FORMULATION AND EVALUATION OF UFASOMAL GEL LOADED WITH POSACONAZOLE FOR TREATMENT OF FUNGAL INFECTION

Shabnam[1]*, Dr. Rajesh Gupta[2], Dr. Nitan Bharti Gupta[3], Hardeep Kaur[4], Ritika Sharma[5], Shaveta Prabhakar[6], ShvetaDevi Billowria[7], Daljeet kaur[8], Shikha[9].

[1, 6, 7, 8,9]Student, Sri Sai college of Pharmacy, Badhani, Pathankot, 145001, India.

[2]Principal, Sri Sai college of Pharmacy, Badhani, Pathankot, 145001, India.

[3]Professor, Sri Sai college of Pharmacy, Badhani, Pathankot, 145001, India.

[4,5]Associate Professor, Sri Sai college of Pharmacy, Badhani, Pathankot, 145001, India.

***Corresponding Author**

***E- mail:** shabnamguleria400@gmail.com*

Contact no. 8360879263

Abstract:

In the present research work ufasomal gel was developed for an effective treatment of fungal infection using posaconazole as model drug. The ufasomes were prepared by thin film hydration method using Oliec acid and drug of molar ratio 8:2. The ufasomal gels were prepared by dispersion method using Carbopol 934 as a gelling agent. The vesicles were characterized on the basis of entrapment efficiency, vesicle size, Poly dispersity Index, Zeta potential, morphological Characterization of ufasomes, SEM. The ufasomal gels were evaluated on the basis of Physical appearance, Drug Content, pH, Rhelogical studies, spreadability, Extrudability, In vitro drug release studies, and stability Studies.

Keywords: Posaconazole, Ufasomes, vesicles, gel, antifungal.

Introduction

Fungal infections are a significant risk to the public, specifically in people with diverse conditions like COVID-19, where they can lead to potentially fatal mycoses. These infections can occur in many different forms, ranging in severity from mucosal to superficial to subcutaneous to cutaneous infections. Immunosuppressive therapies create patients more predisposed to opportunistic infections by pathogens like Candida spp., which end up in situation like invasive candidasises, which can belief threatening. Fungi like Aspergillus, Fusarium, Candida, and molds can cause infections linked to healthcare as well as systemic or opportunistic illnesses in patients with underlying medical conditions.

Annually, fungal sickness consume the lifetimes of over a billion people globally and trigger over 1.5 million deaths. Significantly greater danger of severe fungus infections is associated with conditions such as asthma, cancer, AIDS, corticosteroid medication, and organ transplantation. While the majority of fungi are benign, several can be quite dangerous, especially to those with compromised immune systems. The increasing number of persons with immune-compromising illnesses like diabetes, cancer, and AIDS is contributing to the frightening global incidence of fungal diseases[1].

Fungal infections can take both widespread and superficial forms. Invasive a mold can cause systemic infections that can be fatal, affecting organs like the cartilage, brain's activity, eyes, and blood[12]. Tens of millions of people deal with mucosal candidiasis, and serious fungal illnesses affect an estimated 150 million individuals worldwide, with several instances being deadly or substantially limiting quality of life. Around one billion individuals suffer from fungal diseases of the skin, nails, or hair, which can range from benign mucocutaneous infections to fatal systemic infections. Each year, fungal diseases cause around 160,000 fatalities worldwide[2]. Fungal infections, frequently referred to as mycoses, are defined according to the affected body portion as apparent subcutaneous, or systemic. Common cutaneous tineas (such as those located on the abdomen, groin, hands, feet, and beard) and yeast infections such as pityriasis versicolor are indications for superficial fungal diseases. Although not all fungus are toxic, many are widely distributed in the environment.

Antifungals can be classified as fungal killer or fungistatic based on whether they truly eliminate the mold or stop it from growing.Mucous membranes are fungus infections' primary targets. Millions of people worldwide are impacted by superficial infections such as yeast vaginitis and oral thrush, which affect the skin or mucous membranes. However, they rarely cause death. In a short length of time, most superficial fungal infections can be successfully cured. Fungal that reach into the circulatory system may trigger aggressive infections, which are often lethal. Since invasive fungal infections are becoming more common, it is more important than ever before to carefully select and distribute antifungal medications[3].

Amphotericin B, flucytosine, echinocandins (such as caspofungin), and triazole antifungals were medications taken to treat invasive fungal infections. Posaconazole is a novel triazole antifungal medications that has broad-spectrum activity. Posaconazole and itraconazole vary principally in their molecular makeup, with fluorine substituting chlorine and a furan ring replacing the dioxolane ring. Posaconazole is being found to be a successful antifungal treatment in immunocompromised persons with serious filamentous fungal infections, including the throat and oesophageal candidiasis. Posaconazole, a highly lipophilic triazole antifungal medicine, was recently approved. It has effective and general-purpose anti-fungal properties versus a wide range of Zygomycetes, endemic fungi, Aspergillus species, Candida spp., and skin disorders, both in vitro and in vivo. Posaconazole has already been shown in trials to be more effective and provide a greater spectrum of activity than fluconazole against clinically relevant strains of Aspergillus spp., C. neoformans, and Candida species. This novel triazole is aimed at combating fungal infections, which are especially prevalent in individuals with major immune system deficiencies, such as those undergoing cancer treatment or organ donation[4].

Posaconazole is the second generation triazole drug that has strong and broad antifungal activity in vitro against a wide range of fungal infections, including Aspergillus or Candida species. Its identical structure to itraconazole leads it to inhibit CYP51 (lanosterol 14α-demethylase), therefore preventing the formation of ergosterol. Precursors that may have fungicidal or fungistatic actions accumulate as a result, decreasing the stability of the cell membrane. Extended-spectrum triazoles like posaconazole have been demonstrated to be useful in prophylaxis against invasive fungal disease (IFD) and in treating refractory IFD. To optimize the absorption of systemic substances, Because it has a significantly increased bioavailability when given with food, posaconazole oral suspension is prescribed in conjunction with food. It may be possible to improve bioavailability of medication by dividing dosages or taking it with an acidic beverage or liquid food supplement. Because posaconazole has a higher molecular weight (log P = 5.66, pKa 3.7) and lipophilicity (log P > 3, pKa 3.6 and 4.6) than itraconazole, it was also expected that its bioavailability would be higher in the fed state. Since the bulk of a posaconazole dose is removed unaltered in the stools, unlike itraconazole, the effects of meals on intestinal and hepatic metabolic enzymes were expected to be insignificant. Posaconazole prophylaxis lowers the risk of invasive fungal infection in comparison to fluconazole; however, the efficacy of the oral suspension formulation is restricted due to its poor absorption. A unique delayed-release tablet formulation demonstrated an improved pharmacokinetic profile in healthy persons[5].

Ufasomes have been created to improve medication penetration through the stratum corneum into viable skin. Lipid carriers found in ufasomes adhere to the skin's surface and facilitate the exchange of lipids across the stratum corneum's outermost layers. This carrier technology seems to hold promise for effective medication delivery. Ufasomes have been produced in addition to liposomes and niosomes because of their potential for topical or transdermal delivery of medications, proteins, peptides, hormones, and other materials. Gebicki and Hicks described the creation of fatty acid vesicles for the first time in 1973. The vesicles were originally referred to as "ufasomes," which stood for unsaturated fatty acid liposomes. Unsaturated fatty acid vesicles, or ufasomes, are suspensions of fatty acid and ionic surfactant-based closed lipid bilayers. Ufasomal suspension has a pH range of 7 to 9. Fatty acid molecules organize themselves into ufasomes so that the carboxyl groups stay in touch with water and the hydrocarbon tails point toward the inner side of the membrane[6]. Ufasome represents a novel approach to enhance the skin absorption of opioids. Unsaturated fatty acids, such as oleic and linoleic acids are employed as herbal permeability enhancers in the ufasome manufacturing process. Surfactants and fatty acids are commonly utilized to increase skin suppleness and medicine distribution through the skin membrane. For a long time, ufasomes have improved the properties of medicinal medication retention inside the skin cell membrane. Ufasomes are small vesicles of fatty acids. Membrane fatty acids have carboxyl groups that come into contact with water, but their hydrocarbon tails are oriented closer to the membrane's core, creating a bilayer structure. Ufasomes are soapy-looking closed lipid bilayer solutions mainly composed of fatty acids. They often inhabit the pH range of 7 to 9 in nature[7].

Decrease toxicity and extend the drug's time in systemic circulation, because the medication is delivered straight to the location, selective absorption of the medication is possible. Increases bioavailability, particularly for medications that are poorly soluble Drugs that are

lipophilic or hydrophilic can be included in ufasomes. Postpones the removal of medications that are quickly metabolized. If the medication is applied topically, it can permeate the skin with ease.Compared to liposome and niosomes, ufasomes are more affordable. The drug's entrapment efficiency is noteworthy[8].

Materials and Method

List of materials used

Table 1: List of Chemicals

S.no	Chemical Name	Manufacturer
1	Posaconazole	Jackson laboratory, Amritsar
2	Oleic acid	Central Drug House(P) Ltd, Delhi
3	Span 80	Croda Pharma , Mumbai
4	Methanol	Rama chemicals, Delhi
5	Phosphate buffer	Wagle industrial estate, thane, Maharashtra
6	Carbapol 934	Qualikems Fine Chemicals pvt. Ltd , Cochin
7	Triethanolamine	Nice Chemicals pvt Ltd , Cochin
8	Propylene glycol	Hexon Laboratories Private Ltd , Nashik
9	Methyl paraben	Hexon laboratories private Ltd, Nashik

Table2: List of Equipment

Sr.no	Equipment	Manufacturer
1	Digital Weighing Balance	Shimadzu , Japan
2	UV/VIS Spectrophotometer	Shimadzu, Japan
3	Magnetic Stirrer	Remi Equipments , Mumbai
4	Melting Point Apparatus	Remi Equipments , Mumbai
5	pHmeter	Ohaus, USA

6	Infrared Spectrophotometer	Perkin Elmer , Germany
7	Water Bath	Sunshine Scientific Equipments , Delhi
8	Brookfield Digital Viscometer	Dolphin Pharmacy Instruments Pvt. Ltd , Mumbai

FORMULATION

Formulation of Ufasomes:

Oleic acid vesicles were prepared using the film hydration process, with minor modifications. Various batches of ufasomes were created utilizing varying oleic acid, medication, and surfactant concentrations. To summarize, the accurately weighed oleic acid, span 80, and posaconazole were dissolved in ethanol in a clean, dry, round bottom flask, followed by solvent evaporation under vacuum using a rotary evaporator (Perfit equipments, Ambala, India) under reduced pressure at 40°C to remove any remaining organic solvent. A dry film was created in a rotary evaporator and left overnight to remove any residues of ethanol and to prevent emulsion formation due to leftover organic solvent. The dried film was then hydrated with PBS (pH 7.4) at ambient temperature for 1 h followed by sonication to form the uniform size vesicular dispersion[9].

