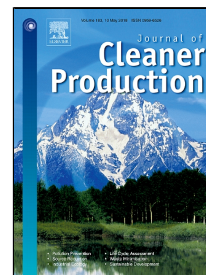


# Accepted Manuscript

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**A microwave-assisted process for the in-situ production of 5-hydroxymethylfurfural and  
furfural from lignocellulosic polysaccharides in a biphasic reaction system**

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## Abstract

In this study, a biphasic reaction system was developed for the microwave-assisted production of 5-hydroxymethylfurfural (HMF) and furfural. The proposed biphasic reaction system is a possible solution in the transition of current industrially state-of-the-art technologies which use C6 carbohydrates to an industrial process where lignocellulosic biomass can be processed, thus being a true sustainable process. In this respect, cellulose and xylan were chosen as model compounds since they are considered as the major building blocks of lignocellulosic polysaccharides. The reaction system consisted of an acidified aqueous phase and methyl isobutyl ketone (MIBK) as the organic phase. Upon the formation of HMF and furfural in the water phase, an instantaneous extraction into MIBK took place. The proposed biphasic reaction system offers many advantages over a monophasic reaction system, including (i) upon formation, furfural and HMF are continuously extracted into the MIBK layer, leading to the suppression of unwanted rehydration reactions, (ii) no unwanted solid particles are formed, and (iii) HMF and furfural can more easily be recovered from the reaction mixture. The goal of this study was to develop the microwave-assisted process in such a way that both cellulose and xylan were simultaneously converted. To this end, optimum process parameters in terms of HCl concentration ( $C_{\text{HCl}}$ ), temperature (T) and reaction time (t) were determined. A maximum HMF yield of  $33.65 \pm 0.46$  w% (or 43.27 mol%) and a maximal furfural yield of  $33.30 \pm 1.30$  w% (or 45.79 mol%) were achieved. To validate the proposed biphasic system, bamboo (*Phyllostachys aureosulcata*) was applied as a lignocellulosic feedstock, which resulted in a HMF yield of 42.44 mol% and a furfural yield of 48.90 mol%, based upon the cellulose and hemicellulose fraction of the bamboo particles. Since similar yields are observed compared to the model compounds, it is concluded that the lignocellulosic structure does not influence the reaction pathway. This means that the proposed biphasic system can be generalized for a wide variety of lignocellulosic feedstocks.

## Keywords

Microwave, Biphasic reaction system, Cellulose, Xylan, HMF, Furfural

## 1. Introduction

In recent years, research towards the production of platform chemicals derived from renewable resources to replace the current fossil based chemicals has expanded significantly. Furanic derivatives for instance, obtained from renewable biomass resources can be used as building blocks for the production of a variety of plastics and fine chemicals (Putten et al., 2013). The key of creating an industrially viable process lies within the simultaneous conversion of lignocellulosic C5 and C6 sugars into their corresponding derivatives. However, most papers focus on the production of one specific platform chemical from a certain lignocellulosic feedstock since each polysaccharide requires different process conditions for their conversion to platform chemicals (Sweygers et al., 2017a). As seen in Table 1, research groups often focus on one specific sugar monomer and its conversion to a desired product. Glucose, fructose or xylose is often used as a starting material mainly because of two reasons: (i) starting from the monomer, no hydrolysis of cellulose or hemicellulose is required leading to shorter reaction times, higher product yields and milder reaction conditions, (ii) since the hydrolysis step is avoided, no water is required for the conversion of polysaccharides into their monomers leading to higher HMF yields, because the rehydration to levulinic acid and formic acid is limited. Therefore, the simultaneous conversion of C5 sugars to furfural and C6 sugars to 5-hydroxymethylfurfural (HMF) has been chosen as the cornerstone of this study by using a biphasic reaction system. HMF has gained much attention over the past years because it is the key precursor in the production of bio-based plastics and biofuels such as 2,5-furandicarboxylic acid, which can be used for the synthesis of polyethylene furanoate (PEF) (Davis, 2015). Despite its many advantages, the production of HMF from lignocellulosic biomass is still not industrially viable because of the instability of the molecule in a water rich environment, the high production costs, the difficulty in purification processes and the difficulty in recycling and reusing both the solvent and catalysts (Gomes et al., 2015; Ma et al., 2015). Furfural, a similar chemical to the increasingly popular HMF is regaining attention as a bio-based alternative for a variety of fossil-based chemicals. Furfural is the most commonly produced chemical from

lignocellulosic biomass and, therefore, considered as one of the top-value added chemicals derived from biomass (Gallo et al., 2013; Sweygers et al., 2017a; Wettstein et al., 2012).

The reaction pathway of cellulose to HMF is depicted in Figure 1. In a first step cellulose is hydrolyzed in the presence of water to glucose monomers followed by an isomerization of glucose to fructose. Subsequently, HMF is formed through the dehydration of fructose in the presence of an acid catalyst. When the reaction is carried out in a monophasic aqueous system, a fast rehydration of HMF to levulinic acid and formic acid takes place, resulting in poor HMF yields. The reaction pathway of xylan to furfural is similar and is illustrated in Figure 2. In a first step xylan is hydrolyzed in an aqueous environment to xylose followed by an isomerization to xylulose. Xylulose is thereafter dehydrated to furfural in the presence of an acid catalyst. A ring-opening reaction does not occur, due to the absence of a hydroxyl group (which is present in HMF).

Water is a major issue in the reaction pathway. On the one hand, it is necessary to hydrolyze cellulose into glucose but on the other hand, adding water to the system enhances the rehydration of HMF to levulinic acid and thereby decreases the yield of HMF. The presence of water also causes unwanted side reactions, leading to the formation of solid particles (humins). The conversion processes that are currently employed at a commercial level start from monomeric sugars (i.e., fructose, glucose), without the need for water addition. AVA Biochem for instance, uses fructose as a feedstock, so no water needs to be added to the system and HMF can be formed. A second company, called Avantium, also starts from C6 carbohydrates (glucose, fructose) in an alcohol solution to form MMF. However, these technologies are limited because they only work with C6 carbohydrates as a feedstock. Both companies mention that the transition of C6 carbohydrates to second-generation non-food crops will be the key in creating a true sustainable process. However, since lignocellulosic biomass consists of polymeric cellulose and hemicellulose, the presence of water is required to hydrolyze these polymers and, therefore, a different technology than what now is commercially available needs to be applied. In

75 this respect, the technology that is proposed in this study offers a possible solution in such a way that  
76 lignocellulosic biomass can be effectively used in the simultaneous production of HMF and furfural.

77 The dilute acid hydrolysis of lignocellulosic carbohydrates using both heterogeneous and  
78 homogeneous acidic catalytic systems has been reported extensively (Girisuta et al., 2013; Li et al.,  
79 2014; Sweygers et al., 2017a; Wyman, 2013). The conversion of cellulose and xylose can be well  
80 catalyzed by strong mineral acids, salts, acidic ionic liquids, zeolites and acidic cation exchange resins  
81 (Morone et al., 2015; Pileidis and Titirici, 2016; Wang et al., 2014). Besides the effectiveness of the  
82 catalyst for achieving a high yield in HMF and furfural production, the applied reaction system also  
83 plays an important role in enhancing these yields. Various types of reaction systems have been  
84 reported in the literature, from aqueous monophasic systems to organic solvents and their biphasic  
85 mixtures (Saha and Abu-Omar, 2014a; Wrigstedt et al., 2016). Generally, adding a second solvent to  
86 the reaction mixture to create a biphasic mixture, increases the complexity and thus the cost of the  
87 process. In this respect, aqueous systems are favored although they are inefficient due to poor HMF  
88 yields caused by a fast ring opening reaction of HMF to levulinic acid and polymerization reactions to  
89 solid particles (i.e., humins) in the presence of water. Therefore, the addition of a second organic  
90 solvent can increase the efficiency of the aqueous monophasic systems (water is necessary for the  
91 hydrolysis of cellulose and xylose to glucose and xylose), towards a higher HMF selectivity by reducing  
92 unwanted side reactions. Since HMF and furfural are immediately transferred to this organic solvent,  
93 the ease of separation increases, rendering the process economically and environmentally competitive  
94 (Saha and Abu-Omar, 2014a). In Table 1, a literature overview of a variety of biphasic mixtures is  
95 presented.

