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FORMULATION AND EVALUATION OF ECONAZOLE TRANSFEROSOMAL GEL

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Abstract

The aim of the present research work is to formulate a transfersomal gel of Econazole for deeper penetration into skin via topical route. Optimization of transfersomes and their characterization for different parameters are performed. The optimized preparation is evaluated for in vitro efficacy. The selected research work was divided into three phases. The first phase comprised of selection of drugs and excipients, Preformulation studies, preparation, optimization and in vitro characterization of selected carriers, nanovesicular transfersome. Drugs selected were Econazole and nanovesicular carriers selected. In the second phase of work, preparation and characterization of transfersomal gel formulation containing selected novel carrier was carried out. In third phase, prepared delivery system was evaluated for in vitro studies to ensure the behavior of delivery system. The entrapment efficiency percent of deformable vesicles was detected to be in the range of 61.84 %±3.15 % to 79.87 %±2.35 %. The formula F4 showed the highest percent encapsulation entrapment (79.87 %±2.35 %), small particle size (179.5 nm), and good release pattern. Accordingly, the formula F4 was used to be incorporated to formulate gel. Use of certain skin permeation enhancers with transferosomal Econazole gel is available and potentiates the permeation of the drug. This technique can serve as a potential tool for delivery of various topical drugs without altering the skin structure.

Keywords: Econazole; Transfersomes; Nanovesicular; Preformulation; Particle size

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. 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. These advancements have led to the development of several novel drug delivery systems that could revolutionalise the method of medication and provides a number of therapeutic benefits. Novel drug delivery system can be broadly divided into two classes

1. Sustained release drug delivery system.
2. Controlled release drug delivery system.

Sustained Release Drug Delivery System

Sustained release drug delivery system is described as a pharmaceutical form formulated to retard the release of a therapeutic agent such that its appearance in the systemic circulation is delayed and/or prolonged and its plasma profile is sustained in duration. The onset of its pharmacological action

is often delayed and the duration of its therapeutic effect is sustained (e.g. coated granules).

Controlled Release Drug Delivery System

Controlled release drug delivery system has a meaning that goes beyond the scope of sustained drug release. It implies a predictability and reproducibility in the drug release kinetics. The release of drug ingredients from a controlled release drug delivery system proceeds at a rate profile that is not only predictable kinetically but also reproducible from one unit to another. Controlled release drug delivery system can be classified into four categories:

1. Rate-Preprogrammed drug delivery system.
2. Activation-Modulated drug delivery system.
3. Feedback-Regulated drug delivery system.
4. Site-Targeting drug delivery system.

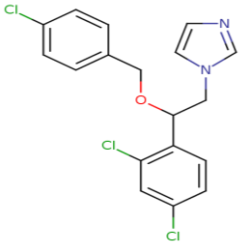
Rate-Preprogrammed Drug Delivery System

In this system, the release of drug molecules from the drug delivery system has been preprogrammed at specific rate profiles. This was achieved by system designing which controls the molecular diffusion of drug molecules in and/or across the barrier medium with in or surrounding the delivery system. (e.g.) implants, transdermal system3.

MATERIAL & METHODS

DRUG PROFILE

Selected Drug: Econazole



Molecular Formula: C18H15Cl3N2O
Molecular Weight: 381.7 g/mol
Chemical name: 1-[2-[(4-chlorophenyl) methoxy]-2-(2, 4-dichlorophenyl) ethyl] imidazole

Preformulaion 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. These studies are designed to determine the compatibility of initial excipients with the active substance for a biopharmaceutical, physicochemical and analytical investigation in support of promising experimental formulations.

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 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-octanolwas 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 standard calibration curve of Econazole Nitrate in PBS 7.4 pH Buffer

From the above Econazole Nitrate standard stock solution (1000µg/ml), 1ml solution was diluted to 10 ml using PBS pH 6.8solution to get concentrations of 100 µg/ml. from this solution, aliquots of, 0.5 ml, 1 ml, 1.5 ml, and so on from standard drug solution were diluted to 10 ml to prepare 10-50 µg/ml dilutions. The absorbance of these solutions was measured against PBS pH 7.4 as a blank.

