Original Article

Statistical Optimization Amalgamated Approach on Formulation Development of Nano Lipid Carrier Loaded Hydrophilic Gel of Fluticasone Propionate

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ABSTRACT

Introduction: Formulation of a nano lipid carrier loaded hydrophilic gel of a corticosteroid, fluticasone propionate (FP) was investigated systemically with response surface model (RSM) for promising dermal delivery of the drug. **Objectives:** To achieve a better penetration of the drug and to overcome the generally associated adverse reactions of corticosteroids, the present study, explored the formulation and evaluation of nano lipid carriers (NLCs) of FP in a hydrophilic gel base. **Methods:** A central composite design was proposed to study the effect of processing materials on the physicochemical properties of the NLC. High shear homogenization method with stearic acid, isopropyl myristate and poloxamer 407 was used to make different batches of FP-NLCs. The model was optimized at a significance level of $P<0.05$. FTIR, DSC and surface morphology studies were carried out for the optimized product. The optimized product was incorporated in the Carbopol P940 gel base and was evaluated for its mechanical and rheological properties, *ex-vivo* permeation and skin irritation study. **Results:** It was observed that using the proposed model, a nano size (179 nm) stable (Zeta potential -26 mV) optimized product of FP-NLC with 85% entrapment efficiency was achieved. The nanogel exhibited a spreadability of 4.2 gm.cm/sec and a viscosity of 92.6 cp. Approximately 3.5 times improvement in *ex-vivo* permeation and no skin irritations on animals were reported on application of the nanogel of FP. **Conclusion:** Hence the investigation created a paradigm to explore the efficacy of nanogel of FP for dermal application with improved permeation and promising therapy for dermatitis.

Key words: Fluticasone propionate, Niosome, Central composite design, Gel, *Ex-vivo* permeation.

INTRODUCTION

Nanostructured lipid carriers (NLC) are novel lipidic formulations of blend of solid lipid (SL) and liquid lipids (LL). They provide greater drug encapsulation and stability for the entrapped drug in its irregular imperfect matrix.[1] The enhancement of drug loading capacity and minimal expulsion of drug from the matrix on storage are the additional beneficial effect of the imperfect matrix in NLC. They are suitable for dermal delivery.[2] Targeting at the deepest layer of epidermis can be attained as it can penetrate deeper layers of skin without skin thinning, which is generally associated with topical administration of corticosteroids.[3] Hence, they are reported as an optimistic lipid carrier for dermal penetration and permeation.[4,5]

Fluticasone propionate (FP), a corticosteroid, is generally used for the treatment of dermatitis and eczema.[6] It is marketed in conventional dermal preparations e.g., creams and ointments. The topical application of FP is associated with local adverse effects like skin atrophy, dermatoses and contact allergy.[7] Brown PH *et al.* reported that conventional dosage form of FP might result in induced vasoconstrictions in patients.[8] Therefore, a novel dermal delivery of FP can be designed for achieving

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enhanced skin penetration and good control over the adverse reactions for its indications. Review of literature revealed that an emulgel of FP showed better dermal effectivity on *in-vitro* permeation study.[9]

Therefore, the current investigation focuses on the delivery of nanostructured lipid carriers of FP dispersed in a hydrophilic gel as a promising mode of delivery of drug for topical use.[10] The nano carriers loaded gel shows greater efficacy for poorly soluble drugs in intracellular penetration by enhancing the contact period at the target area resulting in lesser side effects.[11] They are biocompatible and show versatile skin applications. As NLCs are a blend of solid and liquid lipid, a systematic approach through response surface design was integrated in the present study by varying the material attributes to investigate the variations in the responses like drug content, entrapment efficiency of drug in the lipid and its release from the matrix. The *ex vivo* permeation of FP nano gel through rat skin was also estimated.

MATERIALS AND METHODS

Materials

Fluticasone propionate was acquired from Vamsi lab Ltd, Hyderabad, India. Stearic acid and isopropyl myristate was bought from Central drug house (P) Ltd., New Delhi, India. Poloxamer P 407 was a gift from Dr. Reddy's laboratories, Hyderabad, India.

