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Formulation and Characterization of Ketoconazole Transferosomal Gel for Effective Topical Fungal Treatment

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ABSTRACT

study focuses on the formulation and characterization of a ketoconazole-loaded transferosomal gel for effective topical management of fungal infections. Transferosomes, ultra-deformable vesicular carriers, were employed to enhance drug penetration through the skin and improve therapeutic efficacy. Ketoconazole transferosomes were prepared using the thin-film hydration method and optimized based on vesicle size, entrapment efficiency, and deformability. The optimized formulation was incorporated into a Carbopol-based gel and evaluated for physicochemical properties including pH, spreadability, viscosity, and drug content. In vitro drug release and ex vivo skin permeation studies demonstrated sustained and enhanced release compared to conventional formulations. Antifungal activity against *Candida albicans* confirmed improved efficacy of the transferosomal gel. Stability studies revealed good formulation stability under refrigerated conditions. Overall, the developed ketoconazole transferosomal gel presents a promising alternative to conventional topical preparations, offering improved skin penetration, sustained release, and enhanced antifungal activity for effective topical fungal treatment.

Keywords: Ketoconazole, Transferosomes, Topical gel, Fungal infection, Skin permeation, Antifungal activity.

INTRODUCTION

Infections caused by pathogenic fungi and limited to the human hair, nails, epidermis, and mucosa are referred to as superficial fungal infections. Despite the fact that these infections are rarely dangerous or life threatening, they are important because of their worldwide distribution, frequency, person-to-person transmission, and morbidity.[1]Dermatophytes are pathogens, which cause superficial fungal infection. The dermatophytes have the capacity to invade skin, hair and nails of humans and other animals to produce an infection. The dermatophytes have a saprophytic presence. They cause the surface infections through colonization individually of skin, hairs and nails in human beings known as ringworm, jock itch etc.[2] Most dermatophyte infections are not serious in healthy people, although some conditions are easier to treat than others. Infections in glabrous skin usually resolve within 2- 4 weeks with treatment. Common fungal agents are itraconazole, miconazole, ketoconazole and terbinafine[3-5].

Transferosomes[6-10]

Transferosomes represent an innovative approach in pharmaceutical research, particularly for topical drug

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delivery in fungal treatment. These advanced vesicular carriers are unique lipid-based structures composed of phospholipids and edge activators, which provide remarkable flexibility and penetration capabilities. Unlike traditional topical formulations, transferosomes can navigate through the skin's intricate barriers with exceptional ease, offering a promising solution for more effective antifungal treatments.

The structural composition of transferosomes is what makes them particularly remarkable. Typically ranging from 50 to 1000 nanometers in size, these microscopic vesicles are designed with an incredibly elastic membrane that allows them to pass through narrow intercellular spaces. This exceptional characteristic enables them to transport both hydrophilic and lipophilic antifungal agents directly to the site of infection, dramatically improving drug penetration and efficacy compared to conventional topical preparations.

MATERIALS AND METHOD

Materials

The seeds of Cassia tora were purchased from Nutriveda Xpotim Enterprises, Ketoconazole (Provided by SARACA Laboratories), HPMC K15, Carbopol 940, Propylene Glycol (Merck Limited), Triethanolamine, Isopropyl Alcohol, Soya phosphatidylcholine, Cholesterol (S.D. Fine Chem Ltd.), Dicetyl phosphate (DCP), Methanol (Merck Limited). All the chemicals and reagents used were of analytical grade.

Extraction and Isolation of Chrysophanic acid 9 anthrone from *Cassia tora seed.*

Seeds were washed with tap water; shade dried, powdered in a kitchen blender and was stored in an air tight plastic bag. Then powdered seeds passed through sieve # 10 was defatted by the whatman filter paper and introduced into the soxhlet apparatus using petroleum ether (60-80) as a solvent. After complete defatting, powder was air dried for removing trace of the petroleum ether then packed in whatman filter paper and introduced into the soxhlet apparatus and extract with benzene as a solvent for complete extraction. The extract was filtered, concentrated and dried in water bath. Dried extract was transferred into air tight bottles and the percentage yield was calculated and stored at cool place [11].

Preformulation Studies

Organoleptic properties

Take a small quantity of sample and spread it on the white paper and examine it visually for Color, odour, and texture.

Determination of Melting point

The melting point of Ketoconazole and Chrysophanic acid 9 anthrone was determined by capillary tube method according to the USP. A sufficient quantity of Ketoconazole powder was introduced into the capillary tube to give a compact column of 4-6 mm in height. The tube was introduced in electrical melting point apparatus and the temperature was raised. The melting point was recorded, which is the temperature at which the last solid particle of Ketoconazole in the tube passed into liquid phase.

