

## ARTICLE

# 5-(Chloromethyl)furfural production from glucose: A pioneer kinetic model development exploring the mechanism

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## Abstract

Conversion of glucose to 5-(chloromethyl)furfural (CMF) is one of the well-known high yield unit processes in lignocellulosic biomass valorization. A kinetic modeling study was not reported for the reaction, owing to the complexity in quantification of CMF. Herein we have successfully developed a rapid, sensitive, and specific HPLC method (reverse phase) to quantify the generated CMF (range: 10–650  $\mu\text{g/mL}$ ) in a dichloroethane solvent. The Box–Behnken design of experiment method employed for the statistical optimization. A kinetic model was developed based on the homogeneous first-order kinetic model, and the results are in good agreement with the experiment data. The formation of CMF, 5-(hydroxymethyl)furfural, formic acid, levulinic acid, and humins from glucose and HCl were modeled using a serial parallel reaction mechanism. The apparent activation energy ( $E_a$ ) for glucose decomposition and CMF formation is 99 and 31 kJ/mol.

## KEYWORDS

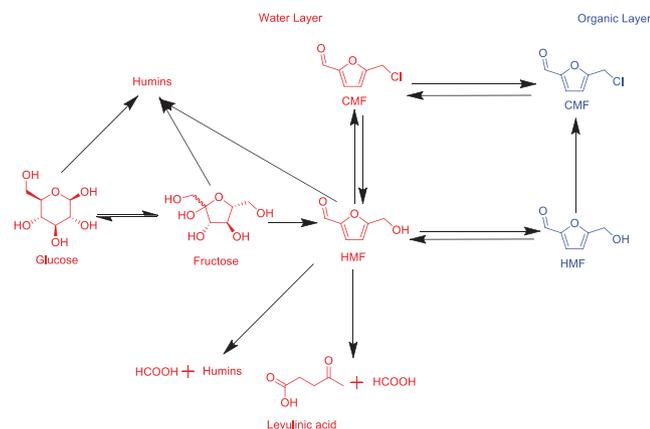
5-(chloromethyl)furfural, design of experiment, glucose dehydration, kinetic model, nonlinear least-squares method

## 1 | INTRODUCTION

Lignocellulose from agro-industrial waste is a key biomass resource, which has highest availability ( $200 \times 10^9$  tons/year) and nonedible.<sup>1,2</sup> Ecofriendly production of feedstock chemicals from such biomass resources remains a challenge owing to the complexity of biomass structure and the need of technical knowledge in reaction engineering.<sup>3</sup> The intention of developing a kinetic model for glucose to 5-(chloromethyl)furfural (CMF) conversion to understand the reaction network in the acid catalyst medium. CMF is one of the high yielding intermedi-

ate produced from cellulose/lignocellulosic biomass using concentrated HCl.<sup>4,5</sup> Like conversion of CMF to feedstock chemicals, conversion to fuel is also a well-studied reaction.<sup>6,7</sup> Well-established industrial production of HCl and recovery of used HCl using membrane techniques renders it a potential catalyst.<sup>8–10</sup> CMF has been used as an intermediate chemical for the synthesis of drugs like ranitidine.<sup>11,12</sup> Chang et al. used CMF as an intermediate for the synthesis of prothrin, a synthetic insecticide, in a six-step synthesis with 65% yield.<sup>13</sup> Three US companies have succeeded in the commercial synthesis of CMF for the production of fuels, fuel additives, and *p*-xylene.<sup>6,14</sup> CMF can also be utilized for the synthesis of highly pure 5-(acetoxymethyl)furfural under mild reaction conditions in a continuous reaction.<sup>15</sup>

**Abbreviations:** CMF, 5-(chloromethyl)furfural; DCE, dichloroethane; FA, formic acid; HMF, 5-(hydroxymethyl)furfural; LA, levulinic acid; MIBK, methyl isobutyl ketone



**SCHEME 1** Possible reaction pathways for conversion of glucose to CMF [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

CMF production is a biphasic reaction, and the possible reaction pathway involves multiple unitary reactions as given in Scheme 1. The kinetic analysis of conversion of glucose to CMF by exploring the underlying mechanism has few reports in contrast to other feedstock chemicals like 5-(hydroxymethyl)furfural (HMF) or levulinic acid (LA).<sup>16–19</sup> This might be due to the unavailability of analytical methods for the quantification of CMF, that is, in the literature, the CMF was quantified by complex procedures like solvent evaporation followed by column chromatography (to remove other furan-based soluble polymers). In a kinetic study, time/temperature variation may lead to mild deviation in the yield/conversion, and it should be quantified accurately to develop a well-defined kinetic model. So, the above-reported method is cumbersome for the quantification of CMF yield. Yet other reports have employed a NMR-based method and an UV–vis spectroscopy based method for the quantification of CMF.<sup>20,21</sup> Consequently, the development of a sensitive, specific, and valid analytical method for the routine analysis of CMF remains a primary requisite.

