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Formulation and Evaluation of Liposomal Gel Incorporated with Aloe vera Gel

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A B S T R A C T

Fungal skin infections are among the most common dermatological disorders, often associated with discomfort, inflammation, itching, and reduced quality of life. Conventional topical antifungal formulations of clotrimazole are effective; however, limited skin penetration, poor retention at the application site, and frequent dosing requirements may reduce therapeutic efficacy. The present study aimed to develop and evaluate a clotrimazole-loaded liposomal gel incorporated with Aloe vera gel to enhance topical drug delivery and improve antifungal activity.

Clotrimazole-loaded liposomes were prepared using the thin-film hydration method with varying concentrations of soya lecithin and cholesterol. Preformulation studies including organoleptic properties, solubility analysis, melting point determination, UV spectrophotometric analysis, and Fourier Transform Infrared (FTIR) spectroscopy were performed to confirm drug characteristics and compatibility with excipients.

The viscosity of the formulations ranged from 6850 ± 45 cP to 8920 ± 70 cP. The spreadability values of all formulations were found between 5.80 ± 0.11 to 6.85 ± 0.12 g•cm/sec. The extrudability values ranged from 82.5 ± 1.2% to 93.5 ± 1.2%, indicating excellent ease of removal from the container. Formulation F9 exhibited maximum extrudability (93.5 ± 1.2%). The highest drug content was observed in F9 (99.05 ± 0.70%), which may be attributed to enhanced drug entrapment due to higher lipid concentration. The cumulative drug release after 12 hours was found to be in the range of 84.75 ± 1.60% to 93.20 ± 1.75%. Formulation F1 showed maximum drug release (93.20 ± 1.75%), whereas F9 showed controlled release (84.75 ± 1.60%) due to increased rigidity of the liposomal bilayer caused by higher cholesterol and lecithin concentration.

The findings of the study suggest that Aloe vera-based clotrimazole liposomal gel can serve as an effective topical drug delivery system with improved skin retention, controlled drug release, and enhanced antifungal potential. This novel formulation approach may provide better therapeutic outcomes for the management of superficial fungal infections.

I. Introduction

Liposomal drug delivery systems

Liposomal drug delivery systems have emerged as an effective approach to overcome these limitations. Liposomes are vesicular systems composed of phospholipid bilayers capable of encapsulating both hydrophilic and lipophilic drugs. When applied topically, liposomes enhance drug penetration into the skin, prolong drug retention, and reduce systemic absorption, thereby improving therapeutic efficacy and safety.

Liposomal drug delivery systems are one of the most significant advancements in pharmaceutical technology, offering an efficient and targeted approach for the delivery of therapeutic agents. Liposomes are microscopic, spherical vesicles composed of one or more phospholipid bilayers surrounding an aqueous core. Because their structure closely resembles that of biological cell membranes, liposomes are biocompatible, biodegradable, and non-toxic. Since their discovery by Alec D. Bangham in 1965, liposomes have been extensively investigated as carriers for a wide variety of

drugs, including anticancer agents, antibiotics, antifungal drugs, peptides, proteins, nucleic acids, vaccines, and herbal bioactive compounds.

The unique structure of liposomes enables them to encapsulate both hydrophilic and lipophilic drugs. Hydrophilic drugs are entrapped within the aqueous core, while lipophilic drugs are incorporated into the phospholipid bilayer. This dual encapsulation capability makes liposomes versatile drug carriers suitable for a broad range of pharmaceutical applications. Liposomal formulations improve drug stability, protect active pharmaceutical ingredients from enzymatic degradation, prolong circulation time, and enhance therapeutic efficacy while minimizing systemic toxicity.

Structure of Liposomes

A liposome consists of phospholipid molecules arranged in a bilayer, with hydrophilic (water-attracting) heads facing the external and internal aqueous environments and hydrophobic (water-repelling) tails facing each other. Cholesterol is commonly incorporated into the lipid bilayer to enhance membrane rigidity, reduce permeability, and improve stability. Depending on their size and number of lipid bilayers, liposomes are classified into:

- **Small Unilamellar Vesicles (SUVs):** 20–100 nm in diameter with a single lipid bilayer.
- **Large Unilamellar Vesicles (LUVs):** 100–1000 nm in diameter with a single bilayer.
- **Multilamellar Vesicles (MLVs):** Consist of multiple concentric phospholipid bilayers resembling an onion-like structure.

