Factorial Design for Optimization of Microwave Assisted Synthesis of 5-Hydroxymethylfurfural

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Synthesis of 5-hydroxymethylfurfural (5-HMF) by microwave assisted dehydration of fructose was performed under various operating conditions. A statistical analysis based on a 2^3 factorial plan was used to optimize the synthesis process. Operating temperature (110, 130 °C), specific mass of HCl catalyst (0.4, 0.6 mg/mg$_s$), and reaction time (8, 12 min) were selected as process factors. A regression equation linking the process performance expressed as 5-HMF yield (7.40-30.60%) to process factors was established. The statistical model emphasized a better performance for higher levels of all process factors.

Keywords: 5-hydroxymethylfurfural, fructose, microwave assisted synthesis, design of experiments, acid catalyst

The factorial design provides efficient tools for the optimization of variable factors for chemical processes. This method has also been successfully employed for different processes of separation and biomass transformation in valuable products [1-5].

Due to the growing concerns about environmental pollution, global warming, and diminishing reserves of fossil resources, an increasing demand to find an alternative source for the production of chemicals and biofuels has been regarded [6-8]. In this respect, biomass is one of the most attractive and sustainable renewable resource due to its abundance, inexpensiveness, and worldwide distribution. Biomass consists of carbohydrates, lignin, lipids, proteins, fatty acids, etc. Besides oil and coal, carbohydrates represent by far the widely available natural source of carbon [9, 10]. In addition, biomass consists of numerous bioactive compounds such as essential oils, flavonoids, tannins, vitamins, minerals, carotenoids, etc. with medicinal and nutritional potential [11,12]. Between the organic compounds that can be obtained from renewable resources, 5-hydroxymethylfurfural (5-HMF) is considered to be one of the top platform molecules. It can be synthesized by catalytic dehydration of carbohydrates, generally from monosaccharides, and further converted into highly valuable intermediates [13]. Its derivatives including furan, 2,5-furandicarboxylic acid, 2-(hydroxymethyl)furan, 2,5-furfuryldiamine, 2,5-furfuryl diisocyanate, 2-methylfuran, 2,5-dimethylfuran, 5-hydroxymethyl furfurylidenester, formic, levulinic, and adipic acids [14] are suitable starting compounds for the preparation of biofuels, polymeric materials, organic acids, solvents, pharmaceuticals, etc. [15]. In recent years, numerous methods have been developed for the efficient dehydration of hexoses such as fructose and glucose to 5-HMF [16]. Many conditions are established for dehydration of fructose to HMF in acidic water, subcritical or supercritical media, organic solvents, and ionic liquids [17] in combination with diverse catalysts such as mineral or organic acids, metal chlorides, cation exchange resins, zeolites, supported heteropolyacids and nanocatalysts [18]. Microwave assisted organic synthesis is an unconventional efficient method for dehydration of fructose to 5-HMF. The advantages of this method are represented by a shorter reaction time and high yield and selectivity. The dehydration of fructose to 5-HMF in acidic water by conventional methods is a slow process. However, by microwave irradiation a good conversion of fructose in water can be achieved in some minutes. Moreover, regarding the toxicity of organic solvents and the demand of focusing on green chemistry, water represents an eco-friendly solvent [19].

This study describes the microwave assisted synthesis of 5-HMF from fructose by acid catalyzed dehydration. A 2^3 factorial design of experiments (DoE) was used to study the effects of process independent variables (temperature, the amount of catalyst, and the reaction time) on the 5-HMF yield. The temperature levels were 110, 120, and 130 °C. The level of specific mass of HCl catalyst were 0.4, 0.5, and 0.6 mg/mg$_s$ and the reaction times were 8, 10, and 12 min. The controllable factors and their levels for the process parameters were selected based on our preliminary work [20].

Experimental part

Materials and methods

Fructose (≥99%), HCl (≥37%, p.a.), 5-HMF (≥99%) used as standard for HPLC analysis and methanol (HPLC grade) were purchased from Sigma-Aldrich and used without further purification. Deionized water was used for the preparation of aqueous solutions.

Dehydration of fructose

The microwave-assisted fructose dehydration was performed using a microwave system (Biotage Initiator). The Biotage reactor (20 mL) was charged with aqueous fructose solution (10 wt.%, 3 mmol), and the required amount of HCl aqueous solution (0.3 – 0.5 mg/mg substrate (mg$_s$)) was added. The experiments were carried out at different temperatures and a stirring rate of 900 rpm.

