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DEVELOPMENT, OPTIMIZATION AND EVALUATION OF HERBAL GEL FORMULATION

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Keywords:

Acne, Carbopol 934, Propylene glycol, Quercetin, Curcuminoids, Berberine HCl

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ABSTRACT: Acne vulgaris is one of the most common chronic inflammatory skin diseases affecting more than 85% of adolescents worldwide. Quercetin, curcuminoids, and berberine HCl have anti-acne, anti-inflammatory, antibacterial, and antioxidant characteristics. This study aimed to develop, optimize and evaluate herbal gel containing quercetin, curcuminoids, and berberine HCl. A preliminary trial was conducted for the screening of polymers. A 3^2 full factorial design was applied to investigate the combined effect of the two independent variables, i.e., the concentration of carbopol 934 and the concentration of propylene glycol, on the dependent variables viscosity and cumulative percent drug release at 8 hrs. The optimized formulation (D0) shows a viscosity of 78123.67±0.69 cps, cumulative percent drug release of quercetin 85.99±1.03%, berberine HCl 35.38± 0.45% and curcuminoids 70.28± 1.18%. An FTIR investigation of drug excipient compatibility revealed no interactions between drugs and excipients. Based on all parameters and experimental design evaluations, it was determined that viscosity increased with increasing carbopol 934 and propylene glycol concentrations; cumulative percent drug release decreased with increasing carbopol 934 concentrations and increased with increasing propylene glycol concentrations.

INTRODUCTION: Acne vulgaris is a common skin disorder, due to chronic inflammation of sebaceous follicles, is characterized by tender inflammatory papules and nodules. Acne usually arises on the face, forehead, chest, upper back, and shoulders since these are the areas of skin with the most oil glands. According to the Global Burden of Disease research, acne vulgaris affects more than 85 percent of young people worldwide and can strike at any age. It typically appears throughout puberty and worsens during adolescence and is classified as an adolescent disease that affects almost 80% of the population between the ages of 11 to 30 [1, 2, 3].

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Acne is treated with retinoids, topical or systemic antibiotics, and other medications. The most serious issue with antibiotic use is resistance and its consequences; oral isotretinoin is teratogenic [4]. Plants are a natural source of medicine that can be utilized to treat a wide range of dermatological problems due to their efficacy and devoid of side effects [5].

Based on literature evaluations, we selected quercetin, curcuminoids, and berberine HCl for herbal gel formulation since they have anti-inflammatory, anti-acne, antibacterial, and antioxidant characteristics [6-12]. As a result, this study aimed to develop, optimize and evaluate herbal gel formulation for acne treatment.

MATERIAL AND METHODS:

Reagents and Chemicals: Quercetin, berberine HCl and curcuminoids were procured from Yucca enterprises, Mumbai; Sodium alginate, Na CMC and HPMC K100M were procured from Astron chemicals (India); HEC were procured from

Yarrow chem product, Mumbai; Carbopol 934 were procured from Research-lab fine chem Industries; Propylene glycol and Triethanolamine were procured from S.D. fine chemicals, Mumbai.

Drug Excipients Compatibility Study using FTIR: The IR spectra were acquired using an FTIR using the KBr pellet technique, and the wavelength range was between 4000 and 400 cm^{-1}. The spectra obtained for drugs and physical mixtures of drugs with polymers were observed [13].

Screening of Polymers: Preliminary screening was performed to confirm the effect of various polymers on herbal gel formulation Composition of preliminary trial batches of herbal gel is shown in **Table 1.** The resulting gel was evaluated for viscosity, homogeneity, and clarity [14-18].

TABLE 1: PRELIMINARY TRIAL BATCHES OF HERBAL GEL FOR SCREENING OF POLYMERS

Ingredients	Composition (%w/w)														
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}	F_{13}	F_{14}	F_{15}
Carbopol 934	0.5	1	2	--	--	--	--	--	--	--	--	--	--	--	--
HPMC K100M	--	--	--	2	3	4	--	--	--	--	--	--	--	--	--
HEC	--	--	--	--	--	--	1	2	3	--	--	--	--	--	--
Na CMC	--	--	--	--	--	--	--	--	--	4	5	6			
Sodium alginate	--	--	--	--	--	--	--	--	--	--	--	--	5	6	7
Triethanolamine	q.s.	q.s.	q.s.	--	--	--	--	--	--	--	--	--	--	--	--
Propylene glycol	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Distilled water q.s to make	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100

HPMC K100M- Hydroxy propyl methyl cellulose K100M, HEC- Hydroxy ethyl cellulose, Na CMC- Sodium carboxy methyl cellulose.