Methods

Formulation and design of NLC

The drug database of Fluticasone propionate (FP) has reported a poor solubility and less permeability of the drug for skin penetration.[12] Therefore, the entrapment of the drug in NLC to render effective penetration through the skin was the main aim for formulation of FP-NLC. Reported studies on solubility and partitioning of drug in lipids revealed that the drug content (DC), entrapment efficiency (EE) and % drug release of nano particles were greatly influenced by the constituents of the formulation SL:LL and concentration of surfactant (% SAA).[13,14] In preformulation experimentations it was observed that the solubility and partitioning of the FP in the specified levels of lipid ratio as mentioned in Table 1 influenced its entrapment and dissolution. The preformulation studies also revealed that at a fixed shear rate of 10000 rpm for 10 min the particle size was not varied significantly within the extreme level of lipid ratio and found to be within the range of less than 180 nm. Thus, a central composite uniform precision design using JMP V 13 was exercised to evaluate the effect of critical formulation variables on DC, EE and % drug release of the prepared NLC. The design yielded eleven experimental runs with two centre points to have effective control over pure error with the star points (-1.414 and +1.414) as rotatable circumscribed CCD. The independent variables ranges are listed in Table 1.

Table 1: List of independent and dependent variables.

Independent variables			Dependent variables
	High	Low	Drug content
SL: LL (Lipid ratio)	10:1	30:1	%Entrapment efficiency
%SAA	5	10	*In-vitro* drug release

Preparation of NLC

High shear homogenization (HSH) method was used for preparation of FP-NLC's.[15] A preformulation study on the solubility of FP in different solid lipids like stearic acid and glyceryl monostearate was performed and the solubility of FP was observed visually under normal light. The liquid lipid was chosen among olive oil, palm oil and isopropyl myristate after determining the solubility by bath shaker method for 24 h.[16] Stearic acid and isopropyl myristate were chosen for solid and liquid lipid from the preliminary solubility studies, respectively. The calculated quantity of lipid mixture was warmed up to 70°C on a water bath. The drug was incorporated to lipid mixture at a percentage 5 %w/w. An aqueous warm solution of Poloxamer P 407 (2 %w/v) was incorporated under HSH (10,000 rpm for 10 min). The resultant emulsion was poured into a petri dish and was left to solidification at room temperature for overnight.[17]

Assessment of drug loaded NLC

Drug content

A fixed quantity of formulation was disrupted in methanol in vortex shaker for 5min and from this, an aliquot was pipetted out. A syringe filter of 0.22 µm was used to filter the aliquot. It was further diluted with methanol. The drug content of the sample was determined spectrophotometrically at 236 nm. Three assessments were done for each formulation.[18]

Entrapment efficiency

The percentage encapsulation of all the prepared formulations was estimated by measuring the amount of unbound drug in the formulation by ultra-centrifugation method.[5] A known quantity of the sample was dispersed in phosphate buffer (PB pH 7.4) and was centrifuged at 5000 rpm for 30 min using Remi centrifuge. An aliquot of the supernatant layer after dilution with methanol, was analysed spectrophotometrically at 236 nm to estimate

the free drug.[19] In each case, a blank formulation was treated in the above manner and the dilution of the aliquot from it was used as a blank to negate the interference of excipient. The % entrapment efficiency was calculated using equation. All the formulations were tested in triplicates.

$$\%\text{Entrapment efficiency} = \{(\text{Total drug-Free drug}) \div \text{Total Drug}\} \times 100$$

In vitro drug diffusion studies

Dialysis membrane 70 (Himedia) (Pore size 2.4 nm, Molecular weight 12,000Da) was used for the *in vitro* study in the Franz diffusion cells. The membrane was soaked in the media for overnight. The diffusion medium selected was PB pH 7.4. In the donor compartment formulation (equivalent to 0.3 mg FP) was taken for the study. The experimentation was conducted at a temperature of 37 ±1°C with a stirring at 100rpm. At a regular interval (upto 90 mins), from the receptor chamber 2ml of sample was withdrawn and replaced with the same volume of the fresh medium. The aliquots were suitably diluted with methanol and analysed spectrophotometrically by the developed method at 236nm. All the readings were taken thrice to avoid errors in prediction.[20]

Particle size (PS) and Zeta potential (ζ) analysis

The PS of the optimized FP-NLCs were determined (Horiba SZ-100). Double distilled water was used to dilute the sample. The measurement of the PS and ζ potential were done through the principle of dynamic light scattering and electrophoretic light scattering, respectively at 25.2°C. Three tests were made for each sample.[21]

FTIR Spectroscopy

FTIR study (IRAffinity-1S, Shimadzu, Japan) of the FP, blank and drug loaded optimized formulation were performed by potassium bromide (KBr) pellet method. The spectra were detected in the range from 500 to 4,000cm^{-1} using a resolution of 1cm^{-1} and were analysed for compatibility of the drug and the lipids.[22]

Differential Scanning Calorimetry (DSC)

