Research Article

Formulation, Optimization and Characterization of Tolnaftate-Loaded Transferosomal Hydrogel for Topical Antifungal Drug Delivery

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Abstract

Background: Tolnaftate is a topical antifungal agent used in the treatment of dermatophytosis. Vesicular drug delivery systems may offer an alternative approach to formulating topical antifungal preparations. Methods: Transferosomes were prepared using the thin-film hydration method with soya lecithin, cholesterol and Tween 80. Six formulations (F1–F6) were evaluated for entrapment efficiency, drug content and in-vitro drug diffusion. The selected formulation was characterized for particle size, polydispersity index, zeta potential and morphology before incorporation into a Carbopol-based hydrogel. The hydrogel was evaluated for physicochemical properties and in-vitro drug release. Results: Formulation F5 was reported to exhibit an entrapment efficiency of 85.89%, drug content of 87.30%, particle size of 124.9 nm, polydispersity index of 0.353 and zeta potential of −20.2 mV. Its cumulative drug diffusion was reported as 88.4% at 24 hours. The hydrogel formulation designated G2 showed a pH of 5.58, viscosity of 8,750 cP, drug content of 84.50% and cumulative drug release of 83.15% at 24 hours. Conclusion: The findings support the feasibility of formulating tolnaftate-loaded transferosomes and incorporating them into a hydrogel. Further verification of the experimental records and additional evidence of skin permeation and antifungal performance are needed to establish the formulation's potential advantages over conventional topical preparations.

Keywords: Tolnaftate; transferosomes; hydrogel; topical drug delivery; dermatophytosis; in-vitro drug release.

1. Introduction

Dermatophytosis is a superficial fungal infection caused by dermatophytes that affect keratinized tissues, including the skin, hair, and nails. Topical antifungal therapy is commonly used for localized infections. Tolnaftate is a synthetic antifungal agent used in the treatment of dermatophyte infections. However, the effectiveness of a topical formulation can be influenced by drug release, formulation characteristics, and the ability of the drug to reach the intended site of action.

Transferosomes are highly deformable vesicular carriers composed of phospholipids and edge activators. Their flexible structure makes them a potential approach for topical drug delivery. Soya lecithin can serve as the phospholipid component, while surfactants such as Tween 80 act as edge activators. Cholesterol may also be incorporated to modify vesicle membrane properties. Nevertheless, the performance of these vesicles depends on their composition and preparation conditions and must be established experimentally.

Hydrogels are semisolid dosage forms that provide convenient application to the skin. Incorporating drug-loaded vesicles into a hydrogel may combine the formulation advantages of vesicular carriers with the ease of application of a topical gel. Carbopol 934 is commonly used as a gelling agent in topical formulations. Important evaluation parameters include vesicle size, polydispersity index, zeta potential, entrapment efficiency, drug content, pH, viscosity, spreadability, in-vitro drug release, and stability.

Therefore, the present study aimed to formulate and evaluate tolnaftate-loaded transferosomes using the thin-film hydration method and incorporate the optimized vesicular formulation into a hydrogel. The prepared formulations were characterized using relevant physicochemical parameters, and the hydrogel was evaluated for its pharmaceutical properties and in-vitro drug release. Antifungal activity was also assessed against *Trichophyton rubrum*, as documented in the study records.

Need of Study

- The study is needed to improve the poor skin penetration of tolnaftate observed in conventional topical formulations
- .The study helps in enhancing the bioavailability of tolnaftate at the site of infection through advanced vesicular delivery.
- There is a need to overcome the barrier function of the stratum corneum for effective antifungal therapy.
- The study focuses on reducing the frequency of application by providing sustained and controlled drug release.
- It aims to minimize systemic side effects by achieving targeted and localized drug delivery.
- The study is required to improve therapeutic efficacy in the treatment of fungal skin infections.
- There is a need to develop a patient-friendly dosage form with better spreadability and ease of application.
- The study helps in utilizing transferosomes as nanosized carriers to enhance drug permeation.
- It is required to increase the entrapment efficiency and stability of tolnaftate in the formulation.
- The study aims to compare the performance of transferosomal hydrogel with conventional gels.
- There is a need to develop a stable and effective formulation with improved shelf life.

The study contributes to the advancement of nanotechnology-based topical drug delivery systems.

2. Materials and Methods

2.1 Materials and Instrumentation

Tolnaftate was obtained from Dhamtec Pharma, Navi Mumbai. Soya lecithin and cholesterol were procured from Cosmo Chem, Pune, while ethanol, propylene glycol and Carbopol 940 were obtained from Labware Chemicals, Latur. Tween 80, chloroform and methanol were used in the preparation of transferosomes. Phosphate buffer (pH 7.4) was used for hydration of the lipid film. Carbopol 940 was used as the gelling agent in the hydrogel formulation, along with propylene glycol, glycerine, methylparaben, propylparaben and triethanolamine. Distilled water was used as required.

The instruments used included a Shimadzu BL-220H digital balance, magnetic stirrer and probe sonicator (Athena Technology), VMP-D melting-point apparatus (Veego), Lab India digital pH meter, rotary vacuum film evaporator, PerkinElmer FTIR spectrophotometer, Shimadzu UV-1800 spectrophotometer, Remi centrifuge, refrigerator, stability chamber (Thermolab Scientific) and light microscope.

2.2 Preformulation Studies

Preformulation studies were performed to evaluate the physical characteristics and suitability of tolnaftate for formulation development. The drug was examined for its physical appearance, colour, odour and taste. Melting-point determination was performed using the capillary method. Solubility was assessed in water, ethanol, chloroform and methanol. The melting point of tolnaftate was reported as 115°C.

