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ORIGINAL ARTICLE

Formulation and Evaluation of a Transferosomal Gel of Famciclovir for Transdermal Use

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ABSTRACT

Objectives: Famciclovir, the drug of choice for cold sores and recurrent genital herpes, has poor oral bioavailability and is associated with numerous side effects. The study aimed to explore the possibility of transdermal application of famciclovir through a transferosome-loaded gelling system to localize the drug at the site of application with improved penetrability, therapeutic effects, and comfort.

Materials and Methods: Transferosomes of famciclovir were prepared using tween 80, phospholipid, and cholesterol. To optimize drug entrapment and the vesicular size of the transferosomes, a central composite design was employed. The optimized formulation was evaluated for physicochemical characteristics, surface morphology, and degree of deformability. The optimized product was included in the Carbopol 940 gelling system. The gel was evaluated for *ex vivo* permeation, skin irritation, drug deposition at various skin layers, and histopathological analysis.

Results: The design optimization yielded an optimized product (FAMOPT) of nanosized (339 nm) stable vesicles of the transferosome of famciclovir. The surface morphology analysis revealed the formation of nanovesicles without aggregation. Compatibility between the drug and excipients was established. The elasticity of the vesicles demonstrated resistance to leakage. The permeation of the drug was enhanced by 2.8 times. The gel was found to be non-irritating and non-sensitizing to the animal skin. The drug deposition at various skin layers was remarkably improved, indicating effective drug penetration. The histopathological examination further demonstrated the penetration of nano-vesiculate drugs through deeper layers of the skin.

Conclusion: Hence, nano-vesicular famciclovir delivery is a promising alternative to conventional famciclovir delivery with enhanced local and systemic action for herpes treatment.

Keywords: Famciclovir, transferosome, deformable vesicle, transdermal penetration, skin deposition

INTRODUCTION

The era of nanotechnology offers novel therapeutic avenues for antivirals to treat viral diseases successfully. Generally, the side effects associated with these small molecules need attention. The novel delivery of drugs in nanocarriers attempts to lower viral loads in a more efficient manner than conventional dosage forms.

Famciclovir is a guanine analog used to treat herpes virus infections of the skin, which are expressed through cold sores around the mouth, sores around the anus, and genital herpes.[1] The drug has poor oral bioavailability but suffers from many side effects when administered orally.[2] The dose of the drug is relatively high, and the treatment lasts for more than 7 days. Hence, a new mode of delivery of famciclovir through the transdermal route could be beneficial for the efficacy of the therapy.

Transdermal delivery of drugs through the stratum corneum is a challenge. One of the most important factors to consider for a successful transdermal formulation is the penetration of the drug through the skin, which is mostly dependent on the physicochemical properties of the drug. Drugs with optimal lipophilicity are best suited for transdermal delivery. Hence, a hydrophilic drug must penetrate the skin to elicit a systemic effect. As a result, in the last decade, lipid-based vesicles or carriers have been routinely studied for topical drug delivery.[3] Niosome, ethosomes, liposomes, and transferosomes have

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been investigated as promising vesicular carriers for enhancing transdermal drug delivery of drugs.[4,5]

Transferosomes are vesicles of phospholipids with edge activators and are one of the superior drug delivery systems for topical application.[6] They are elastic in nature, which enables them to squeeze themselves as intact vesicles through the narrow pores of the skin. The presence of edge activators is responsible for the deformable properties of the transfersomes.[7] The elastic transport is propelled by the trans-epidermal osmotic gradient between the surface of the skin and interior of the skin. Their flexibility facilitates their passage through pores that are smaller than themselves.[8]

Famciclovir has a log *p* value of 0.6, which does not support transdermal permeation. Hence, a novel carrier system is necessary for famciclovir to cross the stratum corneum and localize at the site of action.[9] The composition of transferosomes allows the vesicles to self-optimize to cross dermal barriers efficiently.[10] Therefore, the present study focused on the development and characterization of ultra-deformable vesicles of famciclovir for transdermal delivery in the treatment of herpes. [11]

MATERIALS AND METHODS

Materials

Famciclovir was obtained from Strides Pvt. Ltd., (Bangalore). Acetonitrile, methanol, cholesterol, and carbopol-940 were purchased from SD Fine Chemicals Ltd. (Mumbai, India). Tween 80, soya lecithin was supplied by Central Drug House Pvt, Ltd. (Delhi). All other chemicals were of analytical grade, and distilled water was used throughout the study.

Methods

Design of experiments

Considering the vesicle size, polydispersity index (PDI), and entrapment of sparingly soluble famciclovir as dependent variables, the transfersomes of famciclovir were prepared by optimizing three prime independent factors of the formulations, namely the phospholipid (SPC) and cholesterol ratio (CH), surfactant concentration (tween 80) (*w/v*%), and phase volume ratio. The central composite design was performed using the Design Expert V11 software. The correlation between independent and dependent factors was analyzed using the response surface methodology. The design generated 13 experimental runs with three center points. Two-level [low (-1) and high level (+1)] testing of each independent variable was performed to estimate the effect of composition on the responses, as listed in Table 1.[12] Table 2 explains the formulation table as per the design.

