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Formulation, Development and Evaluation of Posaconazole Loaded Invasomal Gel for Topical Applications

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ABSTRACT

Topical drug delivery allows for localized treatment through various routes such as ophthalmic, rectal, vaginal, and cutaneous. For skin diseases caused by fungi, antifungal agents like Posaconazole are utilized. This study aimed to develop and evaluate Posaconazole-loaded Invasomal gels, enhancing topical drug delivery. Invasomes were created using a mechanical dispersion method with phosphatidylcholine, terpenes, and ethanol. Formulations (F1-F6) were assessed for appearance, pH, vesicle size, drug content, entrapment efficiency, zeta potential, and in-vitro drug diffusion. The vesicle size ranged from 206 to 262 µm, with drug content between 74.40% and 81.35%. The entrapment efficiency varied from 52.56% to 82.49%, with formulation F5 showing the highest drug diffusion of 92.78% after 8 hours. The optimized Invasomal gel (IG-2) showed favorable properties including a pH of 5.2, viscosity of 3156 cps, and drug diffusion of 91.77%. Stability studies confirmed IG-2's stability over time. This study demonstrates that Invasomal gels can significantly enhance the bioavailability of topical antifungal treatments.

Keywords: Invasomes, Phosphatidylcholine, Terpenes, Ethanol, Mechanical Dispersion.

INTRODUCTION

Transdermal drug delivery systems

Transdermal delivery systems eliminate the need for injections or oral consumption by providing an alternate route of distribution to the systemic circulation. The stratum corneum, the skin's outermost layer, serves as the body's main barrier, protecting the skin from potentially hazardous environmental

substances and limiting the amount of moisture that escapes into the outside world. Intercellular lipids in the stratum corneum are essential for preserving the skin's equilibrium and supporting both its protective and general integrity.[1]Transdermal medication delivery allows for the direct injection of bioactive molecules into the systemic circulation while avoiding hepatic metabolism, increasing patient compliance, and reducing the chance of tissue harm. By offering a practical and efficient way to take medication while reducing the possibility of adverse effects connected with alternative routes of administration, this strategy constitutes a substantial development in pharmaceutical delivery.[1,2] Transdermal delivery is becoming more and more popular in formulation development since it increases the bioavailability of many medications. Nevertheless, medications used topically have the potential to negatively impact the epidermal barrier. This effect highlights how crucial it is to give careful thought to formulation optimization in order to minimize potential adverse effects and maximize therapeutic efficacy.[2,3] Vesicular systems have attracted a lot of interest lately as possible drug carrier systems for transdermal and cutaneous medication delivery. To increase the number of medications that are feasible for transdermal administration, new drug delivery methods must be investigated. Drug permeability through the skin is improved by a variety of chemical procedures using liposomes, invasomes, transferosomes, and ethosomes, as well as physical techniques like iontophoresis, sonophoresis, microneedles, and penetration enhancers. These methods present viable ways to enhance transdermal medication delivery's adaptability and effectiveness, enhancing patient care and therapeutic results.[4-6] Drugs that are hydrophilic or lipophilic can be incorporated into liposomal vesicular systems with flexibility, which facilitates the incorporation of agents into the skin. Because of their better ability to penetrate drugs and interact with the skin, novel elastic vesicles-which feature penetration enhancers-outperform conventional liposomes.

Invasomes

Liposomal vesicles known as invasomes contain small amounts of ethanol and terpenes, or terpene combinations, and they have the ability to penetrate the skin more deeply than other carriers. When it comes to skin penetration, invasomes are more common than liposomes and ethosomes. Improved drug efficacy, patient compliance, and comfort are just a few of the benefits that come with invasomes.[7,8] Invasomes are a unique category of vesicles that are generally responsible for improving the transdermal penetration of active medicinal substances. These vesicles' structure

includes phospholipids, ethanol, and unique terpenes or terpene combinations. As These components exhibited remarkable transdermal penetration abilities.

Advantages of Invasomes

- Non-invasive drug delivery method.
- Drugs that are both lipophilic and hydrophilic can be delivered.
- Has non-toxic raw materials in its composition.
- Compliance among patients since the medication can be applied in a semisolid form (cream or gel).
- An easy approach to administering drugs in contrast to iontophoresis, phonophoresis, and other complex methods.