The Box–Behnken design of experiment (DOE) method employed here circumvented the customary steps, thereby reducing the number of reactions to be performed to 15. Time, temperature, and acid concentration are three important reaction parameters in the conversion of glucose to CMF. As mentioned in Scheme 1, conversion of glucose to CMF may involve multiple steps. A reverse-phase HPLC technique has been successfully developed for quantitative assay of CMF in dichloroethane (DCE) solvent. It must be mentioned here that DCE is the commonly employed solvent for CMF production from mono/polymeric carbohydrates.

Apart from the main product CMF, the other possible intermediates like fructose, HMF, LA, humins, etc. were

also formed during the reaction. Kinetic analysis of main reaction (CMF formation) as well as all intermediate reactions was performed. Different control experiments were also performed to understand the basic reaction mechanism.

The chemical kinetic model was implemented using MATLAB, a matrix-based mathematical software package, for a first-order reaction involving concentrated HCl both as a reactant and a catalyst in a water–DCE biphasic medium. The resultant kinetic studies and models are consistent with the proposed mechanism.

## 2 | EXPERIMENTAL

### 2.1 | Materials

D-(+)-Glucose (97.5%, EMPARTA ACS), D-(–)-fructose (EMPARTA), formic acid (FA; 98–100%; EMPARTA ACS), LA, 1,2-dichloroethane (EMPARTA ACS), and hydrochloric acid (35% EMPLURA) were purchased from Merck chemicals, Germany, and used without any further purification. 5-(Hydroxymethyl)furfural ( $\geq 99\%$  FG) and furfural (99%) were purchased from Sigma Aldrich chemicals. HPLC solvents were acquired from Merck chemicals, Germany, and hydrochloric acid (38%) was purchased from Fisher Chemical, and solutions were prepared using Milli Q water.

### 2.2 | Experimental procedure

Reactions were carried out in a round-bottomed glass reactor with magnetic stirring in a preheated oil bath. For a typical reaction, 150 mg of glucose was added in a reactor tube to which 6 mL of DCE and then selected volume of acid was added. This was placed in a preheated oil bath at desired reaction temperature and stirred at 600 rpm for a specified reaction time. After each reaction, a glass reactor was cooled to room temperature, to which calculated volume of water and DCE was added to obtain a solvent ratio of 6 : 12 mL (water: DCE ratio). This solvent ratio was retained after each reaction to make HPLC analysis simple. This was shaken well to extract all CMF into the organic layer (DCE), and both aqueous as well as organic layer were collected separately. The aqueous layer was diluted and analyzed for glucose conversion along with the yield of LA, FA, and HMF. The aqueous layer was analyzed in a Shimadzu HPLC spectrometer (LC-10AD with RID 6A RI detector) using 0.008N H<sub>2</sub>SO<sub>4</sub> buffer, Bio-Rad Aminex HPX-87H (300 × 7.8 mm) column at 50°C, and results were analyzed using Autochro-3000 software. The organic layer was diluted and analyzed for CMF and HMF yield using

a DIONEX HPLC (Ultimate 3000) chromatograph using a reversed-phase C18 column (150 × 4.6 mm). The optimized mobile phase consists of methanol and 0.5 % acetic acid solvents with 7:3 ratio at 30°C, and the results were analyzed using Chormelon software. The conversion and the yield of the products can be defined by the following equation:

$$\text{Conversion (\%)} = \frac{(\text{moles of initial reactant} - \text{moles of final reactant})}{(\text{moles of initial reactant})} * 100$$

$$\text{Yield (\%)} = \frac{(\text{moles of product})}{(\text{moles of initial reactant})} * 100$$

### 2.3 | Synthesis of CMF

180 mg of HMF ( $\geq 99\%$  Aldrich) added in the glass reactor was dissolved in 6 mL of DCE and placed in an oil bath at 70°C for 5 min to which 12.4 mmol of concentrated HCl was added, and the reaction was continued for 1 h with stirring. After the reaction, 5 mL of water and another 6 mL of DCE were added, and the organic layer was separated. Anhydrous sodium sulfate was added to remove the moisture and DCE removed under reduced pressure. The yellow viscous liquid obtained was dissolved in minimum amount of  $\text{CH}_2\text{Cl}_2$  and purified by column chromatography using silica gel (60–120) and  $\text{CH}_2\text{Cl}_2$  as eluent. This CMF was further characterized using mass spectral analysis, and the result is given in Figure S1 in the Supporting Information.