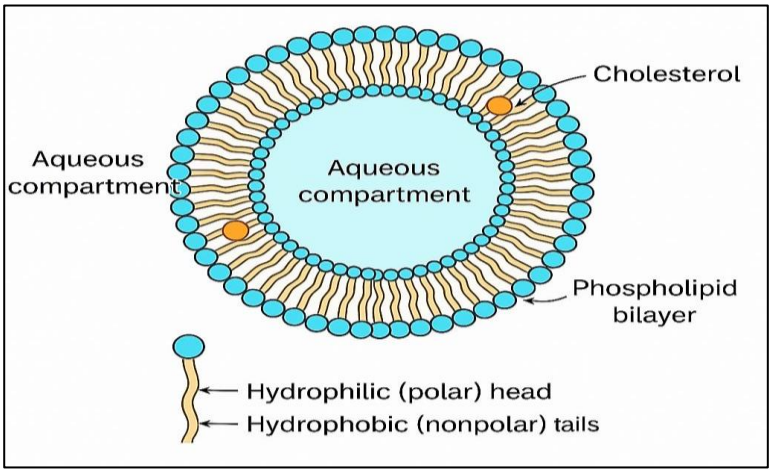

Fig. 1: Structure of Liposomes

Components of Liposomes

The major components used in liposome preparation include:

- **Phospholipids:** Soya lecithin, egg phosphatidylcholine, hydrogenated phosphatidylcholine, or synthetic phospholipids form the structural framework.
- **Cholesterol:** Enhances membrane strength, decreases leakage of entrapped drug, and improves stability.
- **Charge-inducing agents:** Such as stearylamine (positive charge) or dicetyl phosphate (negative charge) prevent vesicle aggregation.
- **Aqueous phase:** Distilled water or phosphate buffer is used for hydration and drug encapsulation.

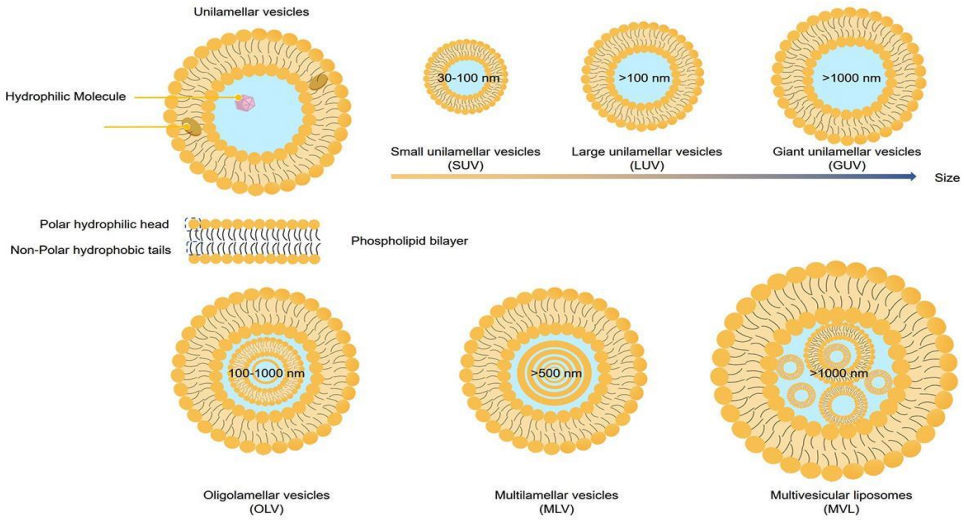

Fig. 2: Components of Liposomes

Mechanism of Drug Delivery

After administration, liposomes interact with biological membranes through several mechanisms. They may adsorb onto the cell surface, fuse with the plasma membrane, undergo endocytosis by target cells, or release the encapsulated drug by diffusion.

Liposomes can accumulate preferentially at diseased tissues due to enhanced permeability and retention (EPR) effects, especially in tumours and inflamed tissues. Surface modification with polyethylene glycol (PEG) or specific ligands further enhances circulation time and targeted drug delivery.

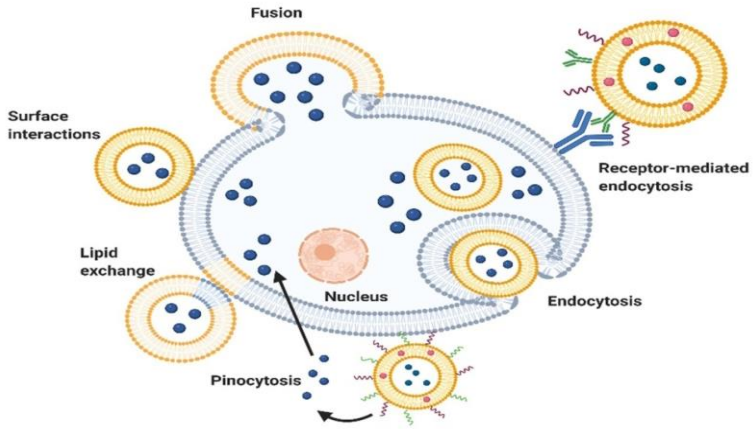

Fig. 3: Mechanism of Drug Delivery

Aloe vera is a natural herbal agent known for its antifungal, anti-inflammatory, wound healing, moisturizing, and soothing properties. Aloe vera gel enhances skin hydration and permeability, making it an excellent natural gel base for topical formulations. Incorporation of liposomes into Aloe vera gel can provide synergistic benefits by combining controlled drug delivery with natural skin healing properties.

Fungal infections of the skin, commonly known as dermatomycoses, are caused by dermatophytes, yeasts, and molds. These infections are prevalent worldwide due to poor hygiene, humid climate, immunocompromised conditions, and prolonged use of antibiotics. Common fungal infections include candidiasis, ringworm, athlete's foot, and jock itch, which primarily affect the superficial layers of the skin.

