A Comparative Study of Alkaline Hydrolysis of Ethyl Acetate Using Design of Experiments

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ABSTRACT: *Alkaline hydrolysis of ethyl acetate is essentially an irreversible and second order reaction. Industrial importance of the reaction product, sodium acetate, necessitate for process improvement in terms of maximum conversion and economical usage of raw materials. Statistical design of experiments was utilized to enhance conversion in both batch and plug flow reactors. A full two level factorial design was used to screen out insignificant factors through analysis of variance followed by examining the significant factors in face-centered central composite design. Reaction conversion in plug flow reactor was investigated, and experimental results after analysis were compared with batch reactor. The experimental data of both the reactors was fitted to develop second order model. Furthermore, graphical residual analysis was used to validate the model. The initial concentration of sodium hydroxide and ethyl acetate for the hydrolysis reaction in both the reactors were reported to be the significant factors. The maximum conversion of 96% was achieved for a residence/reaction time of five minutes at optimum initial concentrations of sodium hydroxide (0.01mol/L) and ethyl acetate (0.07mol/L) in batch and plug flow reactor.*

KEY WORDS: *Design of experiments, Saponification, Process improvement.*

INTRODUCTION

In scientific research experimental work is essential in the process development, selection and optimization. Thus, each experiment has a clear objective before it is being performed. Basically experiments are conducted, in the first instance, to validate a model, a natural or phenomenological law and to investigate response of variables in view of objective optimization. First scenario may lead to an acceptable approximate solution wherein the method of analysis is still a subject of inherent computational intricacy as has been reported elsewhere (*Ruppen et al.*, 1995 [1]; *Rajkumar et al.*, 2008 [2]). Furthermore, process factors are varied arbitrarily one at a time in search of optimum that may result in large number of experimental runs. The computational efforts, required number of experimental runs aimed either to understand the behavior of a model or its validation, time factor and cost can be minimized by developing a systematic procedure. Statistical tools are the potential aspirant for such an organized and systematic procedure and have been applied to a batch reactor (*Asprey & Macchietto*, 2000 [3]).

Unlike classical approaches a more systematic statistical methodology to study the cause and effect relationship of process factors is the newly developed science known as Design of Experiments (DoE).

Design of experiment is an efficient technique of arranging the experiments in a rational way that determines articulate relationship of factors and response; reduces number of experiments and leads to valid statistical inferences (*Montgomery*, 2000 [4]; *Zivorad*, 2004 [5]). It has been reported (*Franceschini & Macchietto*, 2008 [6]) that developments in design of experimental methodology during the last 10 years has made it possible to apply the techniques for complex applications such as chemical/biochemical kinetics, biological processes, heat/mass transfer operations and regression modeling. Recently the studies reported on the enhancement of canthaxanthin production (*Nasrabadi & Razavi*, 2010 [7]), naphtha steam cracking (*Keyvanloo et al.*, 2010 [8]), optimization of ceramic membranes (*Othman et al.*, 2009 [9]; *Ling et al.*, 2010 [10]), optimization of high-purity graphite milling process (*Yang et al.*, 2009 [11]), chemical mechanical polishing process (*Kim et al.*, 2006 [12]), process improvement study of saponification (*Bursali et al.*, 2006 [13]) and recipe improvement for batch reactor (*Zofia*, 1998 [14]) all emphasise on the simplicity and confidence level attained with Design of Experiment (DoE).

There are various methods for statistical design of experiments and the selection of each method strongly depends on the purpose of the experimentation (*Atkinson et al.*, 1998 [15]; *Zivorad*, 2004 [5]). It may be concluded from literature cited that screening design and Response Surface Methodology (RSM) are simple and the most widely used designs for optimization studies. The purpose of the screening design is to figure out the most significant factors affecting the response and consequently RSM is then applied for the optimization of these important factors.

Hydrolysis of carboxylic ester under alkaline conditions, also known as saponification reaction, produces soap and an alcohol. Though sodium acetate, basically a salt produced when ethyl acetate (EtAc) undergoes hydrolysis in alkaline environment, is not used specifically for cleansing purposes as soap but has a wide range of industrial applications such as in pharmaceutical, paint and dying industry, as food additive, in electroplating industry, as meat preservative, photography and purification of glucose etc. whereas ethanol, a by-product, can be used as biofuel. Despite the commercial importance of sodium acetate, no study has been, hitherto, found on process improvement of aforementioned

saponification reaction except by *Bursali et al.*, 2006 [13]. However, the kinetics and reaction mechanism has been reported in numerous studies (*Tsujikawa & Inoue,* 1966 [16]; *Mata-Segreda,* 2002 [17]). Moreover, reports on modeling of plug flow reactor such as constructing concentration profile (*Yusup et al.*, 2005 [18]) and piece wise modeling by numerical methods (*Alopaeus et al.*, 2008 [19]) are available in literature whereas studies related to saponification of ethyl acetate in a plug flow reactor for process improvement are not available in open literature to the best of authors knowledge.

In this study the experimental work of *Bursali et al.,* (2006) [13], after replication for batch reactor has been extended to a continuous flow reactor in order to determine the effect of reactor type on maximum conversion. Therefore, the goal of this work was set forth to investigate the effects of reactant concentrations on conversion, minimization of reaction time and economical usage of the reactants in plug flow reactor. Furthermore, to evaluate optimum robust conditions, subject to maximizing the conversion, the results of plug flow and batch reactor were compared.