Transferosome preparation

A thin-film hydration technique was employed to form transferosomes.[13,14] To optimize the composition of transfersomes, various formulations were prepared using the central composite design. Specific amounts of lipids were dissolved in a mixture of organic solvents consisting of methanol and chloroform (1:3) in a dry round-bottom flask. The evaporation of organic solvents was performed under vacuum using a rota evaporator at 100 rpm, at 48-50 °C. The thin lipid film thus obtained was then hydrated using water containing surfactant and drug (1.5% *w/v*) by rotation for 1 hour at 50 °C. Each formulation was placed in an ultrasonicator bath at 150 W for 20 seconds. A dialysis bag was used to remove the free drug, and the final formulation was stored at 4 °C for further use. Blank transfersomes were prepared using the same method for each formulation.

Evaluation of transfersomes

Vesicle size

The vesicle sizes of the prepared formulations were measured using Horiba SZ100 (Dynamic light scattering technique) at 25 °C. Samples were diluted with Millipore water as a dispersant. The measurements were performed in triplicate.[15]

Zeta potential

Zeta potential was measured using a Horiba SZ100 spectrophotometer. The formulations were diluted with Millipore water before being subjected to measurements, and each measurement was performed in triplicate.[16]

Table 1. List of independent factors

Factors	Low level (-1)	High level (+1)
SPC:CH	1:1	2:1
Surfactant concentration (*w/v*%)	5	20
Phase volume ratio	0.4	0.6

SPC: Phospholipid, CH: Cholesterol

Table 2. Central composite design for transferosome formulation

Runs	Factor 1 SPC:CH	Factor 2 Non-ionic surfactant %	Factor 3 Phase volume ratio
1	1	1	-1
2	0	0	0
3	-1	1	1
4	0	1.41421	0
5	0	0	0
6	0	-1.41421	0
7	-1	-1	-1
8	1	-1	1
9	-1.41421	0	0
10	0	0	0
11	0	0	-1.41421
12	1.41421	0	0
13	0	0	1.41421

SPC: Phospholipid, CH: Cholesterol

Entrapment efficiency

The prepared dispersion was centrifuged at 3000 rpm at 4 °C for 30 minutes. The transfersomes were settled into pellets, and the supernatant layer was collected to determine the amount of unentrapped drug. The pellet was disrupted with an equal volume of methanol in a vortex mixture for 5 minutes. The sample was diluted and analyzed spectrophotometrically using 0.02 M potassium dihydrogen orthophosphate and acetonitrile (80:20) at 307 nm to determine the entrapped drug. The unentrapped drug was determined by analyzing the supernatant layer. Entrapment efficiency was calculated for all formulations in triplicate. The percentage entrapment efficiency is computed using the formula.[17]

$$\% \text{ Entrapment efficiency} = \frac{\text{Entrapped drug}}{\text{Entrapped drug} + \text{Free drug}} * 100$$

Blank transfersomes of each formulation were used as blanks to terminate the effect of the excipients. All studies were performed in triplicate.

Statistical analysis

A central composite design was employed in the study to investigate the experimental variables at five different levels on the responses with a minimum number of experiments. The results were subjected to regression analysis using the Design Expert software V13 to determine the relationship between factors and responses. The use of center points in the design increased the confidence level and helped minimize experimental errors

The 13 formulations thus prepared were evaluated for vesicle size, PDI, and % drug entrapment, and the model validation was established through ANOVA analysis at a significance level of $p < 0.05$. Design optimization was carried out to acieve maximum drug entrapment, minimum vesicle size, andPDI. The optimized formulation (FAMOPT) was adopted for further evaluation.

Fourier transform infrared spectroscopy (FTIR)

FTIR spectrophotometric analysis was performed to investigate the compatibility between the drug and excipients. The Bruker attenuated total reflection alpha technique was used for the analysis. The spectra of the pure drug, the physical mixture of the optimized blank, and FAMOPT were recorded at a temperature of 25.0 ± 0.5 °C by placing the samples on a zinc solenoid crystal plate over the wavenumber 4000 to 400 cm^{-1}.[18]

Transmission electron microscopy (TEM)

The morphology of FAMOPT was examined using a TEM [TEM; FEI Tecnai T20 (North America)]. Transferosome dispersion was placed on paraffin sheets on which carbon-coated grids were placed to allow the samples to adhere. The excess sample was removed by adsorption onto a small piece of filter paper. A drop of phosphotungstate (1%) was added to the grid. The samples were air-dried and imaged.[19]

Degree of deformability

The elasticity of the FAMOPT vesicles was determined by the extrusion method. The transfersomes were extruded at a pressure of 2.5 bar through a polycarbonate membrane (pore diameter, 0.2 microns), (Merck, India). Vesicle size was noted before and after passing through the membrane using Horiba SZ100. The degree of deformability was calculated by estimating the ratio of vesicle size before and after the extrusion process.[20] The entrapment efficiency was also determined after the extrusion method to estimate leakage, if any.

Transferosomal gel preparation of famciclovir

The transferosomal gel of famciclovir was formulated by incorporating FAMOPT (5% *v/v*) in an aqueous dispersion of carbopol 940. Carbopol 940 (0.5% *w/w*) was accurately weighed and dispersed into distilled water in a beaker. Propylene glycol (7% *w/w*) was added to the solution. Stirring was continued at 500 rpm for 2 hours, and the final pH of the gel base was adjusted to 5.5 using sodium hydroxide.[21] A gel of pure drug gel of equivalent strength to the optimized product was prepared using the same composition and used for comparative evaluation for drug release studies.

