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FORMULATION AND EVALUATION OF ECONAZOLE USING TRANSFERSOMAL GEL

Mohd Zubair Ansari*[1], Dr. J. P. Rai[2], Pradeep Kumar Yadav[3] and Dr. A. K. Singhai[4]

[1]Scholar, School of Pharmacy Lnct University Bhopal.

[2]Professor, School of Pharmacy Lnct University Bhopal.

[3]Associate Professor) School of Pharmacy Lnct University Bhopal.

[4]Director School of Pharmacy Lnct University Bhopal.

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***Corresponding Author**
Mohd Zubair Ansari
Scholar, School of Pharmacy
Lnct University Bhopal.

ABSTRACT

The present study aimed to develop and evaluate a transfersomal gel formulation for the enhanced topical delivery of Econazole, an antifungal agent. Transfersomes, vesicular carriers composed of phospholipids, were employed to improve the drug's skin permeation and therapeutic efficacy. The transfersomal gel was characterized for its particle size, polydispersity index, zeta potential, entrapment efficiency, and morphology using dynamic light scattering and transmission electron microscopy. Furthermore, the rheological properties of the gel were examined to assess its suitability for topical application. The in vitro drug release profile was studied using a Franz diffusion cell setup through synthetic cellulose membrane and excised rat skin. The results indicated that the transfersomal gel exhibited a significantly smaller particle size (less than 200 nm), high entrapment efficiency (>80%), and stable zeta potential, indicating the successful formation of transfersomes. The rheological assessment showed a pseudoplastic flow behavior, ideal for topical application, and sustained drug release was achieved over the studied period. In conclusion, the developed transfersomal gel formulation offers a promising platform for the efficient topical delivery of Econazole. Further investigations, including in vivo studies, would be warranted to assess its full potential for clinical application.

KEYWORDS: Novel Drug Delivery System, transfersomal gel, antifungal, Econazole.

INTRODUCTION

For many decades treatment of an acute disease or a chronic illness has been mostly accomplished by delivery of drugs to patients using various pharmaceutical dosage forms including tablets, capsules, pills, suppositories, creams, ointments, liquids, aerosols and injectables, as drug delivery systems are the primary pharmaceutical products commonly seen in the market, even though these drug delivery system ensure a prompt release of drug, it is necessary to take this type of drug several times a day to achieve as well as to maintain the drug concentration with in the therapeutically effective range needed for the treatment. This results in significant fluctuations in drug level.[1,2]

In the past two and a half decades several advancements have been made. They have resulted in the development of new techniques for drug delivery. These techniques are capable of controlling the rate of drug delivery, sustaining the duration of therapeutic activity and targeting the delivery of drug to a cell or tissue. Recently pulsatile drug delivery system is gaining importance.[3]

Fungal infections pose significant health challenges and have become increasingly prevalent in recent times. Econazole is a broad-spectrum antifungal agent commonly used to treat various skin infections caused by fungi. To enhance the therapeutic efficacy and patient compliance, researchers have explored novel drug delivery systems, among which transferosomal gel has shown promising potential.[4]

Transferosomes are lipid-based vesicles designed to enhance the penetration of active ingredients through the skin, allowing for improved drug delivery and targeted action. These vesicles are composed of phospholipids and surfactants, forming flexible, deformable, and highly permeable structures. The transferosomal gel represents an innovative approach to deliver econazole, taking advantage of both the benefits of topical gels and the enhanced drug penetration of transferosomes.[5]

The formulation and evaluation of econazole-loaded transferosomal gel involve a series of studies to ensure its stability, release profile, and effectiveness against fungal infections. Researchers analyze parameters such as vesicle size, zeta potential, entrapment efficiency, drug release kinetics, and in vitro/in vivo antifungal activity.[6,7]

By formulating econazole into a transferosomal gel, potential benefits include improved skin permeation, reduced dosing frequency, enhanced patient compliance, and potentially minimized side effects. This research represents a significant step forward in optimizing antifungal therapy and may open new avenues for drug delivery in the field of dermatology and beyond.[8,9]

The objective of this study is to formulate and evaluate an econazole-loaded transferosomal gel as a novel drug delivery system for the treatment of fungal infections.

MATERIAL

The drug was obtained as a kind gift from GSK Pharmaceuticals Ltd. The supplied powder of Econazole Nitrate was white, odourless White to yellowish white powder. Cholesterol was sourced from S.D. Fine Chem. Ltd., India. Soybean lecithin, ethanol, Sodium cholate pellets, Hydrochloric acid, and Span 80 were obtained from the Chemical Store of the Pharmaceutics Loba Chemie, India. All other reagents used were of analytical grade.

Preformulation study

Preformulation may be described as a phase of the research and development process where the formulation scientist characterizes the physical, chemical and mechanical properties of new drug substances, in order to develop stable, safe and effective dosage forms

ORGANOLEPTIC PROPERTIES

Appearance

Transferred approximately 1gm of the sample on a white paper spreaded uniformly and examined visually.

Colour

A small quantity of pure drug powder was taken in a butter paper and viewed in well illuminated place.

Solubility

Aqueous solubility is an important physicochemical property of drug substance, which determines its systemic absorption and in turns its therapeutic efficacy. Solubility of Econazole Nitrate was determined in water and methanol, ethanol, chloroform and ethyl acetate and other common solvents.

Table 5.1: Solubility Specifications.

Descriptive terms	Approximate volume of solvent in millilitres per gram of solute
Very soluble	Less than 1
Freely soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 to 100
Slightly soluble	From 100 to 1000
Very slightly soluble	From 1000 to 10,000
Practically insoluble	More than 10,000

Melting point determination

Melting point of Econazole Nitrate was determined by Open capillary method.

Determination of Partition Coefficient

25 mg of Econazole Nitrate with aqueous phase and n-octanol was taken in three separating funnels. The separating funnels were shaken for 2 hrs in a wrist action shaker for equilibration. Two phases were separated and the amount of the drug in aqueous phase was analyzed spectrophotometrically. The partition coefficient of the drug in phases was calculated.

Determination of λmax

A solution of Econazole Nitrate containing the concentration 1000µg/ ml was prepared in PBS pH 6.8 and UV spectrum was taken using double beam spectrophotometer(Systronic, 2200). The solution was scanned in the range of 200 – 400 nm.

Preparation of Econazole Nitrate Loaded Transferosomal Formulations[10]

Transferosomes formulations were prepared by a thin film hydration method. Soybean phosphatidylcholine, cholesterol, sodium cholate, span 80, and Brij 35 with different molar ratios were dissolved in 10 mL of a mixture of three organic solvents (methanol:chloroform:ethanol) at (2:2:1) v/v/v ratio, as represented in Table 1.

Using rotary evaporator, thin lipid film on the internal surface of the round-bottomed flask was formed. Econazole Nitrate (100 mg) was dissolved in 20 mL of an isotonic phosphate buffer (pH 5.8). Econazole Nitrate solution was used to hydrate the prepared thin film by rotation at 100 rpm for 2 hours. To form large multilamellar vesicles, the resulting suspensions were kept for 24 hours at 25°C. To form smaller vesicles, the transferosomal dispersions were sonicated for 30 minutes.

The Econazole Nitrate transferosomes were separated from the entrapped Econazole Nitrate by high-speed centrifugation at 20,000 rpm for 3 hours at −5°C using cooling ultracentrifuge. To separate the untrapped Econazole Nitrate, clear supernatant was carefully taken out after the centrifugation. The transferosomes remained as precipitate containing the entrapped Econazole Nitrate. The precipitate was resuspended in 10 mL of isotonic phosphate buffer (pH 5.8) in order to be evaluated. The transferosomal dispersions (free from the untrapped Econazole Nitrate) were kept at a constant temperature of 4°C within glass vials. Laminar air flow hood was used for conducting experimental procedures under aseptic conditions.[11]

Table 5.2: Composition of Transferosomal Formulations.

