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Lignocellulose Treatment Using a Flow-Through Variant of OrganoCat Process

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This study adapts the biphasic OrganoCat system into a flow-through (FT) reactor, using a heated tubular setup where a mixture of oxalic acid and 2-methyltetrahydrofuran (2-MTHF) is pumped through beech wood biomass. This method minimizes solvent-biomass contact time, facilitating rapid product removal and reducing the risk of secondary reactions. A comparative analysis with traditional batch processes reveals that the FT system, especially under severe conditions, significantly enhances extraction efficiency, yielding higher amounts of lignin and sugars with reduced solid residue. Notably, the FT system shows partial hydrolysis of the cellulose, which increases with temperature while not producing significant amounts of furfural or 5-HMF, indicating more efficient depolymerization of polysaccharides without substantial sugar degradation. A statistical design of experiments (DOE) using a Box-Behnken design elucidates the influence of process variables (time, solvent flow rate, temperature) on the yield. Key findings highlight reactor temperature as the dominant factor affecting yields, with process time showing a significant but less pronounced impact. This study demonstrates the potential of the FT OrganoCat system for efficient lignocellulosic biomass fractionation and represents an advancement towards continuous lignocellulose processing, contributing to our knowledge of process optimization for improved biorefinery applications.

Introduction

Transitioning to renewable feedstocks necessitates innovative lignocellulose processing strategies and the enhancement of existing methods to improve the quality and economic viability of lignocellulose-derived materials. Holistic valorization of biomass is essential given the valuable applications of all its components. Cellulose, a β-1,4 glycosidic linked D-glucose polymer, has been historically used in paper and textile industries and is now found in high-tech applications, including nanocrystalline cellulose for biomedical, electronic, and food industries.[1,2] Hemicellulose, mainly composed of accessible pentose and hexose sugars, can be transformed into platform chemicals like 5-hydroxymethylfurfural (HMF) and furfural, and subsequently into solvents, such as 2-methyltetrahydrofuran (MTHF) and polymers.[3] Lignin, the most abundant renewable aromatic resource, remains underutilized due to its complexity, though emerging applications include its use depolymerized for vanillin production or as a fuel additive, and as a polymer for fiber and carbon nanofiber manufacturing.[4] Most industrial biomass fractionation processes concentrate on cellulose for pulp and paper production, resulting in highly condensed lignin that is primarily burned for energy and catalyst recovery. Newer process developments like organosolv aim to use milder conditions to extract functional lignin that is closer to its native structure. Lignin is a polyaromatic molecule composed of three primary monomer subunits: syringyl (S), guyacyl (G), and p-hydroxybenzyl (H). These subunits can be connected through various structures, with the ether linkage via the β-*O*-4 position being the most common. Carbon-carbon linkages, such as resinol (β-β) and (β-5) structures, can also be found.[5] Since ether linkages are chemically more easily accessible than C–C linkages, which require high energy to break, a high proportion of β-*O*-4 linkages and low proportions of β-β and β-5 linkages are desired in a lignin product.[6] The OrganoCat process is a biobased, biphasic lignocellulose fractionation process employing a diluted aqueous acid for selective hydrolysis of non-cellulosic components and a second organic layer of 2-methyltetrahydrofuran (2-MTHF), which can be derived from furfural, to *in situ* extract lignin, and leaves a cellulose-enriched solid residue. Previous research on the OrganoCat process has applied it as a batch process, examining various scales, process conditions, acid catalysts, and biomass types.[7–11] Several promising options for downstream and valorization applications have been investigated for the different product fractions. Cellulose derived from this process has shown enhanced enzymatic digestibility, as highlighted by studies such as the one by Damm et al.[12] and Schrey et al.[13] The hemicellulose

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hydrolysate has been shown to be convertible to platform molecules via catalytic conversion or fermentation even without further purification.[9,14–16] Lignin downstream strategies have been developed[17,18] and further processibility has been confirmed as well.[19,20]

In numerous industrial settings, continuous flow processing is preferred over batch processing for its efficiency and cost-effectiveness in chemical production. This method minimizes downtime and enhances control over reaction conditions, also enabling time-resolved product analysis. Although its application in biomass fractionation, especially for depolymerizing technical lignin, is well-documented,[4] direct biomass solvolysis studies are less common.