In the first stage of experimentation it was decided to examine the additive and interaction effects of all the possible factors on the fractional conversion (X_A) of sodium hydroxide, as response objective. The selected factors were initial concentrations of sodium hydroxide and ethyl acetate, temperature of reaction mixture and agitation rate for batch reactor and feed ratio for plug flow reactor. Experiments were planned in two stages, screening phase and optimization. A two level full factorial (2^k) design aimed to screen out the significant factors and secondly Response Surface Methodology (RSM) was employed to optimize reaction for both types of reactors. Experimental results were verified statistically by analysis of variance (ANOVA) using Fisher's F-test. Finally second order polynomial models were subjected to adequacy tests with Fisher's criterion and graphical residual analysis (*Montgomery*, 2000 [4]).

EXPERIMENTAL SECTION
Theory
Reaction kinetics and mechanism

The saponification of ethyl acetate under alkaline conditions can be represented by the following reaction equation (*Bursali et al.*, 2006 [13]):

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$$NaOH + CH_3COOC_2H_5 \rightarrow CH_3COONA + C_2H_5OH \quad (1)$$
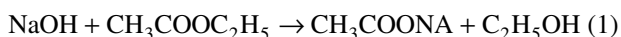
The rate constant, and the reaction mechanism for the aforementioned saponification reaction is given as follows (*Bursali et al.*, 2006 [13]):

$$-r = -r_{NaOH} = kC_{NaOH}C_{EtOAc} \quad (2)$$

Most of the previous studies (*Ortiz et al.*, 1989 [20]; *Balland et al.*, 2000 [21]; *Grau et al.*, 2002 [22]; *Krupska et al.,* 2002 [23]; *Mata-Segreda*, 2002 [17]; *Kim & Baird*, 2004 [24]) in literature regarding the saponification reaction of ethyl acetate have focused on kinetics and reaction mechanism. The saponification reaction is an irreversible, second order overall and first order reaction with respect to reactants. Furthermore, the reaction order decreases, becomes sequential rather than second order when equi-molar concentrations of both the reactants are used (*Tsujikawa & Inoue*, 1966 [16]). In another study (*Sundberg et al.,* 1977 [24]), it was examined that decrease in reaction rate was due to the reverse reaction of transition complex (TS) formation. It is believed that the saponification of ethyl acetate proceeds through direct attack of nucleophile (hydroxide ion) on carbon atom of ethyl acetate (*Tsujikawa & Inoue*, 1966 [16]).

However, *Mata-Segreda* (2002) [17] found that transition complex formation was a result of nucleophilic interaction of water molecule where hydroxide ions generally assist the complex formation.

Hypothesis testing

Fisher's F distribution was used to determine the variance among design data points.

F hypothesis test was defined as

$H_0 :$ $\delta_1 = \delta_2$ Null hypothesis

$H_1 :$ $\delta_1 \neq \delta_2$ Alternative hypothesis

Test statistic: Fisher`s F-value

Significance: significance level α

Where δ_1 is the variance due to a factor at one level and δ_2 is the variance due to same factor at level two.

Null hypothesis is rejected if a factor's F-value is greater than critical F-value at significance level α = 0.1, i.e. the variation in response is due the change in a factor's value (levels). It was assumed that response varies linearly and residuals were distributed normally. Furthermore, errors were assumed to be independently distributed with mean zero.

To subdue the violation of the very assumption, center points were augmented in using rigid F-values. The p-values approach was also adopted.

Analysis of variance (ANOVA)

A statistical technique to determine the variance among data points known as analysis of variance (ANOVA) test was employed in this work. In this approach the magnitude of factor effects are compared with magnitude of experimental error at significance level α = 0.1. If the magnitude of a factor as compared to error is large, null hypothesis is rejected and it is accepted that variation in response is due to the effect of that factor. Fisher's F-test was used, as given in Eq. (3), to screen out insignificant factors:

$$F = \frac{MSS_{effect}}{MSS_{error}} \quad (3)$$

Experimental setup

All experiments were performed on a bench-top lab scale liquid phase chemical reactor service unit (Armfield, Hampshire, England). The block diagram of PFR mounted reactor unit as shown in Fig. 1 has the flexibility to be assembled with both batch reactor and plug flow reactor. In addition to that, the unit is facilitated with temperature controller, conductivity measuring probe, control on stirrer speed, variable feed pumps and hot water circulation unit. The volume of batch and plug flow reactor are 1.0 L. and 0.4 L. respectively. The specific characteristics of individual batch and plug flow reactor are listed in Table 1.

Analytical methods

Palletized sodium hydroxide (Merck, Germany) and ethyl acetate (Scharlau Chemie, Spain) were used to prepare the reactant solution in bulk volumes in order to avoid any chances of error and to keep the concentrations uniform for all experimental runs. Two different molar concentrations, i.e. 0.1 M and 0.01 M for each of the reactant (sodium hydroxide and ethyl acetate) were used taking one combination at a time for one experimental run. The conductivity probe of reactor unit was used to measure conductivities of reaction mixture at specified residence time.

Conductive nature of sodium hydroxide was selected to measure the extent of reaction. Sodium acetate is also conductive but strong electrolytic nature of hydroxide

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Table 1: Characteristics of batch and plug flow reactors employed in experimental work.

