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VARIABLES OPTIMIZATION IN SYNTHESIS OF SURFACTANT FROM HEXADECANOIC ACID AND ARGININE USING CCD AND ANOVA METHOD

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ABSTRACT

Surfactant synthesis from hexadecanoic acid and arginine is influenced by several variables, including catalyst amount (A), mix solvent (B), and arginine to an acid ratio (C). For this reason, Central Composite Design (CCD) and Analysis of Variance (ANOVA) methods are used to optimize the values of the three variables that can produce a maximum surface response. In this work, the synthesis was carried out at a temperature of 60°C for 4 hours and a motor rotation of 250 rpm, using a calcium oxide catalyst and tert-amyl alcohol as a solvent. In addition, the effect of A, B, and C were discussed in terms of the percent conversion of hexadecanoic acid. Of the three variables observed, the percent conversion mainly depends on the arginine to acid ratio and is less influenced by the catalyst amount. The ANOVA results show that the recommended model is a quadratic model, with adjusted R^2 0.8823 and predicted R^2 0.2476.

Keywords: arginine, analysis of variance, central composite design, hexadecanoic acid.

INTRODUCTION

Response surface method (RSM) is an experimental strategy that is useful if the response is influenced by several factors and the aim of the experiment is to find the correct variable value to produce an optimum response [1]. The RSM method makes it easy to determine suitable conditions for a synthesis. RSM is used to observe individual effects and interactions to optimize the effect of variables so that the maximum response is obtained. The most famous and frequently used design in RSM is the Central Composite Design (CCD) [2, 3].

Surfactants are widely used as dispersants, foaming, emulsifier, adhesive components. Surfactants have been made using fatty acids, methyl esters, hexadecanol, and docosanol. In applying fatty acids as a surfactant raw material, fatty acids with a group number of 16 can also be used, one of which is hexadecanoic acid [5-8].

Hexadecanoic acid is a saturated fatty acid composed of 16 carbon atoms (CH3(CH2)14COOH). Hexadecanoic acid is a long-chain saturated fatty acid with a high melting point of 64°C. Plants from the Palmaceae family, such as oil palm, are the primary hexadecanoic acid production. Palm oil contains about 50% hexadecanoic acid. The most famous use of hexadecanoic acid is an essential component in soap making. Hexadecanoic acid is an essential source of calories but has relatively low antioxidant power. Increasing the chain length (number of carbon atoms) causes the irritant potential of the resulting surfactant to decrease while the ability to build viscosity increases [8-10].

The potential of amino acid-based surfactants in bulk detergents for industrial and household cleaning uses is highly dependent on the use of renewable and inexpensive raw materials with rapid biodegradability. Amino acids are alternative ingredients in surfactants and are widely used in various applications. For example, arginine-based surfactants such as N-dodecanoyl arginine are readily prepared from the reaction between oil-soluble dodecanoic acid and arginine [11-13].

Amino acids that can be used are lysine, histidine, and tryptophan. For this reason, arginine-based amino acid surfactants can be considered. Arginine-based surfactants are amphiphilic compounds with excellent self-assembling properties, low toxicity profile, high biodegradability, and broad antimicrobial activity. Therefore, this type of surfactant can be used as a preservative and antiseptic in pharmaceutical, food, and dermatological formulations [14, 15].

Making surfactants has been carried out using NaOH, calcium oxide, H_2SO_4 as catalysts. One of the most widely used catalysts is CaO because it has many advantages such as low price, long catalyst life, high activity, and only requires moderate reaction conditions, although some disadvantages are found in CaO catalysts which have the low surface area and are easy to melt [16-20]. This research used tert-amyl alcohol as a solvent. The use of tert-amyl alcohol has several advantages, including lower toxicity of tert-amyl alcohol and tert-amyl alcohol is inert, so it does not reduce the product mixture and the solvent tert-amyl alcohol is a non-polar solvent [3, 20, 21].

