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Formulation and Evaluation of Ornidazole Loaded Ethasomol Gel for Treatment of Bacterial Infection

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ABSTRACT
The present study focused on the formulation and evaluation of an Ornidazole-loaded ethosomal gel to enhance transdermal drug delivery for the effective treatment of bacterial infections. Preformulation analysis confirmed the physicochemical suitability of Ornidazole, including solubility, stability, and compatibility for formulation. Ethosomes were successfully prepared with particle sizes between 153–172 nm, showing uniform distribution, stability, and high entrapment efficiency, with formulation F4 achieving the maximum (95.34%). Characterization through SEM confirmed spherical, porous vesicles, while the optimized gel exhibited desirable organoleptic properties, appropriate pH (6.2–6.7), viscosity, spreadability, and non-irritating behavior suitable for topical application. In vitro release studies of F4 followed Zero-order kinetics (R^2 = 0.980), indicating controlled and sustained drug release, supported by the Higuchi model (R^2 = 0.972). Antimicrobial evaluation demonstrated significant inhibitory effects against pathogenic bacteria, while stability studies over 90 days confirmed physical and chemical robustness. Overall, the Ornidazole-loaded ethosomal gel showed enhanced bioavailability, therapeutic efficacy, and dermatological safety, highlighting its potential as a promising transdermal drug delivery system for localized treatment of bacterial infections.

1. INTRODUCTION:

Bacterial infections remain a global health concern, often requiring long-term administration of antibiotics. Oral and parenteral routes of administration can lead to systemic side effects, reduced patient compliance, and variable bioavailability. Hence, transdermal and topical delivery systems have gained importance due to their ability to localize drug action, bypass first-pass metabolism, and maintain sustained therapeutic levels **(Laxminarayan *et al.*, 2016).** Transdermal and topical drug delivery systems offer several advantages over conventional oral routes, including bypassing first-pass metabolism, improving drug bioavailability, sustaining drug release, and enhancing patient compliance. In particular, vesicular carriers such as liposomes, niosomes, and ethosomes have gained attention for their ability to enhance penetration of therapeutic agents across the skin barrier **(Bhandare and Nannor 2024).** Among these, ethosomes, which are phospholipid vesicles containing high ethanol concentrations, exhibit superior deformability and skin permeation compared to traditional liposomes. Ethanol not only imparts flexibility to the vesicles but also disrupts the lipid organization of the stratum corneum, facilitating deeper penetration of the encapsulated drug. Ethosomes are novel lipid-based vesicular carriers enriched with ethanol, designed to penetrate the stratum corneum and deliver drugs into deeper skin layers. Compared to conventional liposomes, ethosomes offer higher entrapment efficiency, deformability, and improved transdermal flux **(Ricci *et al.*, 2024).**

Ornidazole, a synthetic nitroimidazole derivative,

Journal of Molecular Science
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exhibits broad-spectrum activity against anaerobic bacteria and protozoa. It is widely used in the management of infections such as bacterial vaginosis, amoebiasis, and giardiasis. However, its clinical application is limited by poor aqueous solubility, variable gastrointestinal absorption, and undesirable systemic effects, including nausea and neurological disturbances **(Kannigadu and N'Da 2020).** These limitations reduce patient compliance and restrict its therapeutic potential when administered orally. Incorporating Ornidazole into an ethosomal gel system offers a dual advantage: the ethosomes enhance drug penetration and provide sustained release, while the gel base improves patient acceptability, ease of application, and prolonged skin residence time. Previous studies on ethosomal systems have reported improved drug entrapment efficiency, enhanced transdermal flux, and increased therapeutic efficacy for both hydrophilic and lipophilic drug **(Pasachhe, 2014).**
This study aimed to formulate and evaluate Ornidazole-loaded ethosomal gel by characterizing its physicochemical, rheological, and antimicrobial properties, followed by stability testing to ensure formulation robustness.

2. MATERIAL AND METHODS:

2.1 Chemicals:

Methyl paraben, Ethanol, Acetonitrile and Propylene glycol, were obtained from Merck. Vizag Chemicals provided the Distilled water. Loba provided the Triethanolamine while Sigma eldrich supplied PVA and Ethyl cellulose. Sulab supply Carbopol 934. Aurobindo Pharma provided the Ornidazole. Methanol obtained from Rankem.