Solubility Studies

Drug sample (10mg) was suspended separately in a 10 ml of different solvents at room temperature in tight closed test tube and shaken by wrist action. The samples were filtered through Whatman filter paper and diluted appropriately with same solvent and concentration was determined by UV- vis spectroscopy. For Chrysophanic acid 9 anthrone, the solubility test was based on the visualization of the presence or absence of drug extract precipitation in the oil phase. Approximately 5-10 mg of extract was weighed accurately and transferred in 5 different 10 ml volumetric flasks. Different solvents (water, ethanol, chloroform, methanol, ether, and acetone) were added to the flask respectively and solubility was determined.

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Determination of maximum absorbance (λ max) of Ketoconazole

A solution containing the concentration 10 µg/ml drug was prepared in 6.8 phosphate buffer and UV spectrum was taken using Lab India Double beam UV-vis spectrophotometer (Lab India UV 3000+). The solution was scanned in the range of 200 – 400 nm.

Construction of standard graph

100 mg of Ketoconazole was dissolved in 100 mL of pH 6.8 phosphate buffer to give a concentration in 1mg/mL (1000µg/mL), 1 ml was taken and diluted to 100 ml with pH 6.8 phosphate buffer to give a concentration of 0.01 mg/ml (10µg/ml). From this stock solution aliquots of 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml, 1 ml, were pipette out in 10 ml volumetric flask and volume was made up to the mark with pH 6.8 phosphate buffer to produce concentration of 2, 4, 6, 8 and 10 µg/ml respectively. The absorbance of each concentration was measured at respective λmax.

Determination of maximum absorbance (λ max) of Chrysophanic acid 9 anthrone

Organic molecules when exposed to light in UV region they absorb light of particular wavelength depending upon the type of electron transition associated with the absorption. The absorption maximum was determined by scanning the drug solution in suitable solvent with double beam ultraviolet spectrophotometer in the range of 300-400 nm.

Preparation of standard stock solution:

1 mg of extract was accurately weighed and dissolved in 10 ml of volumetric flask and dissolved in 10 ml of methanol to give a standard solution of 100µg/ml. 0.1 ml of solution was pipetted out from the stock solution and transferred into the 10 ml of volumetric flask. Absorbance was recorded by using UV-Visible spectrophotometer.

Procedure for standard calibration curve:

The standard solution were prepared by proper dilutions of the primary stock solution with methanol and phosphate buffer pH 6.8 to obtain working standard in the concentration range of 1-10µg/ml. the absorbance was measured at 320nm against a solvent blank and calibration curve was plotted. Similarly absorbance of sample solutions was measured and the amount of Chrysophanic acid 9 anthrone was determined.

Drug – excipient compatibility study: FTIR

The formulations were subjected to FTIR studies to find out the possible interaction between the drug and the excipients during the time of preparation. FTIR analysis of the pure drug and optimized formulation were carried out using an FT-IR spectrophotometer (Bruker FT-IR -Germany).

Formulation development Ketoconazole and *Cassia tora* seed extract loaded transferosomes- thin film hydration method[11]

Start by creating a thin film, this film is likely composed of phospholipids and a surfactant. The mixture of vesicles forming ingredients, that is phospholipids, surfactants and the drug and extract were dissolved in volatile organic solvent (chloroform + methanol). The organic solvent is then evaporated, this is typically done above the lipid transition temperature using a rotary evaporator, leaving behind a lipid film. Any remaining traces of the organic solvent were removed under vacuum conditions overnight. This step ensures that the final vesicle product is free from solvent residues. The deposited lipid films were hydrated with buffer (pH 6.8) by rotation at 60 rpm/min for 1hour at the corresponding temperature. The resulting vesicles were allowed to swell for 2 hours at room temperature. This swelling process helps the vesicles reach their optimal size and stability. To prepare small vesicles, the resulting LMVs were probe sonicated for 30 min at room temperature. The sonicated vesicles were homogenized by manually extruding them through a membrane filter. This step aids in achieving a uniform size and structure for the final vesicles.

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Table No. 2.1 Formulation of transferosomes.

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
Ketoconazole (%)	0.1	0.2	0.1	0.2	0.1	0.2	0.1	0.2
Soya phosphatidylcholine (mg)	20	40	60	80	20	40	60	80
Cholesterol (mg)	20	20	20	20	40	40	40	40
Tween-80 (mg)	30	30	30	30	60	60	60	60
Dicetyl phosphate (mg)	8	8	8	8	8	8	8	8
Extract (mL)	4	4	4	4	4	4	4	4
Methanol (mL)	5	5	5	5	5	5	5	5
Chloroform (mL)	10	10	10	10	10	10	10	10

Preparation of Transferosomal gel

Optimization of Transferosomal gel was done on the basis of concentration of Carbopol-940 (0.2% to 0.8%) as described in the table 6.2 Carbopol-940, a polymer, was dispersed in distilled water to form an aqueous dispersion. The dispersion was subjected to stirring until it exhibited increased viscosity, indicating thickening. Once complete dispersion was achieved, 10 ml of propylene glycol was slowly added to the Carbopol-940 dispersion, along with additional ingredients including 10 ml of isopropyl alcohol and 5 ml of triethanolamine. Furthermore, 10 ml of transfersomes dispersion was incorporated into the Carbopol gel with continuous stirring. To achieve a final volume of 100 g of gel, an appropriate quantity of distilled water was added.

