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Investigation of Effects of *Shata Dhauta Ghrita* on The Skin Permeation of Fluconazole Loaded Topical Antifungal Nanolipogel

Pande Vishal V[1].*, Patel Vipul P.[2], Zarekar Nilesh S.[3], Pandit Shubham R.[4], Pote Ajinkya K.[5]

Department of Pharmaceutics (PG), Sanjivani college of pharmaceutical education and research, Kopargaon ,Maharashtra-423603, India.
[3,4,5] Research Scholars

Abstract

Shatadhautaghrita (SDG) is used as a natural permeation enhancer in topical products. It is prepared by washing cow ghee 100 times with water. *Shatadhautaghrita* is (*shata* = one hundred, *dhauta* = washed) clarified butter fat that has been washed 100 times. Nine formulations of nanolipogel were prepared using different concentrations of carbopol and *shatadhautaghrita* and evaluated on the basis of their physical stability and phase separation. The optimized batch of nanolipogel (F7) was evaluated for pH, percentage yield, drug content, extrudability, rheology and stability. The consistency and spreadability were assessed through texture profile analysis and a spreadability test. A zetasizer study was conducted where in the formation of nanosize particles in the *shatadhautaghrita* and formulation was observed. *In-vitro* drug release and *ex-vivo* permeation studies were performed in a phosphate buffer of pH 6.8 using a Franz diffusion cell apparatus. *Candida albicans*was used as a model fungus to evaluate the antifungal activity of the prepared nanolipogel, with a commercially available gel (0.5%) used as a control. The nanolipogel produced better results compared with the commercial preparation. The *in-vitro* drug release and *ex-vivo* permeation studies showed that the highest values of formulation F7 (80.50% and 83.65%) after 5 hours were better than those of nanolipogel compared with a commercial preparation. Also, the formulation F7 showed the highest antifungal activity. From the present study, it may be concluded that nanolipogel is a better formulation for increasing the release, permeation rate and antifungal activity of topical application.

Keywords: Topical nanolipogel, *shata dhauta ghrita*, fluconazole, permeation, particle size.

INTRODUCTION

Fluconazole (FLZ) is an antifungal agent used mainly in topical formulations to treat various skin disorders such as oropharyngeal candidiasis, cryptoccocal meningitis and cutaneous dermatophyte infections. FLZ is a synthetic triazole derivative that acts as an antifungal. FLZ preferentially inhibits fungal cytochrome P-450 sterol C-14 alpha-demethylation [1]

Shata dhauta ghrita (SDG) is used as a natural permeation enhancer in topical products. It is prepared by washing cow ghee 100 times with water. *shata dhauta ghrita* is (*shata* = one hundred, *dhauta* = washed) clarified butter fat that has been washed 100 times. The use of *shata dhauta ghrita* in managing conditions such as burns, chicken pox, scars, wounds, herpes, leprosy and other skin diseases and as a vehicle for drugs for external application are mentioned in traditional texts. The characteristic odour and granular, oily consistency of cow ghee are not present in *shata dhauta ghrita*, and so it is a homogeneous, smooth, non-oily product that is easier to apply. Thus, patient compliance is improved. The neutral pH of *shata dhauta ghrita* compared with the acidic pH value of ghee makes *shata dhauta ghrita* beneficial by preventing skin irritation. The reduced particle size of *shata dhauta ghrita* makes the product non-granular, non-sticky and homogeneous, which makes it easy to apply it on the skin and may result in an increased rate of absorption through the skin. Washing results in a homogeneous oil-in-water emulsion with better consistency and viscosity, which makes it suitable for use in topical applications. [2, 3]

FLZ is a Class III drug having low permeability and high solubility. Hence it is necessary to increase its permeability so that the desired bioavailability is achieved. This is needed for formulating topical dosages. The aim of the present study was to prepare a topical antifungal nanolipogel (NLG) using the hundred-times-washed cow ghee base known as *shata dhauta ghrita*. It may be used as a permeation enhancer to increase the permeation rate of fluconazole.

MATERIALS

Fluconazole was received as a gift from Cipla Pharmaceuticals Ltd., Mumbai. Carbopol 934P, propylene glycol, triethanolamine, propylparaben and methylparaben were obtained from Research Lab Fine Chem Industries, Mumbai. All chemicals used were of analytical grade.

METHODS

Preparation of *shata dhauta ghrita*

Copper vessels were used to prepare *shata dhauta ghrita*. The vessels were cleaned thoroughly and rinsed with purified water. 2.5 kg cow ghee was taken in one copper vessel, and 1.5 L of purified water was added to it. The mixture of cow ghee and water was mixed for 15–20 minutes in a Kenwood apparatus. The contents of the vessel were allowed to settle down. The water was decanted carefully, avoiding any loss of ghee. A fresh slot of 1.5 L purified water and previously washed cow ghee was taken, and the same procedure was repeated. This operation was carried out 100 times to obtain *shata dhauta*

ghrita. Sample of the *shata dhauta ghrita* was collected and stored in copper containers at room temperature. [2]