Disadvantages of Invasomes

- The high expense of production.
- Drug/molecule leakage and fusion.
- Potential phospholipid hydrolysis/oxidation that could compromise the stability of the formulations.

Composition

Little amounts of ethanol are present in the soft liposomal vesicles known as invasomes, which can function as carriers with enhanced skin penetration. They also include different terpenes or terpene combinations. Along with terpenoids (such citral, limonene, and cineole), water, and a small amount of ethanol (around 3-3.3 percent by volume), they also contain phospholipids and somewhat alcohol. Terpenoids (such as eugenol and citral), water, and ethanol are other ingredients. Terpenes (C_5H_8) have a generic formula that helps with the absorption of hydrophilic and hydrophobic drugs together. Essential oils terpenes are frequently employed as penetration enhancers. Terpenes are less irritating to the skin in little doses. The FDA likewise views terpenes as safe.[9] Invasomes having the composition of Ethanol, Terpenes and Phospholipids.

MATERIALS AND METHODS

Materials:

The drug Posaconazole was purchased from Yarrowchem products, Mumbai.Other materials used in research work with analytical grades are used as supplied by manufacturer. Distilled water used throughout the study.

Methods:

A. Formulation of Posaconazole loaded Invasomes:

Posaconazole (100mg) was loaded in to invasomes by mechanical dispersion technique as per Table 1. Following a five-minute vortex, 0.5 to 0.75% w/v of soy phosphatidylcholine was added to ethanol. After adding the drug and terpenes (0.25% to 0.75%) and continuously vortexing the mixture, it was sonicated for five minutes. Fine stream of Phosphate buffer saline (upto 10% w/v) was added with syringe under constant vortexing.[10-13] For an extra five minutes, it was vortexed to obtain the invasomal preparation.

Table 1: Formulation Table of Posaconazole loaded Invasome

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Posaconazole (mg)	100	100	100	100	100	100
Phosphatidylcholine (%w/v)	0.25	0.5	0.75	0.25	0.5	0.75
Terpenes (%v/v)	0.25	0.25	0.50	0.50	0.75	0.75
Ethanol (ml)	10	10	10	10	10	10

B. Preparation of Invasomal Gel:

To achieve the necessary drug concentration in the gel base, invasomes preparation equivalent to 0.1% w/w of medication was added.The gel was sonicated on a bath sonicator for 10 minutes at a volume of 100 ml in order to eliminate air bubbles. The pH was finally adjusted to 6.5. The already prepared Invasomes formulation was added to the Invasomes-containing gel, which was made using the same process. After adding 0.05 N sodium hydroxide solution dropwise to the mildly acidic solution that as formed, mixing was repeated until the gel turned translucent.After an hour of constant stirring at 800-1200 rpm, 10 milliliters of propylene glycol wasadministered to the mixture. Specifically weighed, Carbopol 940 (0.5-1.5% w/v - Invasome based gel formulation, i.e., IG-1 of 0.5% w/v, IG-2 of 1.0%

w/v, and IG-3 of 1.5% w/v) was distributed into 80ml of double distilled water in a beaker by stirring.[14, 15] Gel was prepared by taking ingredients mentioned in Table 2.

Table 2: Formulation table of Invasomal Gel containing Posaconazole

Ingredients	IG-1	IG-2	IG-3
Drug (Invasomes equivalent to 0.1%)	0.1	0.1	0.1
Carbopol 940 (gm)	0.5	1	1.5
Propylene glycol (ml)	10	10	10
Water (ml)	Upto100	Upto100	Upto100

C. Evaluation of Invasomes

a. Appearance:

The drug loaded Invasomal dispersion was evaluated for appearance by visual perception.

b. pH:

The pH values are measured for invasomes formulation batch F1 to F6 using a digital pH meter of a glass electrode. pH essentially indicates the level of hydrogen ion activity in a solution. A certain amount of the formulation was taken and diluted with calibrated distilled water and mixed well. To measure the pH value, the electrode was immersed in the prepared formulation.

c. Vesicle Size and Shape:

The average size of produced invasomes was measured using microscopic analysis [6]. The glass slide was taken and one drop of the mixture was applied, followed by a cover slip and distilled water dilution. Using a trinocular microscope, the slide was examined at 400 X magnification. Over 150 vesicles had their diameters randomly measured using an electroscopic microscope, an ocular micrometer, and a stage micrometer that were calibrated. Utilizing Saglo software, one may ascertain the microscopic composition of invasomes.

d. Drug content analysis:

After lysing the invasomes in 95% ethanol and thoroughly shaking the vesicles to ensure full lysis, the dosage of the drug in the formulation was calculated. After suitable dilution with the PBS pH 7.4 the absorbance of the solution was measured at 262 nm in the UV visible spectroscopy using empty invasomes as blank. Using a formula, the %drug content was determined from the standard curve.

% Drug content = (Sample absorbance /Standard absorbance) × 100

e. Entrapment Efficiency (EE):

Invasomes entrapment efficiency was estimated by Ultracentrifugation method where the dispersion of invasomes centrifuged at 15000 rpm for 90 minutes. The clear supernatant from the resulting centrifuged solution was diluted using pH 7.4 phosphate buffer and analyzed for Posaconazole spectrophotometrically and the percentage entrapment efficiency then calculated by using following formula.

% Entrapment Efficiency = [(Total drug - Diffused drug)/ Total drug] × 100

f. Zeta Potential:

The microemulsion 1ml was dispersed in a disposable zeta cell. Palladium electrode was inserted in distilled water in the cuvette and the analysis was performed at 25°C.The calculations were carryout in triplicate fashion and average value was reported, which measures the distribution of the electrophoretic mobility of particles using the laser Doppler velocity technique.

g. In-vitro drug diffusion studies:

The membrane diffusion technique was used to study the in-vitro drug diffusion of the invasomal formulation. In-vitro diffusion cell was made using cellophane membrane which was previously soaked in warm water for activation. The diffusion cell consists of a beaker, magnetic stirrer with temperature control and test tube with both ends open. One end of the test tube was closed using treated cellophane membrane and the other end was kept open to introduce invasomal formulation. The diffusion medium was freshly prepared PBS (pH 7.4) of 100 ml and maintained temperature 37°C± 0.5 °C. The invasomal formulation 5ml was placed inside the diffusion cell through open end of the test tube on the cellophane membrane. To maintain a constant volume (sink condition), aliquots (5 ml) of the medium were periodically removed and replaced with fresh PBS (pH 7.4) diffusion media. The samples were analyzed for drug using UV-Visible spectrophotometer at 262 nm.

h. Stability study:

The International Conference on Harmonization "(ICH Q1A (R2)" [ICH, 2003] was used to conduct stability studies of novel drugs and products. A stability study was carried out on the improved formulation (F5) of the Posaconazole invasome. The mixture was placed in a 20 ml glass vial that was sealed and kept for three months at 4 ± 2°C. Every month, samples from each batch were taken out and their in-vitro drug release and entrapment efficiency analyzed.

D. Evaluation of Invasomal gel

a. Appearance:

To find out if any particular material was present, the formulations were tested. One of the most crucial aspects of the topical formulations is their clarity. Visual assessment is used to determine appearance and clarity.

b. pH:

pH of the produced formulations was checked by using a digital pH meter. Small amount of Invasomal gel was diluted in 20ml of distilled water and the pH is measured by dipping the glass electrode of the Digital pH meter and the reading is noted.

c. Viscosity:

The viscosity OF formulations was assessed using an Ametek DV2T Brookfield viscometer equipped with an S-6 spindle running at an ideal 50 rpm. The percentage of drug diffused from the preparation decreases with increasing viscosity.

d. Spreadability:

An instrument that includes a wooden block with a pulley at one end determines the Spreadability. The "Slip" and "Drag" properties of the invasomal gel are used to calculate the Spreadability. This block has a fixed ground slide. This ground slide has an excess of the invasomal gel under evaluation (about 2 grams). Next, place this slide and another glass slide between the invasomal gel. To create a consistent layer of Invasomal gel between both the slides and release any trapped air, a 1 kg weight is positioned on top of each slide for a duration of 5 minutes. With a weight of one kilogram, the amount of time (measured in seconds) needed for the upper slide for moving 7.5 cm with the

assistance of a string connected to the hook is recorded. Better the Spreadability shorter the interval, as determined by the formula.

