

# Preparation of a monolithic sorbent using a response surface methodology

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## Abstract

A 17-run Box-Behnken Design (BBD) was introduced to optimize the synthesis conditions of a monolithic sorbent. The effects of the amount of monomer (mL), crosslinker (mL) and porogen (mL) were investigated. The experimental data was fitted to a second - order polynomial equation by multiple regression analysis, which was examined using statistical methods. The adjusted coefficient of determination ( $R^2_{Adj}$ ) in this model was 0.9867. The probability value ( $p < 0.0001$ ) revealed the high significance of the regression model. A mean amount of 5057.4 mg polymer was produced under the following optimized synthesis conditions: 0.51 mL monomer, 2.94 mL crosslinker and 2.84 mL porogen. The actual experimental result was in good agreement with the predicted model value.

**Keywords:** Preparation; Monomer; Crosslinker; Porogen; Response Surface Methodology.

## 1. Introduction

A monolithic sorbent is a single rod with high permeability, efficiency, effective porosity, and low column backpressure [1]. Monolithic sorbents have many other advantages, including simple preparation, good peak capacity, high permeability, and versatility in surface modification [2-4]. Compared to conventional packing columns, such as a particulate-based  $C_{18}$  or silica columns, monolithic sorbents are characterized by their high reproducibility and rapid mass transport. Furthermore, polymer-based monolithic sorbents are expected to behave as excellent stationary phases in HPLC [5], [6], particularly as solid-phase extraction (SPE) materials.

The potential properties of polymer-based sorbents have been studied using a range of methods [7], [8]. Among these, the response surface methodology (RSM) described by Box and Wilson is an effective optimization tool for situations where many factors and interactions affect the desired response. The main point of RSM is to optimize the conditions for the response of the designed experiments [10], which will be arranged and interpreted easily using this efficient design [11-14]. RSM features two main experimental design methods: the Box-Behnken design (BBD) and the central composite design (CCD). These experimental designs were fitted to a second-order polynomial using a least squares technique. BBD, which has only three levels, requires fewer experiments and is more efficient, making it easier to arrange and interpret experiments compared to other methods [15], [16].

Because RSM can be used to obtain the predicted values of a non-experimental range in just a few experiments, it is useful for the efficient synthesis of monolithic sorbents (polymer, PHEMA), which is affected by many variables. This study examined three variables (the amounts of monomer, crosslinker and porogen) to optimize the synthesis of a monolithic sorbent using BBD in RSM.

## 2. Experimental

### 2.1. Materials

2-Hydroxyethyl methacrylate (2-HEMA) was obtained from Sigma (St Louis, MO, U.S.A.). Ethylene glycol dimethacrylate (EGDMA) was purchased from Fluka (Buchs, Switzerland). Dodecanol was acquired from Acros organics (New Jersey, U.S.A.). 2,2'-azobis (isobutyronitrile) (AIBN) was supplied by Junsei Chemical Co. Ltd. (Japan) and refined prior to use. Methanol (MeOH) was obtained from Duksan Pure Chemical Co., LTD (Ansan, Korea).

### 2.2. Preparation of monolithic sorbent

According to Tian et al. [17], the substrate polymers were prepared by in-situ polymerization. Briefly, 50 mg of AIBN was dissolved in 1.0 mL of methanol. The resulting solutions were then added to the designed amounts of monomer, crosslinker and porogen. Subsequently, polymerization was allowed to proceed at 60 °C for 24 h. The vials with the polymers were then washed three times over a 3 day period with methanol for remove the porogen. Finally, the polymers were dried at 70 °C for 24 h.

### 2.3. Experimental design

A 17-run BBD was applied to optimize the monolithic sorbent. The amounts of monomer, crosslinker and porogen were selected as the parameters.

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

Where Y is the dependent variable (amount of polymer), and  $A_0$ ,  $A_i$ ,  $A_{ij}$ , and  $A_{ij}$  are the coefficients estimated by the model.  $X_i$  and

$X_j$  are the levels of the independent variables representing the linear, quadratic and cross-product effects of the  $X_1$ ,  $X_2$  and  $X_3$  factors on the response, respectively. The independent variables were used to evaluate the model according to each effect on the response. The experimental design was analyzed, and the data was predicted to estimate the response of the independent variables using Design-Expert software (v.8.0.6, Stat-Ease, Inc., Minneapolis, USA). An additional experiment was performed to confirm the validity of the statistical experimental strategies.