Preparation of nanolipogel

Carbopol 934P and purified water were taken in a beaker, and the Carbopol 934P was allowed to soak for 24 hours. Fluconazole was dissolved in propylene glycol and added to the above solution. Other excipients (methylparaben and propylparaben) were also added. The pH value of the gels was brought to skin pH using triethanolamine. The final weight of the gel was adjusted to 100 g with purified water. After this gel base was prepared, the *shata dhauta ghrita* was added with continuous stirring. Nine nanolipogel formulations were prepared using different concentrations of Carbopol and *shata dhauta ghrita*. These formulations were evaluated on the basis of physical stability and phase separation. Table 1 provides the compositions of the nine formulations. [4, 5]

Characterization of *shata dhauta ghrita* and nanolipogel

Drug–excipients compatibility studies

Differential scanning calorimetry (DSC)

DSC studies were performed on the drug, the physical mixtures and a 1:1 drug–carbopol mixture. The samples (3–4 mg) were placed on an aluminium pan and heated at a rate of 0°C⁄minute to a temperature of 200°C using a differential scanning calorimeter (Metler Toledo) [1]

Fourier transform infrared spectrophotometry (FTIR)

FTIR studies were carried out on the drug using an FTIR spectrophotometer (FT-IR 8400; Shimadzu Co., Kyoto, Japan) and the formation of nanolipogel was determined using an FTIR spectrophotometer (JASCO-4600LE) with an ATR Pro ONE accessory. The disks were scanned over the wave number range 4000–400 cm^{-1}). [1]

Physical examination

The *shata dhauta ghrita* and nanolipogel formulation were inspected visually for colour, homogeneity, consistency and spreadability. [6]

PH determination

The pH values of the *shata dhauta ghrita* and nanolipogel were determined using a digital pH meter (PICO+ pH meter, LAB INDIA). One gram of each sample was added to 100 ml of distilled water and stored for 2 hours. The pH values of the *shata dhauta ghrita* and nanolipogel were determined in triplicate, and the average values were calculated. [7]

Percentage yield

An empty container was weighed. The gel formulation was transferred to it, and the container was weighed with the gel formulation. The weight of the empty container was subtracted from the weight of the container with the gel formulation, giving the practical yield. Then the percentage yield was calculated using the formula. [8]

$$\text{Percentage yield} = \frac{\text{Practical yield}}{\text{Theoretical yield}} \times 100$$

Drug content

The drug content was determined by dissolving 1 g of the formulation in phosphate buffer of pH 6.8. The solution was stirred continuously for 2 hours using a magnetic stirrer. The resultant solution was transferred to a 100 ml flask, and the final volume adjusted to 100 ml using phosphate buffer of pH 6.8. After suitable dilution of the drug, the absorbance was determined using a UV–visible spectrophotometer at 258 nm with a phosphate buffer of pH 6.8 [9]

Tube extrudability

A collapsible aluminium tube was filled with the gel formulation. The tube was pressed to extrude the material, and the extrudability of the formulation was checked. [10]

Rheological study

Rheology may be defined as the science concerned with the deformation of matter under increased stress, which may be applied perpendicular to the surface of a body, tangential to the surface of the body or at any angle to the surface of the body.

Rheological studies were carried out on the optimized batch of the nanolipogel formulation using a Brookfield viscometer (RST-CC Rheometer) with coaxial cylinder spindles using the following four blocks:

1) Rotation ramp measuring block. CSS. lin. 0 -> 50 Pa 60 s. M points
2) Rotation ramp measuring block. CSS. lin. previous value -> 0 Pa 60 s. 6 M points
3) Analysis basics
4) Thixotropy.

Non-Newtonian systems such as plastics, pseudoplastics and dilatant systems show time-dependent changes in the viscosity at varying shearing stresses at a given temperature. This behaviour is known as thixotropy. [5, 11]

Texture profile analysis

Texture profile analysis (TPA) of the *shata dhauta ghrita* and nanolipogel (F7) was performed using a CT3 texture analyser in TPA mode. The formulations were transferred into the lower cone. Care was taken to avoid introducing air into the samples. A conical analytical probe (45°) was forced down into each sample at a defined test speed (2 mm/second) and to a defined depth (12 mm). At least five replicate analyses of each sample were performed at 25°C and at 30°C. From the resulting force–time plots, the hardness (the force required to attain a given deformation), compressibility (the work required to deform the product during the first pass of the probe) and adhesiveness (the work necessary to overcome the attractive forces between the surface of the sample and the surface of the probe) were derived. [12, 13]

Spreadability test

Spreadability denotes the area over which a topical formulation spreads when applied to affected parts of the skin. A spreadability test was carried out on the *shata*

dhauta ghrita and nanolipogel (F7) using a CT3 texture analyser in compression mode. The formulations were transferred into the lower cone. Care was taken to avoid introducing air into the samples. A conical analytical probe (45°) was forced down into each sample at a defined test speed (2 mm/second) to a defined depth (12 mm). At least five replicate analyses of each sample were performed at temperatures of 25°C and 30°C. From the resulting force–time plots, the firmness and the spreadability were derived [14].

Particle size

The particle sizes of the *shata dhauta ghrita* and nanolipogel (F7) were measured using a Malvern zetasizer (Ver. 6.20). The mean particle size and particle size distribution (PDI) were determined using this equipment.

