International Journal of Advanced Science and Research
ISSN: 2455-4227, Impact Factor: RJIF 5.12
www.allsciencejournal.com
Volume 1; Issue 9; September 2016; Page No. 01-07

Optimized synthesis conditions of two porous polymers using 20-runs CCD from response surface methodology

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Abstract
In order to optimize the synthesis conditions of porous polymers, the amount of two monomers, the amount of crosslink and porogen as the three major influence factors are considered. Simultaneously, response surface methodology is introduced to analysis and predict the optimized conditions using 20-runs CCD. According to the analysis of significant factors of quadratic polynomial model, the amount of three major factors are given (0.47 mL, 1.06 mL and 2.84 mL for MAA, crosslink and porogen; 0.33 mL, 3.45 mL and 3.49 mL for 2-HEMA, crosslink and porogen). The final amount of obtained polymer is verified, and the predicted values corresponded well to actual values.

Keywords: Central composite design, response surface methodology, porous polymer, methyl methacrylate, 2-hydroxyethyl methacrylate

1. Introduction
With the development of separation technologies, there are lots of advanced methods using currently. Among them, adsorption with a sorbent is one of the most widely used method in separation process. The properties of the sorbents are crucial for the performance of separation, and the choice of a suitable material is critical. Of the available materials, polymer had received more attention because of easy preparation, low cost, its excellent mechanical properties and good chemical stability over a wide pH range [1-3]. Furthermore, because of the large specific surface area, pore size and functional groups, porous polymers are already utilized [4-6].

In order to exhibit the advantage of porous polymer adequately, an elaborate design is needed during the synthesis process. For all types of reactants, monomer, crosslink and porogen are the three major factors could affect the final quality properties obviously. As the monomer, methyl methacrylate (MAA) and 2-hydroxyethyl methacrylate (2-HEMA) are two common reactants to be used in functional polymer [7].

Previous method needs a large number of experiments, and in order to decrease the numbers with increasing the accuracy, mathematic technology need to be introduced. In this case, a estimation and prediction method called response surface methodology (RSM) is involved. RSM explore variations in polymer product quality when levels are changed in the formulation. This technique is a mathematical and statistical tool used to simultaneously evaluate several factors and estimate their linear, quadratic and interaction effects [8].

RSM has been used to optimize the conditions of extraction, but to optimize the synthesis amount of polymer is uncommonly. Therefore, the synthesis conditions which are influenced by different variables, especially monomer, crosslink and porogen, are estimated. RSM uses an experimental design such as the Central Composite Design (CCD) to fit a model by least squares technique. This method is suitable for fitting a quadratic surface, and it helps to optimize all the effective factors with a minimum number of experiments simultaneously and also to analyze the interaction between the parameters [9, 10].

In this research, 20-runs CCD method (three main levels with two additional levels) is used to optimize the volume of two monomers, crosslink and porogen in synthesis process. The final amount of obtained polymers will be predicted and validated.

2. Materials and Methods
2.1 Materials
Methyl methacrylate (MAA) and 2-hydroxyethyl methacrylate (2-HEMA) as monomers were purchased from Sigma (St Louis, MO, USA). Ethylene glycol dimethacrylate (EGDMA) as crosslink was from Fluka (Buchs, Switzerland). Dodecanol as porogen, methanol and other organic solvents were obtained from Duksan Pure Chemical Co., LTD (Ansan, Korea). 2, 2'-Azobis (isobutyronitrile) (AIBN) as initiator was purchased from Junsei Chemical Co. Ltd. (Tokyo, Japan) and refined prior to use.

2.2 Preparation of porous polymers
Set amounts of two monomers, crosslink, and porogen were dissolved in methanol, after degassing 50 mg of AIBN was added and fully mixed in vials. Polymerization was then allowed to proceed at 60 ^{o}C for 24 h. Subsequently, the vials in polymers were fully washed for several times by methanol in order to remove porogen and unreacted chemicals. The polymers were then dried at 70 ^{o}C in a vacuum oven for 24 h and weighed by electronic scale.

