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Design, Optimization and Characterization of a Transferosomal Gel of Acyclovir for Effective Treatment of Herpes Zoster

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ABSTRACT

A transferosome is the first generation of an elastic liposome prepared from phospholipids and edge activators. An edge activator is often a single-chain surfactant with a high radius of curvature that destabilizes the lipid bilayers of vesicles and increases the deformability of the bilayers, thereby making the vehicle ultra-deformable. Acyclovir is a synthetic purine nucleoside analog derived from guanine, is the most widely used antiviral agent. It is effective in the treatment of herpes simplex virus (HSV), mainly HSV-1 and HSV-2 and varicella-zoster virus. However, it has low skin permeability. Hence, the objective of this study was to prepare acyclovir using transferosomes to overcome the barrier function of the skin. The present study deals with the development of transferosomal gel containing acyclovir by handshaking method for painless acyclovir delivery for use in the treatment of skin disease through 33 Fractional factorial design in which amount of Phospholipid (A), Cholesterol (B) and Tween 80 (C) was selected as independent variables and vesicle size (X1) Polydispersity index (X2) and %entrapment efficiency (X3) as dependent variables. The prepared transferosomes were evaluated with respect to entrapment efficiency (EE %), particle size, and quantity of in vitro drug released to obtain an optimized formulation. The optimized formulation of acyclovir transferosomes was incorporated into a Carbapol 934 gel base which was evaluated for drug content, pH, spreadability, viscosity and in vitro permeation. The prepared acyclovir transferosomes had a high EE% ranging from 65 to 81%, with small particle sizes ranging from 181.9 to 401.8nm. The in vitro release study suggested that there was an inverse relationship between EE% and in vitro release. The formulation TF2 have better *in-vitro* drug release profile which contains carbopol 980 concentration 2 %w/w. The kinetic analysis of release profiles of TF2 was found to follow the Korsmeyer-Peppas model. All independent variables had a significant effect on the dependent variables (p-values < 0.05). Therefore, acyclovir in the form of transferosomes can penetrate the skin, overcoming the stratum corneum barrier.

Keywords: Transferosome gel, Acyclovir, 33 Fractional factorial designs, Carbapol 934, Korsmeyer-Peppas model

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INTRODUCTION

Nanotechnology involves fabrication of nanoscale structures which are observed visibly under high resolution. These molecular assemblies are specially designed for attaining their target functions[1]. Based on their critical packing parameter and hydrophilic-lipophilic balance (HLB), these molecules are self-assembled to various morphologies including micelles, sheets and vesicles (liposomes, transferosomes, exsosomes, niosomes etc.)[2]. Furthermore, these vesicular formulations had been more exploited in the field of transdermal drug delivery[3]. They offer many advantages over conventional delivery systems like biocompatibility, non-toxicity, and ability to modify drugs' bioavailability[4]. In addition to the utilization of vesicular carriers for transdermal drug delivery, nano transfection approaches (TNT) have been recently introduced for topical and controllable delivery of reprogramming factors across the skin. These approaches allow delivery of controlling factors by applying an intense and highly focused electric field using arrayed nano-channel. Hence, TNT can deliver the cargo to the skin in a rapid and non-invasive manner[5]. In this manuscript, the strategy of using transferosome s as a vesicular nano-carrier has been selected and investigated for efficient transdermal delivering of drugs and bypassing their oral problems. Transferosomes are ultra-flexible vesicles with a bilayer structure. They can penetrate the skin easily and overcome the barrier function by squeezing through the intracellular lipid of the stratum corneum[6]. After application of Transferosomes on the skin, they move from the dry stratum corneum to a deep hydrated layer according to the osmotic gradient. The presence of surfactant in their structure helps in solubilizing the lipid in stratum corneum and permits high penetration of the vesicles[7]. Acyclovir [9-(2-hydroxyethoxylmethyl) guanine], a synthetic purine

nucleoside analog derived from guanine, is the most widely used antiviral agent. It is effective in the treatment of herpes simplex virus (HSV), mainly HSV-1 and HSV-2 and varicella-zoster virus. According to the biopharmaceutical classification system, acyclovir is categorized as a class - III drug i.e. having high solubility and less permeability. The pharmacokinetic parameters of acyclovir, following oral administration, are generally highly variable. It has an average plasma half-life of about 3 hours in adults with normal renal function. Its absorption in the GIT is slow, variable and incomplete. The bioavailability of acyclovir after oral administration ranges from 10-30%. Approximately 80% of an oral dose is never absorbed and excreted through feces. Also, the frequency of administration of acyclovir is high, being 200mg five times a day up to 400mg five times a day depending upon the type of infection[8]. Pharmaceutical scientists often face the challenge of finding the appropriate combination of variables that will produce the product with optimum properties[9]. The optimization technique encompasses designing a set of an experiment that will reliably measure the response variables, fitting a mathematical model to the data, conducting an appropriate statistical test to assure that the best possible model is chosen and determining the optimum value of independent variables that produce the best response[10]. In the present investigation, we attempted to develop and optimize transferosomal gel containing acyclovir, for improved transdermal permeation using 33 factorial designs.

EXPERIMENTAL

Materials

Acyclovir was obtained as a gift sample from Macleods Pharmaceuticals, Mumbai. Phospholipid was purchased from Himedia Laboratory, Mumbai. Ethanol, chloroform, cholesterol, tween 80 and carbopol-934 purchased from CDH chemical Pvt. Ltd. New Delhi. Dialysis membrane of Mol Wt cutoff 1200 was purchased from Himedia Laboratory, Mumbai. Demineralized and double distilled water was prepared freshly and used whenever required. All other reagents and chemicals used were of analytical grade.