In-vitro drug release study

An *in-vitro* drug release study of the gel was performed using a cellophane dialysis membrane and modified Franz diffusion cell apparatus. The cellophane membrane was soaked in phosphate buffer (pH 6.8) for 24 hours. The membrane was cut into circles of diameter 3 cm. The receptor compartment was filled with phosphate buffer (pH 6.8). The temperature was maintained at 37±0.5°C using a water jacket. 0.5 gm of the nanolipogel was uniformly spread on the cellophane membrane. The solution in the receptor compartment of the Franz diffusion cell was continuously stirred at 50 rpm using a magnetic stirrer. At specific time intervals, 1 ml of the solution was taken out and immediately replaced with 1 ml of fresh phosphate buffer solution. The concentration of the drug was determining using UV spectroscopy at 258nm [15]

***Ex-vivo* drug permeation study**

A percutaneous permeation study of the gel was carried out using modified Franz diffusion cell apparatus. The membrane used was goat abdominal skin. The skin was cut into circles of diameter 3 cm. Prepared skin samples (goat skin) were mounted on the receptor compartment of the permeation cell with the stratum corneum facing upward and the dermis side facing downward. The donor compartment was kept on the receptor compartment and secured tightly with clamps. The receptor compartment was then filled with 10 ml of pH 6.8 phosphate buffer. The temperature of the medium was maintained at 37±0.5°C using a temperature-controlled water jacket. 0.5 gm of the nanolipogel was spread uniformly on the skin. The solution in the receptor compartment of the Franz diffusion cell was continuously stirred at 50 rpm with a magnetic stirrer. At specific time intervals, 1 ml of the solution was taken out and immediately replaced with 1 ml of fresh phosphate buffer solution. The concentration of the drug was determining by UV spectrophometry at 258nm [12]

Antifungal activity study

Fluconazole acts as a fungistatic and inhibits the biosynthesis of ergosterol, the major sterol found in the fungal cell membrane. The prepared formulation was tested using agar well diffusion against *Candida albicans* stain. Sabouraud dextrose agar was prepared, and the fungal stain (*Candida albicans*) was dispersed in the medium. The medium was poured into a sterile Petri plate and allowed to cool to room temperature. Once it solidified, 6 mm wells were cut using a flamed cork borer. Each of the wells was filled with the prepared formulation and a commercial formulation (0.5%) using a sterile syringe. Each well was observed and the diameter of inhibition calculated and compared with that of the commercial formulation [16, 17]

RESULTS

Nine nanolipogel formulations were prepared using different concentrations of Carbopol 934P and *shata dhauta ghrita*. Batch F7 was selected for further evaluation on the basis of physical stability. Other batches showed phase separation or instability.

Drug–excipient compatibility studies

Any formulation development work has to be preceded by preformulation studies. This preformulation study includes drug-excipients compatibility deliberate by DSC and FT-IR analysis.

DSC

The DSC thermogram of fluconazole is characterized by one sharp endothermic peak at about 139°c, which corresponds to the melting point of fluconazole. The DSC scan of physical mixture also showed a sharp melting at 139°C. It is clear that there is no change in the position of the characteristic peak of the drug in the physical mixture with carbopol. The gel formulation showed a melting point at 124°C indicates slight alteration of melting point it was assumed that the interaction of *shata dhauta ghrita* responsible for alteration of melting point.. This indicates there was no interaction between the drug and all the polymers used in the preparation of gel. The results are shown in Figure 1.

FTIR

The FTIR study showed that there was no major change in the position of the peak obtained in the nanolipogel formulation compared with the drug. This shows that there was no interaction between the drug and the excipients. The results are shown in Figures 2 and 3.

Physical examination

The *shata dhauta ghrita* and nanolipogel formulations were white and viscous, with a smooth, consistent and homogeneous appearance. They were easily spreadable and considered acceptable patients compliance to avoid the risk of irritation upon application to the skin. (Table 2).

Rheological study

Rheological studies were performed on a Brookfield viscometer (RST-CC rheometer) with coaxial cylinder spindles. The shear stress, shear rate and viscosity data generated for the optimized nanolipogel batch (F7) was used to understand the characteristics of the nanolipogel.

Table 1: Composition of formulation batches (% w/w)

Ingredients (%)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Fluconazole	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
SDG	30	50	70	30	50	70	30	50	70
Carbopol-934P	0.35	0.25	0.15	0.7	0.5	0.3	1.05	0.75	0.45
Propylene Glycol	5.95	4.25	2.55	5.95	4.25	2.55	5.95	4.25	2.55
Methyl Paraben	0.007	0.005	0.003	0.007	0.005	0.003	0.007	0.005	0.003
Propyl Paraben	0.035	0.025	0.015	0.035	0.025	0.015	0.035	0.025	0.015
Triethanolamine	1.05	0.75	0.45	1.05	0.75	0.45	1.05	0.75	0.45
Purified Water	70	50	30	70	50	30	70	50	30

SDG, *shata dhauta ghrita*.