Evaluation of gel

Physicochemical characterization of the transferosomal gel of FAMOPT

The transferosomal gel of FAMOPT was tested for appearance, feel, odor, clarity, and homogeneity.[22]

The pH of the gel was determined using a digital pH meter. Viscosity measurements of the prepared transferosomal gel were performed using a Brookfield viscometer with a spindle T-D at an optimum speed of 10 rpm at 25 °C. The measurements were performed in triplicate.[23]

Ex vivo diffusion studies of transfersome-loaded gel and skin deposition

Ex vivo diffusion studies of the transferosomal gel of FAMOPT were conducted using Wistar albino rat skin. The animals were euthanized with excess carbon dioxide, and the abdominal skin was surgically removed. The excised skin was cleaned with saline water and placed in the receptor compartment. The receptor compartment was filled with a freshly prepared buffer solution (pH 5.5). The diffusion medium was stirred at 100 rpm, at 37.0 ± 0.5 °C. The transfersome-loaded gel (500 µL) was placed in the donor compartment, and samples of diffusion medium (1 mL) were collected at different time intervals for 24 hours. The samples were withdrawn at intervals of a specific time, and donor cells were replenished with an equal volume of fresh medium. The samples were analyzed spectrophotometrically. A gel of pure drug of equivalent strength and an optimized drug-loaded transferosomal formulation (FAMOPT) were subjected to a comparative drug diffusion study using the same procedure.

The drug release kinetics was studied by plotting diffusion into different rate kinetics models.

For all selected formulations, the amount of permeated drug (mg/cm^2) over time was also calculated. The flux and permeation constant are calculated using the following formula.[24]

Jss = dq/dt

p = dq/dt.1/AC_D

In which A- diffusion area (4,512)

dq/dt slope of the linear region of the *ex vivo* diffusion curve

C_D-is the donor concentration

At the end of the *ex vivo* permeation study, the skin was removed from the diffusion flask, the remaining gel was swabbed, and the skin was washed repeatedly with 0.02 M potassium dihydrogen orthophosphate and acetonitrile (80:20) solution to remove the excess drug.[25]

The skin was carefully sectioned into the dermis and epidermis layers using a tweezer.[20] The separated layers were homogenized with phosphate buffer and centrifuged at 10000 rpm for 5 minutes, and the supernatant was analyzed by ultraviolet spectrophotometry using spiking (known concentration 10 µg/mL) experiments to estimate drug deposition in various layers of skin.

Skin irritation study

The skin irritation study was conducted using albino Wistar rats. The back of the animal was shaved carefully. The animals were divided into three groups, each containing 6 animals-control, test, and placebo. The optimized formulation was applied on the backside of the animal for 7 days for an irritation study. Changes in skin color, morphology, and the development of erythema and edema were observed daily for 7 days of the study.[26]

Histopathological studies

The skin from the animals of Group I and Group II was taken for histopathological studies. The excised skin was dipped in 10% formalin solution and subjected to histopathological examination. The sections were observed using a light microscope equipped with a digital camera using hematoxylin and eosin stains.[27]

Ethical Aproval

This study approved by Krupanidhi College of Pharmacy Institutional Animal Ethics Committee (approval number: KCP/IAEC-407/2021-22, date: 11.06.022)

RESULTS

Evaluation of experimental design

The experimental runs of the thirteen trials are listed in Table 3. The response surface graphs show the most statistically significant variables for the evaluated responses, as shown in Figure 1. The model was established for all dependent variables at a significance level of $p < 0.05$ as shown in Table 4. The effects of the main factors on the formulation responses are listed below. It was found that the lipid ratio (SPC:CH) had a significant effect on drug entrapment, whereas the non-ionic surfactant had a remarkable impact on particle size. PDI was greatly affected by both the phase volume ratio and surfactant concentration, as indicated in Table 4.

The model optimization was carried out at a desirability of 0.77, and an optimized condition was predicted at an SPC:CH ratio of 1.44:1, surfactant concentration of 6.65 *w/v* %, and phase volume of 0.42 to produce drug-loaded transfersomes with high entrapment efficiency, low vesicle size, and polydispersity. The optimized formulation (FAMOPT) was prepared and exhibited the properties predicted by the design with a bias within 10%, as shown in Table 5. The zeta potential of the optimized formulation was determined to be 9.7 mV. The zeta potentials and vesicle sizes of the optimized formulations are shown in Figure 2.

Table 3. Experimental evaluation of transferosomes according to the central composite design

Formulation code	Entrapment efficiency %	Particle size (nm)	PDI
F1	70.9 ± 0.001	452.9 ± 20.1	0.553 ± 2.32
F2	71.6 ± 0.096	483.0 ± 31.2	0.73 ± 1.45
F3	94.3 ± 0.007	440.7 ± 33.4	0.604 ± 0.95
F4	49.2 ± 0.014	508.5 ± 11.5	0.951 ± 1.02
F5	76.0 ± 0.011	519.0 ± 26.8	0.77 ± 2.01
F6	71.0 ± 0.172	314.2 ± 30.4	0.196 ± 0.95
F7	55.2 ± 0.036	213.7 ± 16.9	0.434 ± 1.48
F8	62.9 ± 0.037	415.8 ± 25.9	0.337 ± 1.21
F9	53.7 ± 0.006	493.5 ± 39.7	0.317 ± 2.13
F10	68.9 ± 0.007	456.0 ± 24.4	0.750 ± 1.06
F11	66.3 ± 0.060	416.8 ± 36.1	0.361 ± 0.78
F12	86.3 ± 0.023	344.9 ± 19.2	0.381 ± 1.71
F13	61.3 ± 0.012	278.6 ± 28.5	0.769 ± 1.82