Formulation of Ufasomal Gel:

Carbopol 934 (1% w/v) was disseminated in filtered water using a vortex shaker (Tarsons, Kolkata, India) and hydrated for 4-5 hours. The pH of the gel was adjusted to 7.4 using triethanolamine. The gel was prepared by carefully agitating the fluid to avoid air entrapment. To create plain medication gel, a 2:1 ratio of posaconazole solution was added to previously made Carbopol gel and gently mixed for 5 minutes. Finally, the ufasomal gel was loaded with posaconazole, and the pH was corrected with triethanolamine[10].

EVALUATION

Evaluation parameters of Ufasomes formulations:

Drug entrapment efficiency:

The drug entrapment efficiency of formulated ufasomes was estimated by separating the ufasomes by ultracentrifugation at 10000 rpm for 30 min. the sum of free posaconazole in the supernatant was calculated by UV spectrophotometer at 232nm. The drug loading efficiency in the prepared ufasomes was calculated by the following formula:

Entrapment efficiency (%) = Tp-Tf/Tp x100

Where, Tp = Total amount drug, Tf =free drug

Vesicle size:

The Ufasomes samples were suspended in Milli-Q water and screened for vesicle size at 25^{o}C by Zetasizer (Nano-ZS90, Malvern Instruments, UK). The disposable cuvettes were used for sample analysis. The results were reported as the mean ± standard deviation for tree replicates

Polydispersity Index

The Ufasomes samples were suspended in Milli-Q water and screened for PDI at 25^{o}C by Zetasizer (Nano-ZS90, Malvern Instruments, UK). The disposable cuvettes were used for sample analysis. The results were reported as the mean ± standard deviation for tree replicates

Zeta Potential:

The ufasomes samples were suspended in Milli-Q water and screened for zeta potential at 25^{o}C by Zetasizer (Nano-ZS90, Malvern Instruments, UK). The disposable cuvettes were used for sample analysis. The results were reported as the mean ± standard deviation for tree replicates[16].

Scanning Electron Microscope(SEM) :

Scanning electron microscope is used to attain scanning electron micrographs of Cefadroxil containing ufasomes. The instrument used for this purpose is Hitachi S-4800scanning electron microscope. The microsphere were assembled directly on the SEM sample stub, using double sided sticking tape, and coated with gold film (thickness 200nm) under reduced pressure (0.001 torr)[11].

Evaluation parameters of Ufasomal Gel formulations:

Physical appearance

The prepared ufasomal gel formulations were inspected visually for their color, homogeneity, consistency, grittiness and phase separation.

Drug content

Drug content of the ufasomal gel was determined by dissolving an accurately weighed quantity of 1 g gel in about 100ml of methanol. 2ml of this solution was diluted to 10ml with methanol solutions were then filtered and spectrophotometrically analyzed for drug content at 285nm. Drug content was determined from the standard curve of cefadroxil[12, 13].

pH Determination

1g of gel was accurately weighed and dispersed in 100ml of distilled water. The pH of dispersion was measured by using digital pH meter.

Rheological studies

Brookfield digital viscometer was used to measure the viscosity (in cps) of the prepared ufasomal gel formulation. The spindle number 62 was rotated at 50rpm for the viscosity measurement. The viscosity of the formulated batches was determined using a cone and plate viscometer with spindle 7(Brookfield engineering Laboratories). The assembly was connected to a thermostatically controlled circulating water bath maintained at 25^{o} C. The formulation whose viscosity was to be determined was added to a beaker covered with thermometer jacket. Spindle was allowed to move freely into the ufasomal gel. And reading was noted.

Spreadability

Spreadabilty of the formulation was determined by using an apparatus designed and developed in the laboratory especially for the project and diagram of the apparatus. Two rectangular glass plates of standard dimension were selected. 500mg of the sample was placed on one of the glass plate. Second plate was placed over the other one to sandwich sample between plates. A 20gm weight was placed on the top of upper plate to provide a uniform thin film of the sample between the plates. Weight was removed excess of the gel sample was scrapped off from the edges. The top plate was then subjected to pull by using string to which 50gm weight was applied. The time required by the upper plate to travel a distance of 6cm and separate from the lower plate was noted. A shorter interval indicated better spreadability. Experiment was repeated and averages of three attempts were calculated for each formulation using formula

Spreadability= (M×L) /T

M= weight tied to upper side

L = length of the glass slide

T= time in second

Extrudability

The development formulations were filled in collapsible metal tubes and crimped at one end. After removing the cap tube is pressed to extrude the product from the tube[14, 15].

In Vitro drug release of ufasomal gel formulations loaded with Posacxonazole

The in Vitro drug release studies were carried out using a modified Franz diffusion (FD) cell. The formulation was applied on dialysis membrane which was placed between donor and receptor compartment of the FD cell. Phosphate buffer pH 7.4 was used as a dissolution media. The temperature of the cell was maintained at 37º C by circulating water jacket. This whole assembly was kept on a magnetic stirrer and the solution was stirred continuously using a magnetic bead. A similar blank set was run simultaneously as a control. Sample (5ml) was withdrawn at suitable time intervals and replaced with equal amount of fresh dissolution media. Samples were analyzed spectrophotometrically at 285nm and the cumulative % drug release was calculated. The difference between the reading of drug release and control was used as the actual reading in each case[16].

In- vitro release kinetics of Ufasomal gel formulations:

Zero- order kinetics:

Following this profile, prescription dosage formulation emits the same volume of medication per unit of time, rendering it the perfect type of drug release for achieving pharmacologically extended operation. This model can be represented in a simple way using the following relation:

$$Qt = Qo + Kot$$

Where Q_t is the amount of drug dissolved in time t, Q_o is the initial amount of drug in the solution (most time, $Q_o = 0$) and K_o is the zero order release constant.

First- order kinetics

The following relation expresses this model:

$$\log Qt = \log Qo + \frac{k1t}{2.303}$$

Where Q_o is the amount of drug dissolved in time t, Q_o is the initial amount of drug in the solution and K1 is the zero order release constant.

A graph of the decimal logarithm of the drug's published number Vs time would be linear as a result. Pharmaceutical dosage formulations that adopt this dissolution profile, such as those containing water- soluble drugs in porous matrices, release medication proportionally to the amount of drug remaining in their interior, resulting in a reduction in the amount of drug released per unit of time.

Higuchi model

Higuchi devised a number of experimental models to investigate the release of water- soluble and low- soluble drugs in semi-solid and solid matrixes. For drug particles scattered in a uniform matrix acting as diffusion media, mathematical expressions were obtained.

The simplified Higuchi model is expressed as:

$$Q = KH.t1/2$$

The amount of drug release in time t is Q, and Higuchi dissolution constant is KH. The Higuchi model depicts drug release as a square root time dependent diffusion mechanism based on Fick's law. This association can be used to explain the degradation of water- soluble medications from a number a modified released prescription dosage formulation, such as transdermal systems and matrix tablets[17, 18].

Korsmeyer- Peppas model:

Korsmeyer et al. used a simple empirical equation to describe general solute release behavior from controlled release polymer matrixes:

$$\frac{Mt}{M\infty} = at^n$$

Where, $M_t/M\infty$ is fraction of drug released is a kinetic constant, t is release time and n is the diffusional exponent for drug release. 'n' is the slope value of log $M_t/M\infty$ versus log time curve. Regardless of the release process, Peppas stated that the above equation could accurately explain the release of solutes from slabs, spheres cylinders and disks. Peppas used this n value in order to characterize different release mechanism, concluding for values for slab, of n= 0.5 for Fickian diffusion and higher values of n, between 0.5 and 0.1, or n= 1.0, for mass transfer following a non- Fickian model. In case of a cylinder n= 0.45 instead of 0.5 and 0.89 instead of 0.1. This equation can only be used in systems with a drug diffusion coefficient fairly concentration independent. To the determination of the exponent n the portion of the release curve where $M_t/M\infty < 0.6$ should only be used. To use this equation, the release must be one- dimensional and the device width – thickness or length- thickness

relationship must be at least ten. To account for the lag time (1) at the start of drug release from the pharmaceutical dosage type, a modified version of this equation was developed:

$$\frac{Mt}{M\infty} = a(t - l)n$$

When there is the possibility of a burst effect, b, this equation become:

$$\boxed{\frac{Mt}{M\infty} = at^n + b}$$

The 1 and b values would be zero if there was no lag time or burst effect, and only atn would be used. This statistical model, also known as power Law has been used to explain the release of a number of prescription adjusted release dosage types on a daily basis[19, 20].

Stability studies

The main objective of stability testing is to give evidence on the changes of quality of drug product with respect to time under the influence of various environmental factors such as temperature, humidity, and light and enables recommended storage conditions; re-test periods and shelf lives to be accomplished. According to the ICH guidelines the optimized formulation was kept for accelerated stability for six months. Microspheres were kept in stability chamber maintained at temperature of 40ºC±2ºC/75% RH±5% RH. During the study period, the formulation was monitored at prearranged time intervals of 0, 15, 30, 45, 60, 75, 90, 180 days for change in physical appearance, drug content and in- vitro release characteristics[21, 22, 23, 24, 25].