Optimization of Formulation as Per 3^2 Full Factorial Design: A 3^2 full factorial design was applied for optimization of the formulation. The concentration of carbopol 934 and the concentration of propylene glycol was taken as independent variables; viscosity and cumulative percent drug release at 8 hrs (Q8) were taken as dependent variables. We evaluated the response using a statistical model that included interactive and polynomial terms **Table 2**.

TABLE 2: VARIABLES IN 3^2 FULL FACTORIAL DESIGN

Independent variables	Levels		
	-1 (Low)	0 (Medium)	1 (High)
X_1= concentration of carbopol	0.75 gm	1 gm	1.25 gm
X_2= Concentration of propylene glycol	5 gm	10 gm	15 gm

Method of Preparation of Gel Formulation: Weighed quantity of carbopol 934 was soaked overnight in purified water containing sodium benzoate to ensure complete swelling of the polymer. Then propylene glycol was added. Drugs were accurately weighed and dissolved in ethanol in a stoppered glass vial, slowly added to the polymeric mixture, and homogenized in Triethanolamine was added in an amount (q.s.) sufficient to neutralize the pH. Then, distilled water was added to make q.s. to 100 gm with continuous stirring using mechanical stirrers Composition of factorial batches is shown in **Table 3** [14, 15, 16, 18].

TABLE 3: COMPOSITION OF FACTORIAL BATCHES

Ingredients	Composition (%w/w)								
	D_1	D_2	D_3	D_4	D_5	D_6	D_7	D_8	D_9
Quercetin	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75
Berberine HCl	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Curcuminoids	2	2	2	2	2	2	2	2	2
Carbopol 934	0.75	1	1.25	0.75	1	1.25	0.75	1	1.25
Propylene glycol	5	5	5	10	10	10	15	15	15
Sodium benzoate	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Triethanolamine	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Distilled water q.s. to make	100	100	100	100	100	100	100	100	100

Evaluation of Gel:

Viscosity: The viscosity of the gel formulation was determined at a temperature of 25.0 ± 0.5 °C using a viscometer (Brookfield DV-III+ Rheometer TC-502 Temperature Controller, USA). Spindle speeds have been adjusted to give the highest torque values in the 10-100% range, as the Brookfield instruction manual recommended. Viscosity was measured using spindles # 64 and 5 rpm [15, 18].

Homogeneity: Visual inspection in the presence of light techniques was adopted to check the homogeneity of gel [18].

pH Measurement: After calibration of pH meter using standard buffer solution at pH 4, 7, 9; the determinations were carried out in triplicate by dipping the glass electrode entirely into the formulation, and the average was calculated [18].

Spreadability: The gel was transferred to a glass slide and covered with an equivalent slide. The slides are arranged to have the gel interposed up to 7.5 cm. A weight of 100 g was placed over the upper slide, which helped in forming a uniform thin layer. The weight was removed, and excess adhering gel was wiped. After that 20 g weight was coupled carefully to upper slide. Time taken to travel a distance of 7.5 cm by upper slide under the influence of weight was recorded. The following formula was used to determine spreadability.

$$S = M \times L / T$$

Where, S - Spreadability M - Weight coupled to the upper slide (20 g) L - Length of the glass slide (7.5 cm) T- Time is taken to separate the slides in seconds [19].

Drug Content: The drug content of the gel was determined by dissolving 0.5 g of the gel in 50 ml of phosphate buffer pH 7.4. The solution was diluted with phosphate buffer pH 7.4 and filtered through a 0.45 µm membrane filter. Absorbance was measured using Shimadzu1800 UV visible spectrophotometer [15].