Recent advances in flow-through processes use hydrotropes to enhance solubility and improve the efficiency of biomass fractionation. For instance, Wang et al. demonstrated the use of *p*-toluenesulfonic acid (p-TsOH) as a hydrotrope, which efficiently dissolves lignin and hemicellulose while preserving the cellulose structure under mild conditions (atmospheric pressure and temperatures below 98 °C).[21] Brandner et al.[22] introduces a method for producing native-like lignin from poplar biomass using flow-through solvolysis with methanol at 225 °C. The flow-through system ensures rapid exposure of solubilized lignin to catalysts, thereby preventing condensation, but also achieves monomer yields comparable to those from batch processes, effectively maintaining the integrity of aryl-ether bonds. Machmudah et al.,[23] investigates the extraction of lignin from Japanese rice straw using hot compressed water in a flow-through reactor system at temperatures of 170–230 °C. The process enables thermal softening of rice straw, facilitating lignin removal through depolymerization reactions. Smit et al.,[24] introduces a semicontinuous aqueous acetone organosolv fractionation for lignocellulosic biomass at 140 °C. The semicontinuous countercurrent flow fractionation design significantly reduces the overall residence time of solubilized sugars and lignin, enhancing fractionation performance by slightly improving sugar and lignin solubilization while notably reducing sugar degradation and enhancing the quality of hemicellulose oligomers. Reductive Catalytic Fractionation (RCF) uses a redox-active catalyst to prevent repolymerization of lignin, yielding low-molecular-weight lignin oils rich in phenolic monomers and carbohydrate-rich pulp. Flow-through RCF systems allow the separation of solvolytic lignin extraction from catalytic depolymerization, facilitating better process control and improved catalyst recovery.[25,26]

In circular process designs, regenerating reagents like acids and solvent, along with closed water loops, reduces waste and chemical consumption. This approach significantly reduces environmental impacts and promotes resource efficiency within biorefinery operations.[27] These principles are crucial in multi-sector applications, where lignin, cellulose, and hemicellulose are fractionated and repurposed across various industries.

In this study, we introduce a flow through variation of the OrganoCat process. To evaluate the influence of the process variables time, temperature and flow rate on the products, we used a design of experiments (DOE) approach. With this time-resolved fractionation of the lignocellulose components, we hope to get valuable insight into the mechanistic details of the process for future adaptations.

Results and Discussion

Set-Up of the Flow-Through OrganoCat

To provide insights into lignocellulose deconstruction mechanisms,[28] the biphasic OrganoCat system was adapted to a flow-through (FT) reactor, using a tube reactor filled with biomass, where the solvents are pumped through the reactor at different speeds and temperatures (Figure 1). Oxalic acid was chosen as catalyst. Beech wood, a well characterized substrate processed by OrganoCat systems,[7,9,29] was chosen to study the FT fractionation process and compare it to the batch modus. The organic solvent 2–methyltetrahydrofuran (2-MTHF) and 0.1 M oxalic acid solution is pumped through stationary lignocellulosic biomass in a heated tubular reactor. This approach minimizes solvent-biomass contact time, facilitating rapid product removal and reducing secondary reaction risks. Additionally, time-resolved fractionation offers insights into the process kinetics.

Statistical Design of Experiments Study of the FT Setup

To investigate the impact of different process variables on product yield and quality, a design of experiments (DOE) approach was utilized. The variables examined included process time (30–90 min), solvent flow rate (pump speed, 0.1–0.3 mL/min each solvent), and reactor temperature (140–180 °C). The center point was replicated three times to estimate the experimental error. A Box-Behnken design with one midpoint each edge was employed for the DOE model. The models for pulp yield, lignin yield, and sugar yield exhibited strong performance, for all responses, the low probability values ($p < 0.05$) revealed that the generated models were significant. Experimental results were well aligned with the generated models as confirmed by analyzing predicted against measured values. (see SI, Figure S1) A linear model was deemed the most suitable for pulp yield and sugar yield, while a quadratic model was found to be the best fit for lignin yield.

A significant model ($p < 0.05$) could also be found for β-*O*-4 linkage proportion with a modified 2FI model. According to the model, higher β-*O*-4 linkage proportion can be achieved at low temperature or high flow rate. Measured points, however, did not always fit the model prediction, which is why these trends need to be viewed with caution. GPC-data of the lignin (see SI, Table S7) did not show any clear trends, which might be caused by the very small amounts produced in a run, which makes it susceptible for high fluctuation. Further information on the models, p-values, R^2, and full ANOVA can be found in the supplementary information (see SI, Table S3, S4, S5). A visual representation of all models is provided in Figure 2. The graphs show one response each over the full range of two variables, while the other variable was fixed at its midpoint.