96 In this study a water immiscible organic solvent, i.e., methyl isobutyl ketone (MIBK), was added to an  
97 acidified water phase to improve the selectivity of the reaction system to HMF and furfural. MIBK is a  
98 green solvent and recommended to use by the CHEM21 guide (Prat et al., 2016). Upon formation, both  
99 HMF and furfural are continuously extracted from the water phase, offering the important advantage

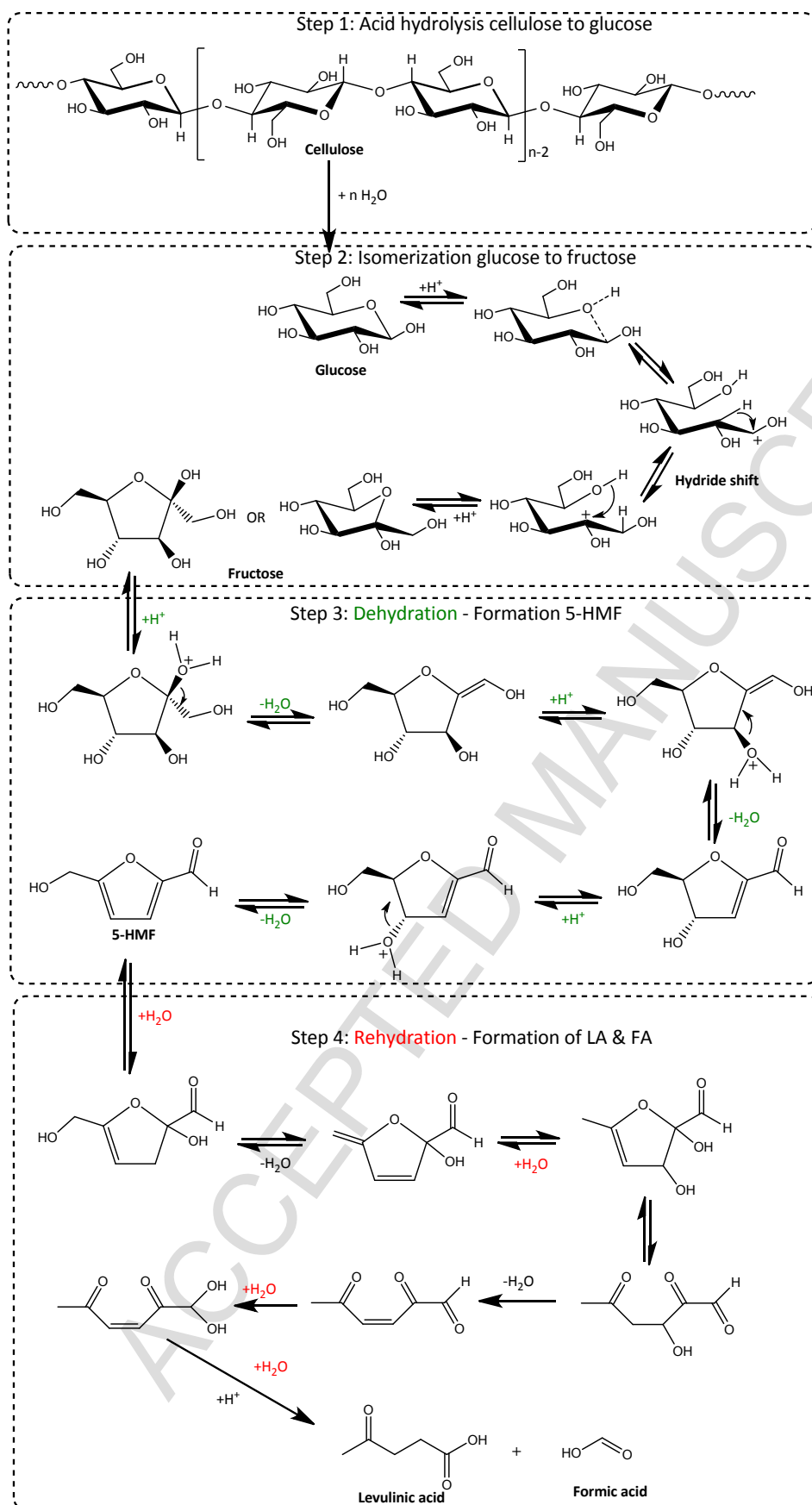
that they are separated from reactants and reaction intermediates and thereby avoiding any unwanted side reactions. Increased reaction temperatures ( $> 100\text{ }^{\circ}\text{C}$ ) were provided by microwave irradiation, which is known to offer many advantages including a highly efficient heating profile to shorten the reaction time considerably (Richel et al., 2011; Yemiş and Mazza, 2011).

To the best of our knowledge, this is the first study to investigate the simultaneous conversion of lignocellulosic polysaccharides to furfural and HMF in a biphasic reaction system. In our opinion, it is crucial that both hemicellulose and cellulose fractions of lignocellulosic biomass are used to create an industrially viable process. The process conditions, HCl concentration ( $c_{\text{HCl}}$ ), temperature ( $T$ ) and reaction time ( $t$ ) are optimized to convert both fractions simultaneously. In this study cellulose and xylan (=hemicellulose) are chosen as model compounds for the conversion to HMF and furfural, respectively, because they are closely related to the native structure of lignocellulosic biomass.

111 **Table 1. Literature overview of platform chemical production using a water/MIBK biphasic reaction system (with MIBK; methyl isobutyl ketone, THF;**  
 112 **tetrahydrofuran, CPME; cyclopentyl methyl ether, GVL;  $\gamma$ -valerolactone, MeTHF; 2-methyltetrahydrofuran, NMP; N-methyl-2-pyrrolidone, SBP; 2-sec-**  
 113 **butylphenol, HPA; hypophosphorous acid )**

| Entry | Feedstock     | Product  | Aqueous phase  | Organic phase | Temperature (°C) | Reaction time (min) | Yield (mol%) | Reference                         |
|-------|---------------|----------|--|---------------|------------------|---------------------|--------------|-----------------------------------|
| 1     | Cellulose     | HMF      | 0.2 mol/L HCl + 71.62 w% ZnCl <sub>2</sub>   | MIBK          | 150              | 40                  | 81           | (Zhang et al., 2016)              |
| 2     | Fructose      | HMF      | H <sub>2</sub> O   | MIBK          | 160              | 120                 | 73.6         | (Ma et al., 2015)                 |
| 3     | Fructose      | HMF      | H <sub>2</sub> O + NaCl + AlCl <sub>3</sub>  | MIBK          | 130              | 5                   | 61.2         | (De et al., 2011)                 |
| 4     | Fructose      | HMF      | 2 mol/L HCl  | MIBK          | 140              | 15                  | 74           | (Brasholz et al., 2011)           |
| 5     | Fructose      | HMF      | 0.25 mol/L HCl   | MIBK          | 180              | 2.5 - 3             | 56           | (Chheda and Dumesic, 2006)        |
| 6     | Fructose      | HMF      | 0.025 mol/L HCl  | MIBK          | 180              | 3                   | 84           | (Shimanouchi et al., 2013)        |
| 7     | Xylose        | Furfural | 0.1 mol/L HCl  | MIBK          | 170              | 50                  | 70           | (Weingarten et al., 2010)         |
| 8     | Glucose       | HMF      | H <sub>2</sub> O + NaCl + 0.1 mmol AlCl <sub>3</sub>   | THF           | 160              | 10                  | 61           | (Yang et al., 2012)               |
| 9     | Starch        | HMF      | H <sub>2</sub> O + NaCl + 0.1 mmol AlCl <sub>3</sub>   | THF           | 160              | 10                  | 50           | (Yang et al., 2012)               |
| 10    | Bamboo fibres | HMF      | H <sub>2</sub> O + NaCl + 0.5 mmol NH <sub>2</sub> SO <sub>3</sub> H                                       | THF           | 180              | 40                  | 52,2         | (Sun et al., 2015)                |
| 11    | Glucose       | HMF      | H <sub>2</sub> O + NaCl + HCl + 0.025 mmol AlCl <sub>3</sub>   | CPME          | 175              | 20                  | 54,5         | (Wang et al., 2017)               |
| 12    | Glucose       | HMF      | 10 mol% CrCl <sub>3</sub> .6H <sub>2</sub> O + 20 mol% H <sub>3</sub> BO <sub>3</sub> + 21 mg Amberlyst 38 | GVL           | 160              | 4                   | 74           | (Wrigstedt et al., 2016)          |
| 13    | Rice straw    | HMF      | 0,5 w% H <sub>2</sub> SO <sub>4</sub>  | THF           | 180              | 180                 | 16           | (Amiri et al., 2010)              |
| 14    | Fructose      | HMF      | HCl (pH 0.6)   | 1-Butanol     | 180              | 20                  | 68           | (Román-Leshkov and Dumesic, 2009) |
| 15    | Glucose       | HMF      | 10 mM AlCl <sub>3</sub> .6H <sub>2</sub> O + 0.1 M HCl   | MeTHF + NMP   | 175              | 80                  | 86,9         | (Atanda et al., 2016)             |
| 16    | Glucose       | HMF      | AlCl <sub>3</sub> + HCl (pH 2.5)   | SBP           | 170              | 40                  | 62           | (Pagán-Torres et al., 2012)       |
| 17    | Glucose       | HMF      | H <sub>2</sub> O + NaCl + HPA/TiO <sub>2</sub> .ZrO <sub>2</sub>   | THF           | 160              | 240                 | 51,3         | (He et al., 2017)                 |





