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## **Appendices**

## **Appendix A**

### **Detail in Statistic Analysis and Glossary of Terms**

## Transformation of the Response

Transformation of the response is an important component of any data analysis. Transformation is needed if the error (residuals) is a function of the magnitude of the response (predicted values). Transformations may be needed to meet the assumptions that make the ANOVA valid. Residuals must be normally distributed with a constant variance.

Check the diagnostic plots to validate these assumptions. If the plots don't look right, come back and try some transformations. Extensive diagnostic capabilities to check if the statistical assumptions underlying the data analysis are met. The normal plot of the residuals tests their normality. The residuals versus predicted response values plot will indicate a problem if a pattern exists. Unless the ratio of the maximum response to the minimum response is large, transforming the response will not make much difference.

Here is a list of the transformations and some data types that may benefit from using that transformation:

Square Root:	Count or Frequency data
Natural Log:	Variance (std dev) or Growth data
Base 10 Log:	Variance (std dev) or Growth data
Inverse Square Root:	
Inverse:	Rate data, Decay data
Power:	
Logit:	Bounded data, Yield data
Arcsin Sqr Root:	Probability, Fraction defective

The appropriate choice of a response transformation relies on subject matter knowledge and/or statistical considerations.

The power transformation allows transformation to any power in the range  $-3$  to  $+3$ , provided the data are positive. A constant may be added to the data to avoid powers of negative numbers. If the standard deviation associated with an observation is

proportional to the mean raised to some power, then transforming the observation by a power gives a scale satisfying the equal variance requirement of the ANOVA. The Box Cox plot is also provided in the Diagnostics plots that can help to choose an appropriate power transformation.

The logit transformation is useful if the response has a finite range, such as 0% to 100%. Logit spreads out the values near the boundaries. The actual response data collected must be between the lower and upper limit, and not equal to either one. When using this transformation, it is very important to correctly set the lower and upper limits to the natural limits of the response.

The arcsine square root should be used for binomial data, for example, fraction defective. For this transformation to be valid, the response data must be in terms of fractions between zero and one, from samples of equal size.

Most data transformations can be described by the power function,

$$\delta = \text{fn}(\mu\alpha)$$

Where; sigma ( $\delta$ ) is the standard deviation,

mu ( $\mu$ ) is the mean

alpha ( $\alpha$ ) is the power.

Lambda ( $\lambda$ ) is  $1 - \alpha$  in all cases. If the standard deviation associated with an observation is proportional to the mean raised to the  $\alpha$  power, then transforming the observation by the  $1 - \alpha$  (or  $\lambda$ ) power gives a scale satisfying the equal variance requirement of the statistical model.

As a reminder, here are the commonly used transformations:

$\lambda = -1$  inverse

$\lambda = 0$  natural log

$\lambda = 0.5$  square root

$\lambda = 1$  no transformation

The lowest point on the Box-Cox plot represents the value of lambda ( $\lambda$ ) that results in the minimum residual sum of squares in the transformed model. The potential for improvement is greatest when the range of the maximum to minimum response value is greater than 3.

Power law transformations can only be performed on responses that are greater than zero, so a constant,  $k$ , may be needed to add to all the responses.

## Fit Summary

Fit summary shows the statistical tables that can be used to identify which model to choose for in-depth study. It is composed of the regression calculations to fit all of the polynomial models to the selected response. The effects for all model terms can be calculated. They can be interpreted line by line as follows:

### Sequential Model Sum of Squares

**Mean:** The sum of squares for the effect of the mean.

**Blocks:** Sequential sum of squares for the effect of blocking (if applicable), after removing the effect of the intercept.

**Linear:** Sequential sum of squares for the linear terms. The F-value tests the significance of adding linear terms to the intercept and block effects. A small p-value (Prob>F) indicates that adding linear terms has improved the model.

**2FI:** Sequential sum of squares for the two-factor interaction (AB, BC, etc.) terms. The F-value tests the significance of adding interaction terms to the linear model. A small p-value (Prob>F) indicates that adding interaction terms has improved the model.

**Quadratic:** Sequential sum of squares for the quadratic (A-squared, B-squared, etc.) terms. The F-value tests the significance of adding quadratic terms to the 2FI model. A small p-value (Prob>F) indicates that adding quadratic terms has improved the model.

**Cubic:** Sequential sum of squares for the cubic terms. The F-value tests the significance of adding cubic terms to the quadratic model. A small p-value ( $\text{Prob}>F$ ) indicates that adding cubic terms has improved the model.

For most response surface methodology (RSM) designs, design points are too small to estimate cubic model. Thus, the cubic model cannot be used.

The column labeled "**DF**" provides the degrees of freedom for each source. In response surface methodology, the total degrees of freedom equals the number of model coefficients added sequentially line by line.

The model that has p-value ( $\text{Prob}>F$ ) that is lower than the chosen level of significance (for example 0.05) should be selected.

### **Lack of Fit**

The lack of fit tests that diagnose how well each of the full models fit the data. Models with a significant lack of fit should not be used for predictions.

The F-value compares the variation of the differences in the average responses at the design points, and the corresponding estimated responses using the model, with the expected experimental variation as estimated from replicated design points (Pure Error). It is the mean square for the model lack of fit divided by the mean square for pure error.

The lack of fit tests compare the residual error to the pure error from replicated design points. A lack of fit error significantly larger than the pure error indicates that something remains in the residuals that can be removed by a more appropriate model. If the lack of fit ( $\text{Prob}>F$  value 0.10 or smaller), don't use the model as a predictor of the response.

The Lack of Fit statistics will not be obtained if there is no replicate and/or design points are not more unique than model coefficients.

### **Model Summary**

The "Model Summary Statistics" table lists other statistics used to compare models.

The Std Dev estimates the standard deviation of the error in the design. Smaller is better.

Both the R-Squared and related Adjusted R-Squared statistics should be close to one. A value of 1.0 represents the ideal case at which 100 percent of the variation in the observed values can be explained by the chosen model.

The Predicted R-Squared estimates the amount of variation in new data explained by the model. It can be negative, but this is very bad and suggests that the model consisting of only the intercept is a better predictor of the response than this model. The closer to 1.0, the better the predicted R-squared.

The PRESS statistic, predicted residual error sum of squares, indicates how well the model fits the data. The PRESS for the chosen model should be small relative to the other models under consideration.

**R-squared:** The multiple correlation coefficient computed as

$$1 - \text{SSresidual} / (\text{SSmodel} + \text{SSresidual})$$

An estimate of the fraction of overall variation in the data accounted for by the model. Use the Adjusted R-squared value for designed experiments.

**Adjusted R-squared:** The R-squared which is adjusted for the number of terms in the model relative to the number of points in the design. An estimate of the fraction of overall variation in the data accounted for by the model.

$$\text{Adjusted R-squared} = 1 - [(\text{SSresidual} / \text{DFresidual}) / ((\text{SSresidual} + \text{SSmodel}) / (\text{DFresidual} + \text{DFmodel}))]$$

**Predicted R-squared:** Measures the amount of variation in new data explained by the model. Generally, a number closer to one is preferred.

$$\text{Predicted R-squared} = 1 - (\text{PRESS} / (\text{SStotal} - \text{SSblock}))$$

**PRESS:** The Predicted Residual Sum of Squares (PRESS) is a measure of how well the model fits each point in the design. The model is used to estimate each point using all of the design points except that one. The difference between the predicted value and actual value at each point is squared and summed over all of the points. The smaller the PRESS statistic, the better the model fits the data points.

## **Model Reduction**

The model selected initially contains all of the terms for that polynomial. If there are terms that considered negligible, they can be dropped from the suggested model or added back to the model. Then the statistics for the new selection of terms will be recalculated. Hierarchy of the effects should be retained for making predictions in the actual factor levels.

Model reduction consists of eliminating those terms that are not desired. It can be done manually or automatically. For each response regression, the starting model can be edited by specifying fewer candidate terms than the full model would contain. In the three automatic regression variations you can control those terms which are forced into the model regardless of their entry/exit alpha values.

There are three basic types of automatic model regression:

1. Step-Wise: A term is added, eliminated or exchanged at each step.
2. Backward elimination: A term is eliminated at each step.
3. Forward selection: A term is added at each step.

For well designed experiments (minimal collinearity problems), all three methods should yield the same reduced model.



### **Step-Wise Regression**

Step-wise regression is a combination of forward and backward regressions. First all blocks and forced terms are fitted to the data. Then begin with a simple regression model using the single term having the highest correlation with the response. After this step, terms are added, eliminated, exchanged, or the procedure stopped.

When two or more terms are in the model:

1. Add to the model the term having the highest partial t-value (or F-value for designs with categorical factors), if it satisfies the alpha-In requirement.
2. Remove all terms (one at a time) having p-values less than the specified alpha-Out. (When categorical factors are in the starting model, terms are added and removed hierarchically.)
3. Stop when there is no further improvement and the alpha-In and alpha-Out values are satisfied.

Note that the coefficient shown is the coefficient at the time the term was added or deleted from the model. This is likely to be different than the coefficient that is generated with the completed model. For designs with categorical factors, the coefficients are not shown.

### **Backward Elimination**

The backward regression procedure differs from stepwise, but the results are often very similar, if not the same. All blocks and forced terms are fit to the data first. Then the remaining candidate factors are considered:

1. Begin with the full model.
2. Remove from the model the term with the highest partial probability value (P-value). For models with categorical factors, terms are removed hierarchically.
3. Stop when the p-value of the next term out satisfies the specified Alpha Out value criterion.

### Forward Selection

When doing forward selection, all blocks and forced terms are fit to the data first. Then the remaining candidate terms are considered:

1. Begin with a simple regression model using the single term having the highest correlation with the response.
2. Add to the model the term with the lowest partial probability value (P-value). For designs with categorical factors, terms are added hierarchically.
3. Stop when the p-value of the next term in does not meet the specified "Alpha In" value criterion.

This algorithm may not be as robust as the others, because some terms may never get the chance to be included in the model. This will only cause concern if the data exhibits a high degree of co-linearity. However, the safest approach may be backward regression.

Note that the coefficient shown is the coefficient at the time the term was added to the model. This is likely to be different than the coefficient that is generated with the completed model. For designs with categorical factors, the coefficients are not shown.

Only blocks and forced terms plus those terms that fail the exit criteria remain. In general, for well-designed experiments with minimal co-linearity, you will see no difference in results. However, the backward method may be the most robust choice since all model terms will be given a chance of inclusion in the model. Conversely, the forward selection procedure starts with a minimal core model, thus some terms never get included.

### ANOVA Output

**Model:** Terms estimating factor effects.

Sum of Squares: Total of the sum of squares for the terms in the model, as reported in the Effects List for factorials and on the Model screen for RSM, MIX and Crossed designs.