$$S = M \times L/T$$

Where,

S= Spreadability

L= Length of glass slides

M= Weight tied to upper slides (1 kg)

T= The amount of time needed to split

e. Extrudability Study:

Extrudability was measured by measuring the quantity of the gel that extruded from a collapsible tube under particular stress conditions.[9] Better extrudability is indicated by a larger extrusion volume. By adding weight to the gel-filled tube, the weight is determined on the basis of extruded amount of gel from the collapsible tube.

f. Drug Content:

A beaker containing 1g of Invasomal gel was accurately weighed, 20 ml of methanol was added, and the mixture was swirled for 30 minutes.[8] Whatman filter paper No. 1 was used for filtering after the solution had been thoroughly mixed. Subsequently, 1.0 mL of the filtered solution was added to a volumetric flask having a 10 mL capacity, and the volume was increased to 10 mL using methanol. The UV Spectroscope was used to determine this solution at λ_{max} 260 nm. The calibration curve was used to calculate the drug content.

g. In-Vitro Drug Diffusion Studies:

Diffusion cells are used to conduct the in-vitro diffusion studies. The glass cylinder that consists the diffusion cell is hollow. The dialysis membrane was placed over one end of the cylinder after being soaked in warm water for a whole day. The 500 ml beaker that was used as the receptor cell held the diffusion cell. The receptor compartment has an effective capacity of about 100 ml and an effective permeation surface area of 3.14 square centimeters. A two-centimeter patch was measured, weighed, and then applied to one side of the membrane that faced the donor compartment. The receptor media is 100 ml of PBS with a pH of 7.4. The receptor chamber is enclosed by a water jacket to maintain a

temperature of 32±0.5°C. Heat is produced using a thermostatic hot plate and a magnetic stirrer. The receptor fluid is stirred by inserting a Teflon-coated magnetic bead into the diffusion cell. At prearranged intervals, fresh buffer saline (pH 7.4) was introduced to the medium volume when the sample was removed.

h. Stability Studies:

For three months, an accelerated stability study was carried out on drug-loaded invasomal gel at a temperature of 40±2°C and a relative humidity of 70±5%. To prevent any interactions between the formulation batches and the container's glass, the formulation that was the topic of the stability investigation was kept in a borosilicate container. The stability study was done to evaluate the effect of storage conditions on essential parameters of gels such as Appearance, pH, Viscosity, Drug content and In-vitro diffusion studies after specified time intervals.

RESULTS AND DISCUSSION

Evaluation Parameters of Invasomes:

a. Appearance:

The Invasomal dispersion was Yellow-Golden in colour. It was stable and did not show sedimentation.

b. pH Measurement:

The pH of the chosen optimum formulations (F1–F6) was measured using a digital pH meter. The pH was discovered to be between 6.2 and 6.8.

c. Vesicle Size and shape:

The size of the vesicle ranged from 206-262 μm (Table 3). Additionally, the form of the intrasomal vesicle was a little round. Figure 1 shows microscopic structure of invasomes.[16,17]

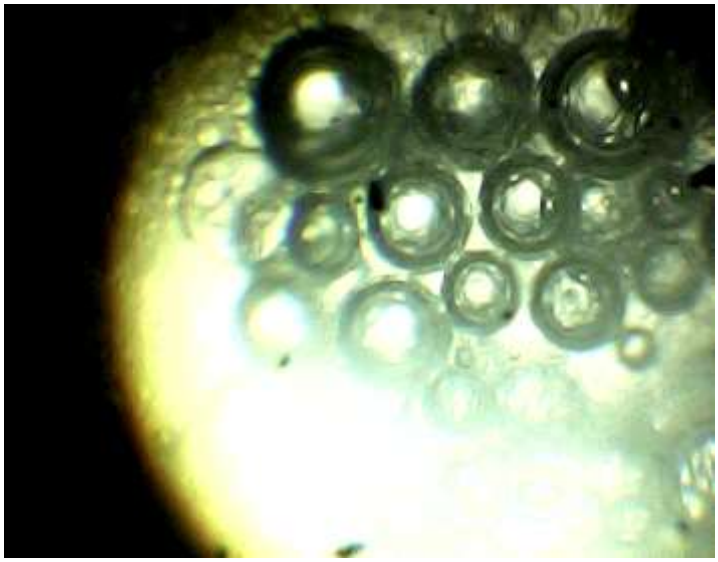

Figure 1: Microscopic structure of Invasomes

Table 3: Vesicle size (μm)