Table No. 2.2 Formulation of transferosomal gel.

Ingredient	**F1 Concentration %**	**F2 Concentration%**	**F3 Concentration %**	**F4 Concentration %**
Transferosome (Drug + Extract)	1	1.5	2	1
Phospholipid	2	2.5	3	3.5
Cholesterol	1	1	1.5	1
Tween 80	0.5	1	1.5	0.5
Carbopol 934P	0.5	1	1.5	2
Triethanolamine	0.1	.25	0.35	0.45
Purified water	q.s.	q.s.	q.s.	q.s.

Characterization of Transferosomes

Particle Size and Zeta Potential[12]

Zeta sizer was used to measure the mean particle size and Zeta potential (ZP) of the transferosome. The mean particle size is an important parameter that governs the degree of permeation through the skin. The stability of the colloidal system in terms of particle size was evaluated based on Zeta Potential values and was established

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based on a Dynamic light scattering technique. For each formulation, three replicate analyses were performed, and data were presented as mean± S.D.

Polydispersity index[13]

PDI is a measure of heterogenicity of a sample based on size, polydispersity can occur because of agglomeration of sample. PDI can be obtained by Dynamic light scattering microscopy (DLS). PDI of less than 0.1 is considered as homogenous and ≥0.4 as heterogenous.

Entrapment efficiency[14]

The entrapment efficiency was determined by using direct method. Detergents are used to break the transferosome membranes 1 ml of 0.1% Triton X- 100(Triton X-100 dissolved in phosphate buffer) was added to 0.1 ml Transfersomes preparations and made up to 5 ml with phosphate buffer then it was incubated at 37oC for 1.5 hrs to complete breakup of the transfersome membrane and to release the entrapped material. The sample was filtered through a Millipore membrane filter (0.25) μm and the filtrate was measured at 240 nm for Mometasone furoate. The amount of Lamivudine was derived from the calibration curve.

The entrapment efficiency is expressed as:

% Entrapment efficiency = Amount of the drug entrapped/Total amount of the drug × 100.

Evaluation of Transferosomal Gel

Physical appearance

All prepared gel formulations have been observed for their visual appearance, such as transparency, colour, texture, grittiness, greasiness, stickiness, smoothness, stiffness, and tackiness. The prepared gels were also evaluated for the presence of any particles. Smears of gels were prepared on glass slide and observed under the microscope for the presence of any particle or grittiness.

pH of Formulation[15]

pH measurement of the gel was carried out by using a digital pH meter. pH of the topical gel formulation should be between 4-6 to treat the skin infections.

Determination of viscosity

Viscosity of the gels were determined by using Brookfield Viscometer (model- RVTP). Spindle type, RV-7 at 100 rpm.

Spreadability[16]

A modified apparatus suggested was used for determining spreadability. The spreadability was measured on the basis of slip and drag characteristics of the gels. The modified apparatus was fabricated and consisted of two glass slides, the lower one was fixed to a wooden plate and the upper one was attached by a hook to a balance. The spreadability was determined by using the formula:

s=ml/t,

where s, is spread ability, m is weight in the pan tied to upper slide and t is the time, l is the distance travelled. for the practical purpose the mass, length was kept constant and ‘t’ was determined.

Homogeneity[17]

All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container for their appearance and presence of any aggregate.

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Drug Content

Gel formulations (100 mg) was dissolved in suitable solvent and filtered and the volume was made. The resultant solution was suitably diluted with solvent and absorbance were measured at 240 nm using UV-Visible spectrophotometer. Drug content was determined from calibration curve.

In-vitro diffusion studies[18]

An In-vitro drug release study was performed using modified franz diffusion cell. Dialysis membrane (hi media, molecular weight 5000 Daltons) was placed between receptor and donor compartments. Transferosomal gel was placed in the donor compartment and the receptor compartment was filled with phosphate buffer, pH 6.8 (24 ml). The diffusion cells were maintained at 37±0.5°c with stirring at 50 rpm throughout the experiment. At different time intervals, 5 ml of aliquots were withdrawn from receiver compartment through side tube and analyzed for drug content by UV visible spectrophotometer and analyzed at 240 nm using phosphate buffer pH 6.8 as blank.

Stability Studies[19]

Stability studies have been carried to point out any physical visual or chemical stability of optimized batch at 25°C ± 2°C/ 60% RH ± 5% RH as per ICH guidelines for 3 months. Samples are taken out at various days 0th, 30th, 60th and 90th and checked their physical property and drug content.