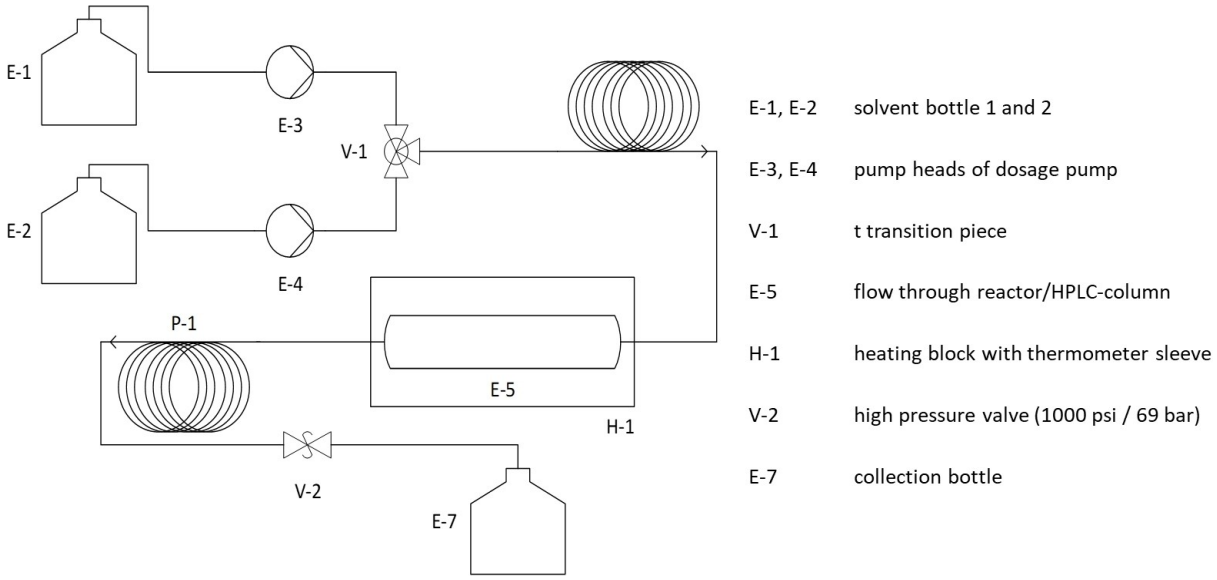

Figure 1. Schematic depiction of flow-through setup for lignocellulose pre-treatment. Two solvents (E-1 and E-2) were pumped (E-3 and E-4) through a T-valve (V-1) into a solid bed reactor (E-5), which was placed inside a heating block (H-1). The solvents were then cooled (P-1), and the pressure was reduced from 70 bar to ambient pressure through a backpressure valve (V-2). The product stream was then collected in fractions afterwards (E-7).

Reactor temperature exerts the greatest influence on pulp, lignin, and sugar yields as well as the β-*O*-4 linkage proportion in extracted lignin. With increasing temperature, more lignin and sugars are extracted, resulting in a reduced weight of the solid residue. The process time also exhibits a significant impact on the yields, showing the same trends as temperature but less pronounced. The influence of process time is most pronounced on lignin yield, which may be due to the longer extraction time required for lignin compared to hemicellulose sugars. The solvent flow rate on the other hand, does not influence the extraction efficiency as much as the other two parameters. There is a slight decrease in pulp yield with increasing flow rate, and for maximal lignin yield a medium flow rate of 0.2 mL/min seems to be favorable.

Overall, a clear correlation is difficult to make out, but a trend is visible that high flow rates result in high lignin yields, with high β-*O*-4 linkage proportion. At high temperatures also high lignin yields were obtained, however, with low β-*O*-4 linkage proportion in the extracted lignin. If looking to maximize lignin yield and β-*O*-4 linkage content, optimal conditions would be found at 160 °C, 0.3 mL/min and 90 min. The system can be adjusted to optimize the yield of the target product. This is in accordance with results, obtained in the batch OrganoCat processes.[9] Consequently, the enhanced cleavage of β-*O*-4 linkages at higher temperature can be partly mitigated with a higher solvent flow rate, reducing the time extracted lignin is exposed to the reaction conditions. This allows for high extraction with low lignin degradation at the cost of higher solvent to biomass ratio.

Time-Resolved Investigation of Flow-Through OrganoCat at Different Temperatures

To receive a more detailed understanding of the extraction of lignin, solvent fractions were collected every 5 minutes over a 90 min timespan using a flow rate of 0.2 mL/min at different reactor temperatures. Results are shown in Figure 3.