A UV spectrophotometric calibration curve was prepared using standard tolnaftate solutions at concentrations of 5, 10, 15, 20 and 25 µg/mL. Absorbance was measured at 252 nm using a Shimadzu UV-1800 spectrophotometer, with methanol as the blank. Drug–excipient compatibility was investigated using FTIR spectroscopy by comparing the characteristic absorption bands of the pure drug and physical mixture. Differential scanning calorimetry was also performed to examine the thermal characteristics of the drug.

2.3 Preparation of Tolnaftate-Loaded Transferosomes

Tolnaftate-loaded transferosomes were prepared by the thin-film hydration method. Accurately weighed quantities of tolnaftate, soya lecithin, cholesterol and Tween 80 were dissolved in a mixture of chloroform and methanol. The organic phase was transferred into a round-bottom flask, and the solvents were evaporated using a rotary evaporator at 40–45°C under reduced pressure to form a thin lipid film on the inner wall of the flask. The film was further dried to remove residual solvent.

The dried lipid film was hydrated with phosphate buffer (pH 7.4) maintained at 30–40°C. Hydration was continued under gentle agitation for 30–60 minutes to obtain a transferosomal suspension. The suspension was sonicated for 5–10 minutes to reduce vesicle size and improve uniformity. The prepared formulations were stored under refrigerated conditions until further evaluation.

2.4 Formulation Design of Transferosomes

Six transferosomal formulations (F1–F6) were prepared by varying the amounts of soya lecithin and Tween 80 while maintaining the tolnaftate and cholesterol quantities constant. Each formulation contained 100 mg of tolnaftate and 20 mg of cholesterol. Soya lecithin was used at 100 or 200 mg, while Tween 80 was varied at 10, 20 and 30 mg. Each batch used 5 mL of methanol and 10 mL of chloroform. Phosphate buffer was used in a quantity sufficient for hydration.

Table No.1: Formulation table of Transferosomes

Ingredient	F1	F2	F3	F4	F5	F6
Tolnaftate (mg)	100	100	100	100	100	100
Soya lecithin (mg)	100	100	100	200	200	200
Cholesterol (mg)	20	20	20	20	20	20
Tween 80 (mg)	10	20	30	10	20	30
Methanol (mL)	5	5	5	5	5	5
Chloroform (mL)	10	10	10	10	10	10
Phosphate buffer	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

2.5 Characterization of Transferosomes

The prepared transferosomal formulations were evaluated for appearance, pH, drug content, entrapment efficiency, particle size, polydispersity index (PDI), zeta potential and vesicle morphology. Drug content was determined using UV spectrophotometric analysis. Entrapment efficiency was evaluated to estimate the proportion of drug entrapped within the vesicles. Particle size, PDI and zeta potential were determined for the selected formulation. Microscopic examination and scanning electron microscopy were used to examine vesicle morphology and distribution.

2.6 Preparation of Tolnaftate-Loaded Transferosomal Hydrogel

The transferosomal hydrogel was prepared using Carbopol 940 as the gelling agent. Carbopol 940 was accurately weighed and slowly dispersed in distilled water under continuous stirring. The dispersion was allowed to hydrate and swell for several hours. The optimized drug-loaded transferosomal suspension was gradually incorporated into the hydrated polymer dispersion with gentle stirring until a homogeneous mixture was obtained.
Propylene glycol, glycerin, methylparaben and propylparaben were incorporated into the formulation. Triethanolamine was added dropwise to neutralize the polymer and produce a smooth hydrogel. The final volume was adjusted with distilled water.

Three hydrogel formulations were prepared by varying the Carbopol 940 concentration while maintaining the other listed ingredients constant.

Table No. 2: Tolnaftate-Loaded Transferosomal Hydrogel

Ingredient	THG1	THG2	THG3
Transferosomal dispersion (mL)	25	25	25
Carbopol 940 (%)	0.5	1.0	1.5
Propylene glycol (mL)	4	4	4
Glycerin (mL)	2	2	2
Propylparaben (g)	0.03	0.03	0.03
Methylparaben (g)	0.10	0.10	0.10
Triethanolamine	q.s.	q.s.	q.s.
Distilled water	q.s.	q.s.	q.s.

2.7 Evaluation of Transferosomal Hydrogel

The prepared hydrogels were evaluated for appearance, consistency, grittiness, uniformity, pH, viscosity, spreadability, gel strength and drug content. For pH determination, 1 g of gel was dispersed in 100 mL of distilled water and allowed to stand for 2 hours before measurement. Viscosity was measured using a Brookfield viscometer. Spreadability was assessed by placing 0.1 g of gel between two glass slides, applying a 100 g weight for 1 minute and recording the time required for slide separation. Drug content was determined using the UV spectrophotometric method.

2.8 In-vitro Diffusion Study

In-vitro diffusion studies were performed for both the transferosomal dispersion and the transferosomal hydrogel using a Franz diffusion cell. A cellophane membrane soaked overnight in phosphate buffer (pH 7.4) was used as the diffusion membrane. The receptor compartment contained 25 mL of phosphate buffer and was maintained at 37 ± 0.5°C under continuous magnetic stirring.

The test formulation was placed in the donor compartment, and samples were withdrawn from the receptor medium at predetermined intervals. An equal volume of fresh buffer was added after each withdrawal to maintain the receptor volume. Drug concentration was determined spectrophotometrically, and cumulative diffusion or release was calculated from the measured concentrations. For the transferosomal dispersion, measurements were recorded at intervals up to 24 hours; hydrogel release measurements were recorded up to 12 hours.

2.9 Stability Studies

The optimized transferosomal formulation was subjected to stability evaluation under accelerated conditions of 40 ± 2°C and 75 ± 5% relative humidity for three months, as reported in the presentation. The formulation was assessed for physical appearance, pH, drug content and drug diffusion.

The optimized hydrogel was evaluated for 30 days under room-temperature conditions (25 ± 2°C/60 ± 5% relative humidity) and accelerated conditions (40 ± 2°C/75 ± 5% relative humidity). The recorded evaluation parameters included appearance, pH, viscosity, spreadability and in-vitro drug release.