| S.No	Characteristics	Batch reactor	Plug flow reactor
1	Working volume	1 Liter	0.4 Liter
2	Residence time	5 min	5 min
3	Conductivity measurement	Immersed probe in reaction mixture	Flow-through type probe at exit
4	Reaction Temperature	Circulating hot water through a coil immersed in reactor	Surrounding hot water across immersed coiled reactor tube
5	Surrounding temperature	No effect (Insulated reactor)	No effect (Maintained by circulating water)
6	Mixing	Variable stirrer	Variable feed pumps
7	Condition	Steady state	Steady state
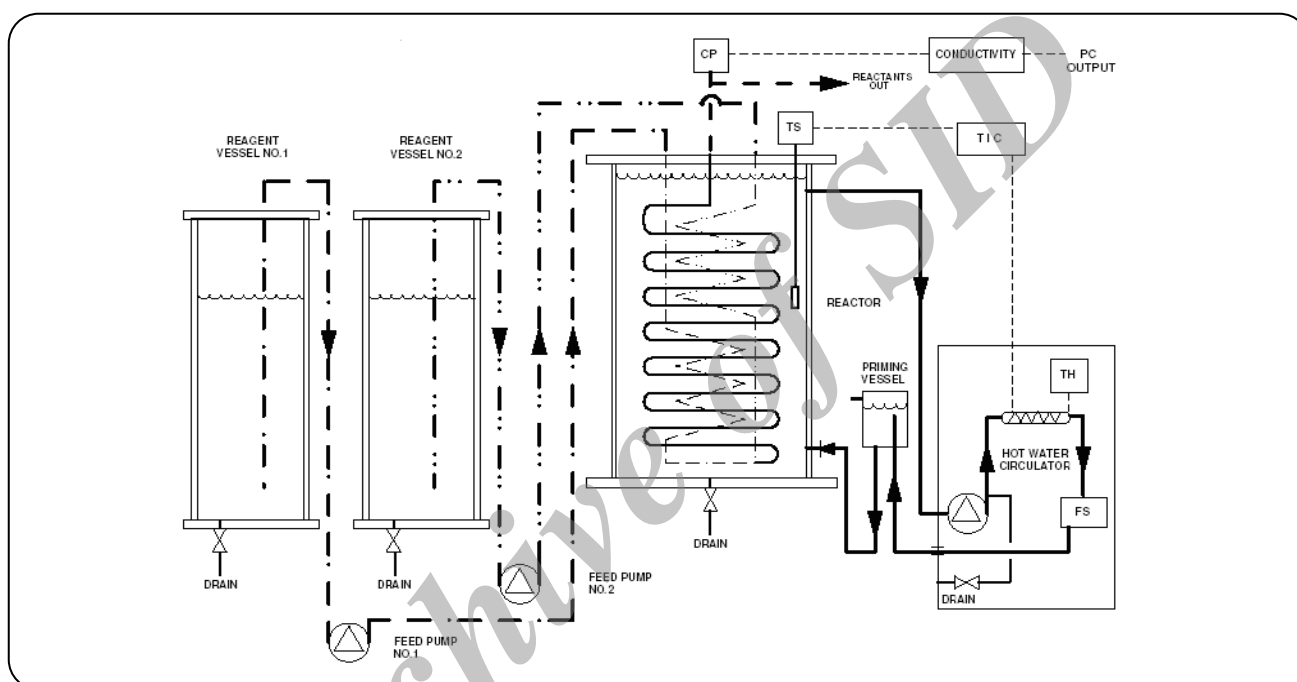
Fig. 1: PFR mounted chemical reactor service unit (adopted from Armfield, Hampshire, England).

suppresses the conductance of sodium acetate. Therefore, the conductivity readings were accounted for the unconsumed hydroxide ions as the reaction proceeds and the conversion of hydroxide ions into sodium acetate was traced back from the changes in conductivity of reaction mixture.

The fractional conversion of sodium hydroxide can be calculated by the following relationship (*Bursali et al.*, 2006 [13]):

$$\frac{C_{NaOH} - C_{NaOH_\infty}}{C_{NaOH_o} - C_{NaOH_\infty}} = \frac{C - C_\infty}{C_o - C_\infty} = 1 - X_A \qquad (4)$$

On the conditions when $C_{NaOH_{,\infty}} \to 0$ as $t \to \infty$, the above equation can be rearranged as follows:

$$X_A = \frac{C_o - C}{C_o - C_\infty} \qquad (5)$$

where X_A is fractional conversion of sodium hydroxide, C is conductivity at time t; C_o is initial conductivity and C_∞ is conductivity at time t_∞, i.e. when reaction stops.

Plan of experiments

Experiments were conducted in two stages, screening experiment and optimization. Finally, same stages of

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Table 2: Factors with natural and codified values.

Factors	Natural Values			Coded Values		
	Higher	Low	Centre	High	low	Centre
Temperature (°C)	45	26	35	1	-1	0
Sodium hydroxide (mol/L)	0.1	0.01	0.055	1	-1	0
Ethyl acetate (mol/L)	0.1	0.01	0.055	1	-1	0
Agitation rate (potentiometer rating)	10	4	7	1	-1	0
Feed ratio (PFR)	2	1	1.5	1	-1	0

design of experiments were employed for batch and plug flow reactors in accordance with same reaction conditions to have an easy comparison.

Screening experiment

Four factors (initial concentration of sodium hydroxide and ethyl acetate, temperature of reaction and agitation rate) for batch reactor at maximum and minimum values were investigated by 2^k full factorial design. In PFR analysis agitation rate was replaced with feed ratio. Natural values of factors were codified, according to Eq. (6), for making computations and analysis easier, as shown in Table 2:

$$X_i = \frac{U_{i,natural}U_{i,avg}}{\Delta U} \tag{6}$$

Where (+1) and (-1) refers to the codified two levels of a factor representing maximum (higher) and minimum (lower) values whereas (0) known as centre point represents the average value.

Volumetric feed rates of reactants, i.e. NaOH and EtOAc, for PFR used at higher level was 55 mL/min and 27mL/min, at lower level was 40 mL/min and 40 mL/min and at center point was 48 mL/min and 32 mL/min respectively.