***In Vitro* Anti-Fungal Activity[20]**

The *in vitro* antifungal activity was assayed through screening of *Aspergillus niger,* by disc diffusion technique on SDA growth medium at pH 6.8. In the study, dilutions of test samples were prepared at various increasing concentrations (25,50,75 and 100 µg/ml).These prepared concentrations were loaded into the well and incubated in inverted positions at 35 °C for 48 h. The size of the zone of inhibition is usually related to the level of antimicrobial activity present in the sample or product, and a larger zone of inhibition usually means that the antimicrobial formulation is more potent. For comparison, amphotericin was used as a standard (10µg/ml). Amphotericin B (Amp B) is one of the best antifungal drugs. It is nephrotoxic. Sample was analysed in triplicate. The test sample at 100 µg/ml concentration showed significant antimicrobial activity against *Aspergillus niger*. Observed results were in concentration dependent manner.

RESULTS AND DISCUSSION

Extraction from Cassia tora seeds:

The initial weight of the powder before extraction – 30 gm.

After defatting by petroleum ether (for 3 hours) weight of the powder was – 29.44 gm.

After defatting by benzene (for 2 hours) weight of the powder was – 27.8 gm.

Organoleptic properties

Table 3.1: Physical properties of Ketoconazole

Parameters	Remarks
General appearance	Crystalline powder
Colour	White to slightly beige-colored
Odour	Odorless crystalline powder

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Taste	Slightly bitter

Table: 3.2 Organoleptic and physical properties of Drug extract

Test	**Observation**
Colour	Brown Powder
Taste	Bitter and astringent
Odour	Characteristic

Solubility Studies

Table 3.3 Solubility of ketoconazole

S. No.	**Surfactant**	**Solubility**
1.	Water	Sparingly soluble
2.	Methanol	Sparingly soluble
3.	Ethanol	Slightly more soluble in ethanol than in methanol
4.	Chloroform	Insoluble

Table: 3.4 Solubility of Cassia tora seed extract

S.No	**Solvent**	**Solubility observed**
1.	Water	Practically insoluble
2.	Methanol	Sparingly soluble
3.	Petroleum ether	Slightly soluble
4.	Benzene	Very soluble

Melting point

Table: 3.5 Solubility of Cassia tora seed extract

Material	**Observation**
Chrysophanic acid 9 anthrone	195°C
ketoconazole	148°C

FTIR study

The FTIR study of drug and excipents mixture was studied and found to be no any other peaks. The results of FTIR peaks revealed that drug and excipents mixture was not show any interaction and suitable for the formulation and development. The FTIR spectra of ketoconazole, Chrysophanic acid 9 anthrone are shown in figure 3.1, 3.2 & 3.3.

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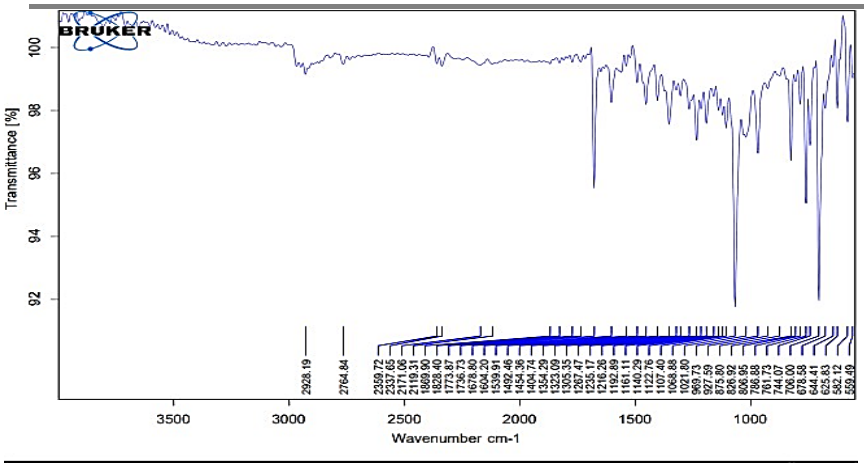

Fig no. 3.1 FTIR Spectra of Ketoconazole

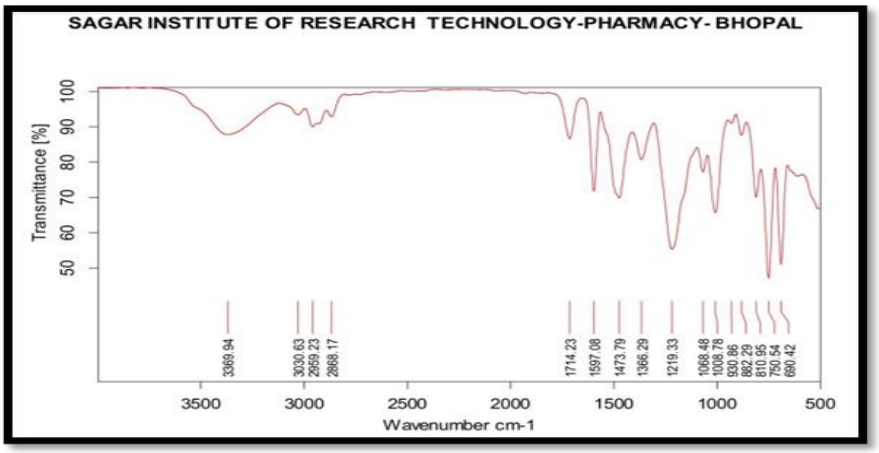

Fig.3.2 IR Spectrum of Chrysophanic acid 9- anthrone (Drug sample)