RESULT AND DISCUSSION

FORMULATION

Formulation of Ufasomes formulations:

Ufasomes were prepared by using thin-film hydration method. Carriers that are used for the preparation of Ufasomes were mentioned in **table 3.**

Table 3: Composition of ufasomes:

S.no	Formulation code	Drug (g)	Oleic acid (g)	Span 80 (g)	Methanol (ml)
1	UFOS 1	25	425	25	25
2	UFOS 2	25	400	50	25
3	UFOS 3	25	375	75	25
4	UFOS 4	25	350	100	25
5	UFOS 5	25	325	125	25
6	UFOS 6	25	300	150	25

Formulation of Ufasomal Gel:

Ufasomal gel was prepared by using sedimentation method. Carriers that are used for the preparation of Ufasomes were mentioned in **table 4.**

Table 4: Formulation of Ufassmal Gel loaded with Posaconazole

S.no	Carbapol934 (g)	Distilled water (ml)	Triethanolamine (ml)
UFG1	5	500	q.s
UFG2	7.5	500	q.s
UFG3	10	500	q.s
UFG4	12.5	500	q.s
UFG5	15	500	q.s
UFG6	17.5	500	q.s

EVALUATION

Evaluation of Ufasomes loaded with Posaconazole

Entrapment Efficiency

Percentage Drug Entrapment and loading of all formulation was given in table 5.

Table 5: Percentage Entrapment efficiency of Ufasomes

S.no	Formulation code	(%) Entrapment Efficiency
1	Ufos 1	50.28±0.17
2	Ufos 2	52.14±0.11
3	Ufos 3	56.78±0.12
4	Ufos 4	65.96±0.13
5	Ufos 5	68.21±0.14
6	Ufos 6	84.75±0.14

mean±SD, n=3

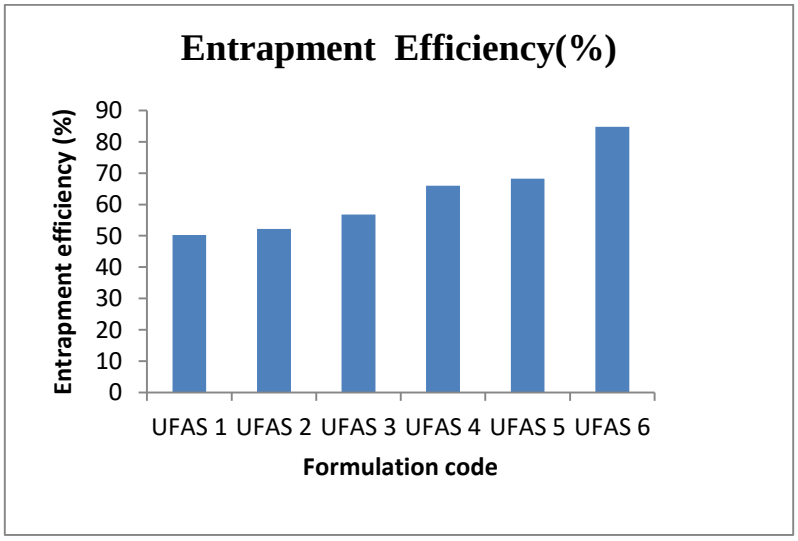

Figure1: Percentages of Entrapment Efficiency of ufasomes formulations

Discussion: The Entrapment efficiency of all formulations UFAS 1, UFAS 2, UFAS 3, UFAS 4, UFAS 5 and UFAS 6 was found to be 56.28, 64.14, 67.78, 75.96, 79.21 and 83.75 were shown in Table5 and Figure1. The higher efficiencies observed in formulation like UFAS 6 (83.75±0.14) and could be attributed to ideal lipid composition and preparation method that promote effective drug encapsulation. Due to low stirring speed, high drug polymer interaction, low solubility of drug in continous phase, low concentration of emulsifier leads to high entrapment efficiencies. Conversely, formulation UFAS 1 (56.28±0.17) and UFAS 2 (64.17±0.11) shows lower efficiencies because of high stirring speed, low drug polymer interaction, high solubility of drug in continous phase, high concentration of emulsifier leads to low entrapment efficiencies.The best entrapment efficiency of UFAS 6 shows best result in entrapment efficiency with range of (83.75±0.14).

Vesicle Size:

Table 6: Vesicle size for different ufasomal formulations

S.no	Formulation code	Vesicle size (nm)
1	UFAS 1	347.75±0.13
2	UFAS 2	376.71±0.22
3	UFAS 3	546.82±0.14
4	UFAS 4	518.95±0.17
5	UFAS 5	474.97±0.21
6	UFAS 6	228.23±0.12

mean±SD, n=3

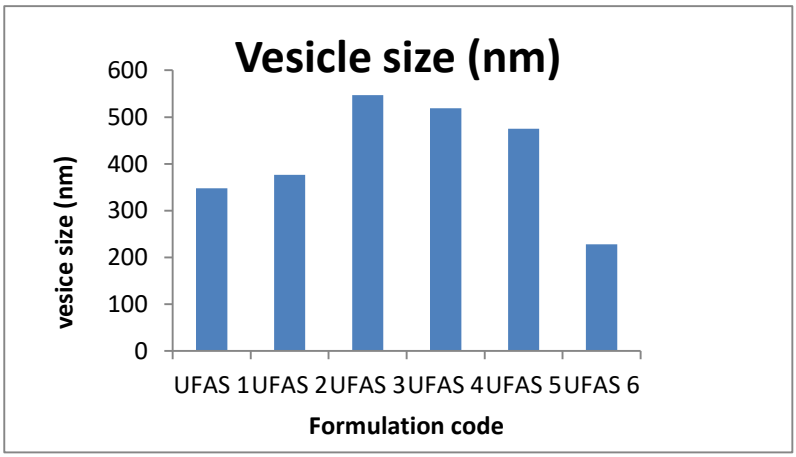

Figure2 : Vesicle size for different ufasomal formulations

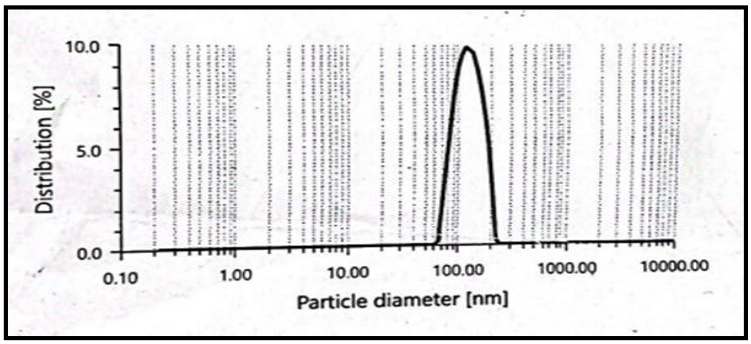

Figure3: Vesicle Size Distribution of UFAS-6 Formulation

Discussion:

The vesicle size of all the formulations UFAS1, UFAS2, UFAS 3, UFAS 4, UFAS5 and UFAS6was found to be 347.75, 376.71, 546.82, 518.95, 474.97and 228.23 were shown in Table 6 and Figure 2 & 3.The smaller vesicle size in UFAS 6 (228.23±0.02) could be due to ideal preparation condition, such as prolonged or adequate sonication time ensures the breakdown of larger vesicles smaller ones. The use of unsaturated fatty acids or a lower concentration of lipids can helps form smaller vesicles. Ideal hydration conditions can produce more uniform and smaller vesicles were shown in Figure 32. In contrast, the larger vesicles size in UFAS 4 (618.95±0.07) and UFAS 5 (674.97±0.01) could of be due to inferior preparation condition, such as unappropriate sonication time, higher concentration of lipids can result in the formation of larger vesicles. Inferior hydration conditions can affect vesicle size, leading to larger vesicles.

The best Vesicle size was found in UFAS 6 (228.23±0.02) smaller vesicle sizes can enhances drug delivery efficiency, cellular uptake, and stability. Smaller vesicles tend to be more stable, reducing the likelihood of aggregation.

Polydispersity Index:

Table7: polydispersity index of ufasomal formulations

S.no	Formulation code	Polydispersity index
1	UFAS 1	0.32±0.12
2	UFAS 2	0.26±0.11
3	UFAS 3	0.23±0.12
4	UFAS 4	0.30±0.15
5	UFAS 5	0.20±0.13
6	UFAS 6	0.17±0.13

mean±SD; n=3

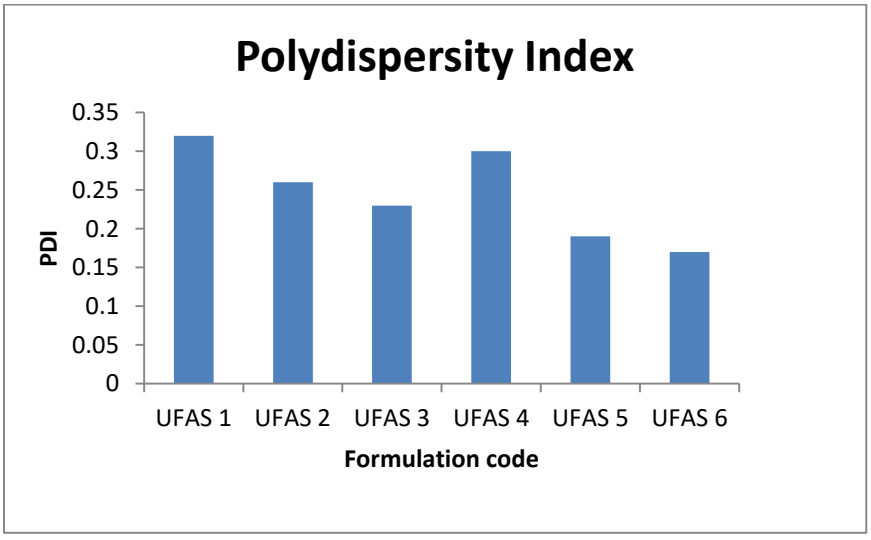

Figure4: Polydispersity index of different ufasomal formulations

Discussion:

The PDI value of all formulations UFAS 1, UFAS 2, UFAS 3, UFAS 4, UFAS 5 and UFAS 6 was found to be 0.32, 0.26, 0.23, 0.30, 0.20, 0.171 were shown in Table 7 and Figure 4. The PDI of UFAS 1(0.32±0.02) and UFAS 4 (0.30±0.05) indicates wider size disrtibution, suggesting more variability in particles size. Potentially less stable and reproducible. The polydispersity index of UFAS 6 (0.171±0.03) is due to ideal method by controlled mixing methods can leads to a more uniform distribution of vesicles size, using high-purity and consistent raw materials can reduce variability in particle formation, concentration of surfactants used can impact the uniformity of vesicle formation leads to lowering the PDI.

