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FORMULATION, DEVELOPMENT AND CHARACTERIZATION OF NEW MICONAZOLE-BASED GLYCEROSOMES FORMULATION FOR TOPICAL DELIVERY

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ABSTRACT

The present study focused on the formulation, development, and characterization of a novel miconazole-based glycerosomal formulation to enhance topical antifungal drug delivery. Pre- formulation studies confirmed the purity and identity of miconazole through organoleptic properties, melting point analysis (176 °C), solubility profiling, UV spectrophotometry (λmax = 273 nm, R^2 = 0.9992), and FTIR analysis, which verified the presence of characteristic functional groups. Five glycerosomal formulations (F1–F5) were prepared and evaluated. All formulations exhibited stable organoleptic properties with no phase separation. Particle size ranged from 120.41 nm (F2) to 208.7 nm (F5), with F2 showing the smallest vesicles, while polydispersity index (18.6–32.6%) indicated uniform distribution, especially in F3. Zeta potential values suggested good stability, with F2 showing the highest negative potential (– 35.4 mV). Entrapment efficiency varied across formulations, with F2 demonstrating the highest drug loading at 96.52%. Scanning Electron Microscopy confirmed spherical, smooth vesicles in the optimized formulation. Overall, formulation F2 exhibited superior physicochemical stability, high entrapment efficiency, and favorable vesicle characteristics, establishing it as the most effective carrier system for topical antifungal therapy. These findings provide a foundation for further in vitro, ex vivo, and clinical investigations.

KEYWORDS: Miconazole, glycerosomes, topical delivery, entrapment efficiency, antifungal therapy, nanovesicles.

1. INTRODUCTION

Topical drug delivery involves the local delivery of drugs anywhere in the body by using vaginal, rectal, ophthalmic and skin as topical route. Skin is the largest organ of the human body for topical delivery of drugs. The idea of using skin for topical delivery of drugs is since ancient time. Different ancient cultures used pastes, creams and plasters in treatment of various diseases **(Gorle, 2016).** But now a day these ancient methods of drug delivery were replaced by novel topical drug delivery systems, which offers a various advantage over conventional systems like reduction in side effects, avoidance of 1st pass metabolism and improves patient compliance. Various strategies are being used for the delivery of drugs by topical routes which include sonophoresis, nanoparticles, patches, microneedles, and vesicular drug delivery systems **(Ramadon *et al.*, 2022).**

Among these, glycerosomes represent an advanced lipid-based vesicular system composed of phospholipids, cholesterol, and high concentrations of glycerol. The presence of glycerol not only imparts elasticity to the vesicles but also enhances hydration of the stratum corneum, thereby facilitating deeper drug penetration **(Sharma *et al.*, 2023).** Compared to conventional liposomes, glycerosomes have shown improved stability, deformability, and drug-loading capacity, making them promising carriers for topical drug delivery. The formulation and characterization of glycerosomes involve careful selection of excipients, optimization of vesicle size, zeta potential, and entrapment efficiency,

followed by evaluation of their physicochemical and in-vitro performance. A well-designed glycerosome formulation can significantly enhance drug permeation through the skin, prolong drug release, and potentially reduce systemic side effects **(Saindane *et al.*, 2022).**

Miconazole, an azole-based model drug with clinical efficacy in the treatment of oral candidiasis, acts by inhibition of 14-α-demethylase (CYP51) implied in the ergosterol biosynthesis and alter the integrity of the fungi cell membrane **(Talianu *et al.*, 2024).** Additional positive effects repurpose miconazole as an anti-inflammatory agent in skin disorders and a promising cytotoxic via molecular antitumor pathways in particular forms of cancer. Miconazole, belonging to the BCS II class, underwent extensive research to improve solubility and sustain an efficient release, thereby enhancing therapeutic efficacy **(Rauf *et al.*, 2025).** The development of miconazole-based systems designed to improve mucoadhesion and achieve a controlled release. In the most recent findings, polymeric materials can provide excellent support for nanosized-based system inclusion, as seen in the case of nanogels and hydrogels loaded with nanoemulsifyable systems **(Kumari *et al.*, 2025).**

The present study focuses on the formulation, development, and characterization of miconazole-loaded glycerosomes for topical delivery. The objective is to improve drug penetration, sustain release, and enhance therapeutic efficacy compared to conventional dosage forms.

2. MATERIAL AND METHODS

2.1 Chemicals

Miconazole were obtained from LGM Pharma, a reputable supplier of analytical reagents. Sulab provided the Cholesterol, and Nippon Fine Chemical, and Croda Pharma provided the Phospholipid. Meru Chem Pvt. Ltd. provided the Methanol. GHCL Limited provided the Chloroform. Glycerol were obtained from Alpha chemical and Sisco Research Laboratories provided the DMSO.

