Isopropyl Myristate Production Process Optimization Using Response Surface Methodology and MATLAB

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ABSTRACT

This work was carried out to optimize the esterification process, between myristic acid and isopropanol, used for the production of isopropyl myristate in a reaction integrated distillation column taking the bottom mole fraction of isopropyl myristate as the objective function and the reflux ratio, the feed ratio and the reboiler duty as the manipulated variables. The experimental setup was built in form of a model using HYSYS 3.2. Response Surface Methodology was used to design the experimental simulations that were carried out. The results of the experimental simulations in addition to the designed experimental parameters were used to develop the model for the bottom mole fraction of isopropyl myristate using Design-Expert 7.0.0. The developed model was theoretically simulated and optimized with the aid of MATLAB R2012a and the theoretical optimum parameters found were used to run the experimental setup. The results obtained showed that the theoretical optimum values obtained with the aid of MATLAB R2012a were valid because the experimental simulation with these values gave the bottom isopropyl myristate mole fraction of 0.9912 that compared very well with the theoretical simulation value of bottom isopropyl myristate mole fraction of 1.0000.

Keywords:optimization, isopropyl myristate, HYSYS, Response surface methodology, MATLAB

1. INTRODUCTION

Fatty acid esters are (natural-based) chemicals used in a broad range of different fields of application, such as the cosmetic industry, the food industry, solvents and plasticisers, the coating industry, lubricants, biodiesel et cetera (Brockmann et al., 2005; Kalish and Pattison, 1968). The fatty acid esters include methyl esters, partial glycerides, wax esters (esters of fatty acids with long-chain fatty alcohols), and ester oils (esters of fatty acids with poly alcohols). (Brockmann et al., 2005; Kalish and Pattison, 1968; Gervajio and Shahidi, 2005). Among the commonly used fatty acid esters is isopropyl myristate which is the main focus of this research.

Isopropyl myristate (IPM), the isopropyl ester of tetradecanoic acid, is used in cosmetics as a substitute for natural oils because it is absorbed easily into the skin and has excellent spreading properties. In addition, IPM can be used as an emulsifier. In topical pharmaceutical creams and transdermal pharmaceutical preparations, IPM is also used as a co-solvent with skin penetration enhancement properties for actives (Klaffenbach and Kronenfeld, 1997).

Conventionally, the fatty acid esters production is of the batch process due to the flexibility in its operation so that it can be used for variety of products (Sonntag, 1979). The conventional process has the advantage of flexibility in multi-product operation for small production capacities but their lower productivity limits for large production volume. The batch process is normally penalized by number of shortcomings such as product quality degradation due to relatively long exposure to heat, necessity of catalyst neutralization and relative high alcohol demand (Moritz, 2003). Consequently, the development of process intensification technologies such as reactive distillation (RD) column for the production of fatty acid esters has been accelerated (Bhatia et al., 2006).

Reactive distillation, otherwise known as reaction integrated distillation, is a process that combines both separation and chemical reaction in a single unit. It combines the benefits of equilibrium reaction with distillation to enhance conversion provided that the product of interest has

the largest or the lowest boiling point (Giwa and Karacan, 2012a). It has a lot of advantages especially for those reactions occurring at temperatures and pressures suitable for the distillation of the resulting components (Giwa and Karacan, 2012b) which include shift of chemical equilibrium and increase of reaction conversion by simultaneous reaction and separation of products, suppression of side reactions and utilization of heat of reaction for mass transfer operation. It has been used in a small number of industrial applications for many years, but the last decade has shown an increase in both research and applications (Al-Arfaj and Luyben, 2002). By carrying out chemical reaction and separation in one process step, the operating and investment costs can be minimized. However, reactive distillation is not extensively used in industry since it is perceived that its operation will always be more difficult and will pose higher requirements on the quality of the design than the conventional flow sheet. This behaviour can be mainly attributed to the complex interactions between the underlying phenomena taking place in the reactive columns (Giwa and Karacan, 2012c). Apart from that, the complexity of this process can also affect its optimum operation. As such, it is very necessary to be very careful in designing the experiments for the determination of the optimum parameters of this process, especially, owing to the fact that it is a multivariable process.