**Figure 1: Cellulose conversion to HMF: key steps of the reaction pathway**

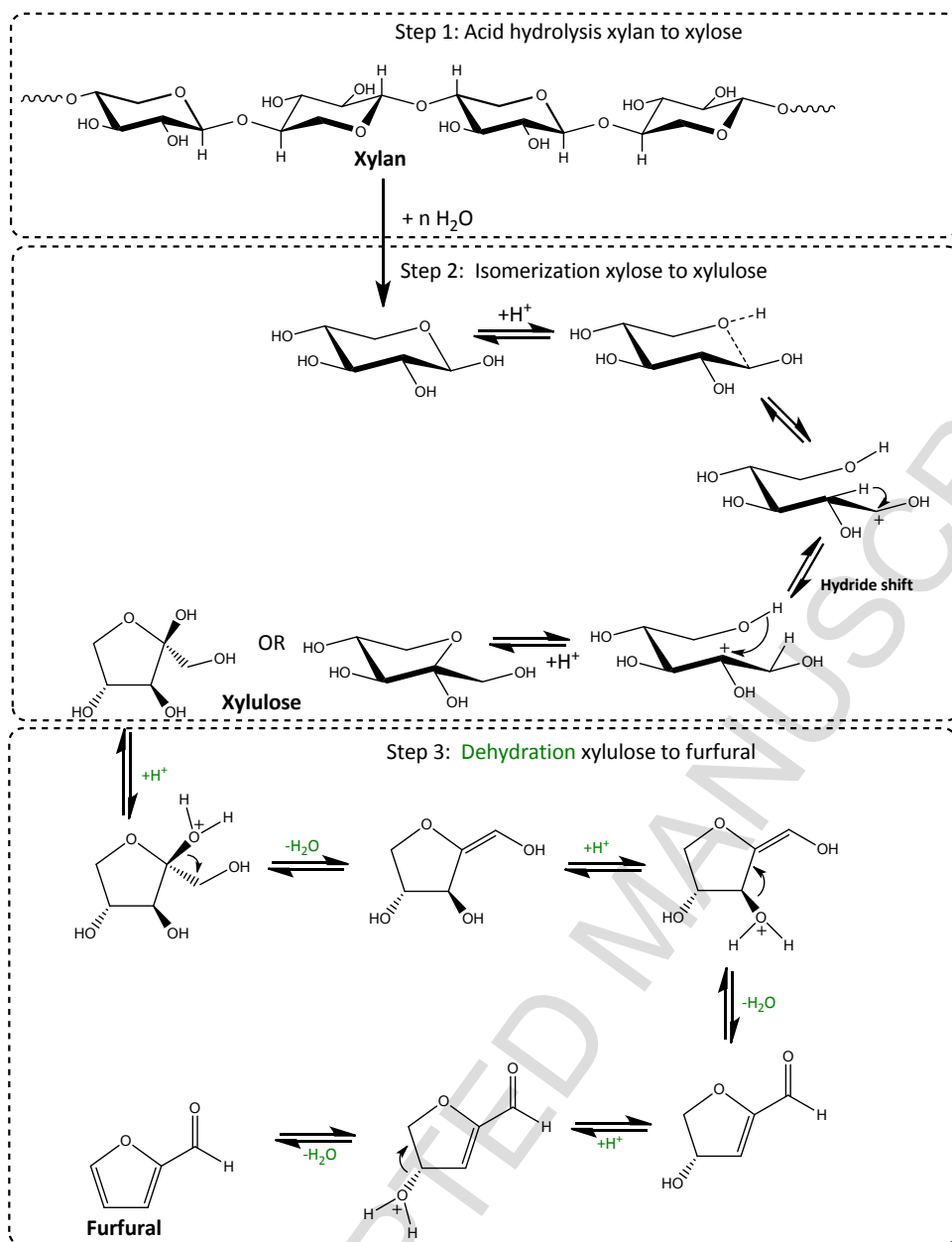


Figure 2: Xylan conversion to furfural: key steps of the reaction pathway

## 2. Materials and methods

### 2.1. Chemicals

All experiments were conducted with cellulose (Sigma Aldrich) and xylan obtained from beechwood (TCI Chemicals), as model polysaccharide constituents of lignocellulosic biomass. The reactions took place in a biphasic reaction medium consisting of an aqueous phase (demineralized water) acidified with HCl (Fisher Scientific, 37 %) and an organic phase consisting of MIBK (Acros Organics, 99.5%).

### 2.2. Experimental set-up

The experiments were carried out in a microwave reactor system (Monowave 300, Anton Paar). The temperature is monitored with a ruby temperature sensor placed inside the reaction vessel. The volume of the reaction vessel is 10 mL. In an experiment, the reaction vessel was filled with 25 mg cellulose or xylan, 250  $\mu$ L acidified water and 4.75 mL MIBK as the organic phase. The stirring rate was set at 800 rpm for all experiments. Maximum power output was set at 800 W. As soon as the reaction time was completed, the glass reaction vessel was cooled rapidly by placing it in an ice bath to prevent further reactions. After cooling, the reaction mixture was filtered to retain any solid particles (Macherey-Nagel glass fiber filters, GF-3). After filtration, HMF, levulinic acid and furfural concentrations were measured in the organic phase and in the aqueous phase. All experiments were conducted in triplicate.

### 2.3. Analytical techniques

A sample (extract of 1  $\mu$ L) of the organic phase was analyzed using an Agilent gas chromatograph (Agilent 7890A-series) equipped with a flame ionization detector (FID) to determine furfural, levulinic acid and HMF concentrations. The GC was equipped with a HP-FFAP column (Agilent, J&W HP-FFAP length 30 m, internal diameter 0.25 mm, film thickness 0.25  $\mu$ m). A sample of the aqueous phase was analyzed using an Agilent HPLC (Agilent 1100 series) equipped with a reversed-phase C18 column (Agilent, Zorbax Eclipse Plus C18 diameter 4.6 mm, length 100 mm, particle size 2.5  $\mu$ m) and a UV detector ( $\lambda$  = 255 nm) to determine furfural, levulinic acid and HMF concentrations. The mobile phase consisted of a mixture of methanol (Acros Organics) and Milli-Q water (10/90) and the injection volume

was 3  $\mu$ L. The mass of particulate matter was gravimetrically determined by filtrating the reaction medium with a glass fiber filter (Macherey Nagel, 0.6  $\mu$ m retention capacity).