Preparation of transferosomes

Transferosomes were prepared by hand-shaking method given by Vyas et al., 2011[11] with slight modification in which. The accurately weighed amounts (80-100 mg) of phospholipids, 10-30mg of cholesterol and Tween 80 (10-30% w/v) were taken in a clean, dry, round-bottom flask and this lipid mixture was dissolved in a minimum quantity of methanol and chloroform mixture in a ratio of 2:1. The round bottom flask was rotated at 45° angle at room temperature. Final traces of solvents were removed under vacuum overnight. The prepared lipid film in the inner wall of the round bottom was hydrated with 10 ml of distilled water containing 10 mg of drug followed by rotating the flask. After complete hydration of film, the prepared formulation of transferosomes was subjected to sonication at 40ºC in 3 cycles of 10 minutes with 5 sec rest between the cycles. The prepared formulation was stored at 4°C in a closed container until further use for analysis.

Experimental design

The response variables which will consider for systematic optimization were Vesicle Size, PDI, and % EE. For studied design, multiple linear regression analysis (MLRA) and ANOVA will be applied using Microsoft Excel® to fit first-order multiple linear equations with added interaction terms to correlate the studied responses with the examined variables. The design expert software trial version will be used to contour and 3-D response curve.

Factorial design and desirability function for optimizing transfersomes

The coefficient estimate represents the expected change in response per unit change in factor value when all remaining factors are held constant. The intercept in an orthogonal design is the overall average response of all the runs. The coefficients are adjustments around that average based on the factor settings. When the factors are orthogonal the VIFs are 1; VIFs greater than 1 indicate multi-collinearity, the higher the VIF the more severe the correlation of factors. As a rough rule, VIFs less than 10 are tolerable. The number of experiments required for these studies is dependent on the number of independent variables selected the multiple linear regression equation given below.

Table 1 List of variables employed in 3^3 factorial designs

Factors	Levels	
	Low (-1)	High (+1)
Acyclovir	30	
Phospolipid	80.00	100
Cholestrol	10.00	30.00
Tween 80	10.00	30.00

ANOVA for Quadratic model

Response 1: Vesicle size

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	62549.33	9	6949.93	5.81	0.0151	significant
A-Phospolipid	2145.13	1	2145.13	1.79	0.2224	
B-Cholestrol	100.11	1	100.11	0.0837	0.7808	
C-Tween 80	9695.28	1	9695.28	8.10	0.0248	
AB	3358.20	1	3358.20	2.81	0.1378	
AC	1040.06	1	1040.06	0.8693	0.3822	
BC	11236.00	1	11236.00	9.39	0.0182	
A^2	14093.48	1	14093.48	11.78	0.0110	
B^2	17020.70	1	17020.70	14.23	0.0070	
C^2	3594.98	1	3594.98	3.00	0.1266	
Residual	8375.24	7	1196.46			
Lack of Fit	4726.17	3	1575.39	1.73	0.2991	not significant
Pure Error	3649.07	4	912.27			
Cor Total	70924.58	16				

The equation in terms of coded factors can be used to make predictions about the response for given levels of each factor. By default, the high levels of the factors are coded as +1 and the low levels are coded as -1. The coded equation is useful for identifying the relative impact of the factors by comparing the factor coefficients. The equation in terms of actual factors can be used to make predictions about the response for given levels of each factor. Here, the levels should be specified in the original units for each factor. This equation should not be used to determine the relative impact of each factor because the coefficients are scaled to accommodate the units of each factor and the intercept is not at the center of the design space.

Final equation in terms of coded factors

Vesicle Size = +216.64+16.38 A-3.54 B+34.81 C-28.98 AB+16.13 AC+53.00 BC+57.85 BC+57.85 A^2+63.58 B^2-29.22 C^2

Final equation in terms of actual factors

Vesicle Size = +4811.11000-99.93150 Phospolipid-10.30825 Cholestrol-9.94325 Tween 80-0.289750 Phospolipid * Cholestrol+0.161250 Phospolipid * Tween 80+0.530000 Cholestrol * Tween 80+0.578550 $Phospolipid^2$+0.635800 $Cholestrol^2$-0.292200 $Tween\ 80^2$

Final equation in terms of coded factors

PDI=+0.2620+0.0050A-0.0050B+0.0125C-0.0250AB+0.0100AC+0.0150BC+0.0265A2+0.0015B2-0.0035C2

Final equation in terms of actual factors

PDI=+2.13050-0.044200 Phospolipid+0.018400 Cholestrol-0.009350 Tween 80-0.000250 Phospolipid * Cholestrol+0.000100 Phospolipid * Tween 80+0.000150 Cholestrol * Tween 80+0.000265 $Phospolipid^2$+0.000015 $Cholestrol^2$-0.000035 $Tween\ 80^2$

Final equation in terms of coded factors

% EE=+72.00+2.25 A+0.0000B-5.25C+1.0000 AB-1.00 AC-1.0000BC

Final Equation in Terms of Actual Factors

%EE= +58.25000+0.225000Phospolipid-0.700000 Cholestrol + 0.575000 Tween 80+ 0.010000 Phospolipid*Cholestrol-0.010000Phospolipid*Tween80-0.010000 Cholestrol* Tween 80

