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LIPOSPHERE-BASED FLUCONAZOLE GEL: AN EFFICIENT TOPICAL CARRIER FOR ANTIFUNGAL TREATMENT

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ABSTRACT

This study aimed to design and characterize fluconazole-loaded lipospheres to enhance the drug's solubility, skin permeation, and local bioavailability. Fluconazole**,** a third-generation triazole antifungal agent, is widely used in the treatment of systemic and superficial fungal infections. As a BCS Class II drug with low aqueous solubility and high permeability, its oral bioavailability remains limited. To overcome these drawbacks, fluconazole-loaded lipospheres were formulated for topical delivery using the melt-dispersion method. **Method and Results:** Preformulation studies included UV-spectrophotometric analysis, drug–excipient compatibility by FTIR, and solubility determination. The calibration curve of fluconazole was linear in the range of 10–100 µg/mL**.** FTIR spectra confirmed no significant interaction between drug and excipients. Lipospheres were prepared using stearic acid and compritol as core lipids and soya lecithin as a stabilizer. The prepared formulations were evaluated for particle size, entrapment efficiency, drug content, and in vitro release**.** Particle sizes ranged from 45 µm to 95.8 µm, entrapment efficiency from 51.7% to 89.5%**,** and drug content from 55.74% to 96.27%**.** Among the batches, formulations F2 and F5 exhibited optimal characteristics and were incorporated into a topical gel. The gel showed a pH of 5.75**,** viscosity of 3144 cP**,** spreadability of 11.33 g·cm²**,** and 96.21% drug release. **Conclusion:** The optimized liposphere-based gel demonstrated enhanced fluconazole release and favorable physicochemical properties compared to conventional formulations.

The findings suggest that lipospheres are a promising delivery system for improving the topical bioavailability and enhanced permeation of poorly water-soluble drugs like fluconazole.

KEYWORDS: Fluconazole, lipospheres, topical delivery, antifungal, melt dispersion, sustained release.

1. INTRODUCTION

Fungal infections are a growing public health concern due to their increasing prevalence and the emergence of antifungal resistance. Fluconazole, a triazole antifungal agent, is widely used to treat both superficial and systemic fungal infections. It acts by inhibiting lanosterol 14-α-demethylase, disrupting ergosterol synthesis and compromising fungal cell membrane integrity. However, conventional fluconazole formulations often exhibit poor skin penetration, limited residence time, and systemic side effects, underscoring the need for improved topical delivery systems.

Liposphere technology offers a promising lipid-based approach to enhance drug stability, biocompatibility, and controlled release. Lipospheres consist of a solid lipid core stabilized by phospholipids, capable of entrapping both hydrophilic and lipophilic drugs while improving skin permeation and sustaining drug release.

The present study focuses on the development and characterization of fluconazole-loaded lipospheres using stearic acid and soya lecithin. The formulations were optimized by varying lipid ratio, concentration of drug, volume of aqueous phase and sonication time, and evaluated for particle size, entrapment efficiency, drug content, in vitro release, and stability, to establish lipospheres as an effective carrier for topical antifungal therapy.[1]

2. MATERIAL AND METHODOLOGY

2.1 Material

The formulation of Fluconazole-loaded lipospheres utilized various chemicals and excipients. Fluconazole was provided by Bioplus Life Sciences Pvt. Ltd., Bangalore. Disodium hydrogen phosphate, potassium dihydrogen phosphate, and sodium chloride were sourced from S. D. Fine Chem. Ltd., Mumbai. Methanol, ethanol, and chloroform were supplied by Qualigens Fine Chemicals, Mumbai. Sodium hydroxide came from Chem pure Specialty Chemicals, Mumbai, and hydrochloric acid from Thomas Baker, Mumbai. Stearic acid and gelatin were

obtained from HiMedia Laboratories, Mumbai, while cetyl alcohol was from Lobachemie, Mumbai, and Tween 80 from Thomas Baker, Mumbai**.**

2.2 METHODOLOGY

2.2.1 Preformulation Studies

Preformulation testing is the first step in the development of dosage form of a drug substance. It can be defined as an investigation of physical and chemical properties of drug substance alone and when combined with excipients. The overall objective of the preformulation testing is to generate information useful to the formulator in developing stable dosage form, which can be mass-produced.