#### 2.4. Response Surface Methodology

HMF is regarded as the most valuable platform chemical to be obtained from lignocellulosic polysaccharides. Therefore, as a first step, the yield of HMF in the organic phase is optimized by means of Response Surface Methodology (RSM), which is a widely used methodology for yield optimization purposes (Chang et al., 2007; Kang et al., 2013; Qu et al., 2014; Yemiş and Mazza, 2012). T, t and  $c_{\text{HCl}}$  are considered as the most important process parameters for the conversion of cellulose to HMF, and were chosen as independent variables. In order to evaluate the combined effect of these variables on the production of HMF, a box-Behnken design in triplicate was employed, leading to 45 experiments. The levels and values of the variables are displayed in Table 2.

**Table 2. Levels of the independent variables, i.e.,  $c_{\text{HCl}}$ , T and t used for the RSM optimization procedure**

| Independent variables                | Unit               | Variable ranges |        |      |
|--------------------------------------|--------------------|-----------------|--------|------|
|                                      |                    | Low             | Medium | High |
| $c_{\text{HCl}}$ ; HCl concentration | M                  | 0.06            | 0.12   | 0.18 |
| T ; reaction temperature             | $^{\circ}\text{C}$ | 150             | 170    | 190  |
| t ; reaction time                    | min                | 20              | 60     | 100  |

The yield of HMF was chosen as the response factor and fitted to the following second-order polynomial model equation:

$$Y = \beta_0 + \sum \beta_i x_i + \sum \beta_{ii} x_i^2 + \sum \sum \beta_{ij} x_i x_j \quad (1)$$

With Y the yield of HMF (w%),  $\beta_0$  the model intercept,  $\beta_i, \beta_{ii}, \beta_{ij}$  the linear, quadratic and interaction coefficients, respectively, and  $x_i$  the independent variables.

The yield of HMF was defined using the weight of raw material (cellulose) as a basis and was calculated from Equation 2:

$$Y_{HMF} = \frac{m_{HMF}}{m_{CEL}} \times 100\% \quad (2)$$

With  $Y_{HMF}$  the yield of HMF,  $m_{HMF}$  the mass of HMF formed (mg),  $m_{CEL}$  the mass of cellulose (mg).

### 3. Results and discussion

#### 3.1. Optimization of HMF yield (via RSM)

As a first step, the HMF yield in the organic phase is optimized, using a Box-Behnken design requiring 15 unique experimental runs (each performed in triplicate). The complete experimental set-up of the independent variables is included in Table 3. The HMF yield in the organic phase was set as a response factor to evaluate the conversion efficiency. The different correlation types (linear, 2-way interaction and quadratic) of the three independent variables  $c_{HCl}$ ,  $T$  and  $t$  were estimated via an analysis of variance (ANOVA) and proved to be significant (as illustrated by the p-values, which are all lower than 0.05). The ANOVA analysis with the yield of HMF as response is shown in Table 4. The obtained model in coded factors is:

$$Y_{HMF} [w\%] = -661.3 + 1.829 \cdot t + 6.338 \cdot T + 1221.9 \cdot c_{HCl} - 0.002304 \cdot t^2 - 0.01495 \cdot T^2 - 794 \cdot c_{HCl}^2 - 0.06973 \cdot t \cdot T - 2.034 \cdot t \cdot c_{HCl} - 5.141 \cdot T \cdot c_{HCl} \quad (3)$$

With  $Y_{HMF}$ : the yield of HMF (w%);  $t$ : the reaction time (min);  $T$ : the reaction temperature (°C); and  $c_{HCl}$ : the HCl concentration (M).

The p-value of the lack-of-fit is 0.159 ( $> 0.05$ ). Therefore, it can be concluded that the proposed model is significant, represented by a coefficient of determination ( $\text{adj } R^2$ ) of 95.81 %, which means it explains 95.81 % of the variability in the responses for the region studied. Equation 3 predicts a maximum HMF yield of 32.58 w% for a  $t$  of 98 min, a  $T$  of 177 °C and a  $c_{HCl}$  of 0.0685 M.

Since all the terms in the proposed model are significant (p-value  $< 0.05$ ) as shown in Table 4, the interaction and quadratic effects of the independent variables cannot be neglected, and, therefore, the variables cannot be analyzed independently. Figure 3 illustrates 2D contour and 3D surface plots

for the HMF yield generated from Equation 3. These plots are constructed by plotting two independent variables ( $t$ ,  $T$  or  $c_{\text{HCl}}$ ) against the HMF yield, while the third parameter is kept at a fixed value, corresponding to the value of this parameter at the predicted optimal HMF yield. Figure 3 visualizes the behavior of the reaction system at the above mentioned optimal reaction conditions leading to a maximum HMF yield of 32.58 w%. In Figure 3A, the temperature is kept at a constant value of 177 °C (predicted optimal  $T$ ). It is clear from the contour plot and the surface plot that at the optimal  $T$ , a maximal conversion to HMF is reached for high  $t$  in combination with low  $c_{\text{HCl}}$ . Figure 3B shows the effect of temperature and reaction time, while the  $c_{\text{HCl}}$  is fixed at 0.0685 M (predicted optimal  $c_{\text{HCl}}$ ). In the contour plot, whilst using the optimal  $c_{\text{HCl}}$ , a minimum temperature of 165 °C is required for a HMF yield of 32 w%. Figure 3B also shows that a higher  $T$  shortens  $t$  considerably, as can be explained by the Arrhenius equation. For instance, to achieve a HMF yield of 32 w%, it takes 100 min at 165 °C and only 60 min at 195 °C. In Figure 3C,  $c_{\text{HCl}}$  is plotted against  $T$ , whilst  $t$  is fixed at 98 min (predicted optimal  $t$ ). It is clear that the reaction is not favorable at low  $T$  (150 °C) and high  $T$  (190 °C). At 98 min, the maximal HMF conversion is situated within a  $T$  range of 175 °C - 182.5 °C and a  $c_{\text{HCl}}$  range of 0.06 - 0.1 M HCl. In all three cases (Figure 3A, B and C) the maximum predicted HMF yield of 32.58 w% lies within the optimal envelope of the 2D contour plot and thus on the highest point of the 3D surface plot.

**Table 3. Experimental Box-Behnken design and results**

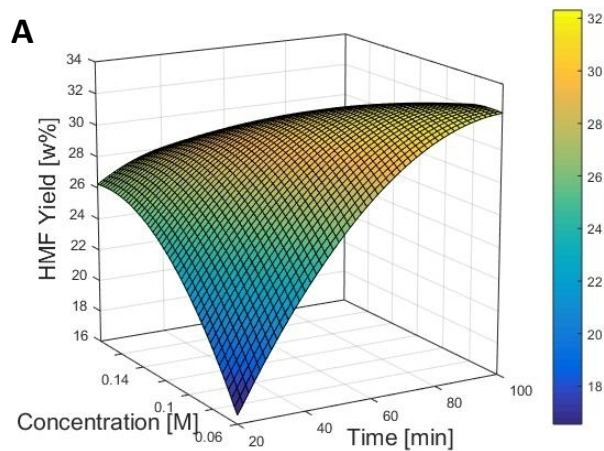
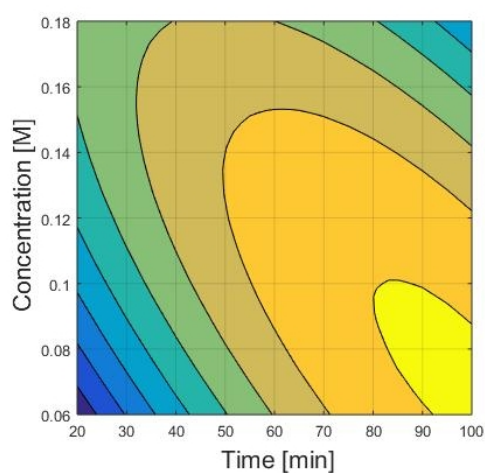
| Run | Experimental variables |          |                      | Response factor - HMF Yield |
|-----|------------------------|----------|----------------------|-----------------------------|
|     | $t$ (min)              | $T$ (°C) | $c_{\text{HCl}}$ (M) | $Y_{\text{HMF}}$ (w%)       |
| 1   | 60                     | 150      | 0.18                 | 24.68                       |
| 2   | 60                     | 170      | 0.12                 | 32.38                       |
| 3   | 100                    | 170      | 0.18                 | 26.48                       |
| 4   | 20                     | 170      | 0.18                 | 25.91                       |
| 5   | 100                    | 190      | 0.12                 | 24.34                       |
| 6   | 20                     | 190      | 0.12                 | 25.11                       |
| 7   | 60                     | 150      | 0.06                 | 7.94                        |
| 8   | 60                     | 150      | 0.06                 | 9.75                        |
| 9   | 60                     | 170      | 0.12                 | 30.47                       |
| 10  | 100                    | 170      | 0.18                 | 27.20                       |
| 11  | 100                    | 170      | 0.06                 | 31.35                       |
| 12  | 20                     | 190      | 0.12                 | 27.07                       |
| 13  | 100                    | 170      | 0.06                 | 32.10                       |
| 14  | 60                     | 190      | 0.06                 | 30.45                       |