The number of experiments incorporating four factors each at two levels (higher and lower) for the analysis of both batch and plug flow reactor according to 2^k full factorial design were $2^4 = 16$. Design matrices as given in Table 3 and Table 4 were randomized in Design Expert 8.0.3 trial version (State-Ease Inc., Minneapolis, USA) and the experiments for both reactors were carried out in that randomized order to protect against noise. Three center point runs were placed in design matrices to detect any curvature in response, i.e. a measure of the quadratic

effects and an indicator to develop appropriate higher order polynomial model to fit data.

Response Surface Methodology

In second stage of experimentation significant factors were augmented with star points to construct face-centered central composite design, a type of RSM to find optimum reaction conditions that maximize the conversion. The optimum factors were regressed into a second order polynomial model. The accuracy of the model was checked with lack of fit (LoF) and R^2 tests and the assumptions made for ANOVA to develop the model were finally subjected to adequacy tests by graphical residual analysis.

Design Expert 8.0.3 version (State-Ease Inc., Minneapolis, USA) was used to construct design matrices, randomize experiments, generate ANOVA, and graphical residual analysis for validation of the developed models.

RESULTS AND DISCUSSION
Screening experiment

The data presented in Tables 3 and 4 was used to make variance analysis for interaction effects and curvature representation in response (fractional conversion). Same reaction conditions of batch reactor were employed in PFR analysis except for replacing agitation rate with feed ratio as shown in Table 1. Variance analysis, as shown in Tables 5 and 6 were carried out using partial sum of squares method and the curvature term was computed from Eq. (8) (*Bursali et al.*, 2006 [13]):

$$SS_{curvature} = \frac{n_F n_C (y_F - y_c)^2}{n_F + n_C} \tag{8}$$

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Table 3: Design matrix for batch reactor.

N	Random order	Std order	X_1	X_2	X_3	X_4	X_A
1	1	13	-1	-1	1	1	0.89
2	15	19	0	0	0	0	0.97
3	16	18	0	0	0	0	0.94
4	2	7	-1	1	1	-1	0.1
5	13	6	1	-1	1	-1	0.1
6	9	9	-1	-1	-1	1	0.97
7	8	10	1	-1	-1	1	0.96
8	17	2	1	-1	-1	-1	0.96
9	18	5	-1	-1	1	-1	0.1
10	6	16	1	1	1	1	0.97
11	12	14	1	-1	1	1	0.89
12	10	8	1	1	1	-1	0.1
13	11	4	1	1	-1	-1	0.87
14	7	15	-1	1	1	1	0.98
15	4	3	-1	1	-1	-1	0.90
16	3	1	-1	-1	-1	-1	0.94
17	14	11	-1	1	-1	1	0.87
18	19	12	1	1	-1	1	0.97
19	5	17	0	0	0	0	0.89

Table 4: Design matrix for PFR.

No	Std order	Random order	X_1	X_2	X_3	X_4	X_A
1	7	1	-1	1	1	-1	0.1
2	16	2	1	1	1	1	0.91
3	2	3	1	-1	-1	-1	0.65
4	5	4	-1	-1	1	-1	0.1
5	15	5	-1	1	1	1	0.97
6	11	6	-1	1	-1	1	0.99
7	14	7	1	-1	1	1	0.82
8	10	8	1	-1	-1	1	0.92
9	6	9	1	-1	1	-1	0.05
10	9	10	-1	-1	-1	1	0.96
11	3	11	-1	1	-1	-1	0.97
12	1	12	-1	-1	-1	-1	0.88
13	8	13	1	1	1	-1	0.05
14	4	14	1	1	-1	-1	0.86
15	13	15	-1	-1	1	1	0.81
16	12	16	1	1	-1	1	0.74
17	17	17	0	0	0	0	0.78
18	18	18	0	0	0	0	0.78
19	19	19	0	0	0	0	0.81

Table 5: Analysis of variance for batch reactor.

Source	SS_{effect}	d.f.	MSS_{effect}	F -value	p-value
X_1	4.84E-04	1	4.84E-04	0.4	0.5938
X_2	1.96E-04	1	1.96E-04	0.16	0.7278
X_3	0.68	1	0.68	556.5	0.0018
X_4	0.74	1	0.74	606.8	0.0016
X_1X_2	2.10E-04	1	2.10E-04	0.17	0.7188
X_1X_3	6.25E-04	1	6.25E-04	0.51	0.5491
X_1X_4	5.52E-04	1	5.52E-04	0.45	0.571
X_2X_3	9.03E-03	1	9.03E-03	7.37	0.1131
X_2X_4	2.45E-03	1	2.45E-03	2	0.2928
X_3X_4	0.66	1	0.66	541.1	0.0018
$X_1X_2X_3$	4.20E-04	1	4.20E-04	0.34	0.6173
$X_1X_3X_4$	1.52E-03	1	1.52E-03	1.24	0.381
$X_1X_3X_4$	7.02E-04	1	7.02E-04	0.57	0.5279
$X_2X_3X_4$	9.92E-04	1	9.92E-04	0.81	0.463
$X_1X_2X_3X_4$	2.03E-03	1	2.03E-03	1.65	0.3272
Curvature	0.11	1	0.11	89.77	0.011
Pure Error	2.45E-03	2	1.22E-03		
Cor total	2.22	18			

Table 6: Analysis of variance for PFR.