2.2 Pre-formulation studies of selected Drug:

Pre-formulation studies are an essential phase in drug development that involve the thorough evaluation of the physical and chemical properties of a drug substance prior to the formulation of the final dosage form. These studies focus on critical parameters such as solubility, stability, particle size, and the potential interactions between the drug and excipients. Understanding these factors is crucial because they directly influence the drug's bioavailability, therapeutic efficacy, and shelf life. The primary aim of pre-formulation investigations is to generate comprehensive data that guide the design and optimization of a stable, safe, and effective pharmaceutical product, thereby minimizing formulation challenges and ensuring consistent performance throughout the product's lifecycle **(Honmane, 2017).**

2.2.1 Organoleptic Properties:

Organoleptic properties encompass the sensory attributes of a drug that can be perceived through sight, smell, taste, and touch **(Clapham, 2022).**

2.2.2 Solubility study:

The solubility of Ornidazole was evaluated by adding a measured amount of the compound to various solvents including water, ethanol, and methanol **(Bhesaniya *et al.*, 2014).**

2.2.3 pH determination:

The pH of an Ornidazole solution was determined to assess its acid-base characteristics, which can influence its solubility and stability **(Nandy *et al.*, 2020).**

2.2.4 Melting Point determination:

A small amount of Ornidazole was carefully packed into a thin capillary tube for melting point determination **(Bhattarai *et al.*, 2018).**

2.2.5 Spectroscopic Analysis and Calibration of Ornidazole:

2.2.5.1 Lambda (λ) max analysis:

A stock solution of Ornidazole was prepared at a concentration of 1 mg/mL using 80% methanol as the solvent. From this, a working standard solution of 100 µg/mL was obtained by appropriate dilution with the same solvent. The solution was scanned over the UV range of 200–800 nm using a Shimadzu 1700 double beam spectrophotometer to determine the absorbance spectrum and identify the wavelength of maximum absorbance (λmax) for Ornidazole.

2.2.5.2 Standard calibration curve analysis:

To prepare the calibration curve for Ornidazole, 100 mg of the drug was accurately weighed and dissolved in 80% methanol in a 100 mL volumetric flask. The solution was diluted to volume with the same solvent to obtain the stock solution. Then, 1 mL of this stock was transferred into a 10 mL volumetric flask and diluted with 80% methanol to prepare the working standard solution. The absorbance of this solution was scanned using a UV spectrophotometer over the wavelength range of 200 to 800 nm to identify the λmax. Following this, a series of Ornidazole solutions at varying concentrations were prepared from the stock solution, and their absorbance readings at λmax were recorded to plot the calibration curve **(Kelani *et al.*, 2023).**

2.2.6 Preparation of calibration curve:

To develop a calibration curve for Ornidazole, a stock solution was first prepared and then appropriately diluted with the selected solvent to obtain a series of working solutions at concentrations of 5, 10, 15, 20, 25, and 30 µg/mL. The absorbance of each solution was measured using a UV-visible spectrophotometer, with the solvent used as a blank to zero the instrument. These absorbance values were then plotted against their

Journal of Molecular Science
Journal of Molecular Science
Volume 35 Issue 3, Year of Publication 2025, Page 606-614
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respective concentrations, with concentration on the X-axis and absorbance on the Y-axis. This generated a standard calibration curve, illustrating a linear relationship in accordance with Beer-Lambert's law across the tested range **(Delgado, 2022).**

2.2.7 Fourier Transform Infrared (FT-IR) Spectroscopy of Ornidazole:

The FT-IR analysis of Ornidazole and its physical mixtures with excipients was carried out to identify any possible interactions between the drug and formulation components. Spectra were recorded in the 4000–400 cm^{-1} range using the potassium bromide (KBr) pellet technique. For each sample, 1 mg of Ornidazole or its blend with excipients was thoroughly mixed with 100 mg of dry, spectroscopic-grade KBr. The mixture was dried under an infrared lamp to remove moisture and then compressed into a transparent disc using a hydraulic press. This KBr disc was placed in the sample holder of the FT-IR spectrophotometer, and the spectra were collected to identify characteristic functional groups and assess compatibility **(Khan *et al.*, 2018).**

2.3 Preparation of Ethosomes containing Ornidazole:

The ethosomal formulation was prepared according to the method reported by Touitou et al. the ethosomal system prepared were composed of 1-3% phospholipid, 10-40% ethanol, drug, 10% propylene glycol and water to 100% w/w. phospholipid and drug were dissolved in ethanol/propylene glycol mixture, the mixture was heated to 30^0 C in a water bath. The double distilled water heated to 30^0 C was added slowly in a fine stream, with constant mixing (mechanical stirrer) at 700 rpm in a closed vessel, mixing was continued for additional 5 min. The system was kept at 30 ºC throughout preparation. The final milky solution of ethosomes was left to cool at room temperature. The preparation was homogenized by using vertex shaker for 15 min **(Sabareesh *et al.*, 2024).**