|    |     |     |      |       |
|----|-----|-----|------|-------|
| 15 | 100 | 190 | 0.12 | 22.06 |
| 16 | 20  | 150 | 0.12 | 6.25  |
| 17 | 20  | 190 | 0.12 | 25.49 |
| 18 | 20  | 170 | 0.18 | 24.58 |
| 19 | 60  | 190 | 0.18 | 22.94 |
| 20 | 60  | 170 | 0.12 | 30.21 |
| 21 | 60  | 190 | 0.06 | 32.90 |
| 22 | 60  | 170 | 0.12 | 27.54 |
| 23 | 60  | 190 | 0.18 | 21.97 |
| 24 | 100 | 150 | 0.12 | 28.06 |
| 25 | 60  | 170 | 0.12 | 31.87 |
| 26 | 20  | 170 | 0.18 | 25.96 |
| 27 | 60  | 170 | 0.12 | 30.93 |
| 28 | 100 | 170 | 0.18 | 26.66 |
| 29 | 20  | 170 | 0.06 | 9.95  |
| 30 | 60  | 170 | 0.12 | 29.07 |
| 31 | 60  | 190 | 0.06 | 27.93 |
| 32 | 60  | 190 | 0.18 | 19.64 |
| 33 | 100 | 150 | 0.12 | 24.88 |
| 34 | 60  | 150 | 0.18 | 27.24 |
| 35 | 20  | 170 | 0.06 | 10.22 |
| 36 | 20  | 170 | 0.06 | 11.80 |
| 37 | 60  | 150 | 0.06 | 8.59  |
| 38 | 20  | 150 | 0.12 | 6.73  |
| 39 | 100 | 190 | 0.12 | 23.70 |
| 40 | 60  | 170 | 0.12 | 26.61 |
| 41 | 100 | 150 | 0.12 | 25.73 |
| 42 | 20  | 150 | 0.12 | 6.32  |
| 43 | 60  | 150 | 0.18 | 21.66 |
| 44 | 60  | 170 | 0.12 | 32.22 |
| 45 | 100 | 170 | 0.06 | 30.99 |

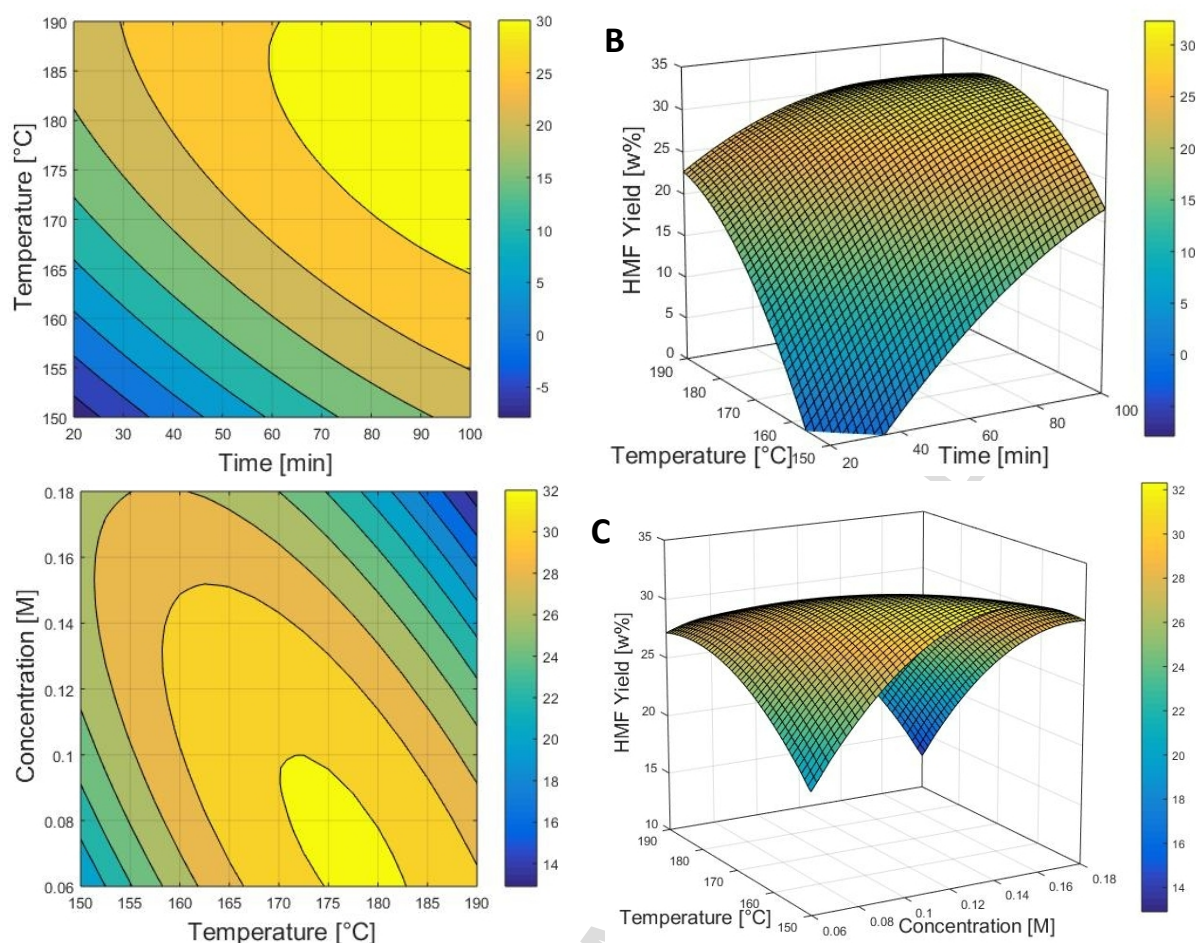
**Table 4: ANOVA of the proposed model for HMF yield ( $R^2 = 96,66\%$ ,  $\text{adj } R^2 = 95,81\%$ ,  $\text{pred } R^2 = 94,65\%$ )**

| Source            | DF | Sum of squares | Mean square | F-value | p-value |
|-------------------|----|----------------|-------------|---------|---------|
| Model             | 9  | 2836.83        | 315.204     | 112.68  | 0.000   |
| Linear            | 3  | 1156.04        | 385.347     | 137.76  | 0.000   |
| T (°C)            | 1  | 466.14         | 466.137     | 166.64  | 0.000   |
| t (min)           | 1  | 581.74         | 581.741     | 207.97  | 0.000   |
| c (M)             | 1  | 108.16         | 108.163     | 38.67   | 0.000   |
| Square            | 3  | 564.71         | 188.236     | 67.29   | 0.000   |
| T (°C) * T (°C)   | 1  | 396.05         | 396.053     | 141.59  | 0.000   |
| t (min) * t (min) | 1  | 150.58         | 150.582     | 53.83   | 0.000   |
| c (M) * c (M)     | 1  | 90.47          | 90.469      | 32.34   | 0.000   |

|                   |    |         |         |        |       |
|-------------------|----|---------|---------|--------|-------|
| 2-way interaction | 3  | 1116.09 | 372.028 | 133.00 | 0.000 |
| t (min) * T (°C)  | 1  | 373.41  | 373.414 | 133.49 | 0.000 |
| T (°C)* c (M)     | 1  | 456.70  | 456.703 | 163.27 | 0.000 |
| t (min) * c (M)   | 1  | 285.97  | 285.968 | 102.23 | 0.000 |
| Error             | 35 | 97.90   | 2.797   |        |       |
| Lack-of-fit       | 3  | 14.43   | 4.810   | 1.84   | 0.159 |
| Pure error        | 32 | 83.47   | 2.609   |        |       |
| Total             | 44 | 2934.74 |         |        |       |