2.10 Antifungal Activity

The antifungal activity of the selected transferosomal gel was evaluated against *Trichophyton rubrum* using the disk diffusion method. The test samples included TFG-2 gel, a pure tolnaftate solution as the positive standard and the gel base as the negative control. Sterile filter-paper discs of 6 mm diameter were impregnated separately with the samples and placed on inoculated agar plates using sterile forceps. Following incubation at 37 ± 2°C for 24–48 hours, the diameter of the zone of inhibition around each disc was measured in millimetres. The antifungal activity of the formulation was compared with that of the standard and negative control.

3. Result and observation

3.1 Preformulation studies

Table No.3: Organoleptic properties of Tolnaftate

Sr. No.	Characters	Result
1	Nature	powder
2	color	White to off white
3	Odour	Odourless
4	Taste	Bitter

a. Solubility studies:

Table No.4: Solubility of Tolnaftate

Sr. No.	solvent	Result
1	Water	Insoluble
2	Methanol	Slightly Soluble
3	Chloroform	Soluble
4	Acetone	Soluble
5	Methanol	Soluble

b. Melting point:

The melting point of Tolnaftate was found to be 115°C.

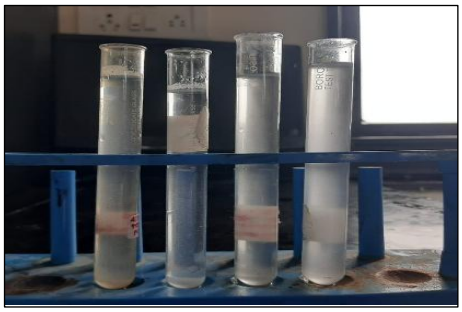




Fig No.1: Melting point determination of Tolnaftate

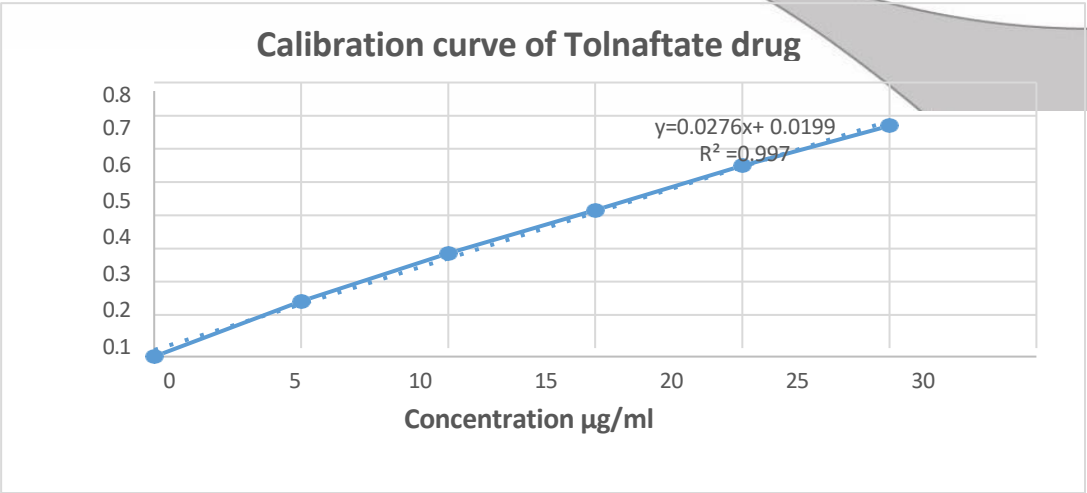
c. Analytical method used in the determination of Tolnaftate:

The UV spectrophotometry method was developed forthe analysis of drug using double beam SchimadzuUV1800 spectrophotometer. Calibration curve for Tolnaftate in methanol.

Preparation of the working standard solution:

Working standard solutions ranging in concentration from 5to25µg/ml were prepared by appropriately diluting the standard solution with methanol. The absorbance of each working standard solution was measured at 252 nm using a Schimadzu UV1800 spectrophotometer using methanol as a blank. Data for each and every experiment was obtained and statistically analyzed. The Calibration curve for Tolnaftate in methanol.

Table No.5: Concentration & absorbance Obtained for calibration curve of Tolnaftate in methanol.



Sr. no	Concentration µg/ml	Absorbance
1	5	0.167
2	10	0.311
3	15	0.441
4	20	0.575
5	25	0.695

Fig No.2: Calibration curve of Tolnaftate drug

Data for each and every experiment was obtained and statistically analysed and that shows linear Calibration curve of Tolnaftate in methanol.

FTIR Spectroscopy of Drug:

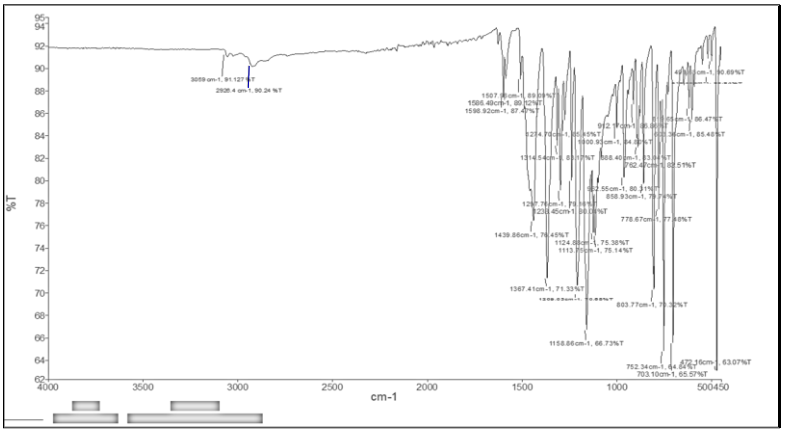


Fig No.3: FTIR spectroscopy of tolnaftate drug

Table No.6: FTIR range of drug

Sr. No.	Functional Group	Standard Range (cm^{-1})	Observed Range (cm^{-1})
1	Aromatic C=C stretching	1600 – 1450	1598 – 1439
2	C–N stretching (Thiocarbamate)	1350 – 1200	1367 – 1209
3	C=S stretching (Thiocarbamate)	1250 – 1050	1238 – 1113
4	C–O–C stretching	1150 – 1000	1158 – 1000
5	Aromatic C–H bending	900 – 700	912 – 703
6	Monosubstituted aromatic ring bending	800 – 690	803 – 703
7	C–S stretching	700 – 500	619 – 499