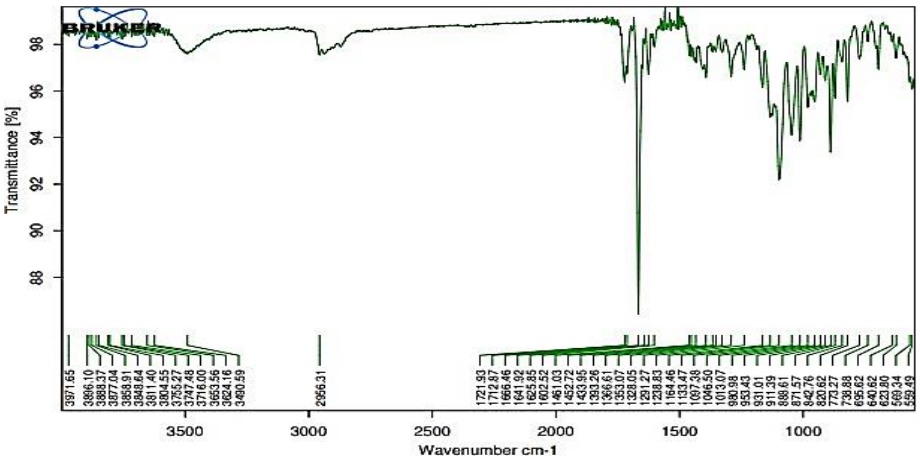

Fig.3.3: FTIR of Drug with Excipients

Determination of Absorbance Maxima of Ketoconazole and Chrysophanic acid 9 anthrone

UV-vis spectra of Mometasone Furoate were measured from 200 to 400 nm and the absorption spectrum was found to be sharp and maximum at wavelength of 240 nm.

After scanning drug solution under UV spectrophotometer it was found that Chrysophanic acid 9 anthrone shows maximum absorbance at 320 nm therefore max of Chrysophanic acid 9 anthrone was found to be 320 nm.

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Table: 3.6 Absorbance Maxima of Ketoconazole and Chrysophanic acid 9 anthrone

