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A SYSTEMATIC STUDY OF THE VARIABLES THAT CONTROL THE SYNTHESIS OF N-ACYL L-LYSINE FROM HEXADECANOIC ACID IN A STIRRED TANK REACTOR

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ABSTRACT

The research carried out is related to developing the process of making surfactants based on amino acids from renewable natural resources. At this stage, the potential for hexadecanoic acid (HA) and L-lysine (L) to be synthesized into a surfactant based on the amino acid N-acyl L-lysine was observed in a stirred tank. For this reason, the research was planned with a specific objective to examine the effect of the substrate ratio, solvent ratio, and catalyst concentration on amide recovery using the Box-Behnken Design. Furthermore, analysis of the interaction effect of the research variables is carried out, compiling an optimization equation model and assessing the optimum reaction conditions to obtain the maximum conversion response. The product purification process is carried out by adding 5 ml of 10% citric acid and then filtration with filter paper then heated at 90 °C to evaporate the remaining solvent. The optimum conversion percentage obtained is 78.084%, which can be generated through six composition options with the same desirability value, 0.851. Among the six options, the substrate ratio of 2.956 (L/HA), the solvent ratio of 2.0 (MS/S), and catalyst concentration of 5% (w/wHA) were selected as the best process variable values at a reaction temperature of 65 °C and reaction time 2 h.

Keywords: N-acyl L-lysine, L-lysine, hexadecanoic acid, mix solvent.

INTRODUCTION

The synthesis of surfactants with various amino acids has been widely carried out from a combination of fatty acids, alcohols, and amines [1]. The utilization of amino acid surfactants can be carried out in various aspects, such as in detergents, cosmetics, pharmaceuticals, and the textile industry [2, 3, 4]. In the surfactant N-acyl amino acids, the amino acid group is called hydrophilic. This part is soluble in water, and the N-acyl group is called lipophilic, where this part is insoluble in water but can dissolve in oil [5]. The synthesis of surfactant N-acyl amino acids is a condensation process of fatty acids and amino acids with a catalyst [6, 7].

One of the long-chain saturated fatty acids is hexadecanoic acid, which is triglycerides and is obtained from vegetable or animal oils. Hexadecanoic acid is an abundant ingredient with a content of 56.84% in palm oil. This compound's chemical formula is $CH_3(CH_2)_{14}COOH$, which is white and solid at room temperature. Hexadecanoic acid is widely used in cosmetics and coloring fields [8,9].

So far, many amides have been produced using a chemical catalyst through a reaction between a fatty acid or fatty acid methyl ester and an amine using a sodium methoxide catalyst. Amide synthesis using biocatalysts has also been carried out through reactions between fatty acids and amines. Apart from using chemical stimuli and biocatalysts, there is also alkanolamide synthesis using metal catalysts. Another alternative can be a modification of a solid catalyst to improve the quality of a product. Calcium oxide is an excellent solid catalyst and can be modified with other catalysts [10, 11, 12].

Surfactants are compounds that have groups that are easy to compound with water (hydrophilic) and groups that are easy to compound with oil (lipophilic). The dominance of one of the groups on the surfactant molecule is one parameter that needs to be known [13]. If the surfactant's polar groups are more dominant than the non-polar groups, the surfactant molecules will be absorbed more strongly by water than by oil. Therefore, to reduce the water content and increase the surfactants' oil absorption ability, it is possible to apply vacuum conditions in a series of experiments [14, 15].

Using a good mixing unit can increase the efficiency of the process and the reaction scale. In a stirred tank where the tank volume is relatively large, the residence time is also considerable, meaning that the reagents can react longer in the tank. It is necessary to design a well-stirred tank so that surfactant synthesis can occur optimally using a catalyst. Factors that need to be considered include tank height, tank diameter, type of stirrer used, and bulkhead. For the tank design, the ratio between height (H) and diameter height (Dt)= 1:1. Turbine impellers are very effective at various types of viscosities. This impeller is powerful and withstands high speeds, and the impeller is very suitable for avoiding dead zones. The number of impeller blades is usually 4 to 16 but generally 6 or 8. The ratio of impeller diameter (Da) to impeller width (W) is 1:8. The balance between the impeller diameter and the tank diameter is in the range = 0.3 - 0.5. The impeller can be positioned 1/3 from the bottom of the tank [16,17].

Research conducted by Zhang *et al*., in 2014 showed that the use of a CaO catalyst as a single catalyst and modified CaO in the synthesis of fatty amide acids from vegetable oils were able to produce good yield values. Calcium oxide is a catalyst that is environmentally friendly and very useful for industrial applications. The

yield results obtained using standard catalysts such as potassium hydroxide, potassium sulfite, and calcium oxide were 72%, 75%, and 89%. This study's optimum operating conditions were catalyst weight of 20% CaO, an operating temperature of 130 °C, and operating time of 3 hours [18]. This study used hexadecanoic acid as a reactant and mixed solvent as the reactant solvent. L-Lysine is a type of amino acid used and a calcium oxide catalyst to support the reaction. It is necessary to scale up for the synthesis of surfactant N-acyl L-lysine from hexadecanoic acid and l-lysine using calcium oxide chemical catalysts with mixed solvents in a stirred tank. In this study, the stirred tank was designed based on literature [19].