2.2.1.1 Identification of pure drug

Identification of Fluconazole was carried out by FT-IR Spectrophotometry.

Procedure

Weighed amount of drug was mixed with IR grade KBr(1:10) and compressed under 10-ton pressure in a hydraulic press to form a transparent pellet. The pellet was scanned by IR spectrophotometer over a range of 4000^{-1} cm to 500^{-1} cm range.

2.2.1.2 Determination of Melting point:

Determination of melting point gives an idea about purity of the drug. Melting point of Fluconazole was determined by capillary tube method. Fine powder of Fluconazole was filled with glass capillary (previously sealed on one end). The capillary tube is tied to thermometer and the thermometer was kept in tube containing liquid paraffin. The Assembly was kept on heating temperature was allowed to increase gradually temperature at which the powder melts was noticed.

2.2.2 Preparation of Calibration Curve of Fluconazole

Stock solution 1: 25mg of Fluconazole was accurately weighed and dissolved in 25ml of phosphate buffer of pH 7.4, which gives the concentration of 1000 □g/ml.

Stock solution 2: 1ml of stock solution 1 was taken and made up to 10 ml with phosphate buffer pH 7.4 which contains the concentration of 100 □g/ml. From stock 2 solution 0.2, 0.4, 0.6, 0.8 and 1.0ml, were taken and made up to 10 ml with phosphate buffer pH 7.4 to get the concentration ranges of 2, 4, 6, 8, and 10□g/ml respectively.

The absorbance was measured against the phosphate buffer pH 7.4 as blank at 210 nm using UV spectrophotometer. The study was carried out in triplicate (n=3). Then the calibration curve was plotted taking concentration on X-axis and mean absorbance on Y-axis.

2.2.3 Preparation of fluconazole loaded lipospheres by melt - dispersion method

In this method, the lipid or lipid mixture was melted and maintained at a temperature slightly above the melting point of the lipid, in which the drug was dispersed. This mixture was emulsified with an external aqueous phase containing a suitable surfactant and phospholipids and it was maintained at a temperature nearly or slightly higher than the lipid phase. The formed emulsion was kept in a sonicator for about 15mins then the formulation was immediately cooled by submerging it in an ice bath with continuous stirring to produce a uniform dispersion of lipospheres. The obtained dispersion was filtered using whatman filter paper and the lipospheres were collected and kept for drying at a room temperature.[2]

Table no 1: Formulation of drug loaded lipospheres.

Formulation	Drug (mg)	Stearic acid (mg)	Compritol (mg)	Soya-lecithin (mg)	PVA (mg)	Tween-80 (ml)	Distilled water (ml)	Time (min)
F-1	200	400	-	200	5	1	10	10
F-2	200	600	-	200	5	1	10	10
F-3	200	800	-	200	5	1	10	10
F-4	200	-	400	200	5	1	10	10
F-5	200	-	600	200	5	1	10	10
F-6	200	-	800	200	5	1	10	10
F-7	150	600	-	200	5	1	10	10
F-8	175	600	-	200	5	1	10	10
F-9	150	-	600	200	5	1	10	10
F-10	175	-	600	200	5	1	10	10
F-11	200	600	-	200	5	1	20	10
F-12	200	600	-	200	5	1	25	10
F-13	200	-	600	200	5	1	20	10
F-14	200	-	600	200	5	1	25	10
F-15	200	600	-	200	5	1	10	15
F-16	200	600	-	200	5	1	10	20
F-17	200	-	600	200	5	1	10	15
F-18	200	-	600	200	5	1	10	20

2.2.4 Evaluation of Fluconazole Lipospheres

All formulations were evaluated for particle size, entrapment efficiency, drug content and In vitro drug release studies.

2.2.4.1 Morphological Characterization

Physical appearance: Visual examination of the generated lipospheres was done to check the shape, size and colour.

Particle size: Particle size was determined by optical microscopy method. The optical microscope using stage micrometer was used to determine particle size of lipospheres. Calibration of microscope was done and the particles were kept on the slide, distance covered by the particle is multiplied by 1 division of eye-piece micrometer to get size of the particle size.