These extraction profiles were also obtained at different temperatures (140 °C, 160 °C, and 180 °C). As illustrated in Figure 3, about two thirds of the overall extracted lignin is already achieved at the 20 min point in case of 160 and 180 °C reactor temperature. At 140 °C two thirds of total lignin yield is achieved after 40 min. The highest extraction rate is obtained within the first 5–10 minutes at all temperatures, showing an almost linear extraction rate. Afterwards, the extraction slows down, until it reaches almost stagnation, and only very little more lignin is extracted, even though the residual solid still contains lignin (see SI, Table S1). This indicates that there is a temperature-dependent maximum of accessible lignin that cannot be exceeded by longer reaction times, which has also been observed in the batch process.[10] The rapid release of lignin in the beginning suggests that a certain fraction of lignin is more readily accessible and does not require substantial hydrolysis within the biomass to be extracted. This is in accordance with observations in other studies, that indicate differences in lignin accessibility, in different parts of the cell wall.[29] Within the investigated temperature range, no clear difference was observed in additional lignin extraction of the later fractions after 40 min. Possibly, even higher temperatures would be necessary to break the specific bonds that keep this residual lignin in the pulp, however this would also lead to enhanced degradation of the extracted lignin and sugars.

As shown in Figure 4, reaction temperature has a significant impact on the total yield of hemicellulose sugars that dissolve