MATERIALS AND METHODS

The materials used are hexadecanoic acid ($C_{16}H_{32}O_2$), calcium oxide (CaO), tert-amyl alcohol ($C_5H_{12}O$), citric acid, and acetone, all from Merck, Darmstadt, Germany. In addition, arginine ($C_6H_{14}N_4O_2$) was purchased from GNC. All other reagents were analytical grade.

The preparation of amide was performed in a 250 mL double-necked conical flask at 60°C using a magnetic stirrer at 250 rpm. The temperature and rpm were controlled automatically. The reaction mixture consisted of hexadecanoic acid (5 grams), and arginine was placed in the reaction vials. The molar ratio and other parameters

were varied as given in Table-1. The optimum reaction temperature was obtained by experimenting with various temperature variations. Different amounts of catalysts, which were generated by RSM with CCD, were subsequently added. The mixture was incubated in mineral oil for four h. Each component was isolated by crystallization in acetone at -4^{o}C, and the product identification was operated by FTIR. This amide product is then analyzed for its acid number and saponification number. The moles of acid reacted were calculated from the values obtained for the blank (without catalyst) and test samples. Finally, the amide formed was expressed as equivalent to the conversion of the acid.

RESULTS AND DISCUSSIONS

The study was conducted to determine the optimum value in the amidation process by optimizing the effects of A, B, and C. To observe the effect of the interaction between the three variables, it was chosen to use RSM, which uses the Desirability Function approach, with a Central Composite Design of 3 variables consisting of 20 treatments and run randomly [1].

The optimization results using CCD and RSM are shown in Table-1. Table-1 shows the optimized components, optimization objectives, upper and lower limits, and the importance of each component. The results in Table-1 show that the highest results were obtained at concentrations of A=1, B=1, and C=1, which was 86.66%. Overall, it is seen that the converted fatty acids are already high, which is greater than 74%. The data from Table-1 will then be analyzed of variance to predict the model describing the relationship between A, B, and C to hexadecanoic acid, converted to N-palmitoyl arginine [7].

Analysis of Variance

The results of the ANOVA are observed with the conclusion that the recommended model is quadratic because the adjusted R-squared and predicted R-square produced are the largest compared to the linear and cubic models. Furthermore, the sequential model sums of squares results also suggest using the quadratic model because the order of the polynomials is the highest (316.01) and the additional terms are significant (0.0001), and the model is not aliased.

The summary statistical model in Table-2 also suggests that the quadratic model is appropriate because it has the maximum adjusted R-squared (0.7765) value. The results of the analysis of variance for the response surface quadratic model are shown in Table-3. The desired parameter function (DF) in Table-3 is used to assess the optimal operating conditions [1]. If the DF is closer to one, the intended response is the best. The model F-value of 8.33 implies that the model is significant. There is only a 0.13% chance that this large F-value could occur due to noise. In addition, this model has a p-value <0.05, so it is a significant model to describe the relationship between variables and responses. In this case, A^2, B^2, C^2 are significant model terms.

This shows that the square of the variables A, B, and C has a positive and significant effect in increasing the conversion of hexadecanoic acid. However, the interaction of AB, AC, and BC had no significant effect on the increase in conversion, indicated by Prob>F greater than 0.0500. Because values greater than 0.1000 indicate, the model terms are not significant. The lack of fit F-value 0f 2.80 implies that the lack of fit is insignificant relative to the pure error. There is a 14.12% chance that a lack of fit this large could occur due to noise. Non-significant lack of fit is good because the model is desired to fit.

The obtained R-squared is 0.8823, and the predicted R-squared is 0.2476. The predicted-R-squared of 0.2476 is not close to the adj R-squared of 0.7765 as one might typically expect. The difference is more than 0.2. This may indicate a significant block effect or a possible problem with the model and data. For this reason, the reduction model needs to be considered. All empirical models should be tested by doing confirmation runs. Adequate Precision measures the signal-to-noise ratio. A ratio greater than 4 is desirable. The ratio of 7,934 indicates an adequate signal. This model can be used to navigate the design space.