The competition between the formation of amides, esters, and amide esters which causes a decrease in surfactant yield, is one of the surfactant manufacture problems. So, the reaction conditions need to be well regulated. One way to optimize the research variables' reaction is to use the Response Surface Method [20]. The most well-known and frequently used research designs include the Central Composite Design (CCD) and the Box-Behnken Design (BBD). The Box-Behnken design has advantages over CCDs. The advantage is that this design is more efficient with fewer trial runs, especially for experiments with 3 or 4 factors [21,22].

MATERIALS AND METHODS

Materials

The primary raw materials used are L-Lysine ($C_6H_{14}N_2O_2$), hexadecanoic acid ($C_{16}H_{32}O_2$), and calcium oxide (CaO) catalyst. While the auxiliary materials used for purification and yield analysis are hexane (C_6H_{14}), 2-propanol (C_3H_8O), potassium hydroxide (KOH), phenolphthalein, and hydrochloric acid (HCl). L-lysine and other materials are obtained from Merck, Darmstadt, Germany.

Methods

The variables observed in this optimization study include the raw material ratio, solvent ratio, and L-lysine concentration, with a box design as in Table-1. The method used refers to the study by Syukri et al. (2019). First, hexane's solvent mixture: 2-propanol is added to the beaker with a ratio of 1: 1 (w/w). Added L-Lysine (Lys) into the beaker glass and homogenized. The reactor is filled with the desired amount of hexadecanoic acid feed. Next, the heating jacket is set to the desired temperature, and the stirrer is turned on. After the hexadecanoic acid reaches the desired temperature, a mixture of l-lysine and solvent is added, and the reactor is heated to a temperature of 70 ^oC. After temperature cooling to 65 ^oC, the reaction was carried out for two h along with 3-7% of CaO addition. Each time interval of 1 hour, samples were taken to analyze the hexadecanoic acid's acid value, the residual reaction [9].

Purification of the product was carried out by adding 5 mL of 10% citric acid, filtering the catalyst, and evaporating the solvent at 90 °C using a rotary evaporator. The product mixture is then washed with acetone to dissolve excess l-lysine and then filtered. The final product will be obtained as a filtrate and cooled at -4 ^oC for 24 hours for further analysis.

Optimization Procedure

Design Expert 10.0.1.0 software is used for making formulation and response designs. Two groups of variables are used, namely fixed variables and independent variables. Reaction time and temperature are used as selected variables because they are considered not to affect the response. In contrast, the substrate ratio, solvent ratio, and amount of catalyst are used as changing variables because these three variables are considered to affect the response.

The Box-Behnken output will bring up the design of the experiment, including the experiment run and its combinations [21]. Furthermore, each run is run based on design of experiment (DOE), then the resulting data on the conversion of fatty acids will be inputted into the Design Expert 10.0.1.0 software to be optimized. Optimization analysis of the condensation process is carried out by processing the data to obtain an accounting of variability, optimization equation models, contour plots, and the optimum conditions for the condensation process [8, 12].

Table-1. Optimization results of n-palmitoyl lysine synthesis.

Run	Factor 1 A: Substrate L/HA	Factor 2 B: Solvent Ratio (MS/S)	Factor 3 C: catalyst (%)	Response 1 HA Conversion (%)
1	2	3	5	72.70
2	3	2	5	73.89
3	4	3	5	77.55
4	4	1	5	76.44
5	4	2	7	76.44
6	4	2	3	71.50
7	2	2	3	71.82
8	3	2	5	74.21
9	3	1	7	74.37
10	3	2	5	74.37
11	2	2	7	72.77
12	3	3	7	73.57
13	3	3	3	74.53
14	2	1	5	71.66
15	3	1	3	74.21

Table-2. Model summary statistics.

Source	Standard Deviation	R-Squared	Adjusted R-Squared	Predicted R-Squared
Linear	1.36	0.5473	0.4239	0.0348
2FI	1.42	0.6427	0.3748	-0.8849
Quadratic	1.52	0.7444	0.2844	-3.0526
Cubic	0.24	0.9973	0.9814	

Table-3. ANOVA for response surface quadratic model.

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob>F
Model	33.52	9	3.72	1.62	0.3098
A-Substrate Ratio	21.06	1	21.06	9.15	0.0293
B-Solvent Ratio	0.35	1	0.35	0.15	0.7132
C-Catalyst	3.24	1	3.24	1.41	0.2888
AB	1.225E-003	1	1.225E-003	5.322E-004	0.9825
AC	3.98	1	3.98	1.73	0.2456
BC	0.31	1	0.31	0.14	0.7272
A^2	0.34	1	0.34	0.15	0.7166
B^2	1.99	1	1.99	0.86	0.3951
C^2	1.92	1	1.92	0.83	0.4031
Residual	11.51	5	2.30		
Lack of Fit	11.39	3	3.80	63.55	0.0155
Pure Error	0.12	2	0.060		
Cor Total	45.03	14			

RESULTS AND DISCUSSIONS

This study chose BBD as a form of experimental design because it is considered a systematic method to obtain interactions between variables. The advantage is that this design is more efficient with fewer trial runs, especially for experiments with 3 or 4 factors [20].