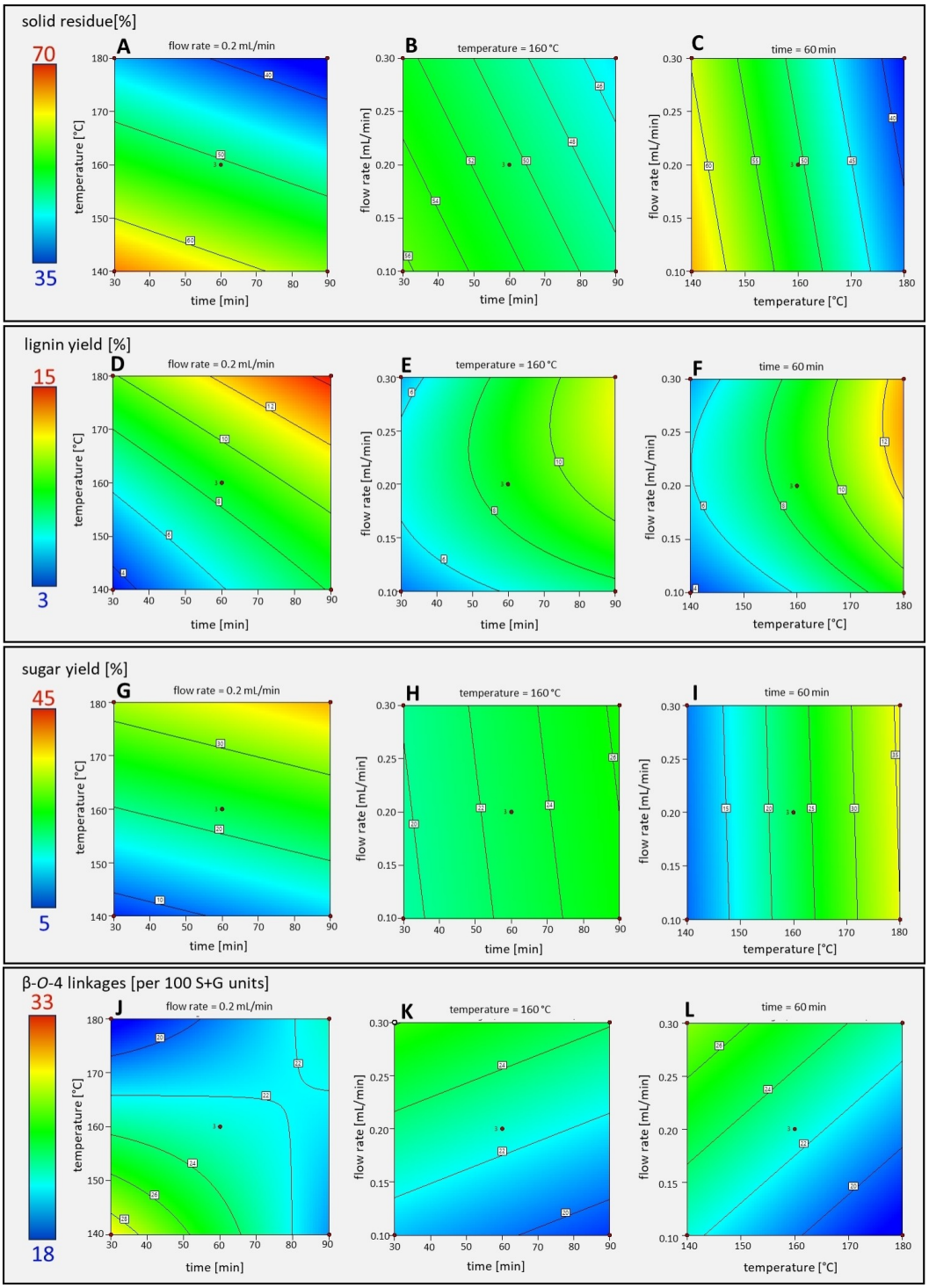

Figure 2. 2D contour models of design of experiments (DOE) study for the lignocellulose fractionation with a flow-through OrganoCat created using Design-Expert® Software Version 13.0.15.0. A, B, C: linear model for the amount of dried solid residue after extraction in wt% of the initial biomass. D, E, F: Quadratic model for lignin yield in wt% of the initial biomass. G, H, I: linear model for sugar yield in wt% of the initial biomass. J, K, L: modified 2FI model for β-O-4 linkages per 100 S + G units in the extracted lignin.

into the aqueous phase over time. Not only does the reaction temperature affect the overall amount of sugars extracted, but it also determines the rate of extraction. Especially in case of the 160 °C, the system is sensitive to small changes in temperature and pressure. These parameters can fluctuate slightly within the setup used for this study, causing high standard deviations at 160 °C. An increase in temperature from 140 °C to 180 °C almost triples the sugar yield. We see a clear increase of extraction speed going from 140 °C, where 46% of the total sugars were extracted after 20 min, to 160 °C, where 74% of the

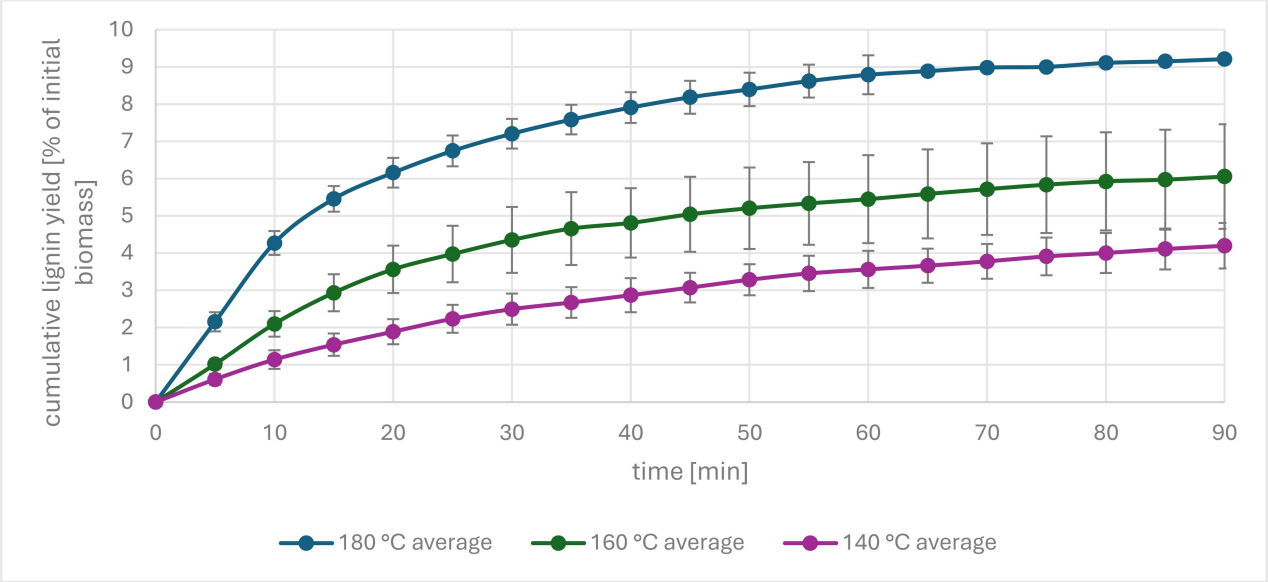

Figure 3. Cumulative lignin yields of the flow-through process at different temperatures. Samples were taken every 5 minutes and lignin was determined gravimetrically. Triplicate experiments were performed for 140 °C and 160 °C 0–90 min and 180 °C 0–60 min, for 180 °C 60–90 min the average of two experiments is shown.

total sugars were extracted after 20 min. However, the trend does not continue at 180 °C, where 69% of the total sugars are extracted after 20 min. While more sugars are extracted after 20 min at 180 °C than the total sugar yield at lower temperatures, the extraction continues at an almost linear rate. This suggests that higher temperatures increase the overall accessibility of sugars. The yield of sugars at 180 °C (32.8%) exceeds the amount of hemicellulose sugars in native beech (22.9%), indicating that the continued sugar extraction is derived from cellulose hydrolysis. This can also be seen when comparing the xylose-to-glucose ratio in the Hemicellulose fraction of the untreated biomass (8.3) to the ratio in the hydrolysate after extraction at 140 °C (5.4), 160 °C (3.9) and 180 °C (1.9). While some enhancement of glucose proportion in the beginning might be derived from starch as well, the continuous sugar extraction at 180 °C in combination with enhancement of the glucose proportion is most likely derived from the cellulose hydrolysis. Interestingly, we found only traces of further sugar degradation with low amounts of 5-HMF and furfural in the extract, which can be promising for a straightforward fermentation.