DF: Degrees of freedom for the model. It is the number of model terms, including the intercept, minus one.

Mean Square: Estimate of the model variance, calculated by the model sum of squares divided by model degrees of freedom.

F Value: Test for comparing model variance with residual (error) variance. If the variances are close to the same, the ratio will be close to one and it is less likely that any of the factors have a significant effect on the response. Calculated by Model Mean Square divided by Residual Mean Square.

Prob > F: Probability of seeing the observed F value if the null hypothesis is true (there is no factor effect). Small probability values call for rejection of the null hypothesis. The probability equals the proportion of the area under the curve of the F-distribution that lies beyond the observed F value. The F distribution itself is determined by the degrees of freedom associated with the variances being compared. In other words, if the Prob>F value is very small (less than 0.05) then the terms in the model have a significant effect on the response.

**Term**: Each of the listed terms is currently in the model and individual statistics are calculated for them.

Sum of Squares: For factorial terms the sum of squares equation reduces to: the number of factorial experiments divided by 4 times the squared factor effect.

DF: Degrees of freedom for the term. It is the number of levels for the term, minus one.

Mean Square: Estimate of the term variance, calculated by the term sum of squares divided by term degrees of freedom.

F Value: Test for comparing term variance with residual (error) variance. If the variances are close to the same, the ratio will be close to one and it is less likely that the term has a significant effect on the response. Calculated by term Mean Square divided by Residual Mean Square.

Prob > F: Probability of seeing the observed F value if the null hypothesis is true (there is no factor effect). Small probability values call for rejection of the null

hypothesis. The probability equals the proportion of the area under the curve of the F-distribution that lies beyond the observed F value. The F distribution itself is determined by the degrees of freedom associated with the variances being compared.

**Residual:** Consists of terms used to estimate experimental error.

Sum of Squares: This equals the sum of squares for all the terms not included in the model.

DF: The corrected total DF minus the model DF.

Mean Square: The estimate of process variance. The square root of this provides an estimate of the process standard deviation.

**Lack of Fit (LOF):** This is the variation of the data around the fitted model. If the model does not fit the data well, this will be significant.

Sum of Squares: Residual sum of squares after removing the pure error sum of squares.

DF: The amount of information available after accounting for blocking, model terms, curvature, and pure error.

Mean Square: Estimate of lack of fit.

F Value: Test for comparing lack of fit variance with pure error variance. If the variances are close to the same, the ratio will be close to one and it is less likely that lack of fit is significant.

Prob>F: Probability of seeing the observed F value if the null hypothesis is true. Small probability values call for rejection of the null hypothesis that lack of fit is not significant. In "plain English", if the Prob>F value is very small (less than 0.05) then lack of fit is significant. In other words the variation in the model points significantly differs from the variation in the replicated points. Consider adding more terms to this model. You want the Prob>F value for lack of fit to be greater than 0.10.

**Pure Error:** Amount of variation in the response in replicated design points.

Sum of Squares: Pure error sum of squares from replicated points.

DF: The amount of information available from replicated points.

Mean Square: Estimate of pure error variance.

**Cor Total**: Totals of all information corrected for the mean.

Sum of Squares: Sum of the squared deviations of each point from the mean.

DF: Total degrees of freedom for the experiment, minus one for the mean.

**Summary statistics for the model:**

Std Dev: (Root MSE) Square root of the residual mean square. Consider this to be an estimate of the standard deviation associated with the experiment.

Mean: Overall average of all the response data.

C.V.: Coefficient of Variation, the standard deviation expressed as a percentage of the mean. Calculated by dividing the Std Dev by the Mean and multiplying by 100.

PRESS: Predicted Residual Error Sum of Squares – A measure of how the model fits each point in the design. The PRESS is computed by first predicting where each point should be from a model that contains all other points except the one in question. The squared residuals (difference between actual and predicted values) are then summed.

R-Squared: A measure of the amount of variation around the mean explained by the model.

$$1 - (\text{SSresidual} / (\text{SSmodel} + \text{SSresidual}))$$

Adj R-Squared: A measure of the amount of variation around the mean explained by the model, adjusted for the number of terms in the model. The adjusted R-squared decreases as the number of terms in the model increases if those additional terms don't add value to the model.

$$1 - ((\text{SSresidual} / \text{DFresidual}) / ((\text{SSmodel} + \text{SSresidual}) / (\text{DFmodel} + \text{DFresidual})))$$

Pred R-Squared: A measure of the amount of variation in new data explained by the model.

$$1 - (\text{PRESS} / (\text{SS}_{\text{total}} - \text{SS}_{\text{block}}))$$

The predicted r-squared and the adjusted r-squared should be within 0.20 of each other. Otherwise there may be a problem with either the data or the model.

Adequate Precision: This is a signal to noise ratio. It compares the range of the predicted values at the design points to the average prediction error. Ratios greater than 4 indicate adequate model discrimination.

### Post ANOVA and Prediction Equations

This section provides definitions for the post-ANOVA information for the individual terms.

**Factor**: Experimental variables selected for inclusion in the predictive model.

**Coefficient Estimate**: Regression coefficient representing the expected change in response  $y$  per unit change in  $x$  when all remaining factors are held constant. In orthogonal designs, it equals one half the factorial effect.

**Coefficient Estimate for General Factorial Designs**: Coefficients for multi-level categorical factors are not as simple to interpret. They do not have a physical meaning, but do have a mathematical meaning.  $\beta_1$  is the difference of level 2 from the overall average.  $\beta_2$  is the difference of level 3 from the overall average.  $\beta_k$  is the difference of level  $(k+1)$  from the overall average. The negative sum of the coefficients will be the difference of level 1 from the overall average.

**DF**: Degrees of Freedom – equal to one for testing coefficients.

**Standard Error**: The standard deviation associated with the coefficient estimate.

**95% CI High and Low**: These two columns represent the range that the true coefficient should be found in 95% of the time. If this range spans 0 (one limit is positive

and the other negative) then the coefficient of 0 could be true, indicating the factor has no effect.

**VIF:** Variance Inflation Factor – Measures how much the variance of the model is inflated by the lack of orthogonality in the design. If the factor is orthogonal to all other factors in the model, the VIF is one. Values greater than 10 indicate that the factors are too correlated together (they are not independent.)

**The predictive model:** is listed in both actual and coded terms. The coded (or pseudo) equation is useful for identifying the relative significance of the factors by comparing the factor coefficients. This comparison cannot be made with the actual equation because the coefficients are scaled to accommodate the units of each factor. The equations give identical predictions. These equations, used for prediction, have no block effects. Blocking is a restriction on the randomization of the experiment, used to reduce error. It is not a factor being studied. Blocks are only used to fit the observed experiments, not to make predictions.

## Glossary of Terms

**Factor:** The independent variable to be manipulated in an experiment.

**Level:** The setting of a factor.

**Response:** A measurable product or process characteristic thought to be affected by the experimental factors.

**Effect:** The change in average response when a factor goes from its low level to its high level.

**Model:** The model is the empirical mathematical model that is fit to the data.

**Standard Order:** A conventional "textbook" ordering of the array of low and high factor levels.

**Actual Value:** The measured response data for this particular run.

**Predicted Value:** The value predicted from the model, generated by using the prediction equation. Includes block and center point corrections, if present.

**Appendix B**

**Data of Dependent Variables**

**Of Curcuminoids-PLGA Nanoparticles**



Table Appendix B-1. Nanoparticles recovery, curcuminoids content, and entrapment efficiency of formulation number 1 to 15

Formulation number		Nanoparticles recovery				Entrapment efficiency	
		(%)				(%)	
		2-replicate	Average	2-replicate	Average	2-replicate	Average
1	Rep-1	61.49	69.03	0.0245	0.0244	0.75	0.80
	Rep-2	69.03		0.0243		0.84	
2	Rep-1	67.78	66.11	0.1106	0.0972	1.25	1.07
	Rep-2	64.44		0.0837		0.90	
3	Rep-1	68.73	64.82	0.0491	0.0625	0.56	0.67
	Rep-2	60.91		0.0759		0.77	
4	Rep-1	67.63	65.93	0.1091	0.1101	0.74	0.73
	Rep-2	64.23		0.1110		0.71	
5	Rep-1	67.43	68.68	0.0538	0.0540	1.81	1.85
	Rep-2	69.93		0.0541		1.89	
6	Rep-1	57.64	62.50	0.0494	0.0454	1.42	1.41
	Rep-2	67.36		0.0414		1.39	
7	Rep-1	68.96	66.42	0.0905	0.0950	1.04	1.05
	Rep-2	63.88		0.0995		1.06	
8	Rep-1	63.19	61.31	0.0923	0.0952	0.97	0.97
	Rep-2	59.43		0.0981		0.97	
9	Rep-1	65.40	62.08	0.0872	0.0864	0.95	0.89
	Rep-2	58.76		0.0855		0.84	
10	Rep-1	64.31	62.26	0.1167	0.1209	0.75	0.75
	Rep-2	60.21		0.1250		0.75	
11	Rep-1	66.72	63.54	0.0944	0.0932	0.63	0.59
	Rep-2	60.36		0.0920		0.56	
12	Rep-1	64.33	61.35	0.0444	0.0430	1.43	1.32
	Rep-2	58.37		0.0415		1.21	
13	Rep-1	66.34	67.54	0.0984	0.0984	1.09	1.11
	Rep-2	68.74		0.0984		1.13	
14	Rep-1	59.26	63.99	0.0621	0.0618	0.61	0.66
	Rep-2	68.72		0.0614		0.70	
15	Rep-1	68.70	68.02	0.1327	0.1389	0.91	0.94
	Rep-2	67.34		0.1450		0.98	

Table Appendix B-2. Mean particle size and polydispersity index of formulation number 1 to 15

Formulation Number	Mean Particle Size (nm)				Polydispersity Index			
	Rep-1	Rep-2	Rep-3	Average	Rep-1	Rep-2	Rep-3	Average
1	310	300	310	307	0.57	0.60	0.60	0.59
2	320	320	320	320	0.85	0.82	0.82	0.83
3	320	320	320	320	0.76	0.79	0.76	0.77
4	320	320	320	320	0.75	0.73	0.74	0.74
5	330	330	330	330	0.85	0.83	0.84	0.84
6	310	300	310	313	0.76	0.74	0.75	0.75
7	320	320	320	320	0.81	0.79	0.83	0.81
8	320	320	320	320	0.70	0.73	0.70	0.71
9	300	310	290	300	0.70	0.68	0.69	0.69
10	320	320	320	320	0.72	0.73	0.71	0.72
11	310	310	310	310	0.72	0.73	0.74	0.73
12	300	310	310	307	0.75	0.75	0.78	0.76
13	310	320	330	320	0.78	0.75	0.78	0.77
14	310	310	310	310	0.80	0.83	0.80	0.81
15	310	300	300	303	0.82	0.84	0.86	0.84