Clotrimazole is a broad-spectrum imidazole antifungal agent widely used in the treatment of topical fungal infections. It acts by inhibiting ergosterol synthesis, leading to disruption of the fungal cell membrane. However, conventional clotrimazole formulations such as creams and ointments suffer from limitations including poor skin penetration, frequent dosing, low residence time, and local irritation.

Anatomy and Physiology of Skin

The human body has two systems that protect it from the harmful organisms existing in the environment. The internal defence system destroys microorganisms and bacteria that have already attacked the body. The external defence system prevents microbial microorganisms to enter the body. Skin is biggest external defence system. Skin covers the outside of the body but has other functions beside the defence mechanism. It serves as a mechanical barrier between the inner part of the body and the external world. Temperature of skin varies in a range of 30 to 40°C degree depending on the environmental conditions.

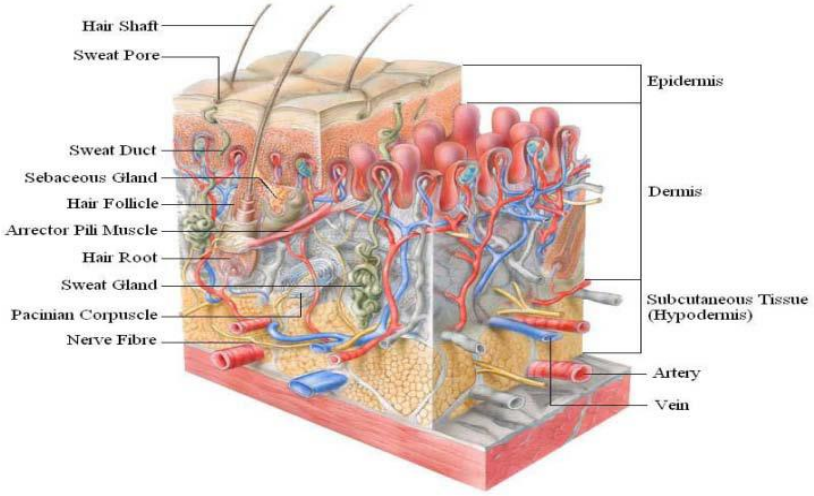

Fig. 4: Longitudinal section of skin

The skin is the largest organ of the body. Its large surface area in direct contact with the environment presents tremendous opportunities for drug delivery. The human skin is organized into two distinct layers, namely the epidermis and dermis directly beneath. The highly vascular dermis is made up of a connective tissue matrix containing the nerves, hair follicles, pilosebaceous units and sweat glands. The epidermis is avascular and its outermost layer, the stratum corneum, consists of keratinrich, dead epidermal cells called corneocytes embedded within a lipid rich matrix. The stratum corneum forms the primary barrier for drug permeation especially to watersoluble compounds. Consequently, drug delivery across the stratum corneum has become the essence in the design of many dermal delivery systems.

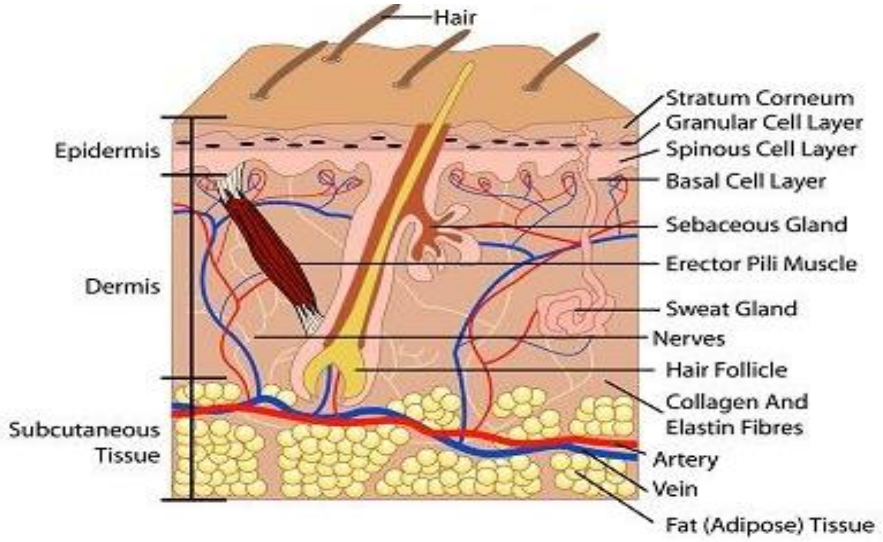

Fig. 5: Skin Layers Diagram

Structure of Gels

A gel consists of a natural or synthetic polymer forming a three dimensional matrix throughout a dispersion medium or hydrophilic liquid. After application, the liquid evaporates leaving the drug entrapped in a thin film of the gel – forming matrix physically covering the skin25. The presence of a network formed by the interlocking of particles of the gelling agent gives rise to the rigidity of a gel. The nature of the particles and the type of form that is responsible for the linkages determine the structure of the network and the property of the gel.