Formulation code	Econazole Nitrate	Cholesterol	Lecithin	Sodium Cholate	Span 80	Brij 35
TF-1	100	2	1	4	-	-
TF-2	100	2	1	3	-	-
TF-3	100	2	1	2	-	-
TF-4	100	2	1	-	4	-
TF-5	100	2	1	-	3	-
TF-6	100	2	1	-	2	-
TF-7	100	2	1	-	-	4
TF-8	100	2	1	-	-	3
TF-9	100	2	1	-	-	2

Evaluation of Transferosomal Formulations

Morphological Study

The vesicle formation was confirmed by optical microscopy in 45× resolution. The Transferosomal suspension placed over a glass slide and fixed over by drying at room temperature, the dry thin film of Transferosomal suspension observed in the formation of vesicles. The microphotography of the transferosomal so obtained from the microscope by using a digital camera. The detailed surface characteristic of the selected transferosome formulation was observed using a scanning electron microscope.

Particle size analysis[12]

The vesicle sizes of transferosomes were determined by light scattering based on laser diffraction using a Malvern Mastersizer (Malvern Instruments, Malvern, UK). The apparatus consisted of a HeNe laser (5 mW) and a small-volume sample-holding cell. The sample was stirred using a magnetic stirrer bead to keep and maintain the sample in suspension.

Zeta potential

The significance of zeta potential is that its value can be related to the stability of colloidal dispersions. The zeta potential indicates the degree of repulsion between adjacent, similarly charged particles in dispersion. The zeta potential for the Transferosomal dispersion was determined using Malvern instruments.[12]

Entrapment efficiency

The percentage of Econazole Nitrate loading in transferosome was determined by using 4.0 mL of dispersion. Free Econazole Nitrate was separated from the transferosomal dispersions by subjecting the transferosomes to a high-speed centrifugation at 21,000 rpm at 10°C model T-70BL (Laby Instrument Industry, Haryana, India) for 3 hours. The supernatant was siphoned-off and analyzed using a UV spectrophotometer. The precipitate separated from supernatant was redispersed in 4 mL of isotonic phosphate buffer (pH 7). To perform the lysis of transferosomes for liberating the encapsulated Econazole Nitrate molecules, a 500 µL was diluted ten times with methanol (HPLC grade, ≥99.9%). The concentration of drug was determined spectrophotometrically.[13]

$$\% \text{ Entrapment efficiency} = [(TD-FD)/TD] \times 100$$

Where TD is the total drug amount, and FD is the amount of free drug.

***In-Vitro* Drug Release Study**

The in vitro release study was performed via a dialysis membrane according to Hao's method. Briefly, an equivalent amount of 10 mg Econazole Nitrate -loaded transferosomal dispersion was introduced into dialysis bags with a molecular weight cutoff 12,000 kDa. The dialysis bags were suspended in an isotonic buffer solution (250 mL, pH 6.8, 37°C±2°C) at speed of rotation 1,500 rpm and placed within the dissolution flask of the USP dissolution apparatus. The samples (5 mL) were withdrawn and analyzed spectrophotometrically every 45 minutes for 12 hours. The withdrawn samples were replaced with the same volume of fresh an isotonic buffer solution (pH 6.8). The concentration percentage of Econazole Nitrate at time (t) was estimated.[14]

Formulation of Transferosomes Entrapped Econazole Nitrate Gel

The gel was prepared by the same procedures described by Schmolka (1972). In brief, in 10 mL distilled water, a required quantities of poloxamer 407 and HPMC k15 were added slowly and stirred with the help of magnetic stirrer at 50 rpm for 1 hour. To ensure the maximum dissolution of polymers, the prepared solution was left in the quiescent state for 12

hours in a refrigerator. Then, the solution (poloxamer with HPMC k15) was stirred slowly at 5°C for 5 hours until a gel was formed. Various formulations were prepared as shown in Table 5.5.

Table 5.3: Composition of Transferosomal Gel Formulations.

Formulation code	Poloxamer 407	HPMC k15	Propylene glycol	DMSO
TFG-1	0	15	-	-
TFG-2	10	20	-	-
TFG-3	10	25	-	-
TFG-4	10	20	0.5	-
TFG-5	10	20	-	0.5

Evaluation of Transferosomal Gel

Physical appearance

The prepared gel was examined for clarity, colour, homogeneity and the presence of foreign particles.

pH

The pH of the dispersion was measured by using a digital pH meter.

Rheological Study

Viscosity measurement: Viscosity was determined by Brookfield programmable DV III ultra viscometer. In the present study, spindle no. CP 52 with an optimum speed of 0.01 rpm was used to measure the viscosity of the preparation.

Content Uniformity

The drug content of the prepared gel was carried out by dissolving accurately weighed quantity of gel equivalent to 10 mg of the drug and triton X-100 (1%) in small amount of water shaken it vigorously and taken in 100 ml volumetric flask and volume was made up to 100 ml with methanol. The content was filtered through Whatman filter paper No. 41. 5 ml of above solution was taken into a 25 ml volumetric flask and volume was made up to mark with methanol. The content of Econazole Nitrate was determined against blank by using the Shimadzu UV/visible spectrophotometer. The drug content was determined from the calibration curve of drug.

In Vitro Drug Release Study

The apparatus consists of a glass cylinder open at both ends. A dialysis membrane soaked in distilled water (24 h before use) is fixed to the one end of the cylinder with the aid of an adhesive. Gels equivalent to 10 mg of drug is taken inside the cell (donor compartment) and the cell is immersed in a beaker containing 100 ml of PBS pH 7.4 containing 10% v/v methanol (to maintain sink condition), act as receptor compartment. The whole assembly is fixed in such a way that the lower end of the cell containing gel is just above the surface of the diffusion medium (1-2 mm deep) and the medium was agitated using a magnetic stirrer at the temperature 37 ± 0.5°C. Aliquots (5 ml) are withdrawn from the receptor compartment periodically and replaced with same volume with fresh buffer. The samples were analyzed by using UV-visible spectrophotometer. The tests were carried out in triplicate.

Stability studies

As soon as the product is developed, it is subjected to ageing; as a result, its physical properties, chemical composition and even its biological availability may be changed. To assess long-term stability, gel-based formulations were stored in gel tube at (4°C±1°C, 25°C±1°C, and 40°C±1°C), 75% relative humidity (RH) ±5% for a period of up to 3 months. They were evaluated periodically for the following parameters:[15]

- Appearance
- Viscosity
- pH
- Drug Content analysis
- % Drug Release

RESULTS

Physical Appearance

Melting Point

Melting point of Econazole Nitrate was determined by melting point apparatus (Tempo) and found to be 174.5±2°C.

Table 6.1: Solubility of Econazole Nitrate in different solvents.

S.No.	Solvent	Solubility
1.	Water	Slightly Soluble
2.	Methanol	Sparingly Soluble
3.	Ethanol	Sparingly Soluble
4.	DMSO	Soluble

5.	Phosphate buffer	Soluble

++++ = Freely soluble 1-10 parts, +++ = Sparingly soluble 30-100 parts, ++ = Soluble 30-100 parts, + = Slightly soluble 100-1000 parts, – = Practically insoluble >10000 parts

Table 6.5: Evaluation of Econazole Nitrate Loaded Transferosomal Formulation.