DSC analysis of FP and optimized FP -NLC formulation were performed using SHIMADZU DSC-60 instrument. The operation was performed under nitrogen environment at a heating rate of 10°C per min from a temperature 50°C to 350°C. An empty aluminium pan was used as reference standard. The thermograms and the phase transition behaviour were recorded as outcome of the analysis.[13]

Scanning electron microscopy

The external morphology of the optimized FP-NLC sample was imaged with scanning electron microscope (Vega 3 tescan). A smear of sample in double distilled water was air dried on a slide. The slide was investigated at 10kV and photographs were taken at 10 KX magnification.[23]

Preparation of nanogel

The preparation of nanogel, Carbopol 940 P was used as a gelling agent. It was dispersed (0.5%w/w) in distilled water containing 7% w/w of propylene glycol at 500rpm for 2hr. The FP-NLC equivalent to 5mg FP was dispersed in the 10 gm of gel (0.05%w/w) using magnetic stirrer (Remi, India) at 1500 rpm for 15min. The pH of the final dispersion was adjusted to 5.5 by addition of few drops of sodium hydroxide. The entrapped air in the gel was removed by letting it stand undisturbed overnight.[4,24]

Assessment of the gel

Appearance

The formulated FP-NLC loaded gel was tested for appearance, odour and feel upon application such as stickiness, stiffness, greasiness and smoothness.

Drug content

A specific quantity of gel was mixed with 1 ml methanol and vortexed for 15min. An aliquot of 0.1 ml was pipetted out diluted with methanol and analysed spectrophotometrically at λ-max of 236nm. The concentration of FP was estimated from the calibration curve. The investigation was carried in triplicates.[18]

Spreadability

To determine the spreadability of the gel, an excess of gel was placed between two glass slides. A weight (500gm) was placed on the top slide for few minutes to make a uniform spreading of the gel. Spread ability was determined by placing a lower weight (100g) on the upper slide and made to drag the slide over a fixed distance. The spread length and the time taken to spread were determined. Spread ability was calculated by the formula

$$\text{Spreadability} = \text{Mass}*\text{Length}/\text{Time}$$

The experimentation was done in triplicates.[25]

Viscosity

Determination of the viscosity of the gel was accomplished by placing a small quantity of gel in Brookfield

viscometer using spindle 2 at 10 rpm at 25C for 5min. The measurements were made in triplicates and the values were recorded.[26]

pH measurement

The pH of the gel was determined using digital pH meter (Digisun Electronics services, Hyderabad). The pH meter was calibrated before use with buffer tablets of various pH (pH 4, 7 and 9.2) ranges. The readings were taken in triplicates.

Ex-vivo permeation study

Rat skin was used to estimate the *ex-vivo* permeation of the nano gel of FP. The animals were used after procuring approval certificate from the Institute Ethical Committee (Approval No. KCP/IAEC/PCEU/28/2019). Excessive carbon dioxide infusion was given to euthanize the rats. The abdominal skin was taken, shaved and washed preliminary with saline solution followed by PB pH 7.4. The *ex-vivo* permeation studies were executed in Franz diffusion apparatus.[27] The receptor chamber was filled with 45 ml freshly prepared buffer solution. The rat skin was fixed between the donor and receptor compartment so that the dermal side was facing with receptor compartment. The temperature in the diffusion cell was maintained at 32±0.5°C and was stirred at 100 rpm. A weighed quantity of 1.5 g of gel was spread on the surface of the skin in the donor compartment. Permeation of the drug was measured in course of time at a stipulated interval for 4 h. The samples were analysed spectrophotometrically at 236 nm. The permeation data were compared with a marketed formulation (Cream) of fluticasone propionate and pure drug dispersed in same quantity of gel base.

Skin irritation test

The study was conducted on eighteen albino Wistar rats distributed in three groups. Group-I served as control where no application was done. A placebo topical gel was added to group II. The test FP-NLC gel was applied to group-III animals. After depletion of the hairs from the back of the animals, the areas were marked. The gels were applied on the marked areas once a day for 7 days and observed for any sensitive reactions.[28]

Statistical analysis

The *ex-vivo* data was subjected for Dunnett's multiple comparison test and analysed with Graphpad prism software Version 5 at a significance level of $P<0.05$.

RESULTS AND DISCUSSION

Evaluation of FP-NLCs

The drug content of all the FP-NLCs was found to be more than 80%. The entrapment of the drug in the lipid matrix was varied from 72- 97 % varied mainly due to the difference in composition of lipid as evidenced from the other reported studies.[28] The % release of the drug was varied from 49 to 69% and the release was good for the formulations which had high concentration of surfactant. The data are in represented in Table 2.