The best PDI was found in UFAS 6, (0.171±0.03) due to its more uniform particle size distribution, which contributes to better stability and reproducibility**.**

Zeta Potential:

Table 8: Zeta potential of ufasomal formulations

S.no	Formulation code	Zeta potential (mv)
1	UFAS 1	-29.09
2	UFAS 2	-36.06
3	UFAS 3	-26.03
4	UFAS 4	-33.02
5	UFAS 5	-28.05
6	UFAS 6	-45.04

mean±SD, n=3

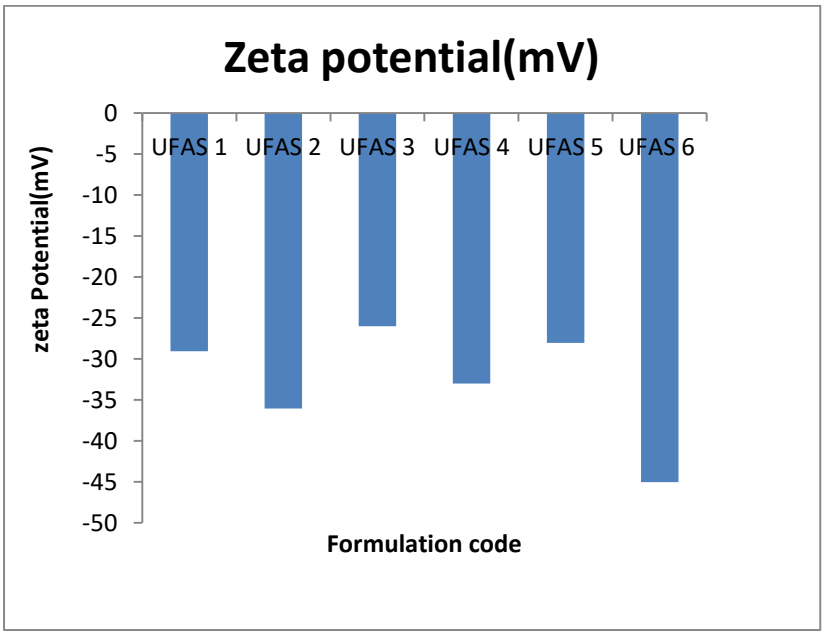

Figure5: Zeta Potential of Different Formulations of Ufasomes

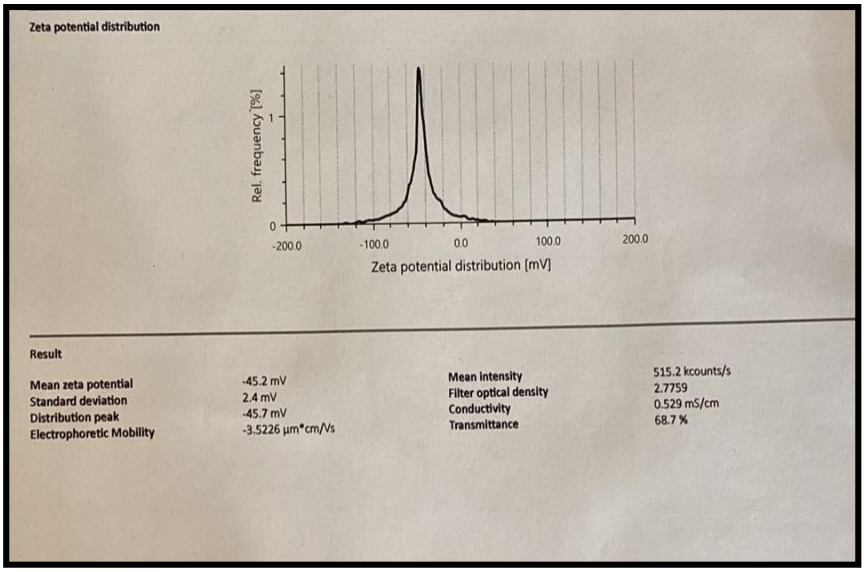

Figure6: Graph represents the zeta potential of the UFAS-6 Formulation

Discussion: The zeta potential of all the formulations UFAS 1, UFAS 2, UFAS 3, UFAS 4, UFAS 5, UFAS 6 was found to be -29.09mV, -36.06mV, -26.03Mv, -33.02mV,-28.05mV, -45.04mV were shown in Table 8 and Figure 5 and 6. The high zeta potential of UFAS 6 (-45.04mV) is likely due to a ideal values such as lipid composition, inclusion of charged molecules, the pH and iconic strength of the dispersion medium, presence of stabilizing agent, and the preparation methods used. The type and concentration of lipids used in UFAS 6 might leads to a higher surface charge density. In contrast, while other formulations shows low zeta potential such as in UFAS 1 (-29.09mV), UFAS 3 (-26.03mV), UFAS 5 (-28.05mV) is likely due to inferior values such as lipid composition, presence of impurities, particle aggregations and inferior preparation methods. The best zeta potential was in the UFAS 6 (-45.04Mv) ensures better colloidal stability, reduces risk of aggregation, and contributes to improved performance and longer shelf life of the formulation.

Morphological characterization of ufasomes formulations:

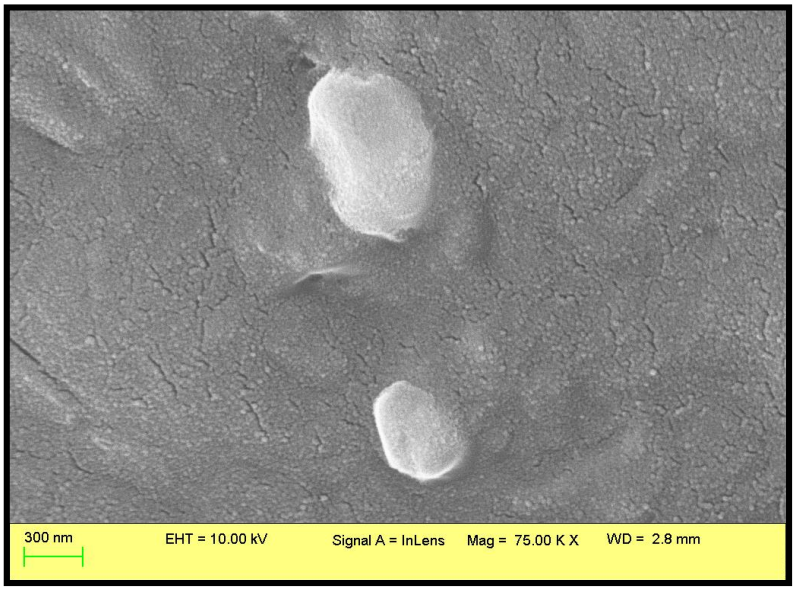

Figure7: Representation of Scanning Electron Microscopy of Ufasomal Formulation (UFAS-6)

Discussion: The UFAS 6 likely contain an ideal mix of lipids that favors the formation of spherical vesicles. The preparation methods for UFAS 6 is probably designed to produce and maintain spherical shape were shown in Figure7 . The high zeta potential of UFAS 6 results in strong repulsive force, reducing aggregation and helping maintain a spherical shape. While, the other formulations like UFAS 1, UFAS 3, UFAS 5 likely contain an inferior mix of lipids that favors rod like structures. Variation in preparation conditions such as temperature, hydration rate, or lack of sufficient shear forces could lead to rod like structures. Lower zeta potential results in weak repulsive forces , leading to more aggregation and less control over shapes. Hence, The Best Representation of scanning electron microcopy was found in UFAS 6 which shows proper spherical shape and less aggregation of particles.

Evaluation of Ufasomal gel formulations:

Physical appearance:

Table 9: Physical appearance of ufasomal gel formulations

S.no	Formulation code	Color	Homogeneity	Consistency	Grittiness
1	UFG-1	White	Satisfactory	Satisfactory	Gritty particles
2	UFG-2	Opaque	Good	Good	Smooth
3	UFG-3	White	Very Good	Very Good	Smooth
4	UFG-4	White	Good	Good	Smooth
5	UFG-5	White	Good	Good	Smooth
6	UFG-6	White	Good	Good	Smooth

Discussion: The UFG 1 shows gritty particles is due to insufficient mixing during the formulation process can lead to incomplete dispersion of ingredients, results in the formations of aggregates or clumps that appears as gritty particles were shown in Table 9.The use of excipients that do not fully dissolve or disperse in the gel matrix cause grittiness.

In contrasts, the UFG 3 maintain white color with better overall properties, like homogeneity of UFG 3 ensuring the uniform distribution of the active ingredients throughout the gel and have smooth texture without any gritty particles**.**

The physical appearance of UFG 3 was selected as the optimal formulation due to their superior physical characteristics.