The condensation parameters were normalized as coded variables so that they could affect the response more completely. From this design, it is obtained the interaction of three variables, namely the substrate ratio (A), the solvent ratio (B), and the weight of the catalyst (C). Optimization results of the synthesis of N-acyl L-lysine in percentage conversion values are shown in Table-1. The synthesis of n-palmitoyl lysine surfactant was obtained from the difference between the acid number at the beginning and the end of the reaction.

ANOVA analysis was performed for each response variable. An appropriate ANOVA model was chosen among the suggested models, namely the one capable of producing the highest level of significance. In this design, there are linear, quadratic, special cubic, and cubic ANOVA models. The equation obtained is then tested with model verification, residual assumption test, resulting contour plot, and optimum conditions [20, 22].

Model Verification

Verification is carried out after the optimum process conditions are obtained. Verification is carried out with two repetitions, and the results of the verification obtained will then be compared with the value of the response variable predicted by RSM, which has been equipped with a prediction of the value of each response so that its suitability can be seen at the verification stage [21]. The relationship between the actual value and the predicted value is expressed by a standard graph plot of residuals, as shown in Figure-1. It is found that the actual value will approximate the predicted result, which is indicated by the data points that usually spread and approach a straight line.

To evaluate the developed model, the correlation coefficient and standard deviation are used. If the value of R^2 is close to 1, it means that the standard deviation is more minor, and the model is better at predicting the response. The summary statistical model shown in Table 2 states that the standard deviation obtained is relatively tiny, namely 1.52, and the R^2 value is relatively high, namely 0.7444.

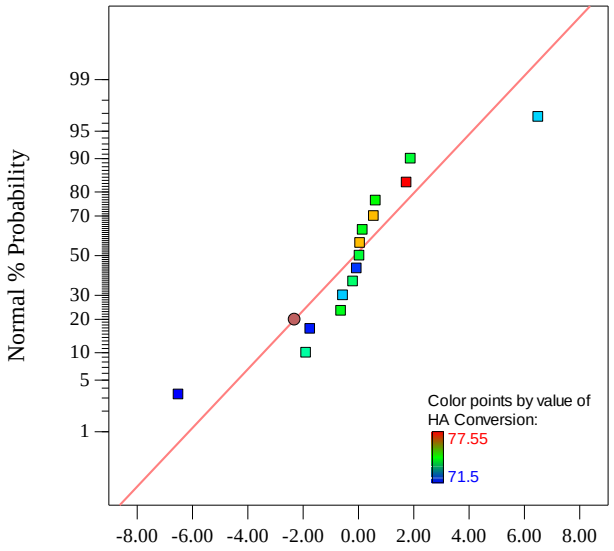

Figure-1. Standard graph plot of residuals.

Table-2 also states that the quadratic model for the R1 response is not aliased, which means that the quadratic model can describe the relationship between the hexadecanoic acid conversion response to the interaction of the substrate ratio, solvent ratio, and catalyst concentration.

Model verification is done by three tests, namely the simultaneous regression coefficient test, individually, and the lack of fit test. The regression coefficient test was conducted to review whether independent variables had a significant effect on the response. This test is carried out simultaneously and individually. The lack of fit test is conducted to determine whether the model is acceptable or not [20].

Table-3 shows the results of the ANOVA for the response surface quadratic model. The regression coefficient test results simultaneously can be seen in Table-3, where the F_{count} value is obtained at 1.62. If the F_{count} value of each response is compared with F_{table}, which is 4.772, then the conclusion is $F_{count} < F_{table}$. That is, H_0 is accepted. The accepted null hypothesis indicates that the model is statistically acceptable, and there is at least one independent variable that has a significant effect on the response. If none of the independent variables has a significant effect on the response, then the null hypothesis is rejected, and the model cannot be accepted statistically [21].

Data from the individual regression coefficient test results for each response can also be seen in Table-3. If the α value is set (the level of significance), the allowable error is one minus confidence level. The confidence level used is 95% so that the value of $\alpha = 0.05$ is obtained, meaning that the research results have a 95% chance of being correct and a maximum error tolerance of 5%. The regression coefficient test results individually can be seen based on the regression coefficients of the

independent variables, the independent variables' squares, and the interaction between the independent variables [8].

In Table-3, it can be seen that the p-value of each variable substrate ratio, solvent ratio, and catalyst weight is 0.0293; 0.7132, 0.2888, respectively. If the value is smaller than α (p-value <0.05), this variable has a significant effect.

Using the Design-Expert Software, we also get an equation model, where the equation model is used to get the model's conversion value. Next, the model conversion value is used as a comparison with the actual conversion value. The final equation in terms of coded factors is as follows.

$$HA\ Conversion = 74.16 + 1.62A + 0.21B + 0.64C + 0.018\ AB + 1.00AC - 0.28BC - 0.30A^2 + 0.73B^2 - 0.72C^2$$

The equation in terms of coded factors can be used to make predictions about the response for each factor's given levels. Where A = Substrate Ratio (mol lysine / mol Hexadecanoic acid), B = Solvent Ratio (vol. Mix solvent / vol. Substrate), C = Weight of catalyst (gram CaO / gram substrate).

The equation in terms of coded factors can be used to make predictions about the response for each factor's given levels. Figure-2 shows the comparison of the actual conversion value with the model conversion value. It can be seen that there is an insignificant deviation in the resulting conversion value. The deviation is obtained from the standard deviation value of the model.