Analytical methods

5-HMF aqueous solutions were filtered through a syringe filter prior to analysis by high performance liquid chromatography (HPLC). The analyses were undertaken using a Jasco HPLC equipped with UV-2075 detector, PU-2080 plus pump, LG-2080_4 gradient unit, DG-2080_4 degasser, and Teknokroma Nucleosil 100 C18 (10 μm, 250×0.4) separation column. Analyses were performed

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Table 1
PROCESS FACTOR LEVELS AND VARIATION INTERVALS

j	Process factor z_j	Level			Variation interval
		minimal	central	maximal	
1	t (°C)	110	120	130	10
2	c (mg/mg$_s$)	0.4	0.5	0.6	0.1
3	τ (min)	8	10	12	2

at a flow rate of 0.5 mL/min using water with 2% v/v acetic acid (solvent A) and methanol (solvent B) under the following gradient program: 0-9 min 70% A, 9-18 min 60% A, 18-60 min 50% A, and then returned to initial condition for a 10 min re-equilibration with a total run time of 70 min. 5-HMF was identified by comparison of retention times from samples with pure standard compound. HMF concentrations were determined using calibration curves and product yields (%) were calculated.

Experimental design

A 2^3 factorial design of experiments (DoE) was used to study the effects of process independent variables (factors) on process performance (response) [1-4]. Operating temperature (t=110-130 °C), specific mass of HCl catalyst (c=0.4-0.6 mg/mg$_s$), and reaction time (τ =8-12 min) were selected as process factors, whereas the process performance was expresses as 5-HMF yield (y). The levels of process factors (z_j) and their corresponding variation intervals (Δz_j) are summarized in table 1.

Results and discussions

A 2^3 factorial DoE combined with statistical methods of data analysis were used for optimizing the 5-HMF synthesis by microwave assisted dehydration of fructose. Values of process factors and response for 8 experiments conducted according to a 2^3 factorial plan are presented in table 2 (exp. 1-8), where values of dimensionless factors (x_1, x_2, and x_3) were determined by eq. (1). Characteristic regression coefficients of eq. (2), β_j (j=1...N=8), were obtained by processing the data from table 2 according to the specific procedure of a 2^3 factorial experiment. Regression equation (2), linking the process response to dimensionless factors, emphasizes enhanced 5-HMF yield (y) for higher levels of all process factors (x_1, x_2, and x_3) and lower levels of their interactions (x_1x_2, x_1x_3, x_2x_3, and $x_1x_2x_3$).

$$x_j = \frac{z_j - z_{j,0}}{\Delta z_j}, j=1..3 \quad (1)$$

$$y = 20.089 + 8.119x_1 + 0.566x_2 + 0.879x_3 - \\ -1.444x_1x_2 - 1.366x_1x_3 - 1.159x_2x_3 - 0.844x_1x_2x_3 \quad (2)$$

In order to test the significance of regression coefficients in eq. (2), 4 replicates within the central point (N_0=4) were performed and corresponding values of process response, y_{0r} (r=1.. N_0), were specified in table 2 (exp. 9-12). The mean value of response, $y_{0,mn}$, number of degrees of freedom, ν, and reproducibility standard dispersion, σ_{rp}, associated to the replicates, were determined by eqs. (3)-(5), whereas the standard dispersion associated to β_j (j=1...N=8) regression coefficients, $\sigma\beta_j$, was given by eq. (6) [3, 4].

$$y_{0,mn} = \frac{\sum_{r=1}^{N_0} y_{0r}}{N_0} = 29.39\% \quad (3)$$

$$\upsilon = N_0 - 1 = 3 \quad (4)$$

Table 2
EXPERIMENTAL MATRIX FOR 2^3 FACTORIAL EXPERIMENT

Exp.	t (°C)	c (mg/mg$_s$)	τ (min)	x_1	x_2	x_3	y (%)
1	110	0.4	8	-1	-1	-1	7.40
2	130	0.4	8	1	-1	-1	27.57
3	110	0.6	8	-1	1	-1	12.05
4	130	0.6	8	1	1	-1	29.82
5	110	0.4	12	-1	-1	1	12.52
6	130	0.4	12	1	-1	1	30.60
7	110	0.6	12	-1	1	1	15.91
8	130	0.6	12	1	1	1	24.84
9	120	0.5	10	0	0	0	28.97
10	120	0.5	10	0	0	0	29.84
11	120	0.5	10	0	0	0	29.41
12	120	0.5	10	0	0	0	29.34

$$\sigma_{rp} = \sqrt{\frac{\sum_{r=1}^{N_0}(y_{0i} - y_{0,mn})^2}{\upsilon}} = 0.357\% \quad (5)$$

$$\sigma_{\beta_j} = \frac{\sigma_{rp}}{\sqrt{N}} = 0.126\% \quad (6)$$

Values of Student random variable, $t_{\beta,j}$=4.49-159.27, estimated by eq. (7), were larger than theoretical value of Student variable, $t_{\alpha,\nu}$=4.3, obtained considering a significance level (α) of 0.05, accordingly all β_j coefficients are significant. Statistical model described by eq. (2) can be applied to predict the process performance for values of process factors in the fields considered in the experimental study.