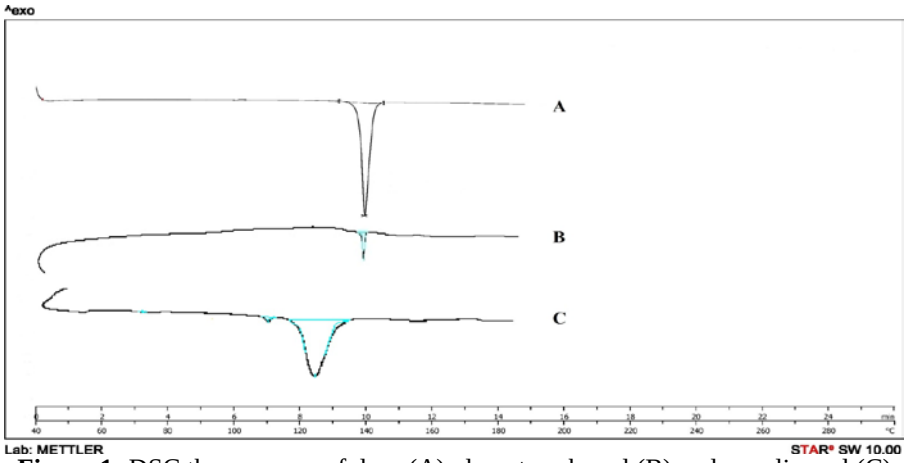

Figure 1: DSC thermogram of drug (A), drug + carbopol (B) and nanolipogel (C)

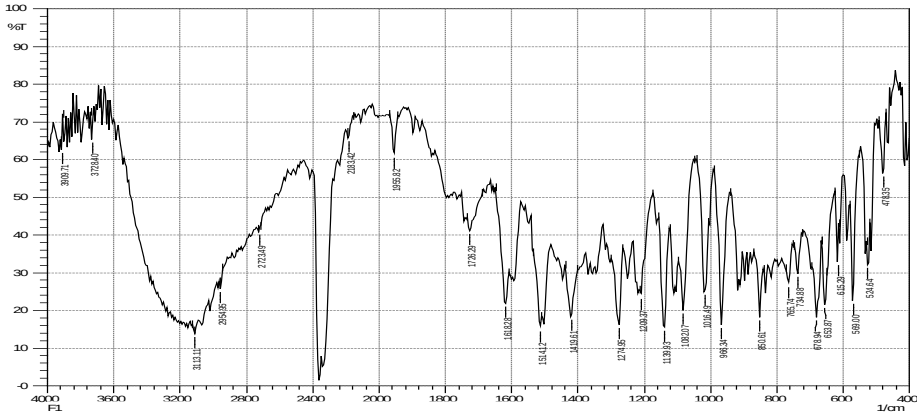

Figure 2: IR spectrum of drug

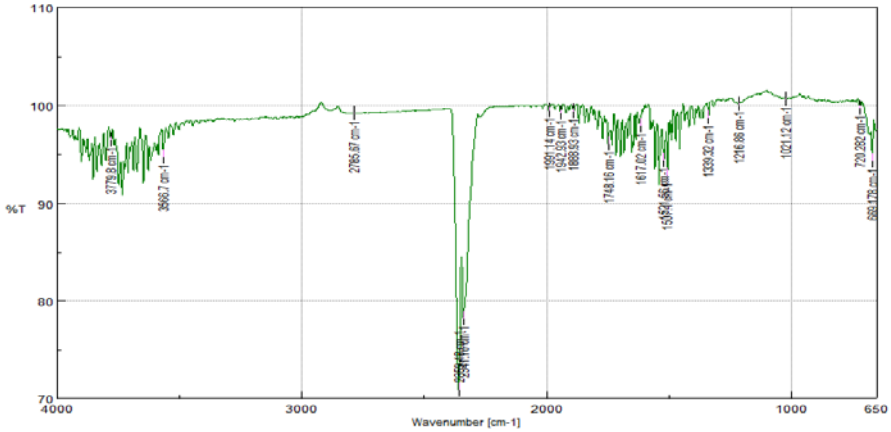

Figure 3: IR spectrum of nanolipogel (F7)

Table 2: Appearance and pH of *shata dhauta ghrita* and nanolipogel

Sr. No.	Formulation	Appearance	pH
1	SDG	White, Smooth, Non oily	6.1±0.27
2	NLG (F7)	White, Smooth, Viscous	7.2±0.15

SDG, *shata dhauta ghrita*; NLG, nanolipogel.

Table 3: Percentage yield, drug content (%) and tube extrudability of nanolipogel

Percentage Yield	Drug Content (%)	Tube Extrudability
98.45	97.12±0.19	Excellent

The results of the rheological studies indicate that the formulation was a non-Newtonian system (dilatant) because the viscosity of the nanolipogel changes with a change in the applied shear force.

The results of the thixotropy analysis indicate that the formulation was a non-Newtonian system (dilatant) because as the shear rate changed the formulation showed a change in viscosity. All the rheograms and the results of thixotropy analysis are shown in Figures 4 and 5, respectively. The shear stress, shear rate, viscosity and temperature data are shown in Table 4.

Table 4: Data of rheological study

Sr. No.	Time (s) T	Shear Stress (Pa) ƮƮ	Shear Rate (1/s) Ẏ	Viscosity (Pa.s) Ƞ	Temp (°C) T
1	10	0.000	0.000	0.0000	1000.0
2	20	9.984	0.000	0.0000	1000.0
3	30	19.989	0.022	906.6497	1000.0
4	40	29.993	0.065	462.5318	1000.0
5	50	39.998	0.185	215.6723	1000.0
6	60	49.982	0.654	76.4675	1000.0
1	70	49.998	0.888	56.2622	1000.0
2	80	39.998	0.441	90.7092	1000.0
3	90	29.993	0.195	154.1773	1000.0
4	100	19.989	0.039	513.7682	1000.0
5	110	9.984	0.001	0.0000	1000.0
6	120	0.000	0.000	0.0000	1000.0

Texture profile analysis

Texture profile analysis (TPA) of *shata dhauta ghrita* and the nanolipogel was carried out using a CT3 texture analyser in TPA mode. TPA is a method used to determine mechanical properties in which a conical analytical probe (45°) is depressed twice into the sample at a test speed (2 mm/second in this study) to a depth (12 mm in the study). A predefined period is provided between the end of the first depression and the beginning of the second depression of *shata dhauta ghrita* and the nanolipogel (Figures 6 and 7, respectively).