Table 1: Composition of Ethosomes Formulation

Formulation code	Phospholip id (mg)	Ethanol (%)	Drug (%)	Propylene glycol (%)	Water (ml)	Temperature (^{0}C)
F1	100	5.0	2.0%	10%	q.s	30^0C
F2	200	10.0	2.0%	10%	q.s	30^0C
F3	300	15.0	2.0%	10%	q.s	30^0C
F4	400	20.0	2.0%	10%	q.s	30^0C
F5	500	25.0	2.0%	10%	q.s	30^0C
F6	600	30.0	2.0%	10%	q. s	30^0C

2.4 Evaluation parameter of Ornidazole loaded ethosomes formulation:

2.4.1 Physical appearance of Ornidazole-Loaded Ethosomes

The physical appearance of the Ornidazole-loaded ethosomes was carefully examined to assess their overall quality and stability. Visual inspection was conducted to evaluate their shape, uniformity, and color **(Jain *et al.*, 2015).**

2.4.2 Particle Size Measurement:

The particle size of Ornidazole-loaded ethosomes was determined using dynamic light scattering (DLS) with a particle size analyser **(AlEbadi and Al-Lami 2022).**

2.4.3 Zeta Potential Measurement:

The zeta potential of Ornidazole-loaded ethosomes was determined using a Malvern Zetasizer (Malvern Instruments). **(Iizhar *et al.*, 2016).**

2.4.4 Drug Entrapment Efficiency:

To accurately evaluate the entrapment efficiency of Ornidazole in ethosomes, 10 mL of the Ornidazole-loaded ethosomal dispersion was mixed with 5 mL of methanol in a volumetric flask. The mixture was vortexed for one minute to ensure complete disruption of the vesicles and release of the entrapped drug. The resulting solution was then diluted to a final volume of 10 mL with an appropriate solvent. After filtration, the concentration of Ornidazole was quantified using UV-Visible spectrophotometry. The entrapment efficiency was calculated to assess the drug loading capacity of the ethosomal formulation **(Pathan *et al.*, 2018).**

$$\%EE = \left(\frac{\text{Initial amount of drug added} - \text{Amount of drug in supernatant}}{\text{Initial amount of drug added}}\right) \times 100$$

2.4.5 Scanning Electron Microscopy (SEM) Analysis:

The surface morphology and structural characteristics of Ornidazole-loaded ethosomes were examined using Scanning Electron Microscopy (SEM). Prior to imaging, a thin conductive coating (approximately 2–20 nm) of gold, platinum, or palladium was uniformly deposited onto the dried sample using a sputter coater under high vacuum conditions. This metal coating minimized charging effects and enhanced the quality of electron imaging. The coated samples were then subjected to an electron beam within the SEM chamber. Interaction between the incident electrons and the sample surface generated various signals, including secondary and Auger electrons. According to principles derived from Rutherford

Journal of Molecular Science
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DoI-10.004687/1000-9035.2025.083

scattering and Kramers' law, secondary electrons emitted predominantly at a 90-degree angle were selectively captured to construct high-resolution images. The resulting micrographs provided detailed insights into the surface architecture, size distribution, and overall morphology of the ethosomal vesicles, which are critical parameters for evaluating the formulation's stability and drug delivery potential. **(Raychaudhuri *et al.,* 2020).**

2.5 Preparation of Gel formulation:

The formulation of the Ornidazole-loaded ethosomal gel was carried out in a systematic manner to ensure homogeneity, stability, and optimal drug delivery characteristics. Initially, Solution A was prepared by dispersing Carbopol-934 in 100 mL of warm distilled water. The dispersion was allowed to stand undisturbed for approximately two hours to ensure complete hydration and swelling of the polymer. Following this, the mixture was stirred at a constant speed of 600 rpm using a magnetic stirrer to obtain a smooth and uniform gel base. Solution B was prepared separately by dissolving Carboxymethyl cellulose (CMC) and Methyl paraben in another 100 mL of warm distilled water. This solution was stirred continuously until a thick, homogenous gel-like consistency was achieved. Once both solutions were fully prepared, they were combined under continuous stirring to ensure thorough blending. To adjust the pH and enhance gel stability, Triethanolamine was added gradually in a dropwise manner until the desired pH level (typically around 6.0–6.5) was reached. Subsequently, the Ornidazole-loaded ethosomal suspension was incorporated into the gel base under continuous stirring to ensure even distribution of the drug throughout the formulation. Formulations I was prepared by incorporating 2% w/w concentrations of Ornidazole to evaluate the effect of drug loading. Finally, Propylene glycol was added as a permeation enhancer to facilitate improved dermal absorption of the active drug. The final gel mixture was stirred continuously until a smooth, uniform, and stable gel suitable for topical application was obtained **(Zhang *et al.,* 2021).**