The optimization of the proposed design was carried out at a significance level of $P<0.05$ and yielded actual vs, predicted graph as shown in Figure 1. The graph revealed that the yielded P value <0.05 was obvious for estimation of the effects of different lipids and surfactant on drug content, entrapment efficiency and *in-vitro* drug release. The regression coefficient value (Rsq) more than 0.8 proved further the significance of the model with respect to all the responses as indicated in Figure 1.

The factor sensitivity analysis showed that the lipid ratio and %SAA had notable effect on the responses as listed in Table 3.

Table 2: Evaluation of FP-NLC as per central composite design.

Formulation code	SL: LL	%SAA	% Drug content	% Entrapment Efficiency	%CDR at 90 min
F1	-1	-1	84.9±0.02	97.3±0.01	56.0±0.03
F2	-1	+1	81.0±0.01	94.2±0.02	66.6±0.01
F3	0	0	85.0±0.04	85.7±0.03	58.0±0.02
F4	+1	+1	88.0±0.03	78.3±0.03	65.7±0.03
F5	0	0	86.0±0.05	88.3±0.02	56.0±0.02
F6	0	-1.414	87.0±0.03	88.5±0.01	49.0±0.01
F7	0	+1.414	84.0±0.07	89.7±0.04	69.0±0.04
F8	+1	-1	89.0±0.01	72.8±0.02	58.6±0.02
F9	0	0	85.6±0.02	84.1±0.01	59.0±0.06
F10	+1.414	0	89.0±0.04	69.0±0.02	64.3±0.04
F11	-1.414	0	80.7±0.07	79.8±0.01	53.0±0.01

The prediction expression shows the positive effect of lipid ratio and %SAA on drug content entrapment and % drug release and it was also evidenced from the contour plot in Figure 2.

The prediction expressions in Table 3 revealed the influence of the factors on the different responses and considering the significant effect of the factors on dependent variable, the formulation was optimized considering maximum entrapment and drug content above 85% and %CDR above 60% at desirability of 0.68. The optimization yielded a formulation condition of the desired predictions at lipid ratio 20:1 and %SAA at 8.75%.

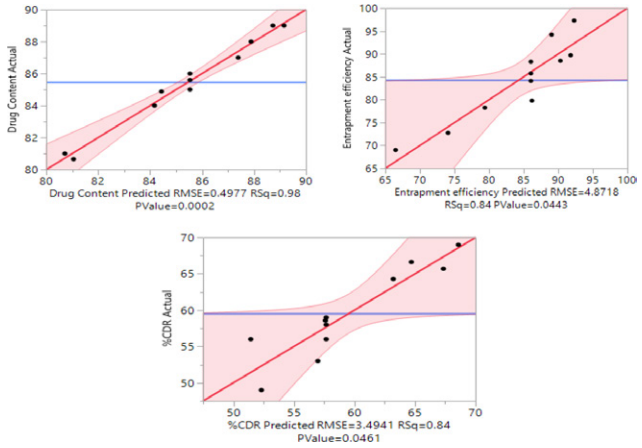


Figure 1: Actual vs. predicted plot for all three responses.

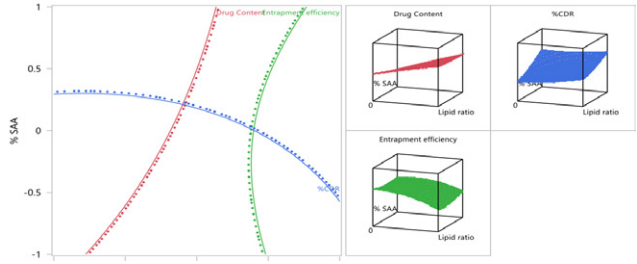


Figure 2: The contour plot and 3D surface plots of the responses with the factors.

The optimized FP-NLC was formulated at that predicted conditions and were analysed for the responses which revealed that the % bias between the predicted and observed responses were less than 5% as listed in Table 4. Therefore, the central composite design for preparation of FP-NLC by varying the lipid ratio and the % SAA was found to be effective in predicting a suitable formulation parameter of NLCs.[29]

The optimized formulation was analysed for PS and ζ potential and found that optimized product had a PS of 179 nm with ζ potential of -26 mV as shown in Figure 3. Hence it was further proved that the method of preparation with the design model could yield a nano sized stable nano lipid carrier of FP with high DC, EE and % drug release.