Table-1. Optimization results using CCD and RSM.

Run	A-Catalyst Amount	B-Mix Solvent	C-Arginine to Acid Ratio	R1- Conversion (%)
1	1	1	1	88.22
2	1	-1	-1	83.77
3	0	0	0	76.00
4	0	0	-1.682	82.44
5	1.682	0	0	80.44
6	0	0	1.682	83.55
7	1	1	-1	86.66
8	1	-1	1	84.66
9	0	0	0	74.44
10	0	0	0	75.11
11	-1	1	-1	79.77
12	-1	-1	-1	82.66
13	0	-1.682	0	85.33
14	-1	-1	1	82.00
15	-1.682	0	0	82.89
16	0	0	0	78.89
17	0	0	0	75.11
18	0	0	0	75.11
19	0	1.682	0	86.00
20	-1	1	1	90.00

Table-2. Model Summary Statistics.

Source	Standard Deviation	R- Square	Adjusted R-Square	Predicted R-Square
Linear	4.93	0.0663	-0.1088	-0.3375
2 FI	5.30	0.1223	-0.2829	-1.6411
Quadratic	2.21	0.8823	0.7765	0.2476
Cubic	1.58	0.9640	0.8860	-0.1579

Table-3. ANOVA results for response surface, quadratic models.

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob>F
Model	366.84	9	40.76	8.33	0.0013
A-Catalyst Amount	1.66	1	1.66	0.34	0.5732
B-Mix Solvent	11.79	1	11.79	2.41	0.1517
C-Arginine to Acid Ratio	14.12	1	14.12	2.89	0.1202
AB	0.22	1	0.22	0.046	0.8347
AC	6.34	1	6.34	1.30	0.2816
BC	16.70	1	16.70	3.41	0.0944
A^2	73.15	1	73.15	14.95	0.0031
B^2	193.80	1	193.80	39.62	<0.0001
C^2	106.87	1	106.87	21.85	0.0009
Residual	48.92	10	4.89		
Lack of Fit	36.05	5	7.21	2.80	0.1412
Pure Error	12.86	5	2.57		
Cor Total	415.76	19			

Final equation in terms of coded factors:

Acid conversion = +75.75 +0.35*A +0.93*B +1.02*C +0.17*AB -0.89*AC +1.45*BC +2.25*A2 +3.67*B2 +2.72*C2 (1)

The equation in terms of coded factors can be used to make predictions about the response for given levels of each factor. By default, the high levels of the factors are coded as +1, and the low levels of the factors are coded as -1. The coded equation is helpful for identifying the relative impact of the factors by comparing the factor coefficients.

Final equation in terms of actual factors:

Acid conversion = +75.750 +0.349*A +0.929*B +1.017*C +0.168*AB -0.890*AC +1.445*BC +2.253*A2 +3.667*B2 +2.723*C2 (2)

The equation in terms of actual factors can be used to make predictions about the response for given levels of each factor. Here, the levels should be specified in the original units for each factor. This equation should not be used to determine the relative impact of each factor because the coefficients are scaled to accommodate the units of each factor, and the intercept is not at the center of the design space.

The next stage of ANOVA is to carry out the following analysis. The first is the normal probability plot analysis of the studentized residuals to check for normality of residuals, as shown in Figure-1. This plot uses residual values instead of actual values. This plot is useful to see if the data is normally distributed. The normal distribution of data is indicated by plot points around the diagonal line [2]. So it can be concluded from Figure-1 that the plot points are as expected. Next is the analysis of studentized residuals versus predicted values to check for constant errors, as shown in Figure-2. If random points are obtained, as shown in Figure-2, this indicates that a normal distribution of residual values has been obtained, which means that the model obtained is already good [20]. Figure-3 shows further analysis in studentized residuals versus run analysis. The results obtained to state that there is an erratic pattern of the resulting conversion. This is good because it indicates that the resulting regression model is acceptable.