Table Appendix B-3. Nanoparticles recovery, curcuminoids content, and entrapment efficiency of formulation number 16 to 30

Formulation number		Nanoparticles recovery (%)				Entrapment efficiency (%)	
		2-replicate	Average	2-replicate	Average	2-replicate	Average
16	Rep-1	51.63	53.52	0.6457	0.6421	16.67	17.18
	Rep-2	55.41		0.6384		17.69	
17	Rep-1	54.37	52.67	2.2429	2.2860	20.32	20.06
	Rep-2	50.97		2.3291		19.79	
18	Rep-1	52.89	55.03	0.9764	0.9896	8.61	9.08
	Rep-2	57.17		1.0027		9.55	
19	Rep-1	56.97	54.10	1.6791	1.6756	9.57	9.07
	Rep-2	51.23		1.6720		8.57	
20	Rep-1	50.20	46.43	0.9035	0.9025	22.68	20.95
	Rep-2	42.66		0.9014		19.23	
21	Rep-1	59.76	56.14	0.5163	0.5236	15.43	14.68
	Rep-2	52.52		0.5309		13.94	
22	Rep-1	48.71	50.17	1.3669	1.3912	11.10	11.64
	Rep-2	51.63		1.4155		12.18	
23	Rep-1	52.89	57.23	1.4195	1.3908	12.51	13.25
	Rep-2	61.57		1.3621		13.98	
24	Rep-1	57.26	55.84	1.1138	1.1052	10.63	10.29
	Rep-2	54.42		1.0966		9.95	
25	Rep-1	47.51	48.65	3.0050	2.9824	14.28	14.51
	Rep-2	49.79		2.9598		14.74	
26	Rep-1	55.26	51.33	1.3815	1.3881	7.63	7.12
	Rep-2	47.40		1.3946		6.61	
27	Rep-1	57.62	55.15	0.7255	0.7308	20.90	20.15
	Rep-2	52.68		0.7361		19.39	
28	Rep-1	55.94	56.38	1.9269	1.9241	17.97	18.08
	Rep-2	56.82		1.9212		18.19	
29	Rep-1	54.61	51.89	0.9453	0.9616	8.60	8.31
	Rep-2	49.17		0.9779		8.01	
30	Rep-1	53.48	52.44	1.8742	1.8614	10.02	9.76
	Rep-2	51.40		1.8486		9.50	

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Table Appendix B-4. Mean particle size and polydispersity index of formulation number 16 to 30

Formulation Number	Mean Particle Size (nm)				Polydispersity Index			
	Rep-1	Rep-2	Rep-3	Average	Rep-1	Rep-2	Rep-3	Average
16	290	300	300	297	1.01	1.05	1.06	1.04
17	330	340	330	333	1.19	1.20	1.21	1.20
18	280	280	280	280	0.82	0.80	0.78	0.80
19	320	310	320	317	1.14	1.08	1.17	1.13
20	320	320	320	320	1.30	1.34	1.35	1.33
21	290	270	280	280	0.72	0.69	0.72	0.71
22	330	330	330	330	0.87	0.89	0.85	0.87
23	320	320	320	320	0.98	0.99	0.94	0.97
24	330	320	310	320	1.03	0.98	1.02	1.01
25	320	330	320	323	1.01	0.97	1.11	1.03
26	310	320	320	317	0.88	0.89	0.90	0.89
27	300	310	310	307	1.12	1.14	1.13	1.13
28	320	310	310	313	1.55	1.54	1.56	1.55
29	270	280	260	270	1.08	1.10	1.06	1.08
30	340	330	330	333	0.86	0.92	0.89	0.89

Table Appendix B-5. Nanoparticles recovery, curcuminoids content, and entrapment efficiency of formulation number 31 to 45

Formulation number		Nanoparticles recovery (%)				Entrapment efficiency (%)	
		2-replicate	Average	2-replicate	Average	2-replicate	Average
31	Rep-1	52.47	51.40	1.1165	1.1291	29.29	29.01
	Rep-2	50.33		1.1416		28.73	
32	Rep-1	50.79	53.63	2.8709	2.8942	24.30	25.88
	Rep-2	56.47		2.9175		27.46	
33	Rep-1	53.07	51.68	2.8005	2.9025	24.77	24.98
	Rep-2	50.29		3.0045		25.18	
34	Rep-1	46.92	49.92	4.5464	4.5606	21.33	22.77
	Rep-2	52.92		4.5748		24.21	
35	Rep-1	51.08	52.04	1.0610	1.0826	27.10	28.18
	Rep-2	53.00		1.1041		29.26	
36	Rep-1	49.37	47.54	1.0338	1.0545	25.52	25.05
	Rep-2	45.71		1.0752		24.57	
37	Rep-1	48.76	51.59	2.6492	2.6369	21.53	22.67
	Rep-2	54.42		2.6246		23.81	
38	Rep-1	56.84	54.51	2.3754	2.4048	22.50	21.84
	Rep-2	52.18		2.4342		21.17	
39	Rep-1	54.78	52.94	2.6657	2.7115	24.34	23.91
	Rep-2	51.10		2.7573		23.48	
40	Rep-1	49.67	54.33	3.9841	4.1865	19.79	22.84
	Rep-2	58.99		4.3889		25.89	
41	Rep-1	56.09	55.04	4.4843	4.4771	25.15	24.64
	Rep-2	53.99		4.4699		24.13	
42	Rep-1	53.87	54.76	1.1921	1.1872	32.11	32.50
	Rep-2	55.65		1.1823		32.90	
43	Rep-1	52.89	53.24	2.7615	2.9669	24.34	26.34
	Rep-2	53.59		3.1723		28.33	
44	Rep-1	54.05	52.38	3.3429	3.3239	30.11	29.02
	Rep-2	50.71		3.3049		27.93	
45	Rep-1	51.64	53.51	4.8107	5.0000	24.84	26.79
	Rep-2	55.38		5.1892		28.74	

Table Appendix B-6. Mean particle size and polydispersity index of formulation number 31 to 45

Formulation Number	Mean Particle Size (%)				Polydispersity Index			
	Rep-1	Rep-2	Rep-3	Average	Rep-1	Rep-2	Rep-3	Average
31	370	360	360	363	0.92	0.94	0.90	0.92
32	320	330	330	327	0.85	0.87	0.89	0.87
33	390	380	380	383	0.94	0.96	0.95	0.95
34	360	350	350	353	0.86	0.87	0.91	0.88
35	360	370	360	363	0.92	0.92	0.92	0.92
36	390	400	400	397	0.85	0.86	0.84	0.85
37	390	380	400	390	0.97	0.94	0.97	0.96
38	390	380	390	387	0.92	0.94	0.93	0.93
39	380	390	380	383	0.99	0.97	1.01	0.99
40	380	380	380	380	0.94	0.98	0.99	0.97
41	410	390	400	400	0.86	0.89	0.86	0.87
42	400	400	400	400	0.99	0.94	0.98	0.97
43	390	390	400	393	0.94	0.92	0.93	0.93
44	420	430	420	423	0.94	0.95	0.93	0.94
45	390	400	400	397	0.97	0.93	0.98	0.96



**Appendix C**

**Standard Curve and HPLC Chromatogram  
of Curcuminoids**

Table Appendix C-1. Peak area from HPLC analysis of curcuminoids at concentration 0.02 to 0.10 mg/ml

Concentration (mg/ml)	Peak area (x 1,000)					
	1	2	3	Mean	±	S.D.
0.02	3,649	3,673	3,656	3,659	±	1.28
0.04	7,660	7,638	7,633	7,644	±	14.08
0.06	11,245	11,257	11,210	11,237	±	24.13
0.08	14,999	15,137	14,896	15,011	±	120.71
0.10	18,393	18,551	18,426	18,457	±	83.39

Standard Curve

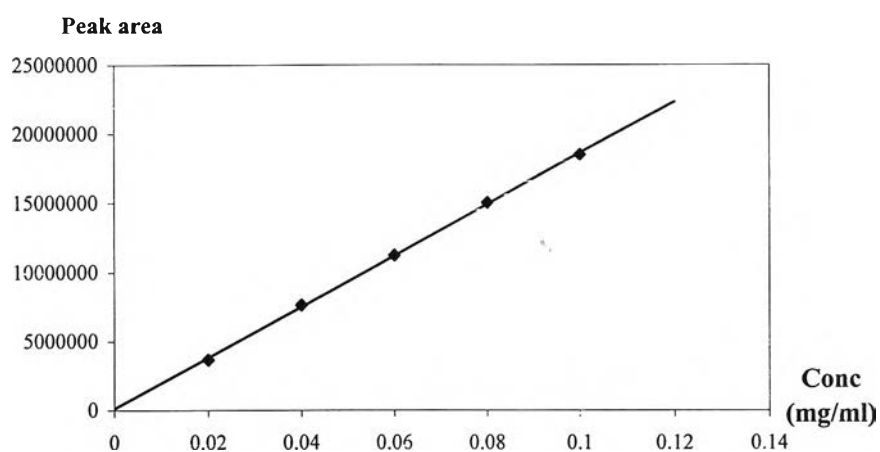


Figure Appendix C-1. Calibration curve of curcuminoids



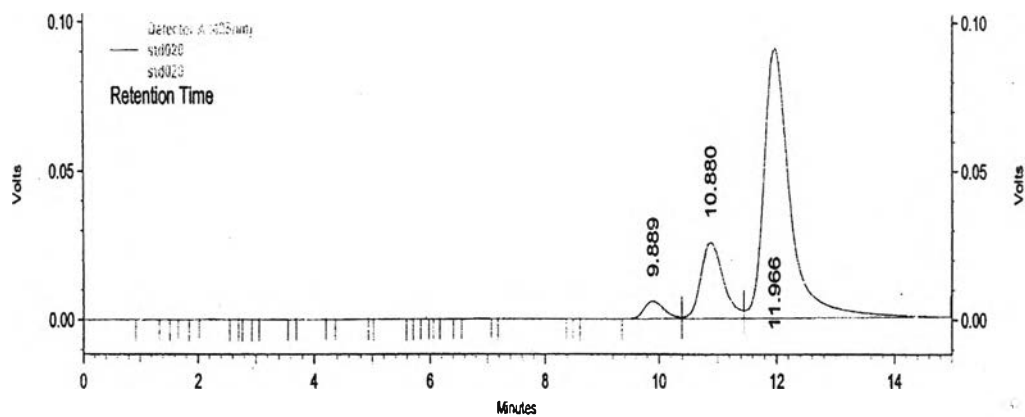


Figure Appendix C-2. HPLC-Chromatogram of curcuminoids

- a) Curcumin (retention time 11.966)
- b) Desmethoxycurcumin (retention time 10.880)
- c) Bisdemethoxycurcumin (retention time 9.889)