Table 2 Array layout as 3^3 factorial screening designs

Formulation	Std	Run	Factor 1	Factor 2	Factor 3
			A:Phospolipid	B:Cholestrol	C:Tween 80
F1	7	1	80	20	30
F2	16	2	90	20	20
F3	8	3	100	20	30
F4	3	4	80	30	20
F5	9	5	90	10	10
F6	17	6	90	20	20
F7	10	7	90	30	10
F8	14	8	90	20	20
F9	15	9	90	20	20
F10	2	10	100	10	20
F11	6	11	100	20	10
F12	13	12	90	20	20
F13	12	13	90	30	30
F14	4	14	100	30	20
F15	11	15	90	10	30
F16	5	16	80	20	10
F17	1	17	80	10	20

Table 3 Optimized formula after post analysis

S. No.	Phospolipid	Cholestrol	Tween 80
1.	98.528	28.302	10.015

Evaluation of acyclovir loaded transferosomes

Microscopic observation of prepared transferosomes

An optical microscope (cippon, Japan) with a camera attachment (Minolta) was used to observe the shape of the prepared transferosomes formulation.

Vesicle size and size distribution

The vesicles size and size distribution were determined by Dynamic Light Scattering method (DLS) (Malvern Zetamaster, ZEM 5002, Malvern, UK).

Zeta potential

The zeta potential was calculated according to Helmholtz–Smoluchowsky from their electrophoretic mobility. For measurement of zeta potential, a zeta sizer was used with a field strength of 20 V/cm on a large bore measures cell. Samples were diluted with 0.9% NaCl adjusted to a conductivity of 50 lS/cm.

Entrapment efficiency

Entrapment efficiency was determined by measuring the concentration of unentrapped free drug in an aqueous medium. About 1 ml of the drug-loaded ethosomes dispersion was placed in the Ependorf tubes and centrifuged at 17000 rpm for 30 min. The ethosomes along with

encapsulated drug were separated at the bottom of the tubes. Plain ethosomes without drug was used as a blank sample and centrifuged in the same manner. In order to measure the free drug concentration, the UV absorbance of the supernatant was determined at 242 nm.

Preparation of transferosomes gels

Carbopol gel was prepared by soaking carbopol 934 (1-3%w/v) in 20 ml of water for 2 hours. Triethanalamine was added to above solution to neutralizing the solution with continuous stirring. The carbopol dispersion was stirred at 200 rpm for 24 hr min to complete hydration and obtaining a homogeneous gel. The previously prepared drug loaded transferomes (equivalent to 20 mg of acyclovir) formulation was added to the above dispersion and stirred again for 20 min at 100 rpm. The pH of the gel was adjusted to 6.5-7.0 by adding triethanolamine. The composition of acyclovir gel formulation was given in table 4.

Table 4 Formulation of transfersomes gel

S. No.	Formulation Code	Carbopol 934 (gm)	Water
1.	TF1	1	100
2.	TF2	2	100
3.	TF3	3	100

Evaluation of gel

Physical characteristic

The Physical characteristic was checked for gel formulations (homogeneity and texture).

Determination of pH

The pH of the gels was determined by digital pH meter. One gram of gel was dissolved in 25 ml of distilled water and the electrode was then dipped into gel formulation for 30 min until constant reading obtained. And constant reading was noted. The measurements of pH of each formulation were replicated two times.

Washability

Formulations were applied on the skin and then ease and extent of washing with water were checked manually.

Extrudability study

The gel formulations were filled into collapsible aluminum tubes. The tubes were pressed to extrude the material and the extrudability of the formulation was checked.

Spreadability

An important criterion for gels is that it must possess good spreadability. Spreadability is a term expressed to denote the extent of the area to which the gel readily spreads on application to the skin. The therapeutic efficacy of a formulation also depends on its spreading value. A special apparatus has been designed to study the spreadability of the formulations. Spreadability is expressed in terms of time in seconds taken by two slides to slip off from formulation, placed between, under the application of a certain load. Lesser the time is taken for the separation of two slides, better the spreadability. It is determined by the formula given below.

Where, S=Spreadability (gcm/sec), m = weight tied to the upper slide (20 grams), l= length of glass slide (6cms), t = time taken is seconds.

Viscosity

The measurement of viscosity of the prepared gel was done using Brookfield Viscometer. The viscosity was measured using spindle no. 6 at 10 rpm and 25ºC. The sufficient quantity of gel was filled in an appropriate wide mouth container which can allow dipping the spindle of the Viscometer. Samples of the gels were allowed to settle over 30 min at the constant temperature (25 ±1ºC) before the measurements.

***In-vitro* drug release studies using the prehydrated cellophane membrane**

The cellophane membrane approximately 25 cm x 2cm was taken and washed in the running water. It was then soaked in distilled water for 24 hours before used for diffusion studies to remove glycerin present on it and was mounted on the diffusion cell for further studies. The drug release studies were carried out using a modified Franz diffusion cell. The cellophane membrane was mounted on the Franz diffusion cell. The formulation was applied through a donor compartment on the dialysis membrane. Reservoir compartment was filled with 25 ml phosphate buffer of pH 7.4 The study was carried out at 37 ± 1°C and a speed of 100 rpm for 8 h. Samples were withdrawn from reservoir compartment at 1 h interval and absorbance was measured spectrophotometrically at 242 nm. Each time the reservoir compartment was replenished with the same quantity of 7.4 pH phosphate buffer[12,13].