The following step was analyzed the predicted versus actual results, as shown in Figure-4. It can be seen that this image has plotting points that follow a diagonal line. This indicates that the predicted value is in line with the actual value obtained from research in the field [3].

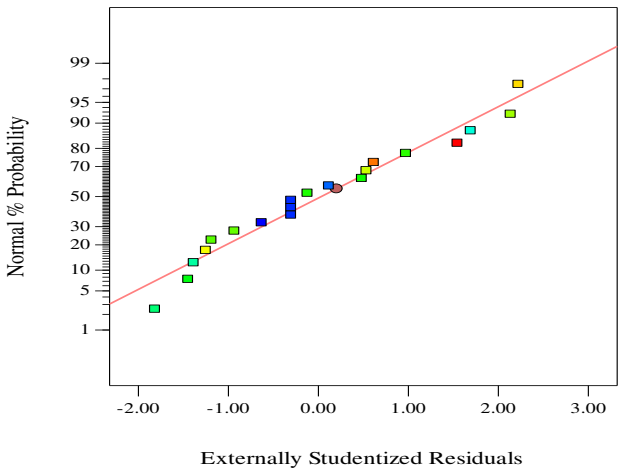

Figure-1. Normal probability plot of the studentized residuals.

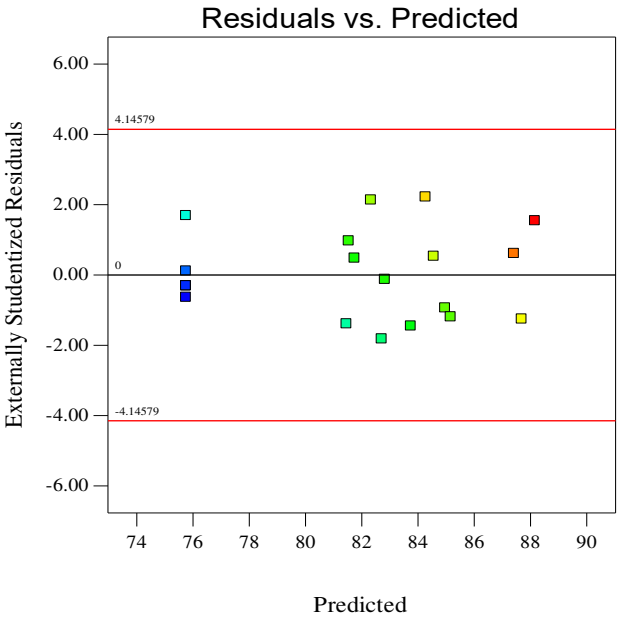

Figure-2. Analysis of studentized residuals versus predicted values.

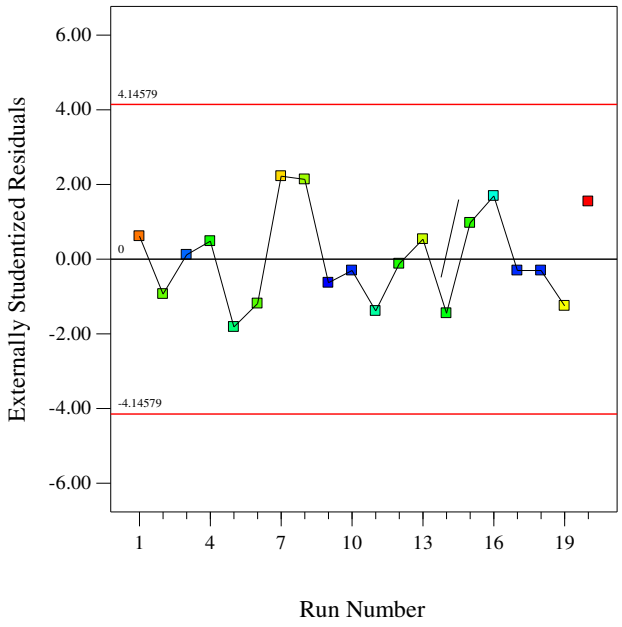

Figure-3. Analysis of studentized residuals versus the run number.

