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Optimisation Study of Taraxacum Officinale Niosomes by Box-Behnken Design

Gajbhiye Sanghadeep[1] , Aate Jayshree[2]
VIVA Institute of Pharmacy, Shirgaon, Virar (E)
Hi- Tech College of Pharmacy, Morwa, Chandrapur

Abstract:- Phytosome process has been applied to many popular herbal extract including Gingko biloba, grape see, hawthorn, milk thistle, green tea and ginseng. The flavonoids and terpenoid components of these herbal extracts lend themselves quite well for the direct binding to Phosphatidylcholine. Phytosomes is produced by binding individual components of herbal extract to phosphatidylcholine, resulting in a dosage form that is better absorbed and thus, produces better result than the conventional herbal extract.

According to this research, design of experiments (DoE) is an efficient, elegant, and cost-effective statistical technique that delivers more knowledge with the least number of runs. Soya lecithin (X1), reaction temperature (X2), and reaction time (X3) were all significant parameters impacting phytosome response characteristics, according to standardised response surface plots, with p 0.05. The precision of the data was demonstrated by significant (p 0.05) model F-values and non-significant (p > 0.05) "lack of fit F-values" for response variables. R2 Adj (adjusted R-squared) and R2 Anticipated (expected R-squared) (R2 Pred) values indicated that the regression coefficients were fairly consistent. A lower PRESS value in regression models indicated a better match. The model discrimination was adequate, according to a high precision (AP) value. The normality of the response data was demonstrated using standard probability plots. Externally studentized residuals vs. expected values of the response parameters revealed the absence of constant error. The absence of lurking variables was investigated using a residual vs. run plot.

Keywords:- *Nisomes, Taraxacum officinale, Box-Behnken Design.*

I. INTRODUCTION

One of the major challenges that limit the direct objectification of factory bioactive constituents into foodstuffs, potables and ornamental and pharmaceutical products is their low water or canvas solubility. Composites with poor water solubility (e.g., carotenoids) can not readily be incorporated into waterless-based products whereas constituents with poor canvas solubility can not fluently be incorporated into canvas- grounded products.

Plants flowers are ornamental and used for worship and flavoring purposes. The leaves, stem, flowers and root all have bioactive pharmaceutical ingredients that can be used for treatment and therapy of certain types of ailments. Full factorial experimental design is one of the best tools to study the effect of different variables on the quality determinant parameters of any formulation. A statistical model was developed to optimize the Taraxacum offcinal loaded niosomal formulation, which is a very important aspect of formulation development, to understand the theoretical formulation and target processing parameters, as well as the range for each excipient and processing parameter. The aim of this study was to investigate the combined influence of 3 independent variables on the preparation of Taraxacum officinale loaded niosomes by the reverse evaporation method and thereby improve the entrapment efficiency and particle size of Taraxacum officinale loaded niosomes.

Fig 1: Flowering Plant of Dandelion (Taraxacum officinale)

II. OPTIMIZATION OF PHYOTOSOMES

Box-Behnken Design (BBD) was used to optimise the formulation parameters of *Taraxacum officinale* phytosomes (LA-PHY) in order to increase yield, drug loading capacity, and particle size. We used Soya Lecithin (X1), reaction temperature (X2) and reaction time (X3) as independent variables to build an optimum carrier device since these three process parameters have a significant impact on the quality of the resulting product. Particle size (Y2), % Entrapment Efficiency (Y1), and cumulative drug content (Y3) were used to evaluate the final product (Y3). Response surface technique was used to design the screening in order to minimise the number of trials while still collecting as much information as possible about the product's characteristics. It was shown that individual responses could be predicted by doing experiments with 17 distinct combinations of

independent variables, and then plugging the results into the equation: Y B0 + B1X1 + B2X2 + B3x3.

Respondents answered with a yes, the intercept was b0 (the average of the 17 runs), and the estimated factor coefficients ranged from b1 to b9. The dependent variable was Y, and the intercept was b0. It was decided that independent variables would be coded at three different levels: 1, 2, and 3. Selective variable level values tables 5.19 and 5.20 demonstrate the structure of the central composite design batches.

Table No 1: Levels of three independent variables used in Box-Behnken Design

Independent variable	Coded symbol	Levels	
		Low	High
Soya Lecithin (mg)	X1	2.00	5.00
Reaction temperature (ºC)	X2	30.00	70.00
Reaction time (min)	X3	30.00	70.00
Entrapment Efficiency (%)	Y1	Maximize	
Vesicle Size (nm)	Y2	Maximize	
Cumulative Drug Release (%)	Y3	Maximize	

➢ *ANOVA- Analysis of variance*

- *Fitness & Analysis of Response Model*

Analysis of variances (ANOVA) was used to construct the quadratic polynomial equation, which was then statistically verified. Response surface (2 & 3-D) models were used to test and validate statistically significant coefficients and R-square values of seventeen duplicate centre locations in order to identify the optimum compositions across the experimental zone (Table 2). Linear regression plots were used to compare the actual response values to the anticipated response values to determine the practical vs. theoretical predicted values.

To 5 mL of chloroform, we added a precisely measured amount of LA-PHY (equivalent to 10 mg of LA Extract). Free (non-aggregated) LA was soluble in chloroform but not the phytosome or non-reacted phospholipids (Tan et al., 2012). The non-aggregated or free *Taraxacum officinale* was separated as a precipitate after filtering the dispersion. This non-aggregated LA was dissolved in methanol and analysed for *Taraxacum officinale* at 664 nm using a UV–visible spectrophotometer (Model: V-630, JASCO International Co. Ltd., Tokyo, Japan).

III. RESULTS AND DISCUSSION

➢ *Optimisation of Formulation by Box-Behnken Design (BBD):*

Table No 02: BBD Experimental design and response for the dependent variables

Run	X1	X2	X3	Y1	Y2	Y3	Zeta	PDI
1	3.5	70	30	88.6±1.1	145±7.9	84.3±4.6	-24.50	0.40±0.03
2	3.5	50	50	84.3±2.6	184±4.5	79.8±1.3	-28.11	0.58±0.02
3	3.5	70	70	83.5±2.4	176±7.9	68.9±2.6	-29.72	0.38±0.02
4	3.5	30	70	86.5±0.9	205±5.6	75.8±4.6	-24.53	0.39±0.01
5	3.5	50	50	84.5±0.8	185±4.5	79.8±5.4	-29.41	0.49±0.03
6	2	50	70	86.6±0.7	125±7.9	86.2±1.3	-24.50	0.51±0.02
7	5	50	70	87.2±1.2	185±4.5	72.3±2.6	-32.41	0.35±0.02
8	3.5	50	50	84.5±2.7	184±6.4	79.8±2.6	-24.91	0.43±0.02
9	2	30	50	80.3±4.6	149±9.2	73.6±4.6	-28.73	0.54±0.01
10	5	70	50	86.6±1.3	153±8.8	70.8±5.8	-27.62	0.52±0.02
11	5	50	30	89.1±4.6	92±9.1	94.5±1.3	-32.45	0.48±0.03
12	3.5	30	30	79.8±0.6	160±5.8	82.3±2.6	-30.60	0.35±0.01
13	2	70	50	83.3±2.9	140±8.2	74.3±5.8	-24.91	0.32±0.03
14	2	50	30	84.6±3.6	125±9.1	86.6±1.3	-28.73	0.43±0.01
15	3.5	50	50	84.5±0.7	184±5.6	79.8±4.6	-27.62	0.39±0.02
16	3.5	50	50	84.3±2.7	184±8.6	84.3±1.3	-25.40	0.42±0.02
17	5	30	50	82.2±1.3	165±4.6	76.1±5.8	-26.13	0.41±0.01

