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From agricultural waste to value: Integrated chemo and biocatalytic biorefinery processes to produce 2-furoic acid

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ABSTRACT

The integration of biocatalysis in biorefineries can lead to synergies for raw material valorization. Enzymes must perform efficient and selective reactions when using crude effluents (to avoid costly downstream units). Herein, this is showcased with the synthesis of 2-furoic acid, starting from rice husk (agricultural waste), via a sequential organic-acid catalyzed pretreatment – to afford xylose and cellulose and lignin –, followed by the microwave-assisted acidic xylose dehydration to furfural, *in situ* extraction in ethyl acetate, and the final biocatalytic selective oxidation of furfural to 2-furoic acid (2-FA). To validate the concept, a xylose-rich hydrolysate (~ 15 g xylose L^{-1}) obtained from rice husk (RH) was used, achieving a furfural yield of 70 % in a biphasic system (water – ethyl acetate). The obtained furfural extracted in the ethyl acetate was subsequently oxidized to 2-furoic acid via an organic peroxide reaction mediated by *Candida antarctica* lipase B (CALB), with an overall yield of 90 %, and, with a yield of 41.72 % based on the initial xylose in biomass. Notably, 20 mg/mL CALB could tolerate up to 400 mM of furfural under optimum conditions of 40 °C, 48 h. The recyclability of the biocatalyst was investigated, enabling an efficient reuse of four consecutive cycles.

1. Introduction

The production of biofuels and biogenic materials from raw (waste) biomass is a highly promising strategy to replace fossil-based resources within the so-called biorefineries [1–3]. Herein, lignocellulose, a non-edible, renewable, inexpensive, and abundant feedstock, may lead to a range of useful platform chemicals through different down-/up-grading approaches [4]. In this area, furanic compounds have found applications in polymer and chemical industries, as well as in the manufacturing of fuel additives and polymer resins [5–7]. In particular, furfural represents an important platform chemical that can be directly obtained via acid-catalysed hemicellulose dehydration (xylose) [8,9]. It is considered as key-compound for biomass valorization, from which different valuable building blocks can be derived [6]. The furfural versatility arises from the fact that it can be subjected to various chemical transformations such as selective oxidation, hydro-deoxygenation, decarbonylation, decarboxylation, hydrogenation, and hydrogenolysis. Among the various achievable products from furfural, its selective oxidation to afford 2-furoic acid has received huge interest [10], because 2-furoic acid can be used as plasticizer, as plastics or fuel additive, or as pharmaceutical intermediate [5].

The chemical conversion of furfural into 2-furoic acid has been reported mainly by means of heterogenous and homogenous catalysts, or electrochemical and photochemical oxidations [5,7,10–13]. From the sustainability perspective, however, developing metal-free processes would result of interest, and the use of enzymes or microbial cells for the furan valorization has been investigated as well [14]. In fact, incorporating biocatalysis to biorefineries may become an important ally to fulfil sustainability aspects by setting-up reactions under mild conditions, and with high efficiency. Recent literature illustrates the potential that enzymatic biotransformations may provide [15–17] Needless to say, industrial competitive conditions must be reached with the biocatalytic alternatives.

In this area, furfural upgrading has received special attention [8,18–20]. Reported processes involve the use of free enzymes or whole-cells. Wild-type microorganisms have been successfully used, yet furfural loadings have become a hurdle, due to its inherent toxicity and inhibitory profiles for enzymes [8]. Wang et al. [21] reported that

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recombinant *Escherichia coli* HMFOMUT displayed tolerance to furfural (up to 50 mM), and to 5-hydroxymethylfurfural (HMF) (up to 150 mM). Cheng et al. [22] investigated the inhibition and toxicity of furans and its carboxylic derivatives on whole cells of recombinant *Escherichia coli* expressing 3-succinoylsemialdehyde-pyridine dehydrogenase (SAPDH). The authors found that this biocatalyst exhibited the highest tolerance toward 5-HMF, up to 200 mM, in the oxidation of furan aldehyde, with lower tolerances toward methoxymethyl furfural (MHF) (up to 150 mM), and to furfural, up to 75 mM. The highest toxicity of furfural may be closely related to its greater hydrophobicity. In. another study, Zheng et al. [23] reported selective oxidation of furfural to 2-furoic acid using whole cells of genetically modified *Pseudomonas putida* KT2440 (incorporated molybdate transporter). To evaluate tolerance limit of *P. putida* KT2440 towards furfural and its bioconversion ability to produce 2-FA, the authors exposed cells to a wide range of furfural concentration from 20 mM −170 mM. The tolerant level of *P. putida* KT2440 was > 175 mM under the cultivation and reaction conditions of this study. Recently, Ma et al. [24] demonstrated a One-pot chemoenzymatic synthesis of 2-FA using a sequential pretreatment with a tin-based argil (Sn-argil) catalyst followed by immobilized *Brevibacterium lutescens* whole cells. The authors exposed whole cells of *Brevibacterium lutescens* to furfural concentrations ranging from 50 mM to 200 mM to assess their maximum substrate tolerance. The cells exhibited the highest tolerance to furfural at a concentration of up to 125 mM.