Process Variable Optimization

After obtaining a mathematical model for the response to the conversion of hexadecanoic acid, then optimization is carried out to obtain the desired response. Optimization aims to minimize the effort and cost required and maximize the desired response. Optimization was carried out by observing the interaction of the three variables to increase the conversion of hexadecanoic acid that reacts with arginine to N-palmitoyl arginine. Figure-5 shows the surface response for A's interaction with B at arginine to acid ratio = 0. This surface response indicates that high palmitoyl arginine will be obtained at A=1 and B=1. The yield of palmitoyl arginine will gradually decrease until it reaches a minimum at A=0 and B is also 0.

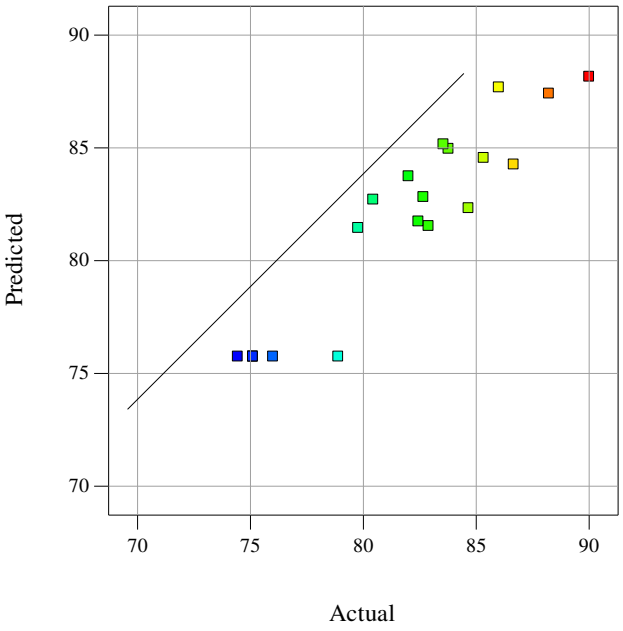

Figure-4. Analysis of predicted versus actual results.

This result is in line with other research studies where using a mixed solvent of hexane/isopropyl alcohol resulted in the best conditions with a percent yield of 70.3%. If the arginine to acid ratio increases to 1, the surface response obtained is shown in Figure-6. This surface response shows two areas where palmitoyl arginine has a maximum value, namely if A=1 and B=1, and A=-1 and B are used. =1. However, Figure-6 shows that the minimum surface response shifts to the right, namely with an increase in the amount of catalyst [16].

Figure-7 will show the surface response if A's interaction with Cis is observed. The response is in the form of conversion of hexadecanoic acid. The mix solvent ratio was fixed at 0. The surface response indicated that the best palmitoyl arginine would be obtained if A and C were used, which were also maximum. The surface also shows that at A=-1, the minimum value will produce the best palmitoyl arginine. So, these two options can be considered in a larger scale synthesis [21].

If the mix solvent ratio increases to 1, the observed A and C interactions are shown as surface responses in Figure-8. This response shows the same trend as Figure-7, where the maximum palmitoyl arginine product obtained at C=1 and A=- 1 or C=1 and A is also 1. At this ratio of mix solvent=1, the minimum surface will shift to the left, i.e., less catalyst. Therefore, it can be concluded that increasing the mixed solvent will decrease the yield of palmitoyl arginine at A, starting from -1 to 0 [20].

The amount of hexadecanoic acid converted to palmitoyl arginine was also observed in the interaction between B and C. The resulting surface response is shown

in Figure-9 for the amount of catalyst 0 and Figure-10 for the amount of catalyst 1. In Figure-9, the best palmitoyl arginine is obtained if B=1 and C are also 1. Reducing the amount of B and C will gradually decrease the conversion until the conversion reaches a minimum level at B=0 and C=0. Furthermore, it was observed that the reduction of B and C until it reached the minimum limit would increase the conversion of hexadecanoic acid, although not maximally.