Drug content: The drug content was determined by dissolving 10mg of lipospheres in 5.8pH phosphate buffer. 1ml from the above solution was again dissolved in 10ml of phosphate buffer. The solution was filtered and resulting solution was analyzed at 210nm in the UV-Visible spectrophotometer.[3]

$$\%\ Drug\ Content = \frac{Amount\ of\ drug\ in\ liposphere}{Total\ amount\ of\ liposphere} * 100$$

Entrapment Efficiency: The entrapment efficiency was determined by indirect method using filtrate.1ml of filtrate added with 10ml of phosphate buffer again, 1ml from this solution was diluted to 10ml. The resulting diluted solution was analysed at 210nm in the UV-Visible spectrophotometer.[4]

$$\%\ EE = \frac{Total\ amount\ of\ drug - Amount\ of\ drug\ unentrapped}{Total\ amount\ of\ drug} \times 100$$

In-Vitro drug release study: In-vitro drug release study was performed by using USP-II (Paddle type) apparatus. Weighed amount of lipospheres (860.82mg) was placed in three different baskets in dissolution medium containing 900ml of phosphate buffer (5.8pH). The paddle was rotated at a speed of 100 rpm by maintaining temperature at 37±1ºC in each test. Samples were withdrawn at regular interval of 1hr as 5 ml of the sample was withdrawn this was continued up to 8hrs by replacing equal quantity of fresh dissolution medium. The filtered samples was analysed at 210nm by using UV Spectrophotometer.[5]

Scanning Electron Microscopy

The powders were imaged by a scanning electron microscope (SEM) run at an accelerating voltage of 10kV using ZEISS EVO 18 SEM. The powder in few µg were fixed on to stub by a double-sided sticky carbon tape and kept inside the SEM chamber and analysed at different

magnification such as 60X, 200X, 500X. 1.10X and 2.50X respectively to obtain better clarity on the particle morphology.[6]

Stability Study of Lipospheres

Stability studies were performed to evaluate the ability of the prepared liposphere formulations to retain their physicochemical characteristics during storage. Parameters such as drug content, entrapment efficiency, particle size, and physical appearance were monitored at regular intervals at room temperature.[7]

2.2.5 Formulation of liposphere Entrapped Fluconazole Gel[8]

An optimized liposphere containing Fluconazole equivalent to 0.5 % w/w was incorporated into gel base composed of carbopol 934 and purified water.

Procedure

0.125g of carbopol 934 was dissolved in 25 ml of purified water and kept for stirring until the carbopol is dissolved completely to form a soft consistant gel. At the end 0.02% of methyl paraben a preservative is added.

Table No. 2: Formulation of gel.

SI. No	Ingredients (Percentage)	Gel A	Gel B	Gel C
1.	Carbopol 934 (mg)	0.25	0.50	0.75
2.	Purified water (ml)	25±5	25±5	25±5
3.	Methyl paraben (ml)	0.02	0.02	0.02
4.	Gel Texture	Low viscous Gel	Soft Gel with good texture	Hard Gel

2.2.6 Evaluation of Liposphere Topical Gel

Physical Appearance: The prepared gel was examined for clarity, color, homogeneity and presence of foreign particles.[9]

pH: The pH of dispersion was measured by using digital pH meter.[10]

Rheological Study by Viscosity Measurement: Viscosity was determined by Brookfield programmable DV-E viscometer. In the present study, we selected spindle no. 63 with an optimum speed of 10 rpm was used to measure the viscosity of the preparation.[11]

Spreadability: The most common method for measuring the spreadability is the parallel-plate method. This method is simple, economical, and time-effective. During the

measurement using the parallel-plate method, 1 g of the sample prepared in 48 hrs before the test was placed between two glass plates. A weight of 100 g was placed on top for 1 minute Then the diameter of the sample between the plates is measured.[12]

In these cases, spreadability is determined by the formula:

$$A = \pi r^2$$

$$Si = d2 * \frac{л}{4}$$

Where

Si = spreading area (mm^2) depending on mass.

d = spreading area diameter (mm)

Content Uniformity[9]

The drug content of the prepared gel was carried out by dissolving accurately weighed quantity of 1gm of gel in 10ml of Phosphate buffer pH 5.8 solution. The content was filtered through Whatmann filter paper No. 41. 1 ml of above solution was taken into 10 ml volumetric flask and volume was made up to mark with Phosphate buffer pH 5.8 solution. The content of Fluconazole was determined at 210 nm against blank by using Shimadzu UV/ visible spectrophotometer. The drug content was determined from calibration curve of Fluconazole. The tests were carried out in triplicate.