The ANOVA analysis results in Table-3 show that the appropriate model for yield response is the quadratic model because this model has a higher R^2 than other models, namely 74.44%.

The lack of appropriate F-value HA conversion response with a value of 63.55 indicates a significant lack of fit. This shows that there is still a mismatch of the conversion response data with the resulting model. There is only a 1.55% chance that a lack-of-fit value, as a result, occurs due to noise.

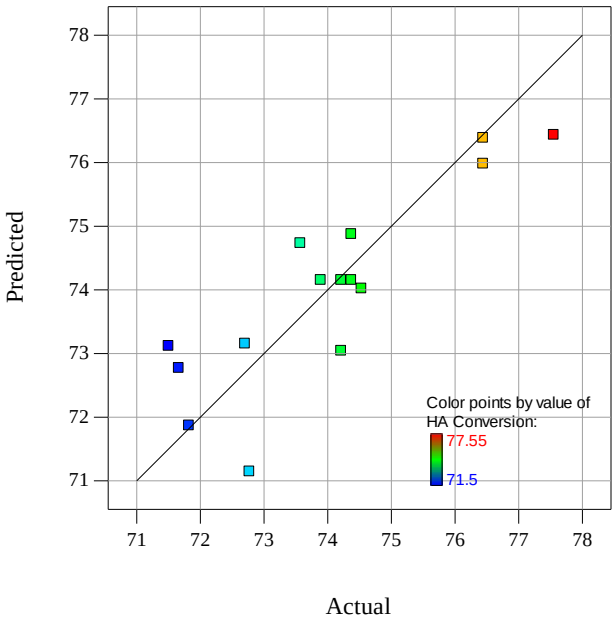

Figure-2. Comparison of the actual conversion value with the model conversion value

Identical and Independent Assumption Test

Identical assumption testing aims to check whether the residual variance of the model obtained is the same. Figure-3, it can see the relationship between the residual conversion value and the predicted conversion value. It can be seen that the residual values are randomly distributed and do not form a specific pattern. This indicates that the exact residual assumption test is fulfilled. If the residual value is not spread out (evenly) and forms a specific pattern, then the exact residual assumption test is not fulfilled [12].

The independence assumption test aims to determine whether the independent variables are interrelated or correlated. Figure-4 is the residual curve for the sequence of experiments. Suppose a residual point does not form a specific pattern in the form of a straight line (random) on different experiments. In that case, it can be concluded that the independent assumptions are fulfilled. On the other hand, if a residual point forms a specific pattern of straight lines on different experiments, it can be concluded that the independent assumptions are not fulfilled. In the curve of Figure-4, it can be seen that the residual points tend not to form a specific pattern in the form of a straight line on different experiments, so it can be concluded that the independence assumption is fulfilled [20].

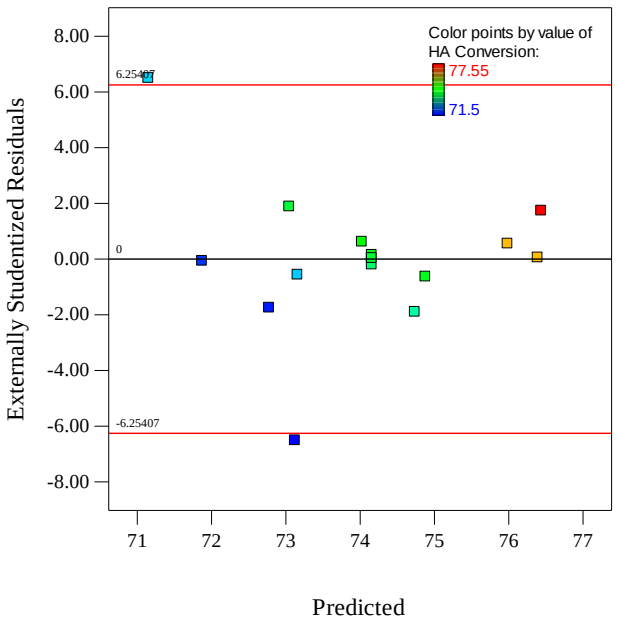

Figure-3. The relationship between the residual conversion value and the predicted conversion value.

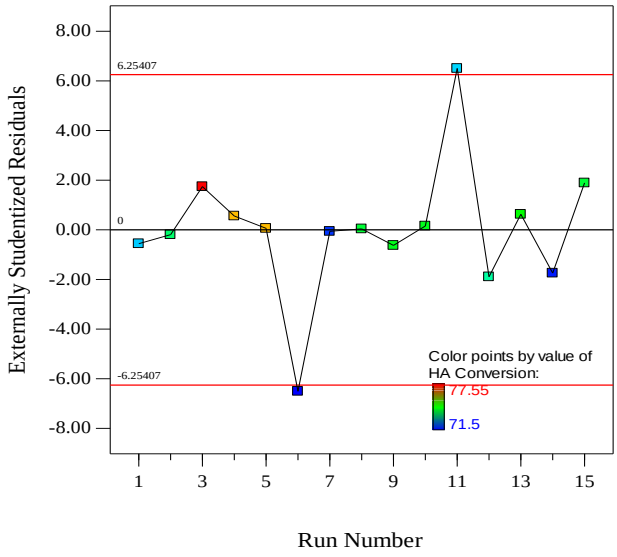

Figure-4. Residual curves against the sequence of experiments.

