HYDROGENATION OF D-GLUCOSE TO D-MANNITOL USING RANEY NICKEL CATALYST

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ABSRACT

Hydrogenation of D-glucose in the presence of Raney nickel as a catalyst was employed for the preparation of D-mannitol. The effects of the reaction time (15-115 min), reaction temperature (15-65 ^{o}C), and catalyst to D-glucose ratio (3-11 %) on the yield of D-mannitol were studied. The experimental design of Box-Wilson method was adopted to find a useful relationship between the effecting variables and the D-mannitol yield. The experimental data collected by this design was successively fitted to a second order polynomial mathematical model. The analysis of variance shows that the reaction time had the greatest effect on the yield of D-mannitol among other variables. An optimum operating conditions of 115 min reaction time, 50 ˚C reaction temperature, and 3 % catalyst to D-glucose ratio gave 14.01 % D-mannitol yield, 81.34 % D-sorbitol yield, and 94.9 % D-glucose conversion. D-Mannitol of purity 99.7 % was obtained after its separation from D-sorbitol, the second product of the hydrogenation process, using the fractional crystallization method.

الخلاصة

يهدف البحث إلى إنتاج المانيتول من الكلوكوز بطريقة الهدرجة و باستعمال (Raney Nickel) كعامل مساعد. تمت دراسة تأثير زمن التفاعل (15- 115 دقيقة)، درجة الحرارة (15- 65 °م)، ونسبة العامل المساعد إلى الكلوكوز (3 - 11 %) على إنتاجية المانيتول. استخدمت طريقة (Box-Wilson) لتكوين علاقة رياضية تربط المتغيرات الثلاثة بإنتاجية المانيتول، وتم تمثيل هذه العلاقة بشكل ناجح بمعادلة من الدرجة الثانية (Second-Order Polynomial) وقد بين التحليل الإحصائي (F-test) إن زمن التفاعل هو المتغير ذو التأثير الأكبر على إنتاجية المانيتول. إن الظروف التشغيلية المثلى التي أعطت إنتاجية مانيتول عالية هي زمن تفاعل (115دقيقة)، درجة حرارة (50°م)، ونسبة عامل مساعد (3%). عند هذه الظروف كانت إنتاجية المانيتول (14,01%)، إنتاجية السوربيتول (81,34%)، ونسبة تحول الكلوكوز (94,9%). تم استخدام طريقة البلورة التجزيئية لفصل المانيتول من السوربيتول، الذي يعتبر الناتج الثاني لعملية الهدرجة، والحصول على مانيتول بنقاوة (99,7%).

KEYWORDS

D-Mannitol, Catalytic Hydrogenation, D-glucose, Raney-Nickel, Box-Wilson Design

INTRODUCTION

D-Mannitol, $C_6H_{14}O_6$, is a hexahydric alcohol with a straight chain of six carbon atoms and six hydroxyl groups. As a pure solid, it is a white, odorless, nontoxic, crystalline material. D-Mannitol has been widely used in the food, pharmaceutical, medicine, and chemical industries. An important use of D-mannitol is for the preparation of mannitol hexanitrate which is a well known vasodilator used in the treatment of hypertension (Von Weymarn, 2002).

D-Mannitol can be extracted from many plant raw materials such as manna, seaweed, and algae. However, the extraction of D-mannitol from these raw materials is not a good commercial source. Both fermentation and catalytic hydrogenation processes are used. The catalytic hydrogenation process has been widely used for the commercial production of D-mannitol (Ojamo et al., 2000).

D-mannitol can be made by the catalytic hydrogenation of three naturally occurring hexoses, D-glucose, D-fructose, and D-mannose. Pure D-mannitol is obtained by the hydrogenation of D-mannose, while an equal portions mixture of both D-mannitol and D-sorbitol is obtained by the hydrogenation of D-fructose. A low portion of D-mannitol as compared with D-sorbitol is obtained when D-glucose is used as the raw material, where a portion of D-glucose is isomerizes to D-fructose and D-mannose. However, D-glucose or a mixture of D-glucose and D-fructose is the practical source because of its greater availability and low cost. Raney nickel catalysts, to which various promoters have been added, are widely used in the hydrogenation process. These catalysts, which are prepared from nickel -aluminum alloys, are approximately as effective as platinum catalysts for promoting many hydrogenations at low pressures and temperatures (Schwarz, 1994).

Different separation processes have been used for the separation of D-mannitol from D-sorbitol. D-Mannitol is readily separated from D-sorbitol by a fractional crystallization from aqueous solutions, in which D-sorbitol is soluble (Devose, 1995). Both D-mannitol and D-sorbitol can be separated chromatographically on a column of calcium poly styrenesulfonate, which professionally retains D-sorbitol (Melaja and Hamalainen, 1975).

Experimental designs are frequently performed in the study of empirical relationships between one or more measured responses and a number of variables. Having such relations, it can specify a combination of variables that will achieve some practical benefit. In the chemical industry, experimental designs are particular applied to the study of process variables and how they affect the product. The basic types of experimental design are factorial design, fractional factorial design, and Box-Wilson design (Montogomary, 1976).