FTIR of Soya Lecithin:

Fig No.4: FTIR spectroscopy of Soya Lecithin

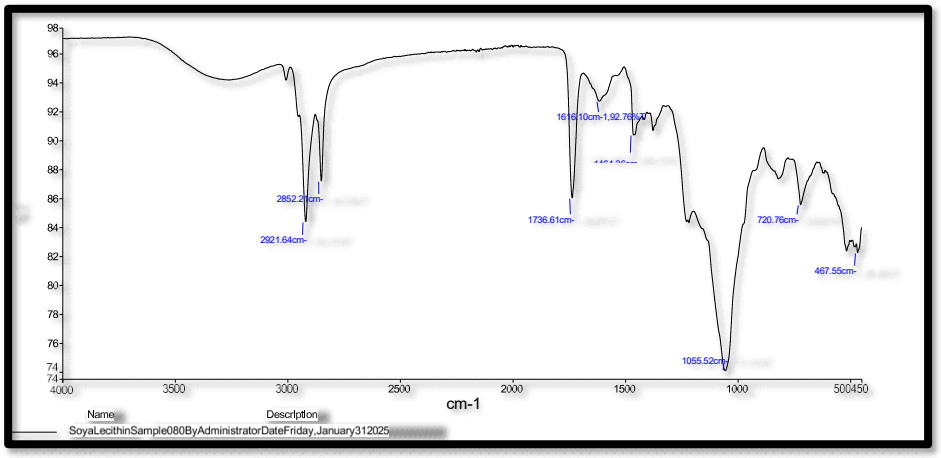


Fig.7.3:FTIR spectra of soya lecithin

Table No.6: FTIR range of Soya Lecithin

Sr. No.	Functional Group	Standard Range (cm^{-1})	Observed Range (cm^{-1})
1	Aliphatic C–H stretching (CH_2 and CH_3)	2950 – 2850	2920 – 2851
2	Ester C=O stretching	1750 – 1700	1735
3	C=C stretching (Unsaturated fatty acids)	1650 – 1600	1615
4	CH_2 bending / Scissoring	1470 – 1450	1464
5	P–O–C / C–O stretching (Phospholipid group)	1100 – 1000	1055
6	=C–H bending (Unsaturated alkene)	850 – 800	818

7	Long-chain CH_2 rocking	730 – 720	720

FTIR study of transferosomes formulation:

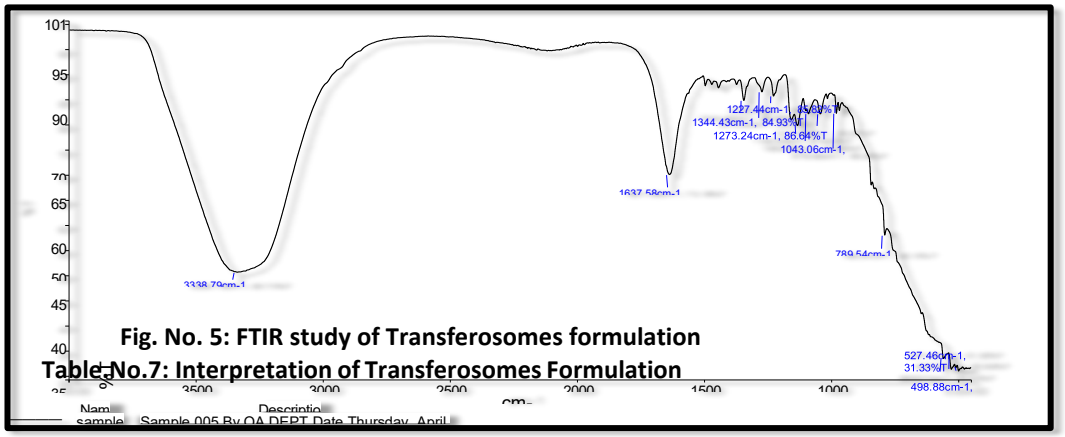


Fig. No. 5: FTIR study of Transferosomes formulation

Table No.7: Interpretation of Transferosomes Formulation

d. pH of transferosomal formulation:

The pH of the prepared transferosomal formulations was found to be in therange of 5.2 to 6.7, which is suitable for topical application and ensures compatibility with skin and nail pH without causing irritation.

Table.No.8: pH of the prepared transferosomal formulations

Sr. No.	Observed Frequency (cm^{-1})	Functional Group
1	3338	O-H stretching
2	1637	Aromatic C=C stretching
3	1344	CH2 Bending
4	1273	C–N stretching (Thiocarbamat group)
5	1089	C-O-C stretching
6	789	Aromatic C–H bending

Sr. No.	Formulation batch	pH
1	F1	5.2
2	F2	6.2
3	F3	5.5
4	F4	5.9
5	**F5**	**6.7**

6	F6	6.5

3.2 Scanning electron microscopy:

The shape and morphology of transferosomes droplet was determined using SEM showing the intact nature. The SEM images of optimized batch showed that a formulated Transferosomes was spherical in shape.