2.3 Experimental design
According to the CCD method from RSM using Design-Expert software (v.8.0.6, Stat-Ease, Inc, Minneapolis, USA), three major factors such as the volumes of monomers, crosslink and porogen, which can significantly affect the

amount of obtained polymer, were selected. According to previous researches, when the volumes of monomers and crosslink were less than 0.1 mL and 0.5 mL, the contributions of them in synthesis process were quite small. However, when the amounts of them were higher than 0.6 mL and 3.0 mL, the process of self-polymerization will reduce the final amount of polymer. Also for the hardness of obtained polymer, it was too hard when the volume of porogen was less than 1.5 mL and too soft when the volume was higher than 3.0 mL. Therefore, three factors of the CCD were designated X_1, X_2, and X_3 and divided into three levels in Table 1. The codes -1, 0, and +1 were assigned as low, intermediate, and high values, respectively.

Table 1: Levels of independent variables used in CCD

Variables	Level		
	-1	0	1
Amount of monomer (mL) (X_1)	0.1	0.45	0.6
Amount of crosslink (mL) (X_2)	0.5	1.75	3.0
Amount of porogen (mL) (X_3)	0.5	1.75	3.0

The three test variables were coded according to the following equation:

$$x_i = \frac{X_i - X_0}{\Delta X} \quad i=1, 2, 3 \qquad (1)$$

In this equation, all x or X are related to the value of independent variables. x_i is the coded value, X_i is the actual value, X_0 is the actual value at the center point, and ΔX is the step change value. A quadratic polynomial model was fitted to the interaction between the response (amounts of obtained polymers) and independent variables (x_i, X_i, X_0, ΔX).

$$Y = A_0 + \sum_{i=1}^{3} A_i X_i + \sum_{i=1}^{3} A_{ii} X_i^2 + \sum_{i=1}^{2} \sum_{j=i+1}^{3} A_{ij} X_i X_j \qquad (2)$$

In the equation, Y is the dependent variable (amount of obtained polymer). The independent variables (X_i and X_j) were used to evaluate the model according to each effect on the response. A_0 is a constant coefficient, and A_i, A_{ii}, and A_{ij} are the coefficients for the linear, quadratic, and interaction effects, respectively. The experimental design was analyzed, and the predicted data were calculated in order to estimate the response of the independent variables. Additional experiments were performed to validate the statistical experimental strategies.

3. Results & Discussion

3.1 Model building and statistical analysis

A 20-runs CCD was used to fit the quadratic response surface and optimize the synthesis conditions of three factors. Among them some runs were at center points and the amount of polymer was obtained as response. Table 2 list the design variables with the predicted and actual values of the response. Comparing the two values from each monomer roughly, the similar amounts of obtained polymers show the accuracy of prediction on a certain level.

Table 2: Arrangement of independent variables with two monomers

Run	Coded variable levels			Amount of polymer (mg)			
				MAA		2-HEMA	
	X_1	X_2	X_3	Actual values	Predicted values	Actual values	Predicted values
1	-1	-1	-1	2137.9	2053.6	2030.8	1975.3
2	1	-1	-1	3341.9	3257.6	2324.9	2269.4
3	-1	1	-1	3701.3	3617	3586.8	3531.3
4	1	1	-1	4237.4	4153.1	4110.8	4055.3
5	-1	-1	1	2534.0	2449.7	2455.4	2399.9
6	1	-1	1	2904.6	2820.3	2898.7	2843.2
7	-1	1	1	4574.2	4489.9	5163.7	5108.2
8	1	1	1	4799.2	4714.9	4774.8	4719.3
9	-1.68	0	0	3068.4	3187.6	2956.5	3035.1
10	1.68	0	0	3432.1	3551.3	3544.8	3623.4
11	0	-1.68	0	4904.2	5023.4	4961.5	5040.1
12	0	1.68	0	1559.1	1678.3	1510.6	1589.2
13	0	0	-1.68	2954.6	3073.8	2864.7	2943.3
14	0	0	1.68	3997.0	4116.2	3885.7	3964.3
15	0	0	0	3314.3	3338.4	3420.6	3417.9
16	0	0	0	3316.5	3338.4	3421.9	3417.9
17	0	0	0	3320.3	3338.4	3478.0	3417.9
18	0	0	0	3412.5	3338.4	3367.7	3417.86
19	0	0	0	3402.5	3338.4	3467.9	3417.9
20	0	0	0	3305.2	3338.4	3378.0	3417.9