The maximum negative force on the graph indicates the adhesive force exerted by the sample; the more negative the value is, the more "sticky" it is. The area under the negative part of the graph is known as the adhesiveness (the energy required to break the probe–sample contact) and can give an indication of the cohesive forces between the molecules within the sample. The peak/maximum force is taken as a measure of the firmness; the higher the value is, the thicker the sample is.

Spreadability test

The spreadability of *shata dhauta ghrita* and the nanolipogel were determined using the CT3 texture analyser in compression mode. Compression is a method of determining the spreadability pattern of a material. When a trigger force of 7 g has been developed, the conical analytical probe (45°) penetrates the sample at a test speed of 2 mm/second to a depth of 12 mm. During this time, the force required to penetrate the sample increases. When the specified penetration distance has been reached, the probe withdraws from the sample at the post-test speed of 2 mm/second. The maximum force value on the graph is a measure of the firmness of the sample at the specified depth. The area under the positive curve is a measure of the energy required to deform the sample to the defined distance (hardness work done). Research has shown that the firmness and energy required to deform a sample to a defined depth can be used to grade samples in order of spreadability. A higher peak load (firmness) and hardness work done value indicate a less spreadable sample. Conversely, a lower peak load (firmness) value coupled with a lower hardness work done value indicates a more spreadable sample. The spreadability values of *shata dhauta ghrita* and the nanolipogel are shown in Figures 8 and 9, respectively.

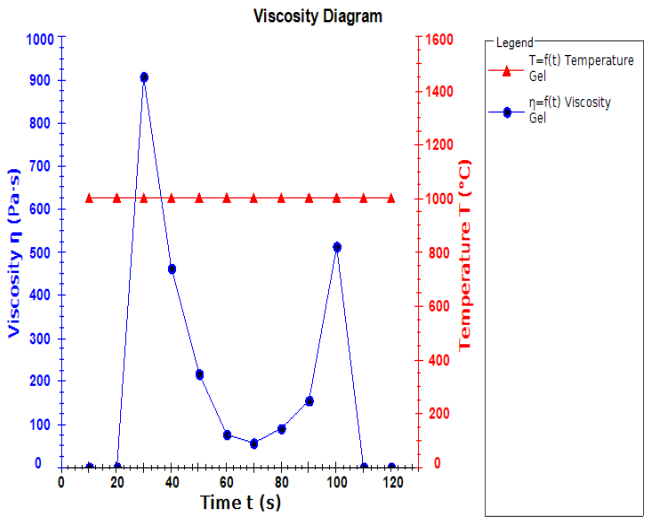

Figure 4: Rheogram of nanolipogel (F7)

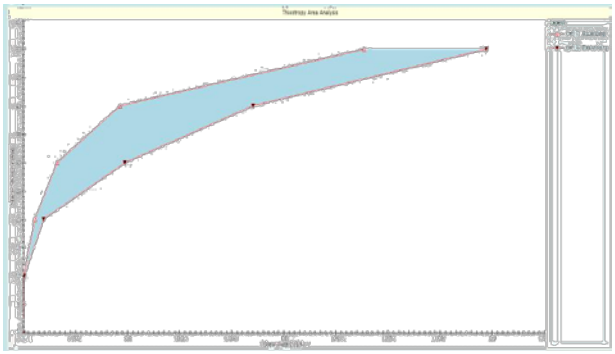

Figure 5: Thixotropy analysis of nanolipogel (F7)

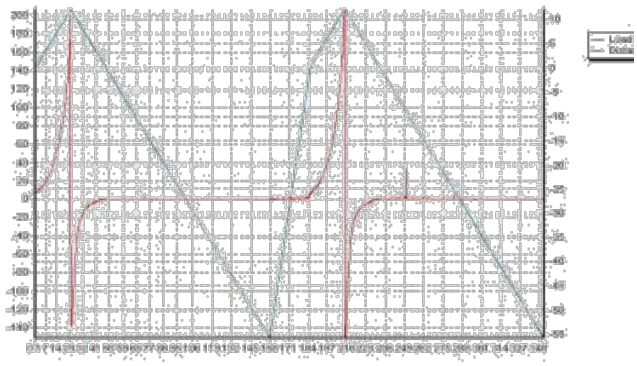

Figure 6: Texture profile analysis (TPA) spectra of *shata dhauta ghrita*

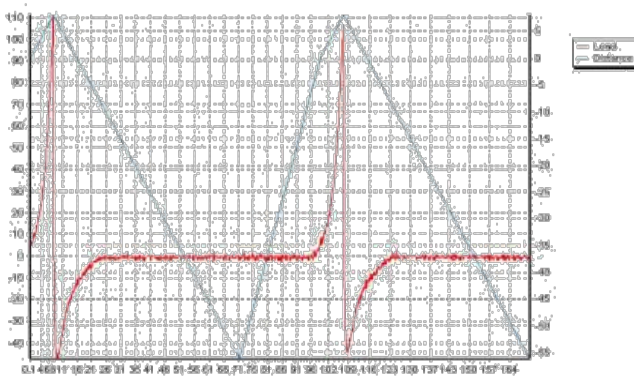

Figure 7: Texture profile analysis (TPA) spectra of nanolipogel (F7)