(Data are expressed as mean ± SD, n =3)

Table No 03: BBD Experimental design and response for R1

Source	Sequential p-value	Lack of Fit p-value	Adjusted R^2	Predicted R^2	
Linear	0.1354	< 0.0001	0.1853	-0.3808	
2FI	0.0340	< 0.0001	0.5382	-0.4628	
Quadratic	**< 0.0001**	**0.0100**	**0.9858**	**0.9072**	**Suggested**
Cubic	0.0100		0.9982		**Aliased**

Table No 04: BBD Experimental design Sequential Model Sum of Squares for R1

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Mean vs Total	1.220E+05	1	1.220E+05			
Linear vs Mean	35.40	3	11.80	2.21	0.1354	
2FI vs Linear	39.10	3	13.03	4.31	0.0340	
Quadratic vs 2FI	**29.58**	**3**	**9.86**	**106.10**	**< 0.0001**	**Suggested**
Cubic vs Quadratic	0.6025	3	0.2008	16.74	0.0100	Aliased
Residual	0.0480	4	0.0120			
Total	1.221E+05	17	7185.23			

Table No 05: BBD Experimental design ANOVA for Quadratic model R1

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	104.08	9	11.56	124.45	< 0.0001	Significant
A-A	13.26	1	13.26	142.70	< 0.0001	
B-B	21.78	1	21.78	234.37	< 0.0001	
-C	0.3613	1	0.3613	3.89	0.0893	
AB	0.4900	1	0.4900	5.27	0.0553	
AC	3.80	1	3.80	40.92	0.0004	
BC	34.81	1	34.81	374.59	< 0.0001	
A^2	0.9600	1	0.9600	10.33	0.0148	
B^2	13.60	1	13.60	146.39	< 0.0001	
C^2	16.47	1	16.47	177.18	< 0.0001	
Residual	0.6505	7	0.0929			
Lack of Fit	0.6025	3	0.2008	16.74	0.0100	Significant
Pure Error	0.0480	4	0.0120			
Cor Total	104.74	16				

The F-value of 124.45 for the model suggests that it is statistically significant. Due to noise, an F-value of this magnitude has a 0.01 percent chance of occurring. Important model terms have P-values of less than 0.0500. In this scenario, the model terms A, B, AC, BC, A2, B2, and C2 are crucial. If the value is more than 0.1000, the model terms are irrelevant. If your model has a lot of irrelevant terms, model reduction can help you improve it (not counting those needed to support hierarchy). The Lack of Fit has an F-value of 16.74, indicating that it is significant. There's a 1.00 percent chance that noise is to blame for a significant Lack of Fit F-value. A significant lack of fit is problematic since we want the model to fit.

IV. FIT SUMMARY

- *Response 2: R2*

Taraxacum officinale phytosomes had an average particle size of 929.1 to 2055.6 nm (minimum particle size of LAPHY). The observed values of mean particle size were compared to the expected values obtained by the model using equation, and the low percent error (5%) revealed strong predictability capacity of the modeled model (Table 4.17). On Y2, the inference of modifying drug: polymer and reaction time was studied (Figure 4.11a and 4.12a). The effects of changing the polymer, reaction time, and temperature ratio (X2 & X3) on mean particle size (Y2) were investigated (Figure 4.11b and 4.12b). The mean particle size grew fast as the polymer ratio rose, as evidenced by an increase in the density of the dispersed phase and the size of the droplets (Hao et al., 2011; Mao et al., 2008;

Shah and Pathak, 2010). The effect of changing drug: polymer and stirring speed on Y2 was investigated when all other factors were held constant (Figure 4.11c and 4.12c). When all other variables were held constant, the effect of varying stirring time (X3) and temperature (X2) on Y2 was investigated.

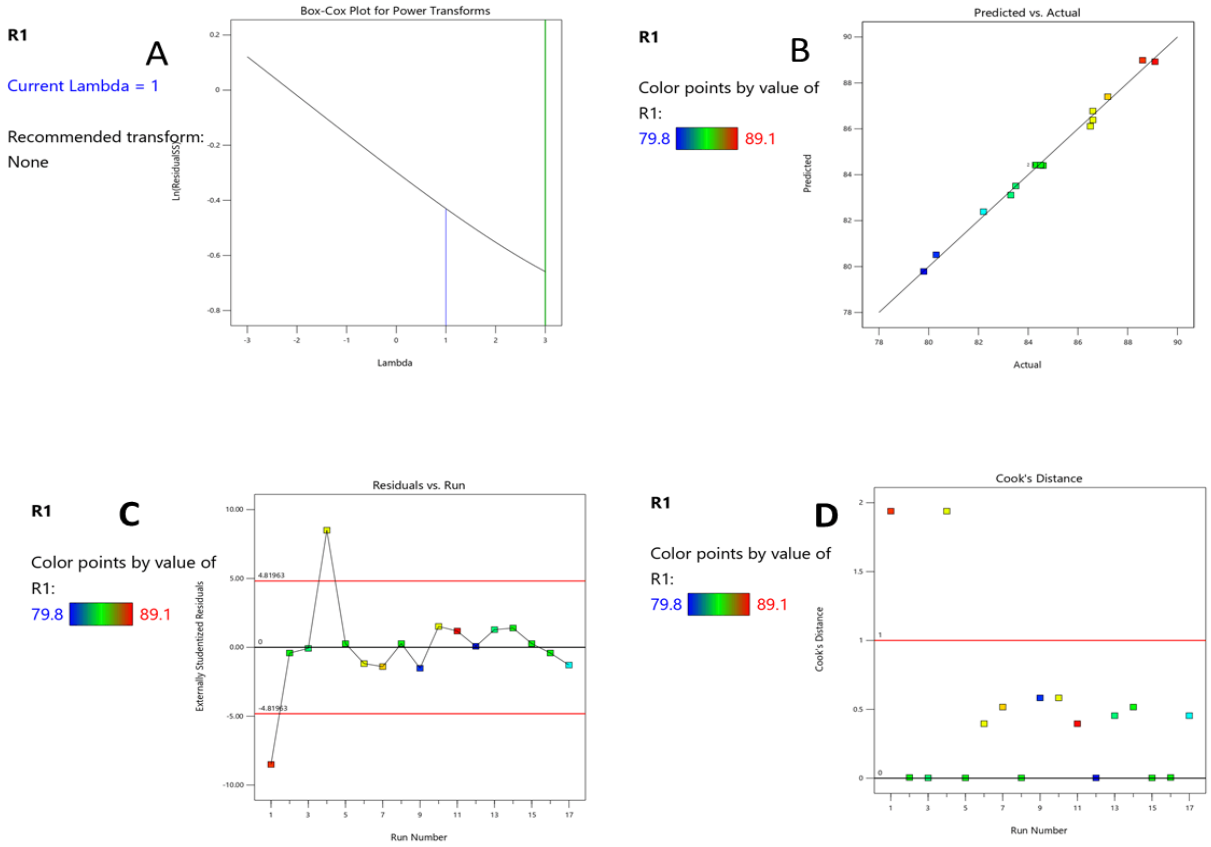

Fig No 02: Diagnostic plot for % EE (a) normal Box-cox (B) residuals versus run number plot (c) Residuals vs. predicted values graph and (d) Cooks Distance values plot for R1