Source	SS_{effect}	d.f.	MSS_{effect}	F -value	p-value
X_1	0.039	1	0.039	3.24	0.1698
X_2	0.01	1	0.01	0.84	0.4261
X_3	0.62	1	0.62	52.35	0.0054
X_4	0.75	1	0.75	63.17	0.0042
X_1X_2	1.87E-03	1	1.87E-03	0.16	0.7183
X_1X_3	0.014	1	0.014	1.21	0.3509
X_1X_4	7.80E-04	1	7.80E-04	0.066	0.8144
X_2X_3	7.56E-04	1	7.56E-04	0.064	0.8173
X_2X_4	2.16E-03	1	2.16E-03	0.18	0.6987
X_3X_4	0.56	1	0.56	47.13	0.0063
$X_1X_2X_3$	4.30E-05	1	4.30E-05	3.61E-03	0.9559
$X_1X_2X_4$	0.011	1	0.011	0.88	0.4164
$X_1X_3X_4$	3.60E-05	1	3.60E-05	3.03E-03	0.9596
$X_2X_3X_4$	0.03	1	0.03	2.55	0.2086
$X_1X_2X_3X_4$	4.34E-03	1	4.34E-03	0.36	0.5885
Curvature	0.035	1	0.035	136.57	0.0072
Pure Error	5.15E-04	2	2.58E-04		
Cor total	2.08	18			

Partial sum of squares take into account the additive effect of individual factors and is independent of the order of the experimentation. Significance of factors was determined by comparing F-values with critical values. The p-values were also adopted as additional affirmative approach to avoid any chances of false rejection of hypothesis. Wherein a factor with a p-value greater than 0.1 is insignificant. The tabulated critical value $F_{0.1(2,18)}$ was 8.526 for batch and PFR (*Montgomery*, 2000 [4]).

By examining variance in Table 5 and Table 6 it was evident that for both reactors that the initial concentrations of sodium hydroxide, ethyl acetate and their interaction terms were significant. Moreover, it was also observed that response did not change linearly when factors were varied from high to low values as detected by significant curvature terms. Therefore, it was decided at the screening stage to develop second order polynomial models which take into account the quadratic effects of the significant factors.

Face-centered central composite design

Two-level face-centered central composite design, a type of RSM suitable when optimum values might not be incorporated outside design space, was applied to obtain a second order polynomial and to investigate the optimum initial concentrations of reactants in saponification reaction. Axial runs (star points $\alpha^* = \pm 1$), which define new extreme optimum values of factors at the boundary of design space, were augmented in previous factorial design. Insignificant factors were removed from factorial designs in further study that resulted in 4 replicates of the sodium hydroxide (NaOH) and ethyl acetate (EtOAc) concentrations. Design matrices for both reactors with 24 run, additional 4 axial runs and central runs are shown in Tables 7 and 8.

Generally a second order model containing two additional quadratic terms can be represented as:

$$X_A = \beta_{\circ} + \beta_3 X_3 + \beta_4 X_4 + \beta_{34} X_3 X_4 + \tag{9}$$
$$\beta_{33} X_3^2 + \beta_{44} X_4^2$$

Where β's are estimates of regression coefficient and can be computed by method of least squares. The model in Eq. (9) includes initial concentrations of sodium hydroxide, ethyl acetate, their interaction and quadratic terms. To validate assumption of normality an arcsine sqrt transformation which is typical for responses varying

between '0' and '1' was employed to develop second order polynomials (*Montgomery*, 2000 [4]). Results of ANOVA for second order polynomial model (Eq. (9)) by using data in Table 7 and Table 8, are shown in Table 9 through Table 11.

For batch reactor the critical F-values for model term, factors effect and LoF were $F_{0.1(5,18)} = 2.19$, $F_{0.1(1,18)} = 3.01$, $F_{0.1(3,15)} = 2.49$ and for PFR these were $F_{0.1(5,17)} = 2.29$, $F_{0.1(1,17)} = 3.03$, $F_{0.1(3,14)} = 2.52$ respectively.

By examining variance in Table 9, the quadratic effect (X_3^2) of sodium hydroxide was insignificant ($F < 3.01$) and was eliminated. The variance analysis after elimination of quadratic effect is shown in Table 10. Finally, the second order model Eq. (10) after regression by method of least squares was obtained:

$$X'_A = \tag{10}$$
$$\text{Sin}^{-1}\sqrt{1.24 - 0.19X_3 + 0.23X_4 + 0.29X_3X_4 - 0.24X_4^2}$$

For PFR, analysis of variance was made using data of Table 8, and ANOVA after eliminating the insignificant quadratic effect of sodium hydroxide as shown in Table 11. By method of least squares regression the second order model for PFR was obtained:

$$X'_A = \tag{11}$$
$$\text{Sin}^{-1}\sqrt{1.91 - 11.34X_3 + 7.96X_4 + 106.78X_3X_4 - 68.12X_4^2}$$

The accuracy of the developed models (Eqs. (10) and (11)) were confirmed by numerical statistical tests such as Fisher`s F-test, lack of fit and correlation coefficient R^2-values. To obtian valid statistical inferences experimental error was split into lack of fit term and pure error. The significant lack of fit term (ratio of residual to pure error) in Table 9 indicates that Equation 9 might be improved by eliminating a factor to fit experimental data. The improvement made by eliminating insignificant quadratic term was obvious by comparing the increase in F-value for model and a reduction in F-value for lack of fit term as shown in Table 10. The lack of fit term was still significant and model accuracy was confirmed by correlation coefficient value. R-squared (a measure of variance in response as explained by the model) value of 0.91 calculated from Eq. (12) satisfied that the proposed model represents the response with reasonable accuracy and only 9 percent of varaibilty in data can not be explained by Eq. (10).

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Table 7: RSM design table for batch reactor.