The following two equations (Eq (3) with MAA and Eq (4) with 2-HEMA) show the relationship between the response and three factors which was predicted from the experimental data:

$$Y = 3338.4 + 108.13X_1 - 994.50X_2 + 309.91X_3 - 101.69X_1X_2 - 143.06X_1X_3 + 184.49X_2X_3 + 10.98X_1^2 + 4.41X_2^2 + 90.73X_3^2 + 65.29X_1X_2X_3 + 1793.72X_1^2X_2 - 135.72X_1^2X_3 + 183.83X_1X_2^2 \quad (3)$$

$$Y = 3417.86 + 174.90X_1 - 1025.96X_2 + 303.55X_3 - 75.29X_1X_2 - 95.46X_1X_3 + 155.31X_2X_3 - 31.35X_1^2 - 36.51X_2^2 + 12.69X_3^2 - 132.76X_1X_2X_3 + 2016.75X_1^2X_2 + 101.37X_1^2X_3 - 65.84X_1X_2^2 \quad (4)$$

Table 3 presents more values from the data analysis. The models F-value of 38.641 from MAA and 105.179 from 2-HEMA imply the models are significant. And only a 0.01% chance for both of models that the F-value could occur due to noise.

Table 3: Analysis of variance of the experimental results and quadratic polynomial models of two monomers

Source	MAA		2-HEMA	
	***F* value**	***p* value (Prob>F)**	***F* value**	***p* value (Prob>F)**
Model	38.641	0.0001	105.179	< 0.0001
X_1	2.573	0.159	14.431	0.009
X_2	217.686	< 0.0001	496.542	< 0.0001
X_3	21.139	0.0037	43.465	0.0006
$X_1 X_2$	3.219	0.123	3.781	0.0998
$X_1 X_3$	6.371	0.045	6.080	0.0487
$X_2 X_3$	10.594	0.0174	16.093	0.0070
X_1^2	0.0676	0.804	1.181	0.319
X_2^2	0.0109	0.920	1.602	0.253
X_3^2	4.6156	0.0753	0.194	0.675
$X_1X_2X_3$	1.327	0.293	11.759	0.0140
$X_1^2X_2$	414.825	< 0.0001	1123.928	< 0.0001
$X_1^2X_3$	2.375	0.174	2.839	0.143
$X_1X_2^2$	4.357	0.0819	1.198	0.316
Lack of fit	60.280	0.0006	30.518	0.0027
R^2	0.988		0.963	
R_{Adj}^2	0.963		0.987	
Adeq. Precision	24.939		38.409	

The *p* value showed the noise probability and it was used as a tool to check the significance of each coefficient. The *p* value less than 0.05 indicates model terms are significant, and both of two monomers are satisfied. Also for each independent value, the number greater than 0.10 indicate the model terms are not significant. So X_2, X_3, X_1X_3, X_2X_3 and $X_1^2X_2$ are significant for MAA, and X_1, X_2, X_3, X_1X_3, X_2X_3, $X_1X_2X_3$ and $X_1^2X_2$ are significant for 2-HEMA. Additionally, the values of MAA (60.280) and 2-HEMA (30.518) imply the lacks of fit are significant. 0.06% and 0.27% chances of the values could occur due to noise, respectively.

Moreover, R^2 and R_{Adj}^2 are close to 1 means the high accuracy of models. The Adeq. Precision measures the signal to noise ratio, and the ratio greater than 4 is desirable. Both of the Adeq. Precision values are quite larger than 4 indicate adequate signals.

3.2 Optimization of procedure

The response surface curves were used to examine the interactions of the variables and to determine the optimal level of each variable for the maximum response. The optimal values of the selected variables were obtained by solving the regression equation to maximize the dependent value *Y*. The variation trends in the results from the both monomer were compared. Because of the differences of functional group, structure, molecular, *et al*, the MAA monomer gave more errors although the result was acceptable. The 3D response surfaces were provided as graphical representations of the regression equation (Figures 1, 2). Figure 3 also confirmed that the error from MAA monomer.

Both Figure 1 and 2 show that when porogen was used as a variable and the volume of monomer or crosslink were fixed, the amount of obtained polymer did not increase with increasing the amount of porogen significantly. These results showed that monomer and crosslink had more influence. Additionally, the amount of crosslink had more obvious effect than monomer.