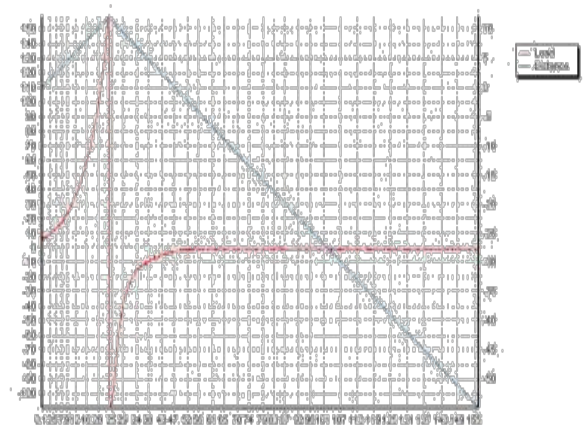

Figure 8 : Spreadability pattern of *shata dhauta ghrita*

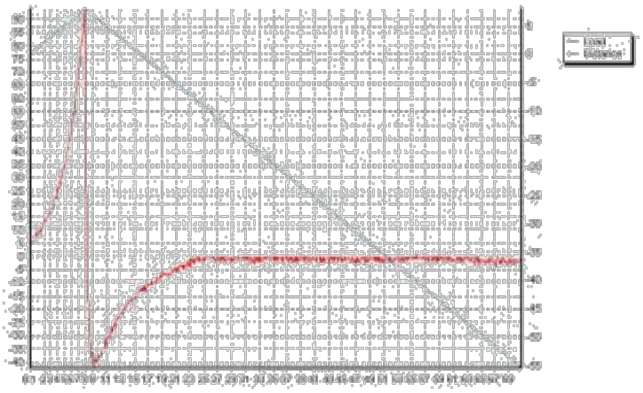

Figure 9 : Spreadability pattern of nanolipogel (F7

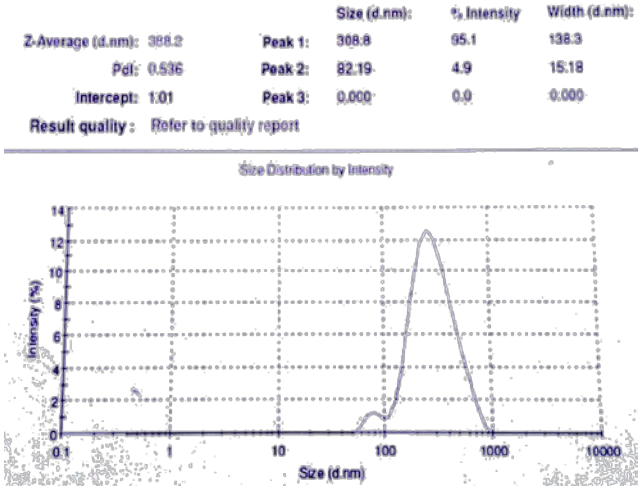

Figure 10: Particle size analysis of *shata dhauta ghrit*

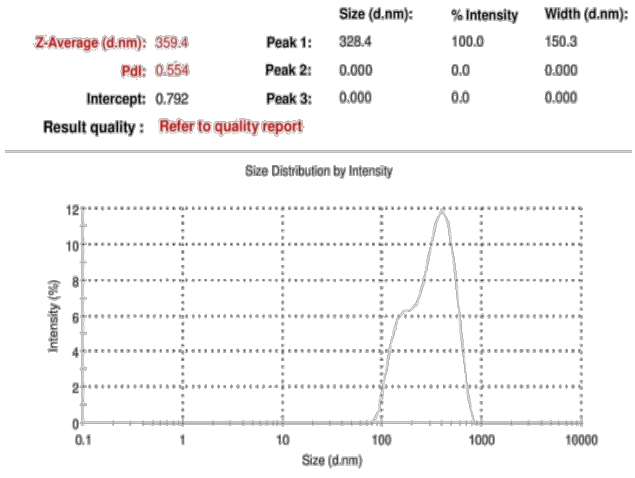

Figure 11: Particle size analysis of nanolipogel (F7)

Particle size

The average particle size of the *shata dhauta ghrita* was evaluated using a Malvern zetasizer. The average particle size was found to be 388.2 nm with a PdI value of 0.536 (Figure 10). The average particle size of the optimized nanolipogel batch (F7) was found to be 359.4 nm, with a PdI value of 0.554 (Figure 11).

***In-vitro* drug release study**

An *in-vitro* drug release study was conducted for plain fluconazole gel (without *shata dhauta ghrita*), the fluconazole nanolipogel and the commercial formulation (0.5%). The release profile obtained is shown in Figure 12. It was observed that the release of the drug from the plain fluconazole gel, nanolipogel (F7) and commercial formulation was 29.36%, 80.50% and 72.24%.

Release kinetics

The *in-vitro* release data were fitted to various release models, namely, the zero order, first order, matrix, Peppas and Hixson–Crowell models, and the best fit model was decided on the basis of the highest r^2 value. The Peppas model had the highest regression value (0.9943 for F7) and was found to be the best fit model for the nanolipogel formulations (Table 6).