Std order	Random order	X_3	X_4	X_A
1	2	-1	-1	0.94
2	14	-1	-1	0.87
3	23	-1	-1	0.96
4	9	-1	-1	0.90
5	4	1	-1	0.1
6	11	1	-1	0.1
7	15	1	-1	0.1
8	6	1	-1	0.1
9	3	-1	1	0.96
10	12	-1	1	0.97
11	8	-1	1	0.86
12	10	-1	1	0.97
13	7	1	1	0.89
14	18	1	1	0.98
15	19	1	1	0.89
16	13	1	1	0.97
17	16	-1(-α*)	0	0.90
18	20	1(+α*)	0	0.55
19	22	0	-1(-α*)	0.18
20	21	0	1(+α*)	0.86
21	1	0	0	0.89
22	5	0	0	0.93
23	24	0	0	0.96
24	17	0	0	0.96

Table 8: RSM design table for PFR.

Std order	Random order	X_3	X_4	X_A
1	19	-1	-1	0.88
2	1	-1	-1	0.65
3	18	-1	-1	0.97
4	4	-1	-1	0.86
5	20	1	-1	0.1
6	23	1	-1	0.045
7	14	1	-1	0.1
8	16	1	-1	0.04
9	3	-1	1	0.95
10	8	-1	1	0.92
11	9	-1	1	0.99
12	13	-1	1	0.73
13	5	1	1	0.80
14	7	1	1	0.82
15	10	1	1	0.97
16	11	1	1	0.91
17	21	-1(-α*)	0	0.98
18	6	1(+α*)	0	0.6
19	12	0	-1(-α*)	0.2
20	2	0	1(+α*)	0.94
21	22	0	0	0.79
22	15	0	0	0.78
23	17	0	0	0.81

Table 9: ANOVA of Second order model for batch reactor.

Source of variation	SS_{effect}	d.f.	MSS_{effect}	F- Value	p-value
Model	3.28	5	0.66	39.29	< 0.0001
X3	0.69	1	0.69	40.99	< 0.0001
X4	0.98	1	0.98	58.41	< 0.0001
X3X4	1.36	1	1.36	81.36	< 0.0001
$X3^2$	6.78E-05	1	6.78E-05	4.06E-03	0.9499
$X4^2$	0.18	1	0.18	10.6	0.0044
Residual	0.3	18	0.017		
Lack of Fit	0.23	3	0.077	16.28	< 0.0001
Pure Error	0.071	15	4.71E-03		
Cor Tot	3.59	23			

Table 10: ANOVA improved second order model for batch reactor.

Source of variation	SS_{effect}	d.f.	MSS_{effect}	F- value	p-value
Model	3.28	4	0.82	51.82	< 0.0001
X3	0.69	1	0.69	43.25	< 0.0001
X4	0.98	1	0.98	61.65	< 0.0001
X3X4	1.36	1	1.36	85.86	< 0.0001
$X4^2$	0.26	1	0.26	16.54	0.0007
Residual	0.3	19	0.016		
Lack of Fit	0.23	4	0.058	12.21	0.0001
Pure Error	0.071	15	4.71E-03		
Cor total	3.59	23			

Table 11: ANOVA of improved second order model for PFR.

Source of variation	SS	d.f.	MSS	F- value	p-value
Model	3.38	4	0.84	43.33	< 0.0001
X_3	1.09	1	1.09	55.96	< 0.0001
X_4	1.47	1	1.47	75.17	< 0.0001
X_3X_4	0.75	1	0.75	38.38	< 0.0001
X_4^2	0.074	1	0.074	3.82	0.0664
Residual	0.35	18	0.019		
Lack of Fit	0.071	4	0.018	0.89	0.4929
Pure Error	0.28	14	0.020		
Cor Tot	3.73	22			

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$$R^2 = \frac{SS_{Model}}{SS_{Total}} \tag{12}$$

The significant model term, insignificant LoF term and R-squared value of 0.90 from variance Table 11 indicates that developed second order model for PFR was also reasonably adequate.

However, in spite of accuracy, the assumptions made for the variance analysis must be verified for the developed models to be valid to represent experimental data. Graphical residual analyses were performed to validate the models of both batch and plug flow reactors over numerical single values because graphical methods give clear representation of the relationship among response and factors (NIST/SEMATECH [26] Handbook of Statistical Methods). The linearity assumption was validated by augmenting center points in aforementioned design tables and accounting for quadratic effects in response. In graphical methods the residuals are re-scaled to a relative unit of estimated standard deviations known as studentized residuals and are plotted against experimental runs, factors or on probability graph to check the root cause of any abnormal deviation.

The normality assumption was verified by plotting the relative magnitude of residuals on normal probability graph as shown in Figs. 2 & 3.

The linear and patterned distribution of residuals about mean zero in normal probability plot as shown in Figure 3 and Figure 4 indicated that proposed models for batch and plug flow reactors were adequate to fit experimental data. The experimental data was subjected to outlier test to check any aberrant deviation or residuals from observed response. One design point in batch reactor analysis showed deviation as shown in Fig. 4.

In batch reactor one design point showed an abnormality of three standard deviations from mean as shown by encircled point in Fig. 4. However, it was confirmed subsequently from Figs. 5 and 6 that encircled point was a mild outlier and it might have been a measurement error instead of any discrepancy in proposed model. The outlier test results for plug flow reactor are presented in Fig. 7. It can be seen from Fig. 7 that there is not discrepancy in the data for plug flow reactor.