The catalytic hydrogenation process was used by different researchers to prepare D-mannitol from different feedstocks using different catalysts. Makkee et al. (1980) used a platinum metal catalyst for the preparation of D-mannitol by catalytic hydrogenation of a mixture of D-glucose and D-fructose. Makkee et al. (1985) prepared D-mannitol by catalytic hydrogenation of D-glucose over a copper on silica catalyst. Toukoniitty et al., (2005) used Raney nickel catalyst for the preparation of D-mannitol by catalytic hydrogenation of D-fructose.

The aim of the present work is to study the catalytic hydrogenation of D-glucose to D-mannitol using Raney nickel catalyst, and the effect of reaction time, reaction temperature, and catalyst ratio on the yield of D-mannitol.

EXPERIMENTAL WORK

Materials

D-Glucose: D-Glucose (supplied by Hopkin and Williams, Searle Company) of purity 99% was used for the preparation of D-mannitol.
Hydrogen: Hydrogen (supplied by Al-Mansour Factory) of purity 99.9% was used for D-glucose hydrogenation.
Catalyst: Highly active Raney nickel catalyst (supplied by Aldrich Company) of pore size 50 µ and surface area 90 m^2/g was used for the hydrogenation of D-glucose to D-mannitol. It was stored as 50% slurry in water. Its nickel content was 75.11%.

Apparatus

A schematic diagram of laboratory experimental unit used for the hydrogenation of D-glucose is shown in Fig.1. This unit consists of a reaction flask which was a pyrex three-necked 500ml glass flask. The feed was charged to the reaction flask through a glass dropping funnel with a capacity of 100ml, and the hydrogen gas was fed to the reaction flask by means of a special perforated bulb tube (Sparser) in order to keep the solution in considerable agitation and to prevent settling of the catalyst. The loss of vapor from the reaction flask was prevented by using a pyrex double pipe glass condenser with an inner pipe of spiral shape. The reaction flask temperature was measured by a glass thermometer range from 0 to 100˚C, and maintained at the desired value by the use of a water bath. The hydrogen gas flow rate was controlled by a needle valve (Micro Hooke mite) and measured by a rotameter (GEC-Elliott). The composition of product was measured by a shimadzu Lc-6A high performance liquid chromatography (HPLC) system consist of: 6mm ID x 150mm L column (Shim-Pack CLC-ODS) and spectrophotometric detector (SPD-6A at 63nm).

Experimental Procedure

20 wt% D-glucose solution was prepared by dissolving 40 g D-glucose in 160 ml distilled water. This solution was brought to pH value of 9 by the addition of 0.01 g calcium hydroxide per 40 g D-glucose and mixed with 2-6 g Raney nickel catalyst to form the reaction slurry. The resultant slurry was charged through the dropping funnel into the reaction flask. When the required temperature was reached, hydrogen gas was fed continuously at a flow rate of 1.86 liter/min through the reaction slurry by means of the perforated glass bulb tube to keep the slurry in considerable agitation during the reaction time. At the end of duration time, the solution was cooled and the catalyst was allowed to settle at the bottom of the reaction flask. The supernatant solution was filtered and by HPLC method for its D-mannitol, D-sorbitol, and D-glucose content. The above procedure was applied at the optimum operating conditions and the D-mannitol was separated from the product solution as follows:

The alkaline product solution (filterate) was first neutralized with dilute sulfuric acid and then concentrated to about 33ml at a temperature of 45 ˚C and under a pressure of 50 mmHg using a glass evaporation-vacuum system. To this solution, 50 ml of 90% ethanol was added and the precipitated salts were removed by filtration. The solution was cooled to 15 ˚C and seeded with D-mannitol. After 2 hours, D-mannitol crystallized in the form of fine needle-like crystals whish were separated by filtration, washed with cold 80% ethanol, and dried at 40 ˚C and 600 mmHg.

The dried D-mannitol crystals were recrystallized twice from ethanol, filtered and dried. Then the purity (assay) of D-mannitol was 99.7.

The D-mannitol yield, D-sorbitol yield, and D-glucose conversion are defined mathematically as follows:

$$\text{D-Mannitol yield (\%)} = \frac{W_m}{W_{gf}} * 100 \tag{1}$$

$$\text{D-Sorbitol yield (\%)} = \frac{W_s}{W_{gf}} * 100 \tag{2}$$

$$\text{D-Glucose conversion (\%)} = \frac{W_{gf} - W_{gp}}{W_{gf}} \tag{3}$$

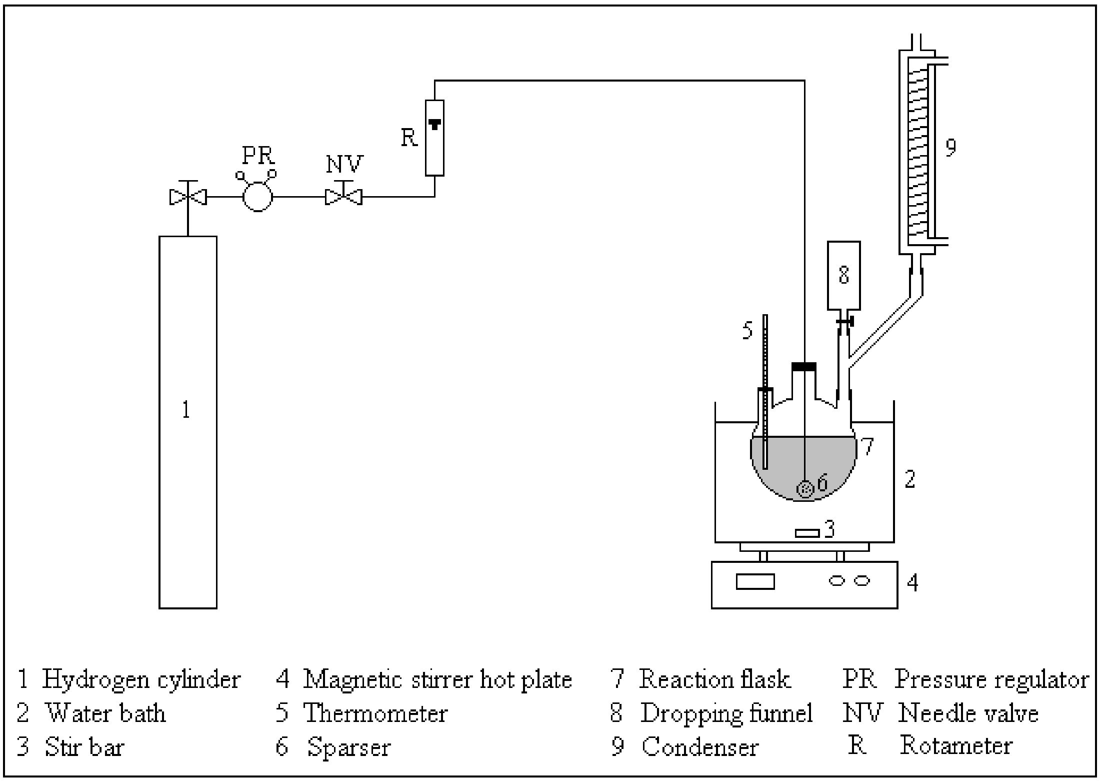

Fig. 1, Schematic diagram of D-Glucose Hydrogenation Unit

Mathematical Modeling

A second order polynomial mathematical model was employed to represent the yield of D-mannitol y as a function of reaction time X_1, reaction temperature X_2, and catalyst ratio X_3. The general form of this model for three variables is represented by the following equation:

$$y = B_o + B_1X_1 + B_2X_2 + B_3X_3 + B_4X_1X_2 + B_5X_1X_3 + B_6X_2X_3 + B_7X_1^2 + B_8X_2^2 + B_9X_3^2 \quad (4)$$

An experimental design based on Box-Wilson central composite method was used to organize the experiments. In order to design the experiments, the operating range of the variables is first specified, thus:

X_1=reaction time from 15 to 115 min.
X_2=reaction temperature from 15 to 65 ˚C.
X_3=catalyst ratio from 3 to 11 %.

The total number of experiments N is computed according to the following equation:

$$N = 2^P + 2P + 1 \quad (5)$$

Then:

$$N = 2^3 + 2(3) + 1 = 15$$

The relationship between the coded variable and the corresponding real variable is as follows:

$$X_{coded} = \left(\frac{X_{actual} - X_{center}}{X_{center} - X_{min}} \right) * \sqrt{P} \quad (6)$$

Then:

$$X_{1coded} = \left(\frac{X_{1actual} - 65}{50} \right) * \sqrt{3} \quad (7)$$

$$X_{2coded} = \left(\frac{X_{2actual} - 40}{25} \right) * \sqrt{3} \quad (8)$$

$$X_{3coded} = \left(\frac{X_{3actual} - 0.07}{0.04} \right) * \sqrt{3} \quad (9)$$

RESULTS AND DISCUSSION

Analysis of Box-Wilson Experimental Results

Table 1 shows the coded and real values of independent variables for the experiments to be conducted according to Box-Wilson method, and the experimental response represented by D-mannitol yield.

A nonlinear least-squares regression program based on Gauss-Newton method was used to fit Eq. (4) to the coded data and experimental D-mannitol yield given in Table 1. This fitting gave the predicted D-mannitol yield y, the residual error e, and the coefficients B of this equation as shown in Table 2. The fitted response surface of Eq. (4) is:

$$\begin{aligned} y &= 9.30 + 2.28X_1 + 1.14X_2 - 2.27X_3 - 0.078X_1X_2 + 0.017X_1X_3 \\ &\quad + 0.037X_2X_3 - 0.638X_1^2 - 0.799X_2^2 - 0.639X_3^2 \end{aligned} \tag{10}$$

The analysis of variance (F-test) was used for testing the significance of each effect in Eq. (2). The calculations are given in Table 3.