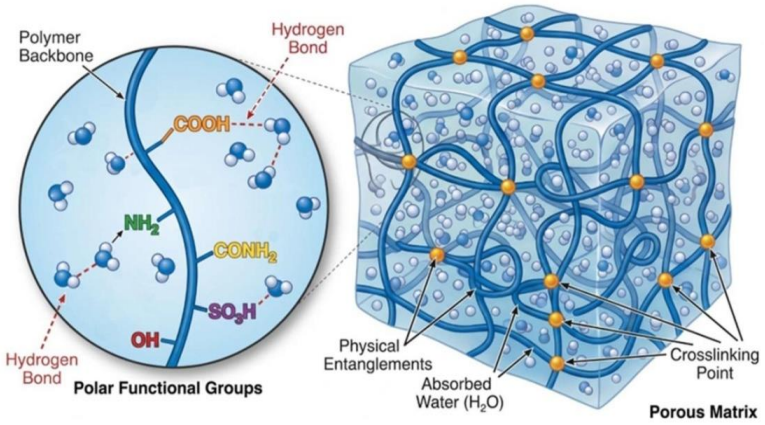

Fig. 8: Structure of gels

Formulation Design

Topical gel may include the following components:

A) Gel forming agent or polymer
B) Drug Substance
C) Penetration Enhancers

2. Materials and Methods

Active Pharmaceutical Ingredient

- Clotrimazole

Lipid Components

- Soya Lecithin
- Cholesterol

Gel Components

- Aloe vera Gel
- Carbopol 934
- Triethanolamine

Solvents and Reagents

- Chloroform
- Methanol
- Ethanol

- Phosphate Buffer pH 7.4
- Distilled Water

Microbiological Media

- Sabouraud Dextrose Agar (SDA)
- Nutrient Broth

Test Organism

- *Candida albicans*

4.2 Methods

4.2.1 Preformulation Studies

A. Characterization of Clotrimazole

1. **Colour**
   The colour of clotrimazole was observed visually under daylight.
2. **Odour**
   The odour was determined by sensory evaluation.
3. **Appearance**
   The physical appearance of clotrimazole was examined visually.

4. **Melting Point Determination**

The melting point was determined using the capillary method and compared with reported values.

B. Solubility Studies

An excess amount of clotrimazole was added to phosphate buffer pH 7.4 and shaken for 24 hours at room temperature. The solution was filtered and analyzed spectrophotometrically.

C. UV Spectrophotometric Analysis

Determination of λmax

A standard solution of clotrimazole was prepared in phosphate buffer pH 7.4 and scanned between 200–400 nm using a UV-Visible spectrophotometer.

Preparation of Calibration Curve

Standard solutions (2–12 µg/ml) were prepared and absorbance was measured at λmax. A calibration curve was plotted between concentration and absorbance.

D. Drug–Excipient Compatibility Study (FTIR)

FTIR spectra of:

- Pure Clotrimazole
- Clotrimazole + Lecithin
- Clotrimazole + Cholesterol

were recorded over 4000–400 cm^{-1} to assess compatibility.

4.2.2 Composition of Aloe vera Based Liposomal Gel

Table No. 1 Composition of Aloe vera Based Liposomal Gel

Ingredients (g/100 g)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Clotrimazole	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Soya Lecithin (X_1)	1.0	1.0	1.0	2.0	2.0	2.0	3.0	3.0	3.0
Cholesterol (X_2)	0.5	1.0	1.5	0.5	1.0	1.5	0.5	1.0	1.5
Aloe vera Gel	10	10	10	10	10	10	10	10	10
Carbopol 934	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Triethanolamine	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Methyl Paraben	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20
Propyl Paraben	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Distilled Water	q.s. to 100 g	q.s. to 100 g	q.s. to 100 g	q.s. to 100 g	q.s. to 100 g	q.s. to 100 g	q.s. to 100 g	q.s. to 100 g	q.s. to 100 g

4.2.3 Formulation of Clotrimazole-Loaded Liposomes

Thin Film Hydration Method

Clotrimazole-loaded liposomes were prepared by the thin film hydration technique. Accurately weighed quantities of clotrimazole, soya lecithin, and cholesterol were dissolved in a chloroform:methanol mixture in the ratio of 2:1 in a round-bottom flask. The organic solvents were evaporated using a rotary evaporator at 40°C under reduced pressure to form a thin, dry lipid film on the inner wall of the flask. The formed lipid film was then hydrated using phosphate buffer solution pH 7.4 with continuous shaking to obtain multilamellar vesicles. The resulting dispersion was subjected to sonication to reduce vesicle size and obtain a uniform liposomal suspension. The prepared liposomal dispersion was stored at 4°C for further use and evaluation.

4.2.4 Formulation of Aloe vera Based Liposomal Gel

Preparation of Gel Base

The gel base was prepared using Carbopol 934 (1% w/w), which was slowly dispersed in distilled water under continuous stirring to avoid lump formation. The dispersion was allowed to swell and hydrate completely. Fresh Aloe vera gel was then incorporated into the hydrated Carbopol dispersion with continuous stirring to obtain a uniform mixture. Triethanolamine was added dropwise to neutralize the system and adjust the pH to form a clear and stable gel base.