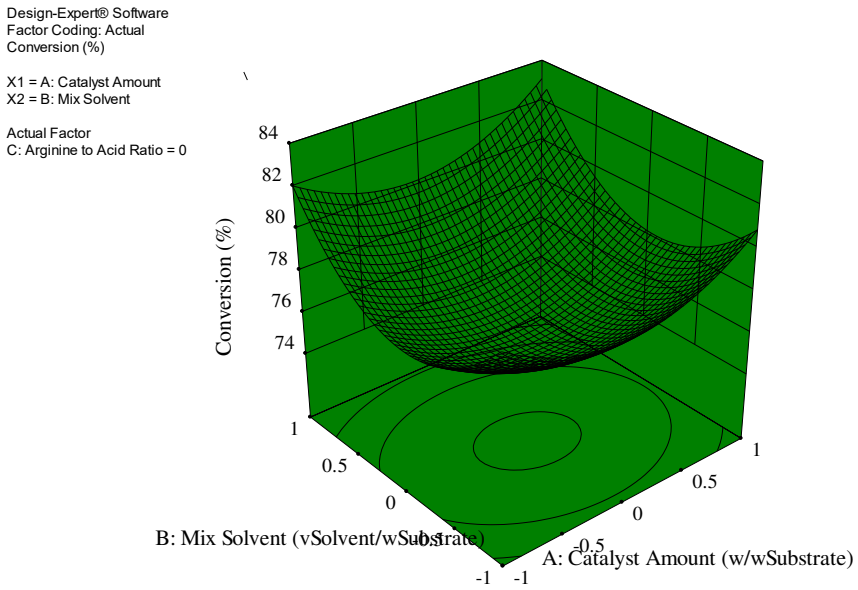

Figure-5. Surface response for interaction A with B at arginine to acid ratio = 0.

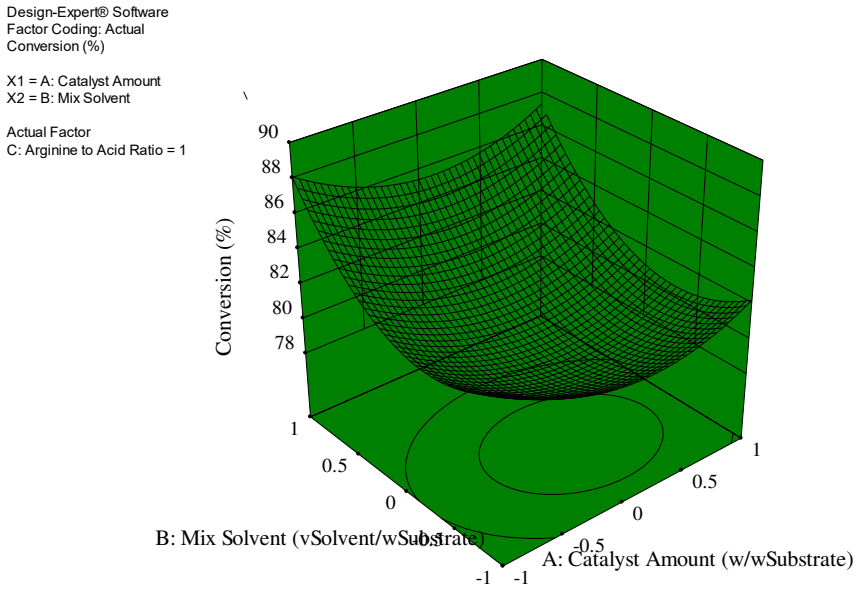

Figure-6. Surface response for interaction A with B at arginine to acid ratio = 1.