Sr. No.	Formulation code	Vesicle Size (μm)
1	F1	256.45±0.23
2	F2	242.65±0.14
3	F3	230.64±0.32
4	F4	218.87±0.78
5	F5	206.10±0.12
6	F6	262.45±0.44

d. Drug Content:

The maximum % drug content is shown in Formulation F5, but the drug content was confirmed to be acceptable for all formulations, ranging from 74.40% to 81.35%. Table 4 detailed appearance, pH & % drug content of all 6 batches

Table 4: Appearance, pH & %Drug Content of all 6 Batches

Formulation code	Appearance	pH	%Drug content
F1	Yellow-Golden	6.3	74.40

F2	Yellow-Golden	6.4	75.98
F3	Yellow-Golden	6.6	76.55
F4	Yellow-Golden	6.6	77.67
F5	Yellow-Golden	6.7	81.35
F6	Yellow-Golden	6.8	80.25

e. % Entrapment Efficiency (EE):

It was discovered that the Posaconazole Invasomes' Entrapment Efficiency (EE) ranged from 52.56% to 82.49%. The results (Table 5) showed that, F5 has a greater entrapment efficiency because of the presence of terpenes at 0.75%v/v and phosphatidylcholine at 0.5%v/v, while ethanol was kept at a constant percentage. The entrapment efficiency in the F5 formulation increases with the concentration of PC (lecithin) and terpenes, but decreases with further increase in the content of phosphatidylcholine.

Table 5: Entrapment Efficiency of all 6 batches

Sr. No.	**Formulation code**	**% Entrapment efficiency**
1.	F1	52.56
2.	F2	58.63
3.	F3	65.52
4.	F4	74.69
5.	F5	82.49
6	F6	78.45

f. Zeta Potential and Particle Size:

The zeta potential of the F-5 batch is measured at -63.0 mV, with an electrophoretic mobility of -0.000489 cm^2/Vs. This negative zeta potential suggests that the particles in the formulation are well-stabilized, as the high negative value typically indicates strong repulsion between particles, reducing the likelihood of aggregation. (Table 6, Figure 2)