Contour Plot of Substrate Ratio and Solvent Ratio

The observations in Figure-5, Figure-6, and Figure-7 show contour plots of the effect of the substrate ratio and solvent ratio on the conversion of N-acyl L-lysine, at constant catalyst weight of 3%, 5%, and 7%, respectively.

The contour plot in Figure-5 shows that the increase in N-acyl L-lysine conversion is sharper when the solvent ratio increases than when the substrate ratio increases. The contour plot in Figure-6 shows that the increase in N-acyl L-lysine conversion is sharper as the substrate ratio and solvent ratio increase. It can be said that in this contour plot, the ratio of the substrate to the solvent is proportional. This contour plot is the best contour plot obtained from the experimental results. The contour plot in Figure-7 shows that the increase in N-acyl L-lysine conversion is sharper when the solvent ratio increases than when the substrate ratio increases.

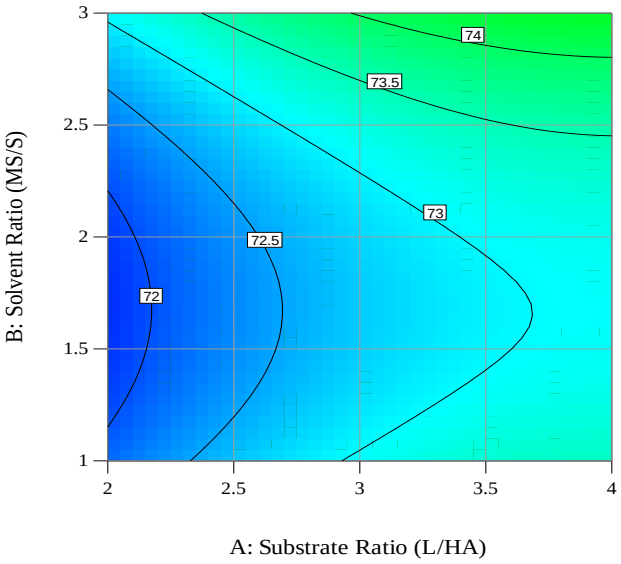

Figure-5. Contour plot of the substrate ratio and solvent ratio at 3% catalyst weight.

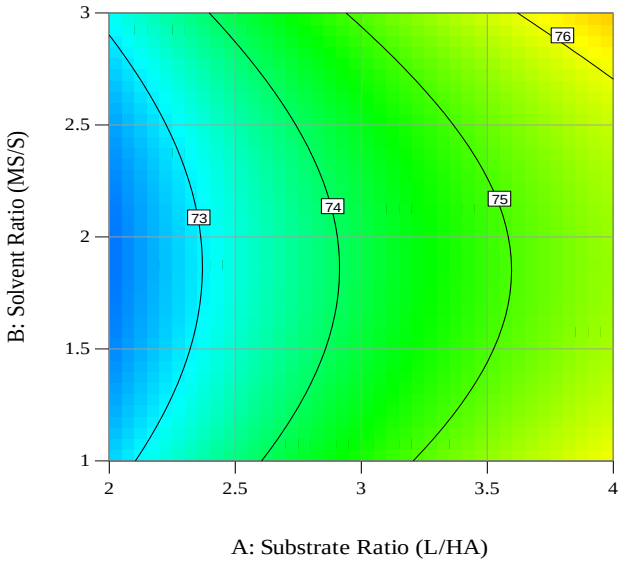

Figure-6. Contour plot of substrate ratio and solvent ratio at 5% catalyst weight.

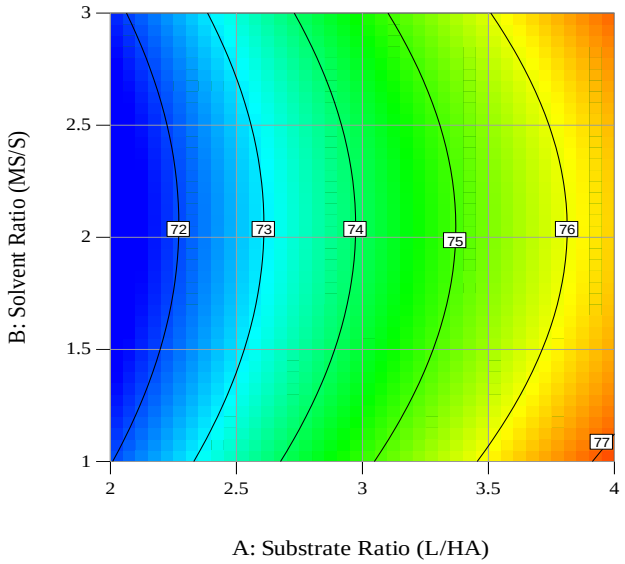

Figure-7. Contour plot of substrate ratio and solvent ratio at 7% catalyst weight.

From the optimization results, the best results were obtained in run IV with the substrate ratio in the ratio 1: 4 (HA: L), while the solvent ratio of 1: 3 (S: MS) with 5% catalyst weight resulted in the best conversion of 77.55% when viewed from the contour plot in Figure 6 with this comparison is in the area with a conversion> = 77%. Surfactants derived from various amino acids that are reacted with palmitic acid have a conversion range between 74 and 81% [1].