Incorporation of Liposomes

The optimized clotrimazole-loaded liposomal dispersion was gradually incorporated into the prepared Aloe vera gel base under continuous stirring to ensure uniform distribution of liposomes throughout the gel matrix. Stirring was continued until a smooth, homogeneous liposomal gel was obtained. The final formulation was filled into clean, airtight containers and stored under refrigeration until further evaluation.

4.2.5 Evaluation of Liposomal Gel

A. Physical Evaluation

The prepared liposomal gel formulations were evaluated visually for colour, appearance, consistency, and homogeneity. The colour and appearance were observed against a white background to detect any particulate matter or phase separation. Consistency was assessed manually by touch, and homogeneity was confirmed by ensuring uniform distribution of drug and absence of lumps or grittiness in the formulation.

B. pH Measurement

The pH of the liposomal gel was determined using a calibrated digital pH meter at room temperature. A small quantity of gel was dispersed in distilled water and the electrode was immersed in the sample until a stable reading was obtained. The pH was recorded to ensure compatibility with skin pH.

C. Viscosity

The viscosity of the formulated gel was measured using a Brookfield viscometer at room temperature. The appropriate spindle was selected and the gel sample was placed in the sample container. The viscosity readings were recorded at different spindle speeds to evaluate flow behavior of the formulation.

D. Spreadability

Spreadability of the gel was determined using the two-glass slide method. A fixed amount of gel was placed between two glass slides, and a known weight was applied on the upper slide. The time required for the upper slide to move a specific distance was recorded. Spreadability was calculated using the formula:

Formula

$S = M \times LT$

Where:

- S = Spreadability
- M = Weight tied to upper slide (g)
- L = Length moved by glass slide (cm)
- T = Time taken (sec)

E. Extrudability

Extrudability of the gel was evaluated by filling the formulation into collapsible aluminum tubes and applying uniform pressure. The amount of gel extruded from the tube was measured and expressed as a percentage. This parameter indicated the ease of dispensing the formulation from the container.

F. Drug Content Determination

For drug content analysis, 1 g of liposomal gel was accurately weighed and dissolved in phosphate buffer pH 7.4 with continuous stirring. The solution was filtered and suitably diluted. The absorbance was measured using a UV-visible spectrophotometer at the predetermined λmax of clotrimazole, and drug content was calculated using the calibration curve.

4.2.6 In-vitro Drug Release Study

Franz Diffusion Cell Method

The in-vitro drug release study was carried out using a Franz diffusion cell apparatus. A dialysis membrane, previously soaked in phosphate buffer pH 7.4, was mounted between the donor and receptor compartments. The receptor compartment was filled with phosphate buffer maintained at 37 ± 0.5°C and continuously stirred. A measured quantity of liposomal gel equivalent to the required dose was placed in the donor compartment. At predetermined time intervals, samples were withdrawn from the receptor compartment and replaced with fresh buffer to maintain sink conditions. The samples were analyzed spectrophotometrically to determine the amount of drug released.

4.2.7 Antifungal Activity Study

Determination of Zone of Inhibition

Agar Well Diffusion Method

1. SDA plates were prepared.
2. *Candida albicans* suspension was spread uniformly.
3. Wells were punched in agar.
4. Liposomal gel samples were placed in wells.
5. Plates were incubated at 37°C for 24–48 h.
6. Diameter of inhibition zone was measured in mm.

4.2.8 Stability Studies

Stability studies were performed according to ICH guidelines to evaluate the physical and chemical stability of the liposomal gel. The formulations were stored under two different conditions: 25 ± 2°C / 60 ± 5% RH and 40 ± 2°C / 75 ± 5% RH. The samples were evaluated at different time intervals (1, 2, and 3 months) for changes in physical appearance, pH, drug content, and in-vitro drug release profile. Any significant variation in these parameters was recorded to determine the stability of the formulation over time.

Storage Conditions

- 25 ± 2°C / 60 ± 5% RH
- 40 ± 2°C / 75 ± 5% RH

Evaluation Parameters

8.1 Physical Stability

- Colour
- Appearance
- Homogeneity

8.2 Drug Content Stability

- Drug assay

8.3 In-vitro Release Stability

- Drug release profile comparison

Study Duration

- 1 Month
- 2 Months
- 3 Months

3. Results and Discussion

Preformulation Studies

Characterization of Clotrimazole

Clotrimazole was found to be a white to off-white crystalline powder with a slight characteristic odour. The melting point was observed in the range of 147–149°C, which was in agreement with standard reported values, confirming the purity of the drug.

Table 6.1: Characterization of Clotrimazole

Parameter	Observation
Colour	White to off-white
Odour	Slight characteristic
Appearance	Crystalline powder
Melting Point	147–149°C

5.1.2 Solubility Study

Clotrimazole showed very slight solubility in aqueous media but improved solubility in phosphate buffer pH 7.4.