Table 6: Zeta Potential of F-5 Batch

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-63.0mV	-0.000489cm2/Vs

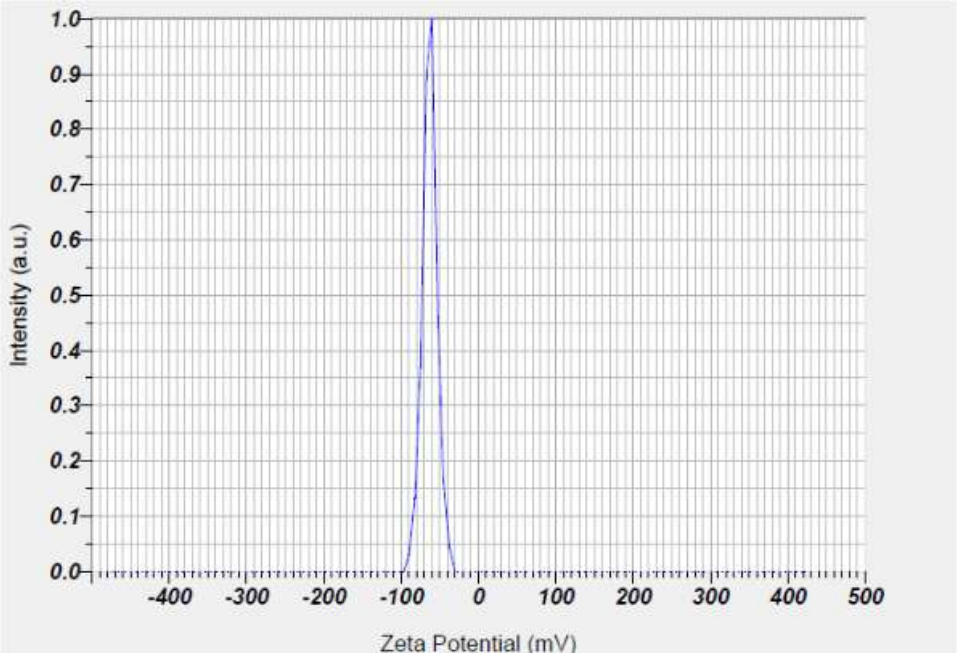

Figure 2: Graph of Zeta Potential (mV)for optimized formulation F-5

Z- Average: 206.10 nm

Polydispersity Index (PDI): 0.338

The particle size analysis shows an average size of 206.10 nm for the optimized F-5 formulation, with a polydispersity index (PDI) of 0.338. The PDI indicates a relatively moderate level of size distribution uniformity, suggesting that the particles are not highly monodisperse but are reasonably uniform in size. The table also lists the mean, standard deviation (S.D.), and mode for a peak area ratio of 1.00, showing values of 163.6 nm, 251 nm, and 160.2 nm, respectively. This data confirms that the particle sizes are close to the Z- average, with some variation in the measured values. (Table 7, Figure 3)

Table 7: Average particle size (nm) and PDI

Peak No.	S.P. Area Ratio	Mean	S.D.	Mode
1	1.00	163.6nm	251nm	160.2nm
Total	1.00	163.6nm	251nm	160.2nm

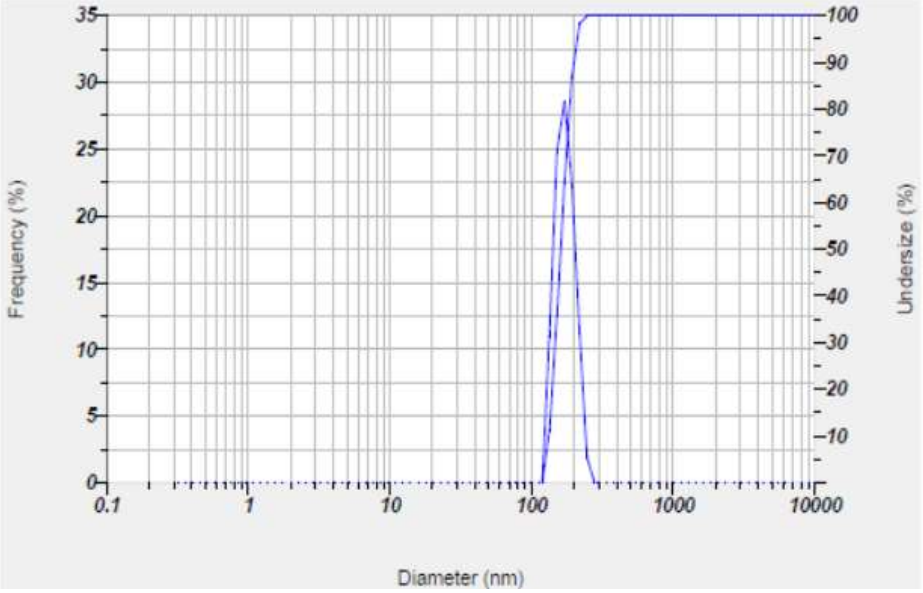

Figure 3: Graph of average vesicle size (nm) of optimized formulation F-5

g. In-vitro drug diffusion studies:

The drug diffusion at 8 hours 92.78% was for the formulation F5 where is it was 67.88%, 76.69%,80.78%, 79.24%,71.78% for F1, F2, F3, F4, F6 respectively. Significant changes in release were observed upon altering the conc. of Phosphatidylcholine and Terpenes. In Invasomal formulations the experimental studies proved that the rate of drug release depends on the percentage of drug entrapment efficiency.From the release studies of F5 showed (Table 8, Figure 4)the slower and prolonged drug diffusion as compared to the other formulations. This is due to higher entrapment efficiency.

