). The drug solution's average pH was 6.41 ± 0.15, making it appropriate for topical formulation, and the pKa was determined to be 6.62.Good flow properties were indicated by micromeritic evaluations, which revealed a true density of 1.2 g/mL, bulk density of 0.370 g/mL, and porosity of 69.13%. The drug's lipophilicity, which makes it perfect for entrapment in lipid bilayer vesicles, was further supported by the partition coefficient (Log P), which varied between 5.62 and 6.18.

The lack of significant peak shifts between the niosomal formulation and pure miconazole was confirmed by FTIR spectroscopy, suggesting that there was no meaningful drug–excipient interaction. Functional group stability indicates that miconazole's chemical identity was unaffected by drug encapsulation.

TLC confirmed the drug's identity with an Rf value of 0.52. Accurate drug quantification in release and solubility studies is made possible by UV spectroscopy, which determined λmax at 223 nm with a calibration curve displaying strong linearity ($R^2 = 0.9994$).

Zeta potential was recorded at approximately **–44.0 mV**, and after one month **-39.0 mV**indicating excellent colloidal stability. Higher negative values reduce vesicle aggregation and suggest long-term physical integrity.

All formulations' initial pH values fell between 6.82 and 7.42, which is within permissible bounds for skin application. Lower temperatures help maintain chemical stability, as evidenced by the more consistent pH retention of refrigerated samples during stability tests compared to the slight pH drops observed under accelerated conditions.

SEM pictures showed multilamellar vesicles that were smooth, spherical, and free of surface roughness or fusion. TEM provided additional proof of particle integrity and homogeneity. These results validate structural consistency and successful vesicle formation.

The use of 285 mg of drug to achieve 200 mg active entrapment was justified by an estimated entrapment efficiency of 70%. According to in vitro drug release studies, FS1 had the lowest cumulative release (~67.6% at 8 hours) and FS4 the highest (~81.3%). Topical antifungal treatment benefits greatly from this pattern of sustained release.

Two months of stability analysis showed that formulations kept at 4°C had slower release and better pH stability, whereas formulations kept at 40°C had both increased release and a pH drop. These findings support the notion that niosome integrity is best preserved by refrigeration.

4. CONCLUSION

Through meticulous preformulation, formulation, and evaluation, the current study successfully developed a miconazole-loaded niosomal suspension. The drug's lipophilicity, purity, and suitability for niosomal encapsulation were all validated by preformulation studies. Zeta potential (–44 mV and -39.0 mV) guaranteed high colloidal stability, and FTIR analysis confirmed chemical compatibility. The ideal pH values for skin application were discovered, and they held up well in cold storage.The development of homogeneous, stable vesicles was validated by morphological evaluations (SEM/TEM). The most promising candidate was the optimized formulation (FS4), which showed the best stability and the highest drug release. Overall, topical administration of lipophilic antifungal agents such as miconazole is made safe, stable, and effective by niosomal technology.

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