Conclusions

The study successfully demonstrates the effectiveness of a flow-through OrganoCat system for lignocellulosic biomass fractionation, offering a promising alternative to traditional batch processes. By comparing the performance under various conditions, it is evident that the FT approach can achieve superior extraction efficiencies, particularly under harsh conditions, with significant enhancements in lignin and sugar yields. The design of experiments (DOE) approach provides insights into the influence of operational parameters on the fractionation process, underscoring the pivotal role of reactor temperature and process time in optimizing yields and minimizing biomass degradation. Notably, the study also elucidates the complex dynamics of β-*O*-4 linkage cleavage within the lignin structure, suggesting potential strategies for mitigating degradation through process optimization. The system allows a fractionated collection of products, which showed that most lignin and sugars are extracted in the early stages of the process. We hope that the findings from this research contribute valuable knowledge towards the development of more efficient and sustainable methods for lignocellulose valorization, with implications for bio-refinery applications and the broader pursuit of renewable resources.

Materials and Methods

Oxalic acid and 2-methyltetrahydrofuran were purchased from Carl Roth and Sigma-Aldrich (Germany) and used without further purification. Beech wood biomass was obtained as already dried material and was milled with a cutting mill (SM 200 (Retsch, Haan, Germany) with a 1 mm sieve.

Lignocellulose Compositional Analysis

Utilizing protocols previously established with minor modifications for wet chemistry analysis of lignocellulose,[30] the procedure was conducted as follows: Alcohol-soluble constituents were first extracted, and subsequent analyses were conducted exclusively on the alcohol-insoluble residues (AIR). For all materials, starch was enzymatically broken down to yield