Drug – Excipient Interaction Studies by FTIR

Infra-red spectra matching approach was used for the detection of any possible chemical reaction between the drug and the excipients. A physical mixture (1:1) of drug and excipients was prepared and mixed with suitable quantity of potassium bromide. About 100 mg of this mixture was compressed to form a transparent pellet using a hydraulic press at 10 tones pressure. It was scanned from 4000 to 150 cm^{-1} in a Bruker FTIR spectrophotometer. The FTIR spectrum of the physical mixture was compared with those of pure drug and excipients and matching was done to detect any appearance or disappearance of peaks.

Preparation of Econazole Nitrate Loaded Transfersomal Formulations

Transfersomes 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.

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 transfersomes 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 transfersomes 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.

Table 2: Composition of Transfersomal Formulations

Formulation code	Econazole Nitrate	Cholesterol	Lecithin	Na. 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 Transfersomal Formulations

Morphological Study

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

Particle size analysis

The vesicle sizes of trandferosome 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 Transfersomal dispersion was determined using Malvern instruments.

Entrapment efficiency

The percentage of Econazole Nitrate loading in transfersome was determined by using 4.0 mL of dispersion. Free Econazole Nitrate was separated from the transferosomal dispersions by subjecting the transfersomes 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 re dispersed in 4 mL of isotonic phosphate buffer (pH 7). To perform the lysis of transfersomes 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.

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

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.

Formulation of Trandferosome 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 3: Composition of Transfersomal 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 Transfersomal Gel

Physical appearance

The prepared gel was examined for clarity, color, 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.

RESULTS & DISCUSSION

Physical Appearance

The drug was obtained as a kind gift from GSK Pharmaceuticals Ltd,. The supplied powder of Econazole Nitrate was white, odour less White to yellowish white powder.

Melting Point

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

Table 4: 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 5: Partition coefficient value of Econazole Nitrate

S. No.	Solvent system	Partition Coefficient
1.	n-Octanol/PBS (pH 6.8)	5.45

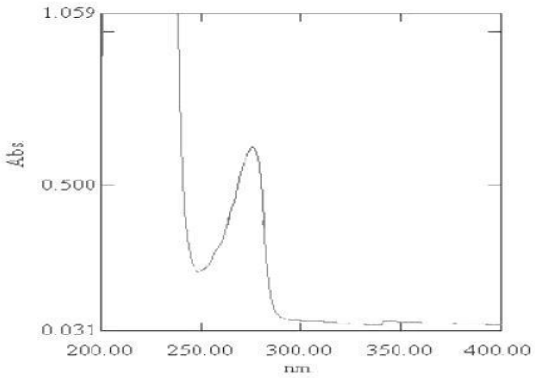


Fig. 1: UV spectra of Econazole Nitrate in PBS Buffer

Infrared Spectroscopy

It was done by making pellets of the drug in KBr. FTIR spectra was taken at Thermo Instrument. The observed peaks were compared with those (Florey, 1973) reported for functional groups.

Table 6: Important band frequencies in FTIR spectrum of Econazole Nitrate

S. No.	Named Group	Reported Band frequency	Band frequency obtained
1.	Imidazole C-N stretching	3140-1475	1409
2.	Aromatic C-H stretching	3000-3100	3107
3.	Aliphatic C-H stretching	2850-3000	2962
4.	C=C aromatic	1450-1590	1587
5.	C-Cl halogen attached at benzene ring	650-800	754
6.	Ether C-O-C stretch ether	1050-1250	1089