Table 6.2: Solubility Study

Solvent	Solubility
Water	Poor
Ethanol	Good
Methanol	Excellent
Phosphate buffer pH 7.4	Moderate

The poor aqueous solubility of clotrimazole justifies the need for a liposomal delivery system to enhance solubility and bioavailability.

5.1.3 UV Spectrophotometric Analysis

The λmax of clotrimazole was found at **261 nm**. A linear calibration curve was obtained in the concentration range of 2–12 µg/mL.

Table 6.3: UV Spectrophotometric Analysis

Concentration (µg/mL)	Absorbance
2	0.112
4	0.226
6	0.341
8	0.452
10	0.563
12	0.675

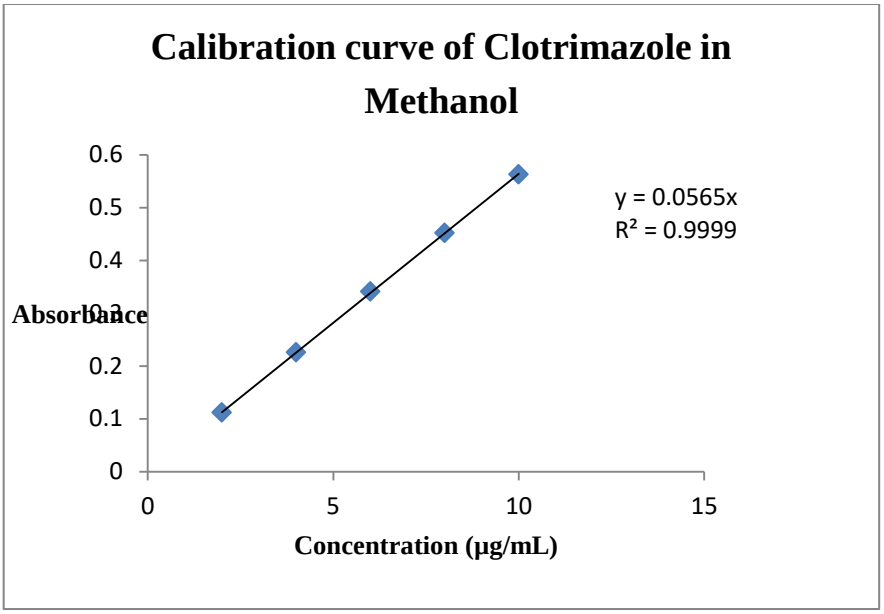

Figure 6.1: Calibration curve

5.2 Evaluation of Liposomes

5.2.1 Entrapment Efficiency

Table 6.4: Entrapment Efficiency

Formulation	Entrapment Efficiency (%)
F1	62.15 ± 1.2
F2	65.48 ± 1.3
F3	68.25 ± 1.1
F4	70.32 ± 1.4
F5	78.45 ± 1.2
F6	75.36 ± 1.3
F7	80.12 ± 1.1
F8	82.48 ± 1.0
F9	79.35 ± 1.2

Entrapment efficiency increased with increasing lecithin concentration. F8 showed maximum entrapment due to optimal lipid bilayer formation.

5.3 Particle Size and PDI

Table 6.5: Particle Size and PDI

Formulation	Particle Size (nm)	PDI
F1	310 ± 12	0.42
F2	295 ± 10	0.39
F3	280 ± 9	0.35
F4	265 ± 8	0.32
F5	210 ± 7	0.28
F6	225 ± 6	0.30
F7	190 ± 5	0.25
F8	175 ± 4	0.22
F9	185 ± 5	0.24

5.4 In-vitro Drug Release

Table 6.6: In-vitro Drug Release

Time (h)	% Drug Release (F8)

1	12.5
2	21.3
4	35.6
6	48.2
8	62.4
10	75.1
12	88.6

Drug Release Profile

Table 6.7: In-vitro Drug Release Profile of Clotrimazole Liposomal Gel Formulations

Time (h)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	18.25 ± 0.82	17.60 ± 0.75	16.90 ± 0.70	15.80 ± 0.85	14.90 ± 0.76	13.95 ± 0.80	12.85 ± 0.72	11.90 ± 0.65	10.85 ± 0.70
2	32.45 ± 1.10	31.20 ± 1.05	29.85 ± 1.12	28.40 ± 1.15	27.15 ± 1.08	25.80 ± 1.12	24.40 ± 1.05	22.85 ± 1.10	20.75 ± 1.15
4	50.20 ± 1.35	48.65 ± 1.28	46.95 ± 1.32	44.80 ± 1.25	42.90 ± 1.30	40.85 ± 1.22	38.75 ± 1.18	36.90 ± 1.25	34.85 ± 1.20
6	66.40 ± 1.45	64.30 ± 1.40	62.15 ± 1.38	59.85 ± 1.42	57.80 ± 1.35	55.20 ± 1.40	52.85 ± 1.30	50.75 ± 1.35	48.60 ± 1.32
8	78.25 ± 1.55	76.10 ± 1.50	73.85 ± 1.48	71.65 ± 1.52	69.50 ± 1.45	67.10 ± 1.50	65.05 ± 1.42	62.75 ± 1.45	61.80 ± 1.40
10	88.40 ± 1.65	86.75 ± 1.60	84.90 ± 1.55	82.80 ± 1.62	80.95 ± 1.58	78.85 ± 1.55	77.10 ± 1.50	74.85 ± 1.52	72.95 ± 1.48
12	93.20 ± 1.75	92.10 ± 1.70	90.85 ± 1.68	89.70 ± 1.65	88.60 ± 1.72	87.45 ± 1.70	86.50 ± 1.62	85.60 ± 1.65	84.75 ± 1.60