All values are mean (n= 3) ± standard deviation, PDI: Polydispersity index

Table 4. Model validation statistics

Response	Suggested fit summary	*p* value	R^2	Model equation
Entrapment efficiency	2FI	0.0243*	0.855	Entrapment efficiency = +68.33+11.51A 7.69B 1.78C 9.54AB 19.43AC+15.43BC
	A-SPC:CH	0.0147*		
	B-% non-ionic surfactant	0.0643		
	C-Phase volume ratio	0.6194		
Particle size	Quadratics	0.0456*	0.966	Particle size = +477.85-52.54A+68.70B-48.86C-96.34AB+2.67AC-106.11BC-23.21A^2-27.13B^2-58.96C^2
	A-SPC:CH	0.0579		
	B-% non-ionic surfactant	0.0296*		
	C-Phase volume ratio	0.0687		
PDI	Quadratics	0.0374*	0.970	PDI = +0.723353+0.022627A+0.0266933B+0.14425C+0.15575AB +0.170433AC+0.059627BC-0.16719A^2-0.05494B^2-0.051919C^2
	A-SPC:CH	0.6085		
	B-% Non-ionic surfactant	0.0067*		
	C-Phase volume ratio	0.0359*		

*Denotes significant, PDI: Polydispersity index, SPC: Phospholipid, CH: Cholesterol

Table 5. Model prediction vs. observed responses for optimized product (FAMOPT)

Responses	Predicted	Observed	Bias %
Entrapment efficiency (%)	84.89	81.78 ± 0.02	3.65
Particle size (nm)	335	340.5 ± 23.7	1.64
PDI	0.383	0.419 ± 1.16	9.39

All values are mean (n= 3) ± standard deviation, FAMOPT: Optimized product

FTIR

The characteristic peaks of $COOCH_3$ stretching, C=C, C=N, and C-0 stretching, and C-N bending of the pure drug were observed at 1745, 1653, 1614, 1211, and 1249 cm^{-1} respectively (Figure 3A). The spectra of the blank formulation (Figure 3B) and FAMOPT (Figure 3C) were analyzed for compatibility.

TEM

The nanovesicles of FAMOPT were observed by TEM as shown in Figure 4.

Degree of deformability

The ratio of the change in the size of the FAMOPT vesicles was found to be less than 1, as listed in Table 6, The % of leakage was calculated to be 3.46%.

Evaluation of the transferosomal gel of famciclovir

The optimized formulation (FAMOPT) was dispersed in a carbopol 940 gel matrix. The gel was found to be translucent; pH was found to be 5.5, with a viscosity of 88.6 centimpoise. The drug content in the gel was estimated at 69.5%.

Ex vivo diffusion studies of transfer some-loaded gels

Ex vivo drug release studies were conducted for FAMOPT, transferosomal gel of FAMOPT, and pure drug gel of famciclovir. The FAMOPT formulation and FAMOPT gel exhibited sustained drug release. The pure drug gel release reached a steady state at 6 hours as shown in Figure 5.

The permeation of the drug from the transferosomal gel and FAMOPT was approximately 2.8 and 3 times higher, respectively, than that from the pure drug gel, as listed in Table 7. The drug deposition in the various skin layers is presented in Figure 6, and permeation of the drug from the transferosomal formulations was remarkably higher compared to the pure drug.

Skin irritation study

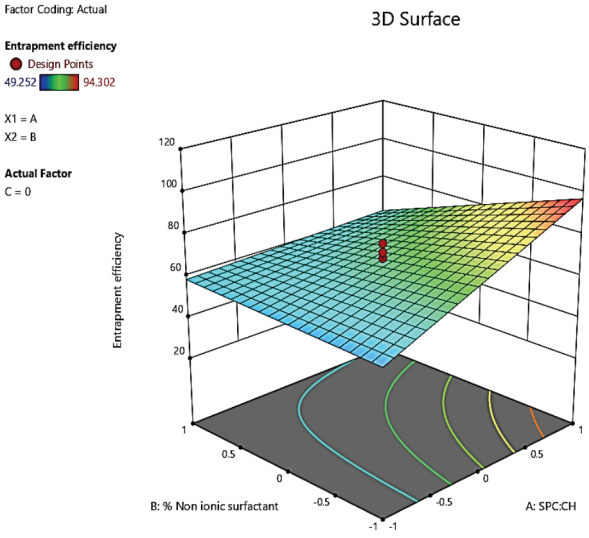
The skin irritation test was performed for the animals such that the first group received control, the second group received placebo, and the third group received test formulation (transferosomal gel of FAMOPT). All animals in the test groups showed no signs of erythema or edema.

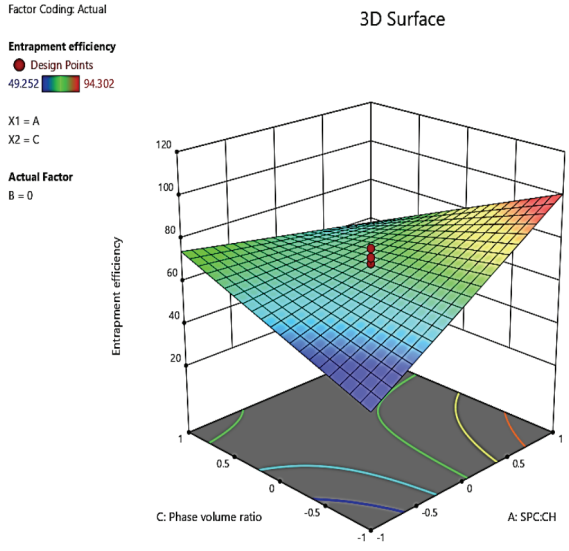
Histopathology study

The histopathology of the rat skin is presented in Figure 7.