### 2.4 | System suitability

The system suitability of HPLC method was analyzed by six replicate analyses of the CMF at a concentration of 210  $\mu\text{g/mL}$ . The acceptance criterion was  $\pm 2\%$  for the percent coefficient of variation (%CV) for the peak area and retention times for CMF.

### 2.5 | Determination of the kinetic parameters

The kinetic parameters were determined based on minimization of the errors between the experimental data and the kinetic model. Error minimization to determine the best estimate of the kinetic parameters was performed using the built-in MATLAB function lsqnonlin, a non-linear least-squares method based on the Trust-Region-Reflective algorithm.

**TABLE 1** Factors selection for optimization of CMF formation by the Box–Behnken design

Independent Factors	Unit	Level (1)	Level (0)	Level (-1)
Acid concentration	mmol	37.2	24.8	12.4
Temperature	°C	80	60	40
Time	h	2	1	0.5

## 3 | RESULTS AND DISCUSSION

CMF is a low melting solid (pure state) at room temperature and is freely soluble in organic solvents like methanol and acetonitrile. Different solvent proportions of methanol, acetonitrile, and 0.1–2% acetic acid solutions were screened to obtain a CMF yield peak with tailing factor  $> 2$ .<sup>22</sup> Acetic acid sharpens the HMF peak, which was broader due to the hydroxyl group, whereas increased methanol ratio resulted in drastic reduction of CMF peak tailing. CMF in DCE was quantitated by a rapid reversed-phase HPLC method (sensitivity: 650–10  $\mu\text{g/mL}$ ).

The isocratic elution of CMF and HMF was done as mentioned in the Experimental Procedure (Figure S2 in the Supporting Information). Moreover, the residual concentration of HMF can also be quantitatively determined under the above conditions. HPLC analysis has shown linearity in CMF concentrations ranging from 650 to 10  $\mu\text{g/mL}$  as shown in Figure S3 in the Supporting Information. The linear regression coefficient obtained using the least square method is 0.991. Temperature, time, and acid volume/concentration are the three crucial factors which influence glucose to CMF conversion using the biphasic medium. Table 1 shows the values of these parameters tested in the Box–Behnken design. The selection criteria of these factors were based on the results reported in the literature. To reduce the complexity of this reaction, the effect of salt addition like LiCl, LiBr, or NaCl was not included in this study. The results obtained from the 17 experimental runs, which were carried out according to the Box–Behnken design with three variable factors, are summarized in Table S1 in the Supporting Information.

The (0,0,0) condition was repeated five times;  $\pm 1\%$  variation in the conversion and selectivity was observed (Table S1). Temperature has a major influence in the conversion of glucose on increasing the temperature, glucose conversion as well as CMF selectivity increased. Under all conditions, reactions at 80°C showed three times higher glucose conversion than at 40°C. The maximum glucose conversion (77.2%) and CMF selectivity (38.1%) was seen for 24.8 mmol acid at 80°C for 3 h reaction time, whereas 37.2 mmol acid at 80°C for 2 h showed 72.6% conversion with 38% CMF yield (entries 8 and 4, Table S1). The cumulative influence of different parameters on the reaction can be expressed by

a quadratic equation as given below:

#### Glucose conversion

$$\begin{aligned} &= 24.39 - 2.5 \times (\text{Acid Conc}) + 26.8 \times (\text{Temp}) \\ &+ 5.2475 \times (\text{Time}) + 3.56 \times (\text{Acid Conc} \times \text{Temp}) \\ &+ 3.4625 \times (\text{Acid Conc} \times \text{Time}) + 5.4225 \\ &\times (\text{Time} \times \text{Temp}) + 3.108 \times (\text{Acid Conc})^2 \\ &+ 14.008 \times (\text{Temp})^2 + 2.15 \times (\text{Time})^2 \end{aligned}$$