ISSN: xxxx-xxxx
Gupta et al., 1(2): 37-47, Dec. 2020

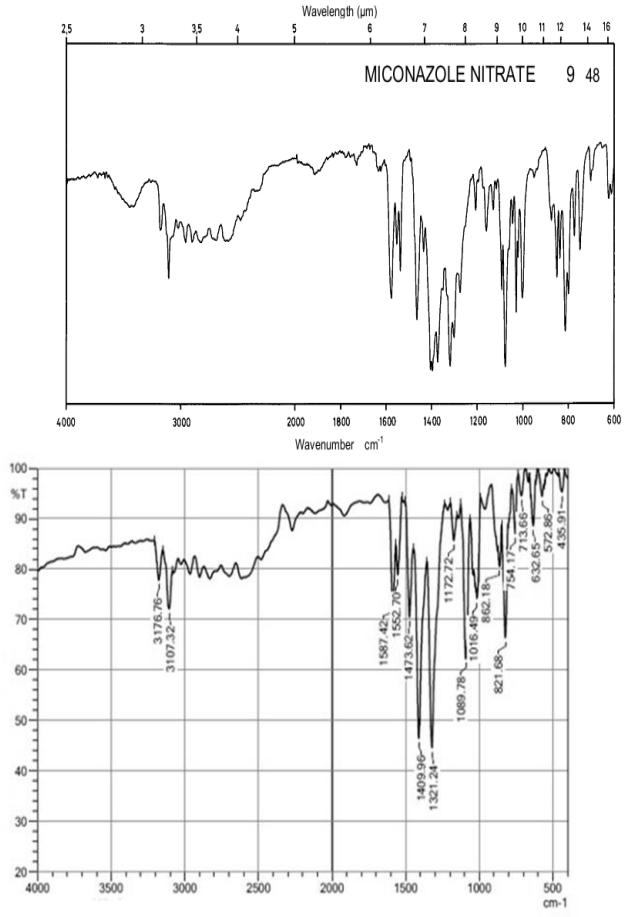


Figure 2: Reference FTIR spectra of Econazole Nitrate & FTIR spectra of Econazole Nitrate

Standard Curve of Econazole Nitrate in Phosphate Buffer Solution (pH 6.8)

All dilutions and measurements were made as above in phosphate buffer solution of pH 6.8 made as per formula (I.P.). The absorbance was taken at λ_{max} 265.6 nm against a reagent blank. The standard curve was plotted between absorbance and concentration.

Table 7: Standard Curve of Econazole Nitrate in Phosphate Buffer Solution (pH 6.8)

S. No.	Drug Conc. (µg/ml)	Absorbance at 272.2 nm
1.	10	0.141
2.	20	0.285
3.	30	0.429
4.	40	0.534
5.	50	0.653

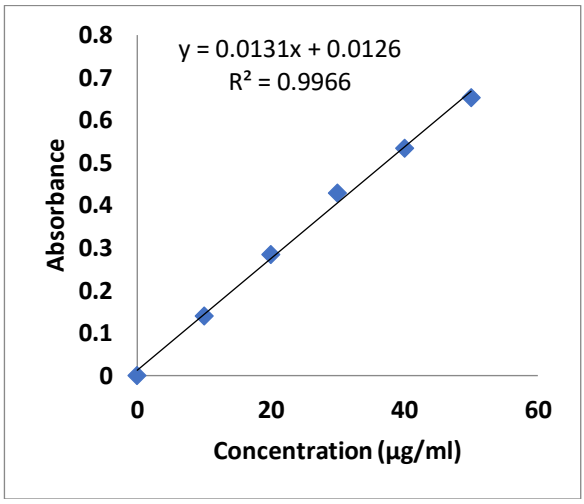


Figure 3: standard curve of Econazole Nitrate in phosphate buffer solution (pH 6.8) at 272.2 nm

Table 8: Evaluation of Econazole Nitrate LoadedTransfersomal 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±1.4	64.93±4.65

ISSN: xxxx-xxxx
Gupta et al., 1(2): 37-47, Dec. 2020

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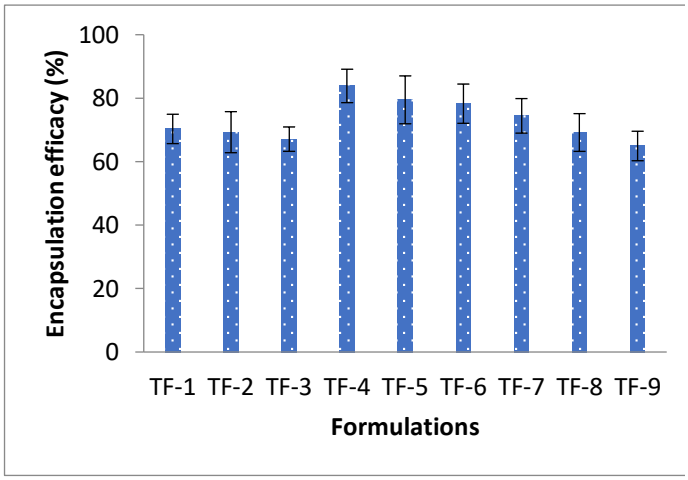
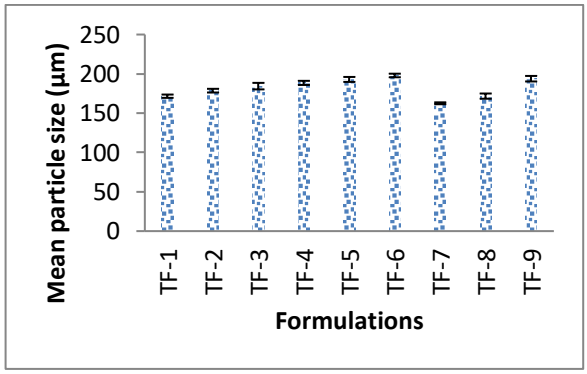