### 3. Results and discussion

#### 3.1. Model building and statistical analysis

A 17-run BBD with three factors (amounts of monomer, crosslinker and porogen) and including five repeats at the center point, was used to fit the second-order response surface to optimize synthesis conditions. Five runs of the center point were carried out to maintain the inherent variability and process stability, and the amount of monolithic sorbent (polymer) was taken as the response. Table 1 lists the F- values and p values of each coefficient. The p value shows the noise probability of the F-value and is used to check the significance of each coefficient, as well as the interaction strength between each independent variable [19]. A F- value of the model with very low probability ( $p < 0.0001$ ) showed that the quadratic regression model is significant. An F-value of 132.71 of the model showed that the model was significant, and the noise probability due to the F- value was lower than 0.0001 %. A “Lack of Fit F- value” of 1.87 showed that the pure error was not significant, and the noise probability due to the “Lack of Fit F- value” was 27.52 %. Table 1 also lists the regression coefficients and corresponding p values.

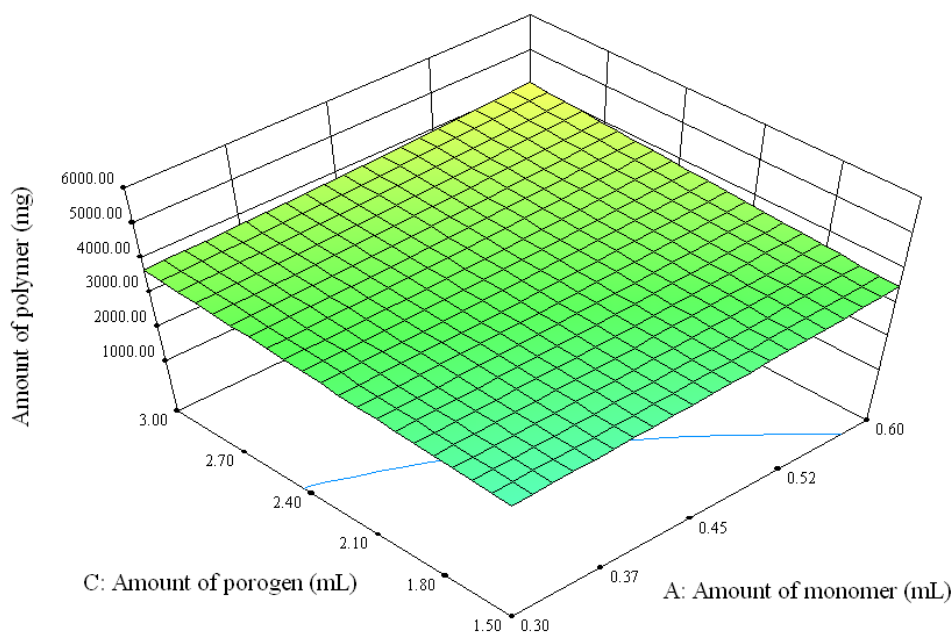
The above data was established by the coefficient of determination ( $R^2 = 0.9942$ ), adjusted coefficient of determination ( $R^2_{Adj} = 0.9867$ ), and coefficient of variation (C.V. = 2.81 %). According to these values, the polynomial model was appropriate. The  $R^2_{Pred}$  value of 0.9418 was in reasonable agreement with the  $R^2_{Adj}$  value.

An “Adeq. Precision” of 38.511 showed that this model could navigate the design space.