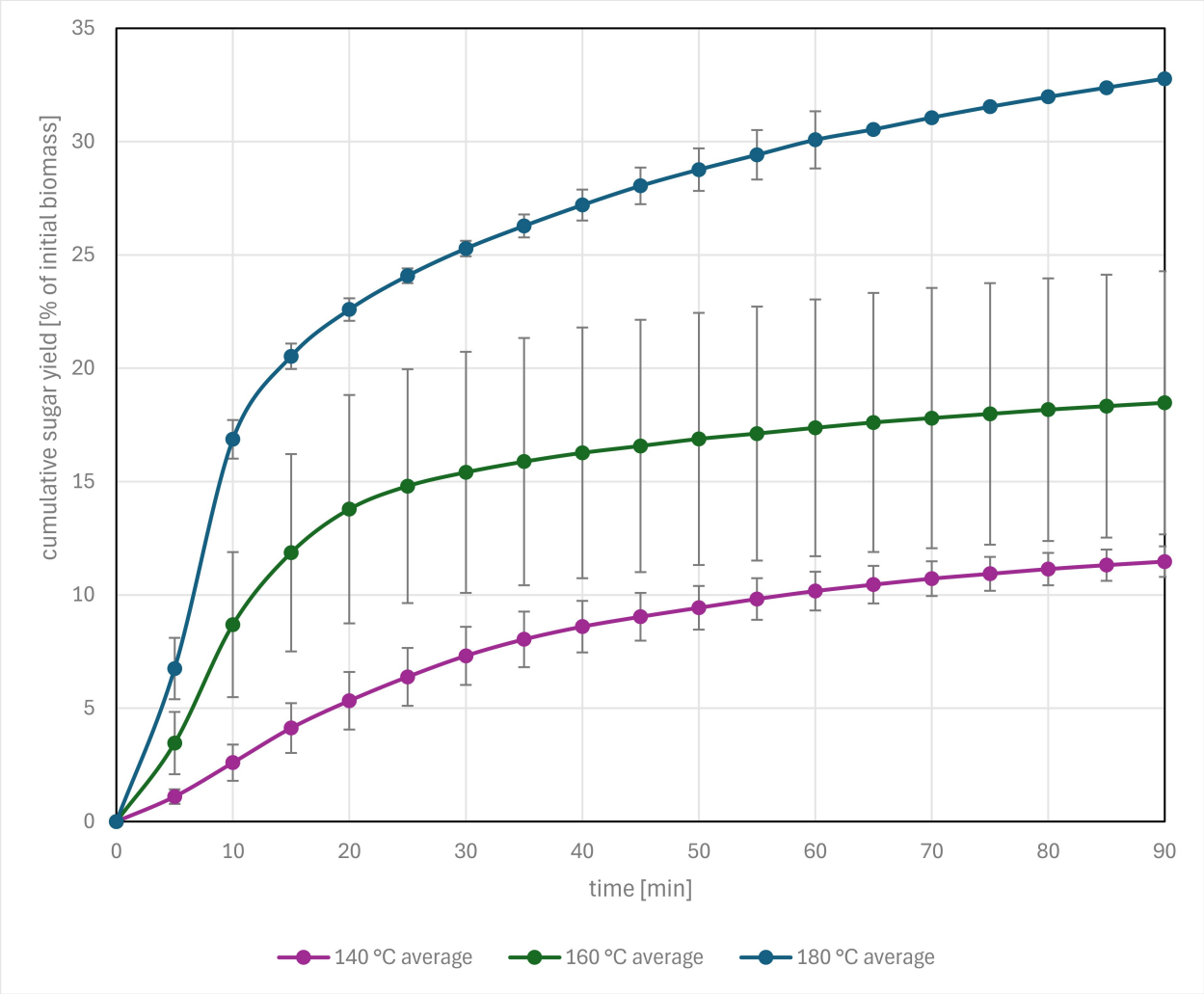

Figure 4. Cumulative sugar yields of the flow-through process at different Temperatures. Samples were taken every 5 minutes and sugar yield was determined by measuring the sugar concentration in the aqueous phase using ion chromatography. Triplicate experiments were performed for 140 °C and 160 °C 0–90 min and 180 °C 0–60 min, for 180 °C 60–90 min the average of two experiments is shown.

destarched lignocellulose samples (dAIR). Lignin content was assessed using the acetyl bromide soluble lignin (ABSL) method, and crystalline cellulose levels were measured applying the Updegraff technique, as detailed by Foster et al.[31,32] The analysis of non-cellulosic polysaccharide composition within dAIR followed, involving hydrolysis with trifluoracetic acid (TFA) and subsequent detection via high-performance anion-exchange chromatography with pulsed amperometric detection (HPAEC-PAD), in line with the method described by Damm et al.[11] The total acetate content in the samples was determined utilizing the acetic acid kit (KACE-TRM, Megazyme, Wicklow, Ireland).

Processing lignocellulose Fractionation in the Batch Reactor

Within a 20 mL high-pressure reactor, beech wood biomass (100 g L^{-1}) was suspended in a biphasic mixture comprising 0.1 M oxalic acid (4 mL, aqueous phase) and 2-methyltetrahydrofuran (MTHF, 4 mL, organic phase), subsequently pressurizing the system with argon to 10 bar.[11] The setup was heated to 140 °C and the temperature was consistently maintained for 180 minutes. Following the heating period, the reactor was allowed to cool and depressurize, after which the liquid phases were separated through decantation. The aqueous phase underwent filtration to procure the cellulose-enriched pulp. This solid residue was subjected to multiple washes with distilled water until achieving a neutral pH, followed by drying to a constant weight. The concentration of sugars in the aqueous phase was quantified using high-performance anion-exchange chromatography with pulsed amperometric detection (HPAEC-PAD), adhering to the methodology detailed by Damm et al.[11] Oxalic acid was removed from the organic phase via precipitation with an equal volume of 0.2 M $CaCl_2$. The organic phase was removed using a rotary evaporator and dried under a vacuum for 24 h. Lignin yields were determined gravimetrically.

Processing lignocellulose in the Flow Through Reactor

The flow through biomass fractionation system (Figure 1) was set up using a stainless-steel tube with an inner diameter of 4.6 mm and length of 15 cm as the reactor. The reactor was placed inside an aluminum heating block (H-1) positioned on a heating plate. Temperature control was achieved by using a thermometer in the block connected to the heating plate. A stainless-steel frit with a pore size of 2 μm was placed at both ends of the reactor to prevent small particles from escaping the reactor. Aqueous oxalic acid solution (0.1 M) and 2-methyltetrahydrofuran (2–MTHF) were provided in solvent bottles (E-1 and E-2). They were simultaneously transported using a high-pressure dosing pump (C09-20.2-200 DK-VA, Fink Chem+Tec GmbH) with two individually controlled pulp heads (E-3, E-4) that could provide up to 200 bar of pressure. The solvents were pumped through 1/16″ stainless steel tubing and mixed in a T-valve (V-1), which was connected to the reactor (E-5). The solvents escaped the reactor through a 1/16″ stainless steel capillary (P-1), which was placed inside an ice bath for rapid cooling of the solvents. The capillary was connected to a backpressure valve (V-2) that kept the reactor at a constant pressure of 70 bar to minimize solvent evaporation when working above its boiling point. The solvents were collected in a glass bottle (E-7).