In-vitro Drug Diffusion Study

In-vitro diffusion study was carried out in a Franz diffusion cell using high media dialysis membrane which was soaked overnight in pH 5.8 phosphate buffer. The membrane mounted between the donor compartment and the reservoir compartment of Franz diffusion cell containing 135 ml of pH 5.8 phosphate buffer. 1g of liposphere gel was placed over the dialysis membrane of donor compartment. The whole assembly was fixed in such a way that the donar compartment of the cell containing gel was just touched to the dialysis membrane and the medium in the compartment was agitated using a magnetic stirrer at the temperature 37±0.5ºC. Care should be taken to avoid the entry of air bubbles below the dialysis membrane through out the study. Aliquots (5 ml) were withdrawn from the receptor compartment periodically and replaced with same volume of fresh buffer. The sample was analyzed by using UV-visible spectrophotometer at 210 nm. The tests were carried out in triplicate (n=3).[13]

Drug Release Kinetic Data Analysis

Several kinetic models have been proposed to describe the release characteristics of a drug from matrix. The following four equations are commonly used, because of their simplicity and applicability. The zero-order model equation (Plotted as cumulative percentage of drug released vs. time); first-order model equation (Plotted as log percent drug remaining vs. time) to study the kinetics of drug release. Higuchi's square-root equation (Plotted as cumulative percent drug released vs. square root of time); and the Korsmeyer-Peppas equation (Plotted as log cumulative percent drug released vs log time) to study the mechanism of drug release.[14]

2.2.7 Anti-Fungal Activity[15]

Cup Plate (Agar Diffusion) Method

- **Medium used**
- Potato dextrose agar (SDA)

- **Test organism**
- *Aspergillus niger*,

- **Procedure**

1. Sterilized SDA medium is poured into Petri plates and allowed to solidify.
2. The surface of the solidified agar is inoculated evenly with the test organism using a sterile swab.
3. Wells (6 mm diameter) are made using a sterile cork borer.
4. A fixed quantity of the **formulated gel**, **plain drug gel**, and **control (blank gel)** are introduced into the respective wells.
5. Plates are incubated at **25–28 °C for 48–72 hours**.
6. After incubation, the **zone of inhibition (in mm)** around each well is measured

2.2.8 Stability study of gel

The stability studies of the prepared gel formulations was (F2, F5) carried out in accordance with ICH guidelines to determine their physical stability. The samples was stored in suitable containers at a temperature (30 ± 2 °C / 65 ± 5% RH), for predetermined periods of 1 month. The gel was evaluated for changes in appearance, color, odour, pH, viscosity and spreadability,. Chemical stability was assessed by determining the drug content and percentage drug released. The obtained results were compared with the initial values to identify significant changes.[15]

3. RESULTS AND DISCUSSION

3.1 Pre formulation studies

3.1.1 Identification of pure dru

The IR spectrum of pure drug was found to be similar to the standard spectrum of Fluconazole. The spectrum of Fluconazole shows the functional groups as per the reference peaks.