Table 8: In-vitro drug diffusion

Time (hr)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	9.15	10.25	12.45	8.65	8.35	14.56
2	16.36	18.63	22.78	17.78	19.54	19.46
3	19.56	23.58	28.65	25.47	32.88	25.78
4	20.63	28.56	37.45	36.12	46.89	39.45
5	35.89	39.45	45.96	48.47	58.78	48.78
6	46.58	55.32	60.75	60.88	72.89	57.12
7	58.78	64.78	70.58	68.38	85.27	66.46
8	67.88	76.69	80.78	79.24	92.78	71.78

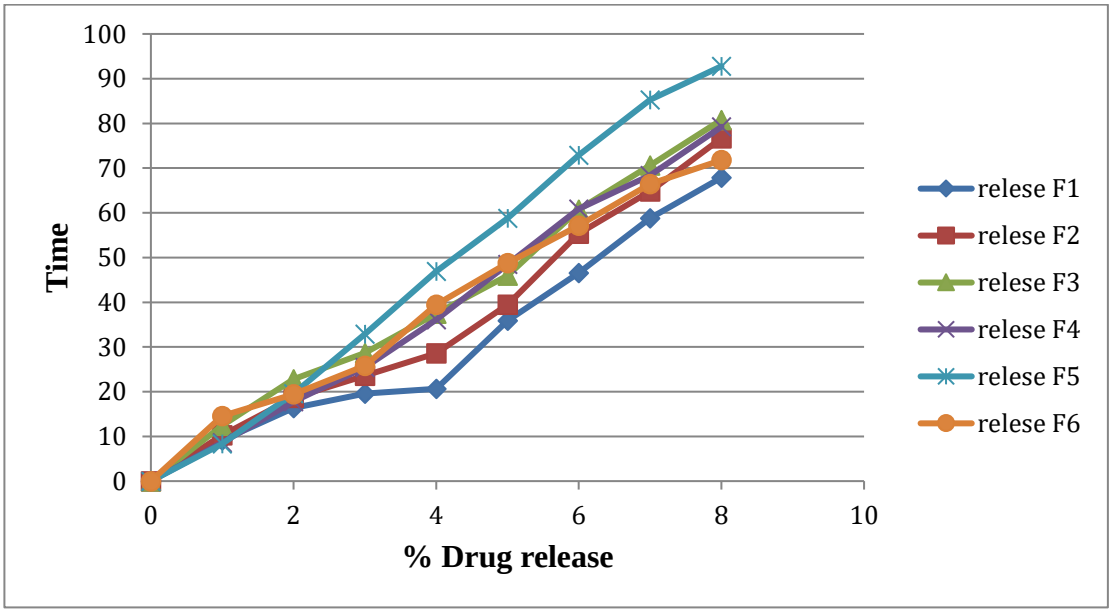

Figure 4: In-vitro drug diffusion study of All 6 Batches

h. Stability studies:

The stability study of the optimized Posaconazole Invasomal formulation (F5) was carried out at 4±2°C. At the interval of one, two and three months the invasomes evaluated for Appearance, pH,

%Drug content, %Entrapment efficiency and in-vitro drug diffusion. The stability study showedin Table 9that Invasomal formulations are more stable at 4°C (refrigerator) temperature.

Table 9: Stability studies of optimized formulation F5 at 4±2°C

Parameters	**Initial**	**After 1 Month**	**After 2 Month**	**After 3 Month**
Appearance	Yellow-Golden	No Change	No Change	No Change
pH	6.7	No Change	No Change	No Change
%Drug content	81.35	81.35	81.26	81.12
%Entrapment efficiency	82.49	82.49	82.36	82.24
% In-vitro drug diffusion	92.78	92.78	92.65	92.52

Evaluation parameters of invasomal gels:

a. Appearance:

The appearance of Invasomal gel was translucent and off-white in colour.

b. pH:

The pH range of 5.2 to 5.8, which is suitable for skin pH, was discovered. The pH of every Gel formulation was proven to be closer to that needed for skin.

c. Drug content:

The drug content of the topical gel was measured using spectrophotometry at 262 nm. All the formulations exhibited fairly uniform drug content. This indicates the drug is delivered to the desired site of action after gel is topically applied. The drug content was found to be within an acceptable range for each formulation. The results revealed that all created formulations had a drug concentration between 86 and 88%as shown in Table 10.