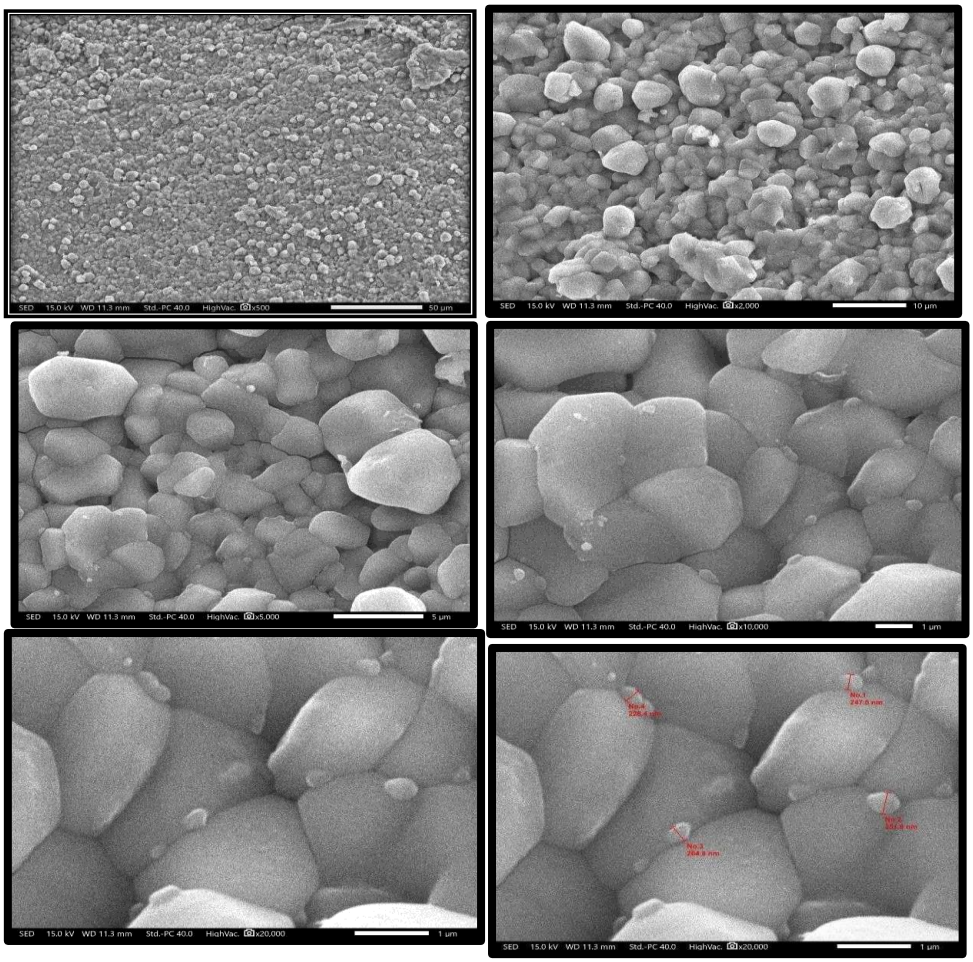


Fig. No.6: SEM images of Tolnaftate Transferosomes

3.3 Particle Size and Poly Dispersity Index:

The particle size of optimized batch is found to be 124.9nm and polydispersity index was found to be 0.353 nm. A low polydispersity index indicates particle size uniformity within the formulation. The particle size of transferosomes should be 100-300nm. The nanometer particle size of the transferosomes formulation influences the good antifungal activity by increasing solubility of drug which increases the bioavailability of drug.

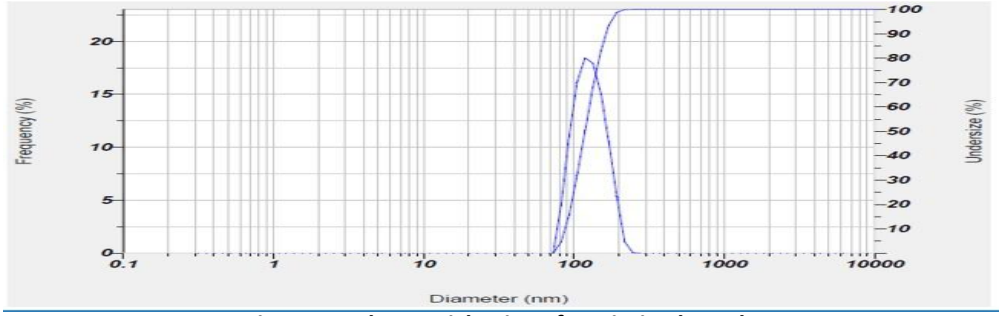


Fig. No.7: The Particle Size of Optimized Batch

3.4 .Zeta potential:

The stability of transferosomes were determine from zeta potential. zeta potential value of optimized batch was found to be -20.2mV. The surface charge on Transferosomes was determined by zeta potential. The zeta potential of transferosomes typically falls in the range of -10 to -60 mV.This negative charge arises from the presence of methanol in the transferosomes formulation, which can impart a negative charge on the vesicle surface.

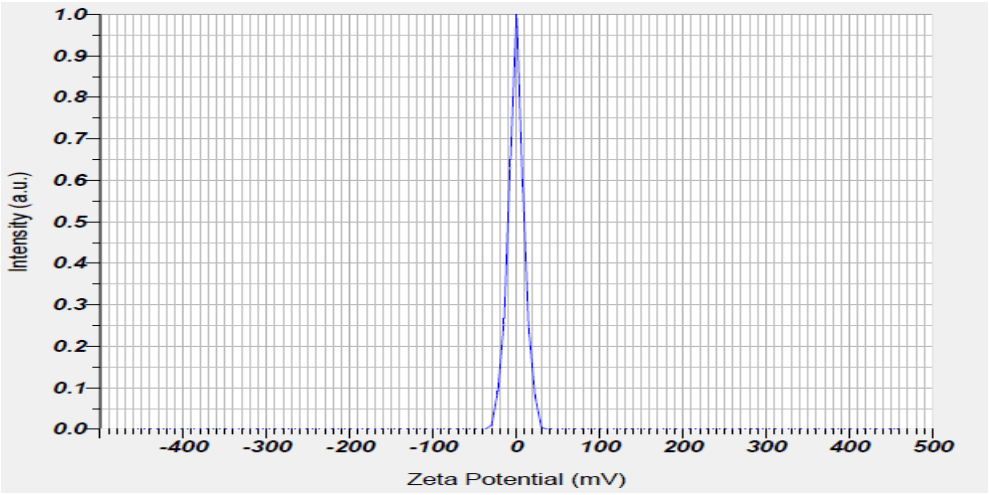


Fig. No.8: The Zeta Potential of Optimized Batch

3.5. Entrapement efficiency

Encapsulation of drug in the transferosomes depends on the amount of soya lecithin to be added in the formulation and also the amount of drug added in the formulation. The results of encapsulation efficiency were shown in below.