Formulation Code	Mean particle size (µm)	Zeta potential (mv)	Encapsulation efficacy (%)
TS-1	171.57±2.10	-53.34±2.27	70.31±4.63
TS-2	178.61±2.35	-38.22±1.35	69.28±6.47
TS-3	184.38±4.13	-25.62±3.65	67.08±3.84
TS-4	188.48±2.61	-45.68±1.45	83.86±5.27
TS-5	192.89±3.16	-40.53±4.61	79.47±7.54
TS-6	197.93±2.27	-35.91±2.72	78.27±6.19
TS-7	162.54±1.20	-33.29±1.16	74.43±5.44
TS-8	171.68±3.32	-30.98±3.57	69.18±5.95
TS-9	193.83±3.50	-28.56±1.42	64.93±4.65

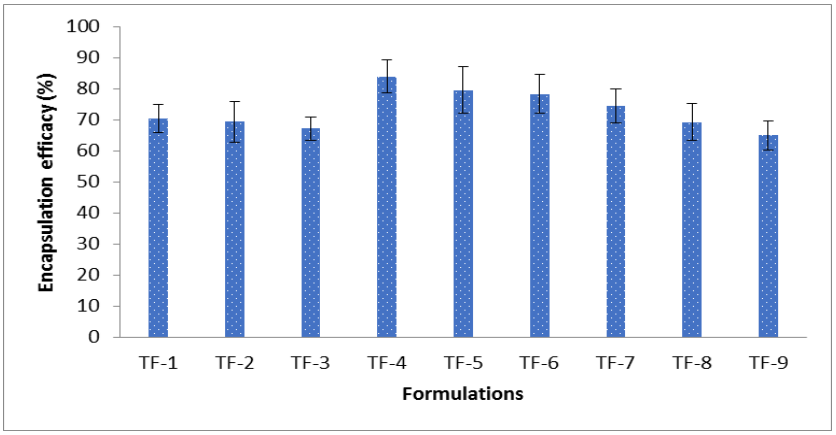

Figure 6.5: Entrapment Efficiency of Econazole Nitrate Loaded Transferosomal Formulation.

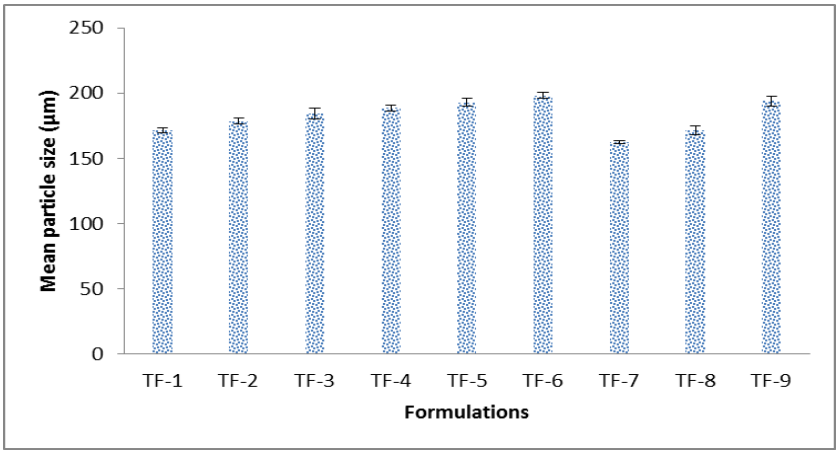

Figure 6.6: Mean particle size (µm)of Econazole Nitrate Loaded Transferosomal Formulation.

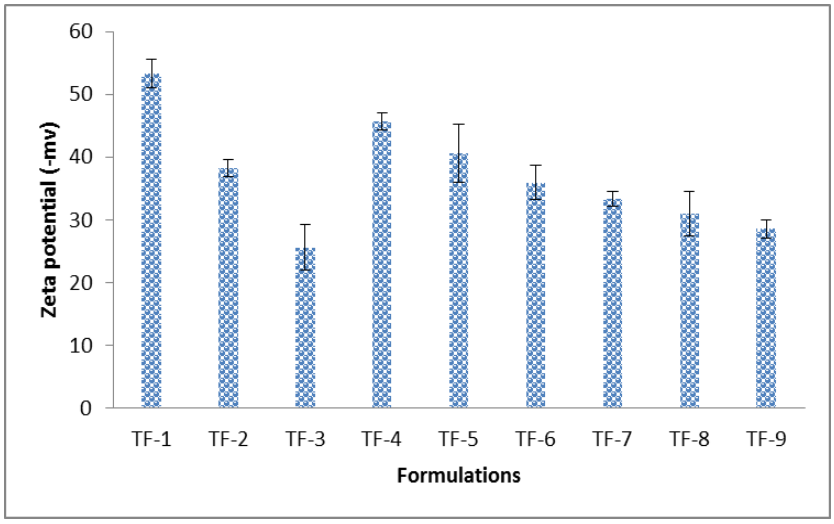

Figure 6.7: Zeta potential (-mv) of Econazole Nitrate Loaded Transferosomal Formulation.

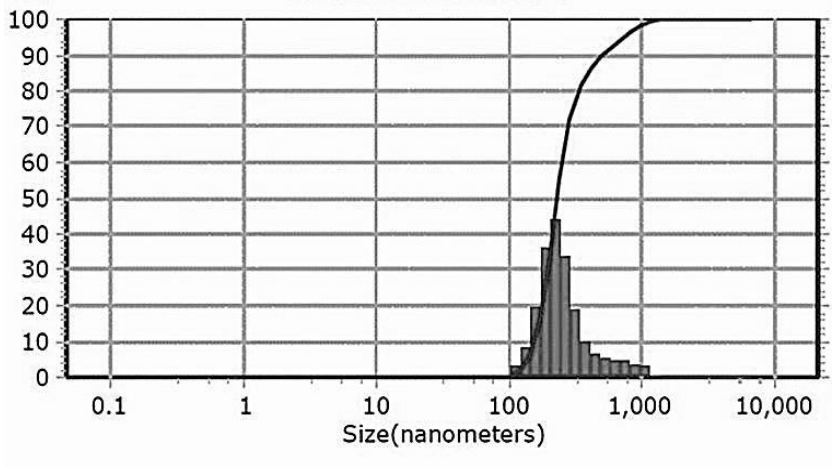

Figure 6.8: Particle Size Distribution of Econazole Nitrate Loaded Transferosomal Formulation (TF3).

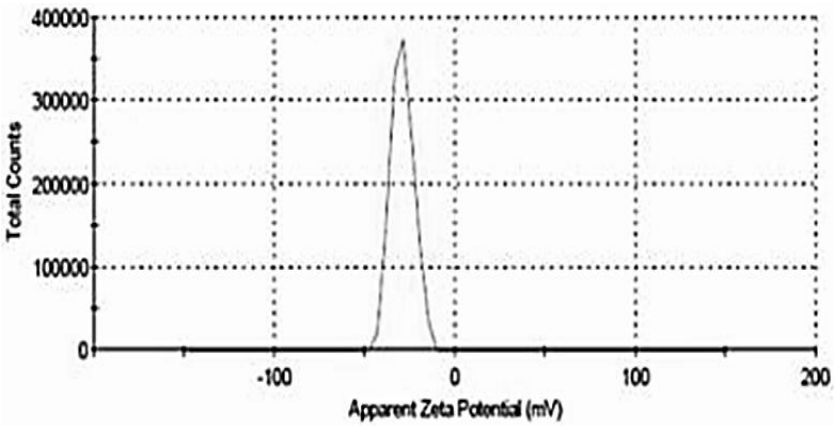

Figure 6.9: Zeta Potential of Econazole Nitrate Loaded Transferosomal Formulation (TF3).