Table 2: Composition of ethosomes gel formulation

Name of Ingredient	Formulation I
Carbopol 940	1.7 gm
Carboxymethyl cellulose	1.5gm
Propylene glycol	0.5 ml
Methyl paraben	0.3 ml
Ethosomes	10 ml
Triethanolamine	q. s
Water	100 ml

2.6 Quality Control Parameters of Ethosomal Gel Formulation

Quality control assessments were performed on the ethosomal gel formulations containing different concentrations of Ornidazole to evaluate critical physicochemical properties including pH, spreadability, and viscosity.

- **pH:** The pH of each gel formulation was measured using a calibrated digital pH meter to ensure skin compatibility and minimize irritation upon topical application.
- **Spreadability:** This parameter was assessed to determine the ease of application of the gel on the skin surface, reflecting its ability to spread uniformly with minimal effort.
- **Viscosity:** Viscosity measurements were conducted using a rotational viscometer to evaluate the gel's flow behavior and consistency, which are important for stability and patient acceptability.
- **Skin irritation studies:** The skin irritation potential of the Ornidazole-loaded ethosomal gel was assessed on healthy Wistar rats. The gel was applied to the skin and monitored for signs of redness, swelling, or irritation at regular intervals. No significant irritation was observed, indicating the formulation is safe for topical use **(Yasir *et al.,* 2023).**

2.7 *In Vitro* Drug Release Study of Ornidazole-Loaded Ethosomal gel

The *in vitro* drug release profile of Ornidazole-loaded ethosomes was evaluated using the dialysis bag diffusion technique. A measured amount of the ethosomal suspension was placed inside a dialysis bag, which was then immersed in a beaker containing 100 mL of phosphate buffer solution (pH 7.4). The system was maintained at 37 ± 2 °C using a magnetic stirrer set at 100 rpm to simulate physiological conditions.

At predetermined time intervals, 2 mL samples were withdrawn from the release medium and replaced immediately with an equal volume of fresh phosphate buffer to maintain sink conditions. The samples were appropriately diluted and analyzed by UV-Visible spectrophotometry at 427 nm to determine the amount of Ornidazole released.

The release data were fitted to various kinetic models to elucidate the drug release mechanism:

2.8 Antimicrobial Activity (Well Diffusion Assay)

2.8.1 Anti-microbial Activity

1. Preparation of Dilutions of the Samples

The samples were diluted to concentrations of 100µg/ml, 150µg/ml, 200µg/ml, and 250µg/ml. The volume was then filled up with distilled water to 1ml.

2. Preparation of Nutrient Agar Media

One liter of distilled water was used to dissolve 28 grams of Nutrient Media. The pH of the media was measured before sterilization. The media was

Journal of Molecular Science
Volume 35 Issue 3, Year of Publication 2025, Page 606-614
DoI-10.004687/1000-9035.2025.083

sterilized in an autoclave at 121 degrees Celsius and 15 pounds of pressure for 15 minutes. Nutrient media was poured into plates and placed in a laminar airflow until the agar solidified.

3. Well Diffusion Assay

The bacterial suspension of *Staphylococcus aureus* was standardized to 10^8 CFU/ml and placed in a shaker. Then, 100 µl of the inoculum (containing 10^8 CFU/ml) was taken using a micropipette and transferred onto fresh, sterile, solidified agar media plates. To evaluate the antibacterial activity of the Ornidazole-loaded ethosomal gel formulation, a well diffusion assay was performed against *Staphylococcus aureus* and *Escherichia coli*. The agar medium was prepared, sterilized, and poured into sterile Petri plates, then allowed to solidify. Fresh overnight bacterial cultures were adjusted to a 0.5 McFarland standard and uniformly spread across the agar surface using sterile cotton swabs to form a bacterial lawn. Wells were then created in the agar using a sterile cork borer, and each well was filled with a fixed volume of the ethosomal gel formulation. A blank ethosomal gel (without drug) served as the negative control, while a standard antibiotic solution or disc was used as the positive control. The plates were left at room temperature for 30 minutes to allow for pre-diffusion, followed by incubation at 37 °C for 24 hours. After incubation, the zones of inhibition around the wells were measured in millimeters to determine the antimicrobial efficacy of the Ornidazole-loaded ethosomal gel against the test organisms **(Aodah *et al.*, 2023).**