The contour plot in Figure-7 shows the best conversion area obtained at the ratio of the substrate ratio (HA: L) 1: 3 and the solvent ratio (S: MS) 1: 3, where the percent conversion is obtained> = 77%. From the three interactions between the substrate ratio and the solvent ratio, it was found that the catalyst changes also affected the amount of hexadecanoic acid converted. In theory, a catalyst is a chemical compound that causes the reaction to be faster to reach equilibrium without experiencing a chemical change at the end of the reaction [18]. The rate of reaction increases as the catalyst concentration increases from 1 to 5% by weight. A further increase in the catalyst concentration did not change the reaction rate significantly. From the results above, it can be concluded that the validation is following the theory in which the catalyst does not affect the reaction, which only affects the reaction speed. If the substrate molar ratio is below 7:1, it is more advantageous to work at temperatures between 70-90 ^{o}C in the surfactant preparation process [7].

Use of the solvent ratio for surfactant synthesis to dissolve the sample, thereby increasing the reaction's homogeneity. When the condensation reaction was carried out using the hexane/2-propanol mixed solvent, this reaction produced the best reaction with a percent yield of 70.3%. This is because amides are more soluble in polar alcohol solvents, while fatty acids are more soluble in non-polar solvents such as hexane [19].

Contour Plot of Substrate Ratio and Weight of Catalyst

The observations in Figure-8, Figure-9, and Figure-10 show a contour plot of the effect of the interaction of the substrate ratio and the catalyst's weight on the conversion of n-acyl-L-lysine at a constant solvent ratio. In general, the three figures show that the resulting increase in the amount of HA converted to amide if the total substrate ratio and the catalyst's weight are also enlarged. The increase also occurs linearly, although the catalyst's weight has a more significant effect in increasing the conversion compared to the substrate ratio from the equation model obtained.

Figure-8 is a contour plot at a constant solvent ratio of 2: 1. It appears that the HA conversion will be more than 76% if> 5.5% catalyst is used. However, in the contour plot in Figure-9, it is observed that if the solvent ratio is constant 1:1, a 76% HA conversion can be achieved if a 5% catalyst is used. If a larger solvent ratio of 3:1 is used, the interaction between the substrate ratio and the weight of the catalyst in Figure-10 shows that it has resulted in a HA conversion of more than 76%, even though the weight of the catalyst used is only 4%. From these three contour plots, it can be concluded that if a high solvent ratio is used, a catalyst can be reduced.

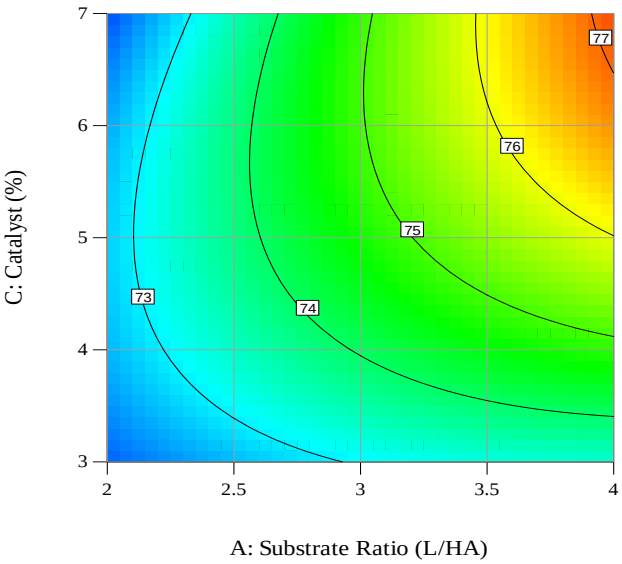

Figure-8. Contour plot of substrate ratio and weight of catalyst at solvent ratio (S: MS) 1: 1.

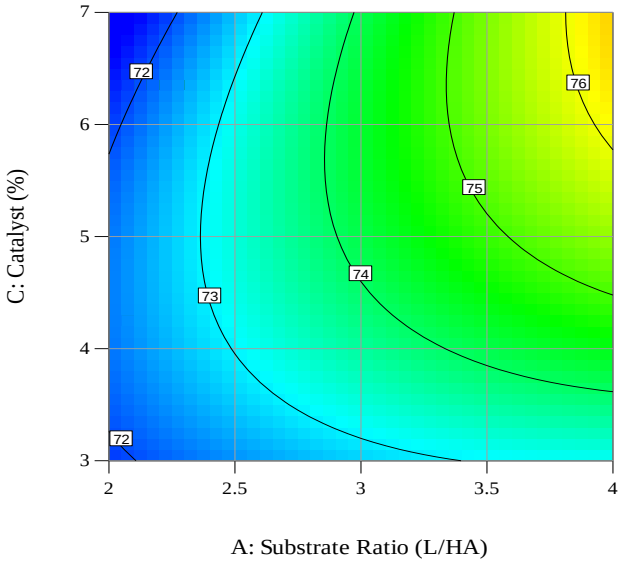

Figure-9. Contour plot of substrate ratio and weight of catalyst at solvent ratio (S: MS) 1: 2.