Material	**Lambda max**
Ketoconazole	240nm
Chrysophanic acid 9 anthrone	320 nm

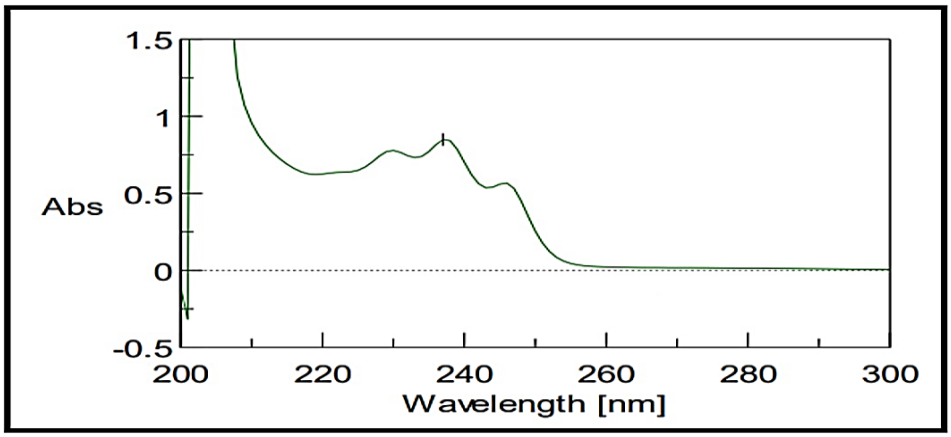

Fig.3.4: Lambda max of Ketoconazole

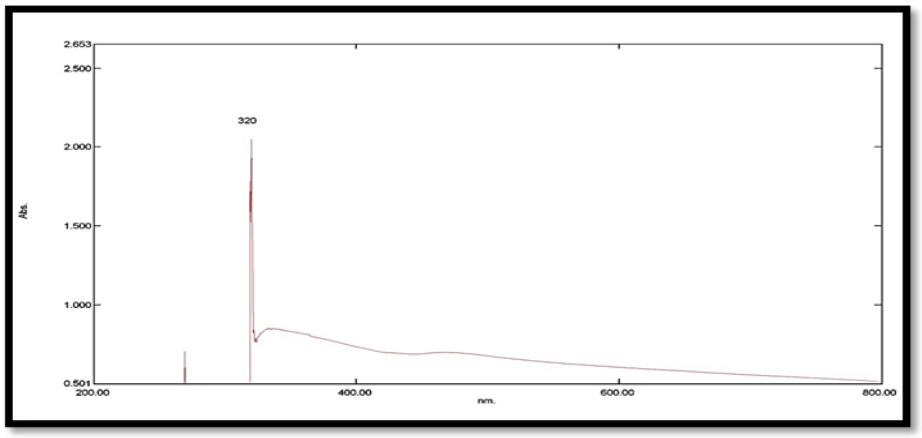

Fig 3.5 Lambda max of Chrysophanic acid 9- anthrone

Calibration curve of Ketoconazole

Table 3.6: Construction of Calibration curve:

Concentration (µg/ ml)	**Absorbance**
0	0
2	0.228±0.10
4	0.424±0.05
6	0.636±0.12
8	0.811±0.09
10	0.999±0.03

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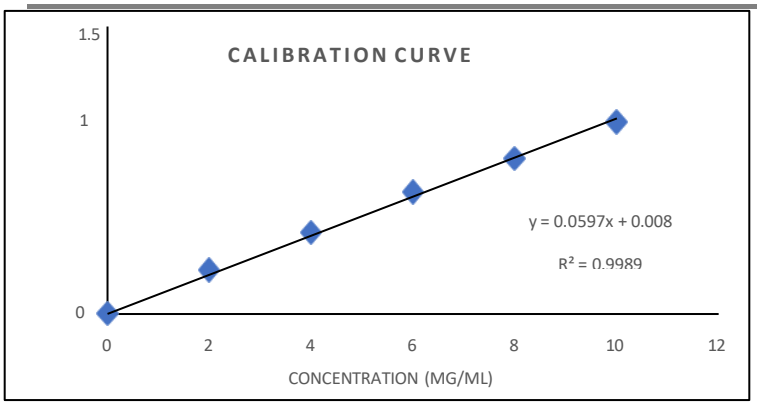

Fig 3.6 Standard calibration curve of Ketoconazole in methanol

Calibration curve of Chrysophanic acid 9 anthrone in methanol

Table 3.7 Calibration curve of Chrysophanic acid 9 anthrone in methanol

Concentration µg/ml	Absorbance nm
3	0.0099
6	0.0210
9	0.0310
12	0.0420
15	0.0520
18	0.0630

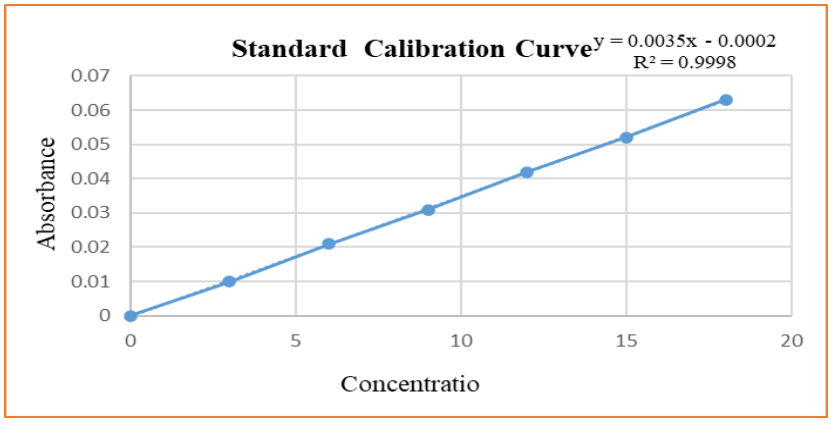

Fig. 3.7 Calibration curve of Chrysophanic acid 9 anthrone in methanol

Characterization of prepared Transferosomes:

Table 3.8: Particle size, PDI, Zeta potential and entrapment efficiency of all formulations

Formulation	Particle Size	PDI	Zeta Potential	Entrapment efficiency	Drug content
F1	171.57±2.10	0.503	-5.44	60.31±1.15	75.43±0.05
F2	162.61±2.35	0.378	-20.62	72.39±0.26	82.19±5.10

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F3	160.38±4.13	0.313	-12.93	79.05±3.02	87.76±1.26
F4	**152.48±2.61**	**0.252**	**-32.55**	**87.16±2.10**	**97.45±2.12**
F5	192.89±3.16	0.987	-18.21	59.22±1.24	66.31±1.41
F6	197.93±2.27	1.235	-10.46	61.79±5.87	78.14±0.25
F7	182.54±1.20	1.503	-16.67	75.63±2.11	88.01±3.40
F8	171.68±3.32	1.378	-15.10	85.48±1.30	91.35±2.09

SD±(n=3)

***IN-VITRO* Diffusion Studies:**

Table 7.9: *In-vitro* diffusion studies of F1-F8 Transferosomes formulations in percentage