FTIR study

The FTIR spectra of FP, blank and FP loaded optimized NLC are shown in Figure 4. The spectra disseminated the compatibility between drug, stearic acid, isopropyl myristate and poloxamer 407. The peaks of the functional groups of the drug were well conserved in the spectrum of optimized FP-NLC. The -OH group peaks at 1415 cm^{1}, -C=C stretch at 1670 cm^{-1}, C-F stretch at 1024 cm^{-1}, ether stretch at 891 cm^{-1} and aromatic benzene ring stretch at 723 cm^{-1} were found in the formulation confirming the compatibility of the drug with the excipients.[30] The harmony of the excipients with the drug was established with the comparative study of the spectra of blank optimized formulation and optimized FP-NLC.

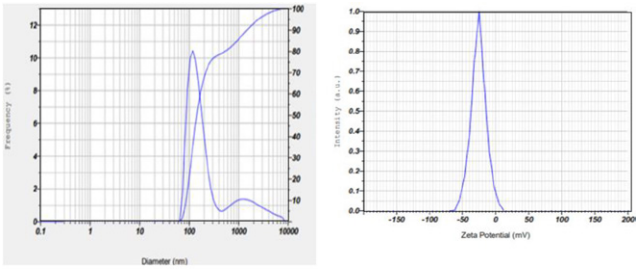
DSC

DSC thermograms permit the quantitative sensing of phase transformation with exploring the change

Table 3: Parameter sensitivity analysis.

Term	Prob> t		
	% Drug Content	% Entrapment Efficiency	% CDR
Intercept	<.0001*	<.0001*	<.0001*
Lipid Ratio	<.0001*	0.0099*	0.1348
%SAA	0.0013*	0.7756	0.0056*
Lipid ratio*%SAA	0.0341*	0.4178	0.6363
Lipid ratio*Lipid ratio	0.3523	0.0642	0.4464
%SAA *%SAA	0.5831	0.2762	0.3870
Prediction expression	85.53+2.87*Lipid ratio+- 1. 14*%SAA+ Lipid ratio. (%SAA*0.72)+Lipid ratio*(Lipid ratio-0.21)+SAA(%SAA*0.12)	86.03+-6.97*Lipid ratio+0.51*%SAA+ Lipid ratio*(%SAA*2.15) + Lipid ratio * (Lipid ratio*-4.85) + %SAA*(%SAA*2.50)	57.67+2.20*Lipid ratio+5.75*%SAA+ Lipid ratio* (%SAA*-0.88) +Lipid ratio* (Lipid ratio*1.21)+%SAA*(%SAA*1.39)

Table 4: Evaluation of optimized formulation.			
Responses	**Predicted**	**Observed**	**%Bias**
Drug content	84.95	86±0.12	1.23
Entrapment efficiency	87	85±0.03	2.29
%CDR	61.17	60.02±0.15	1.88



A B

Figure 3: Particles size (A) and Surface Charge (B) of optimized FP-NLC.

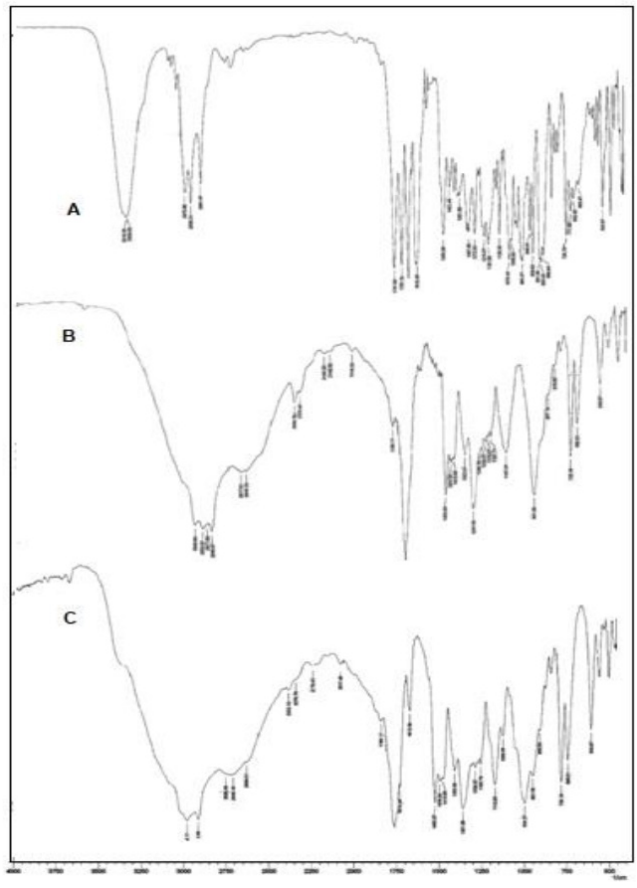


Figure 4: FTIR spectra of pure drug(A), Blank(B) and FP-NLC optimized formulation(C).