#### CMF yield

$$\begin{aligned} &= 9.24 - 0.32 \times (\text{Acid Conc}) + 17.96 \times (\text{Temp}) \\ &+ 4.32 \times (\text{Time}) + 0.21 \times (\text{Acid Conc} \times \text{Temp}) \\ &+ 0.07 \times (\text{Acid Conc} \times \text{Time}) + 2.04 \\ &\times (\text{Time} \times \text{Temp}) + 2.58 \times (\text{Acid Conc})^2 \\ &+ 7.04 \times (\text{Temp})^2 + 0.79 \times (\text{Time})^2 \end{aligned}$$

The cumulative influence of different parameters on glucose conversion and CMF yield obtained by means of Box–Behnken design (response surface methodology [RSM] analysis) using SAS JMP11 software is given in Figure 1. In all different combinations, elevated temperature leads to high glucose conversion and thereby high CMF yield. Humins (furan-based polymer) formation also increased simultaneously with increased temperature. The presence of high humin levels made the product mixture darker in color, thus confirming high humin formation throughout our study (our studies were done without any added salt).

Glucose conversion has a linear relationship with factors like temperature and acid concentration. Regardless of the acid concentration, glucose conversion was high at 80°C. Glucose conversion increased with increasing temperature/acid concentration. However, the acid concentration showed lesser influence than temperature (Figure 1(A)). A trend was observed in CMF yield (Figure 1(B)); at 40°C, no CMF was formed at any of the applied levels of acid concentration and time. Both temperature and time have remarkable influence on glucose conversion/CMF yield; conversion and yield increased with increasing time/temperature. RSM showed that 98% glucose conversion and 53% CMF yield were the maximum possible conversion/selectivity with the different parameters optimized in 24.8 mmol acid concentration.

Correlation between predicted and experimental values of glucose conversion and CMF yield shows that the model is significant and acceptable (Figure 2). The *P* value of the

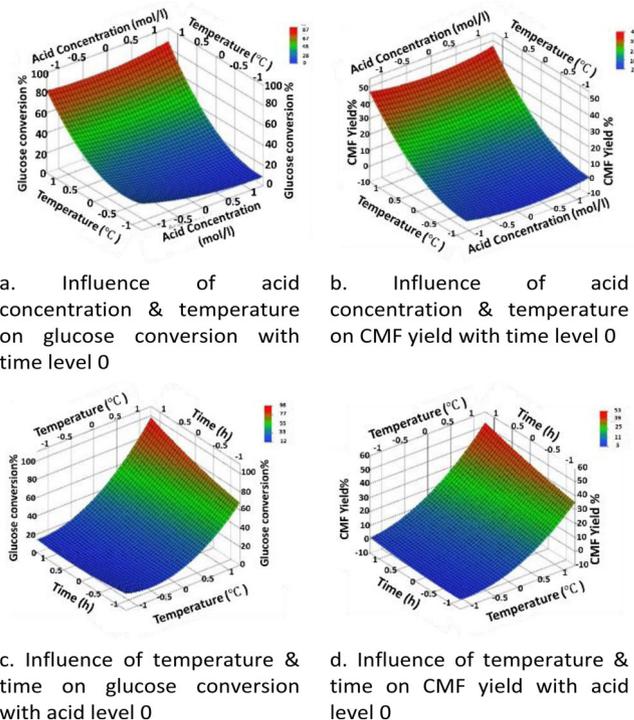


FIGURE 1 Response surface plot for cumulative influence of different parameters on glucose conversion and CMF yield obtained by the Box–Behnken design [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

model is smaller than 0.002, whereas  $R^2$  values of 0.99 for glucose conversion and 0.98 for CMF yield, respectively, reveals the statistically significant relationship between the variables.