The traditional 'one-factor at a time' technique used for optimizing a multivariable system is not only time consuming but also often easily misses the alternative effects between the factors involved in the process. Besides, this method requires carrying out a number of experiments to determine the optimum levels, which may be untrue. These drawbacks of single factor optimization process can be eliminated by optimizing all the affecting parameters collectively with the aid of Central Composite Design (CCD) using Response Surface Methodology (RSM) (Bandaru et al., 2006).

Response Surface Methodology (RSM) is a widely used technology for rational experimental design and process optimization in the absence of mechanistic information (Box and Draper, 1987; Myers and Montgomery, 1995). RSM initiates from Design of Experiments (DoE) to determine the values of the factors to be used for conducting experiments and collecting data. The data are then used to develop an empirical model that relates the process response to the factors. Subsequently, the model facilitates the search for better process response, which is validated through experiment(s). The above procedure iterates until an optimal process is identified or the limit on experimental resources is reached (Chi et al., 2012). RSM has seen diverse applications in almost every area of scientific research and engineering practice, including the development of chemical and biochemical processes (Agatonovic-Kustrin et al., 1998; Baumes et al., 2004; Dutta et al., 2004; Hadjmohammadi and Kamel, 2008; Shao et al., 2007; Tang et al., 2010; Yan et al., 2011a, 2011b).

According to the information obtained from the literature, Giwa and Giwa (2012) applied Design-Expert, using Response Surface Methodology, and Excel Solver for the optimization of a transesterification reaction used for the production of n-butyl acetate and methanol in a reaction integrated distillation column and they were able to achieve the approximate optimum values of the objective functions given by the theoretical optimization carried out using Excel Solver when the theoretical optimum values of reflux ratio and reboiler duty were used to run the experimental simulations.

In this work, the optimization of an esterification reaction for the production of isopropyl myristate in a reaction integrated distillation column was carried out with the aid of Response Surface Methodology and MATLAB taking the reflux ratio, feed ratio and reboiler duty as the independent variables and the mole fraction of isopropyl myristate present at the bottom segment of the column as the dependent variable.

2. PROCEDURES

2.1 Experimental Design

Response Surface Methodology (RSM) was used to design of the experiments for the determination of the optimum parameters of the esterification reaction between myristic acid and isopropanol that was used to produce isopropyl myristate and water with the aid of Design-Expert 7.0.0 (Stat-Ease, 2005). In the experimental design, as mentioned earlier, the dependent variable was taken as the mole fraction of isopropyl myristate collected at the bottom segment of the column while the independent variables of the process were the reflux ratio, the feed ratio and the reboiler duty.

In order to make the writing of the formulation convenient, the variables involved in the process were denoted as shown in Table 1.

Table1. Notations of the factors

Notation	Factor	Unit
A	Reflux ratio	kmol recycled liquid/kmol liquid distillate
B	Feed ratio	mL s^{-1} myristic acid/mL s^{-1} of isopropanol
C	Reboiler duty	kJ/s
Y	Bottom isopropyl myristate mole fraction	

The levels (lower and upper limits) of the independent variables that were used for the experimental design are as shown in Table 2.

Table 2. Levels of independent variables in the experimental plan

S/N	Factor	Lower limit	Upper limit
1	A	2.00	5.00
2	B	1.00	2.00
3	C	0.35	0.70

After fixing the levels to be used for the independent variables, they (the levels) were entered into the Design-Expert 7.0.0 and the experimental design matrix was given as shown in Table 3. According to the methodology used, 20 runs (8 cube points, 6 center points in cube and 6 axial points) were obtained and the alpha value of the design was 1.682.

Table3. The design matrix of the experiment

Run No.	A	B	C
1	3.5	1.5	0.52
2	5	1	0.35
3	5	2	0.35
4	5	2	0.7
5	3.5	1.5	0.52
6	0.98	1.5	0.52
7	2	1	0.35
8	3.5	1.5	0.82
9	3.5	2.34	0.52
10	3.5	1.5	0.52
11	2	2	0.35
12	3.5	1.5	0.52
13	3.5	0.66	0.52
14	6.02	1.5	0.52
15	2	1	0.7
16	2	2	0.7
17	3.5	1.5	0.23
18	3.5	1.5	0.52
19	3.5	1.5	0.52
20	5	1	0.7

With the completion of the design of how the experiments would be carried out, the experimental setup was designed in form of a model using Aspen HYSYS 3.2 (Aspen, 2003).