Apart from these promising prognoses observed from (recombinant) whole-cells, free, isolated enzymes have also been employed under different processing conditions [8,14]. As a potential advantage, compared to whole-cells, free enzymes would enable the set-up of furan oxidations in non-aqueous media, facilitating the integration of synthetic steps within the biorefinery. Thus, whole-cells might be prioritized when aqueous streams from biorefineries are considered, and free enzymes may be the choice if organic media is the option. Moreover, the need of intensified biocatalytic processes with high furfural loadings and conversions, for large-scale production of 2-furoic acid, has been considered, e.g. through the lipase-mediated peracid-oxidation of furfural in non-conventional media (non-aqueous), reaching higher productivities for the desired 2-furoic acid [18].

Following these considerations, another important point is the need of using crude effluents as feedstocks in biorefineries, to avoid the set-up of intermediate, cumbersome and costly downstream units. Herein, the need of "media-agnostic" (bio)catalysts [25], enabling efficient reactions in those crude media, may be of practical importance. With respect to 2-furoic acid production, though, few studies have been performed using either crude furfural or biomass sources, via a sequential chemical xylose production and dehydration, followed by the biocatalytic oxidation [26–28]. For instance, Yang et al. [28] developed a tandem biomass pretreatment and biocatalyst approach to convert furfural produced from bamboo shoot shells into 2-furoic acid, by using an engineered recombinant *Escherichia coli* BH containing horse liver alcohol dehydrogenase to oxidize furfural (30 mM) into 2-furoic acid. Likewise, immobilized *Candida antarctica* lipase B (CALB) has been explored for furanics valorization, being a versatile biocatalyst for selective oxidations, esterifications, and aminations [2,7,18]. Overall, the combination of chemical methods for biomass pretreatment and furfural production with a biocatalytic valorization may become a promising strategy [28,29] that could offer high yields, reduced energy use and solvent consumption, with a minimized waste production (less downstream units). Importantly, the compatibility between the biocatalyst and the previous or subsequent chemical steps – in particular for the solvents, the pH levels, temperature, reagents, etc. –, must be carefully considered [30].

Considering the importance of linking chemical steps with enzymatic upgrading in biorefineries – by using crude effluents –, this work showcases a bio-cascade path from lignocellulose to 2-furoic acid, covering a pretreatment step to depolymerize hemicellulose and release xylose, which is then dehydrated to furfural in a biphasic media (water – ethyl acetate), *in situ* extracted to the organic media, and further oxidized via lipase-mediated peracid formation (Fig. 1). Rice husk (RH) was considered as prototypical agricultural waste for the biorefinery, since it is largely available worldwide (e.g. Mediterranean area, Asia, etc.), and may thus become a good example for its valorization to bio-based products, such as furoic acid, and to trigger the transition towards a circular bioeconomy.

As observed, the process comprises three integrated steps: i) rice husk pretreatment using a microwave-assisted organic acid-catalyzed hemicellulose depolymerization at short reaction times and relatively mild temperatures (1 h, 121 °C). The use of organic acids as catalysts under those mild conditions lowers the by-product formation, enabling the clean separation of xylose from solid lignin and cellulose pulp, which can be subsequently valorized to other products [31–33]; ii) establishment of a biphasic medium (water – ethyl acetate) for the microwave-assisted xylose acidic dehydration to furfural, which is *in situ* extracted to the organic media. These strategies hamper the degradation of furfural, as it remains in the (more inert) organic phase. Finally, the organic phase (ethyl acetate) containing furfural was decanted from the media for the CALB-mediated peracid oxidation to 2-furoic acid.

2. Materials and methods.

2.1. Materials

Rice husk was chosen as the representative lignocellulosic biomass for furfural production. RH biomass was kindly provided by the Cambra Arrossera del Montsià, Catalonia, Spain and was dried overnight in oven at 105 °C. For the microwave-assisted pretreatment, RH was grinded and passed through 400 μm mesh. Oxalic acid, sulfuric acid and *tert*-butanol were purchased from Fischer Scientific (Purity 99 %). Ethyl acetate was purchased from Labkem (Purity 99.5 %). Immobilized lipase B from *Candida antarctica* (Immobilized CAL-B) was a generous gift from Purolite. All chemicals obtained from Sigma Aldrich and Fischer Scientific were used without any modifications.