To comprehend the underlying mechanism of the CMF formation, different control experiments were carried out and the results are given in Table 2. Glucose dehydration performed in aqueous medium without addition of organic solvent produced no CMF; on the contrary HMF, LA, and FA were formed. Similarly, glucose dehydration performed with conc. HCl in the absence of additional water or organic solvent attained only 0.5% CMF along with FA (10.7%), LA (5.9%), and humins. Accordingly, under these reaction conditions, formation of degradation products like LA and FA dominates than the furanic compounds. Owing to no CMF formation, we may have neglected the possibility of direct formation of CMF from glucose for kinetic studies. Chlorination of HMF in DCE yielded the maximum of 75% CMF along with the formation of LA and FA, whereas a similar reaction of HMF in water alone might have generated CMF which possibly could have migrated to organic layer (Table 2, entries 3 and 4). Consequently, no CMF was found in the analysis of the water layer by HPLC. We did not find any CMF in the water layer under biphasic conditions we cannot do kinetic studies for HMF to CMF conversion in the water layer and

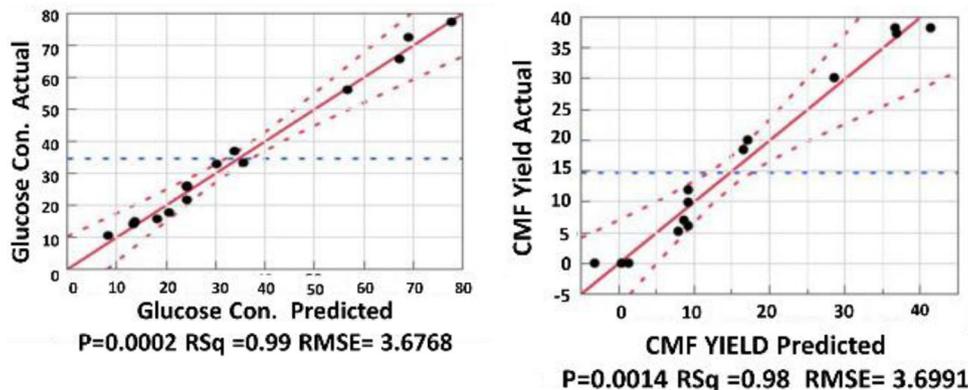


FIGURE 2 Correlation between predicted and experimental values of (A) glucose conversion and (B) CMF yield [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2 Control experiments for the CMF formation mechanism

S. No	Reactants	Glucose conversion (%)	CMF yield (%)	HMF yield (%)	LA yield (%)	FA yield (%)
1	150 mg Glucose, 24.8 mmol HCl, 4 ml H <sub>2</sub> O	17	0	2.1	0.7	3.8
2	150 mg Glucose, 24.8 mmol HCl	28	0.5	2.3	5.9	10.7
3	126 mg HMF, 6 mL DCE, 24.8 mmol HCl	–	74.5	5.3	9.4	10.5
4	126 mg HMF, 4 mL H <sub>2</sub> O, 24.8 mmol HCl	–	0	54.2	21.4	33.2
5	150 mg Glucose, 6 mL MIBK, 24.8 mmol HCl	46	0.13	7.0	0	0

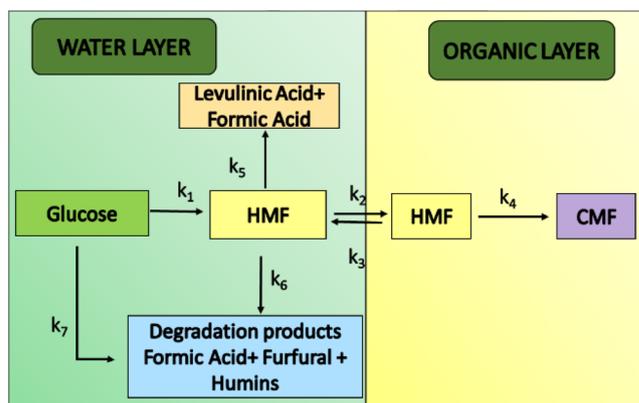
Condition: Temperature 70°C, time 1 h, rpm 650.

its migration without knowing the concentration (Table 2). HMF extracted in the organic phase immediately was converted to CMF. Utilization of nonchlorinated organic solvents like (methyl isobutyl) ketone yielded no CMF from HMF. Chlorinated solvent (DCE) is one of the important conditions for the formation of CMF.