2.9 Stability Studies

The ethosomal gel formulation was sealed and subjected to accelerated stability testing in accordance with ICH guidelines. Samples were stored under two controlled conditions: 25 ± 2 °C with 60 ± 5% relative humidity, and 40 ± 2 °C with 70 ± 5% relative humidity, for a period of three months. Evaluations were conducted at predetermined intervals—on days 30, 45, 60, and 90—to assess any variations in critical parameters such as pH and viscosity. These tests were aimed at monitoring the physical stability of the ethosomal gel to ensure its consistency, quality, and performance throughout the storage period under stressed environmental conditions **(Mohapatra *et al.*, 2023).**

3. RESULTS

3.1 Pre-formulation study of drug

3.1.1 Organoleptic properties

Table 3: Organoleptic properties of Ornidazole

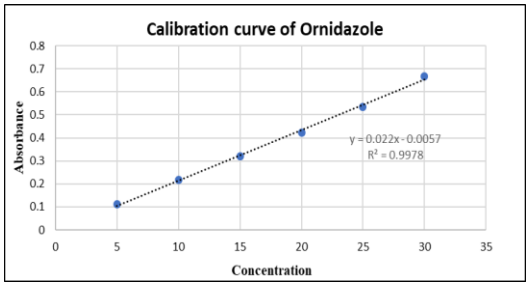
Drug	Organoleptic properties	Observation
Ornidazole	Color	White to off-white powder
	Odor	Characteristic, faint
	Appearance	Crystalline powder
	State	Solid

3.1.2 Melting point, Lambda max and pH determination:

Table 4: - Melting point, Lambda max and pH determination

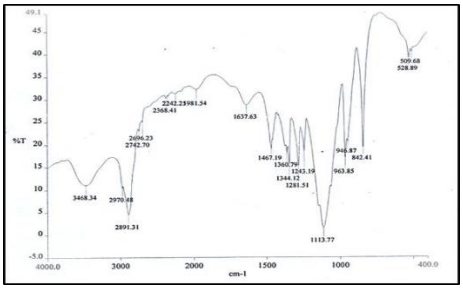
Drugs	Observed (Melting point)	Reference (Melting point)	UV absorption maxima (Lambda max)	Observed (pH)
Ornidazole	90°C	88.0 and 93.0 °C	427.0 nm	6.6

3.1.3 Calibration curve of Ornidazole Table 5: Calibration curve



Graph 2: Calibration curve of Ornidazole

Functional group identified by Infra-Red spectroscopy



Graph 3: FTIR study of Ornidazole

Table 6: Interpretation of IR spectrum of Ornidazole

Peak obtained	Reference peak	Functional group	Name of functional group
3468.34	3500- 3400	N-H stretching	primary amine
2970.48	3000-2800	N-H stretching	amine salt
2742.70	2830-2695	C-H stretching	aldehyde
2368.41	2600-2550	S-H stretching	thiol
2242.25	2260-2190	CΞC stretching	alkyne
1637.63	1648-1638	C=C stretching	alkene
1467.29	1550-1500	N-Ostretching	nitro compound

Journal of Molecular Science
Journal of Molecular Science
Volume 35 Issue 3, Year of Publication 2025, Page 606-614
DoI-10.004687/1000-9035.2025.083

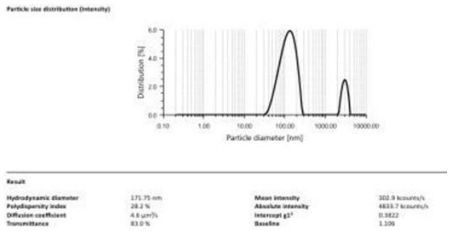
1344.12	1350-1300	S=O stretching	sulfone
1243.19	1250-1020	C-N stretching	amine
946.87	980-960	C=Cbending	alkene