Drug Content:

Table10: Drug Content Profiles of Gel Formulations

Sr.no	Formulation Code	Percent Drug Content
1	UFG-1	65.26±0.15
2	UFG-2	62.5±0.18
3	UFG-3	85.87±0.23
4	UFG-4	64.62±0.11
5	UFG-5	62.54±0.13
6	UFG-6	54.45±0.14

mean±SD, n=3

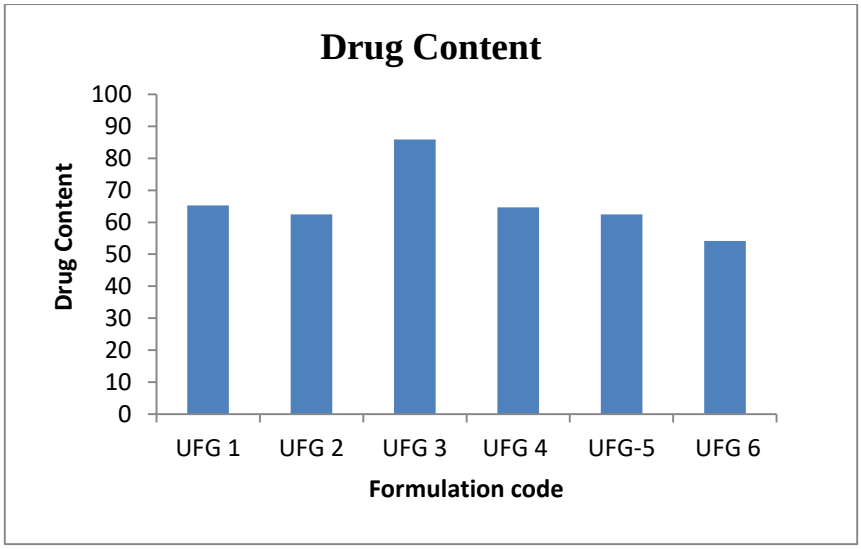

Figure8: Drug content of ufasomal gel formulations

Discussion:

The drug content of gel formulations UFG 1, UFG 2, UFG 3, UFG 4, UFG 5 and UFG 6was found to be 77.26, 82.05, 85.87, 74.56, 83.62, 78.54 were shown in Table 10 and Figure 8. The UFG 1and UFG 6 shows low drug content there is many factors leading to low drug contents, like inferior formulation process (inefficient mixing, encapsulation or stabilization) can lead to lower drug content. Larger particles or unevenly distributed particles may have smaller surface area for drug encapsulation, resulting in lower drug content. In contrast, the UFG 3 shows high drug content due to ideal formulation process include efficient formulation techniques, such as proper mixing , encapsulation can enhances the drug loading capacity of the ufasomes leads to high drug content. Smaller and uniformly distributed particles can provide a larger surface area for drug absorption, increasing drug content.

Thus, the best result shown in UFG 3 with its higher drug content 85% is more suitable for gel formulations. Higher drug content ensures greater efficacy, consistent dosing, and cost effectiveness. The formulation process, particle size, and drug – Excipients compatibility play critical role in achieving high drug content in gel formulations.

pH:

Table 11: pH determination of ufasomal gel formulations

Sr.No	Formulation Code	pH value
1.	UFG-1	7.66±0.169
2.	UFG- 2	7.65±0.128
3.	UFG-3	6.32±0.034
4.	UFG-4	7.67±0.168
5.	UFG-5	7.75±0.047
6	UFG- 6	7.32±0.056

mean±SD, n=3

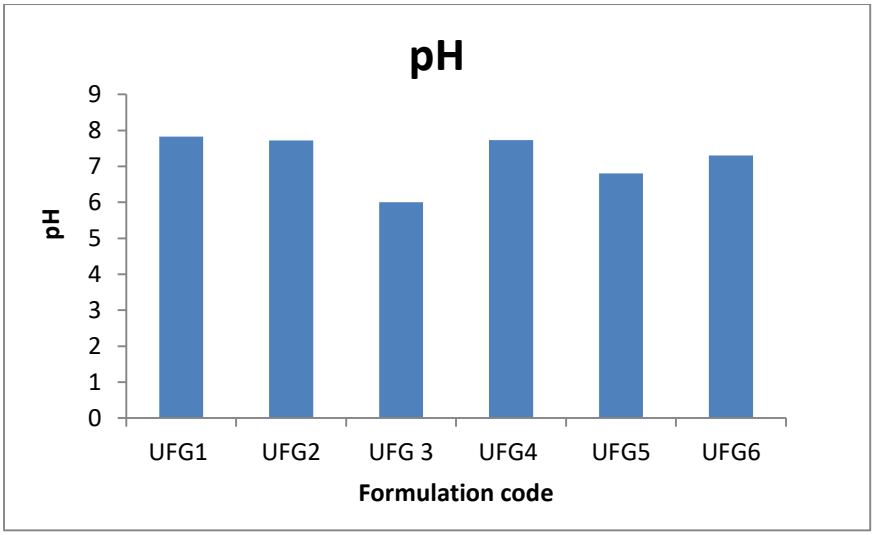

Figure9: pH determination of ufasomal gel formulations

Discussion: The pH of all formulations UFG1, UFG2, UFG 3, UFG4, UFG5 and UFG6 was found to be 7.66, 7.65, 6.32, 7.67, 7.75 and 7.45 were shown in Table 11 and Figure 9. The UFG 3 shows low pH range 6.32±0.034 because active ingredients in gel formulation are more stable and effective at lower pH levels. Acidic pH can enhance the penetration of active ingredient through the stratum corneum, making formulation more effective. Lower pH can help in reducing skin irritation and sensitivity, making the formulation suitable for sensitive skin types. Lower pH environments can inhibit the growth of harmful bacteria and fungi, contributing to the preservation and safety of the product. While, other formulations UFG 6 (7.32±0.056) and UFG 5 (7.75±0.047) shows higher pH can influence the lipophilic drug like Posaconazole tend to have lower solubility in alkaline conditions. This can lead to in adequate drug dissolution, reducing the effectiveness of the formulation. Formulations with a high pH can disrupt the skin's acid mantle, leading to irritation, dryness and increased susceptibility to infections.

The best formulation of UFG 3 with low pH (6.32±0.034) is generally more favorable for gel formulations, especially when dealing with lipophilic drug like Posaconazole, due to improved solubility, skin compatibility and overall formulation effectiveness.

Rheological Studies:

Table12: Viscosity Profile of ufasomal Gel Formulations

Sr.No	Formulation Code	Viscosity (cps)
1	UFG-1	1745.67±0.14
2	UFG-2	1755.08±0.15
3	UFG-3	1545.12±0.22
4	UFG-4	1650.36±0.24
5	UFG-5	1658.18±0.28
6	UFG-6	1743.12±0.45

mean±SD; n=3

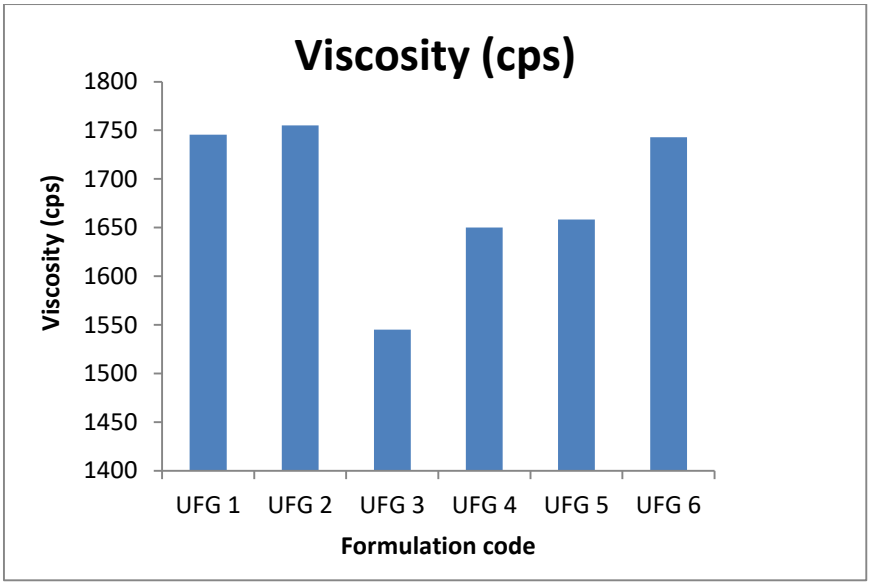

Figure10: Viscosity profiles of ufasomal gel formulations

Discussion: The viscosity of all the formulations UFG1, UFG2, UFG3, UFG4, UFG5 and UFG6 was found to be 1745cps, 1755cps, 1545cps, 1650cps, 1658cps and 1687cpswere shown in Table 12 and Figure 10. The UFG 3 shows low viscosity (1545.12±0.22cps) because the smaller particles or more uniform distribution within the gel can reduce overall viscosity.

Higher temperature can reduce the viscosity of a gel as the molecular motion increases, making gel less viscous. Gelling agents inherently produce gel with lower viscosity. The choice of the gelling agent cam significantly affects the viscosity of the final formulation. While, UFG5 and UFG6 shows high viscosity (1658.22±0.32) and (1687.22±0.32) because using of higher concentration of gelling agents are designed to produce more viscous gels. Lower temperatures generally increase the viscosity of gel as molecular motion decreases.

Thus, the best viscosity profiles of UFG 3 (1545.12±0.22cps**)** shows low viscosity is typically better; because it offers good spread ability, absorption, and ease of application and ensuring the effective delivery of the active ingredient.