2.2. Production of xylose-rich biomass hydrolysates

Xylose-rich hydrolysates from RH biomass were obtained with oxalic acid pretreatment. Exemplarily, 3.0 g of RH was suspended in distilled water (30 mL) containing 0.4 g of oxalic acid, and the mixture was heated in the autoclave at 121 °C for 1 h. After cooling the reaction mixture, the xylose-rich hydrolysate (pH2.0) was separated by filtration. Oxalic acid was removed by adding calcium chloride ($CaCl_2$) to supernatant, stirred at room temperature and filtered. An aliquot of sample was filtered through 0.45 μm nylon filtered and analyzed on (HPLC) (see supporting information, Fig S1 and S2 for HPLC chromatogram of xylose). The xylose-rich hydrolysate was used for further dehydration reaction and the yield of xylose was calculated as shown in equation (1). The analysis of xylose rich-liquid fraction is shown in Table 1 and compositional analysis of RH before and after oxalic acid presented are shown in Table 2

$$\text{Yield of xylose}\,(\%) = \frac{\text{Xylose obtained in g}}{\text{Original xylan in RH}} * \frac{132}{150} * 100 \quad (1)$$

2.3. Synthesis of furfural from xylose rich hydrolysate via dehydration reaction

The acid-catalyzed dehydration of the xylose-rich hydrolysate was conducted in a microwave reactor (Milestone SynthWAVE single reaction chamber (SRC)) as described by Mittal et al. [35] with some modifications. Briefly, a 20 mL glass reactor was charged with 2.50 mL of aqueous xylose-rich hydrolysate (14.38 mg of xylose per mL) containing H_2SO_4 (50 mM), and 7.50 mL of ethyl acetate to form the biphasic system (1:3 v/v). The reaction temperature and stirring were internally

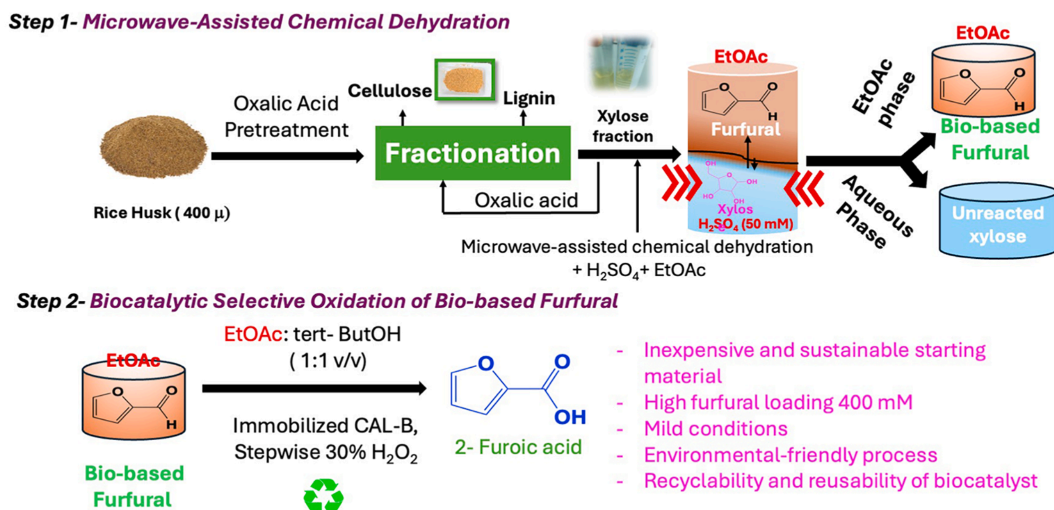

Fig 1. Sequential chemo-enzymatic approach for the conversion of crude furfural – derived from biomass-based xylose into furfural acid through organic-acid catalyzed biomass pretreatment, xylose dehydration, *in situ* extraction, and lipase-mediated peracid oxidation of biobased furfural to 2-furoic acid.

Table 1
Analysis of xylose rich-liquid fraction after oxalic acid pretreatment.

Samples	Xylose yield (%)	Glucose g/L	Xylose g/L	Acetic acid g/L	HMF g/ L
Xylose rich hydrolysate	85.09	2.90 ± 0.32	14.38 ±0.55	0.19 ± 0.37	0.01 ± 0.24

For HPLC chromatogram of xylose rich hydrolysate see supporting information (Fig S1). Xylose rich hydrolysate contains acetic acid and undetected lignin inhibitors.

Table 2
Compositional analysis of RH residue before and after oxalic acid pretreatment.

Samples	Pretreated Solid yield (%)	Glucan Wt %	Xylan Wt %	Lignin Wt %
Raw RH [a]	100	34.85 ±0.85	16.90 ±0.21	25.30 ±0.88
*Solid fraction [b]	57	41.37 ±1.20	3.28 ±0.45	30.56 ±0.32

[a] Raw RH compositional analysis was performed according NREL analysis described by Sluiter et al., (2007) [34].
[b] Solid fraction obtained from oxalic acid pretreatment (see supporting information for HPLC chromatogram and details calculations Fig S2).

measured and monitored by the apparatus, with the maximum power output set to 600 W. The glass reactors were placed in a microwave chamber pre-filled with 250 mL of deionized water. The microwave heating program was set to 170 °C and 30 bar pressure for 20 min. After reaction completion, the glass reactors were removed from the microwave chamber and cooled down to 60 °C. All the experiments were carried out in duplicates. The biphasic system (ethyl acetate – water) was then transferred to a separating funnel. Furfural was extracted into ethyl acetate and the separated aqueous phase was analyzed using HPLC to determine xylose conversion (HPLC program detailed in section 2.6). The ethyl acetate phase containing furfural was analyzed with GC (GC program detailed in section 2.6). The conversion of xylose, partition coefficient, the yield, and selectivity of furfural were calculated using equations (2), 3,4 and 5, respectively.