Release kinetics

To elucidate mode and mechanism of drug release, the *in-vitro* data was transformed and interpreted at a graphical interface constructed using various kinetic models. The zero-order release Eq. (1) describes the drug dissolution of several types of modified release pharmaceutical dosage forms, as in the case of transdermal systems, matrix tablets with low soluble drugs, coated forms, osmotic systems, etc., where the drug release is independent of concentration.

$$Qt = Qo + Kot \quad (1)$$

Where Qt is the amount of drug released in time t, Qo is the initial amount of the drug in the solution and Ko is the zero-order release constant

The first order Eq. (2) describes the release from the system where the release is concentration-dependent e.g. pharmaceutical dosage forms containing water-soluble drugs in porous matrices.

$$\log Qt = \log Qo + K1\ t\ /2.303 \quad (2)$$

Where Qt is the amount of drug released in time t, Q is the initial amount of drug in the solution and K1 is the first-order release constant.

Higuchi described the release of drug from insoluble matrix as a square root of time as given in Eq. (3)

$$Qt = KH\ \sqrt{t} \quad (3)$$

Where Qt is the amount of drug released in time t, KH is Higuchi's dissolution constant[14].

The following plots were made: cumulative % drug release vs. time (zero-order kinetic models); log cumulative of % drug remaining vs. time (first-order kinetic model); cumulative % drug release vs. square root of time (Higuchi model).

Stability studies

Stability study was carried out for drug-loaded transferosomes gel (TF2) at two different temperatures i.e. refrigeration temperature (5ºC±3 ℃) and at room temperature (25±2°C) and 60%±5% RH with for 90 days. The formulation subjected to stability study was stored in borosilicate container to avoid any interaction between the formulation and glass of container. The formulations were analyzed for vesicle size and % drug content.

RESULTS AND DISCUSSIONS

The response surface (3^3) factorial design was applied to optimize the number of formulation and process variables for the preparation of drug bearing transferosomes. Various batches of transferosomes were prepared as obtained by Design Expert Software version 11.1.0 and than characterized for average particles size, PDI and percent drug entrapment efficiency. It was observed that as on increasing the concentration of lipid from 80mg to 100mg the size of transferosomes was increase. Vesicle size and PDI of the transferosomes were measured by photon correlation spectroscopy using a Malvern Zetasizer and entrapment efficiency was determined by measuring the concentration of unentrapped free drug in aqueous medium by UV spectrophotometer the results shown in Table 5 & Figure 1-8.

Table 5 Evaluation of formulations 3^3 factorial design

S. No.	Formulation	Vesicle Size nm	PDI	% EE
1	F1	276.4	0.28	65
2	F2	238.2	0.26	72
3	F3	327.6	0.32	68
4	F4	332.3	0.31	69
5	F5	286.7	0.27	76
6	F6	258.5	0.27	71
7	F7	189.5	0.23	78
8	F8	202.7	0.27	73
9	F9	189.3	0.25	72
10	F10	401.8	0.32	73
11	F11	181.9	0.27	81
12	F12	194.5	0.26	72
13	F13	321.3	0.28	66
14	F14	320.9	0.26	75
15	F15	206.5	0.26	68
16	F16	195.2	0.27	74
17	F17	297.3	0.27	71

The normal probability plot indicates whether the residuals follow a normal distribution or not. In figure 3(a) all the points are showing near the strait line which indicates that a transformation of the response may provide a better analysis. The plot of the residuals versus the ascending predicted response values (not showing in the manuscript) tests the assumption of constant variance. The plot was shown a random scatter (constant range of residuals across the graph) which indicates the no need for a transformation. 2D contour plot and 3D response surface plots for vesicle size clearly shows that as increasing the concentration of phospolipid and cholesterol the average vesicles size was increase. High concentration of lipid may form high dense layers which may result in the formation of multilameller vesicles and the size of the multilameller transferosomes was increase.

The main effect of A, B, and D represents the average result of changing variable at a time from its low level to high level. The interaction terms (AB, AC, BC, A^2, B^2, and C^2) show how the percent drug entrapment changes when 2 variables are simultaneously changed. Among the 3 independent variable the lowest coefficient value is for C (-0.32 & $P<0.05$) indicating that this variable is insignificant in the prediction of percent drug entrapment. It is also observed that the drug entrapment does not significantly change ($P<0.05$) because as on changing stirring speed from 3000 rpm to 5000 rpm there is very little decrease in the percent drug entrapment which shows very less amount of drug loss due to size reduction of the transferosomes.