Fig. 4: Entrapment Efficiency of Econazole Nitrate Loaded Transfersomal Formulation



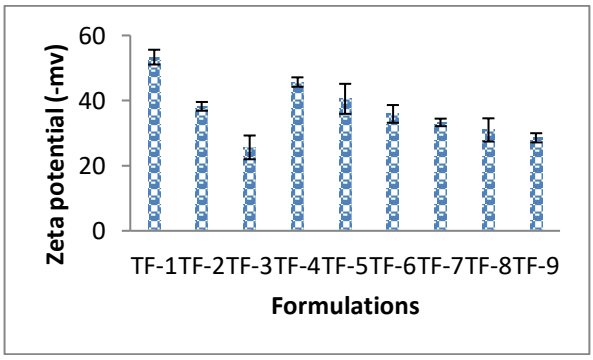
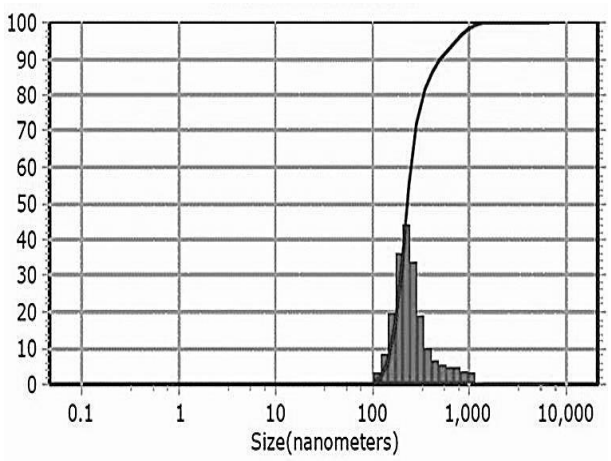


Fig. 5: Mean particle size (µm) & Zeta potential (-mv) of Econazole Nitrate Loaded Transfersomal Formulation



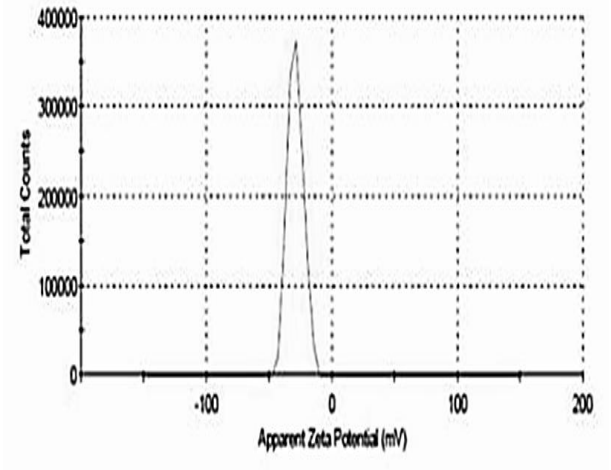
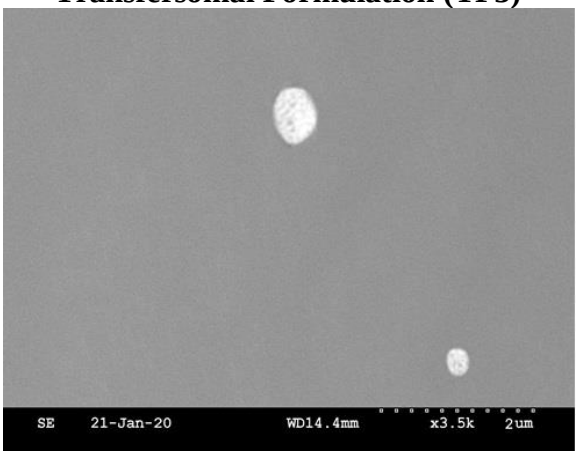