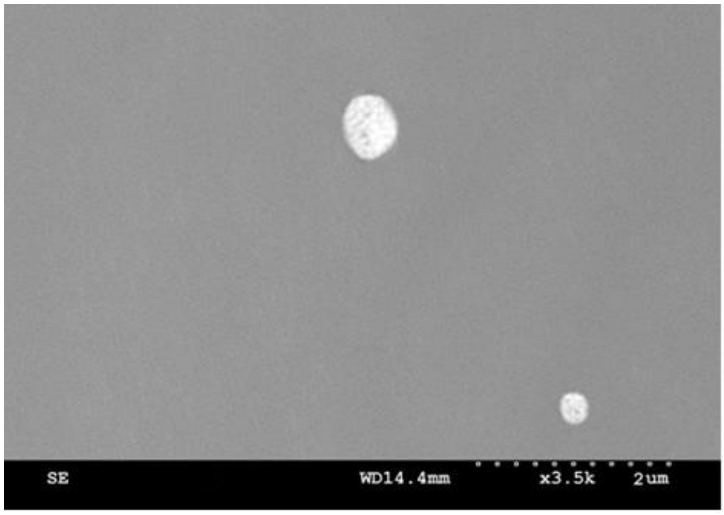

Figure 6.10: SEM Photograph of Econazole Nitrate Loaded Transferosomal Formulation (TF3).

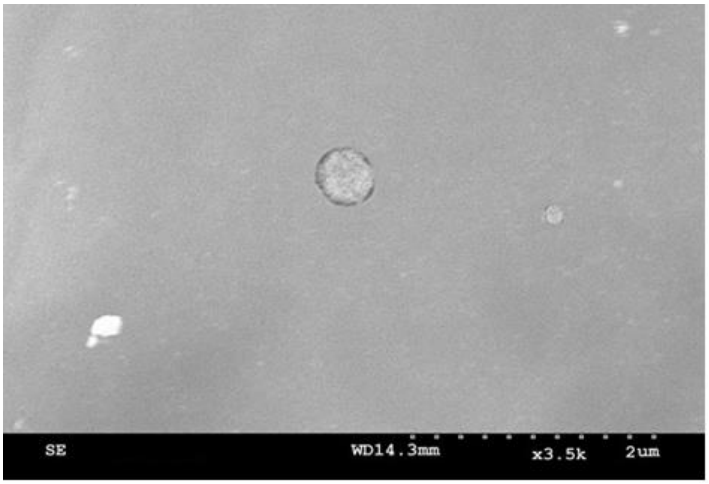

Figure 6.11: SEM Photograph of Econazole Nitrate Loaded Transferosomal Formulation (TF4).

Table 6.6a: Cumulative % of Drug Release of Econazole Nitrate Loaded Transferosomal Formulation.

F. Code / Time	Cumulative % of drug release (in 10 hr.)				
	TF-1	TF-2	TF-3	TF-4	TF-5
0	0	0	0	0	0
0.25	11.85±1.56	9.94±5.33	18.08±1.18	19.32±2.23	17.35±4.66
0.5	22.29±1.32	14.85±1.67	26.61±2.09	29.67±3.86	15.96±4.53
1	37.82±1.98	20.98±3.54	27.32±3.08	35.09±2.06	25.97±3.79
2	45.97±2.15	31.54±5.17	47.98±2.62	47.86±3.56	33.53±3.43
3	55.76±2.28	47.47±6.15	55.47±1.32	62.33±2.98	44.79±3.08
4	63.11±8.06	55.44±5.18	63.8±2.67	67.95±3.54	51.44±1.69
5	72.17±1.33	67.82±2.15	70.43±3.09	79.43±3.08	60.72±3.23
6	78.42±2.18	74.22±3.24	74.62±4.86	88.11±2.15	74.27±2.66

8	80.92±3.23	78.96±3.24	78.11±1.16	96.56±2.86	89.64±2.23
10	82.55±3.75	84.67±2.47	89.95±2.28	99.16±1.62	96.28±4.35

Table 6.6b: Cumulative % of Drug Release of Econazole Nitrate Loaded Transferosomal Formulation.

F. Code / Time	Cumulative % of drug release (in 10 hr.)			
	TF-6	TF-7	TF-8	TF-9
0	0	0	0	0
0.25	22.97±4.35	19.33±2.15	18.91±1.35	12.86±4.66
0.5	36.54±3.66	19.89±4.35	15.59±1.39	16.33±3.23
1	41±5.39	31.69±3.29	27.67±2.38	20.18±2.25
2	48±7.21	37.58±3.09	35.54±2.98	27.23±1.54
3	58.25±3.63	46.19±2.56	41.78±2.32	36.72±2.09
4	63.86±9.52	54.18±2.33	52.99±2.67	47.82±2.06
5	76.51±8.35	65.84±3.67	68.95±1.08	52.88±2.15
6	82.35±2.45	73.94±2.65	79.55±2.18	66.85±3.24
8	94.45±1.74	80.89±1.09	81.95±2.78	79.86±1.25
10	95.83±2.17	89.76±4.86	90.11±1.96	84.35±2.18

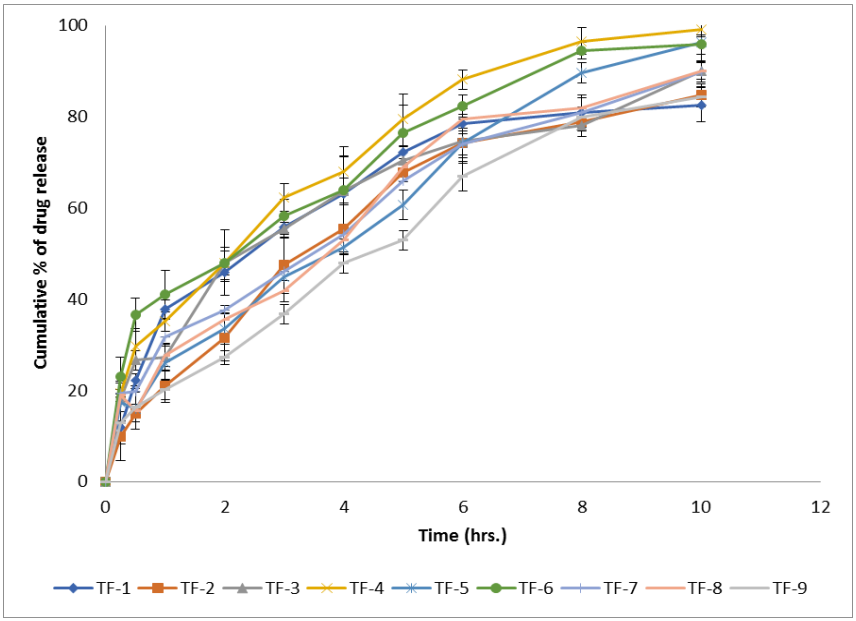

Figure 6.12: Cumulative % of Drug Release of Econazole Nitrate Loaded Transferosomal Formulation.