2.2 Aspen HYSYS Modeling

The experimental setup of the reactive distillation column for the production of isopropyl myristate and water from the esterification reaction between myristic acid and isopropanol, designed in the form of Aspen HYSYS model, developed using General NRTL model, is as shown in Figure 1.

The setup consisted of a condenser, the main column and a reboiler. The column was a packed type with raschig rings and divided into 17 segments. The main column was divided into three sections (rectifying section, reaction section and stripping section). The heavy feed (myristic acid) was passed into the column at the upper feed segment between the rectifying section and the reaction section while the light feed was passed into the column at the lower feed segment between the reaction section and the stripping section at a temperature of 25 ^{o}C and pressures of 1.12 and 1.14 bar respectively for the upper and lower feeds. The condenser pressure was taken to be 1.1 bar while that of the reboiler was taken to be 1.15 bar. For the solution of the reactive column, Sparse Continuation Solver was chosen as the algorithm.

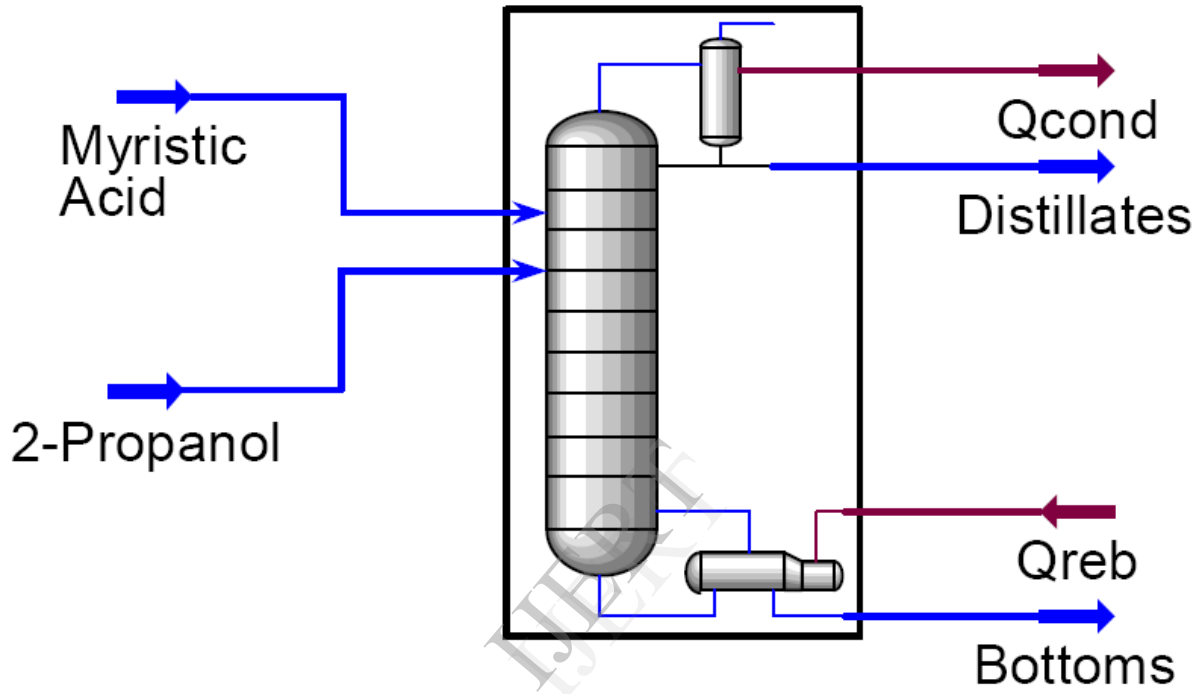

Figure1. Reactive distillation column for the production of isopropyl myristate

The equilibrium esterification reaction occurring in the reaction section of the column is given as shown in Equation 1. Gibbs free energy was used to calculate the equilibrium constant of the reaction in Aspen HYSYS environment.