Raising the stirring speed resulted in a considerable reduction in particle size decrease, which could be caused by the force exerted by high rpm (Shah and Pathak, 2010; Mao et al., 2008; Hao et al., 2011).The effect of altering X2 and X3 on Y2 was investigated when the polymer ratio, stirring time, and temperature ratio were held constant (Figure no. 12)

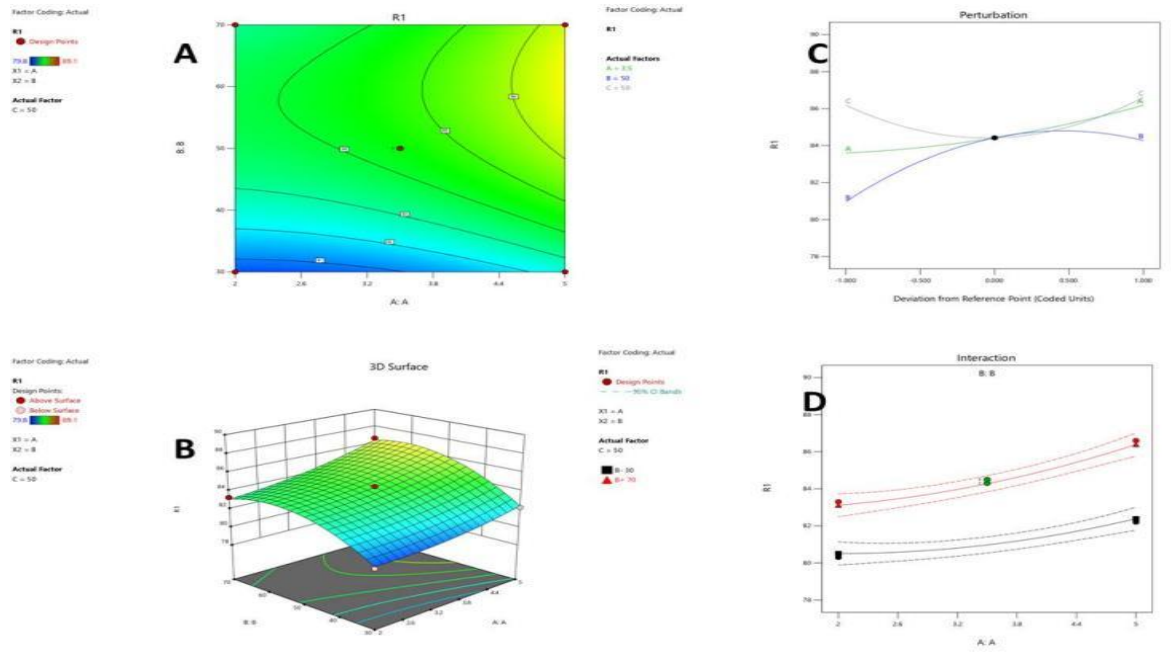

Fig No 03: A&B Response & contour plot for R1 optimized phytosomal preparation of *Taraxacum officinale.* C&D Perturbation and interaction of Independent variables of R1

It was discovered that increasing surfactant concentration would effectively reduce phytosome particle size by lowering surface tension between the scattered and continuous phases (Gullapalli et al., 1999; Ko et al., 2004). Additionally, it can aid in the stabilization of emulsion globules, thereby preventing particle aggregation (Hao et al., 2011; Hamed and Sakr, 2001; Yang et al., 2000). The effect of modifying X4 and X5 on Y2 was confirmed in Figures no. 13.

Since high rpm resulted in particle size reduction, the results showed that mean particle size decreased rapidly with increasing stirring speed(Gullapalli et al., 1999; Ko et al., 2004).

Table No 06: BBD Experimental design Fit SummaryR2

Source	Sequential p-value	Lack of Fit p-value	Adjusted R^2	Predicted R^2	
Linear	0.1481	< 0.0001	0.1725	-0.2217	
2FI	0.4110	< 0.0001	0.1827	-0.8526	
Quadratic	**< 0.0001**	**0.0001**	**0.9827**	**0.8799**	**Suggested**
Cubic	0.0001		0.9998		**Aliased**

Table No 07: BBD Experimental design Sequential Model Sum of Squares R2

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Mean vs Total	4.419E+05	1	4.419E+05			
Linear vs Mean	4490.25	3	1496.75	2.11	0.1481	
2FI vs Linear	2213.50	3	737.83	1.05	0.4110	
Quadratic vs 2FI	**6895.76**	**3**	**2298.59**	**155.38**	**< 0.0001**	**Suggested**
Cubic vs Quadratic	102.75	3	34.25	171.25	0.0001	Aliased
Residual	0.8000	4	0.2000			
Total	4.556E+05	17	26802.88			

Select the highest order polynomial where the additional terms are significant and the model is not aliased.

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Linear	9212.01	9	1023.56	5117.78	< 0.0001	
2FI	6998.51	6	1166.42	5832.09	< 0.0001	
Quadratic	**102.75**	**3**	**34.25**	**171.25**	**0.0001**	**Suggested**
Cubic	0.0000	0				Aliased
Pure Error	0.8000	4	0.2000			

The chosen model should have a minimal lack of fit.

Table No 08: BBD Experimental ANOVA for Quadratic model R2

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	13599.51	9	1511.06	102.15	< 0.0001	Significant
A-A	392.00	1	392.00	26.50	0.0013	
B-B	528.12	1	528.12	35.70	0.0006	
C-C	3570.13	1	3570.13	241.34	< 0.0001	
AB	2.25	1	2.25	0.1521	0.7081	
AC	2162.25	1	2162.25	146.17	< 0.0001	
BC	49.00	1	49.00	3.31	0.1116	
A^2	5487.20	1	5487.20	370.94	< 0.0001	
B^2	56.09	1	56.09	3.79	0.0925	
C^2	1125.57	1	1125.57	76.09	< 0.0001	
Residual	103.55	7	14.79			
Lack of Fit	102.75	3	34.25	171.25	0.0001	significant
Pure Error	0.8000	4	0.2000			
Cor Total	13703.06	16				

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P-values for important model terms are less than 0.0500. A, B, C, AC, A2, and C2 are important model terms in this situation. The model terms are meaningless if the value is greater than 0.1000. Model reduction might assist you enhance your model if it has a lot of useless terms (not counting those needed to support hierarchy).

There is a substantial lack of fit, as indicated by the F-value of 171.25. There is only a 0.01 percent probability that noise will cause a significant Lack of Fit F-value. We want the model to fit, thus a severe lack of fit is bad.