Table 6.7: Evaluation of Econazole Nitrate Loaded Transferosomal Gel Formulation

Formulation Code	TFG-1	TFG-2	TFG-3	TFG-4	TFG-5
Appearance	Off-white	Off-white	Off-white	Off-white	Off-white
Homogeneity	Good	Good	Good	Good	Good
pH	5.88	6.55	7.38	6.76	5.26
Viscosity (Pascal Second)	10.56	16.95	24.12	20.68	17.85
Drug Content (%)	96.66	98.85	97.28	98.56	98.47

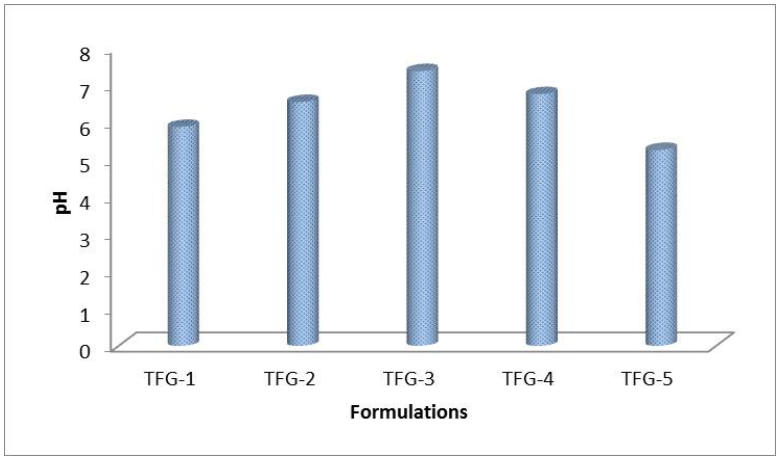

Figure 6.13: Evaluation of pH of Econazole Nitrate Loaded Transferosomal Gel Formulations.

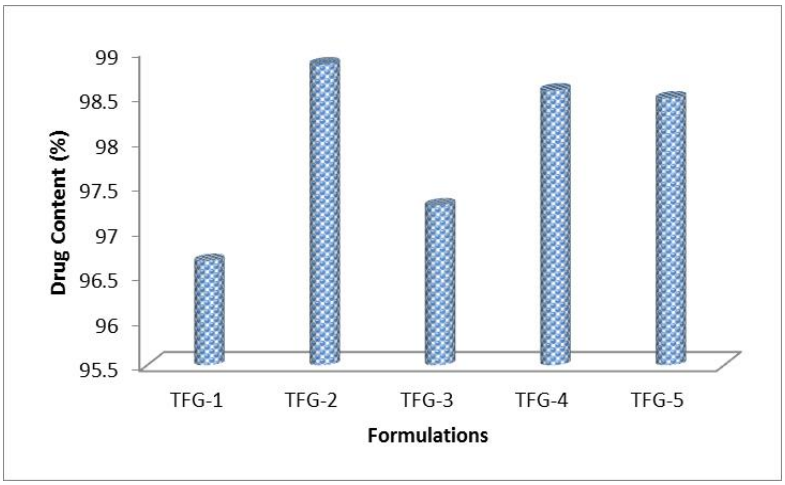

Figure 6.14: Evaluation of Drug Content (%) of Econazole Nitrate Loaded Transferosomal Gel Formulations.

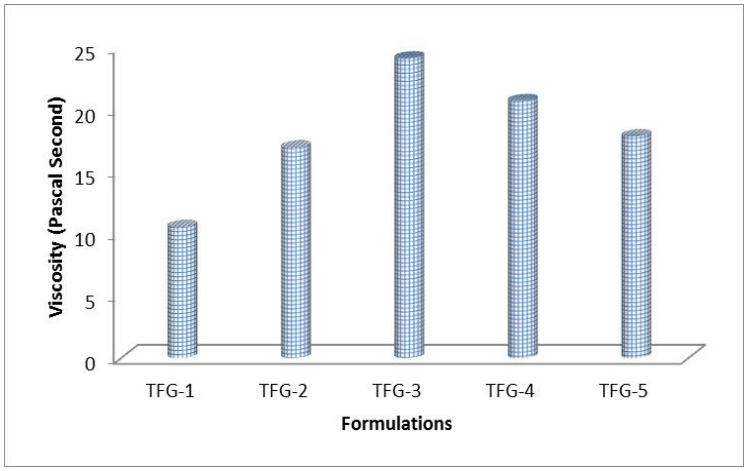

Figure 6.15: Evaluation of Viscosity (Pascal Second) of Econazole Nitrate Loaded Transferosomal Gel Formulations.

Table 6.8: Comparative Cumulative % In Vitro Drug Permeation Study of Econazole Nitrate Loaded Transferosomal Gel Formulation.

Time in(hrs)	Econazole Nitrate Containing Plain Gel	TFG-2	TFG-4	TFG-5
0.25	0	0	0	0
0.5	0	0	0	0
0.75	0	0	0	0
1	0.85±0.12	0.67±1.15	0.93±0.11	2.14±0.55
1.5	1.701±0.68	1.56±0.89	1.861±0.34	4.56±0.67
2	2.552±0.55	2.56±1.34	3.72±0.56	7.85±0.89
2.5	7.658±0.98	5.67±1.7	11.96±0.98	12.87±1.26
3	12.76±1.05	10.11±1.21	16.54±1.15	19.45±1.75
4	18.45±1.23	13.56±1.15	22.85±1.18	25.78±1.89
5	22.97±1.56	22.87±1.24	38.09±1.25	40.45±1.94
6	29.78±1.78	31.46±1.31	43.74±1.14	45.8±1.48
7	30.63±1.34	39.89±1.52	54.6±1.31	55.23±2.13
8	31.88±1.54	45.15±1.48	60.47±1.45	65.78±1.82
9	32.29±1.67	49.55±1.36	70.26±1.98	78.67±1.95
24	36.48±1.53	52.67±1.29	80.77±1.85	84.67±2.35

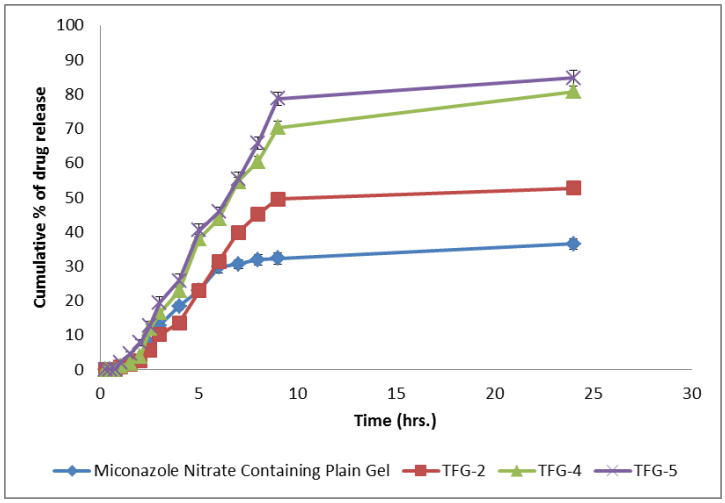

Figure 6.16: Comparative Cumulative % *In vitro* Drug Permeation Study of Econazole Nitrate Loaded Transferosomal Gel Formulation.

Table 6.9: Kinetic Modelling fitting Econazole Nitrate Loaded Transferosome Gel Formulations (TFG-2&TFG-5)

Formulation Code	Model	Kinetic Parameter Value	
	Zero order	y = 7.8672x - 6.5327	R^2 = 0.9302
	First order	y = 20.475x - 17.557	R^2 = 0.8214
TFG-4	Higuchi	y = -0.0413x + 2.0364	R^2 = 0.9036
	Korsemeyer-peppas	y = 0.7577x + 1.0869	R^2 = 0.9974
	Zero order	y = 8.4438x - 5.9999	R^2 = 0.9643
TFG-5	First order	y = -0.0452x + 2.0353	R^2 = 0.9369

	Higuchi	y = 22.27x - 18.223	R^2 = 0.8744
	Korsemeyer-peppas	y = 0.7618x + 1.0746	R^2 = 0.9915

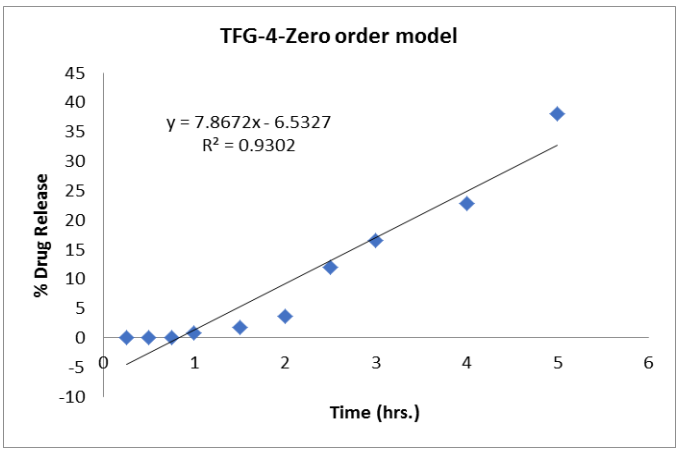

Figure 6.17: Kinetic Model Fitting of Econazole Nitrate Loaded Transferosome Gel Formulations (TFG-4) Zero Order.