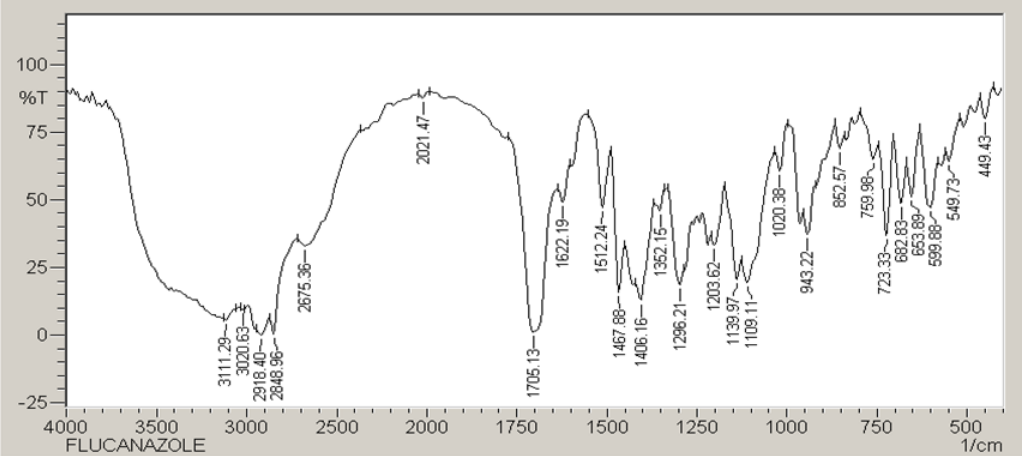


Fig. No. 1: FTIR Spectra of Fluconazole.

Identification of Fluconazole was carried out by using Fourier Transform Infra-Red spectroscopy. It was observed that all the characteristic peaks of Fluconazole were shown as of the standard peaks, so it was concluded that the drug is pure.

3.1.2 Determination of Melting Point: Melting point of Fluconazole was determined by capillary method. The melting point was found to be in the range of 138-142 ℃. Thus, indicating the purity of the drug. The melting point of Fluconazole was found to be 139℃.

3.1.3 Preparation of calibration curve Fluconazole in pH 7.4 Phosphate buffer

The calibration curve of Fluconazole was developed at this wavelength. The calibration curve was linear between 2-10µg/ml concentration ranges in pH 7.4 phosphate buffer. Calibration curve was plotted by plotting mean absorbance on Y-axis against concentration on X-axis. The R^2 and slope were found to be 0.9958 and 0.0107 at 210nm, 0.9902 and 0.0222 at 210nm respectively.

Calibration Data of Fluconazole in PBS pH 7.4 (λ max 210 nm)

Table No. 3: Calibration curve of Fluconazole.

Concentration (µg/ml)	Absorbance (Mean± SD) (n=3)
10	0.171±0.0025
20	0.336±0.0030
30	0.431 ±0.0030
40	0.548 ±0.003
50	0.628 ±0.0036
60	0.762 ±0.0035
70	0.857 ±0.0035
80	0.953 ±0.0035
90	1.052±0.0035

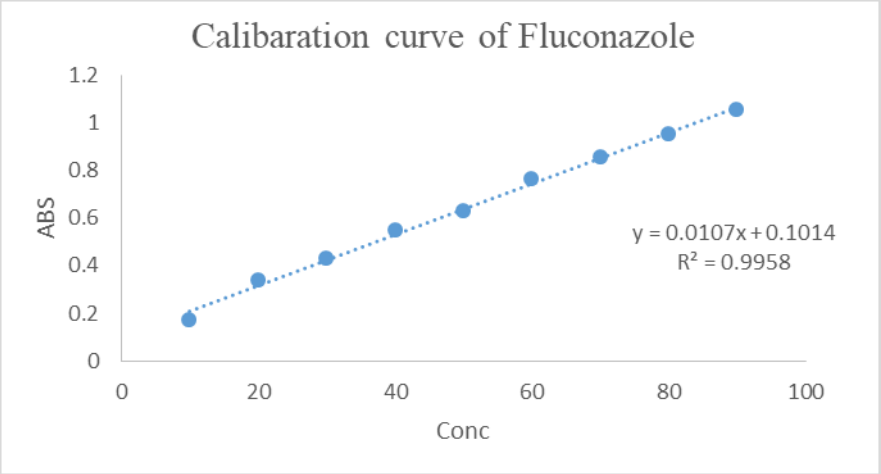


Fig. No. 2: Calibration Curve of Fluconazole in PBS pH 7.4.

Formulation of Lipospheres

Fluconazole loaded lipospheres were successfully prepared by melt-dispersion method. Different lipids were optimized in order to obtain uniform particles.