P-values for important model terms are less than 0.0500. A, B, C, AC, A2, and C2 are important model terms in this situation. The model terms are meaningless if the value is greater than 0.1000. Model reduction might assist you enhance your model if it has a lot of useless terms (not counting those needed to support hierarchy). There is a substantial lack of fit, as indicated by the F-value of 171.25. There is only a 0.01 percent probability that noise will cause a significant Lack of Fit F-value. We want the model to fit, thus a severe lack of fit is bad.

Table No 09: BBD Experimental Fit Statistics R2

Std. Dev.	3.85	**R^2**	0.9924
Mean	161.24	**Adjusted R^2**	0.9827
C.V. %	2.39	**Predicted R^2**	0.8799
		Adeq Precision	37.2475

The difference between the Estimated R2 of 0.8799 and the Adjusted R2 of 0.9827 is less than 0.2, suggesting that the discrepancy is less than 0.2. Adeq Precision calculates the signal-to-noise ratio. It is better to have a four-to-one ratio. You have a strong signal with a transmission ratio of 37.248. This notion can be used to navigate the design space.

Table No 10: BBD Experimental Coefficients in Terms of Coded Factors R2

Factor	**Coefficient Estimate**	**Df**	**Standard Error**	**95% CI Low**	**95% CI High**	**VIF**
Intercept	184.20	1	1.72	180.13	188.27	
A-A	7.00	1	1.36	3.78	10.22	1.0000
B-B	-8.12	1	1.36	-11.34	-4.91	1.0000
C-C	21.13	1	1.36	17.91	24.34	1.0000
AB	-0.7500	1	1.92	-5.30	3.80	1.0000
AC	23.25	1	1.92	18.70	27.80	1.0000
BC	-3.50	1	1.92	-8.05	1.05	1.0000
A^2	-36.10	1	1.87	-40.53	-31.67	1.01
B^2	3.65	1	1.87	-0.7822	8.08	1.01
C^2	-16.35	1	1.87	-20.78	-11.92	1.01

The coefficient estimate displays the expected variance with regard to each change in factor value, while the other variables are kept constant. The intercept in an orthogonal design is the national overall performance of all the runs. The factor parameters influence the coefficients, which are deviations from the average. When factors are orthogonal, the VIFs are 1; larger than 1 indicates multi-colinearity; the stronger the VIF, the more powerful the factor interaction. Tolerance is provided to VIFs of fewer than 10.

$$R2 +184.20 + 7.00A - 8.12B + 21.13C - 0.7500AB + 23.25AC - 3.50BC - 36.10A^2 + 3.65B^2 - 16.35C^2$$

The high levels of the variables are coded as +1, whereas the low values are coded as -1 by default. The factor coefficients can also be used to measure the relative importance of the components using the coded equation.

The equation in terms of actual factors can be used to forecast the solution for certain levels of each factor. Levels should be defined in original units for each factor. This equation cannot be utilized to determine the relative impact of each factor since the coefficients are scaled to fit the units of each element and the intercept is not in the middle of the design space.

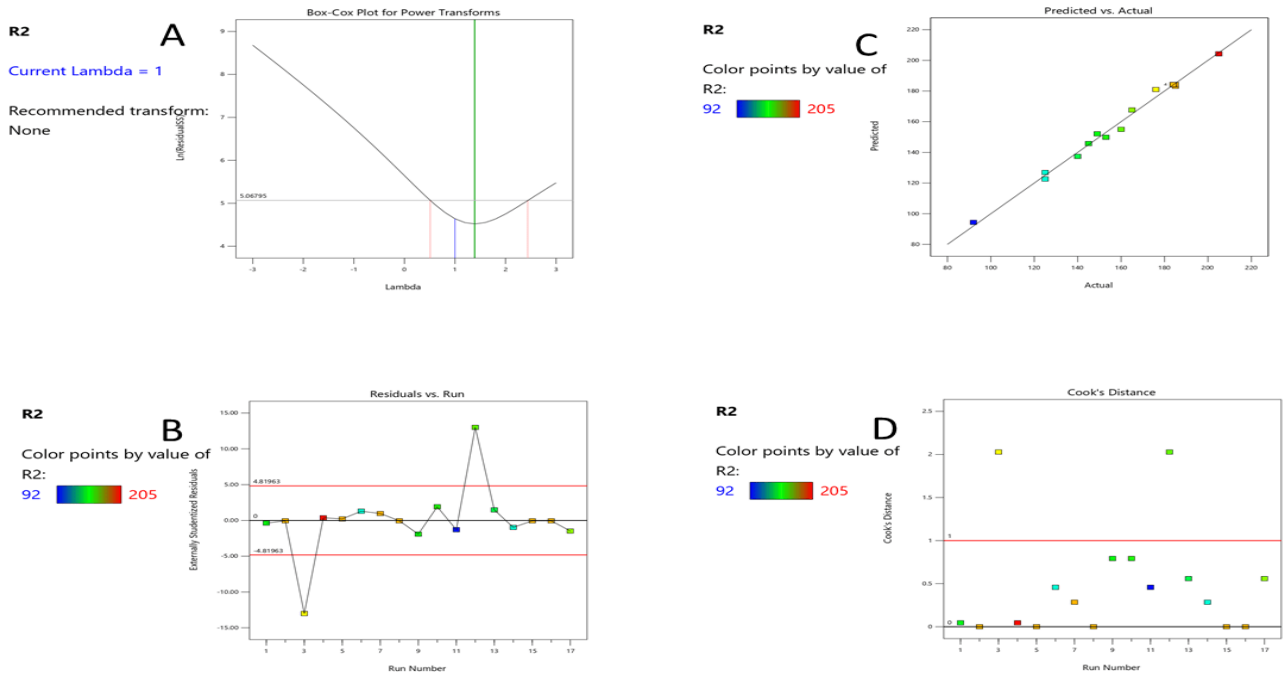

Fig No 04: Diagnostic plot for % Particle size (a) normal Box-cox (B) residuals versus run number plot (c) Residuals vs. predicted values graph and (d) Cooks Distance values plot for R2

Figure no. 14 shows a normal plot of studentized residuals showing that when plotted on a probity scale, the maximum number of color points representing mean particle size followed a straight line, indicating that response data did not need any transformation (Lewis, 2002). Figure no 14 depicted studentized residuals vs. expected values, revealing that all 141 color points representing mean particle size were randomly and uniformly distributed near to the zero-axis, with a constant range of residual across the graph, indicating the absence of constant variance. Figure no. 15 graphically depicted residual versus order of experimental run for mean particle size.