$$myristic\ \ acid + isopropano\ l \ \xleftrightarrow{K_{eq}}\ \ isopropyl\ \ myristate\ + water \qquad (1)$$

After developing the experimental setup in the form of Aspen HYSYS model, it was run according to the experimental design obtained with Response Surface Methodology,given in Table 3,and the desired responses (mole fractions of isopropyl myristate present at the bottom of the column) obtained were entered into Design-Expert where the model equation for the bottom isopropyl myristate mole fraction was developed as a function of reflux ratio, feed ratio and reboiler duty.

2.3 Model Development and Optimization

Using the responses obtained from the experiments, a cubic model was chosen, developed and modified for the bottom isopropyl myristate mole fraction by estimating the model coefficients with the aid of Design-Expert 7.0.0. The developed model equation was then simulated using MATLAB R2012a (MathWorks, 2012). After simulating the developed model equation, it was optimized using a MATLAB R2012a built-in command known as "*fsolve"*. The manipulated variables of the optimization were chosen to be reflux ratio, feed ratio and reboiler duty. In addition, the objective function of the optimization was taken as the maximization of the mole fraction of isopropyl myristate obtained at the bottom segment of the column.

3. RESULTS AND DISCUSSIONS

The results obtained from the experimental simulations carried out using the experimental design obtained with the response surface methodology are as shown in Table 4 below. From the results, it was discovered that the maximum mole fraction of isopropyl myristate obtained at the bottom segment of the column was 0.6425 when the values of reflux ratio, feed ratio and reboiler duty were 0.98, 1.5 and 0.52 kJ/s respectively. In addition, the minimum mole fraction of bottom isopropyl myristate was obtained when the reflux ratio, feed ratio and reboiler duty were 3.5, 1.5 and 0.23 kJ/s respectively to be 0.2581. It can be noticed from the results at the feed ratio of 1.5, the increase in the reflux ratio from 0.98 to 3.5 with the decrease in the reboiler duty from 0.52 to 0.23 kJ/s has reduced the quality of the bottom isopropyl myristate obtained. As can be seen, due to the multivariable nature of the process, even when one of the independent variables was constant, the trend of the mole fraction of the desired product at the bottom of the column could not be said to be either directly proportional or inversely proportional to the remaining two independent variables. This is actually showing the importance of carrying out multivariable experimental design and optimization.

Table 4. Independent and process (dependent) variables of the experiment

Run	A	B	C	Y
1	3.5	1.5	0.52	0.3384
2	5	1	0.35	0.2734
3	5	2	0.35	0.2734
4	5	2	0.7	0.3536
5	3.5	1.5	0.52	0.3384
6	0.98	1.5	0.52	0.6425
7	2	1	0.35	0.3156
8	3.5	1.5	0.82	0.4941
9	3.5	2.34	0.52	0.3384
10	3.5	1.5	0.52	0.3384
11	2	2	0.35	0.3156
12	3.5	1.5	0.52	0.3384
13	3.5	0.66	0.52	0.3384
14	6.02	1.5	0.52	0.2954
15	2	1	0.7	0.6345
16	2	2	0.7	0.6345
17	3.5	1.5	0.23	0.2581
18	3.5	1.5	0.52	0.3384
19	3.5	1.5	0.52	0.3384
20	5	1	0.7	0.3536

Using the results obtained from the experiments (shown in Table 4), the model equation relating the bottom isopropyl myristate mole fraction to the three independent variables was developed with the aid of Design-Expert 7.0.0. Owing to the presence of three different independent variables, the order of the developed model equation was chosen to be cubic in order to incorporate the effects of all the factors that could have resulted from the three independent variables concerned in the work. The developed model equation was not given (shown) by Design-Expert 7.0.0 that was used for the model development because the model contained some terms that were aliased with one another, that is, the developed model was an aliased one. Nevertheless, the model was analyzed and shown in Table 5 are the results of its analysis of variance.