$$\text{Conversion of xylose}\ (\%) = \frac{\text{xylose before dehydration reaction (g)} - \text{xylose after dehydration reaction (g)}}{\text{Intial xylose (g) in sample}} *100 \tag{2}$$

$$\text{Partition Coefficient (P)} = \frac{\text{Furfural in organic phase}}{\text{Furfural in aquouse phase}} \tag{3}$$

$$\text{Yield}\ (\%) = \frac{\text{Furfural produced (g)}}{\text{Initial xylose in hydrolysate (g)}} * \frac{150}{96} *100 \tag{4}$$

$$\text{Selectivity} = \frac{\text{Yield of furfural}}{\text{Conversion of xylose}} *100 \tag{5}$$

2.4. General procedure for the lipase-mediated selective oxidation of furfural to 2-furoic acid via in situ peracid formation

Experiments were conducted following the method outlined by Krystof et al. [18] With some modifications. In brief, 5 mL of ethyl acetate (EtOAc) were added to 5 mL of *tert*-butanol containing furfural (concentration range: 50 mM– 600 mM). After thoroughly mixing, 200 mg of immobilized CALB (20 mg/mL) were added. Under stirring conditions 30 % H_2O_2 (1.6 eq) were added at intervals of 0, 1, 2, 3, 4, 5 h. Aliquots were taken from the reaction mixture at specified times and analyzed on GC. The conversion of furfural, yield, and productivity were calculated using equation (6),7 and 8, respectively.

$$\text{Conversion of Furfural}\ (\%) = \frac{F_0 - F_t}{F_t} *100 \tag{6}$$

$$\text{Yield of 2} - \text{furoic acid}\ (\%) = \frac{\text{Furoic acid in mM}}{\text{Initial Furfural in mM}} *100 \tag{7}$$

$$\text{Productivity of 2} - \text{furoic acid (g/h/L)} = \frac{\text{Concerntration of furoic acid in g/L}}{\text{Time in h}} \tag{8}$$

Where F_0 and F_t are furfural concentrations at 0 and t h, respectively. All experiments were carried out in duplicate.

2.5. 2-furoic acid production from xylose rich hydrolysate via sequential chemical dehydration and biocatalyzed reaction

In a typical experiment, 5 mL of *tert*-butanol were added to 5 mL of ethyl acetate containing ca.30 mM of furfural derived from xylose rich hydrolysate via dehydration reaction, and then 200 mg of immobilized CALB (20 mg/mL) were added. Under stirring conditions 30 % of hydrogen peroxide (H_2O_2, 6*1.6 eq) were added at interval times 0, 1, 2, 3, 4, and 5 h, respectively. The reaction was performed at 40 °C for 24 h. After completion, the reaction mixture was filtered to recover CALB, which was washed with phosphate buffer for its reuse. The filtrate was evaporated under reduced pressure, affording 2-furoic acid as a yellowish oil. Its structure was confirmed by ^{1}H NMR (Bruker Avance 400 MHz) (see supporting information for NMR spectra, Fig S3) ^{1}H NMR (400 MHz, D_2O) δ: 7.72 (d, J = 1.7 Hz, 1H), 7.29 (d, J = 4.2 Hz, 1H), 6.62 (dd, J = 3.8, 1.9 Hz, 1H).

2.6. Analytical methods.

Gas Chromatography: The furfural extracted in ethyl acetate from biomass was identified by using gas chromatography-mass spectrometer detector (GC–MS, Shimazu, GC 2010) and quantified by gas chromatography-flame ionization detector (GC-FID, Agilent 6890 N). GC programme: capillary column meta wax 30 m x 250 µm i.e., 0.25 µm, hydrogen was used as carrier gas for both GC-FID and GC–MS, with H_2 (30 mL /min) and air for the flame for GC/FID (350 mL/ min). The temperature of injector and detector was set 250 °C. Split ratio was 33:1. The column oven programme: initial column temperature 50 °C, increased 10 °C per min to 70 °C, increased 40 °C per min to 300 °C hold 3 min. The quantification of furfural and 2-furoic acid were done using standard calibration curve. The retention time of furfural was 2.9 min and furoic acid was 8.5 min.

HPLC Chromatography: The conversion of xylose into furfural via dehydration reaction was quantified by HPLC (Agilent 1100 series Model) equipped with ICSep ICE-COREGEL 87H3, PrnotoSIL (300 x 3 mm, 5 µm) and refractive index (Agilent G1362A). It was eluted with 5 mM H_2SO_4 mobile phase with flow rate of 0.6 mL per min, at 60 °C column temperature. The retention time of xylose was 9.8 min.

Nuclear Magnetic Resonance (NMR): The structure of 2-furoic acid was confirmed using ^{1}H NMR (Bruker Avance 400 MHz). After completing the reaction, the solvents in the reaction mixture were evaporated using a rotatory evaporator under reduced pressure, affording a yellow oil. The NMR spectrum of the yellow oil was then recorded in D_2O solvent (see supporting information Fig S5).