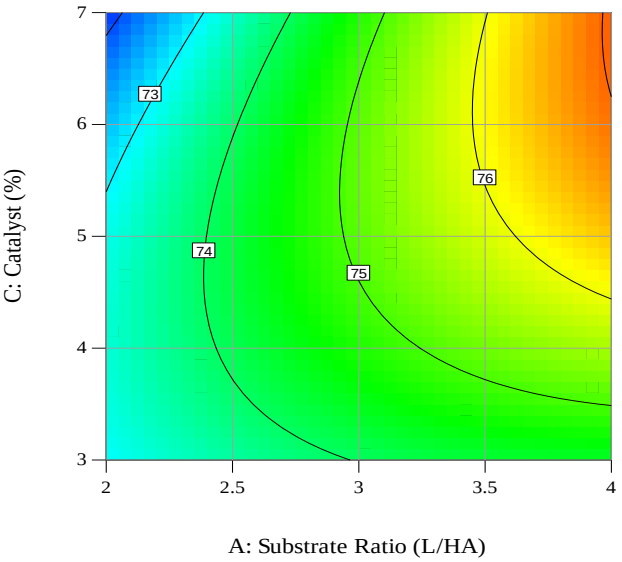

Figure-10. Contour plot of substrate ratio and weight of catalyst at solvent ratio (S: MS) 1: 3.

For this reason, it is necessary to carry out further optimization analysis in order to find the best composition among the three observed independent variables. The acquisition of n-acyl-L-lysine is influenced by the three independent variables used. As illustrated in Figure-8 to 10, HA conversion increases rapidly with the L/HA ratio from 3:1 to 4:1. The highest HA conversion was achieved up to 76% at a 4:1 L/HA ratio and a temperature of 65ºC. This is presumably because the by-product in water is thought not to inhibit the reaction mixture between amines, fatty acids, and catalysts. Therefore, to ensure the amide quality, a substrate ratio of 4:1 can be considered to be selected for further treatment.

The activity of CaO as a solid catalyst was rapidly high, even though the reaction conditions were at a mild level. The low cost of the catalyst and the long catalyst life are other advantages of using CaO catalysts [19]. As the reaction progresses, the acid number will decrease until the reaction is in equilibrium. In this state, the amines' conversion to amides has been optimal, indicated by a significantly reduced acid number.

Contour Plot of Solvent Ratio and Catalyst Weight

The observations in Figure-11, Figure-12, and Figure 13 show contour plots of the effect of the interaction of solvent ratio and catalyst weight on the conversion of n-acyl-L-lysine. The solvent and catalyst ratio interaction at the substrate ratio is kept constant 3:1 (L:HA) is shown in Figure-11. Overall the conversion obtained is more than 70%. The maximum HA conversion is in the range of solvent ratio 2.5-3 and 4-6% catalyst from the value range of the two selected variables. The contour plot of Figure-11 has a horse saddle pattern, where two optimum planes are found. The maximum range is also found from the above ranges when a 1-1.5% solvent ratio and 5-6% catalyst are used. This shows that the optimum HA conversion can be obtained using the maximum solvent ratio and catalyst. However, optimal conversion can also be obtained if the solvent ratio is minimum and the catalyst's weight is maximum. This is in line with the equation obtained, where the effect of catalyst weight is more significant than the solvent ratio to increase HA conversion.

If the substrate ratio is kept constant 2:1, the contour plot obtained in Figure-12 shows a decrease in the average HA conversion obtained, compared to Figure-11, at a constant 3:1 substrate ratio. The optimum field is shown in the use of maximum solvent ratio and minimum catalyst weight. If the substrate ratio is enlarged to 4:1, a contour plot of the interaction of the solvent and catalyst ratio will be obtained, as shown in Figure-13. This contour plot's general pattern shows that the optimum value of HA conversion is calculated when using a 2:1 solvent ratio. It was found that for the entire weight range of the catalyst used, the HA conversion would be maximum at a solvent ratio of 2:1. Increasing the solvent ratio will slightly reduce the HA conversion.

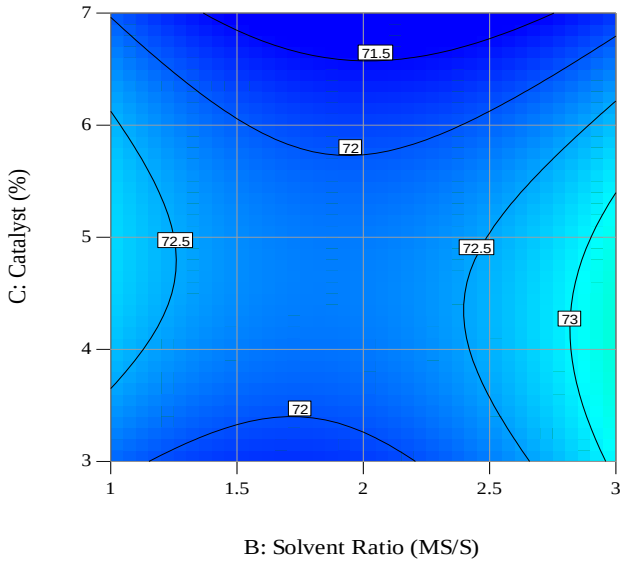

Figure-11. Contour plot of the ratio of solvent and weight of catalyst at 1:2 substrate ratio (AP:L).