It is necessary to be mentioned here that the formation of HMF from glucose is well-studied in the literature, and the possible formation of fructose, reversion products, and levoglucosan from glucose was also reported.<sup>19,23–25</sup> On the contrary, no levoglucosan was found to be produced during our reaction and less than 1% fructose was obtained. Henceforth, we assume that glucose has undergone irreversible reactions like dehydration to HMF as well as degradation to polymers in concurrent to other reports in the literature.<sup>19,24</sup> HMF undergoes a reversible phase transfer between water and DCE layers. HMF could possibly be degraded to LA and FA in the water layer; whereas in DCE, HMF was easily converted to CMF rather than undergoing degradation. The amount of FA formed in the water layer is not stoichiometrically equal to that of LA; this leads to the probable conclusion that HMF was degraded to FA and humins via the intermediate furfural as reported in the literature.<sup>18</sup>

Based on the above products obtained from control reactions including the stoichiometric excess of FA, we propose

a reaction mechanism for CMF formation from glucose in Scheme 2. The kinetic model proposed has the following key steps: (1) glucose dehydration to HMF, (2) HMF phase transfer, (3) HMF chlorination to CMF in DCE, (4) HMF degradation to FA and LA in water, (5) decomposition of HMF in water layer to humins, (6) glucose decomposition to degradation products (FA, furfural, and humins). Here,  $k_1$  is the rate constant for the formation of HMF from glucose;  $k_2$  and  $k_3$  are the rate constants for mass transfer of HMF between water and DCE layer;  $k_4$  is the rate constant



SCHEME 2 Mechanism for CMF formation from glucose [Color figure can be viewed at wileyonlinelibrary.com]

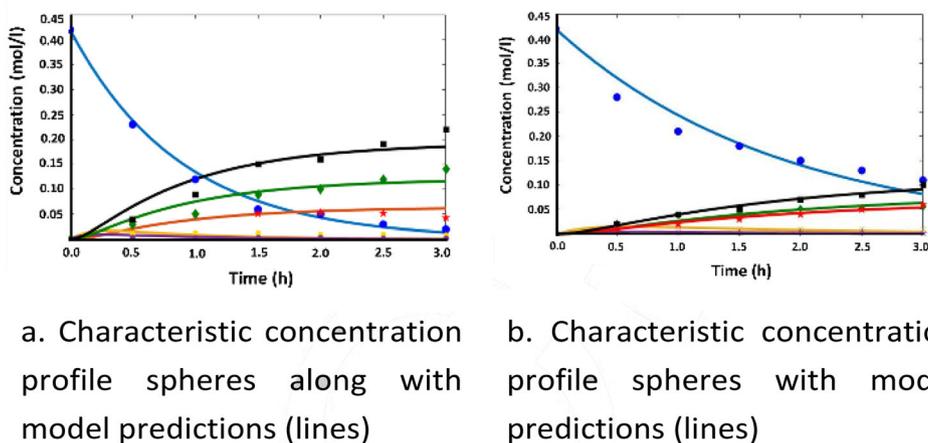


FIGURE 3 Comparison of CMF production from glucose (A) 80°C as a function of time and (B) 70°C as a function of time, (glucose (blue spheres), FA (black spheres), LA (green spheres), CMF (red spheres), HMF in DCE (yellow spheres), and HMF in H<sub>2</sub>O (purple spheres), # Conditions: Glucose 150 mg, HCl 24.8 mmol, DCE 6 mL [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

for the formation of CMF from HMF in DCE layer;  $k_5$  is the rate constant for the degradation of HMF to LA and FA in aqueous phase;  $k_6$  is the rate constant for the degradation to FA and humins;  $k_7$  is the rate constant for the formation of degradation products from glucose.

CMF formation was modeled based on the simplified reaction mechanism given in Scheme 2. Since the concentration of HCl is far greater than the other reactant glucose, all reactions are considered as first order.

The overall rate equation for the biphasic production of CMF from glucose is given below:

$$\frac{d(\text{Glu})}{dt} = -k^1 \times [\text{Glu}] - k^7 \times [\text{Glu}] \quad (1)$$

$$\frac{d(\text{CMF})}{dt} = k^4 \times [\text{HMFo}] \quad (2)$$

$$\begin{aligned} \frac{d(\text{HMFw})}{dt} &= k^1 \times [\text{Glu}] - k^2 \times [\text{HMFw}] - k^6 \\ &\times [\text{HMFw}] - k^5 \times [\text{HMFw}] + k^3 [\text{HMFo}] \end{aligned} \quad (3)$$

$$\begin{aligned} \frac{d(\text{HMFo})}{dt} &= k^2 \times [\text{HMFw}] - k^3 \times [\text{HMFo}] \\ &- k^4 \times [\text{HMFo}] \end{aligned} \quad (4)$$

$$\frac{d(\text{LA})}{dt} = k^5 \times [\text{HMFw}] \quad (5)$$

$$\frac{d(\text{FA})}{dt} = k^5 \times [\text{HMFw}] + k^6 \times [\text{HMFw}]. \quad (6)$$