**Figure 3: 3D Response surface plots and 2D contour plots of the HMF yield (w%) at (A) varying  $c_{HCl}$  and  $t$ ; (B) varying  $T$  and  $t$ ; (C) varying  $T$  and  $c_{HCl}$ .**

As an external validation of the proposed model and to gain insights in the conversion pathway of cellulose to HMF under microwave irradiation, the production of HMF is experimentally tested (in triplicate) at the predicted optimal process conditions (177 °C, 0.0685M HCl), as depicted in Figure 4. The results of these experiments were compared to the calculated values from the model (Equation 3). The yield of HMF is well predicted by the model between 20 and 100 min. For shorter reaction times, the calculated values deviate from the measured ones, as Equation 3 gives a yield of 9.96 w% for a  $t$  of 0 min even though there cannot be any HMF present at this point. For longer reaction times, especially after 140 min, the model becomes inaccurate. For instance, according to the model, HMF

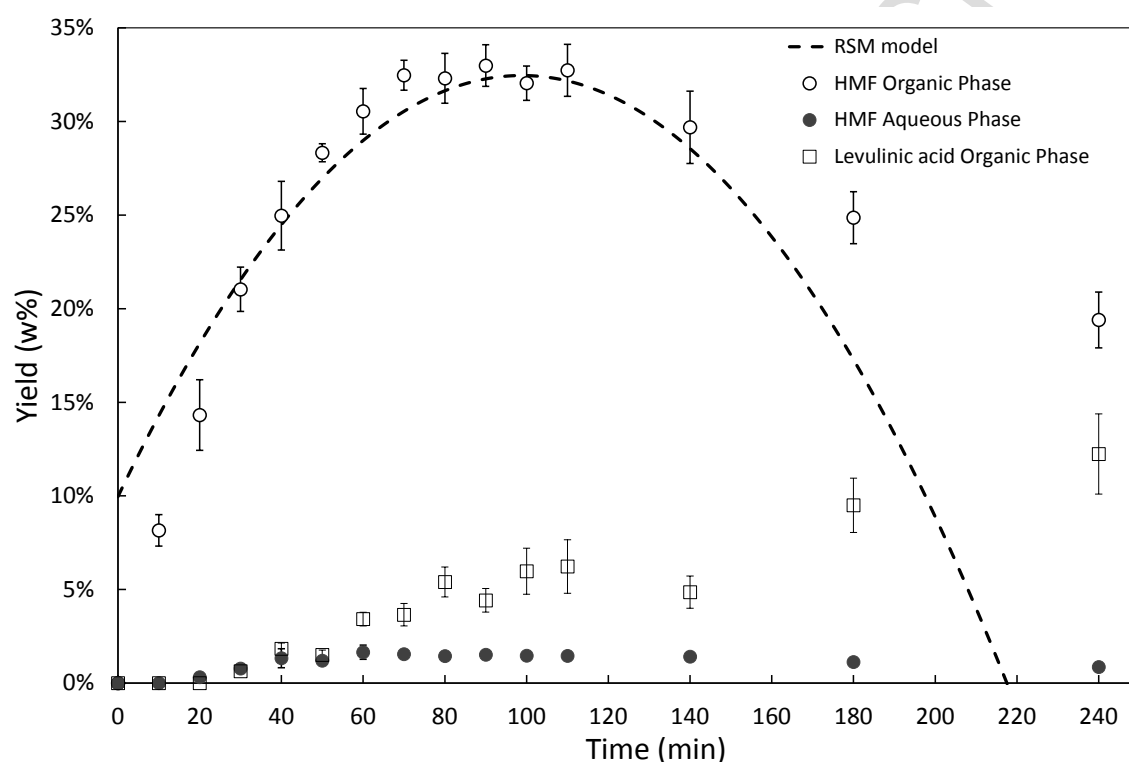
should be completely degraded after a  $t$  of 240 min, but there is still 19.87 w% HMF present in the reaction system. The degradation of HMF is due to the rehydration of HMF to levulinic acid. In contact with water, HMF undergoes a ring-opening reaction leading to the formation of levulinic acid and formic acid. In this biphasic reaction system, the rehydration reaction is rather slow leading to a levulinic acid yield of 12.24 w% ( $\pm 2.14$  w%) after a  $t$  of 240 min. Throughout the experiments, the amount of HMF in the water phase is quite low. This indicates that the HMF is immediately extracted into the MIBK layer. To quantify the in situ extraction process, the partition coefficient ( $K$ ) was calculated, describing the distribution of HMF in the aqueous and organic phase (Equation 4). The average partition coefficient under the conditions given in Figure 4 was 1.15 ( $\pm 0.071$ ). This indicates that the concentration of HMF in the organic phase is slightly higher than the aqueous phase. However, the volume of the organic phase (4.75 mL MIBK) was considerably higher than the volume of the aqueous phase (0.25 mL acidified water) in the reaction system, which means that in absolute terms, a higher amount of HMF was present in the organic phase. For instance, at the datapoint at  $t = 110$  min, 1440 ppm HMF was present in the water phase and 1704 ppm HMF was present in the MIBK phase. This results in a  $K$  of 1.18. However, in absolute terms this equals 0.36 mg HMF for the water phase and 8.094 mg for the MIBK phase since  $V_{\text{water}}$  is 0.25 mL and  $V_{\text{MIBK}}$  is 4.75 mL.

$$K = \frac{c_{\text{HMF,org}}}{c_{\text{HMF,Aque}}} \quad (4)$$

With  $K$ : the partition coefficient;  $c_{\text{HMF,org}}$ : the HMF concentration in the organic phase (ppm);  $c_{\text{HMF,Aque}}$ : the HMF concentration in the aqueous phase (ppm).

In the literature, various research papers describe the formation of solid particles or humins, due to condensation and polymerization reactions of HMF (Girisuta et al., 2013; Patil and Lund, 2011; Tsilomelekis et al., 2016). In this study, during the conversion of cellulose to HMF, no solid particles were formed. A color shift was, however, observed: the reaction medium turned reddish brown during the reaction (darker towards the end). This coloring of the medium can be either due to an increase in HMF concentration, or to the formation of condensation and polymerization products. The latter

would indicate that the formed humins are dissolved in the organic MIBK phase. In the literature, no analytical quantitative methods are available to measure dissolved humins, and, therefore, this hypothesis could not be confirmed.