3.2 Characterization of drug loaded Ethosomes formulation:

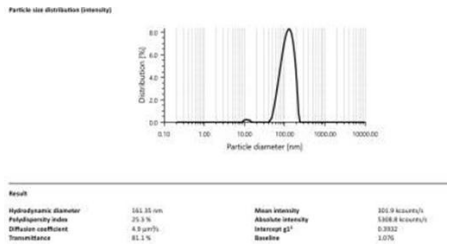
3.2.1 Physical Appearance:

Table 7: Physical Appearance

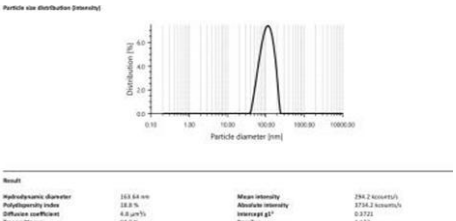
Parameter	Observation
Color	Pale yellow to colorless
Odor	Mild, characteristic
Appearance	Clear to slightly opalescent viscous dispersion
State	Liquid colloidal suspension



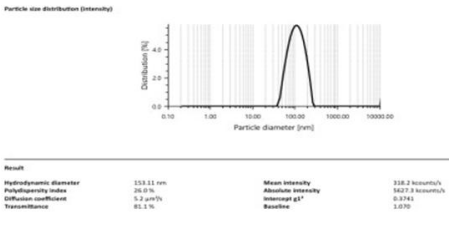
Graph 4: PS F1



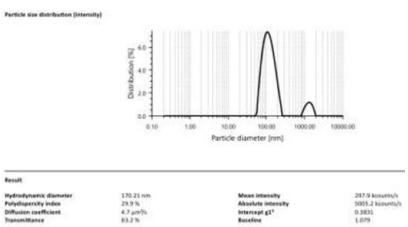
Graph 5: PS F2



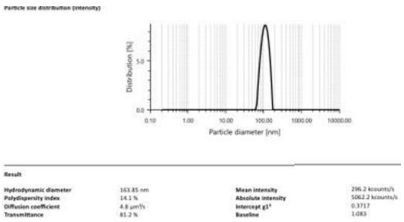
Graph 6: PS F3.



Graph 7: PS F4

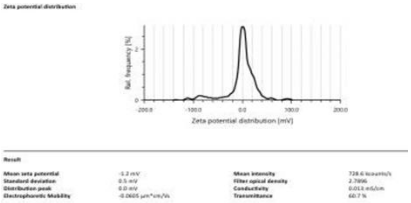


Graph 8: PS F5

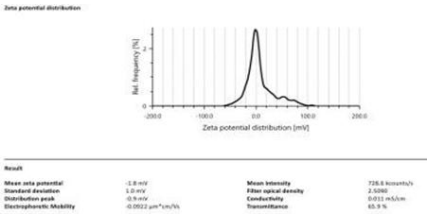


Graph 9: PS F6

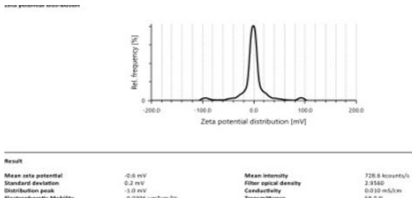
3.2.2 Zeta potential analysis



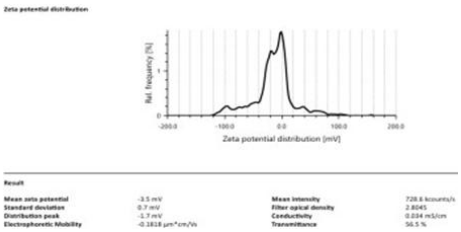
Graph 11: Zeta potential F1



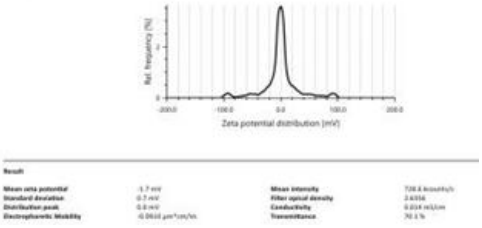
Graph 12: Zeta potential F2



Graph 13: Zeta potential F3

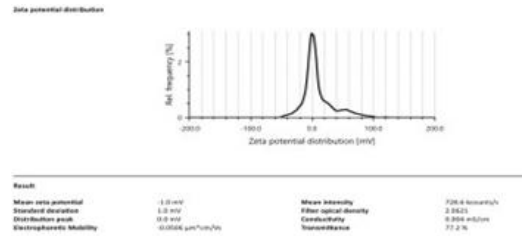


Graoh 14: Zeta potential F4



Graph 15: Zeta potential F5

Journal of Molecular Science
Journal of Molecular Science
Volume 35 Issue 3, Year of Publication 2025, Page 606-614
DoI-10.004687/1000-9035.2025.083