The positive sign in Equation 10 and Eq. 11 is due to additive effect of factor whereas a negative sign shows antagonistic effect. Examining F-values from
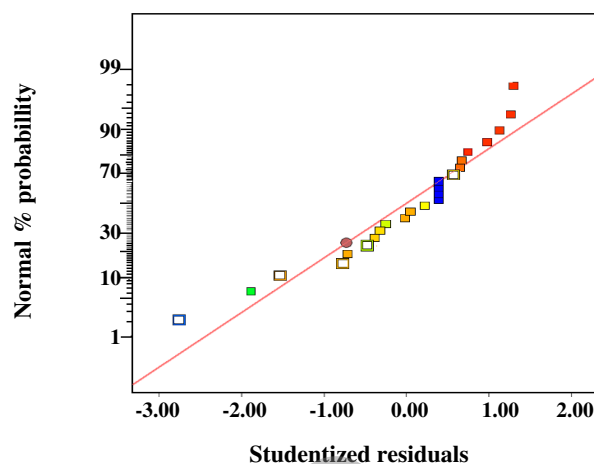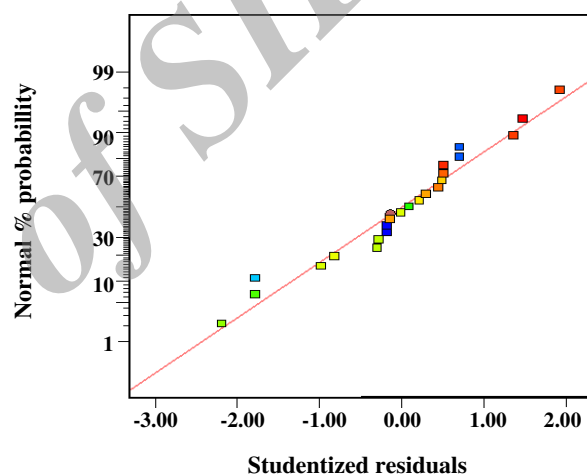

Fig. 2: Graph of residuals for Eq. (10).

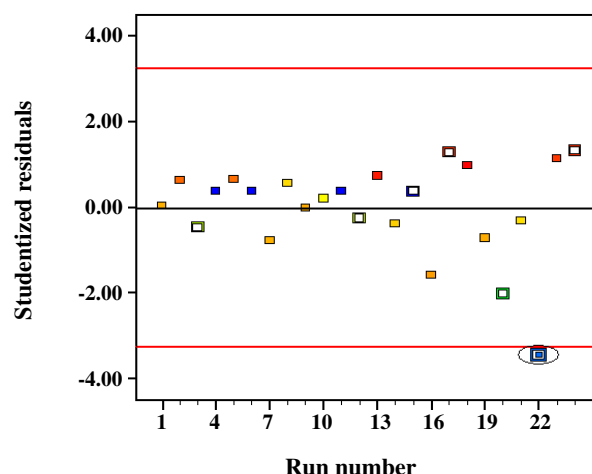*Fig. 3: Normal Graph of residuals for Eq. (11).*

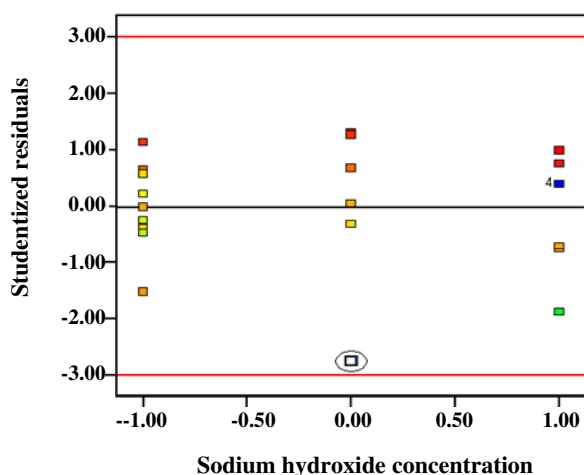*Fig. 4: Outlier t plot of residuals for batch reactor.*

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Fig. 5: Plot of residual Vs Sodium hydroxide concentration.
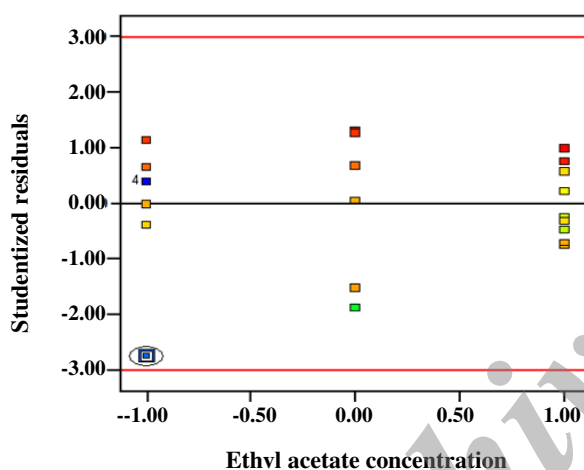

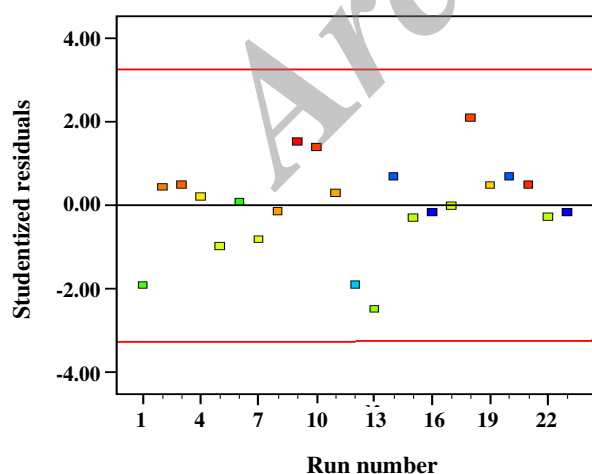*Fig. 6: Plot of residual Vs. Ethyl Acetate concentration.*

Fig. 7: Outlier t plot of residual for PFR.

variance Table 10 the interaction term for batch reactor was the highest effect compared to all factors and was obvious in response surface plot as shown in Fig. 8.