**Appendix D**  
**Design-Expert<sup>®</sup> output of statistical analysis**

Table Appendix D-1. Design-Expert® output for fitting a regression model to the nanoparticles recovery of formulation number 1 to 15

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<b>Response:</b>	<b>Nanoparticles recovery</b>				
<b>*** WARNING: The Cubic Model is Aliased! ***</b>					
<b>Sequential Model Sum of Squares</b>					
	<b>Sum of</b>		<b>Mean</b>	<b>F</b>	
<b>Source</b>	<b>Squares</b>	<b>DF</b>	<b>Square</b>	<b>Value</b>	<b>Prob &gt; F</b>
Mean	62702.10	1	62702.10		
Linear	12.52	3	4.17	0.64	0.6030
2FI	24.19	3	8.06	1.37	0.3207
Quadratic	11.05	3	3.68	0.51	0.6927
Cubic	20.96	3	6.99	0.92	0.5584
Residual	15.18	2	7.59		
Total	62786.00	15	4185.73		
<b>Lack of Fit Tests</b>					
	<b>Sum of</b>		<b>Mean</b>	<b>F</b>	
<b>Source</b>	<b>Squares</b>	<b>DF</b>	<b>Square</b>	<b>Value</b>	<b>Prob &gt; F</b>
Linear	56.20	9	6.24	0.82	0.6590
2Fi	32.01	6	5.34	0.70	0.6879
Quadratic	20.96	3	6.99	0.92	0.5584
Cubic	0.000	0			
Pure Error	15.18	2	7.59		
<b>Model Summary Statistics</b>					
	<b>Std.</b>	<b>Adjusted</b>	<b>Predicted</b>		
<b>Source</b>	<b>Dev.</b>	<b>R-Squared</b>	<b>R-Squared</b>	<b>R-Squared</b>	<b>PRESS</b>
Linear	2.55	0.1493	-0.0827	-0.5741	132.08
2FI	2.43	0.4376	0.0157	-0.9533	163.90
Quadratic	2.69	0.5693	-0.2059	-3.4034	369.47
Cubic	2.76	0.8191	-0.2664		+
+ Case(s) with leverage of 1.0000: PRESS statistic not defined					

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Table Appendix D-2. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the nanoparticles recovery of formulation number 1 to 15

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<b>Response:</b>	<b>Nanoparticles recovery</b>					
	<b>Backward Elimination Regression with Alpha to Exit = 0.050</b>					
<b>Forced Terms</b>	<b>Intercept</b>					
	<b>Coefficient</b>	<b>t for H0</b>				
<b>Removed</b>	<b>Estimate</b>	<b>Coeff=0</b>	<b>Prob &gt;  t </b>	<b>R-Squared</b>	<b>MSE</b>	
A	-0.15	-0.16	0.8788	0.5671	6.05	
B <sup>2</sup>	0.25	0.20	0.8516	0.5643	5.22	
B	0.24	0.30	0.7705	0.5586	4.63	
AC	-0.56	-0.53	0.6137	0.5434	4.26	
C <sup>2</sup>	0.71	0.66	0.5262	0.5214	4.02	
A <sup>2</sup>	1.55	1.49	0.1658	0.4144	4.47	
AB	1.50	1.42	0.1835	0.3071	4.84	
C	-1.22	-1.56	0.1437	0.1658	5.38	
BC	1.87	1.61	0.1319	-0.0000	5.99	

<b>ANOVA for Response Surface Mean Model</b>						
<b>Analysis of variance table [Partial sum of squares]</b>						
	<b>Sum of</b>		<b>Mean</b>	<b>F</b>		
<b>Source</b>	<b>Squares</b>	<b>DF</b>	<b>Square</b>	<b>Value</b>	<b>Prob &gt; F</b>	
Model	0.000	0				
Residual	83.91	14	5.99			
Lack of Fit	68.73	12	5.73	0.75	0.6980	
Pure Error	15.18	2	7.59			
Cor Total	83.91	14				

Std. Dev.	2.45			<b>R-Squared</b>	0.0000
Mean	64.65			<b>Adj R-Squared</b>	0.0000
C.V.	3.79			<b>Pred R-Squared</b>	-0.1480
PRESS	96.32			<b>Adeq Precision</b>	

	<b>Coefficient</b>		<b>Standard</b>	<b>95% CI</b>	<b>95% CI</b>
<b>Factor</b>	<b>Estimate</b>	<b>DF</b>	<b>Error</b>	<b>Low</b>	<b>High</b>
Intercept	64.65	1	0.63	63.30	66.01

**Final Equation in Terms of Coded Factors:**

Recovery = +64.65

**Final Equation in Terms of Actual Factors:**

Recovery = +64.65400

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Table AppendixD-3. Design-Expert® output for fitting a regression model to the particle size of formulation number 1 to 15

Response: Particle Size

\*\*\* WARNING: The Cubic Model is Aliased! \*\*\*

Sequential Model Sum of Squares

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Mean	1.486E+006	1	1.486E+006		
Linear	266.14	3	88.71	1.46	0.2797
2FI	97.51	3	32.50	0.45	0.7215
Quadratic	201.35	3	67.12	0.90	0.5011
Cubic	104.36	3	34.79	0.26	0.8508
Residual	266.67	2	133.33		
Total	1.487E+006	15	99119.47		

Lack of Fit Tests

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Linear	403.22	9	44.80	0.34	0.8982
2FI	305.71	6	50.95	0.38	0.8476
Quadratic	104.36	3	34.79	0.26	0.8508
Cubic	0.000	0			
Pure Error	266.67	2	133.33		

Model Summary Statistics

Source	Std. Dev.	R-Squared	Adjusted R-Squared	Predicted R-Squared	PRESS
Linear	7.80	0.2843	0.0892	-0.2433	1163.80
2FI	8.46	0.3885	-0.0701	-1.0401	1909.59
Quadratic	8.61	0.6036	-0.1099	-1.4249	2269.80
Cubic	11.55	0.7151	-0.9942		+

+ Case(s) with leverage of 1.0000: PRESS statistic not defined

Table AppendixD-4. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the particle size of formulation number 1 to 15

Response: Particle Size

Backward Elimination Regression with Alpha to Exit = 0.050

Forced Terms	Intercept		Prob >  t	R-Squared	MSE
	Coefficient Estimate	t for H <sub>0</sub> Coeff=0			
Removed B	-0.54	-0.18	0.8656	0.6011	62.23
B <sup>2</sup>	-1.54	-0.38	0.7202	0.5917	54.59
BC	1.67	0.45	0.6654	0.5798	49.16
A <sup>2</sup>	-2.26	-0.62	0.5525	0.5597	45.80
AC	-2.50	-0.74	0.4788	0.5329	43.72
AB	-3.92	-1.18	0.2634	0.4674	45.32
A	-3.46	-1.45	0.1741	0.3651	49.52
C	-4.58	-1.84	0.0903	0.1855	58.64
C <sup>2</sup>	6.82	1.72	0.1090	0.0000	66.86

ANOVA for Response Surface Mean Model  
Analysis of variance table [Partial sum of squares]

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Model	0.000	0			
Residual	936.03	14	66.86		
Lack of Fit	669.36	12	55.78	0.42	0.8663
Pure Error	266.67	2	133.33		
Cor Total	936.03	14			

Std. Dev.	8.18	R-Squared	0.0000
Mean	314.73	Adj R-Squared	0.0000
C.V.	2.60	Pred R-Squared	-0.1480
PRESS	1074.52	Adeq Precision	

Factor	Coefficient Estimate	DF	Standard Error	95% CI Low	95% CI High
Intercept	314.73	1	2.11310.21	319.26	

Final Equation in Terms of Coded Factors:

$$\text{Particle Size} = +314.73$$

Final Equation in Terms of Actual Factors:

$$\text{Particle Size} = +314.73333$$

Table AppendixD-5. Design-Expert® output for fitting a regression model to the polydispersity index of formulation number 1 to 15

---

<b>Response:</b>	<b>Polydispersity</b>				
<b>*** WARNING: The Cubic Model is Aliased! ***</b>					
<b>Sequential Model Sum of Squares</b>					
	<b>Sum of</b>		<b>Mean</b>	<b>F</b>	
<b>Source</b>	<b>Squares</b>	<b>DF</b>	<b>Square</b>	<b>Value</b>	<b>Prob &gt; F</b>
Mean	8.60	1	8.60		
Linear	0.010	3	3.358E-003	0.71	0.5659
2FI	6.225E-003	3	2.075E-003	0.36	0.7820
Quadratic	9.452E-003	3	3.151E-003	0.43	0.7385
Cubic	0.028	3	9.358E-003	2.26	0.3210
Residual	8.267E-003	2	4.133E-003		
Total	8.67	15	0.58		
<b>Lack of Fit Tests</b>					
	<b>Sum of</b>		<b>Mean</b>	<b>F</b>	
<b>Source</b>	<b>Squares</b>	<b>DF</b>	<b>Square</b>	<b>Value</b>	<b>Prob &gt; F</b>
Linear	0.044	9	4.861E-003	1.18	0.5410
2FI	0.038	6	6.254E-003	1.51	0.4497
Quadratic	0.028	3	9.358E-003	2.26	0.3210
Cubic	0.000	0			
Pure Error	8.267E-003	2	4.133E-003		
<b>Model Summary Statistics</b>					
	<b>Std.</b>		<b>Adjusted</b>	<b>Predicted</b>	
<b>Source</b>	<b>Dev.</b>	<b>R-Squared</b>	<b>R-Squared</b>	<b>R-Squared</b>	<b>PRESS</b>
Linear	0.069	0.1623	-0.0662	-0.6413	0.10
2FI	0.076	0.2625	-0.2906	-2.2851	0.20
Quadratic	0.085	0.4147	-0.6388	-6.5338	0.47
Cubic	0.064	0.8669	0.0681		+
+ Case(s) with leverage of 1.0000: PRESS statistic not defined					

---

Table AppendixD-6. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the polydispersity index of formulation number 1 to 15

Response: Polydispersity

Backward Elimination Regression with Alpha to Exit = 0.050

Forced Terms	Intercept				
Removed	Coefficient Estimate	t for H <sub>0</sub> Coeff=0	Prob >  t	R-Squared	MSE
A <sup>2</sup>	0.015	0.35	0.7424	0.4006	6.203E-003
B	0.011	0.40	0.7002	0.3843	5.462E-003
AB	-0.017	-0.47	0.6502	0.3646	4.932E-003
C	-0.012	-0.50	0.6282	0.3444	4.523E-003
B <sup>2</sup>	-0.021	-0.60	0.5664	0.3186	4.231E-003
BC	0.025	0.77	0.4598	0.2784	4.074E-003
AC	0.025	0.78	0.4499	0.2381	3.942E-003
C <sup>2</sup>	0.043	1.33	0.2083	0.1258	4.175E-003
A	0.031	1.37	0.1945	0.0000	4.435E-003