Graph 16: Zeta potential F6

3.2.3 Result of Particle size, Zeta potential and entrapment efficiency

Table 9: Particle size, Zeta potential and entrapment efficiency of Ethosomes

Formulation code	Zeta potential	Particle size (nm)	Entrapment efficacy (%)
Zeta potential F1	-1.2 mV	163.64 nm	73.43
Zeta potentialF2	-1.8 mV	161.35nm	81.57
Zeta potentialF3	-0.6 mV	171.75 nm	55.48
Zeta potential F4	-3.5 mV	**153.11 nm**	**95.34**
Zeta potentialF5	-1.7 mV	170.21 nm	76.68
Zeta potentialF6	-1.0 mV	163.64 nm	72.68

3.2.4 SEM analysis of Optimized formulation

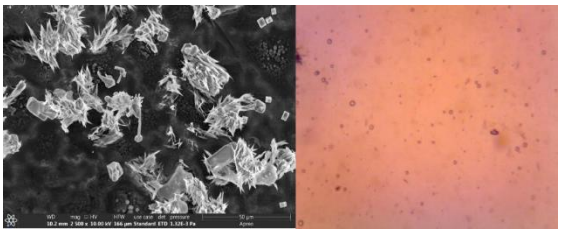


Figure 1: Scanning electron microscope (SEM) and microscopy image

3.3 Evaluation parameter of gel formulation

3.3.1 Organoleptic properties

Table 11: Organoleptic properties

Parameters	Results
Physical appearance	Smooth, consistent gel
Colour	Transparent or light (e.g. white, pale yellow)
Homogeneity	Uniform without lumps or particles

3.3.2 Measurement of pH, Viscosity and Spreadability test of gel formulation

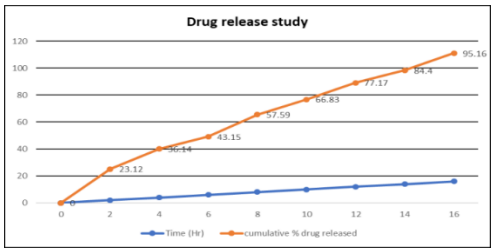
Table 12: pH, Viscosity and Spreadability test

Formulation	pH	Viscosity determination (cps)	Spreadability test (gm.cm/sec)	skin irritation study
Formulation1	6.2	5665±0.81	13.84	Not irritation observed

3.4 *In Vitro* drug release study

Table 13: *In-vitro* drug release studies

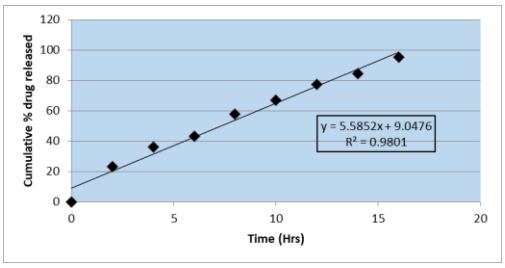
Time (Hr)	cumulative % drug released	% Drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released
0	0	100	0.000	2.000	0.000	0.000
2	23.12	76.88	1.414	1.886	0.301	1.364
4	36.14	63.86	2.000	1.805	0.602	1.558
6	43.15	56.85	2.449	1.755	0.778	1.635
8	57.59	42.41	2.828	1.627	0.903	1.760
10	66.83	33.17	3.162	1.521	1.000	1.825
12	77.17	22.83	3.464	1.359	1.079	1.887
14	84.4	15.6	3.742	1.193	1.146	1.926
16	95.16	4.84	4.000	0.685	1.204	1.978



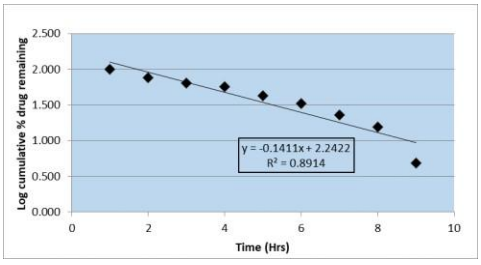
Graph 19: Drug release study

Table 14: Correlation value (R^2 value)