**Figure 4: The external validation of the HMF production in a biphasic reaction medium. Conditions:  $T = 177\text{ }^{\circ}\text{C}$ ,  $c_{\text{HCl}} = 0.0685\text{ M}$ , stirring rate = 800 RPM, reactor content: 25 mg cellulose and 5 mL reaction medium (250  $\mu\text{L}$  acidified water and 4.75 mL MIBK). Dashed lines represent the predicted values of the RSM model.**

### 3.2. Simultaneous conversion of cellulose and xylan to HMF and furfural

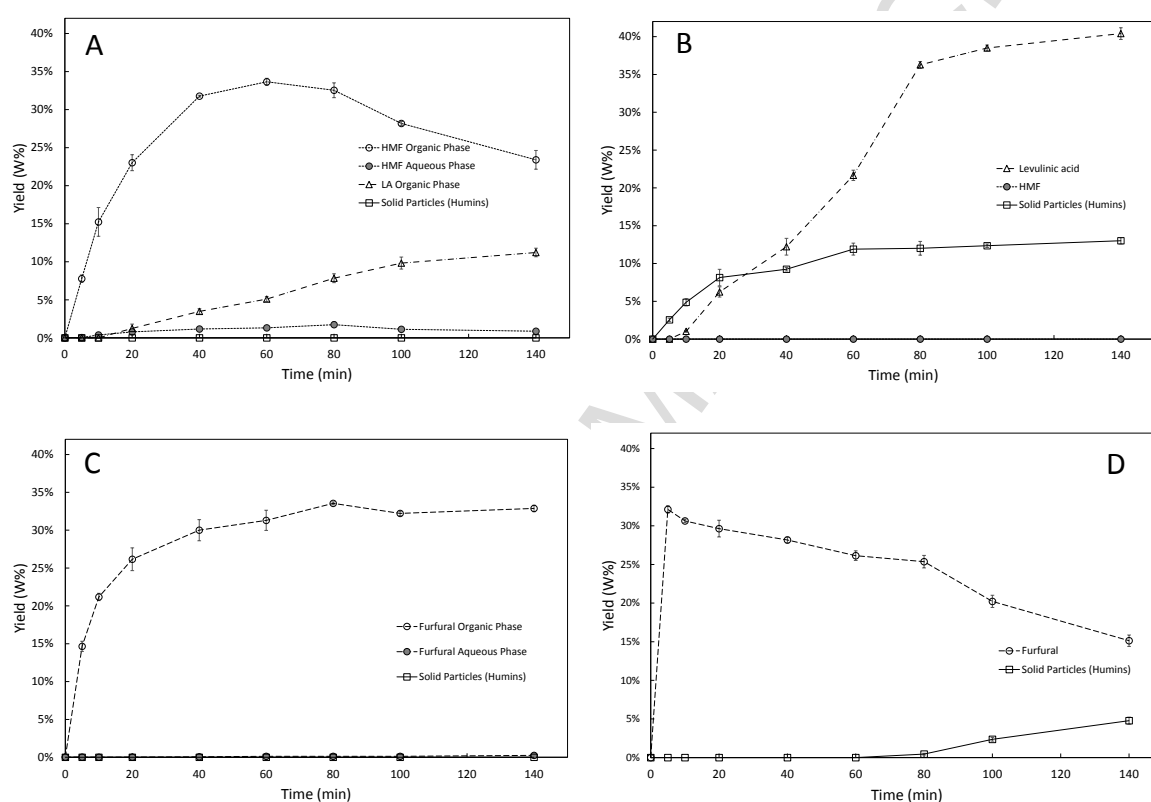
In this study, HMF was chosen over furfural for the optimization procedure. HMF is an unstable molecule being very temperature and acid sensitive. Thus, if furfural was chosen for the RSM procedure, it would be possible that no HMF was detected due to a high(er) optimal temperature and/or acid concentration. The process conditions ( $t$ ,  $c_{\text{HCl}}$ ,  $T$ ) determined during HMF yield

optimization were applied on xylan for its conversion to furfural. Applying a  $c_{\text{HCl}}$  of 0.0685 M, T of 177 °C and t of 100 min resulted in a furfural yield of only 8.66 w%. In order to increase the furfural yield without decreasing the maximal HMF yield,  $c_{\text{HCl}}$  was increased with small increments at a fixed T of 177 °C. A  $c_{\text{HCl}}$  of 0.1285 M and T of 177 °C renders a maximum furfural and HMF yield after a t = 60 min. The incremental increase of  $c_{\text{HCl}}$  to 0.1285 M ensured the lowest  $c_{\text{HCl}}$  possible for a simultaneous conversion of both cellulose and hemicellulose. A low  $c_{\text{HCl}}$  is important in dilute acid hydrolysis processes since it is directly related to the economic viability and environmental implications of the process. As seen in Figure 5A and 5C, the maximum obtained furfural yield was 33.30 w% ( $\pm 1.30$  w%) and the maximum HMF yield was 33.65 w% ( $\pm 0.46$  w%). At this point, the overall goal of this study, i.e., the simultaneous conversion of cellulose and xylan to HMF and furfural, was achieved.

### 3.3. Monophasic versus biphasic reaction system

Figure 5A and 5B compare the conversion of cellulose to HMF in a biphasic and monophasic system. In the absence of an organic phase, HMF is not measured due to the fast rehydration of HMF to levulinic acid and formic acid. Working with solely an aqueous phase also results in an increase in the formation of unwanted solid polymerization products, i.e., humins. In the monophasic system, 13.01 w% ( $\pm 0.41$  w%) solid particles are present after a t of 140 min, and a levulinic acid yield of 40.40 w% ( $\pm 1.78$  w%) is observed. This is in accordance with the literature where humin formation is reported whilst using solely an aqueous reaction medium (Girisuta et al., 2015; Shen and Wyman, 2012; Sweygers et al., 2017a; Yan et al., 2014). In the biphasic system, no solid particles were detected and the rehydration of HMF is suppressed leading to a levulinic acid yield of only 11.22 w% ( $\pm 0.56$  w%) at a similar reaction time. At this point, a HMF yield of 23.40 w% ( $\pm 1.23$  w%) is observed. Figure 5C and 5D compare the conversion of xylan to furfural in the biphasic and monophasic reaction system. Figure 5D shows that furfural in a monophasic system is formed almost instantaneously with a maximal yield of 32.13 w% ( $\pm 0.47$  w%). At the given process conditions furfural decays over time, leading to the formation of solid particles after a t of 60 min, leading to 4.78 w% solid particles after a t of 140 min. In the biphasic system (Figure 5C), the formed furfural is not decomposed and no solid particles were

observed. A maximal furfural yield of 33.30 w% ( $\pm 1.30$  w%) was reached after 60 min. It is well known that limiting unwanted side reactions (i.e. humin formation) is one of the biggest advantages of biphasic reaction systems (Saha and Abu-Omar, 2014b; Wrigstedt et al., 2016). However, in this study no solid particles were observed. However, a color shift indicates the presence of humins. As previously stated, no analytical quantitative methods are, however, available to measure dissolved humins, and, therefore, this hypothesis could not be confirmed (Van Zandvoort et al., 2013; Yan et al., 2014).

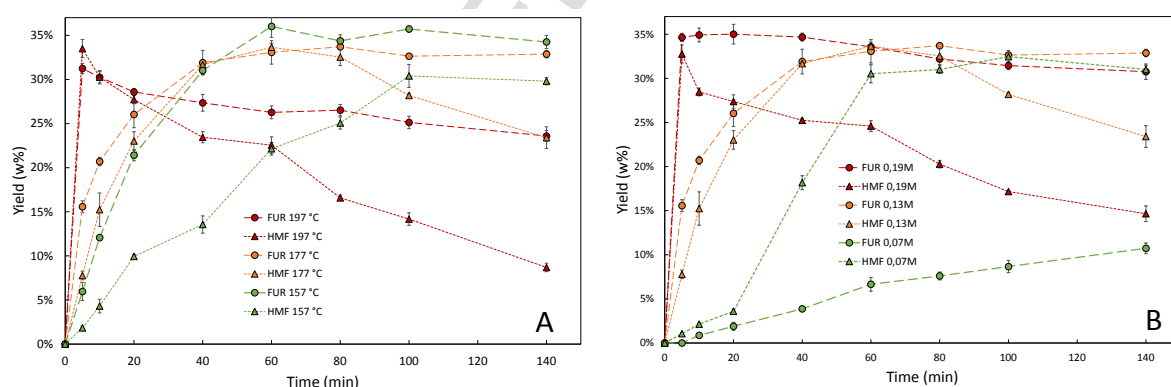


**Figure 5: (A) Conversion of cellulose in a biphasic reaction medium, (B) Conversion of cellulose in a monophasic reaction medium, (C) Conversion of xylan in a biphasic reaction medium, (D) Conversion of xylan in a monophasic reaction medium. Conditions:  $T = 177^{\circ}\text{C}$ ,  $c_{\text{HCl}} = 0.1285$  M, stirring rate = 800 RPM, biphasic reactor content: 25 mg cellulose/xylan and 5 mL reaction medium (250  $\mu\text{L}$  acidified water and 4.75 mL MIBK), monophasic reactor content: 25 mg cellulose/xylan and 5 mL acidified water.**