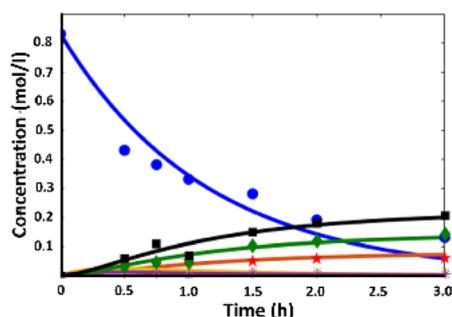
Kinetic studies of all the reactions were modeled by assuming the first-order reaction with respect to the acid

concentration, and kinetic parameters were determined with the same acid concentration. Experimental results were fitted to the kinetic model to calculate the kinetic parameters with the proposed mechanism in Scheme 2. Kinetics of possible reactions involved in CMF formation were independently studied at two different temperatures, and the variable products formed were modeled to fit with experimental results (Figure 3 and Table 3).

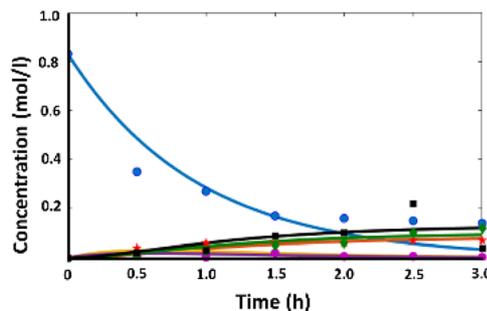
Figure 3(A) shows the experimental results of glucose conversion studied at 80°C with 24.8 mmol HCl, 70% glucose conversion was achieved within 1 h, and LA or FA formation was detected within 0.5 h. FA remains as the major product throughout the reaction at 80°C, which has higher concentration than LA. This confirms the possible formation of humins immediately after the onset of reaction which leads to excess FA. Maximum CMF formation was observed at 2 h and thereafter the CMF concentration decreased this might be due to back extraction of CMF to aqueous layer followed by hydrolysis to HMF and ultimately undergoing decomposition. HMF was present in both water and DCE phases; after 0.5 h, high HMF concentration was obtained. It needs to be mentioned here that a small amount of furfural (<1%) was also detected under these reaction conditions. With the progression of time, the initially formed HMF present in both aqueous layer and organic layer decreased which might be due to the formation of LA, FA, or humins. The effect of both acid concentration and temperature on the glucose conversion, CMF, LA, and FA yield was given in Figure S4 in the Supporting Information. At 70°C, the glucose concentration slowly decreased simultaneously with the formation of CMF, LA, and FA. Up to 1.5 h reaction time, LA and FA showed equal concentrations and thereafter FA dominates. This confirms that up to 1.5 h, HMF prefers to degrade into LA and FA rather than as

TABLE 3 Kinetic parameters for the formation of CMF from glucose in the bi-phasic medium

Entry No	Temperature	$k_1$	$k_2$	$k_3$	$k_4$	$k_5$	$k_6$	$k_7$
1	80	0.70	95.43	50.74	3.00	10.01	5.96	0.44
2	70	0.26	79.99	24.31	2.19	5.60	3.84	0.28
3	$E_a$ (kJ/mol)	98.99	–	–	31.47	58.37	44.12	43.30



a. Characteristic concentration profile spheres along with model predictions (lines)



b. Characteristic concentration profile spheres along with model predictions (lines)

FIGURE 4 Comparison of CMF production from glucose (A) 80°C as a function of time and (B) 70°C as a function of time, glucose (blue spheres), FA (black spheres), LA (green spheres), CMF (red spheres), HMF in DCE (yellow spheres), and HMF in H<sub>2</sub>O (purple spheres) along with model predictions (lines). # Conditions: Glucose 150 mg, HCl 12.4 mmol, DCE 6 mL [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