Table 5: *In-vitro* drug release study of plain gel, marketed formulation and nanolipogel (F7)

Time (min)	Plain Gel	Marketed Formulation (%)	F7 (%)
0	00	00	00
30	2.79	7.91	9.71
60	5.55	15.20	17.33
90	9.24	22.79	25.28
120	11.78	29.53	32.29
150	15.07	36.23	40.64
180	17.42	43.66	47.70
210	21.12	49.81	55.35
240	24.09	56.02	63.28
270	27.33	64.94	72.72
300	29.36	72.24	80.50

Table 6: Release kinetics data of nanolipogel formulations (F7)

Zero order	First Order	Matrix	Peppas	Hixson–Crowell	Best fitting model
0.9869	0.9806	0.8799	0.9943	0.9829	Peppas

Table 7: *Ex-vivo* drug permeation study of plain gel, marketed formulation and nanolipogel (F7)

Time (min)	Plain Gel	Marketed Formulation (%)	F7 (%)
0	00	00	00
30	3.55	8.11	10.41
60	5.78	15.25	18.1
90	8.21	23.95	27.08
120	12.82	30.3	34.78
150	15.02	38.83	42.57
180	17.78	45.66	50.7
210	22.16	52.81	59.33
240	25.33	58.02	67.47
270	27.33	64.09	74.52
300	31.08	71.41	83.65

Table 8: Release kinetics data of nanolipogel formulations (F7)

Zero order	First Order	Matrix	Peppas	Hixson–Crowell	Best fitting model
0.9879	0.9802	0.8803	0.9969	0.9853	Peppas

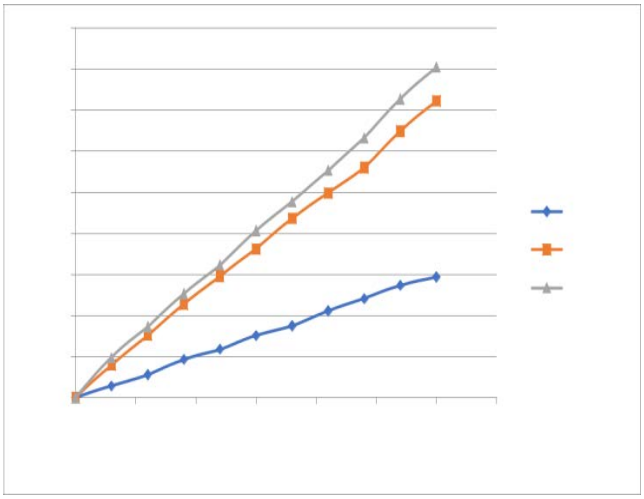

Figure 12 : *In-vitro* drug release study

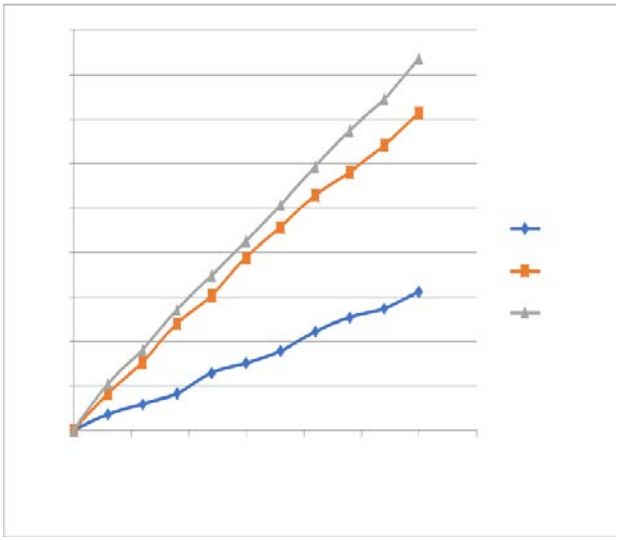

Figure 13: *Ex-vivo* drug permeation study

***Ex-vivo* drug permeation study**

The results of the *ex-vivo* permeation study and the release profile obtained are shown in Figure 13. The release values of the drug from plain fluconazole gel, nanolipogel (F7) and commercial formulation were found to be 31.08%, 83.65% and 71.41%.

Release kinetics

The *ex-vivo* permeation data were fitted to various release models, namely, the zero order, first order, matrix, Peppas and Hixson–Crowell models, and the best fit model was decided on the basis of the highest r^2 value. The Peppas model had the highest regression value (0.9969 for F7) and was found to be the best fit model (Table 8).

Antifungal activity study

In the antifungal studies the fungus used was *Candida albicans*. The zones of inhibition of F7 (18 mm) and the commercial formulation (16 mm) are shown in Figures 14 and 15, respectively.