Table 5. Analysis of variance of the developed bottom isopropyl myristate cubic model

Source	Sum of Squares	df	Mean Square	F Value	p-value
Model	0.28	13	0.022	3032.45	< 0.0001
A	0.06	1	0.06	8496.92	< 0.0001
B	0	1	0	0	1
C	0.028	1	0.028	3927.02	< 0.0001
AB	0	1	0	0	1
AC	0.028	1	0.028	4017.03	< 0.0001
BC	0	1	0	0	1
A^2	0.03	1	0.03	4187.73	< 0.0001
B^2	8.55E-06	1	8.55E-06	1.21	0.3143
C^2	2.28E-03	1	2.28E-03	321.51	< 0.0001
ABC	0	1	0	0	1
A^2B	0	1	0	0	1
A^2C	2.90E-03	1	2.90E-03	409.04	< 0.0001
AB^2	1.67E-03	1	1.67E-03	235.2	< 0.0001
AC^2	0	0			
B^2C	0	0			
BC^2	0	0			
A^3	0	0			
B^3	0	0			
C^3	0	0			
Residual	4.26E-05	6	7.09E-06		
Lack of Fit	4.26E-05	1	4.26E-05		
Pure Error	0	5	0		
Cor Total	0.28	19			

From Table 5, it was discovered that the p-values of some of the factors were greater than the significance level of 0.05. One of factors (B^2) had a p-value of 0.3143 while some (B, AB, BC, ABC and A^2B) had p-values of 1. The very high values of the p-values of these factors made them to be insignificant. Even though the entire model was found to be significant with a Predicted R-Squared value of 0.9665, however, due to the fact that the model developed contained some terms that were aliased with one another which was the reason why the model equation was not shown (given) by Design-Expert 7.0.0, the developed cubic model was modified and the modified developed model equation for the bottom isopropyl myristate mole fraction is as shown in Equation (2).Denoting the predicted bottom mole fraction of isopropyl myristate by Y_p, then,

$$Y_p = -0.6499 + 0.3201A + 0.6374B + 1.6858C - 0.1795AB - 0.7533AC - 0.0193A^2 - 0.2125B^2 + 0.4107C^2 + 0.0751A^2C + 0.0598AB^2 \quad (2)$$

Looking at the model equation very well, it was discovered that some of the factors mentioned before to be insignificant were still contained in the modified model equation (Equation 2). This was necessary to be like that owing to the hierarchical problem of the model.

The analysis of variance of the modified model equation developed was also carried out and the results of the analysis are as shown in Table 6.

Table 6. Analysis of variance of the modified bottom isopropyl myristate model

Source	Sum of Squares	df	Mean Square	F Value	p-value	
Model	0.28	10	0.028	5913.29	< 0.0001	significant
A	0.06	1	0.06	12745.38	< 0.0001	
B	0	1	0	0	1	
C	0.028	1	0.028	5890.53	< 0.0001	
AB	0	1	0	0	1	
AC	0.028	1	0.028	6025.55	< 0.0001	
A^2	0.03	1	0.03	6281.6	< 0.0001	
B^2	8.55E-06	1	8.55E-06	1.81	0.2116	
C^2	2.28E-03	1	2.28E-03	482.27	< 0.0001	
A^2C	2.90E-03	1	2.90E-03	613.56	< 0.0001	
AB^2	1.67E-03	1	1.67E-03	352.81	< 0.0001	
Residual	4.26E-05	9	4.73E-06			
Lack of Fit	4.26E-05	4	1.06E-05			
Pure Error	0	5	0			
Cor Total	0.28	19				

From the results shown in Table 6, it was found out that the p-values of factors B, AB and B2 were still greater than the significance level of 0.05. However, they were included into the model due to the hierarchical problem mentioned before. In addition, even with the presence of these insignificant factors, the overall modified model was found to be significant with a Predicted R-Squared value of 0.9932. It was noticed that the Predicted R-Squared value of the modified model was better than that of the former cubic model equation. This is to say that the modified model equation was better in representing the bottom mole fraction of isopropyl myristate.