***In-vitro* Drug Release Study:** Franz diffusion cell was used for in vitro drug release studies having a receptor compartment capacity of 22.6 ml and an effective diffusion area of 4.52 cm^2. The cellophane membrane of the required thickness was hydrated for 24 hours before use with phosphate buffer pH 7.4. The donor compartment contained 1 g gel, and the recipient compartment contained phosphate buffer pH 7.4. The whole assembly was fixed on a magnetic stirrer, and the solutions in the receptor compartment were continuously stirred using magnetic beads at 50 rpm, and the temperature was maintained at 35±0.5 °C. At regular intervals, sampling was done from the receptor compartment, and an equal volume of fresh phosphate buffer pH 7.4 was added to the receptor compartment. The spectrophotometric method measured the active ingredient contained in the collected sample. The cumulative percentage of drug release was plotted against time [15].

Optimization of Formulation: Optimization of the formulation was done by the software Design Expert 6.0.8 Portable.

Accelerated Stability Study: Accelerated stability study was conducted for optimized gel at 40°C and 75% RH for three months using a humidity chamber. The gel was analyzed for pH, viscosity, and drug content [20].

RESULTS AND DISCUSSION:

Drug Excipients Compatibility Study using FTIR: IR studies have identified key functional group IR bands of pure drugs and physical mixtures and studied the physical and chemical interactions between drugs and the excipients used.

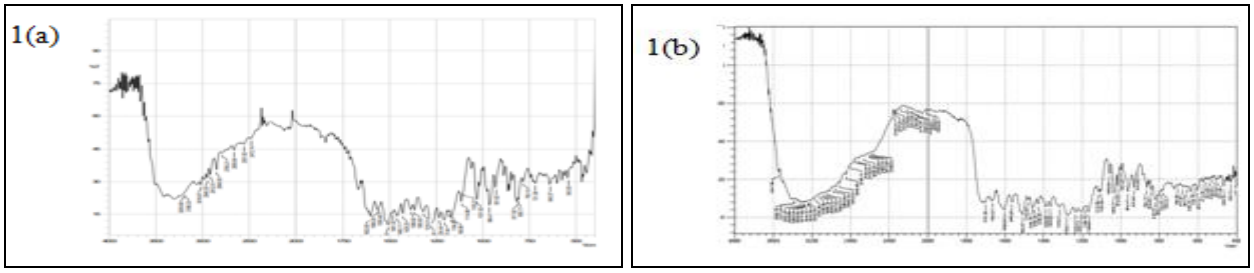

FIG. 1(A): IR SPECTRA OF MIXTURE OF DRUGS; 1(B): IR SPECTRA OF MIXTURE OF DRUGS AND POLYMER

It has been observed that the IR band of the characteristic drug remains unchanged in the IR spectrum of the physical mixture of drug and polymer. IR analysis showed that the drug and polymer are compatible **Fig. 1A, 1B.**

Screening of Polymers: All preliminary trial batches of gel show viscosity variation ranging from 800 to 190000 cps.

The pH values of all prepared formulations range from 6 to 7, which are considered acceptable to avoid the risk of irritation upon application to the skin. Of the five polymers, batch F2 showed optimum viscosity, good clarity, and homogeneity. Therefore, carbopol 934 was chosen for optimization Results of preliminary trial batches of herbal gel is shown in **Table 4.**

TABLE 4: RESULTS OF PRELIMINARY TRIAL BATCHES OF HERBAL GEL FOR SCREENING OF POLYMERS

Batch code	Viscosity(cps)± SD (n=3)	Homogeneity	Clarity
F1	22490±1.63	+++	+++
F2	86370±0.82	+++	+++
F3	132000±1.05	++	+++
F4	55434.33±2.49	+++	++
F5	93580.33±2.05	+++	++
F6	190000±1.98	++	++
F7	15998±2.16	+++	++
F8	25600.33±1.25	+++	+
F9	70299.67±2.05	++	+
F10	800±1.63	++	++
F11	1022.33±2.05	++	++
F12	1120±1.63	++	++
F13	7000±0.82	+	+
F14	23000±2.45	+	+
F15	55700±1.63	+	+

-Not satisfactory, + satisfactory, ++good, +++very good

Evaluation of 3^2 full Factorial Design Batches of Herbal Gel: The factorial design batches were evaluated for viscosity, homogeneity, pH, spreadability, drug content, and cumulative % drug release at 8 hrs Results of 3^2 full factorial design batches of herbal gel is shown in **Table 5, 6.**