3. Results and discussion

Following the protocol described by Krystof et al. [18] on the lipase-mediated peracid furan oxidation, in the first set of experiments furfural (commercial-grade) was converted to 2-furoic acid by stepwise adding 30 % of H_2O_2 at different temperatures and furfural loadings. At temperatures up to 30 °C the furfural conversion remained below 80 % (Fig. 2), while at 40 °C, 95 % conversion of furfural was achieved in 24 h. Further temperature increase (>50 °C) did not lead to any process improvement, and the conversion decreased significantly (less than 50 %). Similar observations were reported in literature [7].

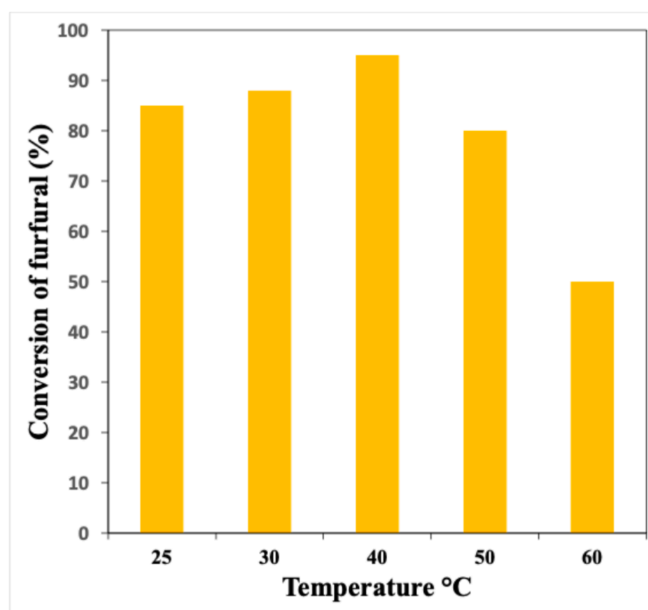

Fig. 2. Effect temperature on CALB-mediated oxidation of furfural. Reaction conditions: 50 mM of furfural(commercial-grade), CAL-B (20 mg/mL), 30 % H_2O_2 (6*1.6 eq). They were added stepwise at 0, 1,2, 3, 4, and 5 h, respectively. Reaction media: ethyl acetate: *tert*-butanol (1:1 v/v).

3.1. Effect of reaction media

The effect of the reaction (organic, non-conventional) media on the CALB-assisted selective furfural oxidation to 2-furoic acid was subsequently assessed. Several commonly used polar protic and aprotic organic solvents were screened, such as 2-MeTHF, cyclopentyl methyl ether (CPME), acetone, *tert*-butanol, isopropyl alcohol, ethanol, and methanol (Table 3). As observed (Table 3), *tert*-butanol resulted a good solvent for the CALB-mediated furfural oxidation, affording 95 % conversion in 24 h with 91 % yield of 2-furoic acid (Table 3), fully consistent with previous literature [18].

Table 3
Effect of organic solvents on the CALB-mediated oxidation of furfural [a].

Organic solvents	Time (h)	Log P [b]	Conversion (%)	Yield (%) [c]
Ethyl acetate [d]	48	0.73	15	5
Tert-butanol	24	0.35	95	91
*Iso*propyl alcohol	48	0.14	73.83	65
Ethanol	48	−0.24	54.31	51
Methanol	48	−0.36	33.84	30
2-MeTHF	24	0.89	n.r	n.r
CPME	24	1.59	n.r	n.r

[a] Reaction conditions: 2.5 mL of solvent, 2.5 mL of ethyl acetate, 50 mM furfural, 200 mg of immobilized CALB, mesitylene as internal standard, 40 °C, 250 rpm; n.r- no reaction.
[b] Log P- partition coefficient at 25 °C.
[c] Yield of furoic acid was calculated by GC analysis.
[d] Reaction performed with EtOAc as acyl donor as well as solvent.

The recent implementation of fermentative processes for isobutylene biosynthesis from glucose, make the potential biogenic route for *tert*-butanol feasible in the future [18,36]. Conversely, other potential bio-based solvents like 2-MeTHF or CPME did not lead to any conversion, presumably because of the interaction of these ether-containing solvents with the formed peracids [37], which would make them not available for the aldehyde oxidation. With respect to the other solvents (Table 3), *iso*propyl alcohol led to acceptable results, while poorer results were obtained in ethanol, ethyl acetate, and methanol.

3.2. Effect of furfural loading

To apply more sustainable biocatalytic reactions, creating intensified processes with high(er) substrate loadings is mandatory, as water and solvent resources are thus better used, and produced wastes are limited [38,39]. Herein, the biocatalytic oxidation reaction was applied at different furfural concentrations from 50 mM to 600 mM (Fig. 3).