An estimate of the variance S_b^2 is obtained by dividing the experimental error variance S_r^2 by the sum of squares of each effect ΣX^2 ,as follows:

$$S_b^2 = S_r^2 / \Sigma X^2$$

Where

$$S_r^2 = (\Sigma e^2) / \gamma$$

$$\gamma = N - n$$

The significance of effects may be estimated by comparing the values of the ratio (B^2/Sb^2) with the critical value of the F-distribution at 95 % confidence level ($F_{0.95}=6.61$). If the ratio $B^2/Sb^2 > 6.61$ then the effect is significant. Thus, according to the results shown in Table 3, it appears that the interaction effects are not significant. The best response function is then conveniently written as follows:

$$y = 9.30 + 2.28X_1 + 1.14X_2 - 2.27X_3 - 0.638X_1^2 - 0.799X_2^2 - 0.639X_3^2 \tag{11}$$

This equation represents the best form of the mathematical model that relates the D-mannitol yield y to the three variables in terms of coded levels. An equivalent equation, in terms of the actual levels will be more useful in estimating the response for any desired conditions in the range of the independent variables. The new equation with a correlation coefficient of 97 % is obtained as follows:

$$\begin{aligned} y &= -7.89313 + 0.181469X_1 + 0.398825X_2 + 75.29651X_3 - 0.000789X_1^2 \\ &\quad - 0.003984X_2^2 - 1239.08X_3^2 \end{aligned} \tag{12}$$

The optimum operating conditions was determined by differentiating both sides of Eq. (12) for each independent variable and equating the derivative to zero. Thus, the optimum conditions corresponding to a maximum D-mannitol yield are 115 min reaction time, 50 ˚C reaction temperature, and 3 % catalyst ratio. At these conditions the optimum theoretical D-mannitol yield calculated from Eq. (12) is 13.66 % and the experimental yield is 14.01 %. Also the experimental D-sorbitol yield is 81.34 % and D-glucose conversion is 94.9 %.

Effect of Reaction Time

Figures 2 and 3 show the effect of reaction time on the theoretical D-mannitol yield at different reaction temperatures and catalyst ratios, respectively.

Figure 2 shows that the yield of D-mannitol increases with increasing reaction time. An increase in reaction time from 15 to 115 min at 50 ˚C and 3 % catalyst ratio leads to an increase in D-mannitol yield from 5.77 to 13.66 %. Figure 3 together with Fig. 2 show that there is no interaction between reaction time and catalyst ratio, and also between reaction time and temperature as summarized in Table 3. The results of this table show that the reaction time has the greatest effect on D-mannitol yield.

Effect of Reaction Temperature

The effect of reaction temperature on the theoretical yield of D-mannitol at different reaction times and catalyst ratios is shown in Figs. 4 and 5, respectively.

These figures indicate that at lower temperature, longer reaction time and smaller amounts of catalyst are necessary to obtain comparable values of D-mannitol yield. At 45 ˚C and 3 % catalyst ratio, 8.2 % D-mannitol yield is achieved in 35 min, while at 19 ˚C and 3 % catalyst ratio, 75 min is needed to achieve the same yield, as shown in Fig. 4. Figure 5 shows that at 45 ˚C and 115 min, 8.2 % D-mannitol yield is obtained using 9 % catalyst ratio, while at 19 ˚C and 115 min it is necessary to use 6 % catalyst ratio in order to reach the same yield.

Figures 5 and 6 also show that the use of high temperatures (above 50 ˚C) reduces D-mannitol yield, because at high temperatures, Raney nickel catalyst losses its activity as explained by Jianping et al. (2004).

Effect of Catalyst Ratio

Figures 6 and 7 show the effect of catalyst ratio on the theoretical D-mannitol yield at different reaction times and temperatures, respectively.

In Fig. 6, the yield of D-mannitol yield decreases with the increase of catalyst ratio. An increase in the catalyst ratio from 3 to 11 % at 50 ˚C and 115 min causes a decrease in the yield of D-mannitol from 13.66 to 5.81 %. The use of low catalyst ratio increases D-mannitol yield, because the rate of isomerization of D-glucose will be greater than its hydrogenation rate, as explained by Makkee et al. (1985). This figure also shows that the time required to reach 8.2 % yield can be reduced from 75 to 35 min by decreasing the catalyst ratio from 9 to 5 %.

Figure 7 shows that there is no interaction between the catalyst ratio and the reaction temperature, as explained in Table 3. This table shows that the catalyst ratio and reaction time have nearly the same effect on the yield of D-mannitol.