The optimized synthesis conditions suggested by the CCD method for MAA (X_1=0.47, X_2=1.06, X_3=2.84) and 2-HEMA (X_1=0.33, X_2=3.45, X_3=3.49) were estimated with the model equation by solving the regression equation and analyzing the response surface contour plots. The predicted amount of polymer was obtained under the suggest conditions. In contrast, the predicted amount of polymer with MAA (5037.48 mg) and with 2-HEMA polymer (5568.87 mg) were slightly higher than the actual amount (4978.6 mg and 5485.5 mg) respectively.

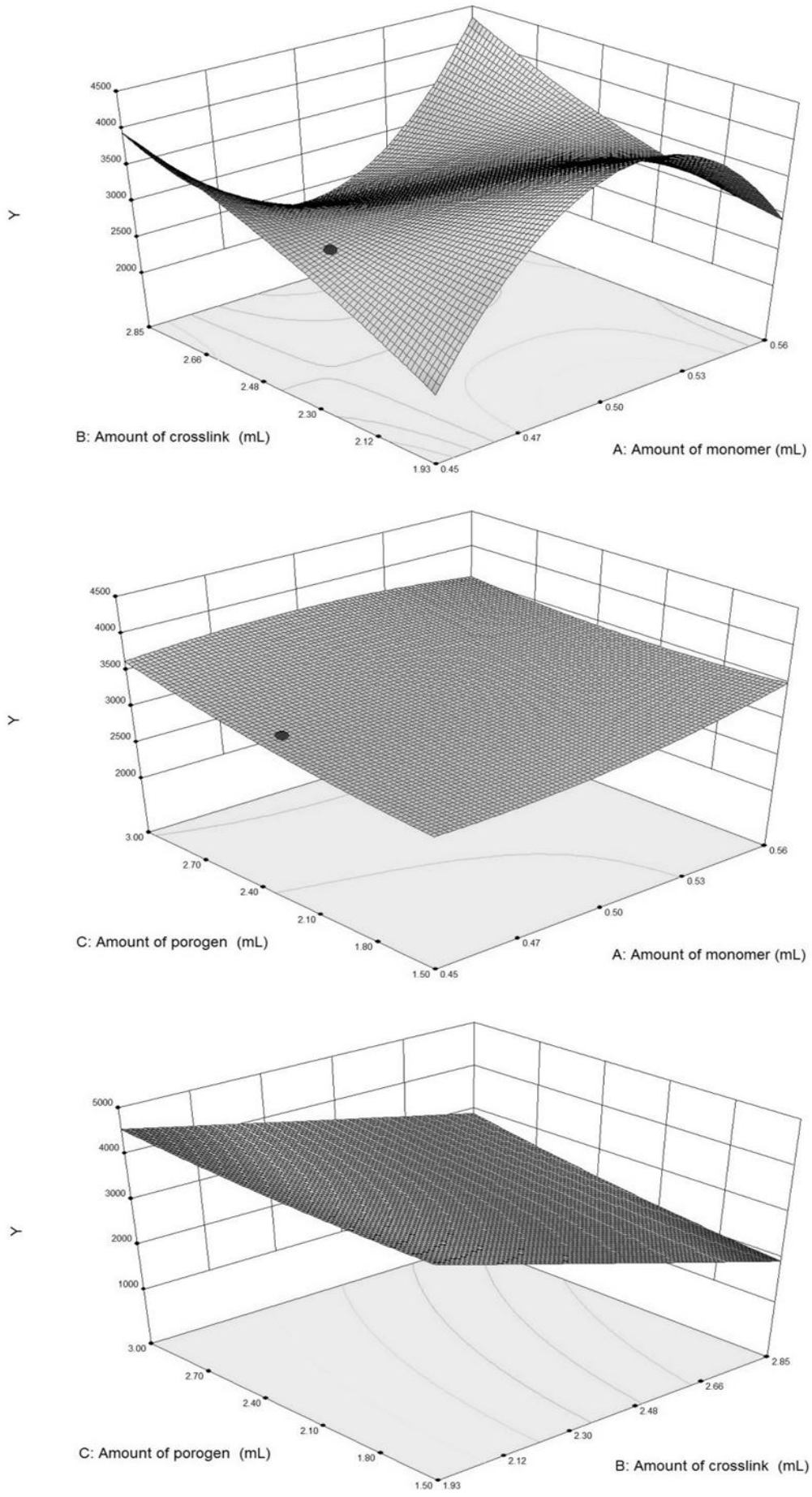

Fig 1: Different conditions and their reciprocal interaction on amount of polymer with MAA.