Table 10: Evaluation Parameters of Invasomal gel

Gel formulation	Appearance	pH	%Drug content
IG-1	Translucent	5.8	86.65
IG-2	Translucent	5.2	88.54
IG-3	Translucent	5.6	87.26

d. Viscosity:

The viscosities of the produced gels were measured using a Brookfield viscometer. For testing the viscosity of the invasomal gels, the Spindle No. 6 is employed at 50 rpm. The viscosities of the three batches, IG-1, IG-2, and IG-3, were found to be 2780, 3156, and 4230 cps, respectively. further testing confirmed the findings that viscosity decreases with increasing viscometer rotational speed, suggesting that easier Spreadability is favored by higher shearing and lower viscosity.

e. Spreadability:

Spreadability is important for patient compliance since it ensures uniform Gel administration throughout a larger surface area. The IG-2 formulation gives the spreadability of 16.40 gms.cm/sec. The Gel dispersed readily and didn't exhibit any grittiness, as seen by its low spreadability coefficient value. The lower spreadability score, which also means that less force was required to spread the gel when applied on the skin.

f. Extrudability:

Extrudability was measured as the volume of gel that extruded from a collapsible tube under particular load conditions. Better extrudability is indicated by a larger extrusion volume. It was done by addition of the wt. on the collapsible tube and noting the weight at which the gel extruded from the tube.Table 11 depicted viscosity, spreadability and extrudability of invasomal gels

Table 11: Viscosity, Spreadability and Extrudability of Invasomal gels

Gel formulations	Viscosity(cps)	Spreadability (gm.cm/sec)	Extrudability(gm)
IG-1	2,780	20.45	210
IG-2	3,156	16.40	224
IG-3	4,230	22.78	245

g. *In-vitro* drug diffusion studies:

The formulated gel formulations released 88.46% **(**IG-1), 91.77% (IG-2), 87.69% **(**IG-3) of drug after 8 hours as shown in the table no. 12.In IG-2 formulation conc. of carbopol 940 have shown good *in-vitro* drug release.

Table 12: In-vitro drug diffusion study of Invasomal Gels

Time (hrs.)	IG-1	IG-2	IG-3
1	10.5	9.5	9.8
2	25.45	27.56	26.25
3	36.89	39.36	33.45
4	49.26	50.89	48.88
5	61.10	66.78	63.14
6	75.48	78.45	76.98
7	82.56	85.72	81.74
8	88.46	91.77	87.69

h. Accelerated stability studies:

The accelerated stability study conducted as per ICH guidelines suggested that the optimized gel formulation (IG-2) maintains its physical appearance, viscosity, and pH consistently over three months (Table 13). The drug content shows only a minor decrease, suggesting that the formulation is relatively stable under accelerated conditions. These results are promising, indicating that the formulation is likely to remain stable over its intended shelf life under normal storage conditions.

Table 13: Accelerated stability studies of optimized gel formulation (IG-2)

Parameters	Initial	After 1 month	After 2 months	After 3 months
Appearance	Translucent	No Change	No Change	No Change
Viscosity	3,156cps	No Change	No Change	No Change
pH	5.2	5.2	5.2	5.2
% Drug Content	88.54	88.54	88.30	88.14

CONCLUSION:

The formulation, development and evaluation of Posaconazole-loaded invasomes and their corresponding gels have demonstrated promising advancements in transdermal drug delivery systems. The optimized formulation, F5, showed superior characteristics including high entrapment efficiency (82.49%), stable vesicle size (206.10 µm), and effective in-vitro drug release (92.78%). The invasomal gels, particularly IG-2, exhibited optimal drug content (88.54%), favorable viscosity (3156 cps), and excellent spreadability (16.40 gm.cm/sec), making them suitable for topical applications. Stability studies confirmed the formulations' robustness under controlled conditions, with no significant degradation in drug content or release profiles. These findings highlight the potential of invasomal systems to enhance drug delivery, improve patient compliance, and minimize adverse effects, offering a significant advancement in pharmaceutical formulation.

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