### 3.4. Influence of temperature and catalyst concentration

Figure 6 depicts the effect of  $T$  and  $c_{\text{HCl}}$  on the conversion of cellulose and xylan to HMF and furfural, respectively. In the first part of the study, the yield of HMF was optimized using RSM. Under optimal

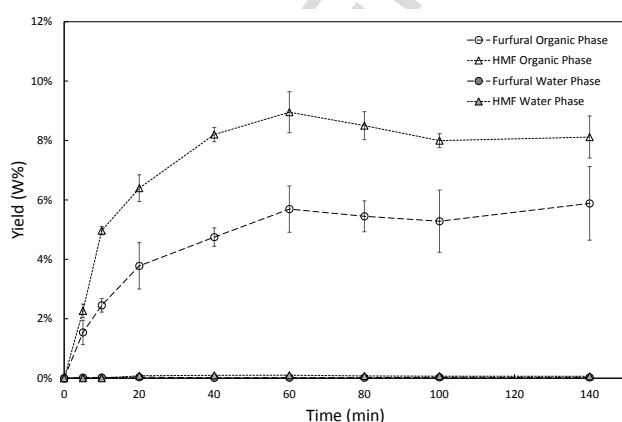
process conditions a maximum HMF yield of 32.46 w% was observed. However, only a poor furfural yield of 8.66 w% was observed under these conditions. A successful simultaneous conversion of cellulose and xylan was ensured after an incremental increase of  $c_{HCl}$ , by applying a  $c_{HCl}$  of 0.1285 M. By using a higher  $c_{HCl}$  of 0.19M, cellulose and xylan were already converted to HMF and furfural after a  $t$  of 5 min, but subsequent degradation of HMF to levulinic acid, however, occurred more rapidly, resulting in a yield of 14.65 w% HMF after a  $t$  of 140 min. Degradation reactions were not observed for the conversion of xylan to furfural whilst using a  $c_{HCl}$  of 0.19 M, resulting in a furfural yield of 31.00 w% after a  $t$  of 140 min. The effect of  $T$  is displayed in Figure 6A. By applying a  $T$  of 197 °C, furfural and HMF are again formed almost instantaneously after a  $t$  of 5 min. It is important to notice that both furfural and HMF were subjected to unwanted degradation reactions at these temperatures. Only 8.69 w% HMF and 23.4 w% furfural were remaining in the reaction system after a  $t$  of 140 min. At a decreased  $T$  of 157 °C, the formation of HMF was stalled, resulting in 29.81 w% HMF after a  $t$  of 140 min. This was not the case with furfural, where a maximal furfural yield of 36.01 w% was observed after 60 min.



**Figure 6: (A Left) Effect of  $T$  on furfural yield and HMF yield at an optimum  $c_{HCl}$  of 0.1285 M (B-Right) Effect of  $c_{HCl}$  on furfural yield at an optimum  $T$  of 177°C. Conditions: stirring rate = 800 RPM, biphasic reactor content: 25 mg cellulose/xylan and 5 mL reaction medium (250 µL acidified water and 4.75 mL MIBK).**

### 3.5. Conversion of Lignocellulosic biomass

The optimal reaction conditions ( $C_{HCl}$  of 0.1285 M and T of 177 °C) for the conversion to HMF and furfural were determined by using the model compounds cellulose and xylose, respectively. However, it is important from a sustainable and economically point of view, that lignocellulosic biomass, being the most abundant and renewable resource on earth, can be used as a raw feedstock for the production these chemical building blocks to create an industrially viable process. (Kumar et al., 2008) In this respect, bamboo (*Phyllostachys aureosulcata*) was used as a lignocellulosic feedstock to validate the proposed biphasic process. From Figure 8 it is clear that a simultaneous conversion of hemicellulose and cellulose to furfural and HMF is achieved. At a t of 60 min, a HMF yield of 8.95 w% and a furfural yield of 5.69 w% was observed. These yields may seem quite low, but should be placed in perspective with respect to the cellulose and hemicellulose fraction of the bamboo particles. The bamboo particles have a cellulose fraction of 29.28 w% and a hemicellulose fraction of 16.62 w% (Sweygers et al., 2017b). This means that a HMF yield of 30.56 w% (8.95 w%/29.28 w%) or 42.44 mol% and a furfural yield of 34.23 w% (5.69 w%/ 16.62 w%) or 48.90 mol% is achieved, based upon the cellulose and hemicellulose fraction of bamboo. This is in good agreement with the yields of HMF (43.27 mol%) and furfural (45.79 mol%) whilst working with the model compounds cellulose and xylose, respectively. This indicates that the lignocellulosic structure does not influence the reaction, and thereby lowering the product yields at the given particle size (<1mm).





**Figure 8: Conversion of bamboo to HMF and furfural. Conditions: T of 177 °C stirring rate = 800 RPM, biphasic reactor content: 25 mg bamboo and 5 mL reaction medium (250  $\mu$ L 0.1285M HCl and 4.75 mL MIBK).**

#### 4. Conclusion

The simultaneous conversion of cellulose and xylan to HMF and furfural in a biphasic reaction system under microwave irradiation was investigated, with an acidified (HCl) phase and MIBK as the organic phase. The process parameters (T, t and  $c_{\text{HCl}}$ ) were optimized in such a way that a simultaneous conversion could be achieved with a maximal HMF yield and furfural yield. A maximum HMF yield of 33.65 w% ( $\pm$  0.46 w%) or 43.27 mol% and a maximal furfural yield of 33.30 w% ( $\pm$  1.30 w%) or 45.79 mol% were achieved when applying a T of 177 °C, a  $c_{\text{HCl}}$  of 0.1285 M and a t of 60 min. The proposed biphasic reaction system is also proven to be applicable to lignocellulosic biomass. The conversion of bamboo (*Phyllostachys aureosulcata*) resulted in a HMF yield of 42.44 mol% and a furfural yield of 48.90 mol% based upon the cellulose and hemicellulose fraction of the bamboo particles. Since similar yields are observed, it is concluded that the lignocellulosic structure does not influence the reaction pathway. In this respect, the proposed biphasic reaction system could be a solution for the transition of current industrially technologies, which use C6 carbohydrates to process where lignocellulosic biomass can be processed, thus being a true sustainable process. From the results it is clear that the proposed biphasic reaction system offers many advantages compared to a monophasic system, as there are; (i) no unwanted solid particles in the biphasic reaction medium, (ii) suppressed rehydration of HMF to levulinic acid leading to the maximal formation of HMF, (iii) at optimum reaction conditions, degradation of furfural and HMF is limited. Working at higher T and  $c_{\text{HCl}}$  resulted in a fast conversion of cellulose and xylan to HMF and furfural. However, at these more extreme reaction conditions, HMF and furfural are more prone to degradation reactions. Hence, it can be concluded that depending on the eventual reactor configuration a tradeoff needs to be made: a fast formation of HMF and furfural applying more extreme conditions and the occurrence of degradation reactions or working at more moderate reaction conditions where the same maximal yield of HMF and furfural is achieved but requiring a longer t in the absence of degradation reactions.



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- Simultaneous formation of HMF and furfural via a microwave-assisted process.
- RSM for the optimization of reaction time, temperature and acid concentration.
- The measured data show a good agreement with the predicted RSM model.
- The biphasic system shows advantages over a monophasic reaction system.