750–800 mg of beech wood were placed in the reactor using light pressure. The reactor was connected to the solvent supply and placed vertically. The solvents were pumped through simultaneously until they exited the reactor. Then the reactor was connected to P-1 and the pump was turned on briefly until the final pressure of 70 bar was reached. The reactor was checked for leakages and then placed into the preheated heating block (H-1). The pumps were started immediately pumping both solvents at the same speed. After the desired process time, the pumps were stopped, and the reactor was cooled in an ice bath. The solid pulp was removed from the tube and washed in a filter using 3×30 mL of water. The liquid phases were separated using a pipette. Oxalic acid was removed from the organic phase via precipitation with an equal volume of 0.2 M $CaCl_2$. The organic phase was removed using a rotary evaporator and dried under a vacuum for 24 h. Lignin yields were determined gravimetrically. The sugar concentration and composition were determined from the aqueous phase using high-performance anion-exchange chromatography with pulsed amperometric detection (HPAEC-PAD).

2D-NMR analysis

Lignin was analyzed by ^{1}H-^{13}C heteronuclear single quantum correlation nuclear magnetic resonance (^{1}H-^{13}C-HSQC-NMR). 25 mg of lignin were suspended in 0.75 mL deuterated dimethylsufoxid DMSO–d_6. The mixture was stirred for 2 h at 60 °C until the biomass dissolved. ^{1}H-^{13}C-HSQC NMR measurements were taken on a Bruker AVANCE 600 MHz NMR spectrometer with the Bruker standard pulse sequence "hsqcetgpsisp.2". The measurement was conducted with a spectral width of 16 ppm in the F2 (1H) dimension with 2048 data points (TD1) and 240 ppm in the F1 (13 C) dimension with 256 data points (TD2), a scan number (SN) of 128, an interscan delay (D1) of 1 s, and an acquisition time of 10 h. The chemical shift was referenced to the solvent DMSO signal ($\delta(^{1}H) = 2.500$ ppm; $\delta(^{13}C) = 39.52$ ppm). The signals of monomer units and linkages were integrated and referenced to the lignocellulose structures, according to literature.[33] The sum of aromatic units was calculated using the following formula:

$$\Sigma(\text{arom.}) = (S_{2,6}/2) + G_2 + (H_{2,6}/2)$$

The percentage of each unit was calculated as

$$S = (S_{2,6}/2)/\Sigma(\text{arom.}) * 100\%$$

$$G = G_2/\Sigma(\text{arom.}) * 100\%$$

$$H = (H_{2,6}/2)/\Sigma(\text{arom.}) * 100\%$$

Linkages are given as linkage per 100 monomer units. Due to overlapping peaks, β-*O*-4 is calculated using only the α proton signal. β-β and β-5 linkages are calculated using all signals of the corresponding linkage. Linkages were calculated according to the following formulas:

$$\beta\text{-}O\text{-}4 \text{ linkages} = \alpha\ \beta\text{-}O\text{-}4/\Sigma(\text{arom.}) * 100\%$$

$$\beta\text{-}\beta \text{ linkages} = (\alpha\ \beta\text{-}\beta + \beta\ \beta\text{-}\beta + \gamma\ \beta\text{-}\beta)/\Sigma(\text{arom.}) * 100\%$$

$$\beta\text{-}5 \text{ linkages} = (\alpha\ \beta\text{-}5 + \beta\ \beta\text{-}5 + \gamma\ \beta\text{-}5)/\Sigma(\text{arom.}) * 100\%$$

Design of Experiments (DOE)

To evaluate the impacts of the three key independent variables – temperature, process time, and solvent flow rate on solid residue, lignin yield, sugar yield and β-*O*-4 linkages – a 3 k factorial Box Behnken design (BBD) was applied using the Design-Expert software version 13.0 (STAT-EASE Inc., United States). The three independent variables were coded at three levels, namely low (−1), central (0) and high. Therefore, 15 experiments were conducted with three replications of the central point for an estimate of pure experimental error. Response factors were solid residue, lignin yield and sugar yield (all in wt% of initial biomass), as well as β-*O*-4 linkage proportion (per 100 S+G units). Contour graphs were chosen to show the interaction of two variables while the other variable was fixed at the midpoint (0).

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: Biorefinery · Lignocellulose · Pretreatment · Flow-through · OrganoCat

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