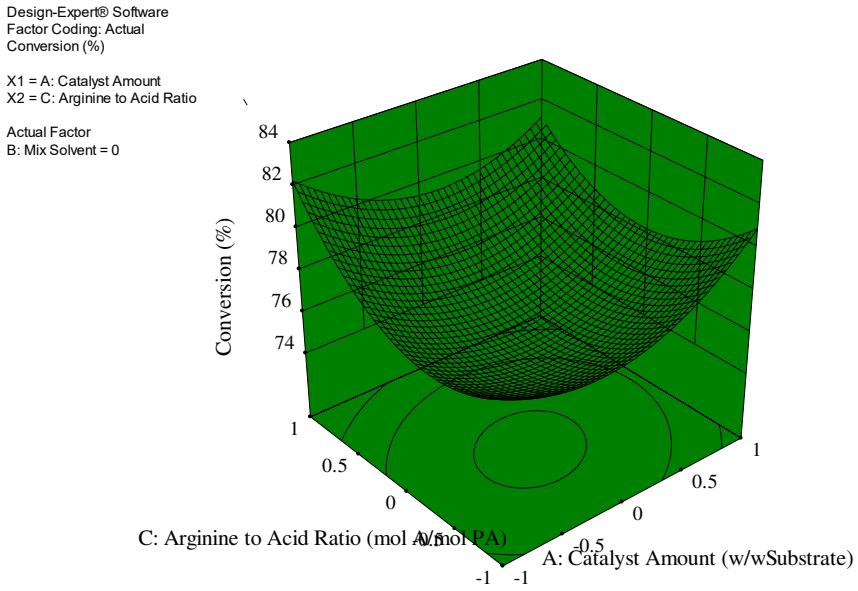

Figure-7. Surface response for the interaction of A with C in the mix solvent = 0.

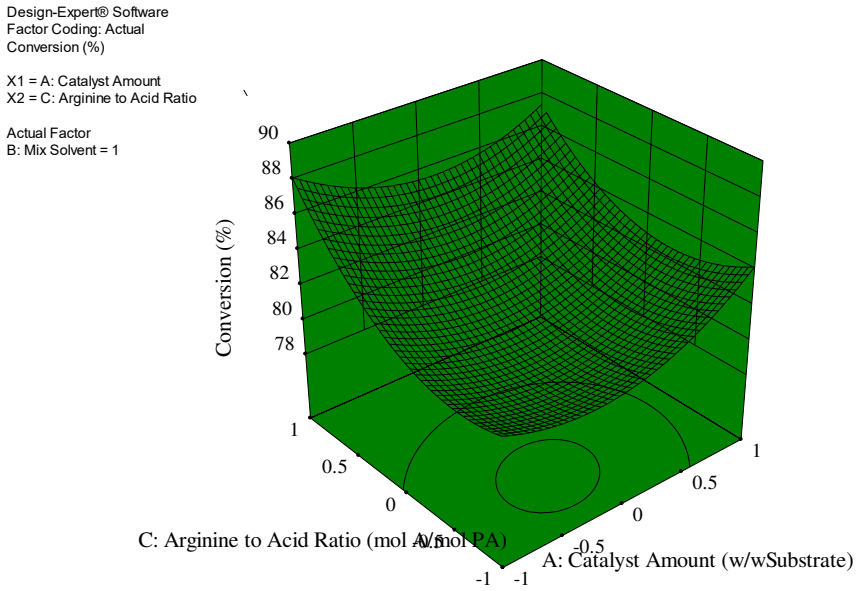

Figure-8. Surface response for the interaction of A with C in the mix solvent = 1.