$$t_{\beta_j} = \frac{|\beta_j|}{\sigma_{\beta_j}} \quad (7)$$

Conclusions

Statistical analysis based on a 2^3 factorial plan was used to optimize 5-HMF synthesis by microwave assisted dehydration of fructose. Operating temperature (110-130 °C), specific mass of HCl catalyst (0.4-0.6 mg/mg$_s$), and reaction time (8-12 min) were selected as process factors. 8 runs at minimal and maximal levels of process factors as well as 4 replicates within the central point were performed in order to determine the regression coefficients and their significance. The correlation obtained between the process performance expressed as 5-HMF yield (7.40-30.60%) and the factors revealed a better performance for higher levels of all process factors and lower levels of their interactions. This statistical model could be used to predict the process performance for values of process factors in the studied ranges.

References

1. DOBRE, T., PARVULESCU, O.C., IAVORSCHI, G., STOICA, A., STROESCU, M., Int. J. Chem. React. Eng., **8**, 2010, p. 1968.
2. DOBRE, T., PARVULESCU, O.C., RODRIGUEZ RAMOS, I., CEATRA, L., STROESCU, M., STOICA, A., MIREA, R., Rev. Chim. (Bucharest), **63**, no. 1, 2012, p. 54.
3. DOBRE, T., STOICA, A., PARVULESCU, O.C., STROESCU, M., IAVORSCHI, G., Rev. Chim. (Bucharest), **59**, no. 5, 2008, p. 191.
4. ION, V.A., PARVULESCU, O.C., DOBRE, T., Appl. Surf. Sci., **335**, 2015, p. 137.
5. PARVULESCU, O.C., DOBRE, T., CEATRA, L., IAVORSCHI, G., Rev. Chim. (Bucharest), **62**, no. 1, 2011, p. 89.
6. TONG, X., MA, Y., LI, Y., Appl. Catal., A., **385**, 2010, p. 1.

7. ZHANGA, X., ZHANGA, D., SUNA, Z., XUEA, L., WANGA, X., JIANGB, Z., Appl. Catal. B., **196**, 2016, p. 50.
8. LUCAS-TORRES, C., LORENTE, A., CABANAS, B., MORENO, A., J Clean Prod., **138**, 2016, p. 59.
9. van PUTTEN, R. J., van der WAAL, J. C., de JONG, E., RASRENDRA, C. B., HEERES, H. J., Chem. Rev., **113**, 2013, p. 1499.
10. MUKHERJEE, A., DUMONT, M. J., RAGHAVAN, V., Biomass Bioenergy, **72**, 2015, p. 143.
11. CALINESCU, I., GAVRILA, A. I., IVOPOL, M., Cent. Eur. J. Chem., **12**, 2014, p. 829.
12. ASOFIEI, I., CALINESCU, I., TRIFAN, A., GAVRILA, A. I., DAVID, I. G., **203**, 2016, Chem. Eng. Commun., p. 1547.
13. de SOUZA, R. L., YU, H., RATABOUL, F., ESSAYEM, N., Challenges, **3**, 2012, p. 212.
14. GOMESA, F. N. D. C., MENDESB, F. M. T., SOUZAA, M. M. V. M., Catal. Today, **279**, 2017, p. 296.
15. LI, L., DING, J., JIANG, J. G., ZHU, Z., WU, P., Chinese J. Catal., **36**, 2015, p. 820.
16. AMARASEKARA, A. S., WILLIAMS, LT. D., EBEDE, C. C., Carbohydr. Res., **343**, 2008, p. 3021.
17. DUTTA, S., DE, S., PATRA, A. K., SASIDHARAN, M., BHAUMIK, A., SAHA, B., Appl. Catal., A., **409– 410**, 2011, p. 133.
18. HU, L., TANG, X., WUA, Z., LINC, L., XU, J., XU, N., DAI, B., Chem. Eng. J., **263**, 2015, p. 299.
19. HANSEN, T. S., WOODLEY, J. M., RIISAGER, A., Carbohydr. Res., **344**, 2009, p. 2568.
20. GAVRILA, A. I., ASOFIEI, I., TRIFAN, A., CHIPURICI, P., RUSEN, E., Rev. Chim. (Bucharest), **68**, no. 3, 2017, p. 435

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