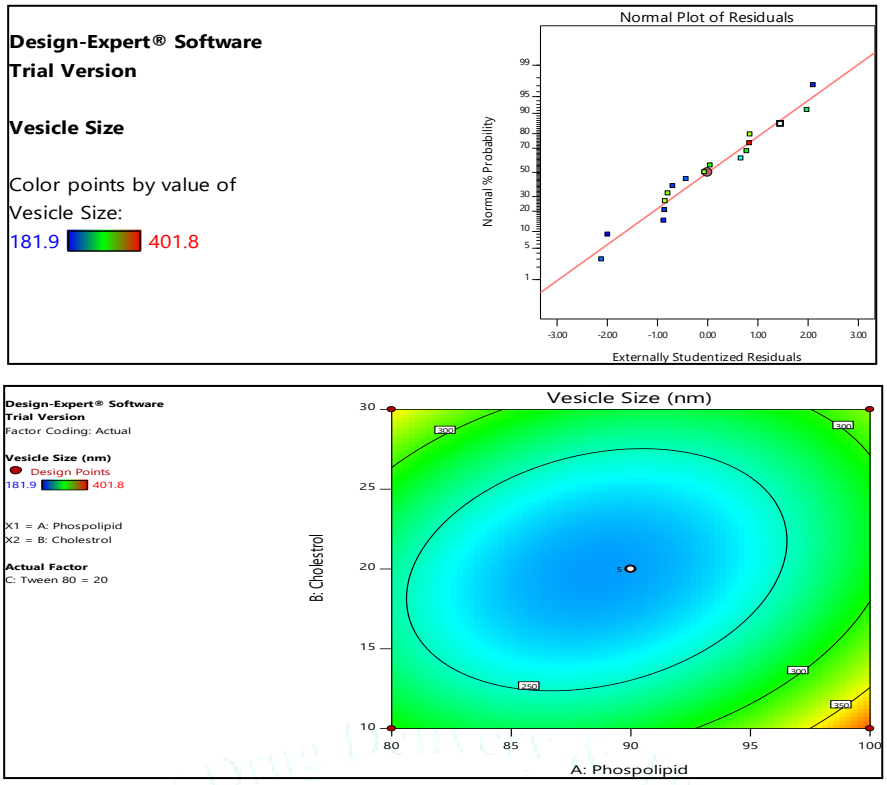


Figure 1 (a) Normal plot of residuals and (b) Contour plots for vesicle size

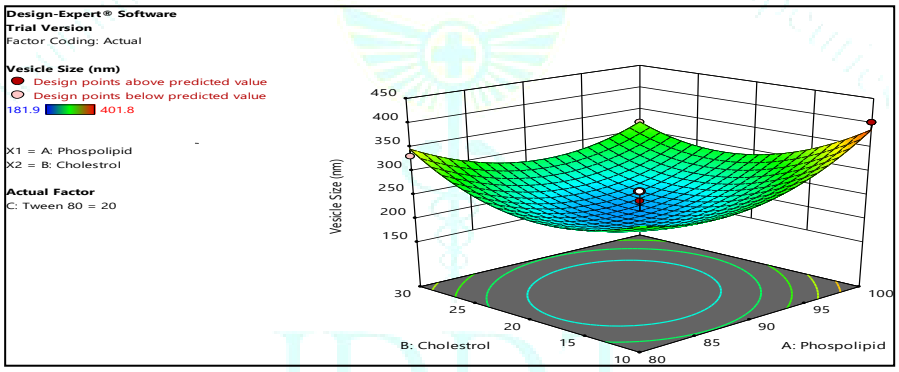


Figure 2 3D Response surface plots for Vesicle Size

In the case of PDI of transfersomes, the normal plot showing that all the points near the strait line of the plot which revealed that a transformation of the response may provide a better analysis. Contour plot and 3D graph were shown that the PDI was increase with increasing the concentration of lipid. Higher concentration of lipid may leads to formation of vesicles of different size.

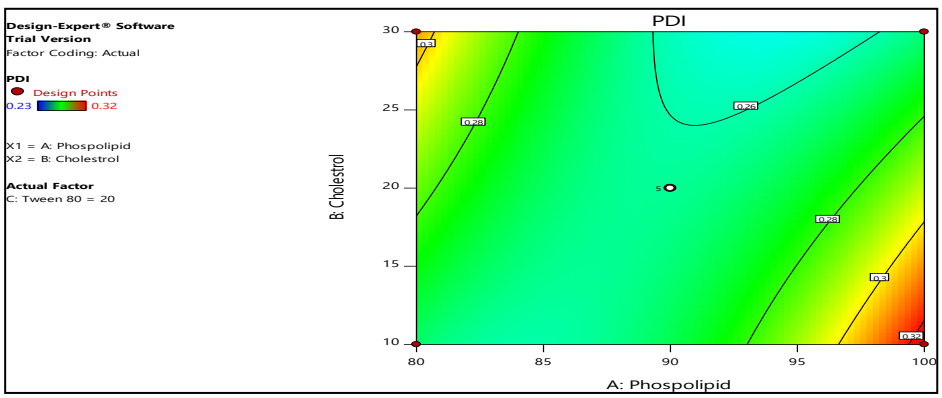
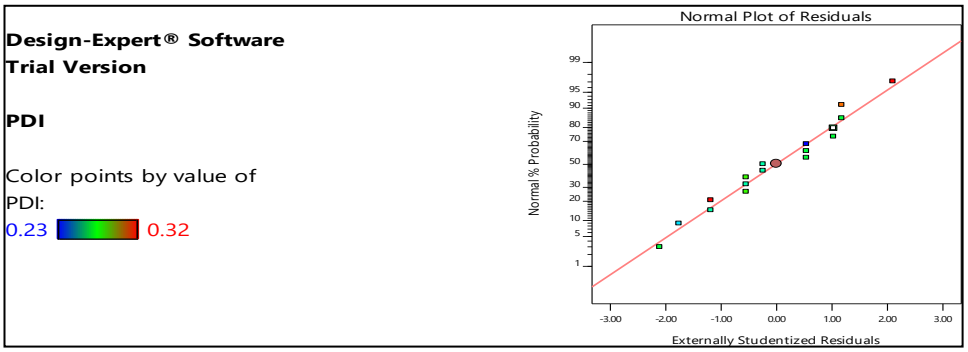