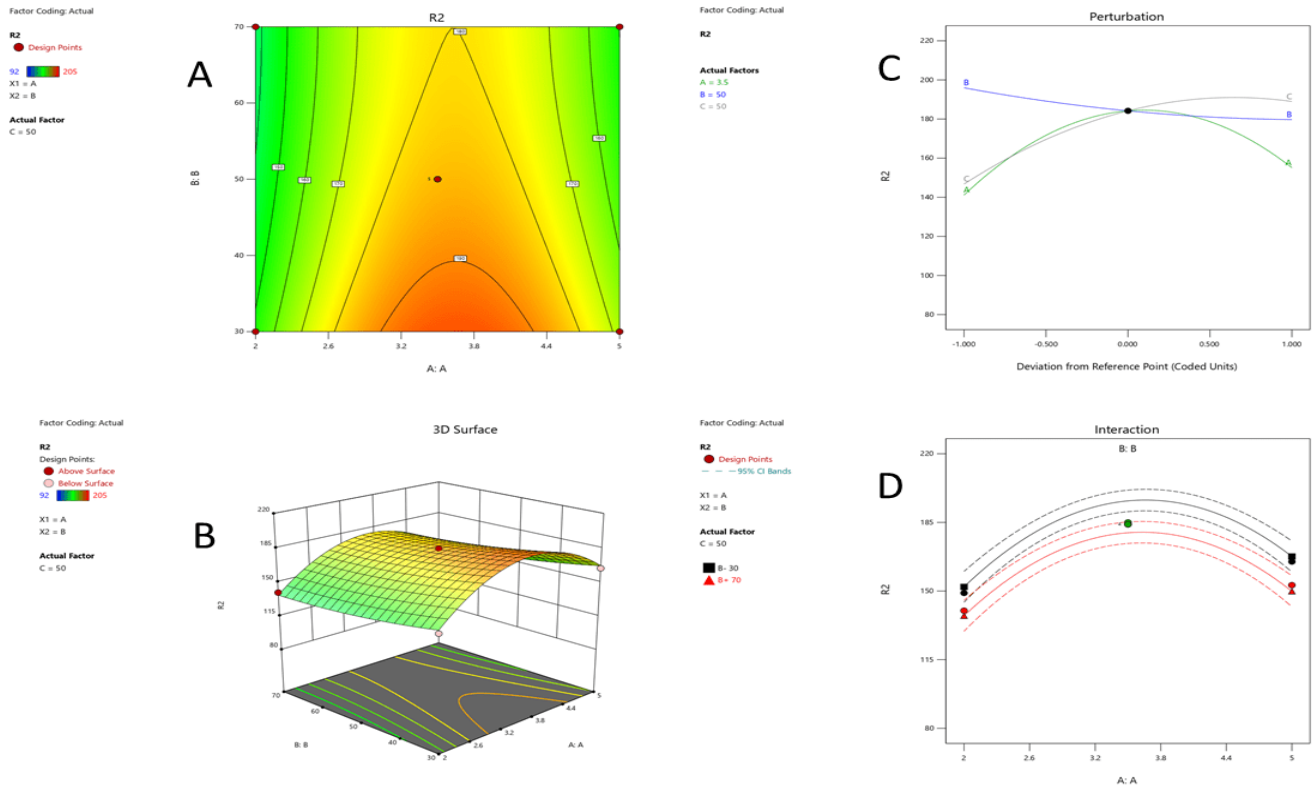

Fig No 05: A&B response & contour plot for R2 of optimized phytosomal preparation of *Taraxacum officinale.* C&D Perturbation and interaction of Independent variables of R2

A straight line drawn from the origin showed that experimentally observed mean particle size values were similar to expected values (Figure no. 04).In a normal probability plot of studentized 142 residuals, the greatest numbers of colour dots corresponding to percent process yield were discovered on a straight line, proving the normality of response data (Figure no. 04). The lack of a megaphone pattern in the plot of studentized residuals vs. expected values showed that the percent process yield data was suitable and that there was no constant error (Figure no. 05).

➢ *ANOVA for Quadratic model:*

Table No 11: BBD Experimental Report of ANOVA for Quadratic model on %CDR (R3).

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	681.86	9	75.76	27.34	0.0001	Significant
A-A	6.13	1	6.13	2.21	0.1807	
B-B	11.28	1	11.28	4.07	0.0834	
C-C	247.53	1	247.53	89.33	< 0.0001	
AB	9.00	1	9.00	3.25	0.1145	
AC	118.81	1	118.81	42.88	0.0003	
BC	19.80	1	19.80	7.15	0.0319	
A^2	0.0059	1	0.0059	0.0021	0.9644	
B^2	208.53	1	208.53	75.25	< 0.0001	
C^2	72.95	1	72.95	26.33	0.0014	
Residual	19.40	7	2.77			
Lack of Fit	3.20	3	1.07	0.2632	0.0092	Significant
Pure Error	16.20	4	4.05			
Cor Total	701.26	16				

Sum of squares is **Type III – Partial**

The F-value of 27.34 suggests that the model is statistically significant. Due to noise, an F-value of this size has a 0.01 percent chance of occurring. Important model terms have P-values of less than 0.0500. The model words in this situation are C, AC, BC, B2, and C2. If the outcome is more than 0.1000, the control variables are meaningless. If your model has a lot of superfluous terms (not including those required to support hierarchy), model reduction may help you improve it.

➢ *Fit Statistics:*

Table No 12: BBD Experimental Report of Fit Statistics on %CDR (R3)

Std. Dev.	1.66	**R^2**	0.9723
Mean	79.36	**Adjusted R^2**	0.9368
C.V. %	2.10	**Predicted R^2**	0.8909
		Adeq Precision	20.5114

The difference between the Predicted R2 of 0.8909 and the Adjusted R2 of 0.9368 is less than 0.2, indicating that the disagreement is less than 0.2. Adequate Precision determines the signal-to-noise ratio. A four-to-one or higher ratio is excellent. You have a strong signal with a signal-to-noise ratio of 20.511. This notion can be used to navigate the design space.

➢ *Coefficients in Terms of Coded Factors*

Table No 13: BBD Experimental Report of Coefficients in Terms of Coded Factors on %CDR (R3)

Factor	Coefficient Estimate	df	Standard Error	95% CILow	95% CI High	VIF
Intercept	80.70	1	0.7445	78.94	82.46	
A-A	-0.8750	1	0.5885	-2.27	0.5167	1.0000
B-B	-1.19	1	0.5885	-2.58	0.2042	1.0000
C-C	-5.56	1	0.5885	-6.95	-4.17	1.0000
AB	-1.50	1	0.8323	-3.47	0.4681	1.0000
AC	-5.45	1	0.8323	-7.42	-3.48	1.0000
BC	-2.22	1	0.8323	-4.19	-0.2569	1.0000
A^2	0.0375	1	0.8113	-1.88	1.96	1.01
B^2	-7.04	1	0.8113	-8.96	-5.12	1.01
C^2	4.16	1	0.8113	2.24	6.08	1.01

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The coefficient estimate depicts the expected variance per unit change in factor value while all other variables are maintained constant. The intercept in an orthogonal design is the cumulative average of all the runs' performance. The factor parameters affect the coefficients, which are deviations from the average. When the factors are orthogonal, the VIFs are one; greater than one indicates multi-colinearity; the higher your VIF, the stronger the factor interaction. Tolerance is given for VIFs of fewer than 10.

The statement in terms of developed can be used to make predictions about the outcome for given values of each element. High-value components are coded +1, whereas low-value components are coded -1. The coded equation can be used to determine the influence factors of the elements by comparing the factor coefficients.