DISCUSSION

The response surface diagrams showed significant effects of lipid composition, surfactant concentration, and phase





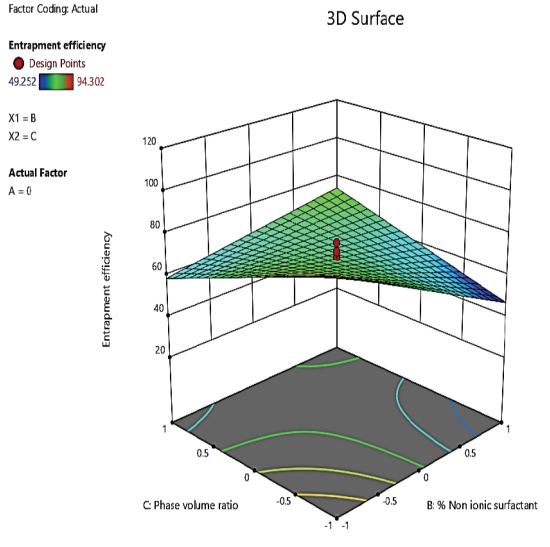
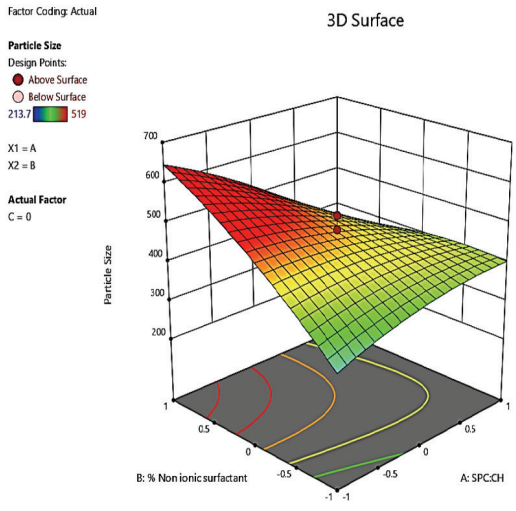
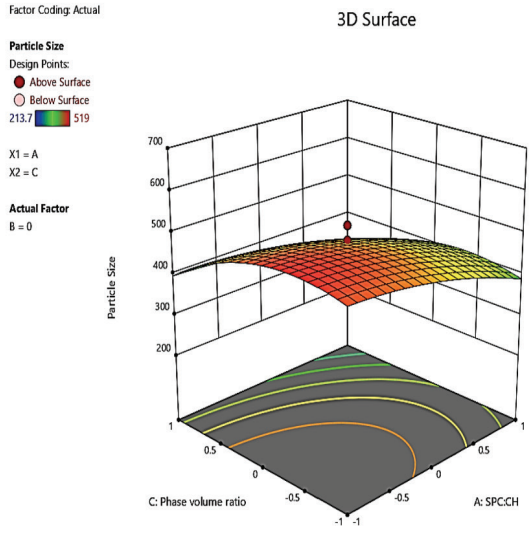