Time (hour)	**CUMULATIVE PERCENT DRUG RELEASE**							
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
0	0	0	0	0	0	0	0	0
1	21.16±0.07	28.10±0.10	32.93±0.02	40.52±0.08	36.60±0.05	28.42±0.11	25.93±0.09	20.40±0.06
2	36.02±0.01	32.36±0.02	43.30±0.12	49.89±0.02	44.56±0.01	35.97±0.05	30.47±0.02	26.99±0.09
3	52.97±0.12	40.29±0.06	49.02±0.06	55.54±0.06	51.06±0.13	42.68±0.15	36.65±0.05	31.02±0.10
4	50.24±0.09	48.95±0.05	56.91±0.15	65.26±0.10	60.30±0.00	48.99±0.09	40.24±0.19	38.87±0.09
5	67.11±0.05	56.61±0.12	65.65±0.12	72.72±0.09	73.49±0.01	59.47±0.02	48.76±0.06	42.24±0.10
8	78.69±0.01	69.61±0.25	72.72±0.09	83.14±0.15	78.20±0.08	64.26±0.06	52.34±0.16	50.34±0.15
9	90.19±0.11	78.20±0.14	82.53±0.12	86.63±0.18	86.16±0.06	76.97±0.04	60.87±0.10	56.91±0.13
10		86.97±0.01	90.26±0.10	95.43±0.05	90.78±0.09	82.34±0.05	71.51±0.15	65.80±0.05
12		91.36±0.14	91.59±0.09	**97.14±0.10**	95.36±0.02	92.92±0.09	85.01±0.12	80.69±0.02

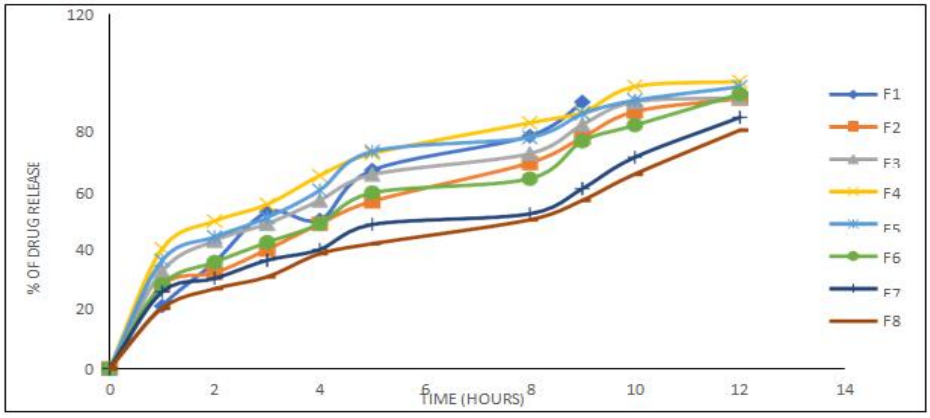

Figure 8: *In-vitro* diffusion studies of F1-F8 Transferosomes formulations in percentage

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Observation: The Transferosomes F4 showed a better release profile of **97.14%** by 12 hours. The prolonged release at 12 hours can be attributed to slow diffusion of drug from lipid matrix.

Characterization of Optimized Formulation

Table 3.10: Gel evaluation Parameters

Polymer	**Formulation**	**pH**	**Viscosity (centipoise)**	**Extrudability**	**Homogeneity**	**Drug Content**	**Skin Irritation test**
Carbopol-940	F4 optimized 0.5 %	6.5	52325	+	Satisfactory	93.29	No
	F4 optimized 1%	6.2	53425	+	Satisfactory	95.56	No
	F4 optimized 1.5%	5.9	54360	+	Satisfactory	96.06	No
	F4 optimized 2%	5.8	**55417**	++	**Excellent**	98.90	No

Table 3.11: Physical evaluation of Transferosomal gel

Polymer	**Formulation**	**Colour**	**Spreadability (g.cm/sec)**
Carbopol-940	F4 optimized 0.5 %	White to off white	0.456±0.01
	F4 optimized 1%	White to off white	0.320±0.12
	F4 optimized 1.5%	White to off white	0.258±0.09
	F4 optimized 2%	**White to off white**	**0.229±0.01**

***In-vitro* diffusion studies:**

Table 3.12: *In-vitro* diffusion studies of Transferosomal gel

Polymer	**Carbopol-940**			
Time	**F4**	**F4**	**F4**	**F4**
(hrs)	**optimized**	**optimized**	**optimized**	**optimized**
	0.5 %	**1%**	**1.5%**	**2%**
0	0	0	0	0
1	40.62±0.01	34.89±0.09	35.96±0.11	30.99±0.04
2	45.10±0.05	40.92±0.02	41.60±0.08	38.06±0.13
4	71.91±0.09	46.06±0.05	48.14±0.05	45.36±0.00
5	76.82±0.13	53.86±0.04	55.30±0.02	56.12±0.05
6	80.86±0.10	69.11±0.03	70.82±0.09	60.79±0.02