Figure 3 contour plots for PDI



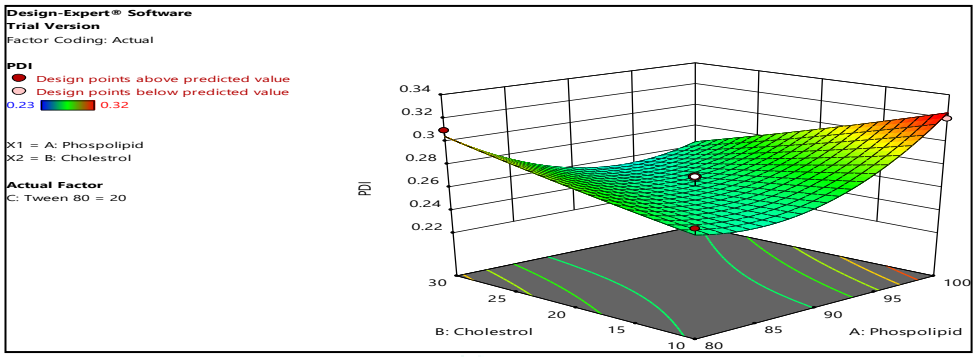
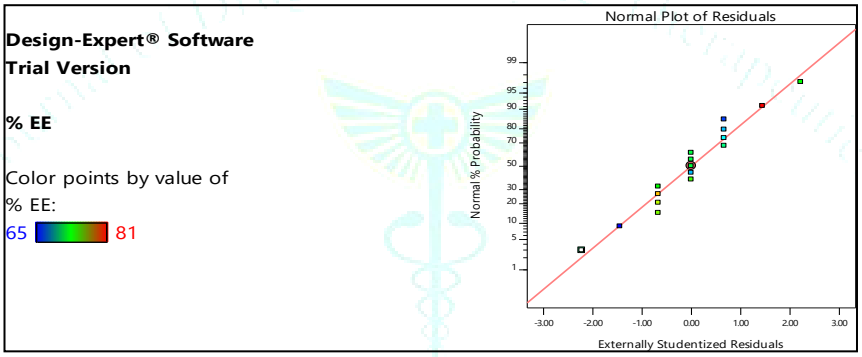