TABLE 5: RESULTS OF 3^2 FULL FACTORIAL DESIGN BATCHES OF HERBAL GEL

Batch code	Viscosity (cps)± SD (n=3)	Homogeneity	pH± SD (n=3)	Spreadability (cm.gm/sec)	%Drug Content		
					Quercetin	Berberine HCl	Curcuminoids
D1	24877.3±1.25	+++	6.23±0.25	5.77	99.89±0.38	100.05±1.02	99.53±0.34
D2	57066±1.63	+++	6.53±0.30	5.36	98.58±1.00	99.39±1.42	99.87±0.44
D3	67078.3±1.25	+++	6.23±0.25	4.69	98.8±1.65	100.09±0.73	99.7±0.33
D4	49566.3±2.05	+++	6.8±0.26	5.17	99.89±0.38	101.03±0.54	100.05±0.25
D5	73598±2.45	+++	6.3±0.17	4.54	101.05±1.00	101.97±1.27	99.26±0.54
D6	98934±1.63	+++	6.16±0.15	4.41	98.37±0.66	101.62±1.61	99.37±0.73
D7	78768.7±2.49	++	6.13±0.25	4.84	100.06±1.36	99.39±1.14	100.09±0.63
D8	97948.3±2.87	++	6.23±0.06	4.55	99.67±1.31	98.1±0.35	98.75±0.25
D9	1,34000±1.98	++	6.87±0.12	3.94	98.15±0.38	99.98±0.73	99.76±0.34

TABLE 6: EXPERIMENTAL RUNS AND MEASURED RESPONSES OF 3^2 FULL FACTORIAL DESIGN BATCHES OF HERBAL GEL

Batch code	X_1= Concentration of carbopol 934 (gm)	X_2= concentration of propylene glycol (gm)	Viscosity (cps)	Cumulative percentage drug release at 8 hrs		
				Quercetin	Berberine HCl	Curcuminoids
D1	0.75	5	24877.3±1.25	66.51±0.72	28.83±0.92	53.87±0.91
D2	1	5	57066±1.63	59.56±0.51	26.49±0.88	49.49±0.89
D3	1.25	5	67078.3±1.25	51.94±0.77	22.41±0.72	43.58±0.85
D4	0.75	10	49566.3±2.05	85.41±0.87	35.54±0.83	68.04±1.01
D5	1	10	73598±2.45	78.34±0.94	32.09±1.71	61.08±0.95
D6	1.25	10	98934±1.63	73.31±0.96	29.47±0.85	55.44±1.16
D7	0.75	15	78768.7±2.49	89.21±0.94	37.52±1.16	69.15±1.14
D8	1	15	97948.3±2.87	79.21±0.52	33.71±1.05	63.05±1.25
D9	1.25	15	1,34000±1.98	72.18±0.78	30.15±1.47	56.89±1.15