Table. No 9: Entrapment efficiency of transferosomal formulation

Formulation batches	Entrapment efficiency (%)
F1	79.94%
F2	83.81%
F3	78.24%
F4	81.43%
F5	**85.89%**
F6	82.85%

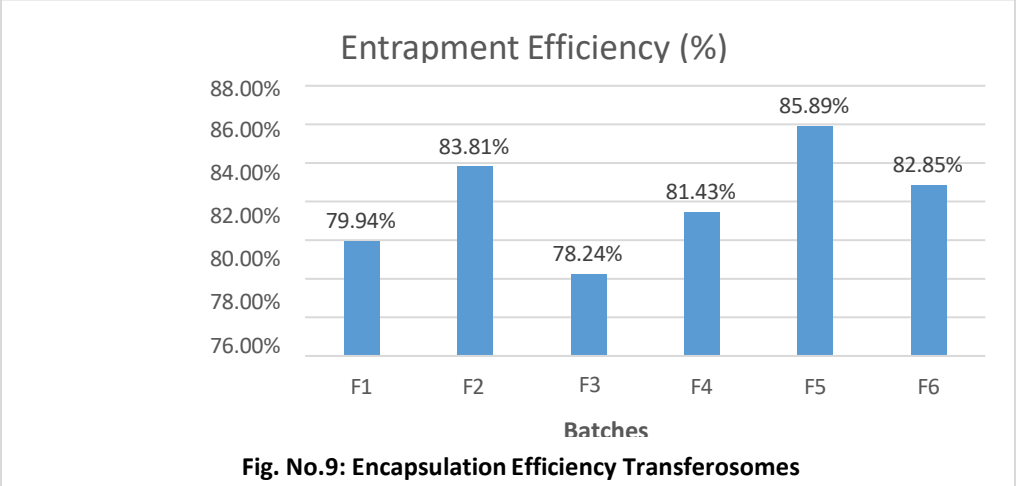


Fig. No.9: Encapsulation Efficiency Transferosomes

3.6. Determination of Drug Content:

The drug content of the transferosomal formulations was expressed as a percentage of the theoretical drug amount. The achieve the drug content 87.30%.These results indicate satisfactory drug loading and good reproducibility across different batches.

Table No 10: Drug content of transferosomal formulation

Formulation batches	Drug content (%)
F1	80.98
F2	79.67
F3	82.81
F4	81.43
F5	**87.30**
F6	83.64

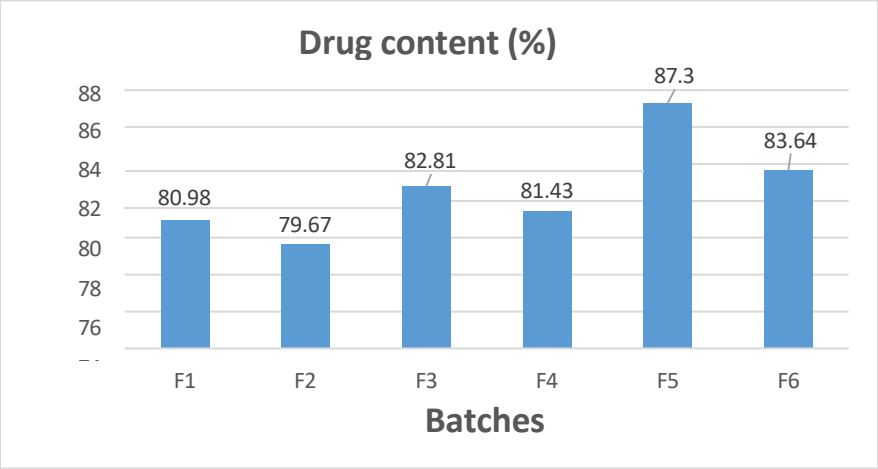


Fig. No.10: Drug content of transferosomal formulation

3.7. Differential Scanning Calorimetry (DSC):

The DSC thermogram of the transferosomal formulation showed a sharp endothermic peak at111.3°C, indicating the melting point of vesicular components. This confirms that thedrug is well-incorporated in the lipid matrix and the formulation is thermally stable.

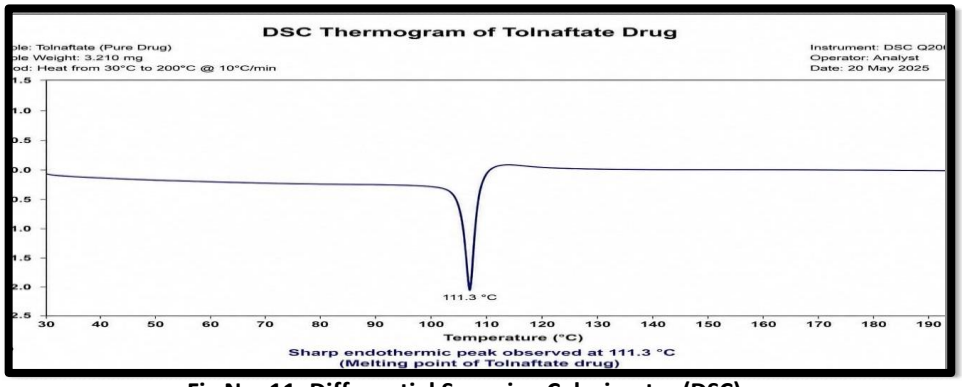


Fig No. 11: Differential Scanning Calorimetry (DSC)

3.8. *In-vitro* diffusion study of transferosomes:

The in vitro drug diffusion study revealed that all transferosomal batches (F1–F6) showed sustained drug release over 24 hours. Among them, F5 batch exhibited the highest cumulative drug diffusion of 88.4%, indicating effective and controlled release. Therefore, F5 was considered the optimized formulation for further studies.