in crystallinity of the pure drug in the formulation. The results of DSC analysis are shown in Figure 5. DSC thermogram of FP showed endothermic peak at 292.69°C (melting point of FP). The blank formulation

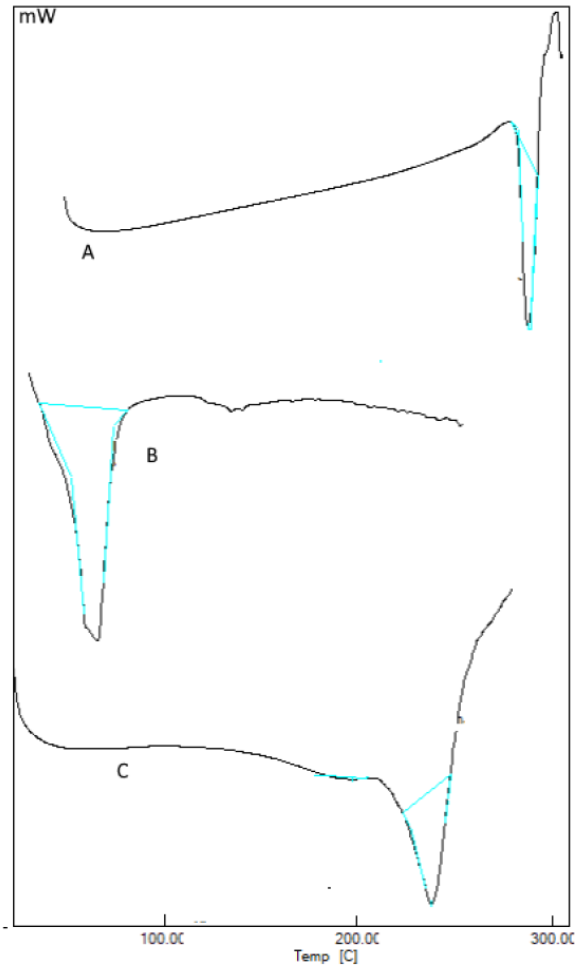


Figure 5: DSC thermograms of pure drug (A), Blank (B) and Optimized FP-NLC(C).

of the optimized formula showed a peak at 59°C. Drug loaded NLC, showed an endothermic peak at 229.90°C. The shift of peak reveals the reduced crystallinity of the drug, molecular dispersion of the drug in lipid matrix and hence high entrapment.[31] Overlay plots of DSC thermogram FP, blank formulation and optimized formulation are shown in Figure 5.

SEM

The studies were carried out for the optimized FP-NLC. It was seen that the particles were discrete without much conglomeration. The surfaces were appeared to be uneven and the particles were slightly spherical in shape as shown in Figure 6.

Evaluation of gel

The gel was found to be translucent and white in appearance. The physical characteristics of the gel showed smooth in consistency without any gritty feelings. The drug content of the formulation was found to be adequate.

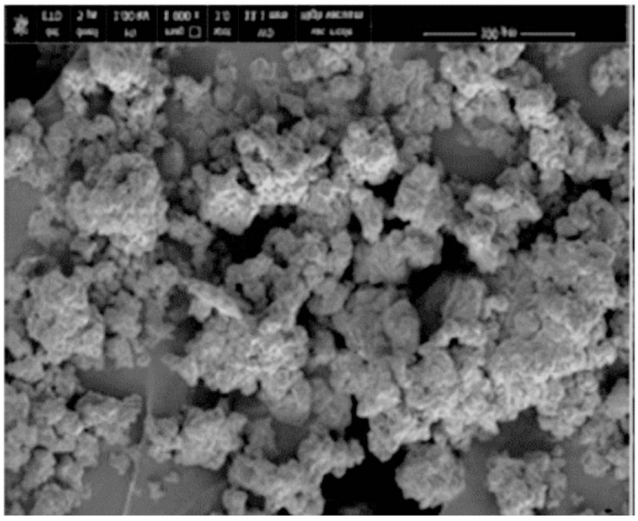


Figure 6: Scanning electron microscopy of optimized FP-NLC.