ANOVA for Response Surface Mean Model  
Analysis of variance table [Partial sum of squares]

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Model	0.000	0			
Residual	0.062	14	4.435E-003		
Lack of Fit	0.054	12	4.486E-003	1.09	0.5757
Pure Error	8.267E-003	2	4.133E-003		
Cor Total	0.062	14			

Std. Dev.	0.067	R-Squared	0.0000
Mean	0.76	Adj R-Squared	0.0000
C.V.	8.79	Pred R-Squared	-0.1480
PRESS	0.071	Adeq Precision	

Factor	Coefficient Estimate	DF	Standard Error	95% CI Low	95% CI High
Intercept	0.76	1	0.017	0.72	0.79

Final Equation in Terms of Coded Factors:

$$\text{Polydispersity index} = +0.76$$

Final Equation in Terms of Actual Factors:

$$\text{Polydispersity index} = +0.75733$$



Table AppendixD-7. Design-Expert® output for fitting a regression model to the curcuminoids content of formulation number 1 to 15

---

<b>Response:</b>	<b>Curcuminoids content</b>				
<b>*** WARNING: The Cubic Model is Aliased! ***</b>					
<b>Sequential Model Sum of Squares</b>					
	<b>Sum of</b>		<b>Mean</b>	<b>F</b>	
<b>Source</b>	<b>Squares</b>	<b>DF</b>	<b>Square</b>	<b>Value</b>	<b>Prob &gt; F</b>
Mean	0.10	1	0.10		
Linear	0.013	3	4.233E-003	29.70	< 0.0001
2FI	1.178E-004	3	3.927E-005	0.22	0.8822
Quadratic	4.151E-004	3	1.384E-004	0.67	0.6069
Cubic	9.847E-004	3	3.282E-004	13.00	0.0722
Residual	5.048E-005	2	2.524E-005		
Total	0.11	15	7.633E-003		
<b>Lack of Fit Tests</b>					
	<b>Sum of</b>		<b>Mean</b>	<b>F</b>	
<b>Source</b>	<b>Squares</b>	<b>DF</b>	<b>Square</b>	<b>Value</b>	<b>Prob &gt; F</b>
Linear	1.518E-003	9	1.686E-004	6.68	0.1369
2FI	1.400E-003	6	2.333E-004	9.24	0.1008
Quadratic	9.847E-004	3	3.282E-004	13.00	0.0722
Cubic	0.000	0			
Pure Error	5.048E-005	2	2.524E-005		
<b>Model Summary Statistics</b>					
	<b>Std.</b>		<b>Adjusted</b>	<b>Predicted</b>	
<b>Source</b>	<b>Dev.</b>	<b>R-Squared</b>	<b>R-Squared</b>	<b>R-Squared</b>	<b>PRESS</b>
Linear	0.012	0.8901	0.8601	0.7910	2.982E-003
2FI	0.013	0.8984	0.8221	0.5696	6.141E-003
Quadratic	0.014	0.9274	0.7969	-0.1122	0.016
Cubic	5.024E-003	0.9965	0.9752		+
+ Case(s) with leverage of 1.0000: PRESS statistic not defined					

---

Table Appendix D-8. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the curcuminoids content of formulation number 1 to 15

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**Response: Curcuminoids content**

**Backward Elimination Regression with Alpha to Exit = 0.050**

Forced Terms	Intercept				
Removed	Coefficient Estimate	t for H0 Coeff=0	Prob >  t	R-Squared	MSE
A	5.975E-003	1.42	0.1846	0.8701	1.545E-004

**ANOVA for Response Surface Reduced Linear Model**  
Analysis of variance table [Partial sum of squares]

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Model	0.012	2	6.207E-003	40.18	< 0.0001
B	0.011	1	0.011	70.99	< 0.0001
C	1.447E-003	1	1.447E-003	9.37	0.0099
Residual	1.854E-003	12	1.545E-004		
Lack of Fit	1.803E-003	10	1.803E-004	7.14	0.1289
Pure Error	5.048E-005	2	2.524E-005		
Cor Total	0.014	14			

Std. Dev.	0.012	R-Squared	0.8701
Mean	0.082	Adj R-Squared	0.8484
C.V.	15.21	Pred R-Squared	0.7902
PRESS	2.993E-003	Adeq Precision	18.162

Factor	Coefficient Estimate	DF	Standard Error	95% CI Low	95% CI High	VIF
Intercept	0.082	1	3.209E-003	0.075	0.089	
B-Curcuminoids	0.037	1	4.394E-003	0.027	0.047	1.00
C-Vit E TPGS	-0.013	1	4.394E-003	-0.023	-3.876E-003	1.00

**Final Equation in Terms of Coded Factors:**

$$\text{Content} = +0.082 + 0.037 * B - 0.013 * C$$

**Final Equation in Terms of Actual Factors:**

$$\text{Content} = +0.059828 + 9.25625E-003 * \text{Curcuminoids} - 6.72500E-003 * \text{Vit E TPGS}$$


---

Table Appendix D-9. Design-Expert® output for fitting a regression model to the entrapment efficiency of formulation number 1 to 15

Response: Entrapment Efficiency

Transform: Inverse

\*\*\* WARNING: The Cubic Model is Aliased! \*\*\*

Sequential Model Sum of Squares					
Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Mean	14.61	1	14.61		
Linear	1.02	3	0.34	6.44	0.0089
2FI	0.042	3	0.014	0.21	0.8871
Quadratic	0.17	3	0.058	0.80	0.5457
Cubic	0.35	3	0.12	18.84	0.0508
Residual	0.012	2	6.217E-003		
Total	16.21	15	1.08		

#### Lack of Fit Tests

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Linear	0.57	9	0.063	10.15	0.0929
2FI	0.53	6	0.088	14.09	0.0677
Quadratic	0.35	3	0.12	18.84	0.0508
Cubic	0.000	0			
Pure Error	0.012	2	6.217E-003		

#### Model Summary Statistics

Source	Std. Dev.	R-Squared	Adjusted R-Squared	Predicted R-Squared	PRESS
Linear	0.23	0.6372	0.5383	0.2312	1.23
2FI	0.26	0.6637	0.4114	-0.7571	2.81
Quadratic	0.27	0.7726	0.3632	-2.5320	5.65
Cubic	0.079	0.9922	0.9456		+

+ Case(s) with leverage of 1.0000: PRESS statistic not defined

Table Appendix D-10. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the entrapment efficiency of formulation number 1 to 15

**Response: Entrapment Efficiency**

**Backward Elimination Regression with Alpha to Exit = 0.050**

**Forced Terms** Intercept

Removed	Coefficient Estimate	t for H0 Coeff=0	Prob >  t	R-Squared	MSE
A	0.091	1.13	0.2845	0.5955	0.054
C	-0.18	-2.15	0.0530	0.4402	0.069

**ANOVA for Response Surface Reduced Linear Model**  
Analysis of variance table [Partial sum of squares]

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Model	0.70	1	0.70	10.22	0.0070
B	0.70	1	0.70	10.22	0.0070
Residual	0.90	13	0.069		
Lack of Fit	0.88	11	0.080	12.91	0.0740
Pure Error	0.012	2	6.217E-003		
Cor Total	1.60	14			

Std. Dev.	0.26	R-Squared	0.4402
Mean	0.99	Adj R-Squared	0.3971
C.V.	26.60	Pred R-Squared	0.1990
PRESS	1.28	Adeq Precision	6.191

Factor	Coefficient Estimate	DF	Standard Error	95% CI Low	95% CI High	VIF
Intercept	0.99	1	0.068	0.84	1.13	
B-Curcuminoids	-0.30	1	0.093	-0.50	-0.096	1.00

**Final Equation in Terms of Coded Factors:**

$$\text{Entrapment Efficiency} = +0.99 - 0.30 * B$$

**Final Equation in Terms of Actual Factors:**

$$\text{Entrapment Efficiency} = +1.43182 - 0.074172 * \text{Curcuminoids}$$

Table Appendix D-11. Design-Expert® output for fitting a regression model to the nanoparticles recovery of formulation number 16 to 30

**Response: Recovery**

**\*\*\* WARNING: The Cubic Model is Aliased! \*\*\***

**Sequential Model Sum of Squares**

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Mean	42344.08	1	42344.08		
Linear	15.98	3	5.33	0.51	0.6860
2FI	26.79	3	8.93	0.80	0.5264
Quadratic	34.58	3	11.53	1.06	0.4441
Cubic	26.43	3	8.81	0.63	0.6614
Residual	27.97	2	13.99		
Total	42475.83	15	2831.72		

**Lack of Fit Tests**

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Linear	87.79	9	9.75	0.70	0.7120
2FI	61.00	6	10.17	0.73	0.6777
Quadratic	26.43	3	8.81	0.63	0.6614
Cubic	0.000	0			
Pure Error	27.97	2	13.99		

**Model Summary Statistics**

Source	Std. Dev.	R-Squared	Adjusted R-Squared	Predicted R-Squared	PRESS
Linear	3.24	0.1213	-0.1184	-0.6337	215.23
2FI	3.33	0.3246	-0.1819	-1.5532	336.37
Quadratic	3.30	0.5871	-0.1562	-2.6870	485.75
Cubic	3.74	0.7877	-0.4864		+

+ Case(s) with leverage of 1.0000: PRESS statistic not defined

Table Appendix D-12. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the nanoparticles recovery of formulation number 16 to 30

---

<b>Response:</b>	<b>Recovery</b>				
<b>Backward Elimination Regression with Alpha to Exit = 0.050</b>					
<b>Forced Terms</b>	<b>Intercept</b>				
	<b>Coefficient</b>	<b>t for H0</b>			
<b>Removed</b>	<b>Estimate</b>	<b>Coeff=0</b>	<b>Prob &gt;  t </b>	<b>R-Squared</b>	<b>MSE</b>
A	0.067	0.058	0.9561	0.5868	9.07
AB	-0.82	-0.55	0.6047	0.5663	8.16
B	-0.59	-0.58	0.5775	0.5451	7.49
A <sup>2</sup>	1.37	0.96	0.3636	0.4924	7.43
AC	-1.71	-1.26	0.2406	0.4033	7.86
BC	-1.76	-1.25	0.2385	0.3096	8.27
C	1.28	1.26	0.2332	0.2097	8.68
C <sup>2</sup>	-1.90	-1.24	0.2379	0.1081	9.04
B <sup>2</sup>	-1.95	-1.26	0.2316	0.0000	9.41