Figure 6: Particle Size Distribution & Zeta Potential of Econazole Nitrate Loaded Transfersomal Formulation (TF3)



ISSN: xxxx-xxxx
Gupta et al., 1(2): 37-47, Dec. 2020

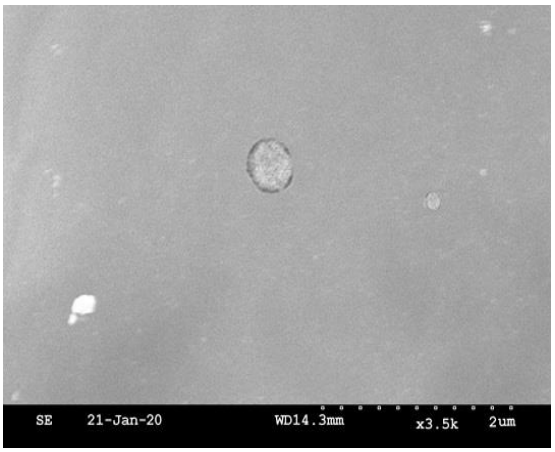


Figure 7: SEM Photograph of Econazole Nitrate Loaded Transfersomal Formulation (TF3 & TF4)

Table 9a: Cumulative % of Drug Release of Econazole Nitrate Loaded Transfersomal 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 9b: Cumulative % of Drug Release of Econazole Nitrate Loaded Transfersomal 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

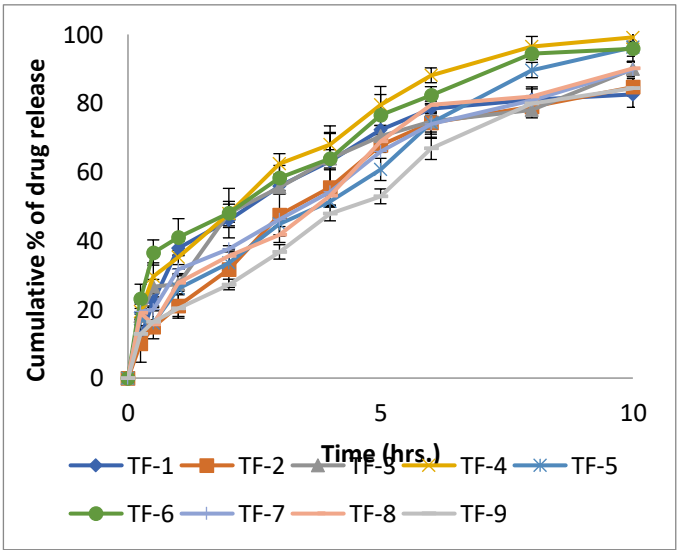


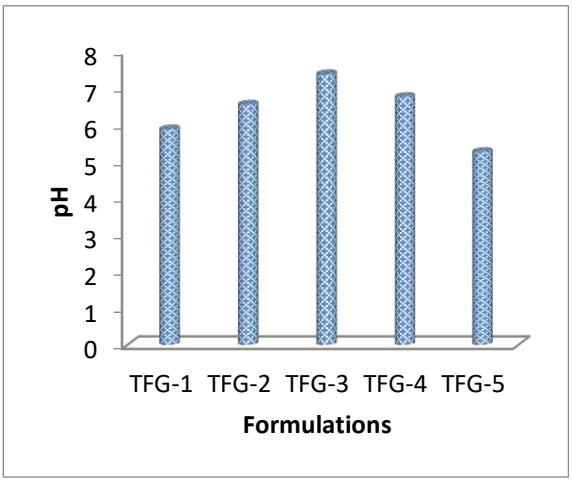
Figure 8: Cumulative % of Drug Release of Econazole Nitrate Loaded Transfersomal Formulation