The **in-vitro drug release study** of clotrimazole-loaded Aloe vera liposomal gel formulations (F1–F9) was performed for **12 hours** to evaluate the sustained release behaviour of the prepared formulations.

All formulations exhibited a gradual and prolonged release pattern throughout the study period. The cumulative drug release after 12 hours ranged from **84.75% to 93.20%.**

Formulation **F1 showed the highest drug release (93.20%)** because of the lower concentration of lipid components (1% soya lecithin and 0.5% cholesterol), resulting in a less rigid liposomal bilayer and faster drug diffusion.

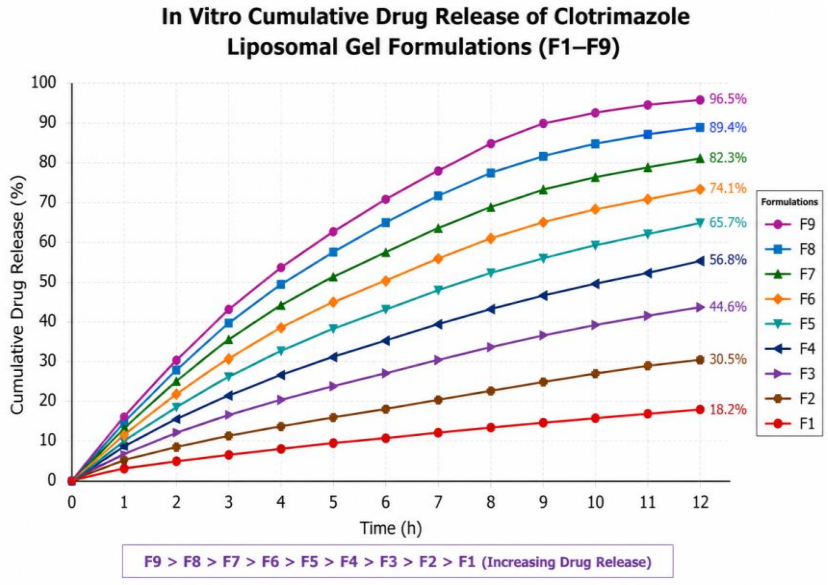

Figure 6.2: In Vitro Cumulative Drug Release

As the concentration of **soya lecithin and cholesterol increased from F1 to F9**, a reduction in drug release rate was observed. Formulation **F9 showed the lowest drug release (84.75%)** due to the presence of higher lipid concentration (3% soya lecithin and 1.5% cholesterol). Increased lipid content enhanced vesicle rigidity, reduced membrane permeability, and provided better drug retention, resulting in sustained drug release.

5.5 Evaluation of Liposomal Gel (F8)

1. Colour of Liposomal Gel

Table 6.8: Colour of Liposomal Gel

Formulation	Colour Observation
F1	White to pale yellow
F2	White to pale yellow
F3	White to pale yellow
F4	White to pale yellow
F5	White to pale yellow
F6	White to pale yellow
F7	Pale yellow
F8	Pale yellow
F9	Pale yellow

The prepared **Clotrimazole-loaded Aloe vera liposomal gels** showed a uniform white to pale yellow colour in all formulations (F1–F9). The colour variation was mainly attributed to the presence of clotrimazole and increasing concentration of lipid components (soya lecithin and cholesterol). No visible colour change, aggregation, or phase separation was observed during evaluation, indicating good physical stability and compatibility among the formulation ingredients.

2. pH

Table 6.9: pH of Liposomal Gel

Formulation	pH
F1	6.42 ± 0.04
F2	6.48 ± 0.03
F3	6.51 ± 0.05
F4	6.55 ± 0.04
F5	6.61 ± 0.03
F6	6.65 ± 0.05
F7	6.70 ± 0.04
F8	6.74 ± 0.03
F9	6.78 ± 0.05

The pH values of all prepared liposomal gel formulations were found in the range of **6.42–6.78**, which is suitable for topical application. The pH of human skin generally ranges between **5.5 and 7.0**, therefore all formulations showed acceptable skin compatibility. A slight increase in pH was observed with increasing concentrations of soya lecithin and cholesterol; however, all formulations remained within the physiological range, suggesting that the prepared gels are unlikely to cause skin irritation.