Remarkably, a high conversion of furfural (87 %) with a 75 % yield of 2-furoic acid, corresponding to a productivity 0.522 g/L/h of 2-furoic

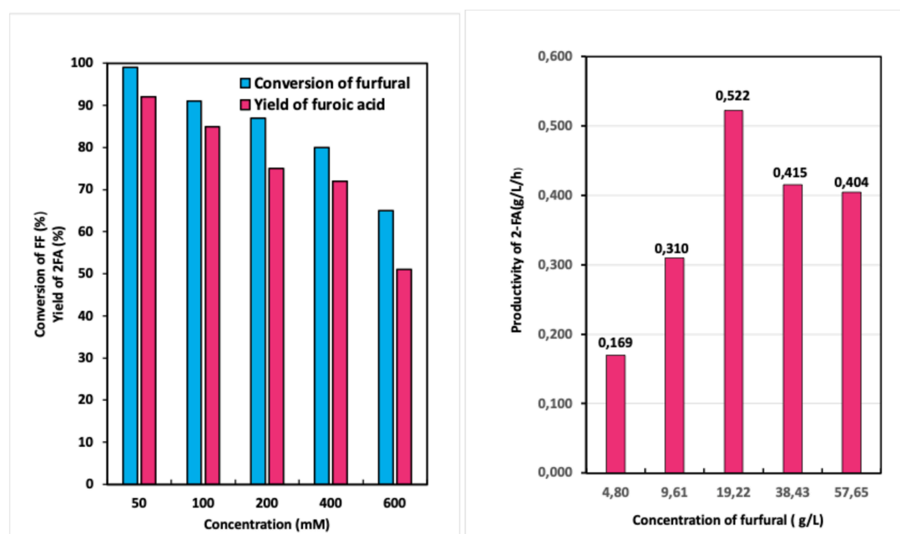

Fig 3. A) Effect of furfural loadings on calb-mediated oxidation of furfural. conditions: commercial grade furfural (50 mM-600 mM), CAL-B (20 mg/mL), H_2O_2 (6 *1.6 eq, 0, 1,2, 3, 4, 5 h), EtOAc: *tert*-BuOH (1:1v/v). The reaction time 24 h for 50 mM-200 mM, 48 h for 400 600 mM furfural loadings (6 *1.6 eq, 0, 1,2, 3, 4, 5, 6, 7, and 8 h). b) Productivity of 2-furoic acid (g/L/h) was calculated for different concentration of furfural 50 mM to 600 mM, herein concentrations of furfural are converted from mM in g/L.

acid (Fig. 3 b), was obtained within 24 h at a furfural concentration of 200 mM. At higher substrate loadings (400 mM), the conversion remained at 72 %, corresponding to 0.415 g/L/h after 48 h of reaction time (Fig. 3 a,b). Previously, Ma et al. [24] reported a 2-furoic acid yield of 50 % at 175 mM furfural loadings in the mixture of ethyl butyrate – water by using immobilized *Brevibacterium lutescens* cells, and lower yields (22 %) were achieved at 200 mM furfural loading. Likewise, Yang et al. [28] investigated the effect of furfural loadings on the biocatalytic activity of whole cells, reporting a 2-furoic acid yield of 99.9 % at loadings of 30 mM, while a lower yield of 60 % was obtained at a furfural loading of 50 mM. The results reported herein reflect the robustness of using lipases in non-conventional media, as they reach furfural conversions of 72 % at 400 mM loading (range of 30 g product L^{-1}) and offer still room for future further improvement (improved stepwise substrate addition, reactor design, continuous flow, etc.).

3.3. *Sequential synthesis of furoic acid from xylose rich hydrolysates*

As stated above, enzymes (and other catalysts) need to show competitive performances in crude media from biorefineries [25]. Thus, the use of real, inexpensive lignocellulosic biomass waste as feedstock is necessary to demonstrate the usefulness of the intended process, adding economic and environmental perspectives to the discussion [29].

Herein, the sequential reaction proposed involved the rice husk pretreatment, the microwave-assisted dehydration of xylose to furfural, and the CALB-mediated selective oxidation of furfural to 2-furoic acid (Fig. 1). As stated above, the applied pretreatment led to the selective xylose release – upon hemicellulose depolymerization –, while enabling the recovery of (solid) lignin and cellulose pulp as future raw materials for the biorefinery. Subsequently, xylose was dehydrated in acidic media to render furfural. To this end, different approaches using homogenous or heterogenous catalysts in a biphasic system reactor have been proposed [7,35,40,41].

Mittal et al. [35] reported 80 % yield furfural from dehydration of pentose rich sugars in water-methyl isobutyl ketone (MIBK) (1:2 v/v) biphasic system containing 50 mM of H_2SO_4 under microwave heating at 170 °C for 20 min. To validate the concept by linking the furfural production and *in situ* extraction to an enzyme-compatible media, herein ethyl acetate was used as the extractive phase, which could be later directly blended with *tert*-butanol to create the biocatalytic media [18].

