

Supplementary Material-I

Table S1 Full factorial central composite design matrix with their observed & predicted responses.

Run	Type	Independent Variable			Response Variable (Flux) ($\mu\text{g}/\text{cm}^2/\text{h}$)	
		Guar gum (X_1) (mg)	Na-CMC (X_2) (mg)	Glycerol (X_3) (mg)	Observed	Predicted
1	Center	450 (0)	450 (0)	2500 (0)	998.343	998.16
2	Axial	450 (0)	450 (0)	3340.9 (+ α)	70.8036	16.83
3	Axial	365.91 (- α)	450 (0)	2500 (0)	1024.52	908.59
4	Center	450 (0)	450 (0)	2500 (0)	998.343	998.16
5	Center	450 (0)	450 (0)	2500 (0)	998.343	998.16
6	Factorial	500 (+1)	500 (+1)	2000 (-1)	522.949	486.83
7	Axial	450 (0)	450 (0)	1659.1 (- α)	464.043	524.43
8	Factorial	500 (+1)	500 (+1)	3000 (+1)	356.65	249.57
9	Factorial	500 (+1)	400 (-1)	3000 (+1)	227.34	277.78
10	Axial	534.09 (+ α)	450 (0)	2500 (0)	562.89	685.24
11	Factorial	400 (-1)	500 (+1)	3000 (+1)	83.256	195.40
12	Factorial	400 (-1)	400 (-1)	3000 (+1)	349.793	381.38
13	Axial	450 (0)	534.09 (+ α)	2500 (0)	208.865	257.83
14	Center	450 (0)	450 (0)	2500 (0)	998.343	998.16
15	Axial	450 (0)	365.91 (- α)	2500 (0)	407.29	364.74
16	Center	450 (0)	450 (0)	2500 (0)	998.343	998.16
17	Center	450 (0)	450 (0)	2500 (0)	998.343	998.16
18	Factorial	500 (+1)	400 (-1)	2000 (-1)	544.656	427.98
19	Factorial	400 (-1)	500 (+1)	2000 (-1)	703.811	648.84

Factorial Design study

Effect on Response: Flux (Y)

Fig. S1 Response surface 2D contour plots showing effects of (a) Guar gum and Na-CMC , (b) Guar gum and Glycerol, (c) Na-CMC and Glycerol on the flux.

Evaluation of Optimum values of the Independent variables

The polynomial equation of our model is;

$$Y = 998.16 - 66.40X_1 - 31.78X_2 - 150.91X_3 + 39.45X_1X_2 - 21.76X_2X_3 + 54.05X_1X_3 - 71.15X_1^2 - 242.85X_2^2 - 257.22X_3^2 \quad \text{Eq. (A.1)}$$

The independent variables were coded according to the following equation for developing the regression equation:

$$X_i = (Z_i - Z_i^*) / \Delta Z_i \quad [\text{where } i=1, 2, 3] \quad \text{Eq. (A.2)}$$

where Z_i stands for the uncoded value of i^{th} independent variable, Z_i^* denotes uncoded value of i^{th} independent variable at center point and ΔZ_i is a step change value. The above equation can be

converted into the uncoded unit.

Maximum and minimum principle of differential calculus was used to have the optimum values of the respective independent variables. From the differential calculus we know that a stationary point on a curve occurs when $dy/dx = 0$. Once we have established where there is a stationary point, the type of stationary point (maximum, minimum or point of inflexion) can be determined using the second order derivative. At this stationary point we will get the optimum values for the variables.

The partial differential equations obtained are:

$$\partial Y / \partial X_1 = -66.40 + 39.45X_2 + 54.05X_3 - 142.3X_1 \quad \text{Eq. (A.3)}$$

$$\partial Y / \partial X_2 = -31.78 + 39.45X_1 - 21.76X_3 - 485.7X_2 \quad \text{Eq. (A.4)}$$

$$\partial Y / \partial X_3 = -150.91 - 21.76X_2 + 54.05X_1 - 514.44X_3 \quad \text{Eq. (A.5)}$$

The second order differential equations are

$$\partial^2 Y / \partial X_1^2 = -142.3 \quad \text{Eq. (A.6)}$$

$$\partial^2 Y / \partial X_2^2 = -485.7 \quad \text{Eq. (A.7)}$$

$$\partial^2 Y / \partial X_3^2 = -514.44 \quad \text{Eq. (A.8)}$$

The negative values of second order partial differential equations denote the presence of the maxima and by solving the equations Eq. (A.3) to Eq. (A.5) which are equated to zero we will have the optimum values of the variables X_1 , X_2 and X_3 . These optimum values lead to achieve the maximum value of response Y.

$$-66.40 + 39.45X_2 + 54.05X_3 - 142.3X_1 = 0 \quad \text{Eq. (A.9)}$$

$$-31.78+39.45X_1-21.76X_3-485.7X_2 = 0 \quad \text{Eq. (A.10)}$$

$$-150.91-21.76X_2+54.05X_1-514.44X_3 = 0 \quad \text{Eq. (A.11)}$$

From the algebraic solution of the above equations [Eq. (A.9) to Eq. (A.11)] the coded values of the variables were obtained which are X_1 (Guar Gum)= -0.6294, X_2 (Na-CMC) = -0.1006 and X_3 (Glycerol)= -0.3552. The corresponding uncoded values were generated by using the equation 4, those are $Z_1 = 418.53\text{mg}$, $Z_2 = 444.97\text{mg}$ and $Z_3 = 2322.4\text{mg}$. According to our model the maximum Flux (i.e., $998.343 \mu\text{g}/\text{cm}^2/\text{h}$) was observed when the values of the variables were Guar gum= 450mg, Na-CMC = 450mg and Glycerol= 2500mg. After optimization using RSM, the maximum flux was increased to $1047.4602 \mu\text{g}/\text{cm}^2/\text{h}$ at the optimum levels of the variables. Therefore statistical approach plays an important role in optimizing the components for the enhancement in the Flux.