In PFR on the basis of variance analysis as shown in Table 11, it was concluded that first order effect of ethyl acetate concentration had the highest impact on response as compared to the effects of other factors.

Response surface contours were developed after validating the proposed models from Eqs. (10) and (11). It was inferred from contours plots as demonstrated in Figs. 8 and 9 that 97 (±1) % conversion of sodium hydroxide in batch and plug flow reactors was obtained at optimum initial concentrations of 0.01 mol/L and 0.07 mol/L for sodium hydroxide and ethyl acetate respectively. It was obvious from variance analysis (Table 10 and Table 11) and Eqs. (10) and Eq. (11) that an increase in absolute initial concentration of ethyl acetate positively increased conversion whereas negative effects of sodium hydroxide tend to decrease the reaction conversion. This phenomenon was graphically represented in Figs. 8 and 9. The effects of initial concentrations of ethyl acetate and sodium hydroxide on conversion were shown on response surface contour plots in Figs. 8 and 9. The linear increase in conversion with increasing ethyl acetate concentration while keeping sodium hydroxide concentration constant was more profound in PFR than batch reactor. The elliptical curved contour lines in Fig. 8 were the consequence of the highest interaction effect in batch reactor. The decrease in conversion rate due to the interaction and quadratic effects of ethyl acetate and sodium hydroxide were marked, more or less, at 0.07 mol/L. In the absence of axial mixing, less volume of sodium hydroxide was available for an element of reaction mixture in PFR at time t which resulted in almost linear behavior of response as shown in Fig. 9 and the inference is further supported from variance Table 11. The experimental finding that sodium hydroxide concentration influences conversion negatively in hydrolysis of ethyl acetate and its presence in small concentrations assist in higher conversions was in agreement with the observations of *Mata-Segreda* (2002) [17].

CONCLUSIONS

The objective of this study was to investigate the alkaline hydrolysis of ethyl acetate reaction to maximize conversion,
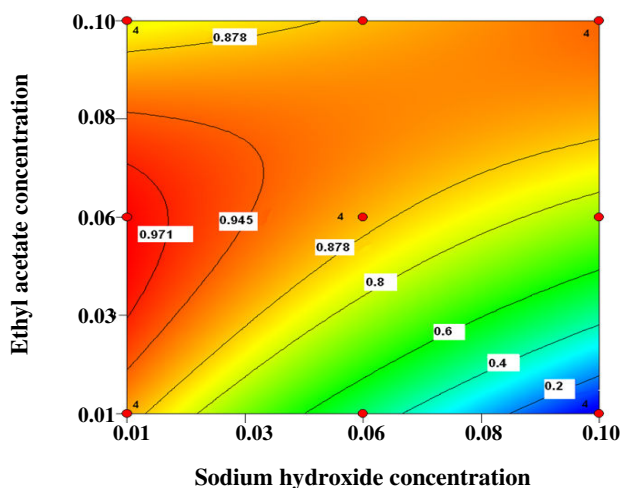
Fig. 8: Contour plot of Equation 10 for batch reactor.

Fig. 9: Contour plot of Equation 11 for PFR.

minimize reaction time and economical usage of the reactants in plug flow reactor. It was observed during trial runs that reaction took 45-60 minutes for completion in batch reactor. Therefore, a residence time of 5 minutes was selected to maximize conversion by varying four factors from a low level to a high level. Design of experiments, a statistical tool was utilized to construct the design matrix and experiments were then conducted accordingly. Experiments were planned in two stages, screening experiment and response surface methodology. In screening stage, factors contributing major changes in the response were determined as significant and in the second phase these significant factors were varied to optimize conversion of sodium hydroxide.

The important factors identified were initial concentrations of sodium hydroxide and ethyl acetate. It was found that response did not change linearly by varying initial concentrations of reactants over two levels. The experimental data was fitted with a second order polynomial model. The least interaction and highest first order ethyl acetate concentration was due to the absence of axial mixing in PFR. The presence of sodium hydroxide along the entire reaction path resulted in higher interaction effects with ethyl acetate. The optimum initial concentrations that resulted in 91(±1)% conversion of sodium hydroxide were 0.01 mol/L, 0.07 mol/L for sodium hydroxide and ethyl acetate respectively in both batch and plug flow reactors.

Acknowledgment

Nomenclature

β	Regression coefficient
C	Specific conductivity at time t, µS
C_{EtOAc}	Concentration of ethyl acetate, mol/L
C_{NaOH}	Concentration of sodium hydroxide, mol/L
$C_{NaOH,o}$	Concentration of sodium hydroxide at t = 0, mol/L
$C_{NaOH,\infty}$	Concentration of sodium hydroxide at t = ∞, mol/L
C_o	Specific conductivity at time t = 0, µS
C_∞	Specific conductivity at time t = ∞, µS
k	Second order rate constant, also number of factors in experimental design
MSS_{error}	Mean sum of squares of error
MSS_{effect}	Mean sum of squares of effect
n_C	Number of center point
n_F	Number of design points
N	Number of experiments
$-r_{NaOH}$	Consumption rate of sodium hydroxide, mol/Ls
$SS_{curvature}$	Sum of squares of curvature
SS_{effect}	Sum of squares of effect
SS_{error}	Sum of squares of error
$U_{i, average}$	Average value of factor
$U_{i, natural}$	Natural value of factor
X_A	Fractional conversion of sodium hydroxide
X_i	Codified value of factor
X1	Codified value of agitation rate
X2	Codified value of reaction temperature
X3	Codified value of initial NaOH concentration

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X4   Codified value of initial EtOAc concentration
Y_C Average response at the center points
Y_F Average response at factorial points
ΔU_i Incremental value of factor

Greek Letters

α   Significance level
α*   Axial runs for face-centered composite design

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