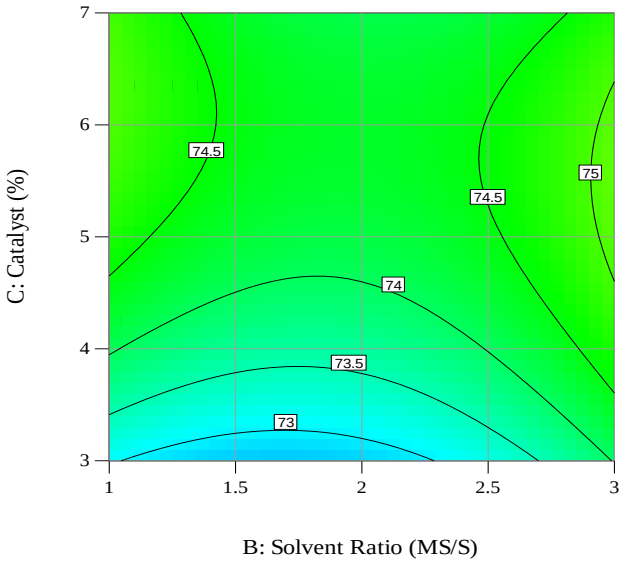

Figure-12. Contour plot of the ratio of solvent and weight of catalyst at 1:3 substrate ratio (AP:L).

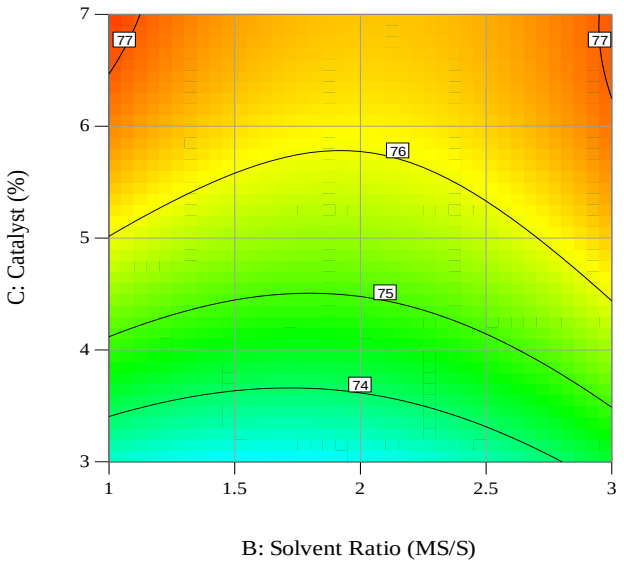

Figure-13. Contour plot of the ratio of solvent and weight of catalyst at 1:4 substrate ratio (AP:L).

The results obtained indicate that small solvents' use does not entirely dissolve the reactants and products produced. However, large amounts of solvent will dilute the reactants and reduce the working efficiency of the catalyst. The use of hexane and 2-propanol mixed solvent seems to be the best way because the fatty acids are more soluble in the non-polar hexane solvent, but the resulting amide is more soluble in the polar 2-propanol solvent [19].

Cao catalysts in the synthesis of fatty acid amides can produce good yields [18]. The weight of the catalyst used in the 3-6% range overall yields the maximum conversion, where the best results will be found at a maximum catalyst use of 6%. For this reason, further analysis is needed to reduce the range of values for the three variables, which will result in the maximum HA conversion.

Hexadecanoic acid is a long-chain fatty acid. The long chain of hydrocarbons will cause a lobe force that converts the fatty acids into alkanolamide. It is estimated that the long chain of hydrocarbons will be more lipophilic than the short-chain. The longer the hydrocarbon chain, the more lipophilic properties will be [13].

Optimization of Results

Result optimization is done according to variable data and response measurement data. The results of this optimization phase are recommendations for several new optimal formulas according to the program. Therefore, the optimal formula will be indicated by the maximum desirability value. The desirability value is the optimization objective function's value, where this value shows the program's ability to fulfill the desires based on the criteria set in the final product [20].

This value ranges from 0 to 1.0. The closer to one, then the shows the program's ability to be more perfect for producing the desired product. Table-4 shows the optimum conditions for the conversion response along with the value of the desirability function. It can be seen in

Table-4 that the optimal condition seen from the desirability value is 0.851.

Table-4. Optimum conditions for HA conversion response.

Number	Substrate Ratio	Solvent Ratio	Catalyst	HA Conversion	Desirability
1	2.956	2.000	5.000	74.084	0.851
2	2.948	2.000	5.000	74.072	0.851
3	2.963	2.000	5.000	74.096	0.851
4	2.933	2.000	5.000	74.047	0.851
5	2.994	2.000	5.000	74.147	0.851
6	3.027	2.000	5.000	74.201	0.850

CONCLUSIONS

Model prediction using Design Expert Software gives Fcount = 1.62, the R^2 value is 74.44%. Analysis of variance showed value (P = 0.0293); (P = 0.7132); (P = 0.2888) where the substrate ratio has a significant effect on the model, while the solvent ratio and the weight of the catalyst do not have a significant effect. The interaction relationship between the substrate ratio and the solvent ratio with the catalyst's weight shows a significant effect on the conversion of n-acyl-L-lysine. The desirability value is 0.851, where the optimal state of the equation can be accepted because the value is close to 1.

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