<b>ANOVA for Response Surface Mean Model</b>					
<b>Analysis of variance table [Partial sum of squares]</b>					
	<b>Sum of</b>		<b>Mean</b>	<b>F</b>	
<b>Source</b>	<b>Squares</b>	<b>DF</b>	<b>Square</b>	<b>Value</b>	<b>Prob &gt; F</b>
Model	0.000	0			
Residual	131.75	14	9.41		
Lack of Fit	103.77	12	8.65	0.62	0.7612
Pure Error	27.97	2	13.99		
Cor Total	131.75	14			

Std. Dev.	3.07		R-Squared	0.0000
Mean	53.13		Adj R-Squared	0.0000
C.V.	5.77		Pred R-Squared	-0.1480
PRESS	151.24		Adeq Precision	

	<b>Coefficient</b>		<b>Standard</b>	<b>95% CI</b>	<b>95% CI</b>
<b>Factor</b>	<b>Estimate</b>	<b>DF</b>	<b>Error</b>	<b>Low</b>	<b>High</b>
Intercept	53.13	1	0.79	51.43	54.83

**Final Equation in Terms of Coded Factors:**

Recovery = +53.13

**Final Equation in Terms of Actual Factors:**

Recovery = +53.13133

---

Table Appendix D-13. Design-Expert® output for fitting a regression model to the particle size of formulation number 16 to 30

---

<b>Response:</b>	<b>Particle size</b>				
<b>*** WARNING: The Cubic Model is Aliased! ***</b>					
<b>Sequential Model Sum of Squares</b>					
<b>Source</b>	<b>Sum of Squares</b>	<b>DF</b>	<b>Mean Square</b>	<b>F Value</b>	<b>Prob &gt; F</b>
Mean	1.448E+006	1	1.448E+006		
<u>Linear</u>	<u>3447.00</u>	<u>3</u>	<u>1149.00</u>	<u>5.86</u>	<u>0.0122</u>
2FI	323.00	3	107.67	0.47	0.7119
Quadratic	1059.67	3	353.22	2.28	0.1973
Cubic	709.00	3	236.33	7.09	0.1261
Residual	66.67	2	33.33		
Total	1.453E+006	15	96887.47		
<b>Lack of Fit Tests</b>					
<b>Source</b>	<b>Sum of Squares</b>	<b>DF</b>	<b>Mean Square</b>	<b>F Value</b>	<b>Prob &gt; F</b>
<u>Linear</u>	<u>2091.67</u>	<u>9</u>	<u>232.41</u>	<u>6.97</u>	<u>0.1317</u>
2FI	1768.67	6	294.78	8.84	0.1051
Quadratic	709.00	3	236.33	7.09	0.1261
Cubic	0.000	0			
Pure Error	66.67	2	33.33		
<b>Model Summary Statistics</b>					
<b>Source</b>	<b>Std. Dev.</b>	<b>R-Squared</b>	<b>Adjusted R-Squared</b>	<b>Predicted R-Squared</b>	<b>PRESS</b>
<u>Linear</u>	<u>14.01</u>	<u>0.6150</u>	<u>0.5099</u>	<u>0.2725</u>	<u>4077.74</u>
2FI	15.15	0.6726	0.4270	-0.3353	7484.70
Quadratic	12.46	0.8616	0.6125	-1.0505	11494.00
Cubic	5.77	0.9881	0.9167		+
+ Case(s) with leverage of 1.0000: PRESS statistic not defined					

---

Table Appendix D-14. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the particle size of formulation number 16 to 30

Response: Particle size

Backward Elimination Regression with Alpha to Exit = 0.050

Forced Terms	Intercept				
Removed	Coefficient Estimate	t for H0 Coeff=0	Prob >  t	R-Squared	MSE
A	-0.50	-0.10	0.9214	0.6146	180.03

ANOVA for Response Surface Reduced Linear Model  
Analysis of variance table [Partial sum of squares]

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Model	3445.00	2	1722.50	9.57	0.0033
B	924.50	1	924.50	5.14	0.0427
C	2520.50	1	2520.50	14.00	0.0028
Residual	2160.33	12	180.03		
Lack of Fit	2093.67	10	209.37	6.28	0.1451
Pure Error	66.67	2	33.33		
Cor Total	5605.33	14			

Std. Dev.	13.42	R-Squared	0.6146
Mean	310.67	Adj R-Squared	0.5504
C.V.	4.32	Pred R-Squared	0.3986
PRESS	3371.24	Adeq Precision	9.499

Factor	Coefficient Estimate	DF	Standard Error	95% CI Low	95% CI High	VIF
Intercept	310.67	1	3.46	303.12	318.21	
B-Curcuminoids	10.75	1	4.74	0.41	21.09	1.00
C-Poloxamer 407	-17.75	1	4.74	-28.09	-7.41	1.00

Final Equation in Terms of Coded Factors:

$$\text{Particle size} = +310.67 + 10.75 * B - 17.75 * C$$

Final Equation in Terms of Actual Factors:

$$\text{Particle size} = +365.54167 + 2.68750 * \text{Curcuminoids} - 5.91667 * \text{Poloxamer 407}$$



Table Appendix D-15. Design-Expert® output for fitting a regression model to the polydispersity index of formulation number 16 to 30

Response: Polydispersity Index

\*\*\* WARNING: The Cubic Model is Aliased! \*\*\*

Sequential Model Sum of Squares

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Mean	16.29	1	16.29		
<u>Linear</u>	<u>0.37</u>	<u>3</u>	<u>0.12</u>	<u>5.14</u>	<u>0.0183</u>
2FI	0.086	3	0.029	1.29	0.3422
Quadratic	0.090	3	0.030	1.70	0.2820
Cubic	0.078	3	0.026	4.98	0.1718
Residual	0.010	2	5.200E-003		
Total	16.92	15	1.13		

Lack of Fit Tests

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
<u>Linear</u>	<u>0.25</u>	<u>9</u>	<u>0.028</u>	<u>5.41</u>	<u>0.1656</u>
2FI	0.17	6	0.028	5.36	0.1654
Quadratic	0.078	3	0.026	4.98	0.1718
Cubic	0.000	0			
Pure Error	0.010	2	5.200E-003		

Model Summary Statistics

Source	Std. Dev.	R-Squared	Adjusted R-Squared	Predicted R-Squared	PRESS
<u>Linear</u>	<u>0.15</u>	<u>0.5838</u>	<u>0.4703</u>	<u>0.1647</u>	<u>0.53</u>
2FI	0.15	0.7195	0.5092	-0.2577	0.80
Quadratic	0.13	0.8610	0.6109	-0.9977	1.27
Cubic	0.072	0.9836	0.8851		+

+ Case(s) with leverage of 1.0000: PRESS statistic not defined

Table AppendixD-16. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the polydispersity index of formulation number 16 to 30

Response: Polydispersity Index

Backward Elimination Regression with Alpha to Exit = 0.050

Forced Terms Intercept

Removed	Coefficient Estimate	t for H0 Coeff=0	Prob >  t	R-Squared	MSE
B	-0.034	-0.62	0.5502	0.5694	0.023
A	0.060	1.13	0.2825	0.5240	0.023

ANOVA for Response Surface Reduced Linear Model

Analysis of variance table [Partial sum of squares]

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Model	0.33	1	0.33	14.31	0.0023
C	0.33	1	0.33	14.31	0.0023
Residual	0.30	13	0.023		
Lack of Fit	0.29	11	0.026	5.09	0.1755
Pure Error	0.010	2	5.200E-003		
Cor Total	0.63	14			

Std. Dev.	0.15	R-Squared	0.5240
Mean	1.04	Adj R-Squared	0.4874
C.V.	14.62	Pred R-Squared	0.3163
PRESS	0.43	Adeq Precision	7.325

Factor	Coefficient Estimate	DF	Standard Error	95% CI Low	95% CI High	VIF
Intercept	1.04	1	0.039	0.96	1.13	
C-Poloxamer 407	-0.20	1	0.054	-0.32	-0.087	1.00

Final Equation in Terms of Coded Factors:

$$\text{Polydispersity index} = +1.04 - 0.20 * C$$

Final Equation in Terms of Actual Factors:

$$\text{Polydispersity index} = +1.85700 - 0.067917 * \text{Poloxamer 407}$$

Table Appendix D-17. Design-Expert® output for fitting a regression model to the curcuminoids content of formulation number 16

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**Response: Curcuminoids Content**

**Sequential Model Sum of Squares**

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Mean	28.72	1	28.72		
Linear	5.50	3	1.83	24.26	< 0.0001
2FI	0.40	3	0.13	2.47	0.1367
Quadratic	0.24	3	0.079	2.01	0.2315
Cubic	0.14	3	0.047	1.73	0.3864
Residual	0.054	2	0.027		
Total	35.05	15	2.34		

**Lack of Fit Tests**

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Linear	0.78	9	0.086	3.17	0.2627
2FI	0.38	6	0.063	2.31	0.3325
Quadratic	0.14	3	0.047	1.73	0.3864
Cubic	0.000	0			
Pure Error	0.054	2	0.027		

**Model Summary Statistics**

Source	Std. Dev.	R-Squared	Adjusted R-Squared	Predicted R-Squared	PRESS
Linear	0.27	0.8687	0.8329	0.7310	1.70
2FI	0.23	0.9318	0.8806	0.6880	1.98
Quadratic	0.20	0.9691	0.9134	0.6232	2.39
Cubic	0.17	0.9914	0.9398		+

+ Case(s) with leverage of 1.0000: PRESS statistic not defined

---

Table Appendix D-18. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the curcuminoids content of formulation number 16 to 30

Response: Curcuminoids content

Backward Elimination Regression with Alpha to Exit = 0.050

Forced Terms Intercept

Removed	Coefficient Estimate	t for H0 Coeff=0	Prob >  t	R-Squared	MSE
A	-0.014	-0.15	0.8848	0.8684	0.069

ANOVA for Response Surface Reduced Quadratic Model  
Analysis of variance table [Partial sum of squares]

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Model	5.50	2	2.75	39.61	< 0.0001
B	3.26	1	3.26	46.98	< 0.0001
C	2.24	1	2.24	32.24	0.0001
Residual	0.83	12	0.069		
Lack of Fit	0.78	10	0.078	2.86	0.2867
Pure Error	0.054	2	0.027		
Cor Total	6.33	14			

Std. Dev.	0.26	R-Squared	0.8685
Mean	1.38	Adj R-Squared	0.8465
C.V.	19.04	Pred R-Squared	0.7619
PRESS	1.51	Adeq Precision	19.815

Factor	Coefficient Estimate	DF	Standard Error	95% CI Low	95% CI High	VIF
Intercept	1.38	1	0.068	1.24	1.53	
B-Curcuminoids	0.64	1	0.093	0.44	0.84	1.00
C-Polxamer 407	-0.53	1	0.093	-0.73	-0.33	1.00

Final Equation in Terms of Coded Factors:

$$\text{Curcuminoids content} = +1.38 + 0.64 * B - 0.53 * C$$

Final Equation in Terms of Actual Factors:

$$\text{Curcuminoids content} = +2.54184 + 0.15964 * \text{Curcuminoids} - 0.17634 * \text{Poloxamer407}$$