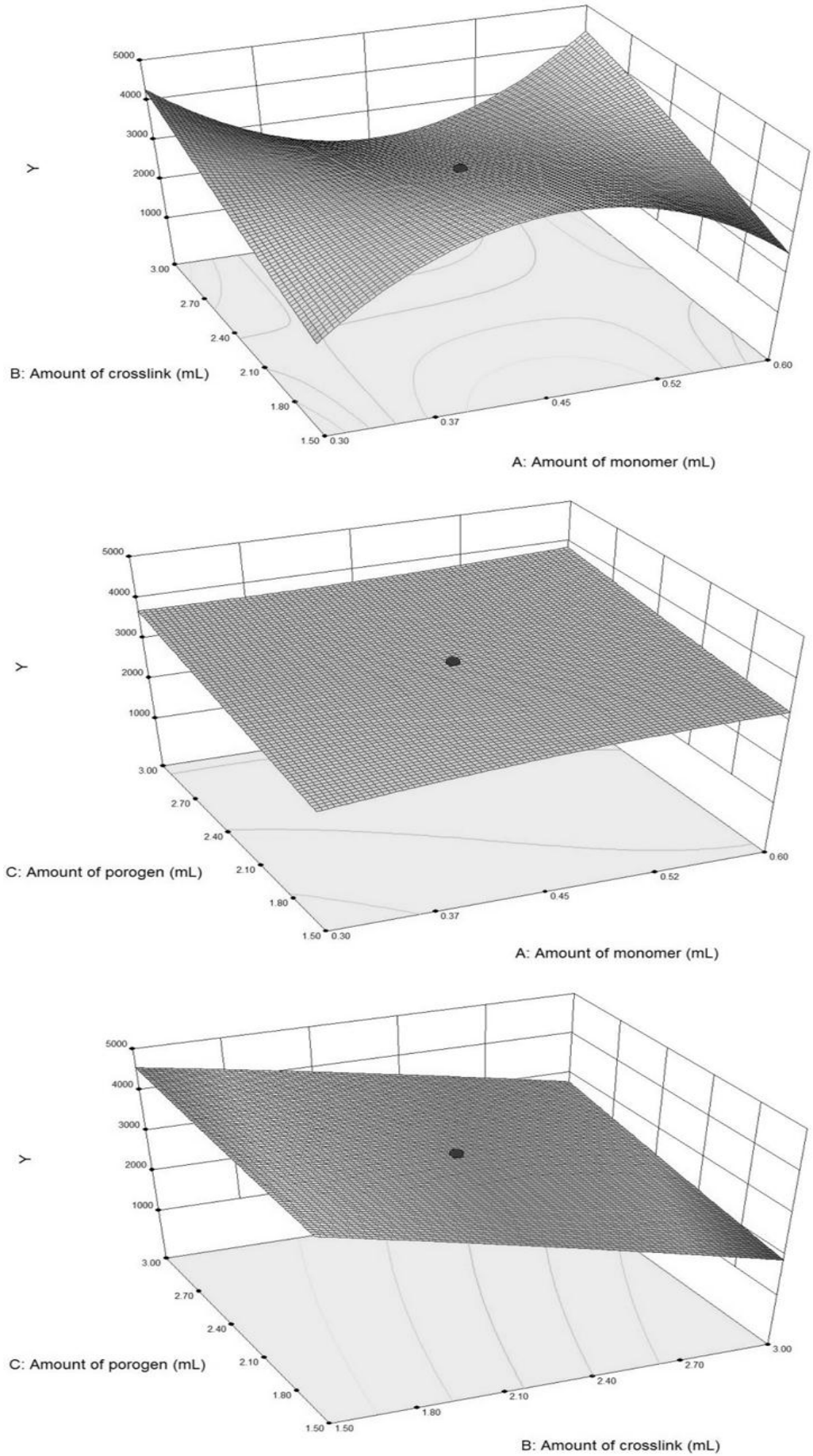

Fig 2: Different conditions and their reciprocal interaction on amount of polymer with 2-HEMA.