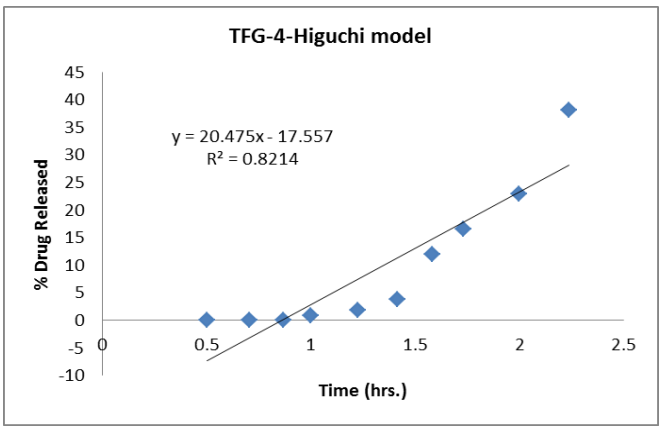

Figure 6.18: Kinetic Model Fitting of Econazole Nitrate Loaded Transferosome Gel Formulations (TFG-4) -First Order

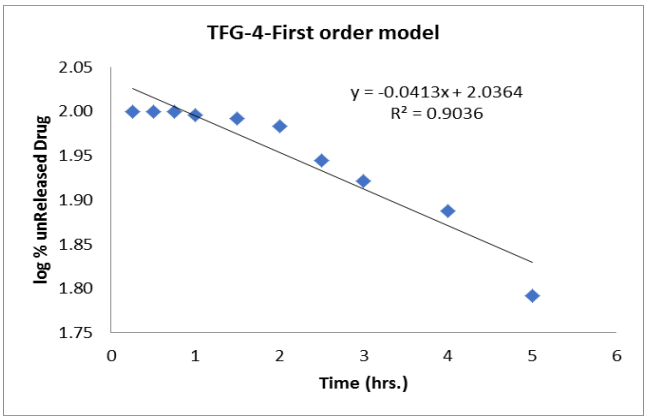

Figure 6.19: Kinetic Model Fitting of Econazole Nitrate Loaded Transferosome Gel Formulations (TFG-4) –Higuchi.

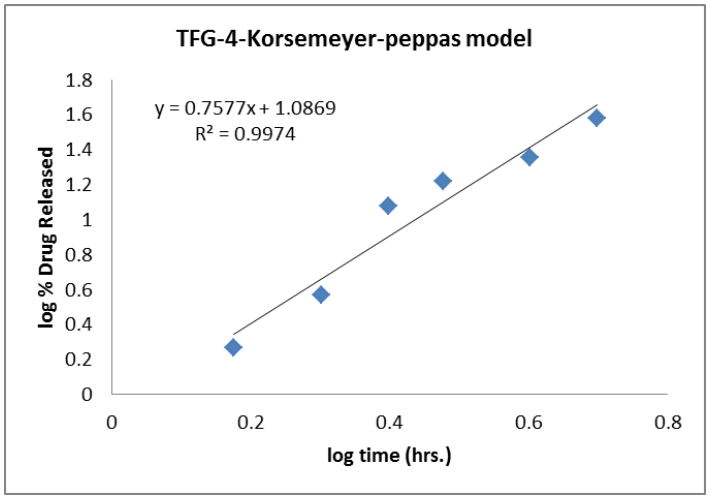

Figure 6.20: Econazole Nitrate Loaded Transfersome Gel Formulations (TFG-4) - Korsemeyer-Peppas.

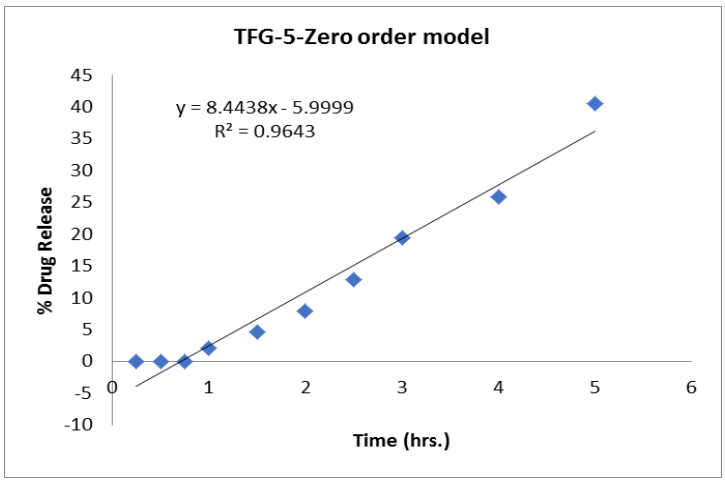

Figure 6.21: Kinetic Model Fitting of Econazole Nitrate Loaded Transferosome Gel Formulations (TFG-5) Zero Order.

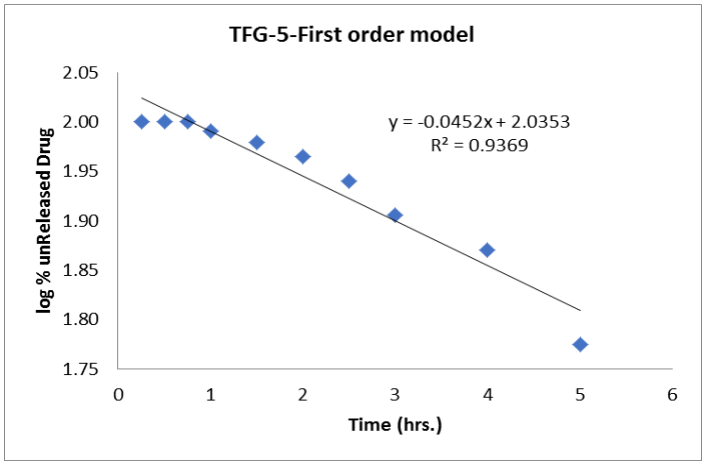

Figure 6.22: Kinetic Model Fitting of Econazole Nitrate Loaded Transferosome Gel Formulations (TFG-5) -First Order.