Apart from using the criteria of significance (with respect to significance level of 0.05) and Predicted R-Squared value to determine the validity of the developed model equation, the model was also simulated with the aid of MATLAB R2012a and the theoretical simulation results were compared to the experimental simulation ones as shown in Figure 2, in forms of composition profiles. The good comparison between the two profiles can be observed from the figure. This good graphical comparison was found to be in support of the high Predicted R-Squared value as well as the significance of the model equation developed for the bottom mole fraction of isopropyl myristate.

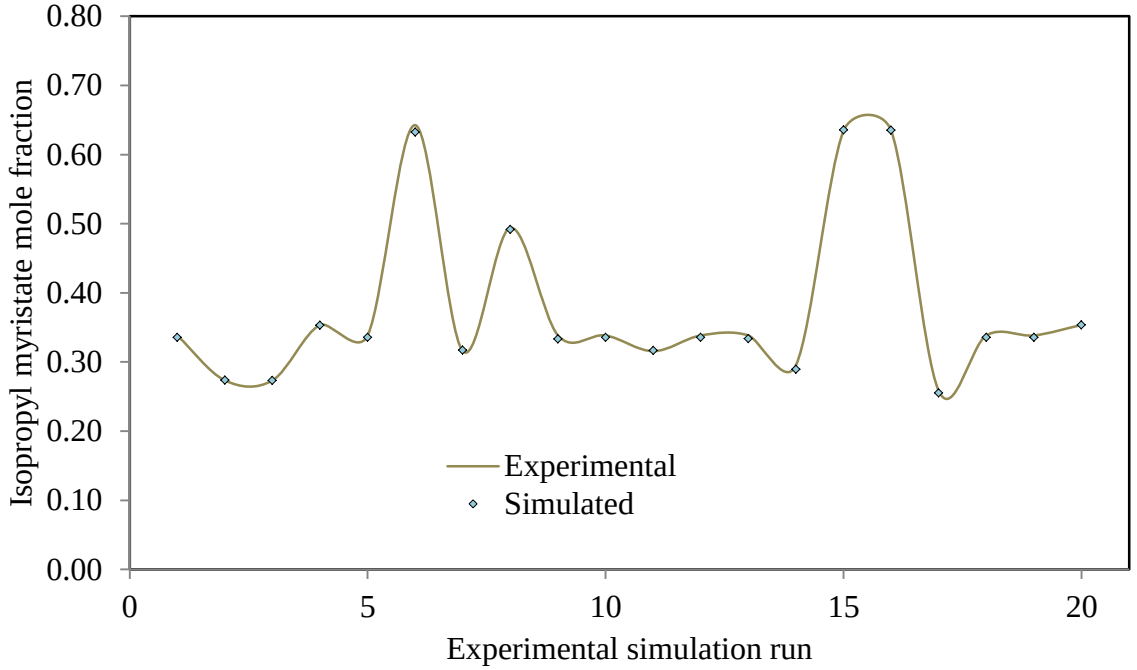

Figure2. Bottom isopropyl myristate mole fraction of experimental and theoretical simulations

Also noticed from the theoretical simulation carried out was that the highest mole fraction of isopropyl myristate obtainable at the bottom segment of the column was 0.6356. This value of the bottom composition was not satisfactory and, therefore, the optimization of the process was carried with the aid of MATLAB R2012a using *fsolve* command.

The results of the optimization (optimum values) are as shown in Table 7. From the table, it was discovered that when the objective function (bottom isopropyl myristate mole fraction) was set to 1.00, the theoretical optimum values of reflux ratio, feed ratio and reboiler duty were 1.96, 1.94 and 0.99 kJ/s respectively.

Table7. Optimum values

Variable	**Optimum value**
Reflux Ratio	1.96
Feed Ratio	1.94
Reboiler Duty (kJ/s)	0.99
Bottom isopropyl myristate mole fraction	1.00

In order to know the validity of the theoretical optimization that was carried out, the theoretical optimum values were used to run the experimental simulation and the steady state mole fractions of the components along the segments of the column obtained from the simulation are as shown in Figure 3.