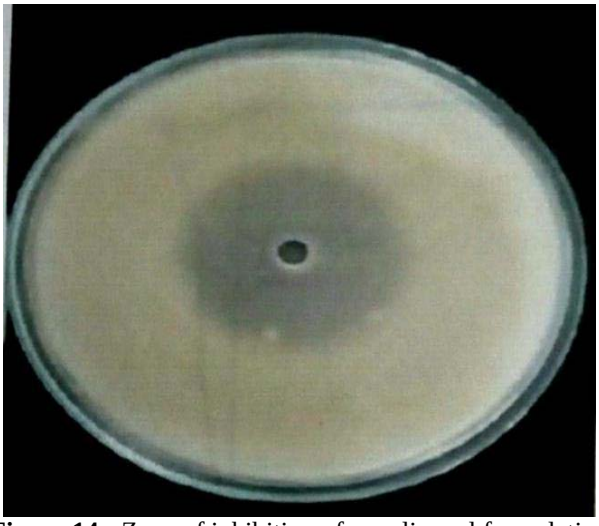

Figure 14 : Zone of inhibition of nanolipogel formulation (F7)

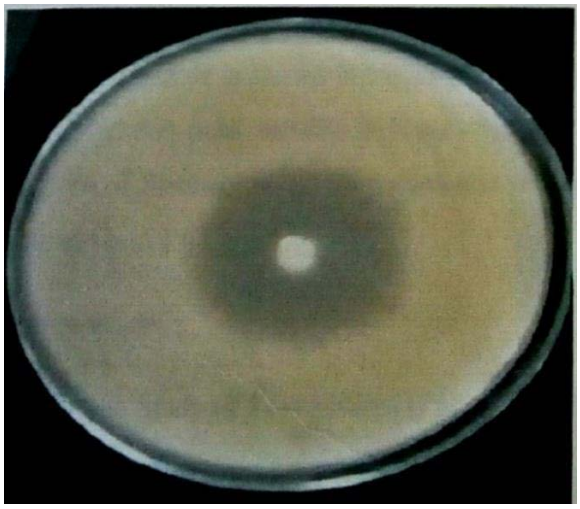

Figure 15: Zone of inhibition of marketed formulation

DISCUSSION:

Fungal infection ok skin is one of the most common dermatological problems. Fungal infection skin cause variety of different rashes, itchy, scaly, dry, red patch of skin that slowly gets bigger. It is mainly treating by applying antifungal formulation directly to the affected area of the skin. The present research work focuses on the formulation, development and characterization of topical antifungal nanolipogel by using *shata dhauta ghrita*. It may be used as permeation enhancer to increase the permeation rate of poorly permeable drugs like fluconazole.

Shata dhauta ghrita is used as natural permeation enhancer in topical product. It is prepared by cow ghee washing with 100 times with water. It is smooth, homogenous, non-oily product, easier to apply and thus improve patient compliance. pH change from acidic to neutral makes it beneficial to prevent skin irritation. Reduction in particle size makes the product non-granular, non-sticky, homogeneous, which makes it easy to apply on skin and may result in increased rate of absorption through skin. It was concluded that *shata dhauta ghrita* used as permeation enhancer in the topical formulation.

The preformulation study contains spectroscopy study, melting point, DSC and physicochemical properties. The FTIR spectra showed principle peak of hydroxyl, azide and benzene oops. The melting point with capillary method and DSC thermogram show same as 139^0 C. The nanolipogel prepared by using gel base and SDG. The nanolipogel formulations were containing different concentration of SDG and carbopol-934P. The optimized nanolipogel batch was contained 30% SDG and 70% gel base with 1.5% carbopol-934P.

In the present study particle size of SDG and formulation was determine using Malvern zetasizer, which showed the Z-average value 388.2 nm and 359.4 respectively. Appearance was determined such as white smooth and viscous. The physical properties were determined by measurement of pH, percentage yield, drug content, extrudability. The pH of SDG and nanolipogel were found to be 6.1 and 7.2 respectively. The stability study was performed for this F7 batch. The reheological study of optimized batch was performed by brookfield viscometer (RST-CC rheometer) to determine the viscosity and flow behaviour of the formulation. F7 batch showed good texture profile analysis and spreadability was observed from ghraph. In-vitro drug release and Ex-vivo permeation study were performed using phosphate buffer pH 6.8 was used as diffusion medium. The results of in-vitro drug release and ex-vivo permeation showed that the highest values of F7 formulation (80.50%) and (83.65%) after 5 hrs showing better results of nanolipogel over marketed preparation. *Penicillium* was used as a model fungus to evaluate the antifungal activity of prepared nanolipogel using marketed gel (0.5%) as control, showing better results of nanolipogel over marketed preparation.

CONCLUSIONS

The purpose of the present study was to develop a nanolipogel formulation of fluconazole using *shata dhauta ghrita* for antifungal drug delivery. The present study showed that *shata dhauta ghrita* may be used as a permeation enhancer in a topical drug delivery system for a poorly permeable drug like fluconazole to increase the permeation rate. The optimized batch showed higher drug release and antifungal activity compared with the commercial formulation. From the present study it can be concluded that the use of a nanolipogel is a better approach for increasing the release, permeation rate and antifungal activity of topical applications.

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Abbreviations:
SDG: Shata dhaura ghrita
FLZ: Fluconazole
NLG: Nanolipogel
TPA: Texture profile analysis
DSC: Diffrential scanning calorimetry

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Not Applicable

Consent for Publication:
Not applicable

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Dr. P.V.V. has given his contribution in the collection of material and finding important tool of research work.
Dr. P.V.P. has given contribution in the selection of preparation method of the formulation.
Mr. Z.N.S. has given his contribution in the study of characterisation part of research work.
Mr. P.S.R. given his contribution in study of ex vivo permeation and checking antifungal activity.
Mr. P.A.K. has given his contribution in to check drug excipient compatibility study.