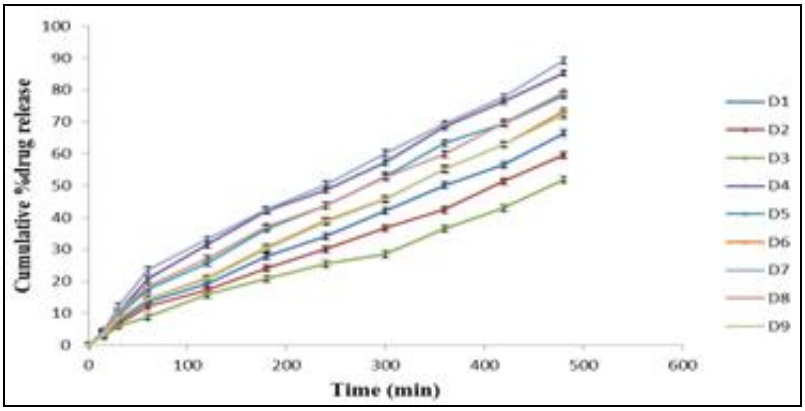

FIG. 2: CUMULATIVE PERCENTAGE RELEASE OF QUERCETIN AT 8 HRS

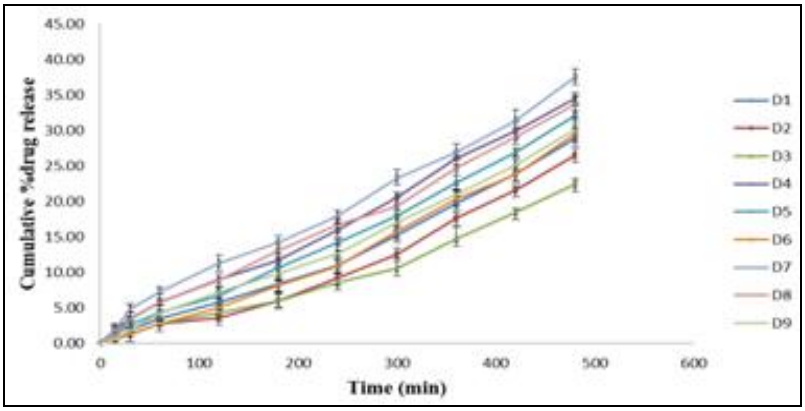

FIG. 3: CUMULATIVE PERCENTAGE RELEASE OF BERBERINE HCL AT 8 HRS

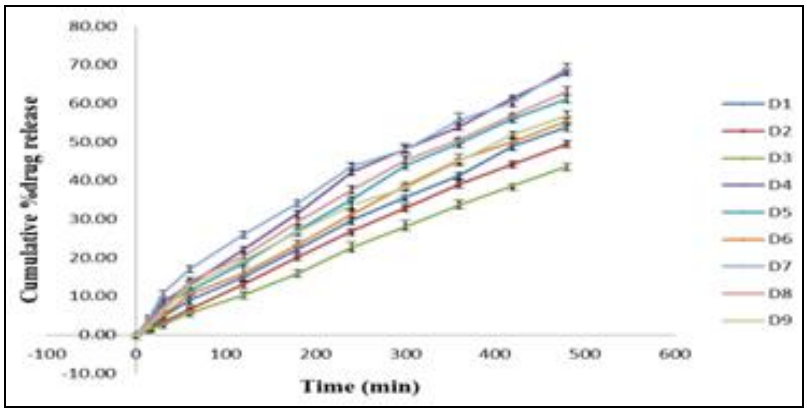

FIG. 4: CUMULATIVE PERCENTAGE RELEASE OF CURCUMINOIDS AT 8 HRS

Regression Analysis:

Regression Analysis for the Effect of X_1 and X_2 on Y_1 (Viscosity): The higher values of correlation coefficients for viscosity indicate a good fit. Here p Value for X_1 and X_2 was less than 0.05. Therefore, Carbopol 934 and propylene glycol significantly affected viscosity Results for regression statistics Y_1 is shown in **Table 7.** From the 3D surface plot **Fig. 5** and regression coefficient values of factors, it was concluded that carbopol 934 and propylene glycol positively affected viscosity. Here the b_2 value is more positive than the b_1 value, indicating that viscosity increases with increasing amounts of propylene glycol compared to carbopol 934 [21, 22, 23].

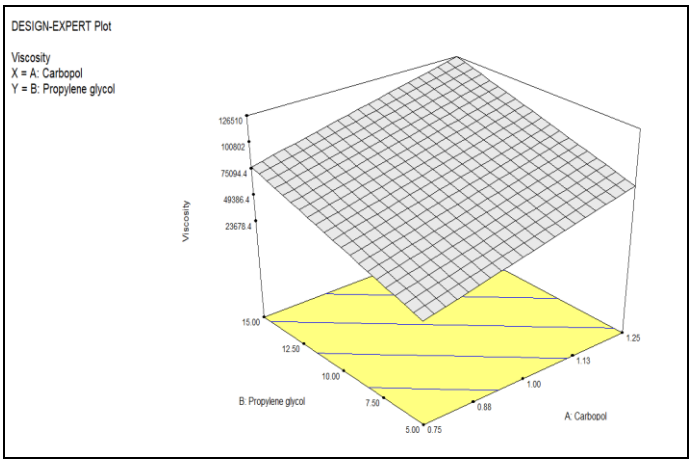

FIG. 5: 3D SURFACE PLOT OF RESPONSE Y_1

TABLE 7: REGRESSION STATISTICS Y_1

R-Squared	**0.976**	
Adj R-Squared	0.971	
Source	**Sum of Squares**	**P value**
Model (Linear)	79493	< 0.0001
X_1	35918	< 0.0001
X_2	43575	< 0.0001