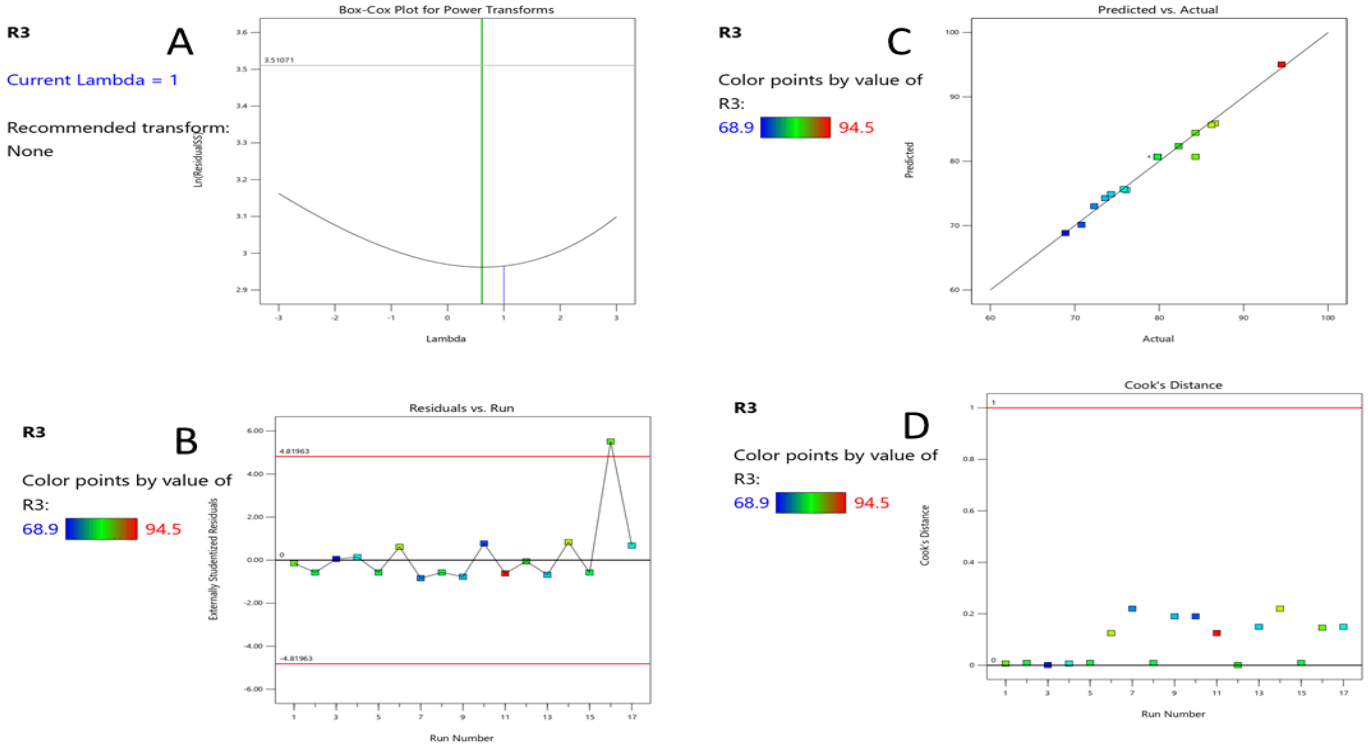
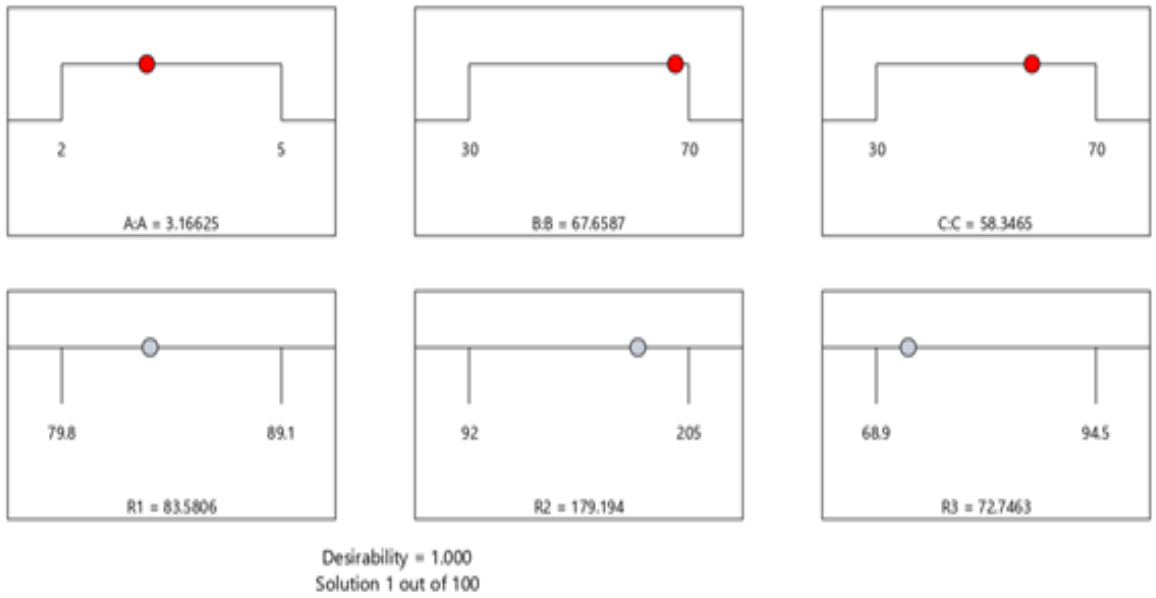


Fig No 06: Diagnostic plot for % CDR (a) normal Box-cox (B) residuals versus run number plot (c) Residuals vs. predicted values graph and (d) Cooks Distance values plot.



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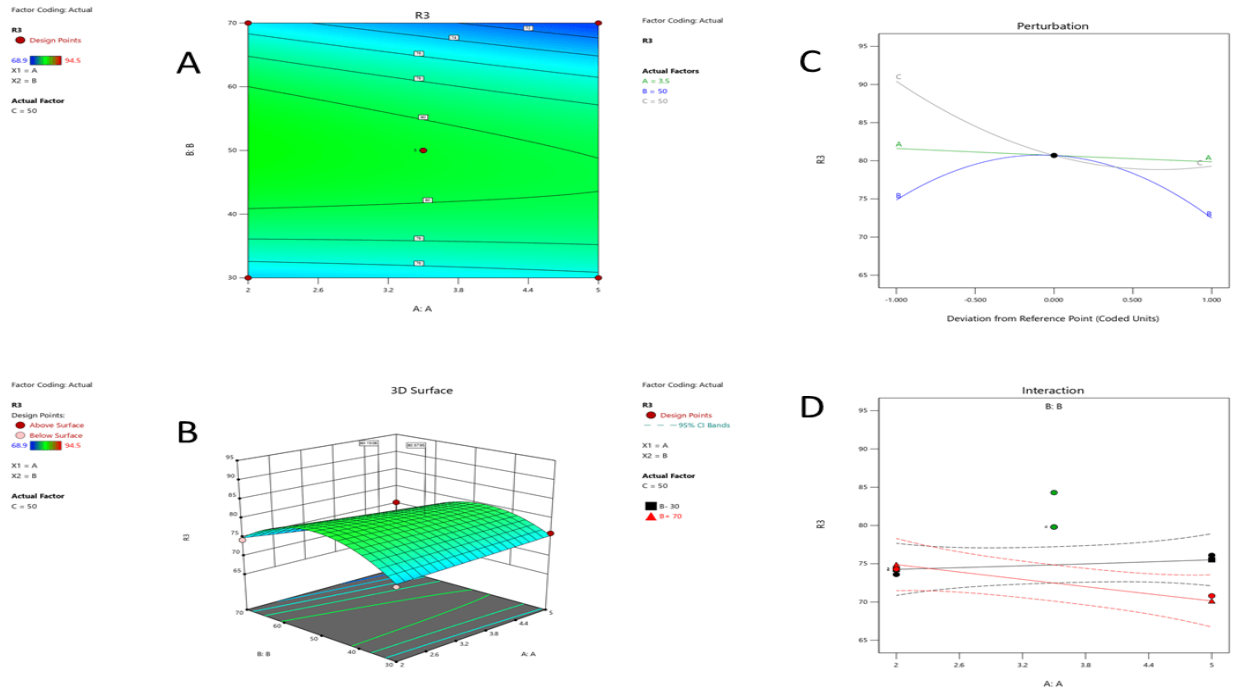