Figure 1A. Response surface diagram for entrapment efficiency





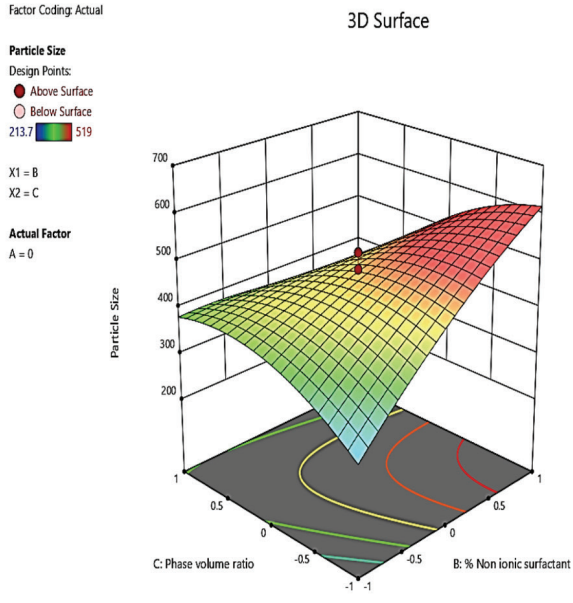


Figure 1B. Surface response for particle size

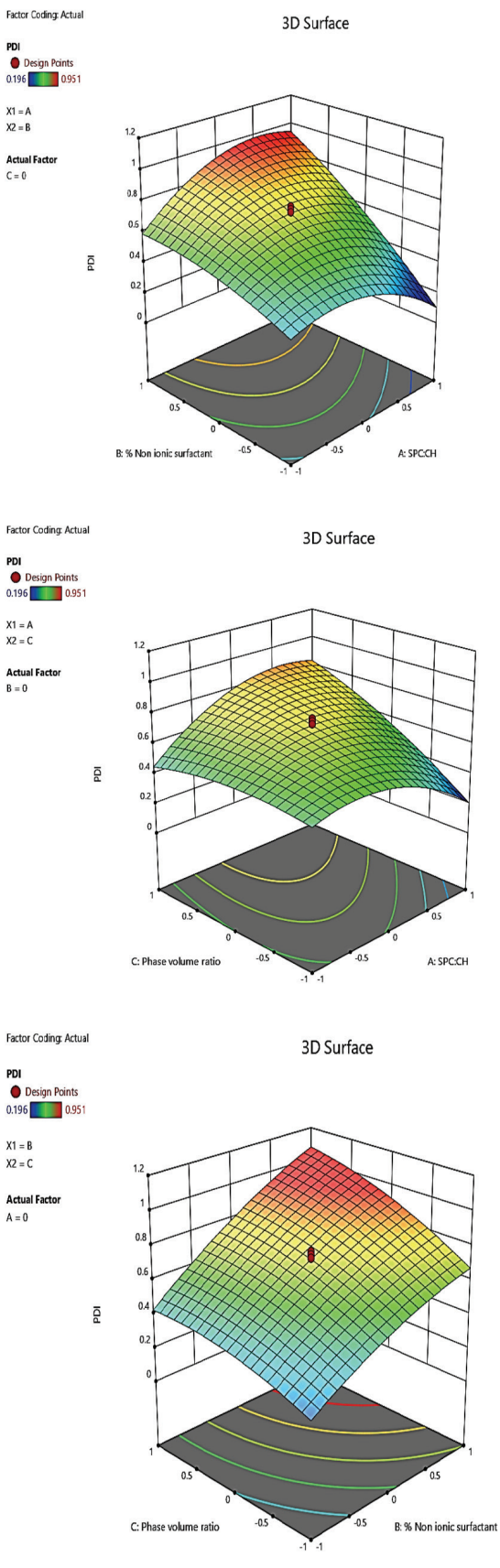


Figure 1C. PDI response surface of
PDI: Polydispersity index

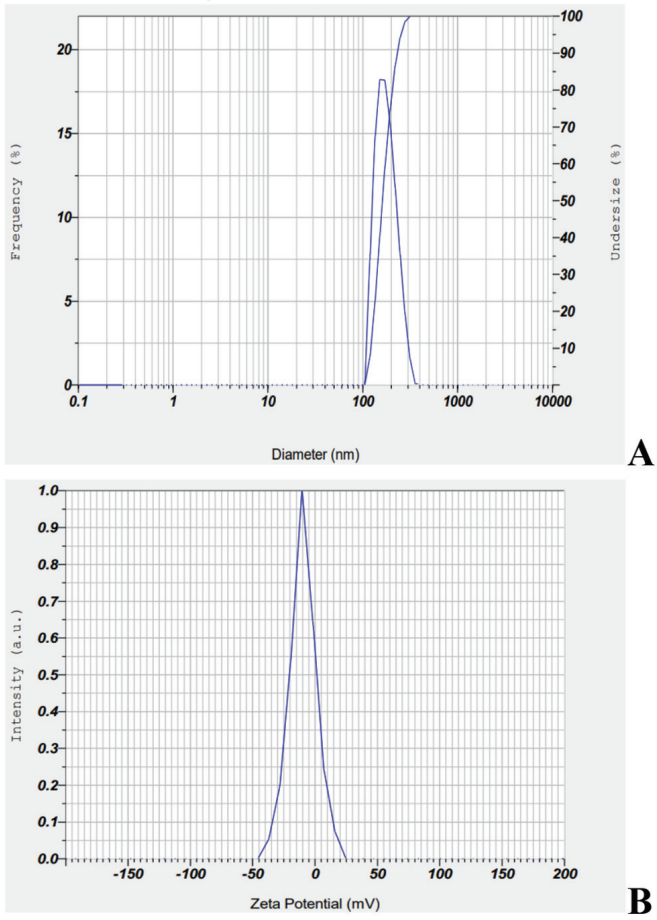


Figure 2. Particle size (A) and zeta potential (B) of FAMOPT
FAMOPT: Optimized product

Table 6. Degree of deformability of the optimized product (FAMOPT)

	Vesicle size (nm)	Entrapment of the drug %
Before extrusion	340.5 ± 0.02	84.15 ± 0.02
After extrusion	320.33 ± 5.05	81.23 ± 0.05
Deformability	0.94	-
%Leakage	-	3.46

All values are mean (n= 3) ± standard deviation, FAMOPT: Optimized product

volume ratio on entrapment efficiency. The vesicle size of the transfersomes was greatly affected by the surfactant concentration and phase volume ratio, as indicated by the extent of curvature in the response surface diagram. The drug has good water solubility; hence, entrapment of the drug in the core of the bilayer vesicle was a challenge. The presence of cholesterol made the bilayer sufficiently stable to prevent drug leakage. The non-ionic surfactant contributed to the elasticity of the vesicles.[28] The effect of the main factors on the properties of the transferosomes was remarkable as evidenced from the model validation.

The model equation provides a fit summary of the factors with the responses. The positive sign in the equation indicates the critical parameters' significant contribution to the responses. The analysis of the variance test showed that the model was significant for approximating the effects of the variables on entrapment efficiency, vesicle size, and PDI. The optimization of the model was carried out considering the high entrapment efficiency of the drug, minimizing the particle size and PDI at high desirability. The vesicle size of FAMOPT after experimentation was found to be within the predicted range, and the surface charge indicated the stability of the vesicles with less aggregation and flocculation.[29]