FA and humins. After 1.5 h, both the degradations were possible which leads to excess LA, the formation of CMF increased up to 3 h. Results obtained from the experiments were fitted to the kinetic model proposed to calculate the kinetic parameters. Moreover, it needs to be mentioned here that the experimental values agreed relatively with the modeling results which validates the proposed mechanism. The activation energy calculated for HMF formation from glucose is 98.99 kJ/mol, whereas formation of HMF directly from glucose was reported 108 and 160 kJ/mol higher than other report.<sup>19,26</sup> Similar reports on conversion in water using H<sub>2</sub>SO<sub>4</sub> and H<sub>3</sub>PO<sub>4</sub> acids were 128 and 121 kJ/mol, respectively, which was higher than our observed activation energy.<sup>27–29</sup> But reactions using ionic liquids and heterogeneous catalysts showed lower activation energy between 22 and 64 kJ/mol.<sup>30–32</sup> The lower activation energy favors the reaction toward the product-specific pathway. The mass transfer of HMF between aqueous and organic layers can be expressed by a distribution coefficient  $K_{eq} = k_2/k_3 = 95.43/50.74 = 1.88$ . Formation of CMF from HMF showed minimum activation energy of 31.47 kJ/mol proves it to be the most likely reaction than other competitive reactions.

HMF degradation in an aqueous layer to LA and FA has an activation energy of 58.37 kJ/mol. Reports showed that the H<sub>2</sub>SO<sub>4</sub>, H<sub>3</sub>PO<sub>4</sub>, and HCl-catalyzed reactions had activation energies of 57, 56, and 95 kJ/mol, respectively.<sup>19,33,34</sup>

Formation of FA and humins in the water layer from HMF showed activation energy of 44.12 kJ/mol, previous reports on this conversion using AlCl<sub>3</sub> had an activation energy of 90 kJ/mol.<sup>18</sup> The degradation of glucose to humins, furfural, and FA has the activation energy of 43.30 kJ/mol; it needs to be mentioned here that the humins and other degradation products formation from glucose is a well-studied conversion with high activation energy 89 kJ/mol.<sup>18</sup>

To study the influence of acid concentration on this kinetic model, similar reaction modeling was done using 12.4 mmol acid concentration and the results are given in Figure 4. Higher initial concentration of glucose was due to the lower volume of the water layer during the reaction. 80°C reaction exhibited a trend similar to the 24.8 mmol acid reaction, and LA remains as the major product. However, at 70°C, CMF prevailed as a major product up to 1 h reaction time, later other products predominated. It needs to be mentioned here that at low acid concentrations, the formation of by-products like LA, FA, and humins was low compared to higher acid concentrations.

To validate the present kinetic model, parity plots were constructed for glucose conversion as well as CMF yield and the corresponding result is shown in Figure 5. Good agreement between prediction and experimental values has been established for all products.

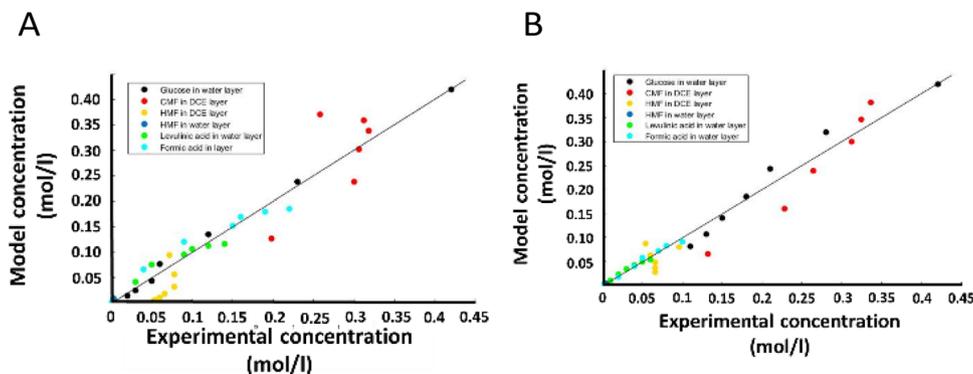


FIGURE 5 Parity plot with experimental and model values at (A) 80°C and (B) 70°C at 24.8 mmol acid concentration [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

## 4 | CONCLUSIONS

A rapid, sensitive, specific, reversed-phase HPLC method for assaying CMF in DCE (sensitivity 650  $\mu\text{g}/\text{ml}$  to 10  $\mu\text{g}/\text{mL}$ ) was developed. The Box–Behnken DOE method was used for statistical optimization of reaction parameters in this biphasic CMF formation in DCE solvent. A kinetic model was proposed for the first time based on an experimental investigation using different variables. The formation of CMF, HMF, FA, LA, and humins was modeled using a serial parallel mechanism. The apparent activation energy ( $E_a$ ) for glucose decomposition and CMF formation is 98.99 and 31.47 kJ/mol.

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## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the Supporting Information of this article.

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#### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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