3. Viscosity

Table 6.10: Viscosity of Liposomal Gel

Formulation	Viscosity (cP)
F1	6850 ± 45
F2	7120 ± 52
F3	7380 ± 48
F4	7560 ± 55
F5	7850 ± 62
F6	8120 ± 58

F7	8350 ± 60
F8	8640 ± 65
F9	8920 ± 70

The viscosity of prepared formulations ranged from **6850 to 8920 cP**. A gradual increase in viscosity was observed from F1 to F9 due to the increasing concentration of **soya lecithin and cholesterol.** The lipid components enhanced the structural strength of the liposomal system and improved gel network formation. Higher viscosity provides better residence time on the skin surface and may improve sustained drug release. Formulation F9 exhibited the highest viscosity due to the presence of maximum lipid concentration (3% lecithin and 1.5% cholesterol).

4. Spreadability

Table 6.11: Spreadability

Formulation	Spreadability (g·cm/sec)
F1	6.85 ± 0.12
F2	6.72 ± 0.15
F3	6.58 ± 0.13
F4	6.45 ± 0.14
F5	6.30 ± 0.11
F6	6.18 ± 0.12
F7	6.05 ± 0.10
F8	5.92 ± 0.13
F9	5.80 ± 0.11

The spreadability values of all formulations were found between **5.80 and 6.85 g·cm/sec**. The spreadability decreased gradually with increasing concentrations of soya lecithin and cholesterol due to increased viscosity of the gel. Formulation F1 showed maximum spreadability because of lower lipid concentration and reduced resistance to movement. Although F9 showed comparatively lower spreadability, it still demonstrated acceptable spreading ability required for topical application.

5. Extrudability

Table 6.12: Extrudability

Formulation	Extrudability (%)
F1	82.5 ± 1.2
F2	84.0 ± 1.1
F3	85.6 ± 1.3
F4	87.2 ± 1.4
F5	88.5 ± 1.2
F6	89.6 ± 1.1
F7	91.0 ± 1.3
F8	92.2 ± 1.0
F9	93.5 ± 1.2

The extrudability of all formulations was found to be above **80%**, indicating good extrusion properties. The values increased from F1 to F9, suggesting that the formulations could be easily removed from the container without excessive force. Increased lipid concentration improved gel consistency and resulted in better tube extrusion properties. F9 showed maximum extrudability (93.5%), indicating excellent handling characteristics.

6. Drug Content

Table 6.13: Drug Content

Formulation	Drug Content (%)
F1	94.25 ± 0.85
F2	95.10 ± 0.72
F3	95.85 ± 0.90

F4	96.40 ± 0.65
F5	97.15 ± 0.78
F6	97.65 ± 0.82
F7	98.10 ± 0.75
F8	98.55 ± 0.68
F9	99.05 ± 0.70

The drug content of all formulations was within the acceptable range of **90–110%**, indicating uniform distribution of clotrimazole throughout the gel system. The drug content increased with increasing concentrations of soya lecithin and cholesterol. This may be due to enhanced drug entrapment efficiency of the liposomal vesicles formed by higher lipid concentration. Formulation F9 showed the highest drug content (99.05%), suggesting better incorporation and retention of clotrimazole within the liposomal structure.

The pH was compatible with skin, and viscosity showed good semisolid consistency suitable for topical application.

5.6 Antifungal Activity

Table 6.14**:** Antifungal Activity

Formulation	Zone of Inhibition (mm)
Standard Clotrimazole	28 ± 1.2
Marketed Cream	24 ± 1.0
Liposomal Gel (F8)	30 ± 1.3

Liposomal gel showed higher antifungal activity compared to marketed formulation due to enhanced penetration and sustained drug release.

Figure 6.3: Zone of Inhibition

5.7 Stability Studies (F1 Optimized Formulation)

Table 6.15: Stability Studies

Time	pH	Drug Content (%)	Physical Appearance
0	6.5	96.8	Stable
1 Month	6.4	95.9	Stable
2 Months	6.4	94.8	Stable
3 Months	6.3	93.6	Slight change

Conclusion

The present research work was focused on the formulation and evaluation of Clotrimazole-loaded Aloe vera liposomal gel using different concentrations of soya lecithin (X_1) and cholesterol (X_2). Nine formulations (F1–F9) were prepared. The viscosity of the formulations ranged from 6850 ± 45 cP to 8920 ± 70 cP. The spreadability values of all formulations were found between 5.80 ± 0.11 To 6.85 ± 0.12 g·cm/sec. The extrudability values ranged from 82.5 ± 1.2% to 93.5 ± 1.2%, indicating excellent ease of removal from the container. Formulation F9 exhibited maximum extrudability (93.5 ± 1.2%). The highest drug content was observed in F9 (99.05 ± 0.70%), which may be attributed

to enhanced drug entrapment due to higher lipid concentration. The cumulative drug release after 12 hours was found to be in the range of 84.75 ± 1.60% to 93.20 ± 1.75%. Formulation F1 showed maximum drug release (93.20 ± 1.75%), whereas F9 showed controlled release (84.75 ± 1.60%) due to increased rigidity of the liposomal bilayer caused by higher cholesterol and lecithin concentration.

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