Table 1, D-Mannitol Yields of Box-Wilson Method Experiments

Run No.	Coded Variables			Real Variables			D-Mannitol Yield (%)
	X_1	X_2	X_3	X_1	X_2	X_3	
1	-1	-1	-1	36	26	0.0469	6.05
2	1	-1	-1	94	26	0.0469	10.29
3	-1	1	-1	36	54	0.0469	8.86
4	1	1	-1	94	54	0.0469	13.01
5	-1	-1	1	36	26	0.0931	1.89
6	1	-1	1	94	26	0.0931	6.42
7	-1	1	1	36	54	0.0931	5.07
8	1	1	1	94	54	0.0931	9.07
9	-1.732	0	0	15	40	0.07	2.57
10	1.732	0	0	115	40	0.07	11.25
11	0	-1.732	0	65	15	0.07	5.09
12	0	1.732	0	65	65	0.07	7.76
13	0	0	-1.732	65	40	0.03	11.52
14	0	0	1.732	65	40	0.11	2.29
15	0	0	0	65	40	0.07	9.30

Table 2, Statistical Analysis Results of Fitting Eq. (4)

No.	X_1	X_2	X_3	Y(%)	y(%)	e(%)	Coefficient B	
1	-1	-1	-1	6.05	6.05	0	B_0	9.30
2	1	-1	-1	10.29	10.73	-0.44	B_1	2.28
3	-1	1	-1	8.86	8.41	0.45	B_2	1.14
4	1	1	-1	13.01	12.78	0.23	B_3	-2.27
5	-1	-1	1	1.89	1.40	0.49	B_4	-0.078
6	1	-1	1	6.42	6.16	0.27	B_5	0.017
7	-1	1	1	5.07	3.91	1.16	B_6	0.037
8	1	1	1	9.07	8.36	0.71	B_7	-0.638
9	-1.732	0	0	2.57	3.43	-0.86	B_8	-0.799
10	1.732	0	0	11.25	11.34	-0.09	B_9	-0.639
11	0	-1.732	0	5.09	4.93	0.16		
12	0	1.732	0	7.76	8.88	-1.12		
13	0	0	-1.732	11.52	11.31	0.21		
14	0	0	1.732	2.29	3.46	-1.17		
15	0	0	0	9.30	9.30	0		

Table 3, Variance Analysis of Variable Effects*

Effect	$\sum X^2$	Coefficient B		Variance $S_b^2 = S_r^2 / \sum X^2$	F-value $= B^2/S_b^2$	$F_{0.95}$ =6.61
	15	B_0	9.30			
X_1	14	B_1	2.28	0.086	60.45	S
X_2	14	B_2	1.14	0.086	15.11	S
X_3	14	B_3	-2.27	0.086	59.92	S
X_1X_2	8	B_4	-0.078	0.151	0.040	NS
X_1X_3	8	B_5	0.017	0.151	0.002	NS
X_2X_3	8	B_6	0.037	0.151	0.009	NS
X_1^2	26	B_7	-0.638	0.047	8.66	S
X_2^2	26	B_8	-0.799	0.047	13.58	S
X_3^2	26	B_9	-0.639	0.047	8.69	S