Spread ability Studies:

Table 13: Spread ability Profile of ufasomal gel formulations

Sr.no	Formulation Code	Spread ability (cm^2)
1	UFG-1	16.21±0.39
2	UFG-2	16.86±0.38
3	UFG-3	22.64±0.22
4	UFG-4	15.95±0.41
5	UFG-5	15.81±0.17
6	UFG-6	16.43±0.44

mean±SD, n=3

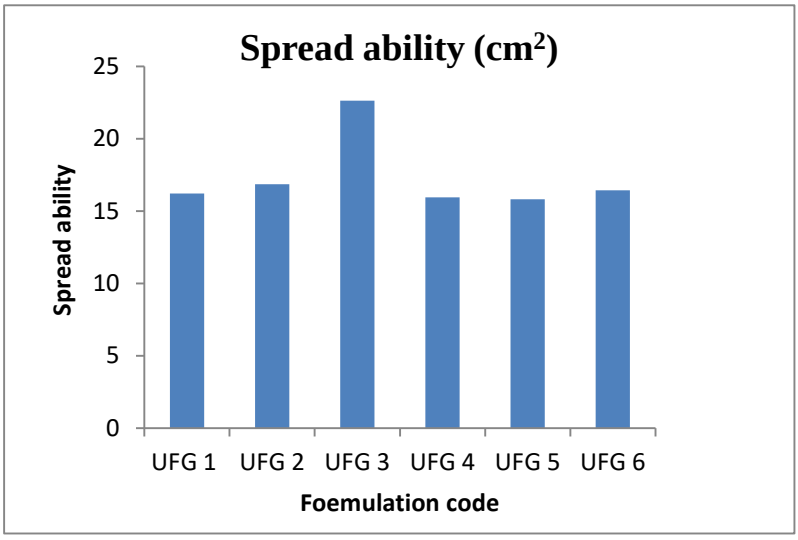

Figure11: Spread ability profiles of ufasomal gel formulations

Discussion:

The spread ability of all gel formulations UFG1, UFG2, UFG3, UFG4, UFG5 and UFG6 was found to be 16.21, 16.86, 22.64, 17.25, 17.95 and 18.81were shown in Table 13 and Figure11. The UFG 1 shows low spread ability (16.21) because larger particle size or unevenly distribution particles can increases resistance to spreading. Higher concentration of gelling agents can lead to lower spread ability. Higher viscosity of UFG 1 which can make the gel thicker and less easy to spread. While, the UFG 3 shows high Spread ability (22.64) because smaller or uniformly distributed particles in gel can lead to better spread ability. Gel with lower viscosity can easily spread over the skin.

Thus, the best result shown in UFG 3 (22.64) with higher spread ability is more suitable for gel formulation. Its lower viscosity and potentially better rheological properties contribute to easier and more effective application, enhancing the overall performance of the gel formulation.

Extrudability studies:

Table14: Extrudability profile of ufasomal gel formulation

Formulation code	Weight of formulation	Weight of gel extruded	Extrudability amount (%)	Grade
UFG-1	15.01	13.24	72.65	Good
UFG-2	15.23	13.45	76.89	Good
UFG-3	15.84	13.89	86.67	Good
UFG-4	15.45	13.43	75.67	Good
UFG-5	15.76	13.87	72.87	Good
UFG-6	15.24	13.26	74.56	Good

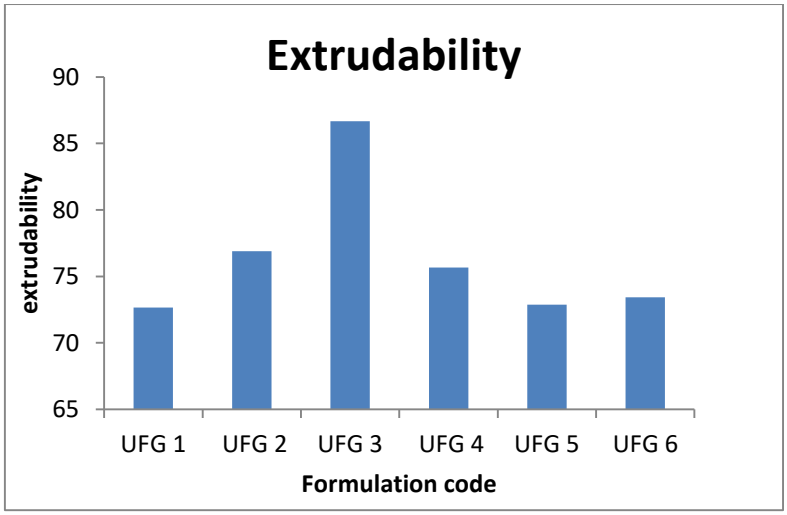

Figure12: Extrudability profile of ufasomal gel formulations

Discussion:

The Extrudability of all gel formulations UFG1, UFG2, UFG3, UFG4, UFG5 and UFG6 was found to be 72.65, 76.89, 86.87, 72.78, 75.67 and 84.87were shown in Table 14 and Figure 12. The UFG 1 shows low extrudability, because higher viscosity making it thicker and more resistant to flow. This requires more force to extrude the gel. Larger or unevenly distributed particles can increase internal friction, making it harder to extrude the gel. While, the formulation UFG 3 shows high extrudability because UFG 3 has a low viscosity making it easier to push through the nozzle of the container. Lower viscosity gels require less force to extrude. Smaller and more uniformly distributed particles can reduce internal friction, allowing the gel to flow more easily.

Thus, the best result shown in UFG 3 with higher extrudability value (86.67) is more suitable for gel formulations. Its low viscosity and potentially better flow properties contribute to easier and ensuring effective application of the gel**.**

***In Vitro* drug release of Ufasomal gel formulations:**

Table 15: Percentage drug release of ufasomal gel formulations for UFG1 to UFG 6

Time (hrs)	**Cumulative (%) Drug Release**					
	UFG1	**UFG2**	**UFG3**	**UFG4**	**UFG5**	**UFG6**
0	0	0	0	0	0	0
0.25	4.34±0.23	4.32±0.21	4.69±0.20	4.65±0.19	4.55±0.18	4.52±0.17
0.5	18.52±0.25	18.5±0.24	21.14±0.23	19.45±0.22	19.42±0.21	19.36±0.20
1	28.87±0.27	31.67±0.26	28.05±0.25	25.34±0.24	24.45±0.23	20.17±0.22
2	38.5±0.17	37.68±0.16	37.09±0.15	34.13±0.14	32.23±0.13	30.56±0.12

3	45.69±0.19	48.16±0.18	45.67±0.17	42.34±0.16	40.12±0.15	38.54±0.14
4	50.48±0.24	56.21±0.23	54.34±0.22	52.32±0.21	49.34±0.20	46.34±0.19
5	58.18±0.28	64.1±0.27	62.32±0.26	60.23±0.25	58.76±0.24	56.76±0.23
6	62.18±0.25	70.56±0.24	60.03±0.23	59.34±0.22	57.46±0.21	54.34±0.20
8	67.82±0.16	81.26±0.15	74.34±0.14	72.45±0.13	69.08±0.12	64.65±0.11
10	75.14±0.24	83.56±0.23	85.43±0.22	82.45±0.21	79.65±0.20	76.56±0.19

Mean±SD, n=3

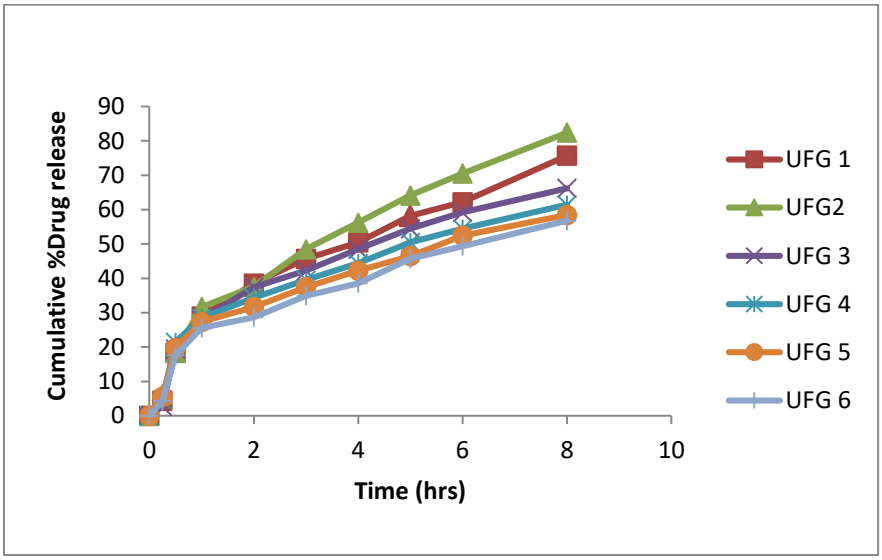

Figure13: In-Vitro drug release of gel formulations UFG1-UFG6

Discussion:

From Table 15 and Figure 13 the in-vitro drug release pattern of initial burst release of surface adsorbed drug was observed followed by slow and sustained release of entrapped drug from the UFGs the initial burst effect on the release of Posaconazole may be due to the loosely associated Posaconazole on the surface of ufasomal gel formulations. The burst release is clinically significant to achieve initial high drug concentrations in the target tissue. The slow release of the drug is controlled by the speed of the degradation of ufasomes. Thus, UFG 3 show a slow and sustained release of drug which found to be the best formulation. These indicate to the growing body evidence supporting the use of ufasomes as a promising delivery system for prolonged drug release.