Table 10: Evaluation of Econazole Nitrate Loaded TransfersomalGel Formulation

Formulatio	TF	TFG	TFG	TFG	TF

ISSN: xxxx-xxxx
Gupta et al., 1(2): 37-47, Dec. 2020

n Code	G-1	-2	-3	-4	G-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



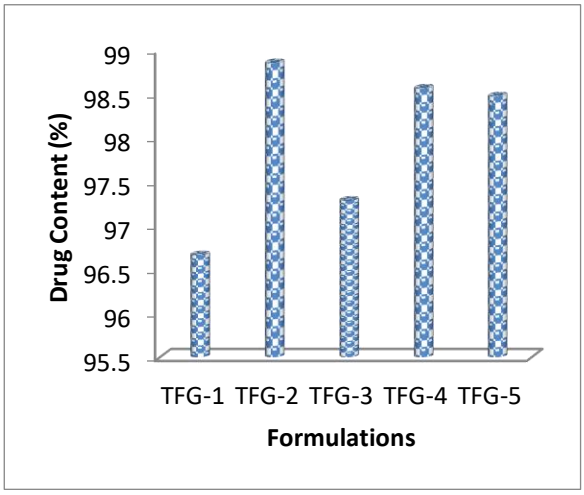


Fig. 9: Evaluation of pH & Drug Content (%) of Econazole Nitrate Loaded Transfersomal Gel Formulations

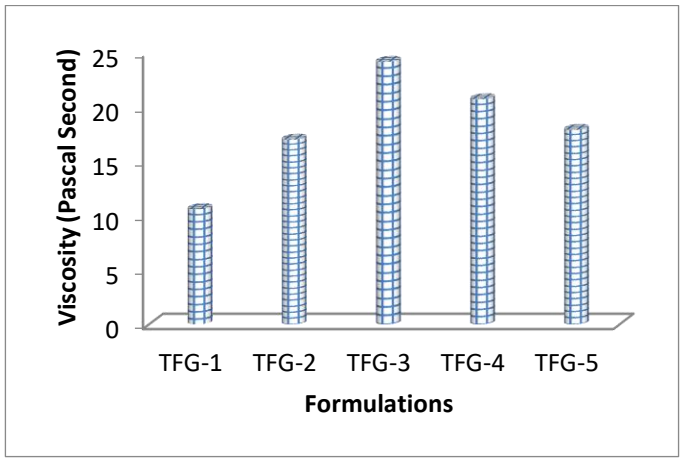


Figure 9: Evaluation of Viscosity (Pascal Second) of Econazole Nitrate Loaded Transfersomal Gel Formulations

Table 11: Comparative Cumulative % In Vitro Drug PermeationStudy of Econazole Nitrate Loaded Transfersomal 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

ISSN: xxxx-xxxx
Gupta et al., 1(2): 37-47, Dec. 2020

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

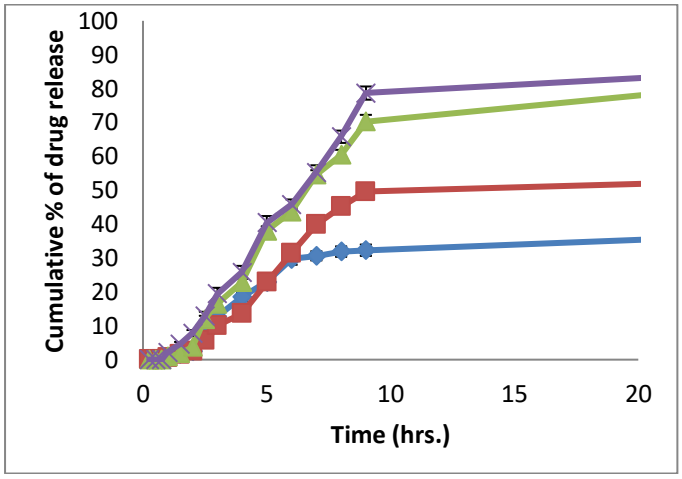


Figure 10: Comparative Cumulative % In Vitro Drug PermeationStudy of Econazole Nitrate Loaded Transfersomal Gel Formulation

Vesicular carriers that they prove to be very promising novel drug delivery units with respect to biocompatibility, reduced toxicity and enhanced sustained release quality that would be essential to address issues pertaining to compromised therapeutic efficacy of the bio-actives especially through topical route of administration. Vesicular formulations shows better therapeutic results as compared to conventional formulations and it has been expected that in upcoming years more vesicular formulations would find their place in therapeutic world. Transfersomes overcome the skin barrier by opening extracellular pathways between cells in the organ and then deforming to fit into such passages. In the process, transfersomes undergo a series of stress-dependant adjustments of the local carrier composition to minimize the resistance of motion through the otherwise confining channels. This process allows transfersomes to transport the drugs associated into and across the skin easily and very reproducibly. The aim of the present research work is to formulate a transfersomal gel of Econazole for deeper penetration into skin via topical route. Optimization of transfersomes and their characterization for different parameters are performed. The optimized preparation is evaluated for in vitro efficacy.