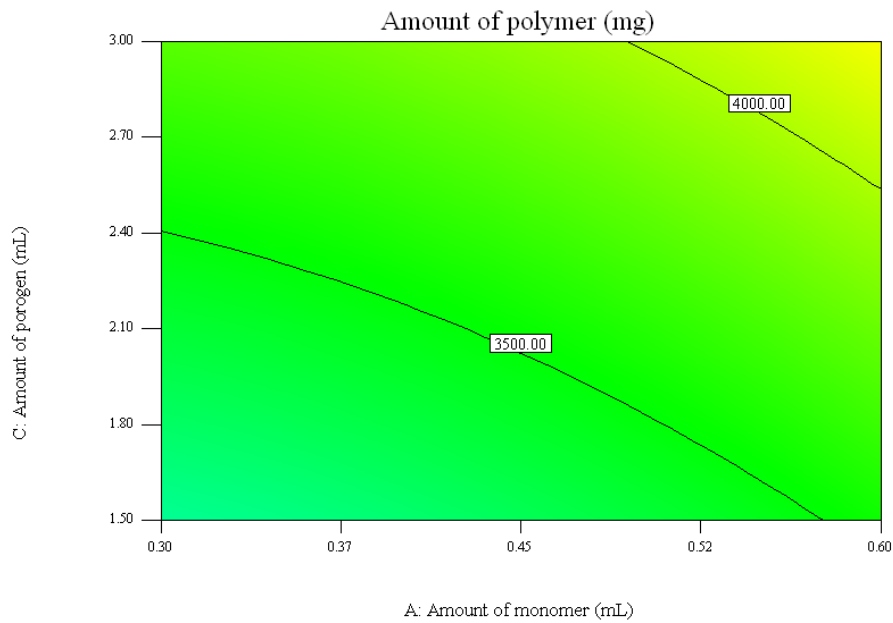
#### 3.2. Optimization of procedure

The surface curves of the response were plotted to show the interactions of the variables as well as the optimal level of each variable for the optimal response [19]. The variable for the optimal values was selected by the regression equation using the Design-Expert software. The 3D response surface and 2D contour plots were established as graphical representations of the regression equation (Figures 1 and 2). When the other factors were fixed to the zero level, each contour curve related an infinite number of combinations of the two variables. The amount of polymer increased sharply with increasing amount of crosslinker, whereas the amount of polymer only increased slightly with larger amounts of monomer. Figures 1 and 2 shows the amount of polymer due to the interactions of the amount of monomer and porogen when the amount of crosslinker fixed at 2.25 mL. The amount of polymer showed large variations according to the amounts of monomer and porogen. As shown in Figures 1 and 2, the crosslinker was the strongest factor affecting polymer synthesis. In addition, the importance of crosslinker can be derived from the F and p- values (Table 1). Therefore, the amount of polymer could be controlled by regulating the amount of crosslinker, which limited the synthesis under sufficient amounts of monomer and porogen.

Figure 3 shows the relationship between the actual and predicted values of the amount of polymer. The residuals were in close proximity to the straight diagonal line. The optimal conditions for the synthesis of polymer were determined as follows: amount of monomer = 0.51 mL, amount of crosslinker = 2.94 mL and amount of porogen = 2.84 mL. These were predicted using the regression equation and by an analysis of the response surface contour plots (Figure 3) using the Design-Expert software. The theoretical amount of polymer (monolithic sorbent) under the above conditions was 4951.233 mg.



**Fig. 1:** Effects of the Amount of Monomer, Porogen and Their Reciprocal Interaction on the Amount of Polymer. (With the Amount of Crosslinker Kept Constant at 2.25 MI) (3D Response Surface).