Full model equation Y_1=75094.38+ 24466.83X_1+26949.17X_2

Regression Analysis for the Effect of X_1 and X_2 on Y_2 (Cumulative Percentage Release of Quercetin at 8 hrs): The higher values of correlation coefficients for drug release at 8 hrs indicate a good fit. Here, the p-values for X_1 and X_2 were less than 0.05. Therefore, carbopol 934 and propylene glycol significantly affected *in-vitro* drug release at 8 hrs Results for regression statistics Y_2 is shown in **Table 8.**

From the 3D surface plot **Fig. 6** and regression coefficient values of factors, it was concluded that carbopol 934 had a negative effect on in vitro drug release and propylene glycol had a positive effect on in vitro drug release, so it was concluded that % drug release decreased with increasing concentration of carbopol 934 and increased with increasing concentration of propylene glycol. The significance levels for the X_1^2 and X_1X_2 coefficients were P= 0.1851and 0.2188, respectively, so they were omitted from the full model to generate a reduced model. The coefficients X_1, X_2, and X_2^2 were significant at P<0.05; therefore, they were retained in the reduced models [21, 22, 23].

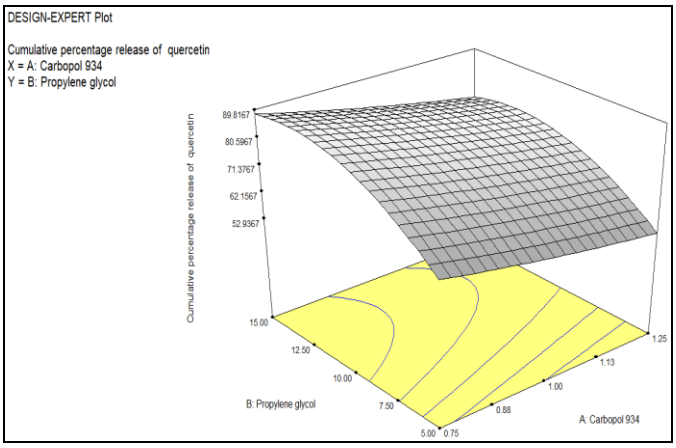

FIG. 6: 3D SURFACE PLOT OF RESPONSE Y_2

TABLE 8: REGRESSION STATISTICS Y_2

R-Squared	**0.995**	
Adj R-Squared	0.992	
Source	**Sum of Squares**	**P value**
Model (Quadratic)	1228.29	< 0.0001
X_1	318.28	< 0.0001
X_2	652.92	< 0.0001
X_1^2	1.79	0.1851
X_2^2	232.24	< 0.0001
X_1X_2	1.51	0.2188

Full model equation Y_2= 78.40-7.28X_1+10.43X_2+0.81X_1^2- 9.17X_2^2 -0.61X_1X_2

Regression Analysis for the Effect of X_1 and X_2 on Y_3 (Cumulative percentage Release of Berberine HCl at 8 hrs): The higher values of correlation coefficients for drug release at 8 hrs indicate a good fit.

Reduced model equation on the basis of p value

Y_2=78.40- 7.28X1+10.43X2-9.17X22

Here p Value for X_1 and X_2 was less than 0.05. Therefore, carbopol 934 and propylene glycol significantly affected *in-vitro* drug release at 8 hrs Results for regression statistics Y_3 is shown in **Table 9.** From the 3D surface plot **Fig. 7** and regression coefficient values of factors, it was concluded that carbopol 934 had a negative effect on *in-vitro* drug release and propylene glycol had a positive effect on *in-vitro* drug release, so it was concluded that % drug release decreased with increasing concentration of carbopol 934 and increased with increasing concentration of propylene glycol. The significance levels of the coefficients X_1^2 and X_1X_2 were P= 0.8817and 0.2458, respectively, so they were omitted from the

full model to generate a reduced model. The coefficients X_1, X_2, and X_2^2 were significant at P<0.05; therefore, they were retained in the reduced models [21, 22, 23].