The selected research work was divided into three phases. The first phase comprised of selection of drugs and excipients, Preformulation studies, preparation, optimization and in vitro characterization of selected carriers, nanovesiculartransfersome. Drugs selected were Econazole and nanovesicular carriers selected. In the second phase of work, preparation and characterization of transfersomal gel formulation containing selected novel carrier was carried out. In third phase, prepared delivery system was evaluated for in vitro studies to ensure the behavior of delivery system. The whole study can be summarized under following points:

- Preformulation studies were done to evaluate the purity of drug by physical/morphological examination, melting point, partition coefficient, FTIR and λmax determination.
- Econazole drug was found to be white to Yellowish powder, odorless and tasteless.
- The melting point of Econazole was found to be 174.5°C.
- The solubility of Econazole was determined in various solvents. It was found that the Econazole were practically insoluble in the water and soluble in methanol, Dimethyl sulphoxide, phosphate buffer, ethanol, acetone and chloroform.
- The partition coefficient (Log P value) of Econazole was found to be 5.42 ±0.132. The λmax of drug were found to be 272.5 nm by UV-Spectroscopy.
- Data obtained from FTIR Spectrophotometric study clearly indicates in significant changes in spectra obtained from physical mixture of Econazole and excipients.
- All transferosomal formulations were found to be in the sub-micron to nanosize range. The formula F7 had the smallest size of 154.8 nm while the formula F6 had the largest size of 188.5 nm.
- The zeta potential values of the formulations were detected to be in the range of −50.8±4.16 mV to −27.2±4.18 mV.
- The entrapment efficiency percent of deformable vesicles was detected to be in the range of 61.84%±3.15% to 79.87%±2.35%. The formula F4 showed the highest percent encapsulation entrapment (79.87%±2.35%), small particle size (179.5 nm), and good release pattern. Accordingly, the formula F4 was used to be

incorporated to formulate gel.

- The scanning electron micrograph of examined transfersome (TF-4) represented the outline and the core of the spherical vesicles proving the vesicular characteristics of the prepared transfersome. The examined transfersome (TF-4) has vesicular shape with large internal aqueous core, with 200–150 nm in diameter.
- The formula TF4 showed significant high percent encapsulation entrapmentand good release pattern. More than 80% of the drug content of all the prepared vesicles was released after 6 hours.
- The optimized formulation of transferosomal suspension (F4) was to be incorporated into the prepared gel. PG and DMSO were used as skin permeation enhancers.
- All formulations had off-white appearance. The pH of the formulated gels of HPMC and different permeation enhancers was found between 5.26 and 7.38.
- The results of various pH values with different permeation enhancers revealed that all examined gels were compatible with skin. The gel prepared with DMSO as a permeation enhancer had pH of 5.26.
- All the examined gel samples exhibited good viscosity & drug Content (%) in the range of 10.56 - 20.68 and 97.28 -96.66 respectively
- The comparative permeation of Econazole from Econazole -containing plain gel, TFG-4 & TFG-5 formulations has also been shown, significant increase in the permeation.
- Significant decrease in entrapment efficiency was detected representing leakage of Econazole from different transfersomes. Decrease in entrapment efficiency may be ascribed to raise temperature that led to enhanced fluidity of lipid bilayer of vesicles.

CONCLUSION

Transfersomes are excellent drug carrier to permeate skin tissues. Embedding of transferosomal Econazole to gel improves permeation of the drug. Moreover, stability of transferosomal vesicles is improved when they are embedded into gel dosage form. Use of certain skin permeation enhancers with transferosomal Econazole gel is available and potentiates the permeation of the drug. This technique can serve as a potential tool for delivery of various topical drugs without altering the skin structure.

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