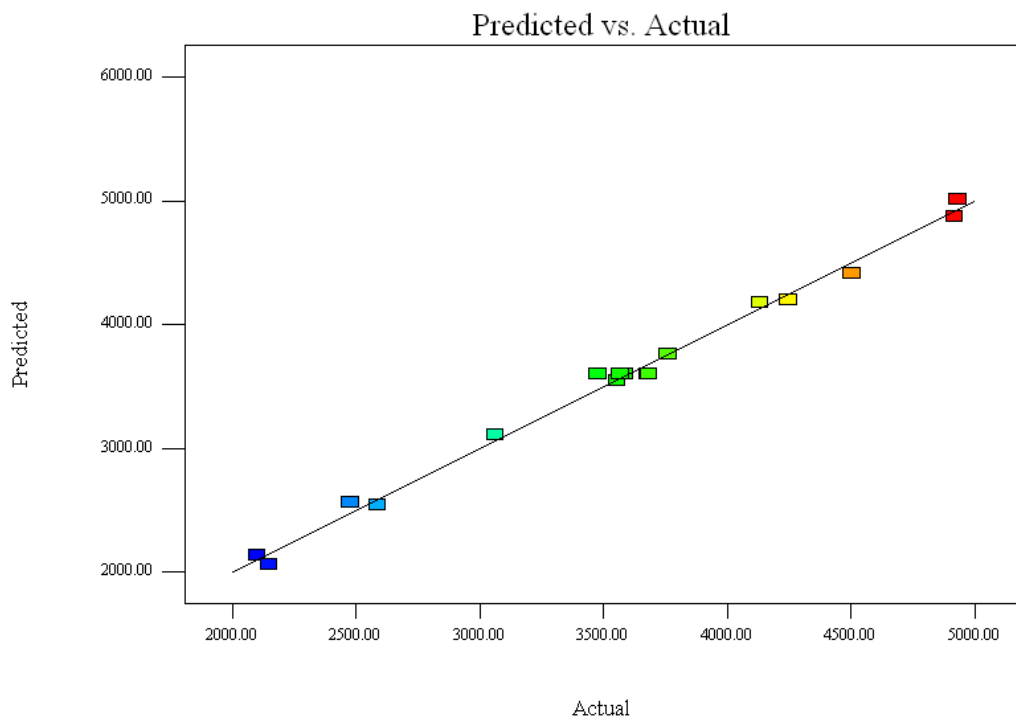


**Fig. 2:** Effect of the Amount of Monomer, Porogen and Their Reciprocal Interactions on the Amount of Polymer. (With the Amount of Crosslinker Kept Constant at 2.25 MI) (2D Contour Plots).

**Table 1:** Analysis of the Variance of the Experimental Results of the Bbd

Source	Sum of Squares	DF	Mean Square	F Value	p-value Prob> F
Model	11900950	9	1322328	132.71	< 0.0001 <sup>a</sup>
A-Monomer	392320.8	1	392320.8	39.37	0.0004 <sup>a</sup>
B-Crosslinker	10507216	1	10507216	1054.55	< 0.0001 <sup>a</sup>
C-Porogen	861262.5	1	861262.5	86.44	< 0.0001 <sup>a</sup>
AB	327.6	1	327.61	0.03	0.8612
AC	7.8	1	7.84	0.001	0.9784
BC	32887.8	1	32887.8	3.30	0.1121
A <sup>2</sup>	12521.2	1	12521.2	1.26	0.2993
B <sup>2</sup>	97783.1	1	97783.0	9.81	0.0165 <sup>a</sup>
C <sup>2</sup>	62.7	1	62.7	0.006	0.9390
Residual	69745.9	7	9963.7	-	-
Lack of Fit	40734.4	3	13578.1	1.87	0.2752
Pure Error	29011.5	4	7252.9	-	-
Cor Total	11970696	16	-	-	-

<sup>a</sup> Means significance (Values of "Prob> F" less than 0.0500)



**Fig. 3:** Scatter Diagram of the Predicted Response versus the Actual Response for the Amount of Polymer.

### 3.3. Validation of the model

The above conditions were applied three times in an actual experiment to validate them. The actual amount of polymer (monolithic sorbent) produced under the selected optimal conditions according to the BBD was 5057.4 mg, which corresponded well to the value predicted from the model equation.

## 4. Conclusions

To optimize the amount of monolithic sorbent, the BBD of RSM worked quite well. In this model, the coefficient of determination ( $R^2$ ) was 0.9942, whereas the probability value ( $p < 0.0001$ ) played an important role in the regression model. In this synthesis of polymer, the optimal conditions were as follows: amount of monomer = 0.51 mL, amount of crosslinker = 2.94 mL and amount of porogen = 2.84 mL. Under these conditions, the actual amount of synthesized polymer was 5057.4 mg, which corresponded well to the predicted value. Overall, the methodology developed in this study can be applied to predict the optimal synthesis in future research.

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