In-vitro drug release Kinetics:

Table16: In-Vitro Drug Release Kinetic for UFG3 Formulation

Time (hrs)	Square root of time (hrs) 1/2	Log time	Cumulative % drug release	Log cumulative % log release	Cumulative% drug remaining	Log cumulative % drug remaining
0	0	0	0	0	0	0
0.25	0.5	-0.602	4.68	0.671	95.31	1.979
0.5	0.707	-0.301	21.14	1.345	78.96	1.876
1	1	0	28.99	1.432	71.34	1.854
2	1.41	0.301	34.18	1.554	65.67	1.814
3	1.73	0.477	39.81	1.578	60.56	1.779
4	2	0.602	44.65	1.634	55.43	1.74
5	2.23	0.698	51.98	1.745	49.65	1.79
6	2.24	0.778	53.23	1.756	45.21	1.69
8	2.82	0.903	65.76	1.734	38.45	1.58
10	3.16	1	69.57	1.842	30.43	1.48

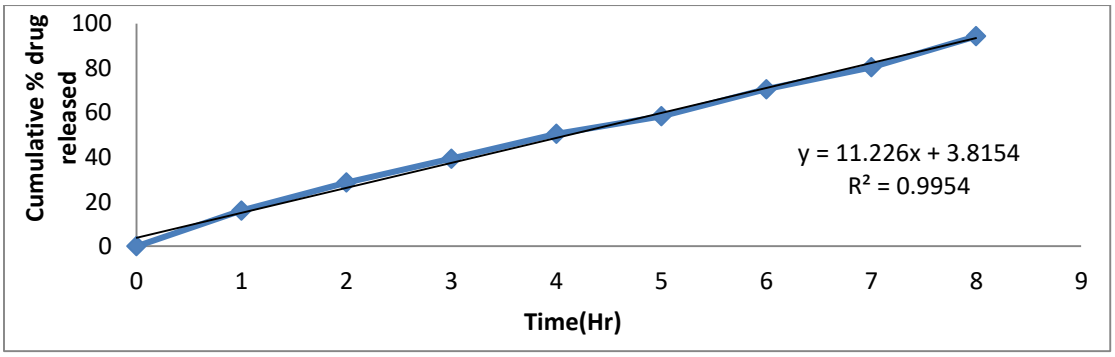

Figure14: (A) zero order kinetics

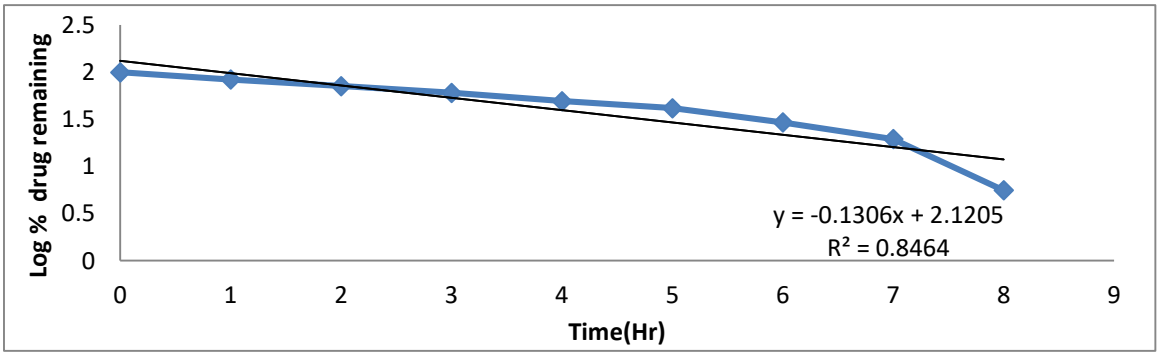

Figure15: (B) First order kinetics

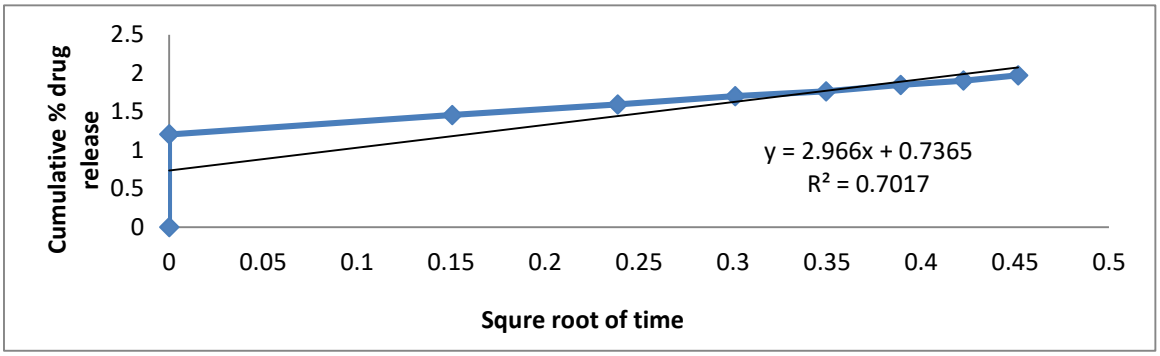

Figure16: (c) Higuchi model

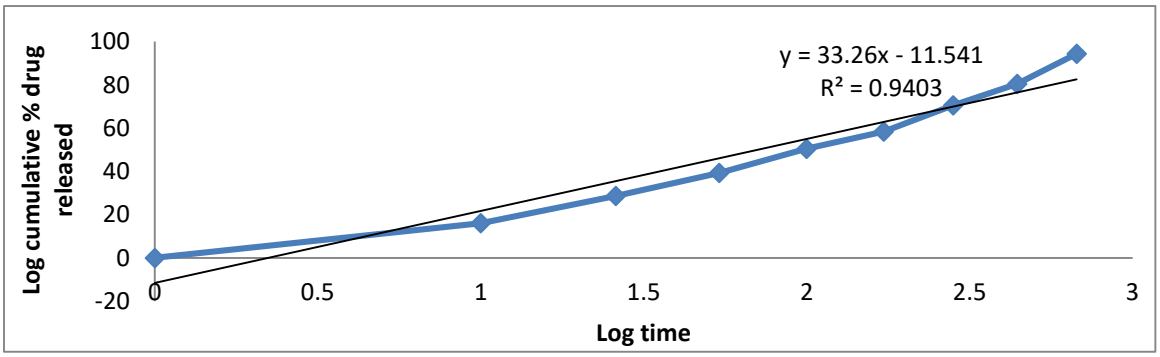

Figure17: (D) Korsmeyer-Peppas model

Table 17: Correlation coefficient values of kinetic models

S. No.	Kinetic model	Correlation coefficient values (r^2)
1.	Zero-order	0.9954
2.	First-order	0.8464
3.	Higuchi model	0.7017
4.	Korsemeyer-Peppas model	0.9403

Discussion:

The attainment of zero–order kinetics with high coefficient of determination (R^2= 0.995) represents a pivotal achievement in the development of the gel formulation investigated in this study were shown Table 16, 17 and Figure 14, 15, 16, 17. Zero–order kinetics indicates that the drug release from the formulation occurs at a constant rate over time, independent of its concentration. This characteristics is highly desirable for topical formulations like gels, as it's ensure consistent and sustained delivery of the active ingredient to the target site. The observed high R^2 value underscore the precision drug release, reflecting optimized formulation parameters such as excipients composition, drug loading, and particle characteristics. Such controlled release kinetics not only enhance therapeutics efficacy by maintaining effective drug levels but also signify formulation stability and robustness. Moreover, achieving zero- order kinetics holds implications for regulatory compliances and clinical applicability, demonstrating the formulation ability to meet stringent safety and efficacy standards.

Hence, the UFG-3 shows zero order kinetics, which shows the optimal formulation and has high coefficient of determination which is best achievement in the development of the gel formulation.

Stability studies:

Table18: Stability study appearance of ufasomal gel UFG-3 Formulation for 6 Month:

Duration (days)	Appearance at 4±2˚C	Appearance at 25±2˚C/65˚%±5%RH	Appearance at40±2˚C/75%±5%RH
0	White in color	White in color	White in color
30	No change	No change	No change
60	No change	No change	No change
90	No change	No change	No change
120	No change	No change	No change
150	No change	No change	No change
180	No change	No change	No change

Table19: Stability of drug content of ufasomal gel UFG-3 Formulation for 6 Month:

Duration (days)	Percentage of drug content at 4±2˚C	Appearance at 25±2˚C/65˚%±5%RH	Appearance at40±2˚C/75%±5%RH
0	85.34±0.14	85.34±0.13	85.34±0.12
30	84.13±0.15	83.16±0.15	82.34±0.13
60	83.14±0.12	82.41±0.17	81.23±0.16
90	82.10±.0.12	81.43±0.14	80.12±0.15
120	81.78±0.13	80.56±0.15	79.80±0.18
150	80.54±0.15	79.76±0.18	77.87±0.16
180	75.14±0.14	77.65±0.17	75.45±0.16

Mean±SD; n=3

Table20: Stability studies of an in vitro drug release of ufasomal gel formulationUFG-3 at 4±2˚C

Time (hrs)	Cumulative drug release at 4±2˚C						
	0 days	30 days	60 days	90 days	120 days	150 days	180 days
0	0	0	0	0	0	0	0
0.25	4.34±0.23	4.33±1.1	4.32±0.8	4.24±0.4	4.17±0.3	4.08±0.2	4.00±1.8
0.5	18.52±0.25	18.13±1.7	21.12±1.6	21.11±1.5	20.45±1.4	19.36±1.3	18.76±1.2
1	28.87±0	28.86±	27.78±1.	27.75±1.	25.67±1.	24.54±1.	23.52

	.27	1.6	5	4	3	2	±1.1
2	38.97±0.17	34.85±1.3	33.83±1.2	32.77±1.1	31.67±0.9	30.58±0.8	29.40±0.7
3	45.69±0.19	45.32±1.9	44.65±1.7	43.23±1.6	42.33±1.5	41.42±1.4	40.65±1.3
4	50.48±0.24	48.44±1.9	47.43±1.8	46.42±1.7	45.41±1.6	44.35±1.5	43.24±1.4
5	58.18±0.28	57.35±1.5	56.56±1.4	55.44±1.3	54.23±1.2	53.67±1.1	52.89±0.9
6	62.18±0.25	61.42±1.7	60.43±1.6	59.42±1.5	58.41±1.4	57.36±1.3	56.32±1.2
8	67.82±0.16	66.54±1.8	65.53±1.7	64.53±1.6	63.78±1.5	62.76±1.4	61.75±1.3
10	75.14±0.24	74.86±1.9	73.85±1.8	72.84±1.7	71.83±1.6	70.82±1.5	69.80±1.4

mean±SD; n=3

Table21: Stability studies of in vitro drug release of ufasomal gel UFG 3 formulations Appearance at 25±2˚C/65˚%±5%RH