Therefore, experiments for the xylose dehydration from the xylose-rich hydrolysate (14.38 mg of xylose per mL) were conducted in a biphasic system (aqueous xylose rich hydrolysates: ethyl acetate 1:3 v/v). This reaction was catalyzed by H_2SO_4 (50 mM) under microwave heating at 170 °C for 20 min, 30 bar pressure. Dehydration of xylose in the presence of mineral acid resulted in a 95 % conversion of xylose and a 70 % yield of furfural, corresponding to a 75 % selectivity and a partition coefficient of 4.2. Our results for furfural yield and selectivity were comparable to those reported by Mittal et al. [35]. Upon pH adjustment of the furfural liquor to 7.0 using NaOH, furfural was extracted into the ethyl acetate phase, which was separated from the aqueous phase, resulting in a concentration of 62 mM furfural. The biocatalytic oxidation of furfural was performed by integrating the immobilized lipase with the starting crude furfural extracted in ethyl acetate as starting material (Fig. 4A). Importantly, when extracted furfural in ethyl acetate was combined with *tert*-butanol (1:1 v/v) for the biocatalytic oxidation reaction, the furfural concentration was diluted to 30 mM. In the same reaction media (ethyl acetate – *tert*-butanol, 1:1 v/v), stepwise additions of 30 % H_2O_2 were employed for lipase-assisted selective oxidation of furfural, being in this case the ethyl acetate the acyl donor. As observed (Fig. 4B), the conversion of bio-based furfural and the subsequent production of 2-furoic acid was complete at 30 h, corresponding to an overall yield of 90 % of 2-furoic acid, based on the initial concentration of (crude) furfural (Fig. 4C). Notably, comparable results were achieved when using commercial-grade furfural (Fig. 4D), indicating that CALB can perform the reaction properly in “real” biorefinery-like effluents, being a “media-agnostic” biocatalyst [25]. In fact, our preliminary screening experiments on the effect of inhibitory compounds on biocatalytic oxidation reactions also show that immobilized lipases are not inhibited by lignin monomers such as vanillic acid (20 mM), 4-hydroxybenzoic acid (20 mM), p-coumaric acid (20 mM) each tested alongside commercial-grade furfural (refer to Supporting Information, Table S1). In any case, no potential inhibitors such as acetic acid, formic acid, or levulinic acid were detected in the ethyl acetate fraction, indicating that these impurities remained in the aqueous phase (refer to HPLC results in Supporting Information) because of this reason not included in Table S1 in supporting information. After the reaction was completed, the immobilized lipases were separated by filtration, and the filtrate was then evaporated under reduced pressure, yielding a yellowish oil. The chemical structure of 2-furoic acid was confirmed by

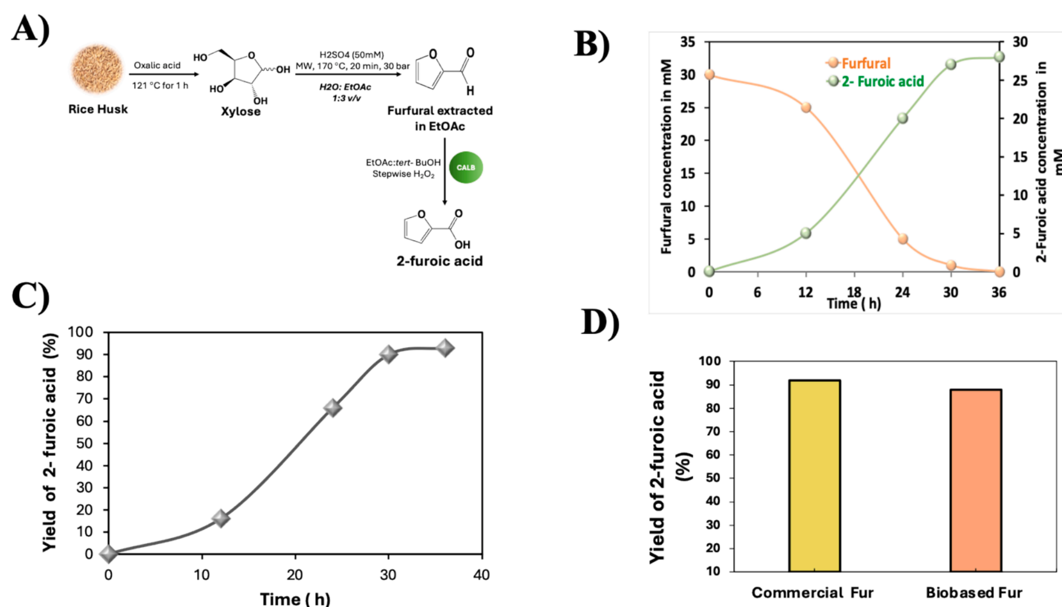

Fig 4. Integrated approach to deliver 2-furoic acid from xylose hydrolysate obtained from rice husk biomass: A) Synthesis of 2-furoic acid; B) Conversion of bio-based furfural to 2-furoic acid; C) Yield of 2-furoic acid using bio-based furfural; D) Yield of 2-furoic acid obtained using commercial grade furfural compared to bio-based furfural.

^{1}H NMR and GC–MS analysis (see supporting information Fig. S3 and S4 GC and GC–MS analysis, Fig S5 for NMR spectra).