Table 5: Evaluation of FP loaded NLC based gel.	
Evaluation parameters	**Observed values**
Drug Content (%)	96.98±0.02
Viscosity (cp)	92.6±0.01
Spreadability(gm.cm/sec)	4.2±0.03
pH	5.5±0.01

*All values are mean±SD

The viscosity of FP nanogel was optimum, the viscosity was an indication of easy spreading which was authenticated by the values of spreadability. The pH of the formulation was found to be decent which conceded that the formulation could be well tolerated by the skin. Results of FP-NLC loaded gel formulation are tabulated in Table 5.

Ex-vivo permeation study

Ex-vivo permeation study was carried out for calculating permeability of FP from the nanogel and the permeation was compared with the marketed cream of FP and pure drug dispersed in same composition gel base of equivalent strength. The cumulative amount of the permeated drug per unit area from the formulated nanogel (FP nanogel), the marketed cream (Cream (MRKT)) and pure drug in plain Carbopol 940 gel (FP gel) at the end of 4 hr was found to be 11.42 μg/cm^2, 7.15μg/cm^2 and 3.13 μg/cm^2 respectively. The optimized formulation in the gel system showed better permeation owing to its nano size and enhanced permeability in a lipid carrier. The drug permeation graph is shown in Figure 7.

The permeation study was further evaluated for calculation of steady state flux (Jss) and permeability coefficient (Kp) for the prepared nanogel and the cream. The steady state flux was calculated from dividing the slope

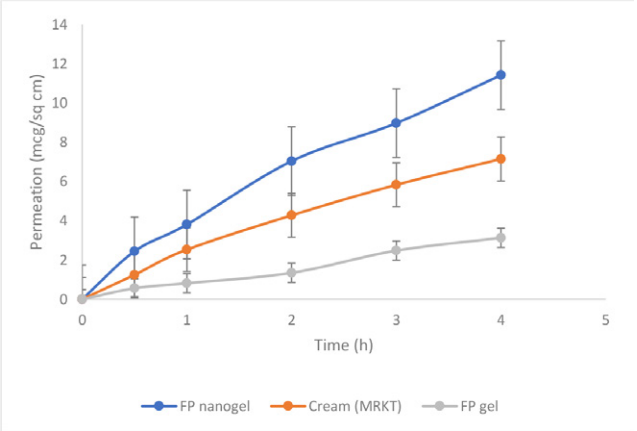


Figure 7: *Ex-vivo* permeation study of FP from different formulations.

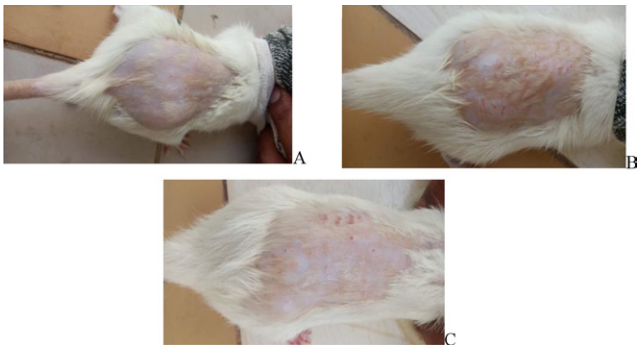


Figure 8: Skin irritation test. (A) Group-I – no application (control), (B) Group-II – placebo topical gel without NLC and (C) Group-III – topical NLC gel loaded with fluticasone propionate (FP).

of the permeation study graph with the cross-sectional area of the diffusion cell. The permeability coefficient was derived from Jss.[4] The Jss value revealed that it was significantly high (0.563 μg/cm^2/ h) compared to the marketed product (0.360 μg/cm^2/h). The Kp value of the nanogel and the cream was 7.5cm/h and 4.80cm/h respectively. The Permeability coefficient of the nanogel was also found to be greater than the marketed cream. The data of the *ex-vivo* permeation study was analysed for determining the kinetics of drug release. It was found that the release of drug from the gel matrix followed Higuchi model with regression coefficient (R^2) of 0.9927. The data when analysed with Ritgers-peppas model showed that the release exponent value (n) was 0.7461 which indicated the drug release followed non Fickian model.[32] This may be attributed to the drug release through erosion of lipid matrix of NLCs in a swellable hydrogel.

Skin irritation test

The results revealed that the gel formulation did not precipitate any symptoms of erythema, edema, or

ulceration. It was found to be non-irritant to the skin as evidenced from the Figure 8. Thus, this formulation was found to be suitable for topical application.