Table No 11*: In Vitro* drug diffusion study of all transferosomal batches (F1–F6)

Time (hrs.)	F1	F2	F3	F4	F5	F6
1	10.5%	12.3%	14.2%	16.5%	18.1%	19.2%
2	18.4%	20.8%	23.1%	26.0%	29.5%	28.0%
4	32.0%	35.4%	38.7%	42.1%	45.6%	44.9%
6	43.5%	47.2%	50.8%	54.0%	57.2%	56.0%
8	55.1%	58.3%	62.1%	66.0%	68.5%	67.8%
12	67.0%	70.2%	74.3%	78.4%	81.0%	80.2%
24	78.5%	82.0%	79.4%	81.6%	88.4%	84.9%

3.9. Stability study

The F5 batch remained physically and chemically stable after 3 months under accelerated conditions (40 ± 2°C/75 ± 5% RH) as per ICH guidelines. There were no significant changes in appearance, pH, drug content, drug diffusion, confirming its stability and suitability for topical use.

Table No 12*:* Stability study of Optimized Transferosomes batch (F5)

Parameters	Initial	1 Month	2 Months	3 Months
Appearance	Homogeneous	No significant change	No significant change	No significant change
pH	6.70 ± 0.04	6.67 ± 0.03	6.42 ± 0.05	6.02 ± 0.04
Drug Content (%)	87.30 ± 0.2	87.09 ± 0.3	86.9 ± 0.2	86.34 ± 0.4
Drug Diffusion Study (%)	88.4 ± 0.4	88.01 ± 0.3	87.62 ± 0.5	87.3 ± 0.4

3.10 Evaluation of Tolnaftate loaded transferosomal hydrogel

a. Appearance and colour

Table No 13: Appearance and colour of Transferosomal hydrogel

Formulation	Appearance	Consistency	Grittiness	Uniformity
G1	offWhite	Smooth	None	Good
G2	offWhite	Smooth	None	Good
G3	offWhite	Smooth	None	Good

B. p of

Tolnaftate transferosomal Hydrogels was found in range of 5.53 – 5.62 which is was near to the physiological pH of the skin .Hence it Concludes that the gel formulation is safe to use topically.

Table No 14: pH of Transferosomal hydrogel

Batch	G1	G2	G3
pH	5.58	5.62	5.53

c. Spreadability

The value spreadability indicates that gel is easily spreadable by applying just a small amount of shear. Spreadability is inversely proportional to the viscosity of prepared gel. Spreadability decreased as the amounts increased.The Spreadability of the prepared carbopol940 gel formulation was in the range of 3.8-4.2 gm.cm/sec. All the formulations showed good spreadability

Table No. 15: Spreadability of Tolnaftate Loaded Transferosomal Hydrogels.

Batch	Spreadability (gm.cm/sec)
G1	3.8
G2	4.5
G3	4.2

d.Viscosity

Viscosity of gel was determined using Brookfield viscometer at 25°C with a spindle speed at 10 rpm. Viscosity values of the formulation are in the range of 8420 cps to 8750 cps.

Table No 16: Viscosity of Tolnaftate Loaded Transferosomal Hydrogels

Batch	Viscosity (cps)	Gel strength
G1	8420	+
G2	8750	++
G3	8680	++

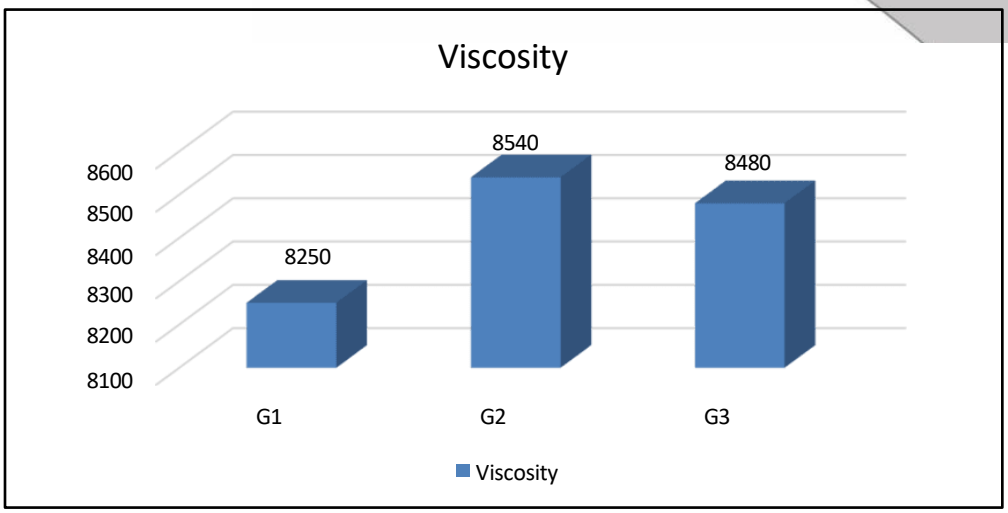


Fig No. 11: Viscosity of Tolnaftate Loaded Transferosomal Hydrogels

e. Drug content

The prepared formulations were evaluated for drug content. It was found that drug content range in the prepared formulation was satisfactory and the drug was uniformly distributed in all formulations. The % drug content was higher for Transferosomes G2 formulation (84.50%) and lowest for the G3 formulation (78.43%).