Table Appendix D-19. Design-Expert® output for fitting a regression model to the entrapment efficiency of formulation number 16 to 30

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<b>Response:</b>	<b>Entrapment Efficiency</b>				
<b>*** WARNING: The Cubic Model is Aliased! ***</b>					
<b>Sequential Model Sum of Squares</b>					
<b>Source</b>	<b>Sum of Squares</b>	<b>DF</b>	<b>Mean Square</b>	<b>F Value</b>	<b>Prob &gt; F</b>
Mean	2779.03	1	2779.03		
Linear	280.21	3	93.40	30.13	< ^.0001
2FI	1.99	3	0.66	0.17	0.9167
Quadratic	13.66	3	4.55	1.23	0.3894
Cubic	13.99	3	4.66	2.09	0.3394
Residual	4.46	2	2.23		
Total	3093.34	15	206.22		
<b>Lack of Fit Tests</b>					
<b>Source</b>	<b>Sum of Squares</b>	<b>DF</b>	<b>Mean Square</b>	<b>F Value</b>	<b>Prob &gt; F</b>
Linear	29.64	9	3.29	1.48	0.4675
2FI	27.65	6	4.61	2.07	0.3612
Quadratic	13.99	3	4.66	2.09	0.3394
Cubic	0.000	0			
Pure Error	4.46	2	2.23		
<b>Model Summary Statistics</b>					
<b>Source</b>	<b>Std. Dev.</b>	<b>R-Squared</b>	<b>Adjusted R-Squared</b>	<b>Predicted R-Squared</b>	<b>PRESS</b>
Linear	1.76	0.8915	0.8619	0.8153	58.04
2FI	2.00	0.8979	0.8212	0.6564	108.00
Quadratic	1.92	0.9413	0.8357	0.2559	233.88
Cubic	1.49	0.9858	0.9008		+
+ Case(s) with leverage of 1.0000: PRESS statistic not defined					

---

Table Appendix D-20. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the entrapment efficiency of formulation number 16 to 30

**Response: Entrapment Efficiency**

**Backward Elimination Regression with Alpha to Exit = 0.050**

**Forced Terms Intercept**

Removed	Coefficient Estimate	t for H0 Coeff=0	Prob >  t	R-Squared	MSE
A	0.11	0.18	0.8568	0.8912	2.85

**ANOVA for Response Surface Reduced Linear Model**

**Analysis of variance table [Partial sum of squares]**

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Model	280.11	2	140.05	49.14	< 0.0001
B	132.28	1	132.28	46.41	< 0.0001
C	147.83	1	147.83	51.87	< 0.0001
Residual	34.20	12	2.85		
Lack of Fit	29.75	10	2.97	1.34	0.5023
Pure Error	4.46	2	2.23		
Cor Total	314.31	14			
Std. Dev.	1.69			R-Squared	0.8912
Mean	13.61			Adj R-Squared	0.8730
C.V.	12.40			Pred R-Squared	0.8387
PRESS	50.71			Adeq Precision	22.159

Factor	Coefficient Estimate	DF	Standard Error	95% CI Low	95% CI High	VIF
Intercept	13.61	1	0.44	12.66	14.56	
B-Curcuminoids	-4.07	1	0.60	-5.37	-2.77	1.00
C-Polxamer 407	-4.30	1	0.60	-5.60	-3.00	1.00

**Final Equation in Terms of Coded Factors:**

$$\text{Entrapment Efficiency} = +13.61 - 4.07 * B - 4.30 * C$$

**Final Equation in Terms of Actual Factors:**

$$\text{Entrapment Efficiency} = +36.90571 - 1.01656 * \text{Curcuminoids} - 1.43292 * \text{Polxamer 407}$$

Table Appendix D-21. Design-Expert® output for fitting a regression model to the nanoparticles recovery of formulation number 31 to 45

Response: Nanoparticles recovery

Sequential Model Sum of Squares

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Mean	41449.87	1	41449.87		
Linear	18.26	3	6.09	1.77	0.2110
2FI	7.10	3	2.37	0.62	0.6241
Quadratic	1.26	3	0.42	0.071	0.9730
Cubic	25.23	3	8.41	3.94	0.2091
Residual	4.27	2	2.14		
Total	41505.98	15	2767.07		

Lack of Fit Tests

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Linear	33.58	9	3.73	1.75	0.4166
2FI	26.48	6	4.41	2.07	0.3615
Quadratic	25.23	3	8.41	3.94	0.2091
Cubic	0.000	0			
Pure Error	4.27	2	2.14		

Model Summary Statistics

Source	Std. Dev.	R-Squared	Adjusted R-Squared	Predicted R-Squared	PRESS
Linear	1.85	0.3255	0.1415	-0.3583	76.22
2FI	1.96	0.4519	0.0409	-1.5562	143.44
Quadratic	2.43	0.4743	-0.4718	-6.3639	413.21
Cubic	1.46	0.9239	0.4672		+

+ Case(s) with leverage of 1.0000: PRESS statistic not defined

Table Appendix D-22. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the nanoparticles recovery of formulation number 31 to 45

Response: Nanoparticles recovery

Backward Elimination Regression with Alpha to Exit = 0.050

Removed	Coefficient Estimate	t for H0 Coeff=0	Prob >  t	R-Squared	MSE
AB	0.057	0.047	0.9641	0.4741	4.92
A <sup>2</sup>	-0.060	-0.052	0.9600	0.4739	4.22
C <sup>2</sup>	-0.22	-0.20	0.8453	0.4708	3.71
AC	0.27	0.28	0.7845	0.4655	3.33
B <sup>2</sup>	-0.54	-0.57	0.5848	0.4464	3.11
C	-0.83	-1.32	0.2150	0.3494	3.32
B	0.88	1.37	0.1980	0.2383	3.56
A	0.91	1.36	0.1988	0.1209	3.79
BC	1.30	1.34	0.2040	-0.0000	4.01

ANOVA for Response Surface Mean Model  
Analysis of variance table [Partial sum of squares]

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Model	0.000	0			
Residual	56.11	14	4.01		
Lack of Fit	51.84	12	4.32	2.02	0.3781
Pure Error	4.27	2	2.14		
Cor Total	56.11	14			
Std. Dev.	2.00		R-Squared	0.0000	
Mean	52.57		Adj R-Squared	0.0000	
C.V.	3.81		Pred R-Squared	-0.1480	
PRESS	64.42		Adeq Precision		

Factor	Coefficient Estimate	DF	Standard Error	95% CI Low	95% CI High
Intercept	52.57	1	0.52	51.46	53.68

Final Equation in Terms of Coded Factors:

$$\text{Recovery} = +52.57$$

Final Equation in Terms of Actual Factors:

$$\text{Recovery} = +52.56733$$



Table Appendix D-23. Design-Expert® output for fitting a regression model to the particle size of formulation number 31 to 45

Response: Particle size

\*\*\* WARNING: The Cubic Model is Aliased! \*\*\*

Sequential Model Sum of Squares

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Mean	2.196E+006	1	2.196E+006		
<u>Linear</u>	<u>6827.25</u>	<u>3</u>	<u>2275.75</u>	<u>33.36</u>	<u>&lt; 0.0001</u>
2FI	230.25	3	76.75	1.18	0.3763
Quadratic	153.18	3	51.06	0.70	0.5933
Cubic	342.25	3	114.08	9.25	0.0991
Residual	24.67	2	12.33		
Total	2.203E+006	15	1.469E+005		

Lack of Fit Tests

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
<u>Linear</u>	<u>725.68</u>	<u>9</u>	<u>80.63</u>	<u>6.54</u>	<u>0.1397</u>
2FI	495.43	6	82.57	6.70	0.1356
Quadratic	342.25	3	114.08	9.25	0.0991
Cubic	0.000	0			
Pure Error	24.67	2	12.33		

Model Summary Statistics

Source	Std. Dev.	R-Squared	Adjusted R-Squared	Predicted R-Squared	PRESS
<u>Linear</u>	<u>8.26</u>	<u>0.9010</u>	<u>0.8740</u>	<u>0.7977</u>	<u>1533.13</u>
2FI	8.06	0.9314	0.8799	0.6754	2459.46
Quadratic	8.57	0.9516	0.8644	0.2700	5531.50
Cubic	3.51	0.9967	0.9772		+

+ Case(s) with leverage of 1.0000: PRESS statistic not defined

Table Appendix D-24. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the particle size of formulation number 31 to 45

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**Response: Particle size**

**Backward Elimination Regression with Alpha to Exit = 0.050**

**Forced Terms Intercept**

Removed	Coefficient Estimate	t for H0 Coeff=0	Prob >  t	R-Squared	MSE
B	0.88	0.30	0.7700	0.9002	63.04

**ANOVA for Response Surface Reduced Linear Model**  
**Analysis of variance table [Partial sum of squares]**

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Model	6821.13	2	3410.56	54.10	< 0.0001
A	4371.12	1	4371.12	69.34	< 0.0001
C	2450.00	1	2450.00	38.86	< 0.0001
Residual	756.47	12	63.04		
Lack of Fit	731.81	10	73.18	5.93	0.1527
Pure Error	24.67	2	12.33		
Cor Total	7577.60	14			

Std. Dev.	7.94	R-Squared	0.9002
Mean	382.60	Adj R-Squared	0.8835
C.V.	2.08	Pred R-Squared	0.8286
PRESS	1298.56	Adeq Precision	23.023

Factor	Coefficient Estimate	DF	Standard Error	95% CI Low	95% CI High	VIF
Intercept	382.60	1	2.05	378.13	387.07	
A-PLA:PGA ratio	23.37	1	2.81	17.26	29.49	1.00
C-PVA	17.50	1	2.81	11.38	23.62	1.00

**Final Equation in Terms of Coded Factors:**

$$\text{Particle size} = +382.60 + 23.37 * A + 17.50 * C$$

**Final Equation in Terms of Actual Factors:**

$$\text{Particle size} = +303.78750 + 11.68750 * \text{PLA:PGA ratio} + 8.75000 * \text{PVA}$$


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Table Appendix D-25. Design-Expert® output for fitting a regression model to the polydispersity index of formulation number 31 to 45