Statistical analysis

Dunnett's multiple comparison test was carried out with the *ex-vivo* data of FP nanogel, marketed cream and pure drug dispersed in Carbopol 940. The statistical analysis was carried out at a significance level $P<0.05$ and the outcome revealed that the FP nano gel has significant effect over marketed cream and FP gel over drug permeation through rat skin as shown in Table 6. The level of significance of the test is presented in Figure 9. This established the superiority of the nano gel of FP over other formulations on skin penetration.

CONCLUSION

Nanostructured lipid carrier of FP can be successfully formulated employing CCD model using stearic acid, isopropyl myristate and Poloxamer 107 by high shear homogenization technique. Studies showed that change in the proportions of lipids and concentration of surfactant influenced the DC, drug entrapment and drug release. The particle size and zeta potential of optimized formulation was 179 nm and -26 mV, respectively. The process was capable to produce nano structured stable NLCs of fluticasone. The optimized NLC of FP was dispersed in 0.5% w/w carbopol gel and was characterized for its mechanical, rheological, physicochemical, skin irritation and *ex-vivo* permeation studies. The nano gel exhibited more effective penetration without skin irritation as compared to the marketed cream and pure drug gel. The permeation was statistically found to be significant. Hence the nano gel of FP can be a superior delivery for the treatment of dermatitis.

Table 6: Dunnett's multiple comparison test of FP nanogel

Dunnett's Multiple Comparison Test Mean Difference		q	*P* < 0.05	Summary
FP nanogel vs Cream (MKTG)	2.53	3.054	0.0034	Significant
FP nanogel vs FP gel	5.07	6.121	0.001	Significant

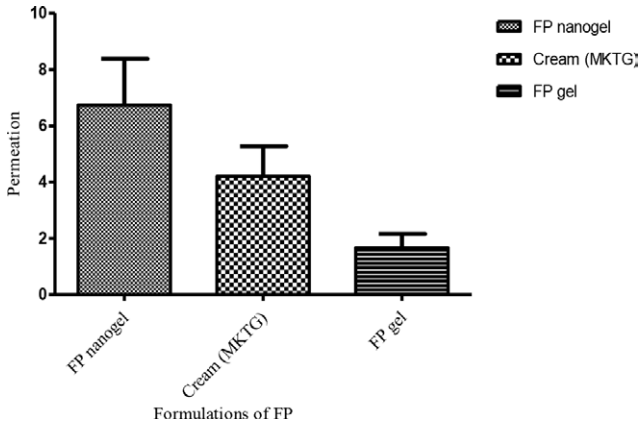


Figure 9: Graphical representation of level of significance of *ex-vivo* permeation study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

FP Fluticasone propionate; **NLCs:** Nano lipid carriers; **FP-NLC:** Nano lipid carriers of fluticasone propionate; **SL:** Solid Lipid; **LL:** Liquid lipid; **SAA:** Surfactant; **EE:** Entrapment efficiency; **DC:** Drug Content; **HSH:** High shear homogenization; **PB:** Phosphate Buffer; **FTIR:** Fourier transform infrared spectroscopy; **DSC:** Differential scanning calorimetry; **SEM:** Scanning electron microscope; **PS:** Particle size; Z: Zeta.

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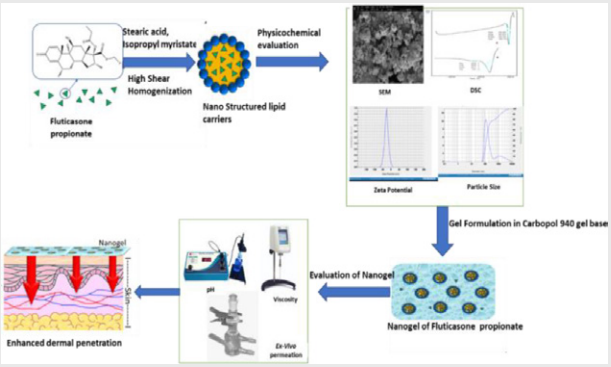
PICTORIAL ABSTRACT



SUMMARY

The intention of the research work was to develop a nanogel of fluticasone propionate, a corticosteroid, for the external application on skin. Initially a nano lipid carrier of the drug was made using stearic acid and isopropyl myristate by high shear homogenization method. The preparation method was assisted with a statistical optimization process. The optimization was executed by central composite design. The nano lipid carriers of the drug were evaluated for various physicochemical aspects, thermal study and surface morphological study. The optimized preparation was loaded into carbopol 940P gel base. The gel exhibited good compatibility and permeation through the skin. A comparative study of the prepared nanogel of fluticasone propionate with a marketed cream showed the superior characteristics of the nano gel in terms of penetration and adherence to the skin. Hence the investigation showed the fulfilment of the objective of the study.

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