Evaluated parameters of Fluconazole lipospheres

EFFECT OF CORE: COAT RATIO

Table No. 4: Results for Effect of Core: Coat Ratio.

FORMULATION	CORE: COAT RATIO	%YEILD	DRUG CONTENT (%)	ENTRAPMENT EFFICIENCY (%)	PARTICLE SIZE (µm)
F-1	1:2	41.74	85.32	58.21	65.5
F-2	1:3	75.67	95.2	74.56	55.6
F-3	1:4	57.80	78.8	51.7	71.51
F-4	1:2	40.05	55.74	52.8	67.46
F-5	1:3	72.63	86.3	74.2	58.67
F-6	1:4	51.96	78.3	50.32	75.8

Increase in coat ratio resulted in increase in percentage yield, drug content, and entrapment efficiency, indicating that this ratio provides an optimal lipid matrix for efficient drug encapsulation. The improved performance can be attributed to sufficient lipid availability for drug entrapment and reduced drug loss during preparation.

Increase in the coat concentration to 1:4 (F3 and F6) led to a decline in yield and entrapment efficiency, possibly due to increased system viscosity and reduced emulsification efficiency. The excess lipid may also promote phase separation and drug leakage.[17]

EFFECT OF CONCENTRATION OF DRUG

Table No. 5: Results for Concentration of Drug.

FORMULATION	AMOUNT OF DRUG	%YELD	DRUG CONTENT	ENTRAPMENT EFFICIENCY	PARTICLE SIZE
F-7	150	58.4	72.67	60.63	45.2
F-8	175	65.23	83.9	69.76	55.87
F-2	200	75.67	95.2	74.56	65.5
F-9	150	64.89	61.43	53.74	50.87
F-10	175	70.18	75.79	65.08	62.36
F-5	200	72.63	86.3	74.02	67.46

Increase in drug concentration led to increase in yield, entrapment efficiency and drug content**.** At constant lipid level when amount of drug increases the concentration of mixture increases until saturation.

EFFECT OF VOLUME OF AQUEOUS PHASE

Table No. 6: Results for Volume of Aqueous Phase.

FORMULATION	QUANTITY OF WATER (ml)	%YEILD	DRUG CONTENT (%)	ENTRAPMENT EFFICIENCY (%)	PARTICLE SIZE(µm)
F-2	10	80.95	95.2	74.56	58.35
F-11	20	62.58	87.46	69.57	65.5
F-12	25	57.14	74.05	63.4	57.8
F-5	10	78.63	86.3	74.02	72.96
F-13	20	75.67	79.65	68.38	67.46
F-14	25	62.90	70.36	61.05	64.68

The effect of aqueous phase volume on formulation characteristics revealed that increasing the volume of water led to a decrease in yield, drug content, and entrapment efficiency. As the volume of aqueous phase increases at constant stirring speed same amount of energy in the form of sonication is applied to more volume. This in turn decreases viscosity of the liquid which reduces the entrapment efficiency, drug content and particle size.[18]

INFLUENCE OF SONICATION TIME:

Table No. 7: Results for Influence of Sonication Time.

FORMULATION	TIME (MIN)	%YEILD	DRUG CONTENT (%)	ENTRAPMENT EFFICIENCY (%)	PARTICLE SIZE (µm)
F-2	10	75.5	95.2	74.56	65.5
F-15	15	68.72	79.57	71.86	63.12
F-16	20	61.39	67.28	62.57	57.7
F-5	10	72.3	86.3	74.2	67.46
F-17	15	70.21	77.93	64.34	61.86
F-18	20	63.98	65.20	59.32	59.68

The effect of sonication time on formulation characteristics revealed that increasing sonication duration led to a decrease in yield, drug content, and entrapment efficiency. Prolonging sonication to 15 or 20 minutes, resulted in a gradual decline in these parameters, likely due to structural disruption and partial drug leakage.[19]

IN VITRO DRUG RELEASE OF OPTIMIZED FORMULATION

Table No. 8: Results for In vitro Drug Release of Optimized Formulation.