2.2 Pre-formulation studies of Drug

2.2.1 Organoleptic Properties

It is practically odorless, which makes it suitable for pharmaceutical formulations intended for topical or oral use. The compound has a slightly bitter taste, typical of many alkaloid derivatives. It is sparingly soluble in water but exhibits good solubility in alcohol and other organic solvents.

2.2.2 Solubility study

Solubility plays a crucial role in pharmaceutical development, directly impacting a drug's absorption, bioavailability, and therapeutic effectiveness. This qualitative evaluation provided initial insights into the drug's solubility behavior, aiding in the rational selection of solvents for further formulation development and compatibility studies **(Jindal *et al.*, 2024).**

2.2.3 pH Determination

The pH value of Miconazole was measured to assess its acid-base behavior, which is essential for predicting stability, solubility, and compatibility with excipients during formulation development. A digital pH meter was employed for the analysis **(Annapurna, 2018).**

2.2.4 Melting point

For Miconazole, the melting point was measured using the open capillary method in conjunction with a Thiele's tube apparatus **(Joshi ang Gupta, 2013).**

2.2.5 Determination of Lambda max and calibration curve of Miconazole

- **Lambda (λ) max**

To determine the wavelength of maximum absorbance λ max for Miconazole, a standard stock solution was prepared by dissolving 1 mg of the drug in 1 mL of methanol. From this, a working solution with a concentration of 100 µg/mL was obtained through appropriate dilution using the same solvent. The UV-visible absorption spectrum of the working solution was recorded within the range of 200–400 nm using a Shimadzu 1700 double-beam UV-Vis spectrophotometer. The λ max was identified as the wavelength corresponding to the highest absorbance on the spectrum. This λ max value was then used for subsequent quantitative analysis. Additionally, a calibration curve was constructed by measuring the absorbance of solutions at varying concentrations to establish a linear relationship for accurate drug quantification in formulation studies (**Kokilambigai and Lakshmi 2021**).

- **Standard calibration curve**

A quantity of 10 mg of Miconazole was accurately weighed and transferred into a 10 mL volumetric flask. The drug was dissolved in methanol, and the volume was brought up to the mark with the same solvent to obtain a primary stock solution (1 mg/mL). From this stock, 1 mL was pipetted into a 10 mL volumetric flask and diluted with methanol to produce a working standard solution with a concentration of 100 µg/mL. This working solution was subjected to UV spectrophotometric analysis using a Shimadzu 1700 double-beam spectrophotometer. The solution was scanned across the wavelength range of 200–400 nm to determine the maximum absorbance wavelength λ max of Miconazole. Subsequently, a series of dilutions were prepared to cover a range of concentrations, and their absorbance values were recorded at the identified λ max. A calibration curve was then constructed by plotting absorbance against concentration. This standard curve served as a reference for determining the concentration of Miconazole in unknown samples during formulation and analysis **(Aprile et al., 2017).**

2.2.6 Preparation of calibration curve

To establish a calibration curve for Miconazole, a standard stock solution was first prepared by dissolving

the drug in methanol. This stock was then serially diluted with the same solvent to produce a series of standard solutions with concentrations of 40, 50, 60, 70, 80, 90, and 100 µg/mL. Each of these solutions was analyzed using a UV-Visible spectrophotometer at the previously determined λ max, using methanol as the blank. The absorbance values corresponding to each concentration were recorded. A calibration curve was plotted with drug concentration (µg/mL) on the X-axis and absorbance on the Y-axis. The resulting graph displayed a linear relationship, which was used to calculate the concentration of Miconazole in unknown formulations or test samples with precision and accuracy **(Eticha *et al.*, 2018).**

2.2.7 Fourier transmission Infra-Red Spectroscopy

Fourier Transform Infrared (FT-IR) spectroscopy was employed to analyze the pure drug and its physical mixture with excipients to identify possible interactions and confirm the presence of characteristic functional groups. The spectra were recorded in the range of 4000–400 cm^{-1} using the KBr pellet method. Approximately 1 mg of Miconazole (or drug-excipient blend) was finely ground and mixed with 100 mg of spectroscopic-grade potassium bromide (KBr), which had been pre-dried under an infrared lamp to remove moisture.