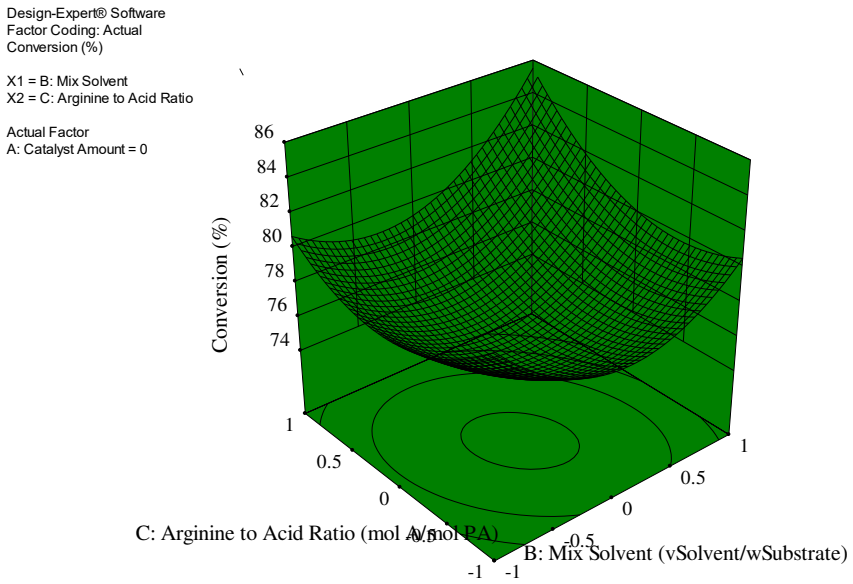

Figure-9. Surface response for interaction B with C at catalyst amount = 0.

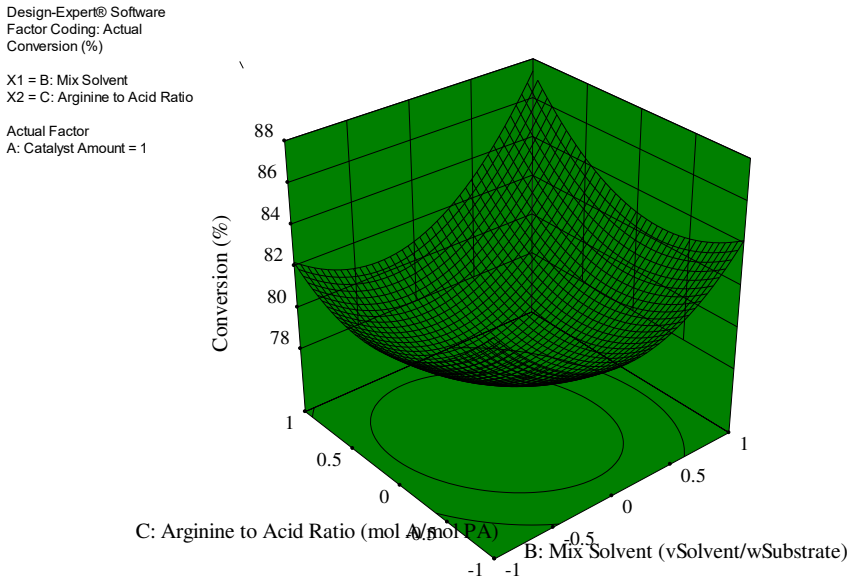

Figure-10. Surface response for the interaction of B with C at catalyst amount = 1.

The surface response in Figure-10 is obtained if the catalyst = 1. The interaction response between B and C shows a more expansive minimum zone if catalyst = 1. The minimum zone of 82% is still within reasonable limits because it is already above 80%. Hexadecanoic acid was converted more than 80% to palmitoyl arginine over the selected variable range. The highest conversions to produce amides were also observed at B=1 and C=1.

CONCLUSIONS

The reaction conditions, including A, B, and C, were studied, and the best hexadecanoic acid conversion surface response of 86.66% was obtained for the values A, B, and C, located at code +1. The normal probability plot analysis results show that the plot points are as expected. The studentized residuals versus predicted value analysis also indicate that the model obtained is also good. The analysis of predicted versus actual results shows plotting points that follow a diagonal line, which indicates that the predicted value is in line with the actual value obtained from research in the field.

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