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<b>Response:</b>	<b>Polydispersity Index</b>				
<b>Sequential Model Sum of Squares</b>					
<b>Source</b>	<b>Sum of Squares</b>	<b>DF</b>	<b>Mean Square</b>	<b>F Value</b>	<b>Prob &gt; F</b>
Mean	12.90	1	12.90		
Linear	4.900E-003	3	1.633E-003	0.88	0.4806
2FI	1.675E-003	3	5.583E-004	0.24	0.8671
Quadratic	5.868E-003	3	1.956E-003	0.76	0.5623
Cubic	0.011	3	3.683E-003	4.09	0.2026
Residual	1.800E-003	2	9.000E-004		
Total	12.92	15	0.86		
<b>Lack of Fit Tests</b>					
<b>Source</b>	<b>Sum of Squares</b>	<b>DF</b>	<b>Mean Square</b>	<b>F Value</b>	<b>Prob &gt; F</b>
Linear	0.019	9	2.066E-003	2.30	0.3402
2FI	0.017	6	2.820E-003	3.13	0.2616
Quadratic	0.011	3	3.683E-003	4.09	0.2026
Cubic	0.000	0			
Pure Error	1.800E-003	2	9.000E-004		
<b>Model Summary Statistics</b>					
<b>Source</b>	<b>Std. Dev.</b>	<b>R-Squared</b>	<b>Adjusted R-Squared</b>	<b>Predicted R-Squared</b>	<b>PRESS</b>
Linear	0.043	0.1937	-0.0262	-0.5302	0.039
2FI	0.048	0.2599	-0.2951	-2.1151	0.079
Quadratic	0.051	0.4920	-0.4225	-6.1501	0.18
Cubic	0.030	0.9288	0.5018		+

+ Case(s) with leverage of 1.0000: PRESS statistic not defined

---

Table Appendix D-26. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the polydispersity index of formulation number 31 to 45

Response: Polydispersity index

Backward Elimination Regression with Alpha to Exit = 0.050

Forced Terms	Intercept				
Removed	Coefficient Estimate	t for H0 Coeff=0	Prob >  t	R-Squared	MSE
B	2.500E-003	0.14	0.8945	0.4900	2.150E-003
A <sup>2</sup>	-3.750E-003	-0.16	0.8816	0.4879	1.850E-003
BC	-7.500E-003	-0.35	0.7376	0.4790	1.647E-003
AB	7.500E-003	0.37	0.7213	0.4701	1.489E-003
C	-0.010	-0.73	0.4822	0.4385	1.420E-003
AC	-0.018	-0.93	0.3749	0.3901	1.402E-003
B <sup>2</sup>	-0.023	-1.21	0.2526	0.3092	1.456E-003
C <sup>2</sup>	-0.032	-1.61	0.1335	0.1601	1.634E-003
A	0.022	1.57	0.1394	0.0000	1.807E-003

ANOVA for Response Surface Mean Model  
Analysis of variance table [Partial sum of squares]

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Model	0.000	0			
Residual	0.025	14	1.807E-003		
Lack of Fit	0.023	12	1.958E-003	2.18	0.3579
Pure Error	1.800E-003	2	9.000E-004		
Cor Total	0.025	14			

Std. Dev.	0.043	R-Squared	0.0000
Mean	0.93	Adj R-Squared	0.0000
C.V.	4.58	Pred R-Squared	-0.1480
PRESS	0.029	Adeq Precision	

Factor	Coefficient Estimate	DF	Standard Error	95% CI Low	95% CI High
Intercept	0.93	1	0.0110.90	0.95	

Final Equation in Terms of Coded Factors:

$$\text{Polydispersity index} = +0.93$$

Final Equation in Terms of Actual Factors:

$$\text{Polydispersity index} = +0.92733$$

Table Appendix D-27. Design-Expert® output for fitting a regression model to the curcuminoids contents of formulation number 31 to 45

Response: Curcuminoids Content

\*\*\* WARNING: The Cubic Model is Aliased! \*\*\*

Sequential Model Sum of Squares

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Mean	120.52	1	120.52		
Linear	23.88	3	7.96	128.41	< 0.0001
2FI	0.092	3	0.031	0.42	0.7461
Quadratic	0.47	3	0.16	6.74	0.0330
Cubic	0.066	3	0.022	0.86	0.5785
Residual	0.051	2	0.026		
Total	145.08	15	9.67		

Lack of Fit Tests

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Linear	0.63	9	0.070	2.74	0.2961
2FI	0.54	6	0.090	3.51	0.2384
Quadratic	0.066	3	0.022	0.86	0.5785
Cubic	0.000	0			
Pure Error	0.051	2	0.026		

Model Summary Statistics

Source	Std. Dev.	R-Squared	Adjusted R-Squared	Predicted R-Squared	PRESS
Linear	0.25	0.9722	0.9647	0.9502	1.22
2FI	0.27	0.9760	0.9580	0.9128	2.14
Quadratic	0.15	0.9952	0.9867	0.9525	1.17
Cubic	0.16	0.9979	0.9854		+

+ Case(s) with leverage of 1.0000: PRESS statistic not defined

Table Appendix D-28. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the curcuminoids content of formulation number 31 to 45

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**Response: Curcuminoids content**

**Backward Elimination Regression with Alpha to Exit = 0.050**

**Forced Terms Intercept**

Removed	Coefficient Estimate	t for H0 Coeff=0	Prob >  t	R-Squared	MSE
C	0.076	0.89	0.3916	0.9702	0.061
A	0.12	1.42	0.1809	0.9652	0.066

**ANOVA for Response Surface Reduced Quadratic Model**  
Analysis of variance table [Partial sum of squares]

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Model	23.70	1	23.70	360.84	< 0.0001
B	23.70	1	23.70	360.84	< 0.0001
Residual	0.85	13	0.066		
Lack of Fit	0.80	11	0.073	2.85	0.2881
Pure Error	0.051	2	0.026		
Cor Total	24.56	14			

Std. Dev.	0.26	R-Squared	0.9652
Mean	2.83	Adj R-Squared	0.9626
C.V.	9.04	Pred R-Squared	0.9546
PRESS	1.11	Adeq Precision	36.785

Factor	Coefficient Estimate	DF	Standard Error	95% CI Low	95% CI High	VIF
Intercept	2.83	1	0.066	2.69	2.98	
B-Curcuminoids	1.72	1	0.091	1.53	1.92	1.00

**Final Equation in Terms of Coded Factors:**

$$\text{Curcuminoids Content} = +2.83 + 1.72 * B$$

**Final Equation in Terms of Actual Factors:**

$$\text{Curcuminoids Content} = +0.25250 + 0.43034 * \text{Curcuminoids}$$


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Table Appendix D-29. Design-Expert® output for fitting a regression model to the entrapment of formulation number 31 to 45

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**Response:           Entrapment Efficiency**

**\*\*\* WARNING: The Cubic Model is Aliased! \*\*\***

**Sequential Model Sum of Squares**

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Mean	9950.57	1	9950.57		
Linear	57.77	3	19.26	3.27	0.0627
2FI	9.45	3	3.15	0.46	0.7202
Quadratic	46.07	3	15.36	8.36	0.0215
Cubic	7.01	3	2.34	2.15	0.3331
Residual	2.17	2	1.09		
Total	10073.05	15	671.54		

**Lack of Fit Tests**

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Linear	62.53	9	6.95	6.39	0.1425
2FI	53.08	6	8.85	8.14	0.1134
Quadratic	7.01	3	2.34	2.15	0.3331
Cubic	0.000	0			
Pure Error	2.17	2	1.09		

**Model Summary Statistics**

Source	Std. Dev.	R-Squared	Adjusted R-Squared	Predicted R-Squared	PRESS
Linear	2.43	0.4717	0.3276	0.0970	110.60
2FI	2.63	0.5489	0.2105	-0.4422	176.63
Quadratic	1.36	0.9250	0.7901	0.0445	117.02
Cubic	1.04	0.9823	0.8758		+

+ Case(s) with leverage of 1.0000: PRESS statistic not defined

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Table Appendix D-30. Design-Expert® output of ANOVA for the reduced model of correlation between formulation ingredients and the entrapment efficiency of formulation number 31 to 45

**Response: Entrapment Efficiency**

**Backward Elimination Regression with Alpha to Exit = 0.050**

Forced Terms		Intercept				
Removed	Coefficient Estimate	t for H0 Coeff=0	Prob >  t	R-Squared	MSE	
C	0.076	0.16	0.8798	0.9247	1.54	
AB	0.12	0.20	0.8499	0.9242	1.33	
C <sup>2</sup>	0.57	0.95	0.3747	0.9144	1.31	
AC	0.89	1.56	0.1585	0.8886	1.52	
BC	1.25	2.03	0.0734	0.8377	1.99	

**ANOVA for Response Surface Reduced Quadratic Model**  
Analysis of variance table [Partial sum of squares]

Source	Sum of Squares	DF	Mean Square	F Value	Prob > F
Model	102.60	4	25.65	12.91	0.0006
A	17.85	1	17.85	8.98	0.0134
B	39.87	1	39.87	20.06	0.0012
A <sup>2</sup>	36.38	1	36.38	18.30	0.0016
B <sup>2</sup>	11.14	1	11.14	5.61	0.0394
Residual	19.87	10	1.99		
Lack of Fit	17.70	8	2.21	2.04	0.3707
Pure Error	2.17	2	1.09		
Cor Total	122.47	14			

Std. Dev.	1.41	R-Squared	0.8377
Mean	25.76	Adj R-Squared	0.7728
C.V.	5.47	Pred R-Squared	0.6328
PRESS	44.98	Adeq Precision	11.166

Factor	Coefficient Estimate	DF	Standard Error	95% CI Low	95% CI High	VIF
Intercept	23.16	1	0.68	21.65	24.67	
A-PLA:PGA ratio	1.49	1	0.50	0.38	2.60	1.00
B-Curcuminoids	-2.23	1	0.50	-3.34	-1.12	1.00
A <sup>2</sup>	3.13	1	0.73	1.50	4.76	1.01
B <sup>2</sup>	1.73	1	0.73	0.10	3.36	1.01



**Final Equation in Terms of Coded Factors:**

$$\text{Entrapment Efficiency} = +23.16 + 1.49 * A - 2.23 * B + 3.13 * A^2 + 1.73 * B^2$$

**Final Equation in Terms of Actual Factors:**

$$\begin{aligned} \text{Entrapment Efficiency} = & +35.21010 - 3.94755 * \text{PLA:PGA ratio} - 1.85721 * \text{Curcuminoids} \\ & + 0.78240 * \text{PLA:PGA ratio}^2 + 0.10826 * \text{Curcuminoids}^2 \end{aligned}$$

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## BIOGRAPHY

Miss Praewpun Boonyasirisri was born on October 22, 1974 in Bangkok, Thailand. She received her Bachelor Degree of Science in Pharmacy from the Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok in 1998. Since graduation, she have been worked as a production planner in the Production Department of the Government of Pharmaceutical Organization (GPO), Bangkok. In 2002, she got a scholarship from GPO for graduate study in Pharmaceutical Technology (International Program), Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok. In 2003, she got a Grant for research publication, provided by the Ministry of University Affairs (or the Commission on Higher Education, Ministry of Education at present), Thailand, from the Graduate School of Chulalongkorn University.