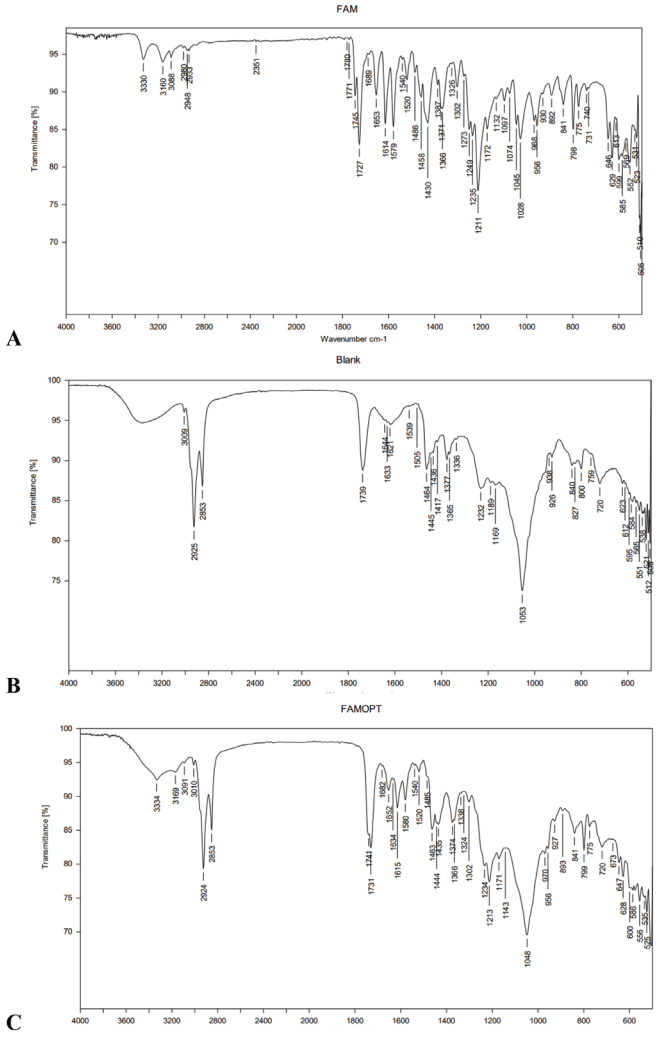


Figure 3. FTIR Spectra of pure drug (A), blank FAMOPT (B), and FAMOPT (C)

FTIR: Fourier transform infrared spectroscopy, FAMOPT: Optimized product

The compatibility of the pure drug with excipients was confirmed by the retention of specific peaks in the fingerprint region of the formulation. The optimized formulation could retain the major peaks of the pure drug and excipients. Hence, it establishes compatibility between the drug and excipients.

The TEM analysis revealed that the vesicles were spherical and did not aggregate. The size range of the vesicles of the optimized product was found to be within the predicted range as per the design.

The degree of deformability of the optimized formulation was calculated by estimating the vesicle size of the formulation before and after extrusion through a polymeric membrane with a lower aperture size. The obtained deformability index (< 1) of the optimized formulation indicates the retention of the vesicle size and proves the minimum leakage of the vesicles.[30] The elasticity of the prepared nanovesicles was determined.

The physicochemical properties of the hydrogel of the optimized formulation in Carbopol 940 were found to be suitable for spreading and application over the skin.

The *ex vivo* diffusion study revealed that drug release from the transferosomal gel of the optimized formulation was very high compared with that from the gel containing the pure drug. The diffusion of the drug from the nanocarriers was much higher and more sustained than that from the gel containing the pure drug. The transferosomal gel of FAMOPT was almost comparable to that of FAMOPT, and a slight reduction in drug release from the gel was attributed to its viscosity. The release of famciclovir from the transferosomal gel was evaluated using first-order kinetics. The exponent of the Korsmeyer-Peppas model (n) is 0.96, which indicates non-fickian anomalous diffusion of the drug from the gel.