Time (hrs)	**Cumulative drug release at 4±2˚C**						
	0 days	**30 days**	**60 days**	**90 days**	**120 days**	**150 days**	**180 days**
0	0	0	0	0	0	0	0
0.25	4.34±0.23	4.33±1.1	4.32±0.8	4.24±0.4	4.17±0.3	4.08±0.2	4.00±1.8
0.5	18.52±0.25	18.13±1.7	18.12±1.6	18.11±1.5	18.08±1.4	17.36±1.3	17.06±1.2
1	28.87±0.27	28.38±1.6	27.67±1.5	27.63±1.4	25.53±1.3	24.21±1.2	23.52±1.1
2	38.5±0.17	37.85±1.3	36.83±1.2	35.77±1.1	34.67±0.9	33.58±0.8	29.40±0.7
3	45.69±0.19	45.32±1.9	44.65±1.7	43.23±1.6	42.33±1.5	41.42±1.4	40.65±1.3

4	50.48±0.24	48.54±1.9	47.65±1.8	46.56±1.7	45.44±1.6	44.35±1.5	43.24±1.4
5	58.18±0.28	57.35±1.5	56.56±1.4	55.44±1.3	54.23±1.2	53.67±1.1	52.89±0.9
6	62.18±0.25	61.42±1.7	60.43±1.6	58.42±1.5	57.41±1.4	56.36±1.3	54.32±1.2
8	67.82±0.16	63.54±1.8	62.53±1.7	61.53±1.6	59.78±1.5	58.76±1.4	57.75±1.3
10	75.14±0.24	76.86±1.9	75.85±1.8	69.84±1.7	68.83±1.6	67.82±1.5	65.80±1.4

mean±SD; n=3

Table 22: Stability studies of in vitro drug release of ufasomal gel formulation UFG 3 Appearance at40±2˚C/75%±5%RH

Time (hrs)	**Cumulative drug release at 4±2˚C**						
	0 days	**30 days**	**60 days**	**90 days**	**120 days**	**150 days**	**180 days**
0	0	0	0	0	0	0	0
0.25	4.34±0.23	4.32±1.1	4.31±0.8	4.23±0.4	4.17±0.3	4.08±0.2	4.00±1.8
0.5	18.52±0.25	17.13±1.7	17.11±1.6	17.09±1.5	16.05±1.4	16.36±1.3	16.76±1.2
1	28.87±0.27	28.38±1.6	27.67±1.5	27.63±1.4	25.53±1.3	24.21±1.2	23.52±1.1
2	38.5±0.17	34.85±1.3	33.83±1.2	32.77±1.1	31.67±0.9	30.58±0.8	29.40±0.7
3	45.69±0.19	45.32±1.9	44.65±1.7	43.23±1.6	42.33±1.5	41.42±1.4	40.65±1.3
4	50.48±0.24	48.54±1.9	47.65±1.8	46.56±1.7	45.44±1.6	44.35±1.5	43.24±1.4
5	58.18±0.28	54.35±1.5	53.56±1.4	52.44±1.3	49.23±1.2	48.67±1.1	46.89±0.9
6	62.18±0	60.42±	59.43±1.	57.42±1.	56.41±1.	54.36±1.	53.32±

	.25	1.7	6	5	4	3	1.2
8	67.82±0.16	65.54±1.8	62.53±1.7	60.53±1.6	59.78±1.5	57.76±1.4	56.75±1.3
10	75.14±0.24	73.85±1.9	70.84±1.8	69.83±1.7	65.82±1.6	62.81±1.5	61.79±1.4

mean±SD; n=3

Discussion: The stability study of UFG 3 Formulation over a 180 days period revealed no change in its physical appearance, maintaining uniform white color, smooth texture, and homogeneity without visible particles. The drug content analysis revealed that the active ingredient remained unchanged after 180 days. This indicates robust chemical stability, as there was no significant degradation of the active components. Stability studies of an in vitro drug release of ufasomal gel formulation UFG-3 at 4±2˚C, 25±2˚C, 40±2˚C for 180 days. This consistent release profile across different temperature indicates that the formulation is stable.

CONCULSION:

A recent approach of Posaconazole loaded ufasomal gel formulation was prepared by a thin film hydration method using the ratios of drug and oleic acid. Formulations UFG 3 exhibited the best formulation. Results showed that optimized formulation had vesicle size <228nm with 94% entrapment efficiency, polydispersity index 0.171 shows high entrapment efficiency, smaller particle with uniform size enhances the spread ability or increase in extrude ability . In vitro drug release of best fit formulation UFG 3 shows 92% drug content in the formulation. The attainment of zero–order kinetics with high coefficient of determination (R^2= 0.995) represents a pivotal achievement in the development of the gel formulation investigated in this study. Zero–order kinetics indicates that the drug release from the formulation occurs at a constant rate over time, independent of its concentration. This characteristics is highly desirable for topical formulations like gels, as it's ensure consistent and sustained delivery of the active ingredient to the target site. Stability studies conducted on UFG 3 at different temperatures over a period of 180 days revealed robust stability characteristics crucial for its pharmaceutical application. This consistent drug release is indicative of the formulation's ability to provide reliable therapeutic efficacy over time, which is essential for its intended use in topical gel formulations. Temperature variations did not adversely affect the stability of UFG 3, underscoring its resilience to environmental factors. These findings validate the formulation design approach taken and highlight UFG 3 potential as a stable and effective pharmaceutical product. Overall, results revealed the capability of ufasomal gel formulation in improving the bioavailability of posaconazole.

ACKNOWLEDGEMENTS: I would like to thank all my colleagues for helping me out with this research work.

REFERENCES:

1. Luger T, Paus R, Slominski A, Lipton J 1999 Cutaneous neuromodulation: the proopiomelanocortin system. Ann NY Acad Sci 885:1–479 .
2. Slominski A, Ermak G, Mazurkiewicz JE, Baker J, Wortsman J 1998 Characterization of corticotropin releasing hormone (CRH) in human skin. J Clin Endocrinol Metab 83:1020–1024.
3. Slominski A, Roloff B, Curry J, Dahiya M, Szczesniewski A, Wortsman J 2000 The skin produces urocortin. J Clin Endocrinol Metab 85:815–823.
4. Grando SA, Horton RM 1997 The keratinocyte cholinergic system with acetylcholine as an epidermal cytotransmitter. Curr Opin Dermatol 4:462–268.
5. Schallreuter KU, Lemke KR, Pittelkow MR, Wood JM, Korner C, Malik R 1995 Catecholamines in human keratinocyte differentiation. J Invest Dermatol 104:953–957 .
6. Schallreuter KU, Wood JM, Pittelkow MR, Guˆ tlich M, Lemke R, Rodl W, Swanson NN, Hitzemann K, Ziegler I 1994 Regulation of melanin biosynthesis in the human epidermis by tetrahydrobiopterin. Science 263:1444–1446.
7. Rossi R, Johansson O 1998 Cutaneous innervation and the role of neuronal peptides in cutaneous inflammation: a minireview. Eur J Dermatol 8:299–306.
8. Thody AJ, Shuster S 1989 Control and function of sebaceous glands. Physiol Rev 69:383–416 36.
9. Thiboutot DM 1995 Dermatological manifestations of endocrine disorders. J Clin Endocrinol Metab 80:3082–3087.
10. Scholzen T, Armstrong CA, Bunnett NW, Luger TA, Olerud JE, Ansel JC 1998 Neuropeptides in the skin: interactions between the neuroendocrine and the skin immune systems. Exp Dermatol 7:81–96 .
11. Al Abadie MS, Kent GG, Gawkrodger DJ 1994 The relationship between stress and the onset and exacerbation of psoriasis and other skin conditions. Br J Dermatol 130:199–203
12. Lee PP, Lau YL. Cellular and molecular defects underlying invasive fungal infections—revelations from endemic mycoses. Frontiers in immunology. 2017 Jun 28;8:735.
13. Bongomin F, Harris C, Hayes G, Kosmidis C, Denning DW. Twelve-month clinical outcomes of 206 patients with chronic pulmonary aspergillosis. PloS one. 2018 Apr 10;13(4):e0193732.
14. fungal infection and host tree health in the endangered American chestnut in Canada. Forest Ecology and Management. 2018 Nov 1;427:60-9.
15. Armstrong-James D, Meintjes G, Brown GD. A neglected epidemic: fungal infections in HIV/AIDS. Trends in microbiology. 2014 Mar 1;22(3):120-7.
16. Enoch DA, Yang H, Aliyu SH, Micallef C. The changing epidemiology of invasive fungal infections. Human fungal pathogen identification: methods and protocols. 2017:17-65.
17. Lai CC, Tan CK, Huang YT, Shao PL, Hsueh PR. Current challenges in the management of invasive fungal infections. Journal of Infection and Chemotherapy. 2008 Jan 1;14(2):77-85.
18. Weitzman I, Summerbell RC. The dermatophytes. Clinical microbiology reviews. 1995 Apr;8(2):240-59.
19. Marynissen G, Dallas W, De Doncker P. An epidemiological survey to assess the prevalence of foot diseases. Janssen Study Report. 1997.

20. Gröschel DH, Toye B. Clostridium difficile infection. Critical reviews in clinical laboratory sciences. 1996 Jan 1;33(3):203-45.
21. Jantunen E, Ruutu P, Niskanen L, Volin L, Parkkali T, Koukila-Kähkölä P, Ruutu T. Incidence and risk factors for invasive fungal infections in allogeneic BMT recipients. Bone marrow transplantation. 1997 Apr;19(8):801-8.
22. Tumbarello M, Tacconelli E, Pagano L, La Barbera EO, Morace G, Cauda R, Leone G, Ortona L. Comparative analysis of prognostic indicators of aspergillosis in haematological malignancies and HIV infection. Journal of Infection. 1997 Jan 1;34(1):55-60.
23. Groll AH, Shah PM, Mentzel C, Schneider M, Just-Nuebling G, Huebner K. Trends in the postmortem epidemiology of invasive fungal infections at a university hospital. Journal of infection. 1996 Jul 1;33(1):23-32
24. Cai W, Lu C, Li X, Zhang J, Zhan P, Xi L, Sun J, Yu X. Epidemiology of superficial fungal infections in Guangdong, southern China: a retrospective study from 2004 to 2014. Mycopathologia. 2016 Jun;181:387-95.
25. Crissey JT, Lang H, Parish LC. Manual of medical mycology. (No Title). 1995.