The mixture was compressed into a transparent disc using a hydraulic press. This disc was carefully placed in the sample holder of the FT-IR spectrophotometer, and the spectrum was recorded. The resulting spectra were analyzed for characteristic absorption peaks, which provided insights into the structural integrity of the drug and any potential interactions between the drug and formulation components (**Nanda *et al.*, 2012)**

2.3 Preparation of drug loaded Glycerosomes formulation by thin film hydration process.

The thin film hydration approach was employed for the preparation of Drug-loaded GMs. Cholesterol (2 to 5%), phospholipid (15 to 35 mg), and Miconazole (2.0 %) were accurately measured and dissolved in chloroform with methanol. The resulting mixture was mechanically stirred at 40^0C for one hour. Subsequently, the mixture was evaporated using a rotary evaporator under reduced pressure, leading to the formation of a clear lipid film on the rounded bottom of the flask. The transparent lipid film allowed for the removal of residual solvents overnight under a vacuum. To hydrate the Drug-loaded-GMs, a glycerol-Phosphate buffer solution 6.8 was used, and the two phases were mechanically stirred at 40^0C for one hour. The vesicles were then subjected to sonication for half cycle. To remove any excess un-entrapped drug, the resulting formulation was centrifuged at 1500 rpm for 10 min at 4 ◦C before being lyophilized for future use **(Gupta *et al.*, 2020).**

Table 1: Composition of Glycerosomes formulation.

Formulation Code	Cholesterol (%)	Phospholipid (mg)	Glycerol (%)	Methanol (ml)	Chloroform (ml)	PBS 6.8 (ml)
F 1	1.0	15	10	10.0	10.0	15.0
F 2	2.0	20	10	10.0	10.0	15.0
F 3	3.0	25	10	10.0	10.0	15.0
F 4	4.0	30	10	10.0	10.0	15.0
F 5	5.0	35	10	10.0	10.0	15.0

2.4 Evaluation parameter of Drug loaded Glycerosome

2.4.1 Physical Appearance

The physical appearance of the drug-loaded glycerosome formulation was visually inspected to assess its clarity, color, homogeneity, and phase separation **(Ahmad *et al.*, 2023).**

2.4.2 Particle Size

In this study, the average particle size and size distribution of the Miconazole-loaded glycerosomes wer e det er mined us ing a Malver n Zetasizer **(Anwer *et al.*, 2025).**

2.4.3 Zeta potential

Zeta potential measurements were conducted to evaluate the surface charge and electrostatic stability of the Miconazole-loaded glycerosomes. The samples were assessed using a Malvern Zetasizer (Malvern Instruments).

2.4.4 Scanning Electron Microscopic (SEM) Analysis

Scanning Electron Microscopy (SEM) was utilized to examine the surface morphology and structural characteristics of the Miconazole-loaded glycerosomes. SEM provides high- resolution images that allow for detailed visualization of particle shape, surface texture, and aggregation state, which are crucial for understanding the formulation's physical properties **(Sharma *et al.*, 2019).**

2.4.5 Entrapment efficiency

The entrapment efficiency of Miconazole in glycerosomes was determined indirectly. The glycerosome dispersion was centrifuged at 15,000 rpm for 30 minutes using a REMI Ultra Centrifuge to separate the free drug from the vesicles. The supernatant containing the unentrapped drug was collected and analyzed by UV spectrophotometry. Using a calibration curve, the concentration of free drug was measured, and the amount encapsulated was calculated by subtracting

this from the total drug added. Entrapment efficiency (%) was then computed using the formula: **(Moolakkadath *et al.*, 2020).**

Entrapment efficiency % = Total drug conc. - Supernatant drug conc. / total drug conc. ×100

3. RESULTS

3.1 Pre-formulation study of drug

3.1.1 Organoleptic properties

Table 2: Organoleptic properties of Miconazole.

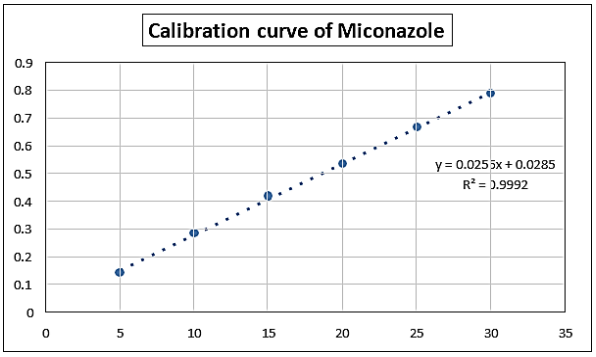
Drug	Organoleptic properties	Observation
Miconazole	Color	White to off-white
	Odor	Odorless or slightly characteristic
	Appearance	Crystalline powder
	State Miconazole	Solid

3.1.2 pH, Melting point and Lambda max determination

Table 3: Determination of pH, Melting point and Lambda max.