* S= Significant, NS= Not Significant

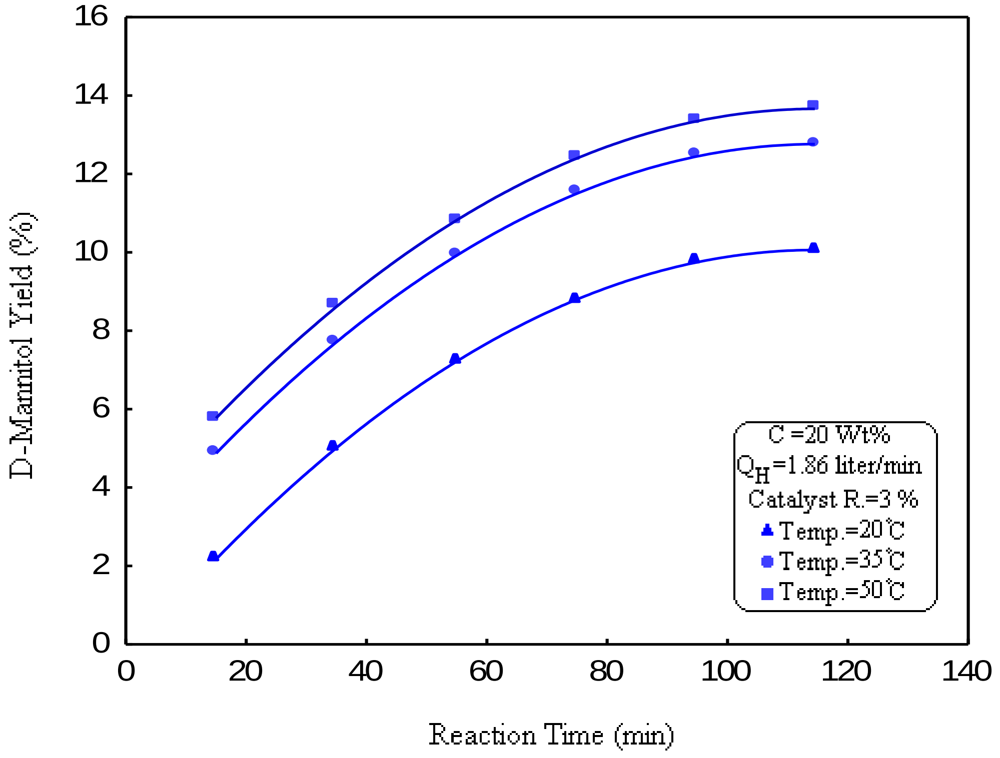

Fig. 2, D-Mannitol Yield Vs. Reaction Time at Different Temperatures

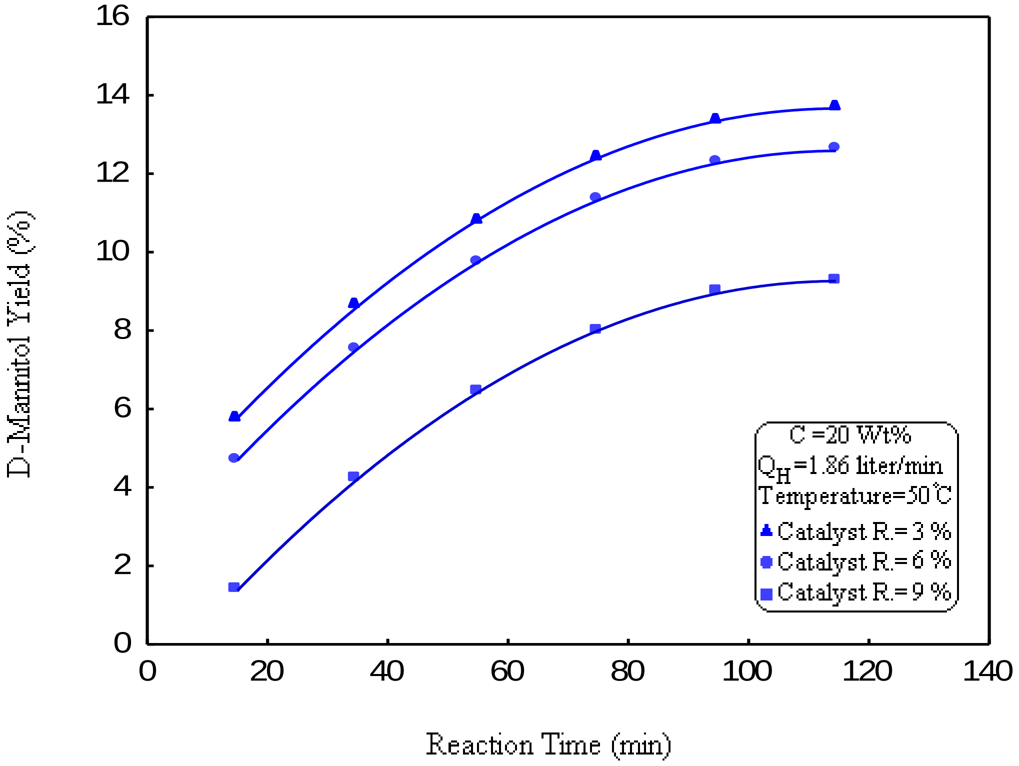

Fig. 3, D-Mannitol Yield Vs. Reaction Time at Different Catalyst Ratios

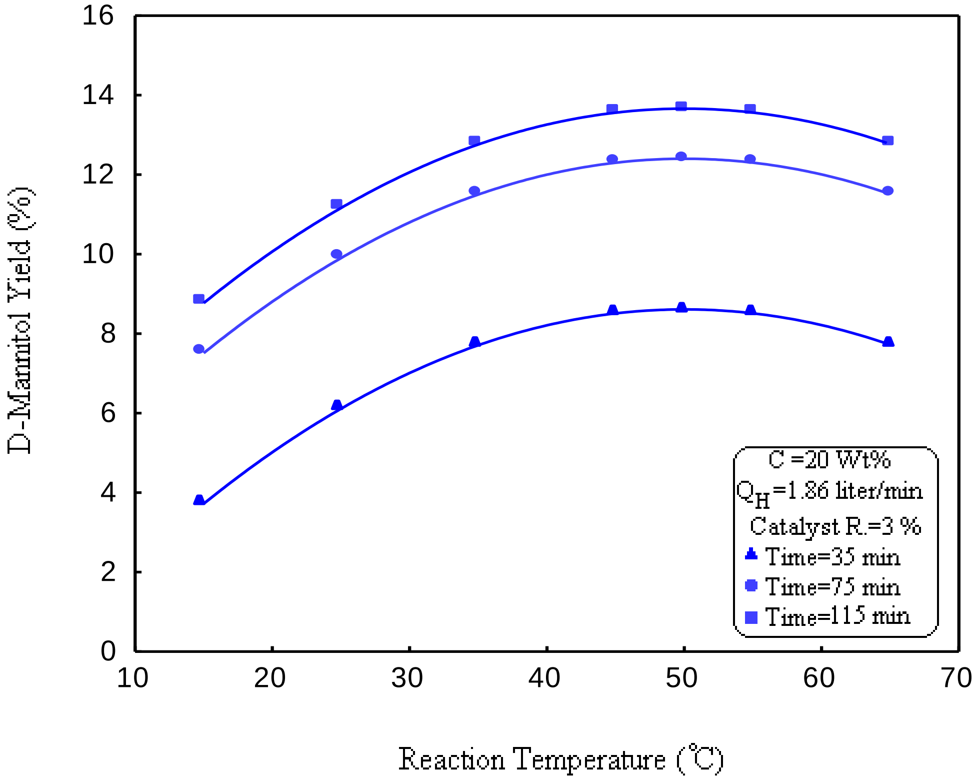

Fig. 4, D-Mannitol Yield Vs. Reaction Temperature at Different Times

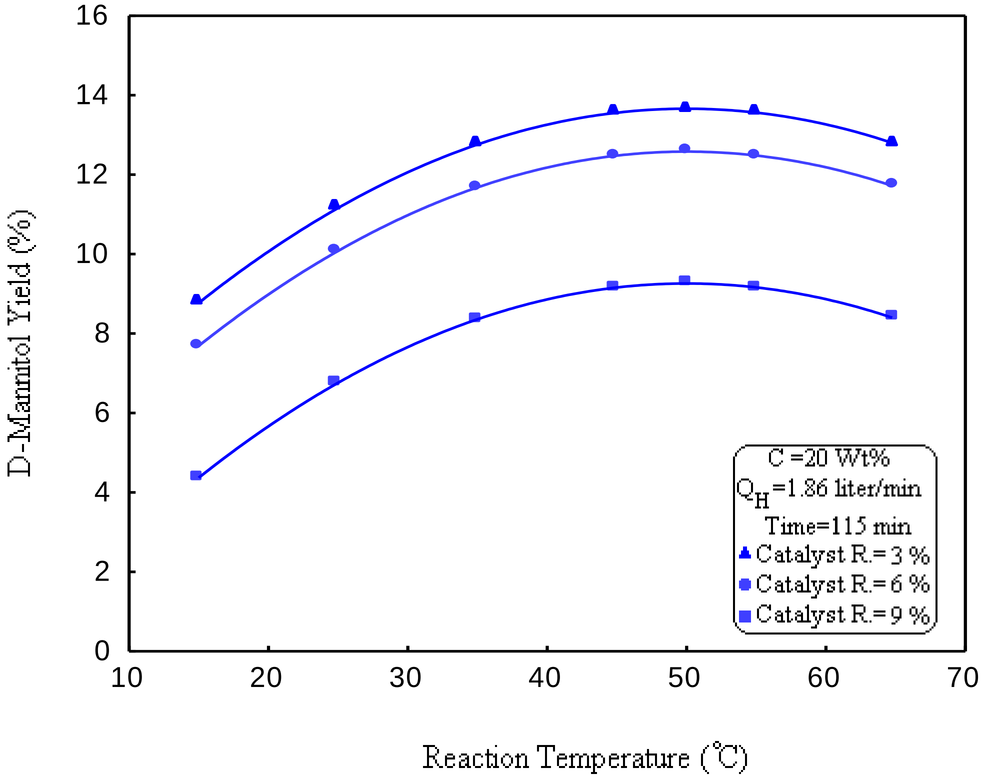

Fig. 5, D-Mannitol Yield Vs. Reaction Temperature at Different Catalyst Ratios

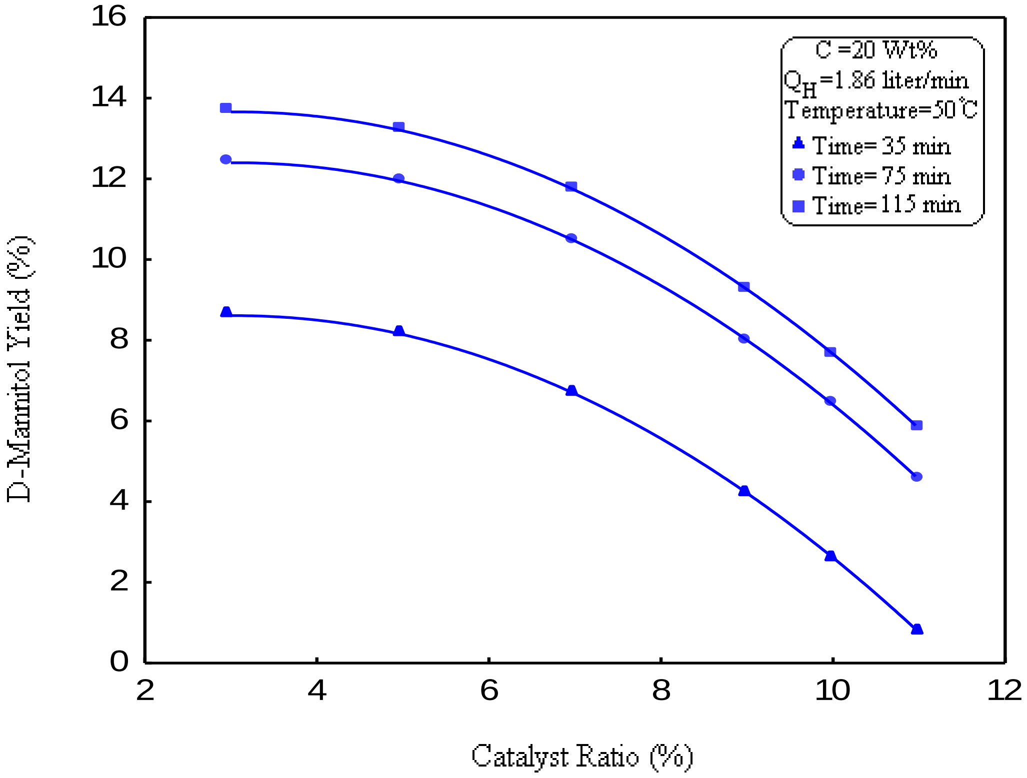

Fig. 6, D-Mannitol Yield Vs. Catalyst Ratio at Different Times

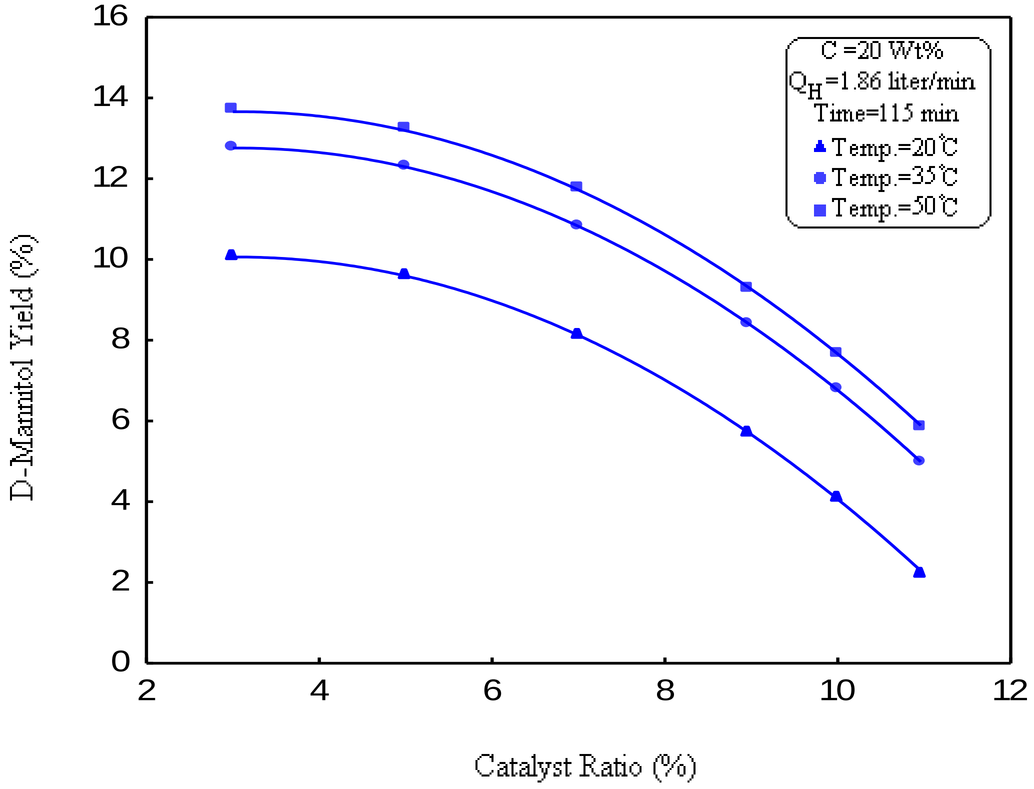