Fig No 07: A&B response & contour plot for R3 of optimized phytosomal preparation of *Taraxacum officinale.* C&D Perturbation and interaction of Independent variables of R3

Table No 14 : BBD Experimental Report of %CDR (R3)

Run Order	Actual Value	Predicted Value	Internally Studentized Residuals	Externally Studentized Residuals	Cook's Distance	Influence on Fitted Value DFFITS	Standard Order
1	84.30	84.43	-0.150	-0.139	0.007	-0.241	10
2	79.80	80.70	-0.604	-0.575	0.009	-0.287	15
3	68.90	68.85	0.060	0.056	0.001	0.096	12
4	75.80	75.67	0.150	0.139	0.007	0.241	11
5	79.80	80.70	-0.604	-0.575	0.009	-0.287	14
6	86.20	85.66	0.646	0.617	0.125	1.068	7
7	72.30	73.01	-0.856	-0.838	0.220	-1.451	8
8	79.80	80.70	-0.604	-0.575	0.009	-0.287	13
9	73.60	74.26	-0.796	-0.773	0.190	-1.338	1
10	70.80	70.14	0.796	0.773	0.190	1.338	4
11	94.50	95.04	-0.646	-0.617	0.125	-1.068	6
12	82.30	82.35	-0.060	-0.056	0.001	-0.096	9
13	74.30	74.89	-0.706	-0.678	0.149	-1.174	3
14	86.60	85.89	0.856	0.838	0.220	1.451	5
15	79.80	80.70	-0.604	-0.575	0.009	-0.287	17
16	84.30	80.70	2.418	5.514(1)	0.146	2.757(2)	16
17	76.10	75.51	0.706	0.678	0.149	1.174	2

Observation with |External Stud. Residuals > 4.82

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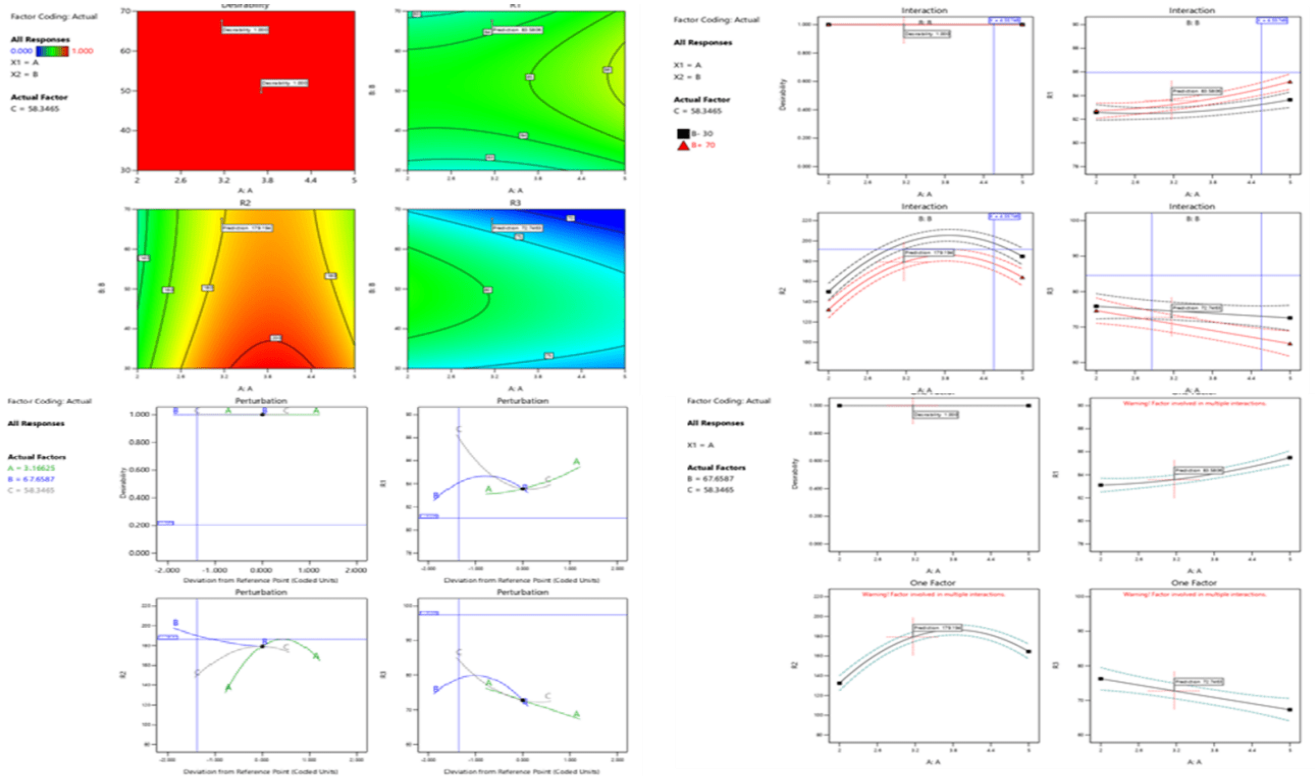

Fig No 08: Response surface plots & contour plot for R1, R2&R3 of optimized phytosomal preparation of *Taraxacum officinale.*

Desirability overlay plots and interactions of factors of dependent & independent variables.As a result, the solubility of formulation in several oils was investigated, including glyceryl Caprylate, oleic acid, and grape seed oil etc. In glyceryl Caprylate and oleic acid, dissolved more than 100 mg/g, with a maximum solubility of more than 1000 mg/g in glyceryl Caprylate. Among the non-ionic surfactants examined for nano-emulgel formations, tween 20, cremophore EL, and cremophore RH demonstrated the highest emulsification efficiency for selected oil phases. For the creation of a homogeneous nano-emulsion with the chosen oil phase, only one 'flask inversion' was required table no 13 trial runs obtained from the BBD design. Figures no. 16, 17, and 18 illustrate the generation of 3D response plots to analyse the effect of solvent and polymer ratio on the responses.