Figure 4 3D Response surface plot for PDI



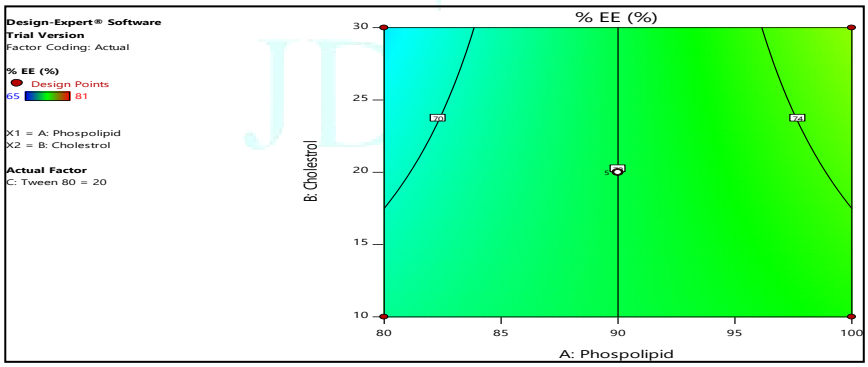


Figure 5 Contour plot for % EE

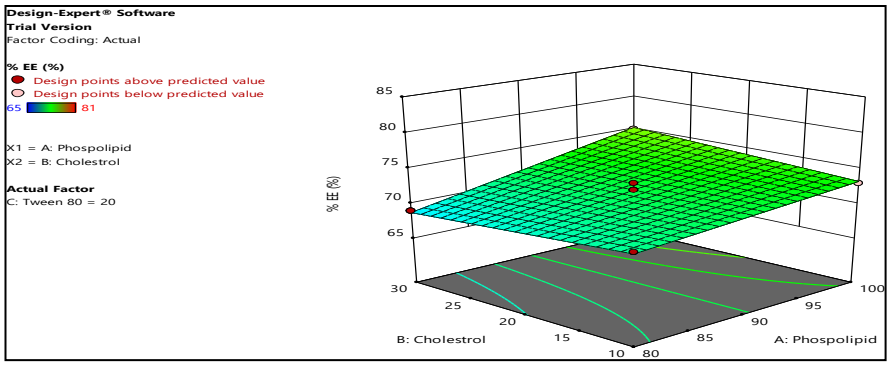


Figure 6 Response surface plot for % EE

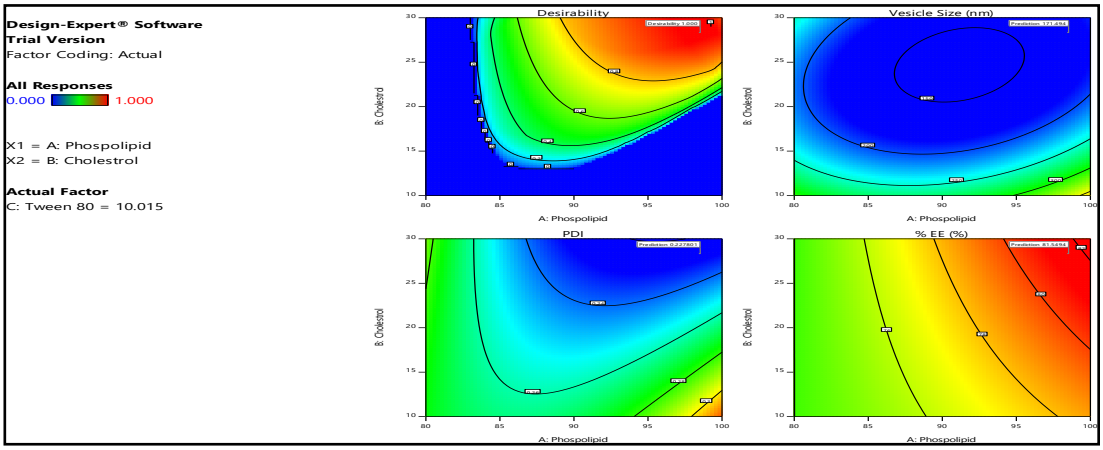


Figure 7 Contour plots for all parameters

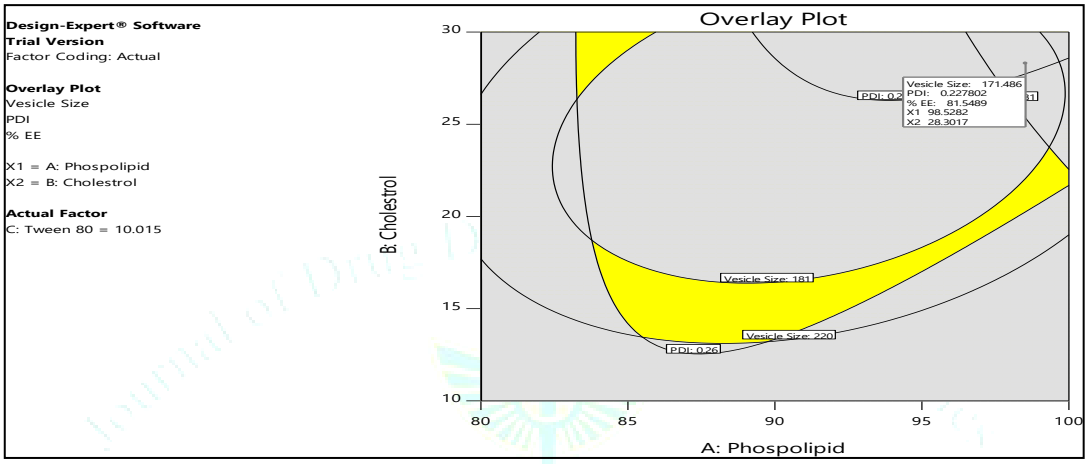


Figure 8 Overlain plot for all parameters

Vesicle size, PDI, % EE and desirability of optimized formulation after post analysis was given in table 6. The vesicle size and % EE of optimized formulation was found to be 171.49 nm and 87.54% respectively.

Table 6 Optimized formulation after post analysis

S. No.	Vesicle Size (nm)	PDI	% EE	Desirability
1.	171.494	0.228	87.549	1.000

Results of the evaluation of transferosomal gel formulation (TF1-TF3) of optimized formulation were incorporated into three different carbapol gel concentration 1, 2 and 3%w/w respectively. Formulation TF2 was found to be good Table 7. Results of *In-vitro* drug release from optimized formulation (TF2) are given in Table 8 was found 62.5 after 72 hrs. The *in vitro* drug release data of the formulation was subjected to the goodness of fit test by linear regression analysis according to zero order, first-order kinetic equation and Korsmeyer's -Pappas models to determine the mechanism of drug release. When the regression coefficient values of were compared, it was observed that 'r' values of the formulation were maximum i.e 0.990 hence indicating drug release from formulations was found to follow Korsmeyer-Peppas model of drug release kinetics Table 9 & Figure 9-12.

Table 7 Optimization of transfersomes gel formulations

Code	Drug content (%)	pH	Spreadability (gm.cm/sec.)	Viscosity (cps)
TF1	97.30±0.23	6.78±0.03	6.84±0.12	4850±12
TF2	98.74±0.45	6.99±0.02	5.16±0.21	4278±15
TF3	97.18±0.36	6.85±0.04	4.65±0.25	5325±10

Table 8 *In-vitro* drug release data for transfersome gel TF2

Time (h)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative*% Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
0.12	0.346	-0.921	5.84	0.766	94.16	1.974
0.5	0.707	-0.301	11.05	1.043	88.95	1.949
1	1.000	0.000	15.39	1.187	84.61	1.927
2	1.414	0.301	18.36	1.264	81.64	1.912
4	2.000	0.602	21.7	1.336	78.3	1.894
6	2.449	0.778	24.11	1.382	75.89	1.880
8	2.828	0.903	25.63	1.409	74.37	1.871
12	3.464	1.079	31.35	1.496	68.65	1.837
24	4.899	1.380	40.16	1.604	59.84	1.777
48	6.928	1.681	50.06	1.699	49.94	1.698
72	8.485	1.857	62.5	1.796	37.5	1.574

Table 9 Release Kinetics Regression values of formulation TF1-TF3

Formulation code	Zero order	First order	Higuchi	Korsmeyer-Peppas
TF1	Y=0.499x+19.33 0.774	Y=-0.003x+1.907 0.839	Y= 4.849x+12.18 0.928	Y= 0.279x+1.197 0.989
TF2	**Y=0.694x+16.61 0.900**	**Y=-0.005x+1.925 0.960**	**Y= 6.464x+7.544 0.989**	**Y= 0.346x+1.130 0.990**
TF3	Y=0.606x+14.81 0.844	Y=-0.004x+1.933 0.905	Y= 5.728x+6.629 0.955	Y= 5.728x+6.629 0.964