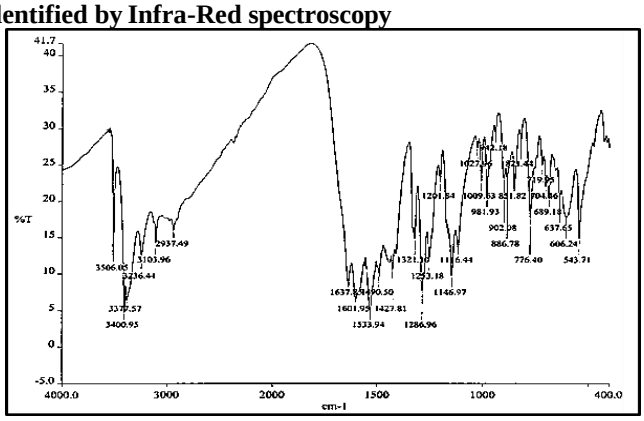
Drugs	Observed (pH)	Observed (Melting point)	Reference (Melting point)
Miconazole	6.2	176 °C	170-185°C

3.1.3 Calibration curve of Miconazole



Graph 1: Calibration curve of Miconazole.

3.1.4 Functional group identified by Infra-Red spectroscopy



Graph 2: FTIR study of Miconazole.

Table 4: Interpretation of IR spectrum of Miconazole.

Peak obtained	Reference peak	Functional group	Name of functional group
3400.95	3400-3300	N-H stretching	Aliphatic primary amine
3103.96	3200-2700	O-H stretching	Alcohol
2937.49	3000-2840	C-H stretching	Alkane
1286.96	1310-1250	C-O stretching	Aromatic ester
1146.97	1225-1200	C-O stretching	Vinyl ether
981.93	995-985	C=C stretching	Alkene
886.78	895-885	C=C stretching	Alkene

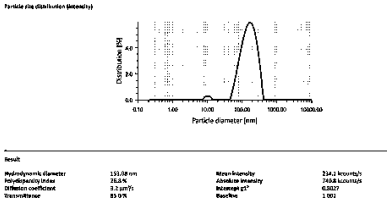
3.2 Characterization of optimized formulation

3.2.1 Physical appearance of drug loaded glycerosome formulation

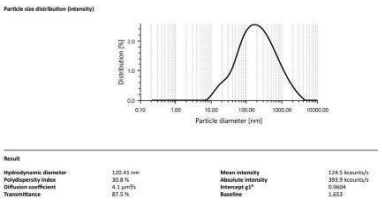
Table 5: Physical appearances.

Physical appearance	Observation
Color	White to pale yellow
Clarity	Opaque to slightly turbid
Consistency	Smooth and semi-solid or gel-like
Odor	Odourless or faint characteristic odour
Phase Separation	Absent

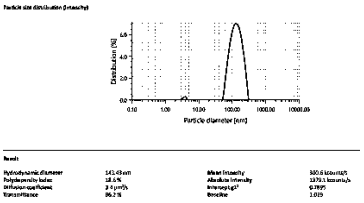
3.2.2 Particle Size



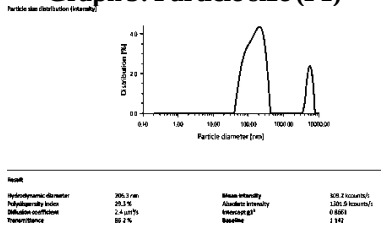
Graph 3: Particle size (F1)



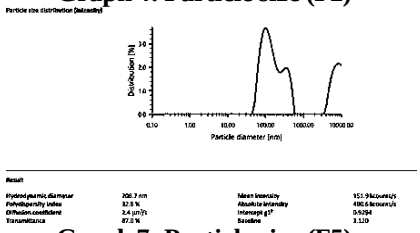
Graph 4: Particle size (F2)



Graph 5: Particle size (F3)



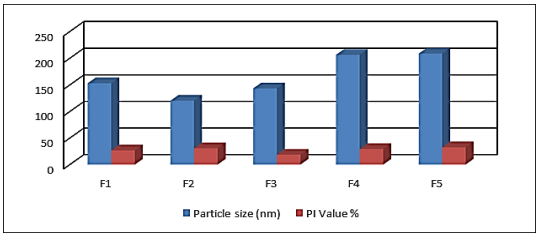
Graph 6: Particle size (F4)



Graph 7: Particle size (F5)

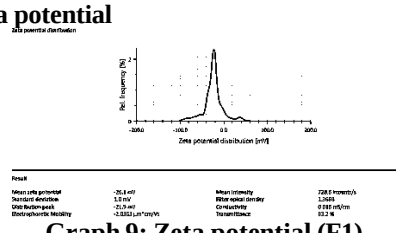
Table 6: Particle size of drug loaded glycerosome formulation.