From Figure 3, it was observed that desired product was the major component present in the bottom segment of the column because the mole fraction of isopropyl myristate found in the bottom segment of the column was approximately 0.9912. This optimized experimental simulation value (0.9912) of mole fraction of bottom isopropyl myristate was found to compare very well with the optimized theoretical simulation value of 1.0000. This is showing that the obtained optimum values were valid ones.

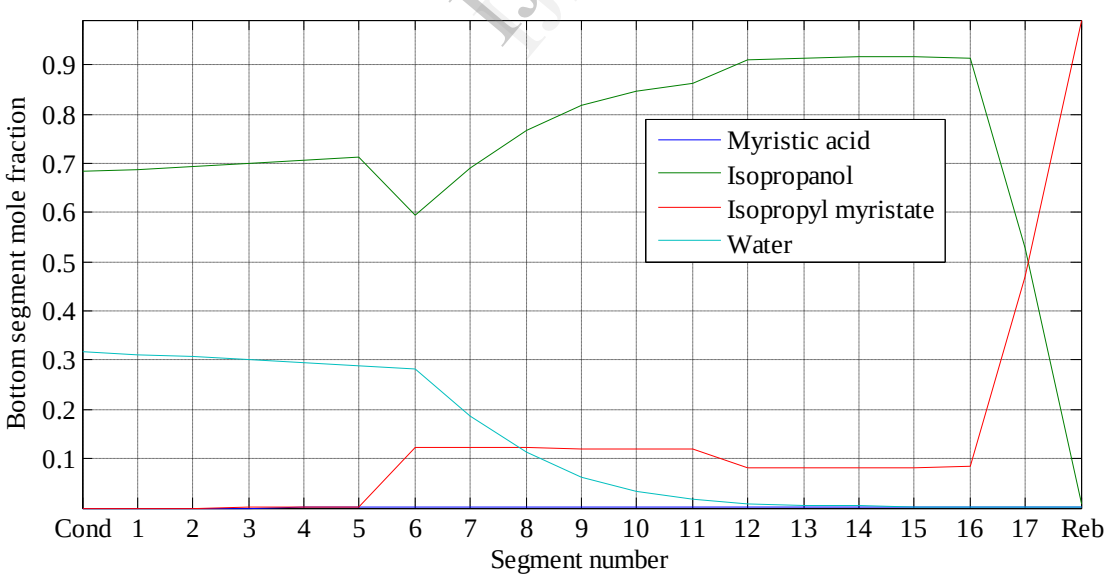

Figure3. Steady state liquid mole fraction profiles of the components obtained from optimization

Apart from the fact that high and good value of mole fraction of the desired product (isopropyl myristate) was obtained from the bottom segment of the column, it was also discovered that the steady state mole fraction of one of the reactants (myristic acid) in the column was approximately zero; the mole fraction of the other reactant (isopropanol) was not zero. This is an indication that the limiting reactant of the process was myristic acid. In other words, at steady state,

all the myristic acid passed into the reaction medium of the reaction integrated column was completely converted.

4.CONCLUSIONS

The results obtained from this work have shown that the modified model equation developed for the bottom isopropyl myristate mole fraction using Design-Expert 7.0.0 can be used to represent the behavior of isopropyl myristate in the bottom segment of the column because the model was discovered to be significant with Predicted R-Squared value of 0.9932. Furthermore, the theoretical optimum values obtained with the aid of MATLAB R2012a were found to be valid because when the theoretical optimum values were used to carry out experimental simulation, the value of bottom isopropyl myristate mole fraction of 0.9912 obtained compared very well with the theoretical simulation value of bottom isopropyl myristate mole fraction of 1.0000.

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NOMENCLATURES

A	Reflux ratio (kmol recycled liquid/kmol liquid distillate)
B	Feed ratio (mL s^{-1} myristic acid/mL s^{-1} of isopropanol)
C	Reboiler duty (kJ/s)
CCD	Central Composite Design
Cond	Condenser
df	Degree of freedom
DoE	Design of Experiment
K_{eq}	Equilibrium constant
NRTL	Non-Random Two-Liquid model
Reb	Reboiler
RSM	Response Surface Methodology
Y	Bottom isopropyl myristate mole fraction
Y_p	Model bottom isopropyl myristate mole fraction

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