TIME (Hrs)	F-2	F-5
0	0	0
1	13.48 ± 0.39	11.63 ± 0.96
2	28.18 ± 0.71	24.82 ± 0.12
3	36.72± 0.63	35.35 ± 0.24
4	48.71 ± 0.55	46.28 ± 0.77
5	56.97 ± 0.55	54.91 ± 0.72
6	63.27 ± 0.63	61.05 ± 0.24
7	82.27 ± 0.71	80.49 ± 0.71
8	96.56 ± 0.71	93.51 ± 0.64

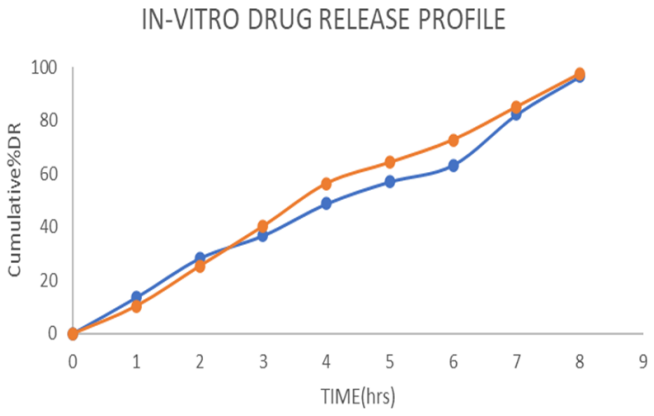


Fig. No. 3: In vitro release of F2 and F5 Formulation.

STABILITY STUDIES

Table No. 9: Results for Stability Studies of Lipospheres.

Sl. No	Evaluation parameters	Short term stability (F-2)		Short term stability (F-5)	
		Initial	After 1 month	Initial	After 1 month
1	Physical appearance	Off white	Off white	Off white	Off white
2	Average Particle size	65.5(µm)	64.2(µm)	67.46(µm)	65.89(µm)
3	Drug content	95.2%	94.6%	86.3 %	83.5 %
4	Entrapment efficiency	74.56%	74.12%	73.2 %	70.8 %

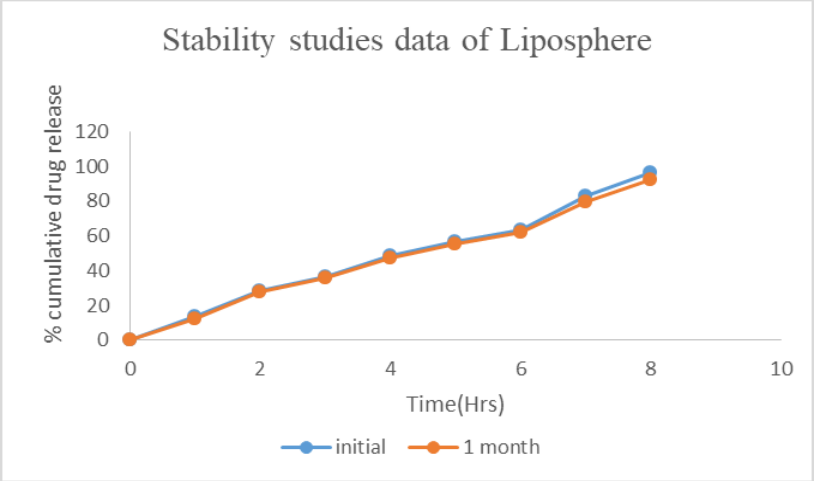


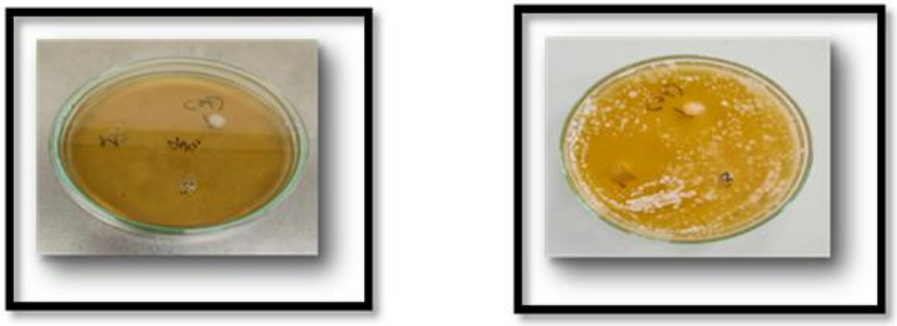
Fig. No. 4: Stability studies data of Lipospheres.