Formulation	Model	Kinetic parameter values
Ethosomal Formulation	Zero Order	R^2 = 0.980
	First Order	R^2 = 0.891
	Higuchi	R^2 = 0.972
	Korsmeyerpeppas	R^2 = 0.810

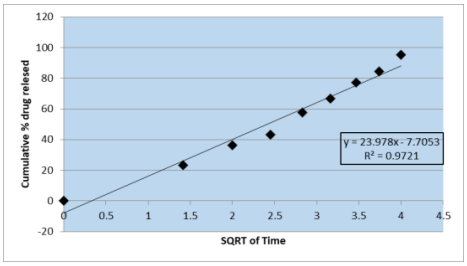


Graph 20: Zero order

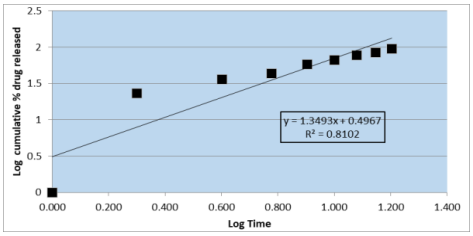


Journal of Molecular Science
Journal of Molecular Science
Volume 35 Issue 3, Year of Publication 2025, Page 606-614
DoI-10.004687/1000-9035.2025.083

Graph 21: First Order



Graph 22: Higuchi



Graph 23: Korsmeyer peppas

3.5 Antimicrobial Activity (Well Diffusion Assay)

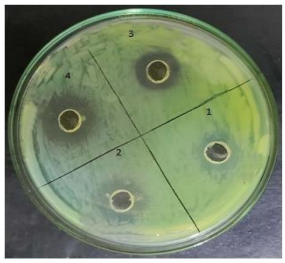
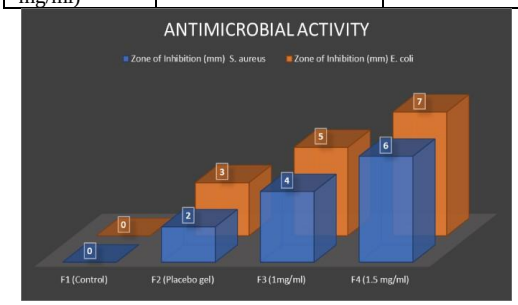


Figure 2: *In-vitro* antimicrobial activity

Table 15: Antimicrobial activity of drug loaded ethosomal gel formulation

Sample name	Zone of Inhibition (mm) *S. aureus*	Zone of Inhibition (mm) *E. coli*
F1 (Control)	0.0 mm	0.0 mm
F2 (Placebo gel)	2 mm	3 mm
F3 (1mg/ml)	3 mm	5 mm
F4 (1.5 mg/ml)	6 mm	7mm



Graph 24: Graphical representation of ethosomal gel formulation

3.6 Stability study:

Table 16: Stability Study of optimized formulation (Ethosomes)

Time (Days)	25^0C±2 ^{0}C and 60 ± 5% RH		40^0C±2 ^{0}C and 70 ±5% RH	
	Viscosity	pH	Viscosity	pH
0	3416	5.9	3416	5.9
30	3231	5.2	3520	6.3
45	3349	6.4	3242	5.4
60	3450	6.3	3376	4.9
90	3783	5.0	3489	5.1

4. CONCLUSION:

The Ornidazole-loaded ethosomal gel was successfully developed and exhibited favorable physicochemical characteristics, including optimal viscosity, pH, spreadability, and homogeneity, which are essential for effective topical application. Among the various formulations tested, the F4 formulation demonstrated the highest drug entrapment efficiency, desirable particle size distribution, and excellent stability under different storage conditions. In vitro release studies revealed that the F4 formulation followed Zero-order kinetics, indicating a consistent and controlled release of Ornidazole over an extended period. This sustained release profile is particularly beneficial for enhancing therapeutic efficacy while minimizing dosing frequency. Moreover, the antimicrobial activity assessment confirmed that the ethosomal gel retained the potency of Ornidazole, showing significant inhibitory effects against a broad spectrum of bacterial strains.

Skin irritation studies further affirmed the formulation's dermatological safety and compatibility, making it suitable for transdermal application. Overall, the results highlight the potential of ethosomal gels as an effective and patient-friendly transdermal drug delivery system for Ornidazole. This novel formulation strategy not only improves drug bioavailability but also offers a promising alternative approach for the localized treatment of bacterial infections.

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