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8	94.01±0.04	75.70±0.01	78.14±0.10	75.66±0.09
10		82.59±0.08	85.97±0.09	80.90±0.15
11		97.05±0.10	90.36±0.02	95.36±0.10
12			93.75±0.04	**98.22±0.12**

Stability Studies:

Table 3.13: Stability Study of F4 Transferosomal Gel

Formulation	**F4**			
Storage Condition	**25℃± 2℃/ 60 % RH ± 5 % RH**			
Time interval (days)	**0**	**30**	**60**	**90**
Colour	White to off white	White to off white	White to off white	White to off white
Homogeneity	+++	+++	+++	+++
pH	5.8	6.0	6.0	6.1
Viscosity (cP)	55417	54120	54012	52059
Spreadability (g.cm/sec)	0.229±0.01	0.226±0.05	0.225±0.02	0.224±0.06
Extrudability	++	++	++	++
Drug content uniformity (%)	98.90	98.82	98.72	98.60
+++ Excellent, ++ Good, + Satisfactory, - Poor, -- Fail				

DISCUSSION

There was not much more variation in the properties of transferosomal gel F4 under stability study as the formulation retained all the properties when stored at specified storage conditions over a while, indicating that the transferosomal gel was very much stable.

In-Vitro Antifungal activity

Table 3.14: *In-Vitro* Antifungal activity of Transferosomal gel

S. No.	**25ug/ml**	**50ug/ml**	**75ug/ml**	**100ug/ml**	**Amphotericin B (10µg/ml)**
1.	08.00	13.00	14.00	23.00	26.00
2.	09.00	13.00	14.50	23.00	
3.	09.00	11.00	17.00	20.00	
Mean	08.66±0.57	12.33±1.15	15.16±1.60	22.00±1.73	

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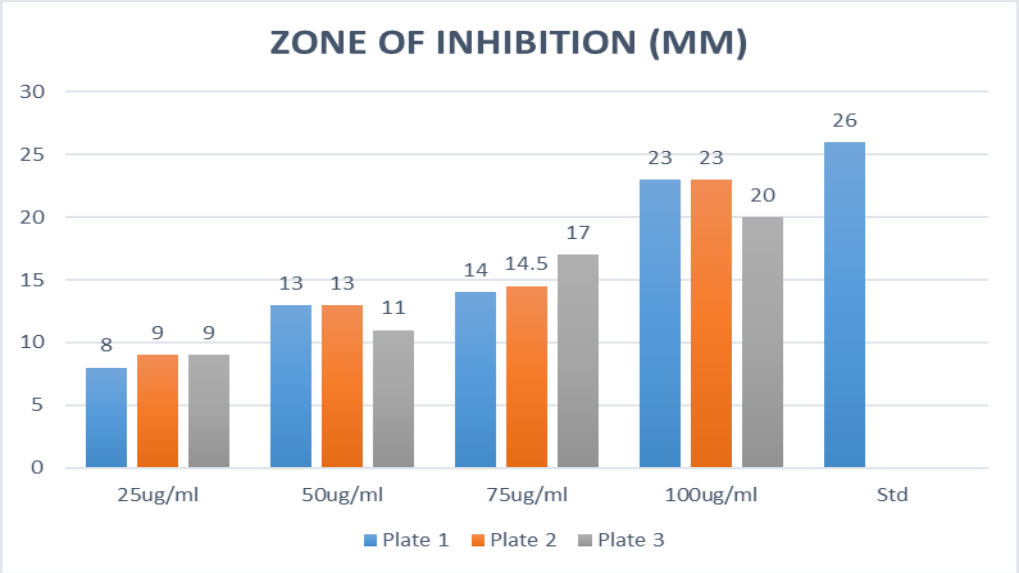

Fig 3.6 Zone of inhibition (mm) at various concentrations.

This study shows that Transferosomal gel had a potential source for inhibition of fungi and could be used as efficient drug with minimum side effects.

SUMMARY AND CONCLUSION

Summary: A transferosomal gel was formulated using ketoconazole and Cassia tora seed extract (Chrysophanic acid 9-anthrone). Extraction and characterization confirmed their purity, solubility, and compatibility with excipients. Among all formulations, F4 showed the best properties with smallest particle size (152.48 nm), highest entrapment efficiency (87.16%), and maximum drug release (97.14%) over 12 hours.

The optimized F4 was incorporated into Carbopol 940 gel, with the 2% gel showing the best spreadability, drug content (98.90%), and stability over 90 days. In-vitro antifungal testing confirmed strong activity with increasing concentrations.

Conclusion: The developed F4 transferosomal gel with 2% Carbopol 940 is stable, shows excellent drug release, and effective antifungal activity. It is a promising formulation for topical antifungal treatment with sustained release and minimal side effects.

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