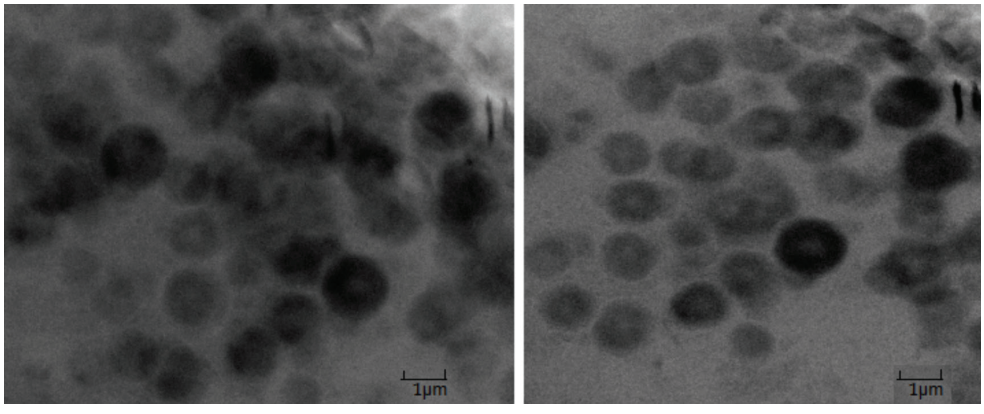


Figure 4. TEM images of transferosomes of famciclovir

TEM: Transmission electron microscope

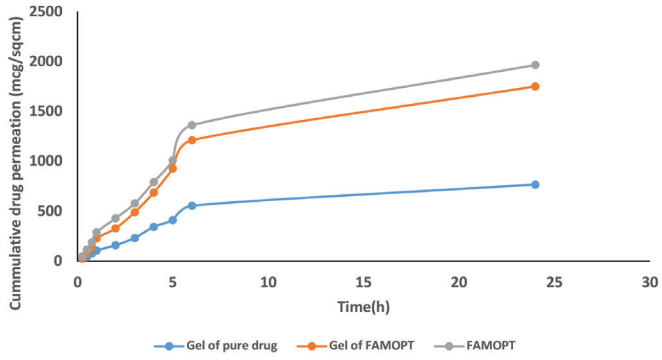


Figure 5. *Ex vivo* diffusion curve of famciclovir
FAMOPT: Optimized product

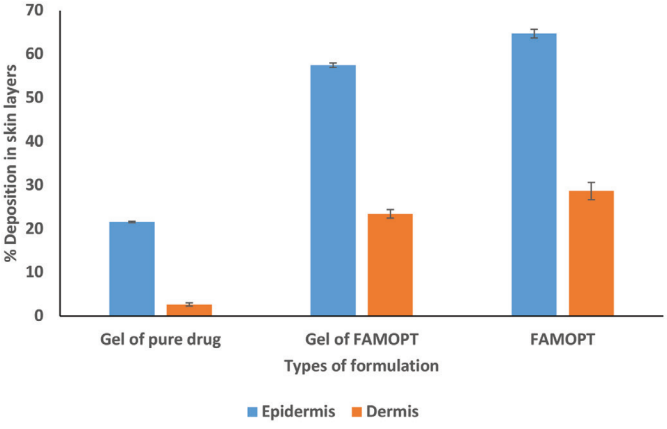


Figure 6. Estimation of famciclovir deposition in skin
FAMOPT: Optimized product

Skin permeation studies showed significantly higher permeation of the drug from the nanocarriers; hence, the penetrability of famciclovir was significantly improved.[30]

The drug deposition in various layers represents a high deposition of the drug in the layers of the skin from the gel of the nanovesicles compared with the gel of the pure drug, and the result was in conformation with the *ex vivo* permeation study. This further confirmed the efficient permeation of the drug into different layers of the skin from the nanovesicles.[29]

The gel was found to be non-sensitive to the skin. Histopathology revealed that there were no sensitization or irritation on the different layers of skin following the application of the nano gel, and a near-normal morphology was observed, similar to the control group. Focal inflammation in the dermal layers upon transferosomal gel application provides evidence of nanovesiculate drug penetration.

CONCLUSION

In this study, novel deformable famciclovir vesicles was developed and evaluated as a nanocarrier for transdermal delivery. These nanosized vesicles exhibit deformable properties. These properties of the vesicles allow drug delivery into deeper layers of the skin. Moreover, the incorporation of the drug into the carbopol 940 gel enhanced the penetration and deposition of the drug into the dermis layer. The permeation of famciclovir was significantly enhanced by the transferosomal gel compared with that of the pure drug. The transferosomal gel was non-sensitive and did not irritate the animal skin. Hence, it can be concluded that transdermal application of transferosomal gel of famciclovir could be an alternative for conventional delivery to reduce virus

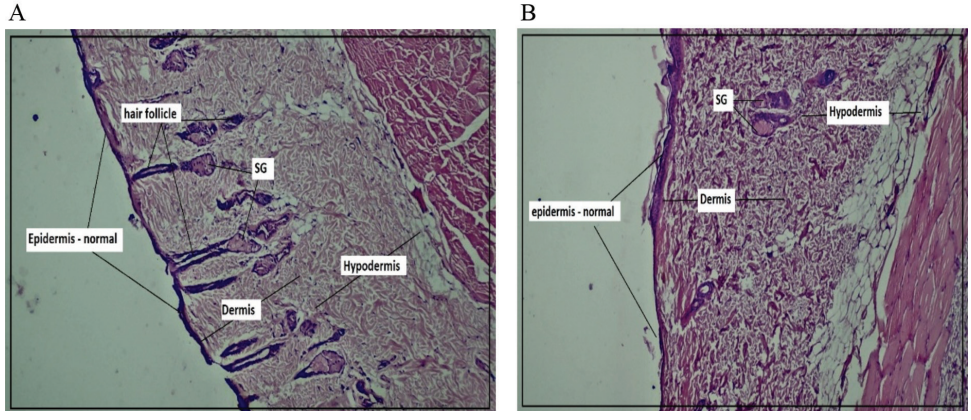


Figure 7. Histopathological examination of rat skin (A) control and (B) after application of transferosomal gel

Table 7. Permeation data of famciclovir after 24 hours

Formulation	Permeated amount of drug at 24 h (μg/cm²)	Drug flux (μg/cm²/h)	Permeability coefficient (Kp) (cm/h)	Permeation of pure drug gel enhanced
FAMOPT	1977	46.32	579	3
Gel of FAMOPT	1751	42.7	534	2.77
Gel containing pure drug	767	19.26	192	-

FAMOPT: Optimized product, Kp: Permeability coefficient

load and could be a non-invasively promising technique for the treatment of cold sores and genital herpes.

Ethics

Ethics Committee Approval: This study approved by Krupanidhi College of Pharmacy Institutional Animal Ethics Committee (approval number: KCP/IAEC-407/2021-22, date: 11.06.022).

Informed Consent: Not applicable.

Authorship Contributions

Concept: S.B., Design: S.B., K.T.L., A.M., Data Collection or Processing: S.B., K.T.L., A.M., Analysis or Interpretation: S.B., K.T.L., Literature Search: S.B., K.T.L., A.M., Writing: S.B., K.T.L.

Conflict of Interest: No conflict of interest was declared by the authors.

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