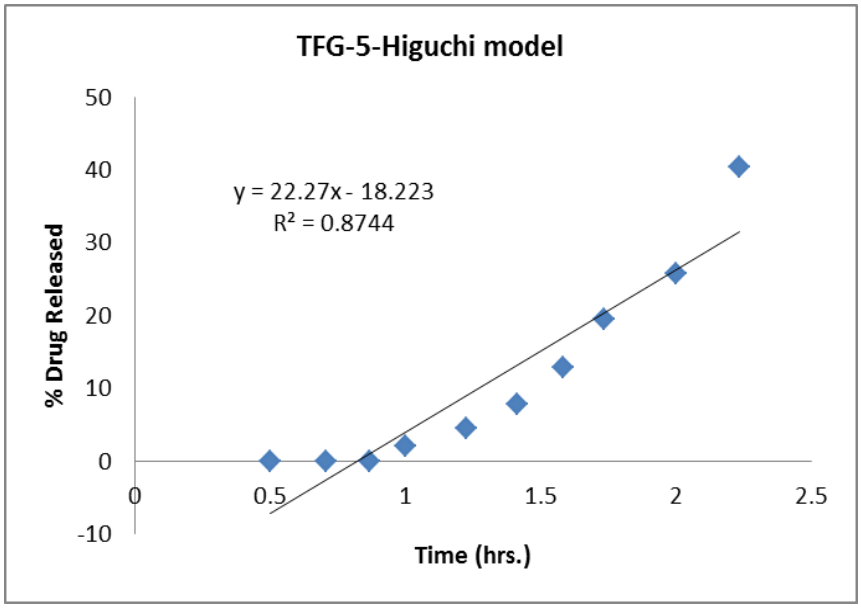

Figure 6.23: Kinetic Model Fitting of Econazole Nitrate Loaded Transferosome Gel Formulations (TFG-5) –Higuchi.

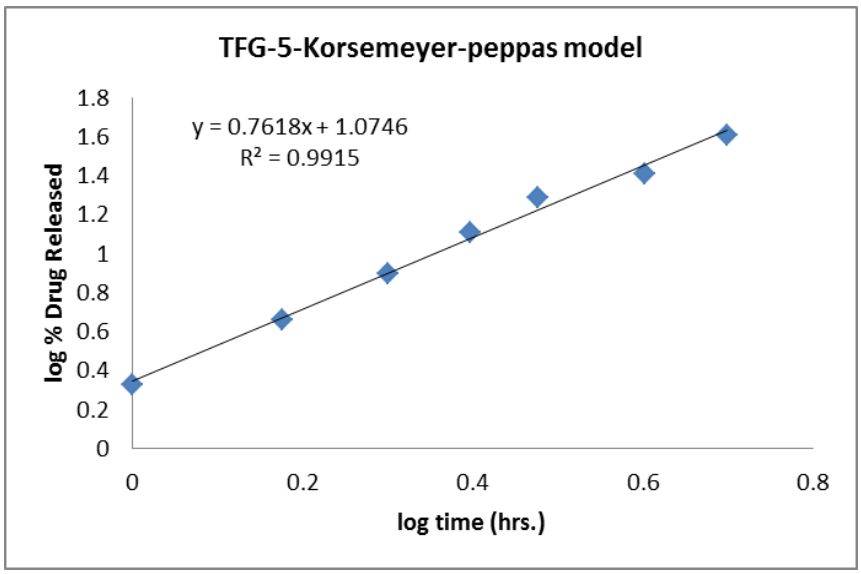

Figure 6.24: Econazole Nitrate Loaded Transferosome Gel Formulations (TFG-5) - Korsemeyer-Peppas.

Table 6.10: Stability Study of Econazole Nitrate Loaded Transferosome Gel Formulations (TFG-4 & TFG-5).

Time	Stability Condition/ Parameters					
	4°C± 2°C		25°C± 2°C		40°C± 2°C	
1.	Appearance					
	TFG-4	TFG-5	TFG-4	TFG-5	TFG-4	TFG-5
Initial	Off-white	Off-white	Off-white	Off-white	Off-white	Off-white
30 Days	Off-white	Off-white	Off-white	Off-white	Off-white	Off-white

60 Days	Off-white	Off-white	Off-white	Off-white	Off-white	Off-white
90 Days	Off-white	Off-white	Off-white	Off-white	Off-white	Off-white
2.	**Ph**					
	TFG-4	**TFG-5**	**TFG-4**	**TFG-5**	**TFG-4**	**TFG-5**
Initial	6.76	5.26	6.76	5.26	6.76	5.26
30 Days	6.67	5.20	6.55	5.13	6.42	5.10
60 Days	6.62	5.15	6.45	5.09	6.35	5.04
90 Days	6.58	5.10	5.82	5.07	5.29	4.95
3.	**Viscosity(Pascal Second)**					
	TFG-4	**TFG-5**	**TFG-4**	**TFG-5**	**TFG-4**	**TFG-5**
Initial	20.68	17.85	20.68	17.85	20.68	17.85
30 Days	20.62	17.84	20.59	17.79	20.65	17.71
60 Days	20.60	17.80	20.55	17.72	20.62	17.68
90 Days	20.55	17.75	20.48	17.70	20.59	17.65
4.	**% Drug Content**					
	TFG-4	**TFG-5**	**TFG-4**	**TFG-5**	**TFG-4**	**TFG-5**
Initial	98.56	98.47	98.56	98.47	98.56	98.47
30 Days	98.52	98.42	97.50	96.16	96.77	95.05
60 Days	98.55	98.40	96.46	95.32	95.23	93.16
90 Days	98.50	98.38	95.41	94.29	93.14	91.68
5.	**% Drug Release (After 9 hr.)**					
	TFG-4	**TFG-5**	**TFG-4**	**TFG-5**	**TFG-4**	**TFG-5**
Initial	70.26	78.67	70.26	78.67	70.26	78.67
30 Days	70.12	78.62	70.10	77.95	69.65	77.12
60 Days	70.05	78.55	68.91	74.28	67.18	75.92
90 Days	69.15	78.46	67.86	73.53	65.25	72.89

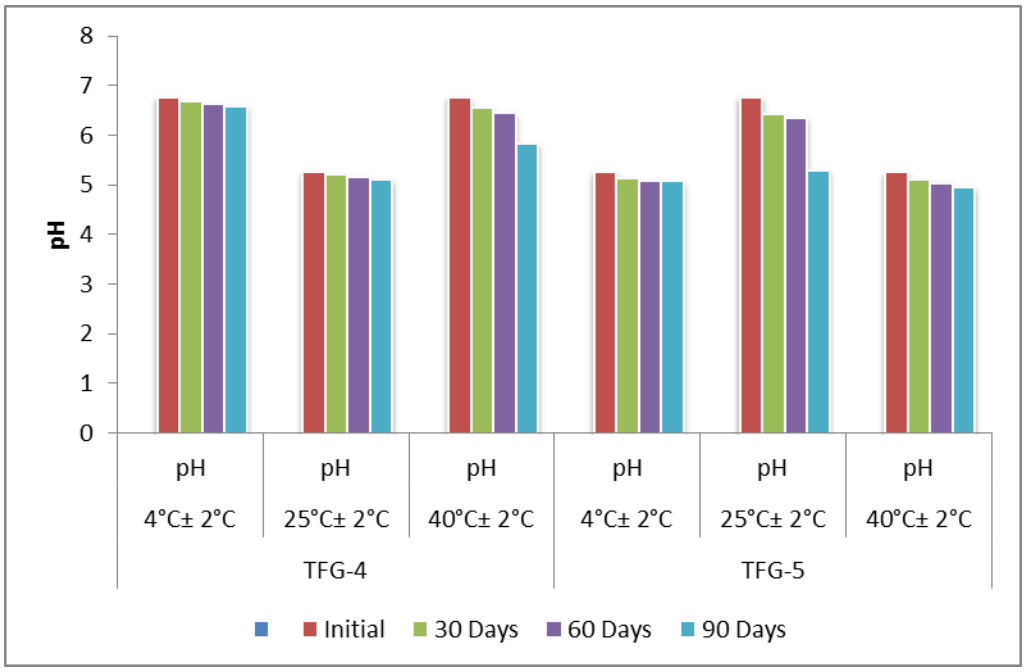

Figure 6.25: Stability Study (pH) of Econazole Nitrate Loaded Transferosome Gel Formulations (TFG-4 & TFG-5).