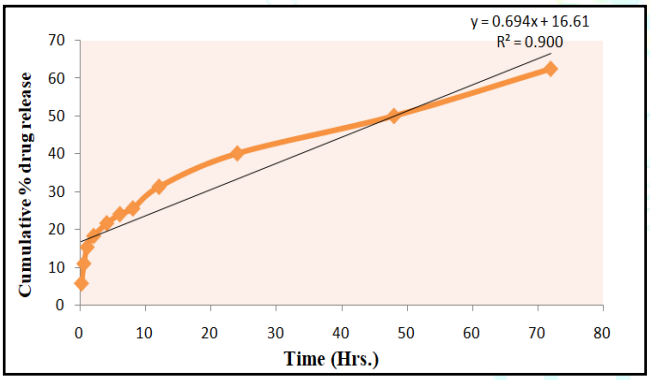


Figure 9 Graph of Zero order Release Kinetics of transfersome gel TF2

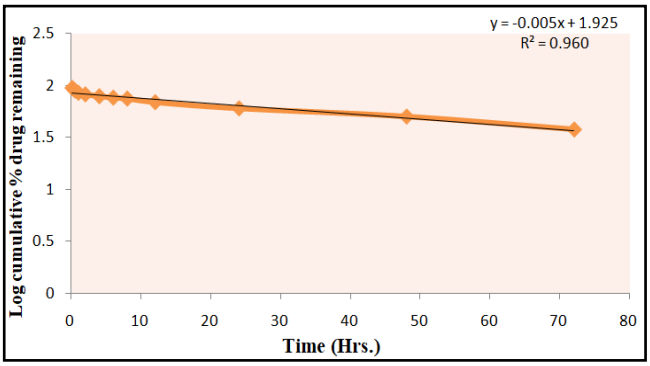


Figure 10 Graph of first order Release Kinetics of transfersome gel TF2

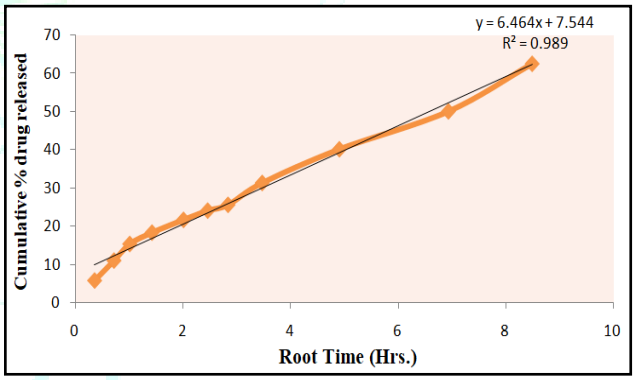


Figure 11 Graph of Higuchi release Kinetics of transfersome gel TF2

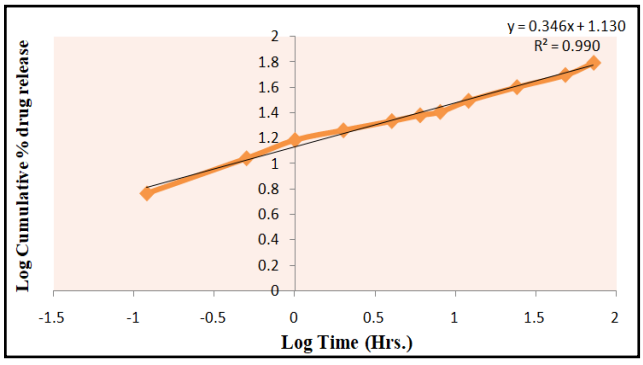


Figure 12Graph of Korsmeyer-Peppas release Kinetics of transfersome gel TF2

Stability study was carried out for drug loaded transferosomes gel (TF2) at two different temperatures i.e. refrigeration temperature (4.0±0.5°C) and at room temperature (28± 0.5°C) for 90 days. The formulations were analyzed for any vesicle size and drug content (figure 13 & 14).

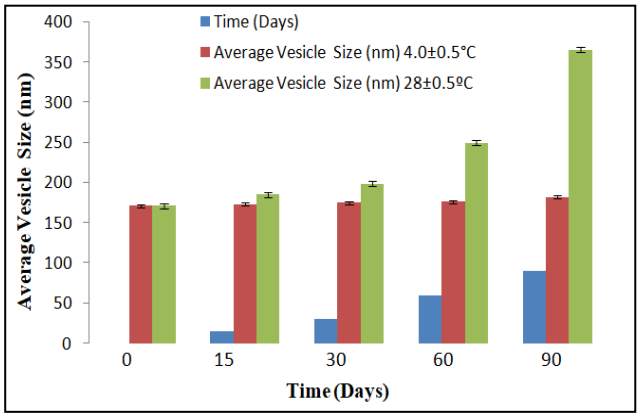


Figure 13 Effect of storage temperature on the vesicle size

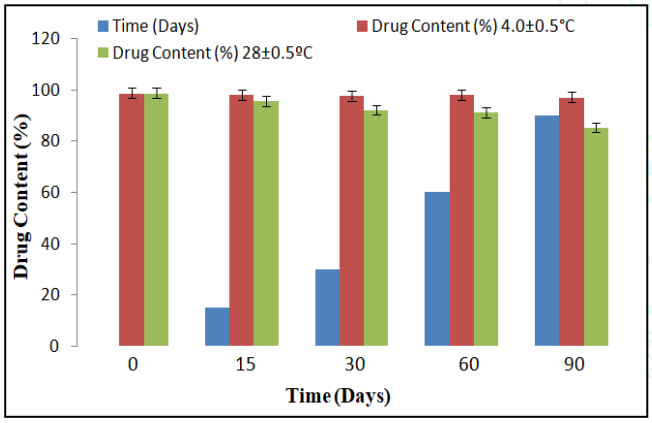


Figure 14 Effect of storage temperature on drug content

CONCLUSION

From this study, it was concluded that the factorial design (3^3) coulcould obtain an optimized formula of acyclovir, with high EE%, small particle size, and high transdermal flux. Also, the preparation of acyclovir as transfersomal gel can overcome the barrier properties of the skin and increase the antiviral activity and avoiding its oral problems and consequently improving patient compliance.

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