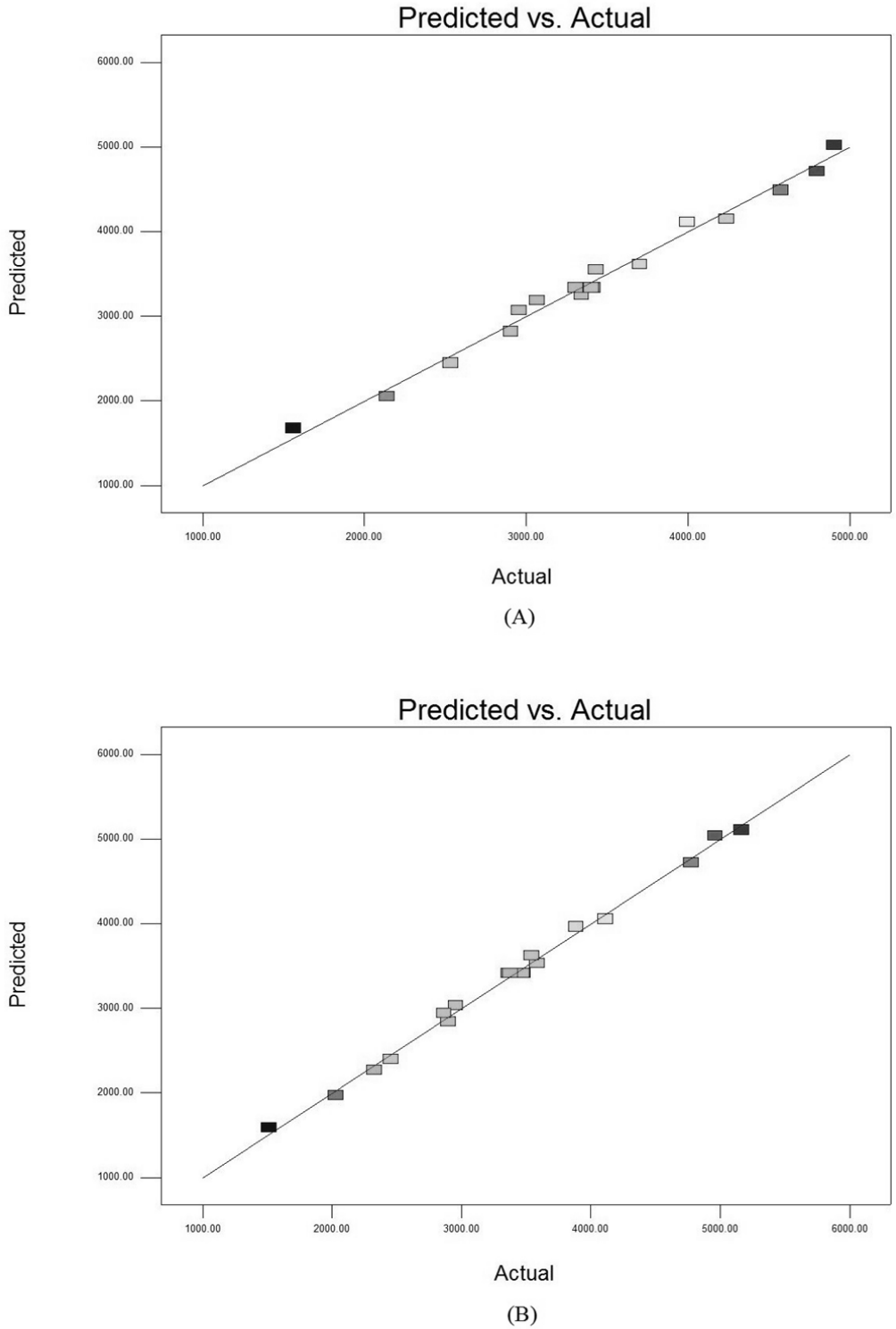

Fig 3: The correlation between predicted and actual results of monomer (A) MAA and (B) 2-HEMA.

4. Conclusions

20-runs CCD were successfully used to optimize the synthesis conditions of polymers with two monomers. The high adjusted coefficient of determination and high significant proved the accuracy of the model. With the suggested conditions, the predicted amounts of obtained polymers corresponded well to actual values.

5. Acknowledgements

This work was supported by the National Natural Science Foundation of China (No. 51503020) and Foundation of Hubei Education Committee (No. Q20151310)

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