Table No 14.: Solution provided by the BBD design for phytosomal formulation of *Taraxacum officinale*

CONSTRAINTS								
Independent Variables								
Name				Goal		Lower Limit		Upper Limit
X1: Soya lecithin				Is in range		2.00		5.00
X2: Reaction temp				Is in range		30.00		70.00
X2: reaction time				Is in range		30.00		70.00
Dependent Variables								
Entrapment Efficiency (%)				Maximize		79.8±0.6		89.1±4.6
Vesicle Size (nm)				Minimize		92±9.1		205±5.6
Cumulative Drug Release (%)				Maximize		68.9±2.6		94.5±1.3
Optimized Formulation								
F	**X1**	**X2**	**X3**	**R1**	**R2**	R3	PDI	Zeta
11	5	50	30	89.1±4.6	92±9.1	94.5±1.3	-32.45	0.48±0.03

V. CONCLUSION

According to this research, design of experiments (DoE) is an efficient, elegant, and cost-effective statistical technique that delivers more knowledge with the least number of runs. Soya lecithin (X1), reaction temperature (X2), and reaction time (X3) were all significant parameters impacting phytosome response characteristics, according to standardised response surface plots, with p 0.05. The precision of the data was demonstrated by significant (p 0.05) model F-values and non-significant (p > 0.05) "lack of fit F-values" for response variables. R2 Adj (adjusted R-squared) and R2 Anticipated (expected R-squared) (R2 Pred) values indicated that the regression coefficients were fairly consistent. A lower PRESS value in regression models indicated a better match. The model discrimination was adequate, according to a high precision (AP) value. The normality of the response data was demonstrated using

standard probability plots. Externally studentized residuals vs. expected values of the response parameters revealed the absence of constant error. The absence of lurking variables was investigated using a residual vs. run plot.

The plot of expected vs. real values shows that the actual values of response parameters were quite close to the projected values. The influence of changing operating circumstances on response parameters in 2-D and 3-D was shown using a contour plot or response surface plot. The effects of X1, X2, and X3 on percent EE, particle size, and percent CDR were found to be important. X1 and X3 had a major synergistic and antagonistic effect on mean particle size, respectively. Both X1 and X2 had significant effects on percent CDR. X1 had a surprising antagonistic effect on percent EE. In the current research, the ideal LA-PHY formulation with a desirability function of 0.920 was found to be 1:3 drug/polymer (w/w), 5 (w/v), 50 reaction temperature, and 30 minute stirring time. Optimized LA-PHY had a biphasic Fickian diffusional publication pattern from the polymer matrix, with an initial 'burst release' of approximately 22.32 percent loosely bound NFH on or near the particle surface within the first 0.5 hours, followed by 52.41 percent drug release over the next 4 hours. Following that, due to diffusion from the polymer matrix, drug release was maintained, with a median drug release of 86.13 percent over 24 hours. In comparison to rotary evaporation (210.92nm and 74.60.9) and solvent evaporation (140.76nm and 78.91.8), solvent evaporation provided the smallest particle size (929.1nm) and highest entrapment efficiency (89.14.6). As a result, phytosomes were produced by solvent evaporation, and optimization was complete factorial design was used to carry out the experiment. 11.0.4.0 Expert in Design (Evaluation version) Using Stat-Ease, Inc., USA, the impact of each variable on the designated response, i.e. particle size, percent CDR, and entrapment efficiency, was studied. To determine the statistical significance, an ANOVA was used. Particle size ranges from 929.1 to 2055.6nm in *Taraxacum officinale* loaded phytosomes, percent CDR ranges from 68.92.6 to 94.51.3, and entrapment efficiency ranges from 79.80.6 to 89.14.6 percent for all 17 formulations. The functional characterization includes in vitro release tests and in vivo anti-psoriasis activity. Zeta potential values of -32.45mv and -24.50mv imply the formation of a stable formulation. As the temperature rose, the polar section of the phospholipid moved, causing phase shift and isomerization in the phospholipid structure.

At various time intervals, the percentage of drug released from the optimised formulation was tested, and it was observed that the body produced a steady fraction of the medication at regular intervals. The kinetic models zero order; first order, Higuchi model, and Korsmeyer-Peppas model were used in this investigation. The Korsmeyer–Pappas model was chosen based on the regression values. As demonstrated by a comparison of FTIR spectra, the interaction with phospholipids induces changes in specific locations in the extract. Changes in the stretching frequency in the optimised formulation show the presence of intermolecular interactions during phytosome formation.

REFERENCES

[1]. Agarwal R, Patil C, Katare OP. Preparation and pharmacological evaluation of silibinin liposomes, Medicinal Aromatic plant Science Biotechnology, 2003;53, Page no.420-427.
[2]. Ajazuddin, S. Saraf, Applications of novel drug delivery system for herbal formulations, Fitoterapia 81 (2010), Page no. 680–689
[3]. Battacharya S. Phytosomes: Emerging strategy in delivery of herbal drugs and nutrceuticals. Pharm Times 2009; 41, Page. no.3-9.
[4]. Bhattachrya S. Phytosomes: The new technology for enhancement of bioavailability of botanicals and nutraceuticals. International Journal of Health Research 2009; 2, Page no.225-234
[5]. Bombardelli E, Spelta M: Phospholipid-polyphenol complexes: A new concept in skin care ingredients, Cosmetics and oil 1991; 106, Page no. 69-76.
[6]. Bombardelli E., Mustich G. Bilobalide-phospholipid complex, their uses and formulation containing them US Patent No. EPO-275005,1991
[7]. Chauhan N. S, Gowtham R, Gopalkrishna B. Phytosomes: A potential Phyto-phospholipid carriers for herbal drug delivery. Journal of Pharmaceutical Research 2009; 2, Page no. 1267-1270.
[8]. Comoglio A., Tomasi A., Malandrino S., et al. Scavenging effect of silipide-A new silybinphospholipid complex, on ethanol derived free radicals. Biochemical Pharmacology,1995, 50, Page no.1313- 1316.
[9]. Dipierro F: Composition Comprising Ginkgo Biloba Derivatives For Treatment of Asthmatic and Allergic Conditions Patent No. EP 1813280, 2007.
[10]. Facino RA, Carini M, Aldini G: Free Radicals Reaction and Anti- Enzymic Activities of VitisVinifera: A Mechanism For Capillary Protection, Arzeniem Forsch, 2010, Page no. 247-254.
[11]. Facino RM, Carini M and Aldini G. Free Radicals Sea Action Arzneim. 1994; 44, Page no. 592-601.
[12]. Jain N, Gupta B P, Thakur N; Phytosome: A novel drug delivery system for herbal medicine. International journal of Pharmaceutical Science and Drug Research. 2010; 2(4)-, Page no. 224-2.
[13]. Jain N. K, Controlled and Novel Drug Delivery, 1st Edition, CBS Publisher, 2005, 321-326.
[14]. Jing Li, Xuling Wang, Ting Zhang, Chunling Wang, Zhenjun Huang, Xiang Luo, Yihui Deng, A review on phospholipids and their main applications in drug delivery systems, asian journal o f pharmaceutical sciences,2014, Page no.1-18.
[15]. Joseph a. Kareparamban, Pravin H. Nikam, Aruna P Jadhav Vilasrao J Kadam, Phytosome: a novel revolution in herbal drugs, international journal of research in pharmacy and chemistry, 2012, 2(2), Page no. 299-310
[16]. Kumar vishal saurabh, Asha kesari, Herbosome-a novel carrier for herbal drug delivery international journal of current pharmaceutical research, vol 3, issue 3, 2011. Page. No. 142-155.