Fig. 7, D-Mannitol Yield Vs. Catalyst Ratios at Different Temperatures

CONCLUSSIONS

- The reaction time had the greatest effect on D-mannitol yield, as compared with the other variables.
- There was no interaction between the reaction time, reaction temperature, and catalyst ratio.
- A quantitative relationship between D-mannitol yield and the three variables was well represented by a second order polynomial mathematical model.
- A maximum D-mannitol yield of 13.66% was obtained at 115 min reaction time, 50˚C reaction temperature, and 3 % catalyst ratio.

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NOMENCLATURE

Notation

B	Coefficient of estimated model (%)
C	Initial concentration of D-glucose solution (wt. %)
e	Residual error (%)
n	Number of coefficients in the model
N	Number of experiments
NS	Not significant
P	Number of variables
Q_H	Volumetric flow rate of hydrogen (liter/min)
S	Significant
S_b^2	Variance of coefficient B
S_r^2	Residual variance
W_{gf}	Weight of D-glucose in the feed (g)
W_{gp}	Weight of D-glucose in the product (g)
W_m	Weight of D-mannitol in the product (g)
W_s	Weight of D-sorbitol in the product (g)
X_1	Reaction time (min)
X_2	Reaction temperature (˚C)
X_3	Catalyst ratio (%)
y	Theoretical or predicted value of D-mannitol yield (%)
Y	Experimental or observed value of D-mannitol yield (%)

Greek Leters

γ	Number of degree of freedom