Reduced model equation based on the p-value

$Y_3 = 32.20-3.31\ X_1+3.94\ X_2-2.37\ X_2^2$

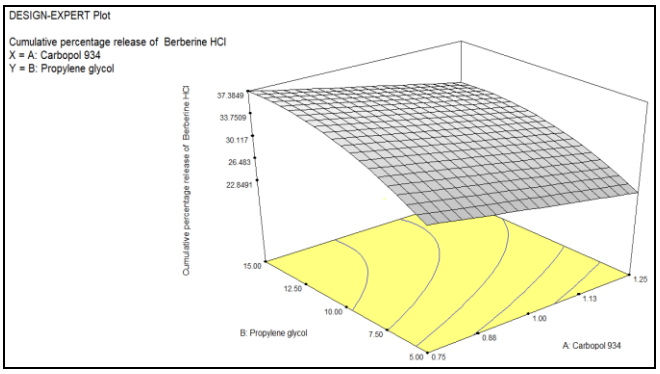

FIG. 7: 3D SURFACE PLOT OF RESPONSE Y_3

TABLE 9: REGRESSION STATISTICS Y_3

R-Squared	**0.994**	
Adj R-Squared	0.991	
Source	**Sum of Squares**	**P value**
Model (Quadratic)	177.13	< 0.0001
X_1	65.74	< 0.0001
X_2	93.22	< 0.0001
X_1^2	0.003	0.8817
X_2^2	15.52	< 0.0001
X_1X_2	0.23	0.2458

Full model equation $Y_3 = 32.20-3.31\ X_1+3.94X_2+0.035X_1^2-2.37X_2^2-0.24\ X_1X_2$

Regression Analysis for the Effect of X_1 and X_2 on Y_4 (Cumulative Percentage Release of Curcuminoids at 8 hrs): The higher values of correlation coefficients for drug release at 8 hrs indicate a good fit.

Here p Value for X_1 and X_2 was less than 0.05. Therefore, carbopol 934 and propylene glycol significantly affected *in-vitro* drug release at 8 hrs Results for regression statistics Y_4 is shown in **Table 10**.

From the 3D surface plot **Fig. 8** and regression coefficient values of factors, it was concluded that carbopol 934 had a negative effect on *in-vitro* drug release and propylene glycol had a positive effect on *in-vitro* drug release, so it was concluded that % drug release decreased with increase in the concentration of carbopol 934 and increased with increasing concentration of propylene glycol. The significance levels of the coefficients X_{12} and X_1X_2 were P= 0.6123 and 0.0736, respectively, so they were omitted from the full model to generate a reduced model. The coefficients X_1, X_2, and X_{22} were significant at P<0.05; therefore, they were retained in the reduced models [21, 22, 23].

Reduced model equation based on a *p-value*

$Y_4 = 61.23-5.86\ X_1+7.03\ X_2\ -5.32\ X_2^2$

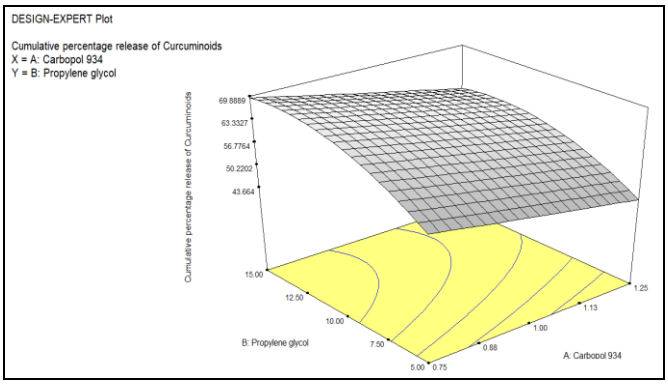

FIG. 8: 3D SURFACE PLOT OF RESPONSE Y_4

TABLE 10: REGRESSION STATISTICS Y_4

R-Squared	**0.997**	
Adj R-Squared	0.996	
Source	**Sum of Squares**	**P value**
Model (Quadratic)	592.57	< 0.0001
X_1	205.92	< 0.0001
X_2	296.10	< 0.0001
X_1^2	0.062	0.6123
X_2^2	78.18	< 0.0001
X_1X_2	0.97	0.0736

Full model equation $Y_4 = 61.23-5.86X_1 + 7.03X_2 + 0.15\ X_1^2-5.32\ X_2^2-0.49\ X_1X_2$

Optimization of Formulation: The optimum formulation was chosen based on the criteria of minimum & maximum values of the response variables. From **Fig. 9**, we can conclude that the batch with X_1 = 0.79 and X_2 =14.60 was selected as the optimized batch with desirability 1.