Formulation code	Particle size (nm)	PI Value
F1	153.08 nm	26.8 %
F2	**120.41 nm**	**30.8 %**
F3	143.43 nm	18.6 %
F4	206.3 nm	29.3 %
F5	208.7 nm	32.6 %

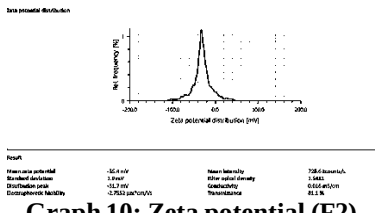


Graph 8: graphical representation of particle size of glycerosomes.

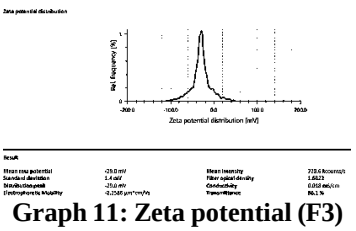
Zeta potential



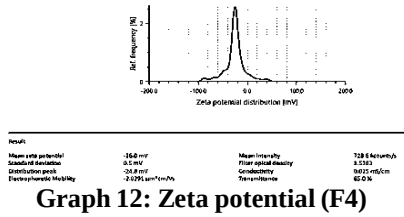
Graph 9: Zeta potential (F1)



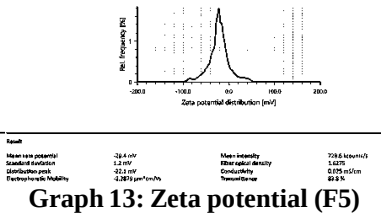
Graph 10: Zeta potential (F2)



Graph 11: Zeta potential (F3)



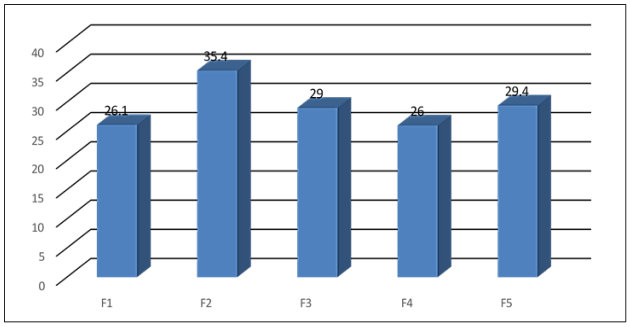
Graph 12: Zeta potential (F4)



Graph 13: Zeta potential (F5)

Table 7: Zeta potential of drug loaded glycerosome formulation.

Formulation Code	Zeta potential mV
F1	-26.1
F2	**-35.4**
F3	-29.0
F4	-26.0
F5	-29.4



Graph 14: graphical representation of Zeta potential of drug loaded.

Glycerosome Formulation

3.2.3 Entrapment efficacy

Table 8: Entrapment efficacy.

Formulations (F1-F5)	Entrapment efficacy (%)
Glycerosome (F1)	85.31
Glycerosome (F2)	**96.52**
Glycerosome (F3)	80.28
Glycerosome (F4)	75.40
Glycerosome (F5)	71.68

3.2.4 Scanning electron microscope (SEM)

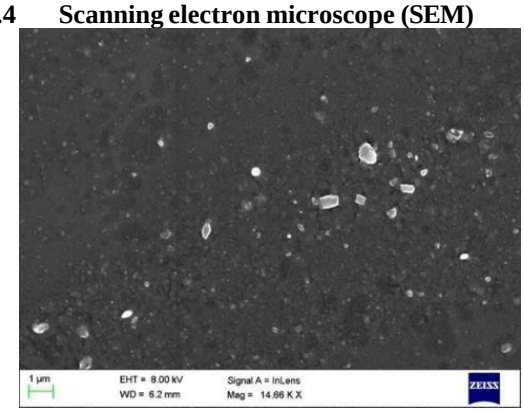


Figure 1: Scanning electron microscope (SEM)

4. CONCLUSION

In conclusion, the comprehensive data from physicochemical, spectroscopic, and formulation characterization strongly support that Formulation F2 is the most effective and optimized Miconazole glycerosome. Its small particle size, high zeta potential, excellent entrapment efficiency, and uniform vesicle morphology make it a highly suitable carrier for topical antifungal therapy. The study lays a strong foundation for further *in vitro*, *ex vivo*, and clinical evaluations to validate its therapeutic potential, stability, and patient compliance in real-world applications.

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