Results indicated that drug content remained within the acceptable pharmacopeial limits throughout the study period, suggesting that the drug was chemically stable in the lipid matrix. Entrapment efficiency showed no changes with time. Particle size analysis revealed slight growth during storage, which could be due to aggregation or fusion of lipospheres over time. In terms of appearance, no significant color change or phase separation was observed.

Evaluation of liposphere gel

1. **pH:** The pH of the formulated gel was found to be 5.75 and 5.47 for F2 and F5 formulations respectively.
2. **Viscosity:** The viscosity of the formulated gel was found to be 3144cp and 3418cp respectively for F2 and F5 formulations.
3. **Spreadability:** The spreadability of the formulated gel was found to 8.23g cm^2 and 9.71g cm^2 respectively for F2 and F5 formulations.
4. **Zone of Inhibition:** The zone of inhibition of the formulated gel was found to 2.1±0.2cm and 1.9±0.2cm respectively for F2 and F5 formulations.

Anti-fungal activity of f-2(stearic acid) and f-5(compritol) formulation



F2 Before Activity **F2 After Activity**

F5 Before Activity **F5 After Activity**

Fig. No. 5: F2 and F5 formulation before and after anti fungal activity.

IN VITRO DIFFUSION STUDY OF GEL

Table No. 10: Results for In Vitro Diffusion Study of gel.

%Cumulative Drug Release			
Time(Hrs)	Marketed Gel	F-2 Gel	F-5 Gel
1	24.51	21.71	19.22
2	36.70	31.12	28.82
3	42.47	41.43	39.73
4	50.90	50.83	47.47
5	59.65	57.34	55.25
6	71.26	61.67	60.06
7	92.72	86.98	79.23
8	94.67	90.85	87.63

COMPARISION OF MARKETED PRODUCT AND LIPOSPHERE LOADED GEL

Table no 11: Results for Comparison of Marketed Product and Liposphere Loaded gel.

EVALUATION TESTS	MARKETED PRODUCT	LIPOSPHERES LOADED GEL F-2	LIPOSPHERES LOADED GEL F-5
pH	5.5	5.75	5.47
Spreadibility	9.96 g cm^2	8.23g cm^2	9.71g cm^2
Viscosity	5174cp	3144cp	3418cp
Zone of Inhibition	2.3±0.2cm	2.1±0.2cm	1.9±0.2cm

Stability data of liposphere gel

Table No. 12: Results for Data of stability data of Liposphere gel.

TESTS	INITIAL F-2	F-2 AFTER 1 MONTH	INITIAL F-5	F-5 AFTER 1 MONTH
pH	5.75	5.65	5.47	5.43
Spreadibility	8.23g cm^2	8.20g cm^2	9.71g cm^2	9.50g cm^2
Viscosity	3144cp	3132cp	3418cp	3403cp
% Drug release	90.85%	90.04%	87.63%	86.58%

Two formulations of the liposphere gel were stored at 25 ± 2 °C / ~60% RH for 1 month. Physical appearance, pH, viscosity, entrapment efficiency and drug content limits were evaluated at 0 and 1 month. Both formulations showed minimal changes in all the parameters, No phase separation or color change was observed. These results indicated short-term stability of the formulation at room temperature over 1 month.

CONCLUSION

- Our research mainly focused on Design and characterization of liposphere gel of fluconazole for topical anti-fungal activity, followed by their evaluation and **incorporation into a gel**
- The study demonstrated that by **optimizing various formulation parameters**, such as the **core: coat ratio**, **concentration of drug, volume of aqueous phase and sonication time**, the desired drug release profiles and physical characteristics of lipospheres could be achieved.
- Overall, the study concludes that liposphere-based drug delivery systems are a promising approach for **improving the penetration and controlled release of Fluconazole**. The gel formulation developed offers an efficient and stable means of delivering Fluconazole topically, which could enhance the permeation, patient compliance and therapeutic outcomes.

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