TABLE 11: RESULTS OF EVALUATION PARAMETERS OF OPTIMIZED BATCH (D0)

Parameters	Results
Viscosity (cps)	78123.67±0.69
pH	6.4±0.18
Spreadability (cm.gm/sec)	4.73
% Drug content of quercetin	99.89±0.38
%Drug content of berberine HCl	98.1± 1.42
%Drug content of curcuminoids	98.75± 0.75
Cumulative % drug release of quercetin at 8hrs	85.99±1.03
Cumulative % drug release of berberine HCl at 8hrs	35.38±0.45
Cumulative % drug release of curcuminoids at 8hrs	70.28±1.18

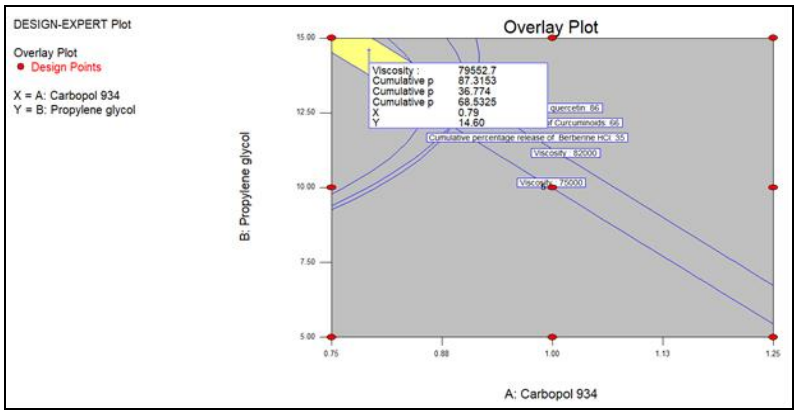

FIG. 9: OPTIMIZED BATCH FROM OVERLAY PLOT

TABLE 12: COMPARISON BETWEEN RESPONSES OF OPTIMIZED BATCH (D0)

Evaluation parameters	Actual value	Predicted value	% Error
Viscosity (cps)	78123.67	79552.7	1.80
Cumulative %drug release of quercetin at 8hrs	85.99	87.32	1.52
Cumulative %drug release of berberine HCl at 8hrs	35.38	36.77	3.78
Cumulative %drug release of curcuminoids at 8hrs	70.28	68.53	2.55

The actual response of the optimized batch was measured and compared with the predicted response of the checkpoint batch, and % Error was found to be less than 5%. So it shows a good correlation between observed and predicted values. Hence it was concluded that this design was valid.

TABLE 13: ACCELERATED STABILITY STUDY OF GEL FORMULATION

Stability conditions	Sampling time	pH	Viscosity (cps)	Drug content (%)			Cumulative percent drug release at 8 hrs		
				Quercetin	Berberine HCl	Curcuminoids	Quercetin	Berberine HCl	Curcuminoids
Accelerated condition (40±2°C and75±5% RH) (Batch D_0)	Initial (0 day)	6.4± 0.18	78123.67 ± 5.13	99.89± 0.38	98.1± 1.42	98.75± 0.75	85.99	35.38	70.28
	30 days	6.45± 0.32	78134± 4.58	98.37± 0.66	99.98± 0.73	99.53± 1.34	86.16	34.59	69.34
	60 days	6.43± 0.21	78132± 2.65	99.67± 1.36	99.39± 1.07	99.87± 0.44	86.32	35.15	68.4
	90 days	6.33± 0.45	78127.33 ± 2.08	98.15± 2.31	99.28± 1.42	98.37± 1.73	85.17	36.12	70.13

This study showed that drugs remained stable in gel formulation at accelerated conditions for 90 days. No significant variations in pH, viscosity, % drug content and cumulative percent drug release at 8 hrs were observed at mentioned conditions.

CONCLUSION: The present investigation was to develop, optimize and evaluate herbal gel formulation using polymers such as carbopol 934 and propylene glycol. An FTIR investigation of drug excipient compatibility revealed no interactions between drugs and excipients. From all parameters and experimental design evaluation, it was concluded that viscosity increased with increasing carbopol 934 and propylene glycol concentrations; cumulative percent drug release

decreased with increasing carbopol 934 concentrations and increased with increasing propylene glycol concentrations.

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