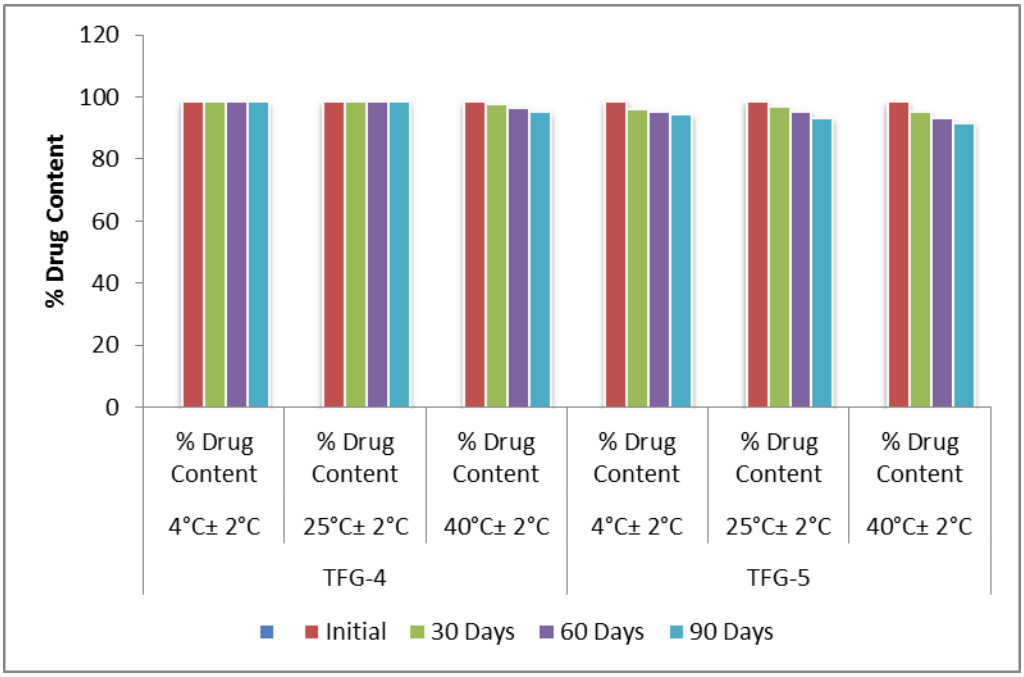

Figure 6.26: Stability Study (% Drug Content) of Econazole Nitrate Loaded Transferosome Gel Formulations (TFG-4 & TFG-5).

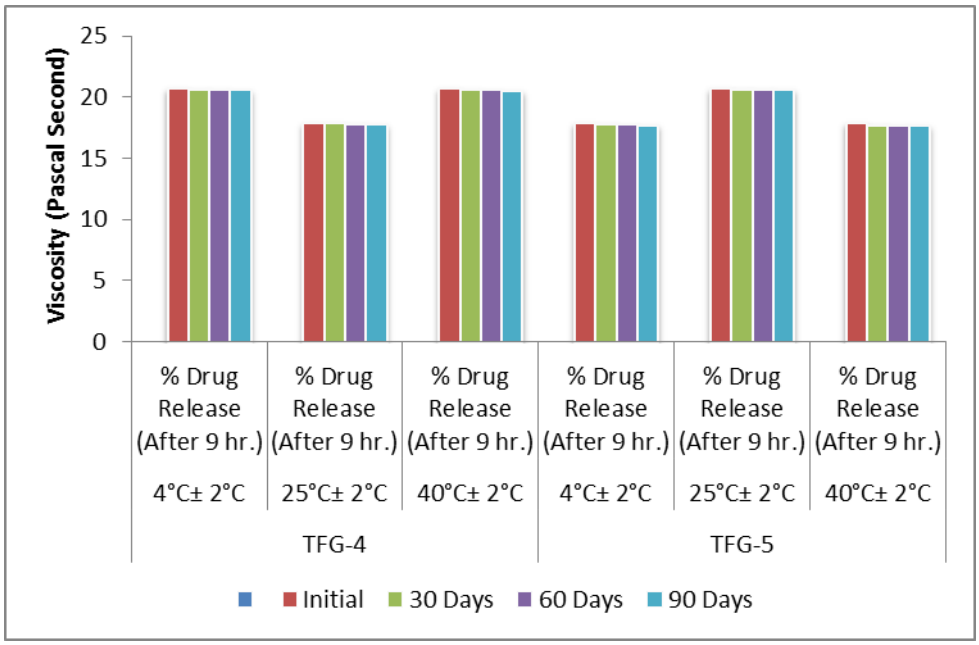

Figure 6.27: Stability Study (Viscosity) of Econazole Nitrate Loaded Transferosome Gel Formulations (TFG-4 & TFG-5).

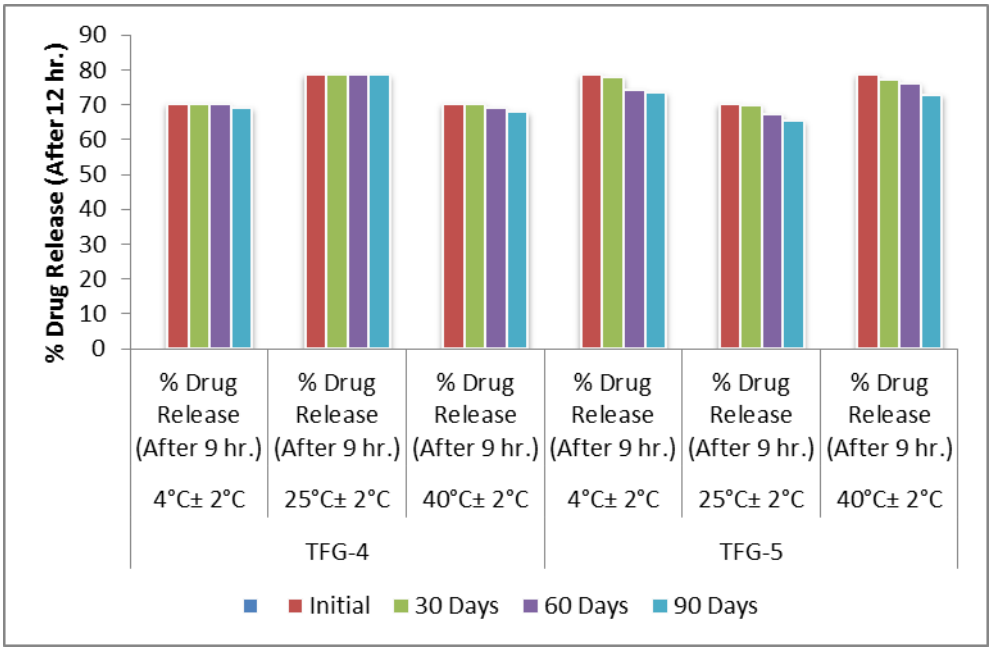

Figure 6.28: Stability Study (% Drug Release after 9 hr.) of Econazole Nitrate Loaded Transferosome Gel Formulations (TFG-4 & TFG-5).

CONCLUSION

This study aimed to formulate and evaluate econazole-loaded transferosomal gel for enhanced antifungal therapy. Preformulation studies confirmed drug purity and solubility. Transferosomes were prepared with sizes ranging from 154.8 nm to 188.5 nm, with good entrapment efficiency (61.84% to 79.87%). The optimized formula F4 exhibited good release and permeation properties. Gel formulations showed good viscosity and drug content. The transferosomal gel demonstrated a significant increase in drug permeation compared to plain gel. Kinetic analysis indicated a delayed drug release behavior. Stability studies showed refrigeration improved vesicle stability. Overall, transferosomal gel with econazole can enhance drug permeation through the skin, making it a promising approach for topical antifungal therapy.

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