Table No.17 : Drug Content(%)Tolnaftate Loaded Transferosomal Hydrogels

Batch	Drug content (%)
G1	80.52%
G2	84.50%
G3	78.43%

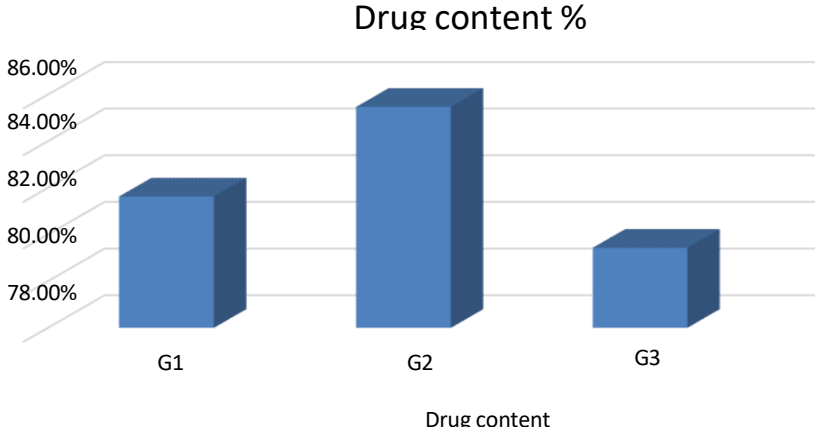


Figure No 12: %Drug content of Transferosomal hydrogel

f. *In Vitro* drug diffusion(%)

TableNo.18: In vitro drug diffusion of Tolnaftate Loaded Transferosomal Hydrogel

Time (hr)	THG1	THG2	THG3
1	5.41	8.2	6.84
2	8.38	10.53	9.48
3	11.75	14.4	16.13
4	15.2	21.32	18.64
5	21.15	28.22	24.62
6	30.78	38.08	35.8
8	45.47	54.21	51.68
10	52.32	66.84	61.19
12	65.92	75.12	72.69
24	78.32	83.15	80.49

g. Anti-fungal activity study

The antifungal activity of TFG-2 against *Trichophyton rubrum* was evaluated using the disk diffusion method. Following incubation at 37 ± 2°C for 24–48 h, TFG-2 exhibited a clear zone of inhibition, indicating significant antifungal activity. The standard formulation also showed effective inhibition, whereas the control exhibited negligible or no antifungal effect.

TableNo.19: The antifungal activity of TFG-2 against Trichophyton rubrum

Sr. No.	Formulations	Fungal Strain
		Trichophyton rubrum
1.	Standard (+)	18.6 ± 0.4 mm
2.	TFG-2 Gel	17.8 ± 0.5 mm
3.	Control (-)	0 mm

- Standard (+) : Pure drug solution
- TFG-2 : Formulated Gel
- Control(-) : Gel base

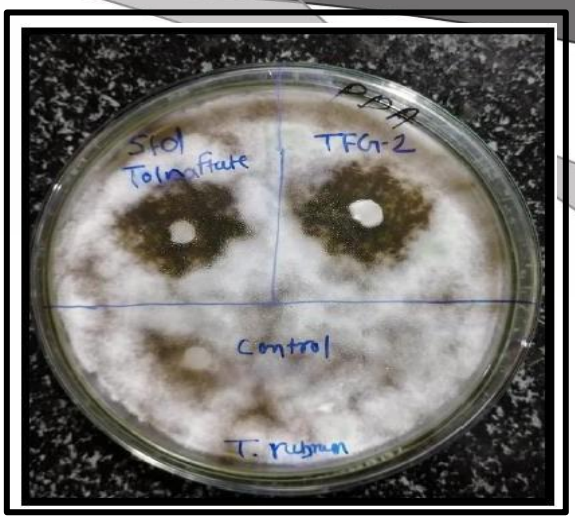


Figure No 13: The antifungal activity of TFG-2 against Trichophyton rubrum

h. Stability Study

Optimized topical gel was assessed for stability test for 3 months by exposing the sample at room temperature (25 ± 2 °C/60 ± 5%RH) and accelerated condition (40 ± 2 °C/75 ± 5%RH) in Stability chamber, after 30 days stability of the gel is evaluated for appearance, pH, viscosity, Spreadability, in vitro diffusion release(%).

TableNo.20: Stability study of Optimized topical gel

Parameters	**Initial**	**1 Month**	**2 Months**	**3 Months**
Appearance	Homogeneous	No significant change	No significant change	No significant change
pH	5.6	5.6	5.4	5.3
(%) cumulative drug release	83.15	83.15	82.86	81.72

4. Conclusion

The present study successfully demonstrated the formulation and evaluation of a tolnaftate-loaded transferosomal hydrogel for topical application. Among the six transferosomal formulations, F5 showed the most favourable overall characteristics, with a particle size of 124.9 nm, polydispersity index of 0.353, zeta potential of −20.2 mV, drug content of 87.30%, and entrapment efficiency of 85.89%. The optimized transferosomal formulation exhibited 88.4% drug diffusion, while the selected hydrogel formulation (THG2) demonstrated 83.15% drug release at 24 hours. The hydrogel also showed satisfactory physicochemical properties, including pH, viscosity, spreadability, and physical stability during the evaluated storage period.

In the antifungal study against *Trichophyton rubrum*, the transferosomal hydrogel produced a zone of inhibition of 17.8 ± 0.5 mm, compared with 18.6 ± 0.4 mm for pure tolnaftate, whereas the control gel base showed no inhibition. These findings indicate that the formulated hydrogel retained the antifungal activity of tolnaftate. Overall, the developed transferosomal hydrogel appears to be a promising topical delivery system for tolnaftate. However, further studies involving comprehensive skin permeation, and in-vivo evaluation are required to establish its therapeutic performance and suitability for clinical application.

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