An important note to be stressed here is the apparent low furfural loading used in the process with *real* xylose hydrolysates (62 mM, from which a final actual concentration of 30 mM was set). While CALB can handle much higher aldehyde loadings (see Fig. 3A), the concentration of *real* xylose must be adapted to the previous lignocellulose pretreatment. Under our conditions, 3 g of biomass were suspended in 30 mL media (that is, ~ 100 g biomass L^{-1}). The conditions are in the range of common pretreatments (~ 10 wt%) [28–30,42], and due to mass transfer limitations, it appears challenging to enhance that solid-to-liquid proportion. In any case, envisaging a pre-concentration of the *real* xylose would not become problematic for CALB, given its acceptance furfural range (50–400 mM, Fig. 3A).

To quantify the overall use of lignocellulosic resources in the proposed integrated process, a mass balance rice-husk-to-furoic-acid was performed. Fig. 5 illustrates the components of the xylose-rich hydrolysate, as well as the concentrations of furfural and 2-furoic acid. An oven-dried RH (3.0 g) was pretreated with oxalic acid (0.4 g) in 30 mL of water in an autoclave at 121 °C for 60 min. In the pretreated slurry, the solid RH fraction was mainly composed of 0.70 g of glucan and 0.51 g of lignin, respectively. The xylose-rich hydrolysate comprised 0.4 g of xylose as the major component, 0.09 g of glucose, 0.06 g of acetic acid, and negligible amounts of HMF and furfural (due to the mild pretreatment conditions applied). Subsequently, the microwave-assisted diluted acid-catalyzed dehydration of xylose hydrolysates yielded 0.17 g based on the initial biomass weight. Then, furfural derived from xylose rich hydrolysates was converted into 2-furoic acid via enzymatic selective oxidation reaction at 40 °C for 36 h, whereby 0.17 g of furfural were completely converted into 0.18 g of 2-furoic acid. The yield obtained of

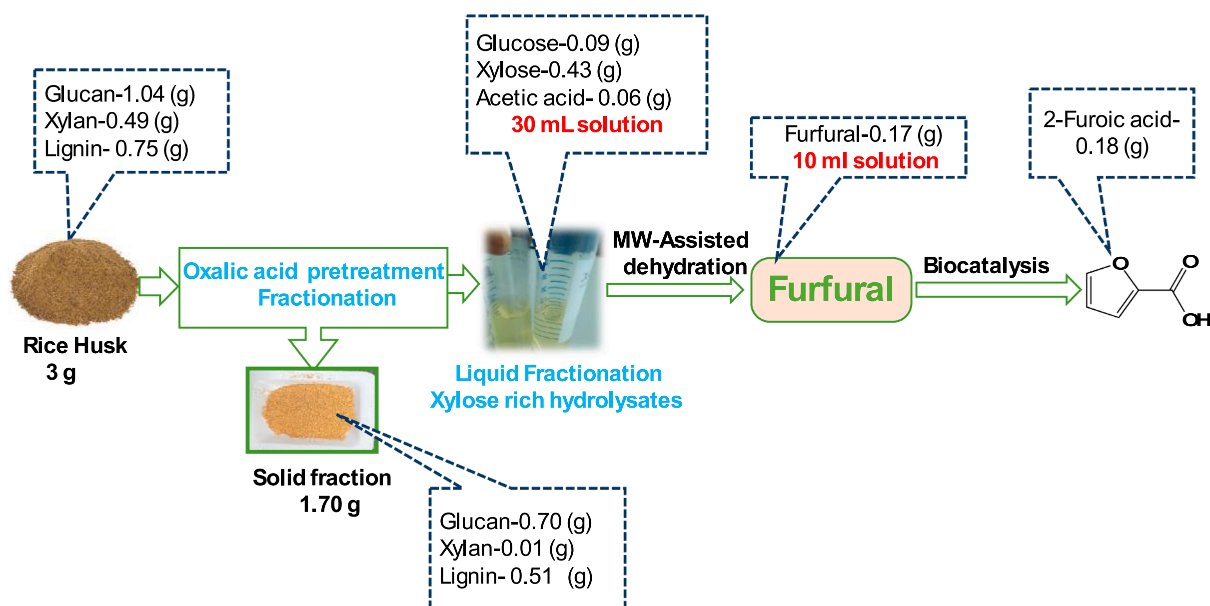

Fig 5. Mass balance analysis on production of 2-furoic acid based on starting material xylose.

furoic acid is 41.72 % based on initial xylose present in the biomass. Therefore, the concept shows that starting from RH as lignocellulosic agricultural waste, it is possible to valorise xylan for the synthesis of furan-based building blocks, by means of cascade chemo-enzymatic processes.

3.4. Recyclability of biocatalyst

Apart from showing its "media-agnostic" profile, the robustness of CALB was further assessed by recovering and reusing the immobilized enzyme, from where both economic and environmental positive impacts can be generated [43]. Herein, the recycling was evaluated using crude bio-based furfural from xylose dehydration. Notably, CALB could be effectively recycled for four consecutive cycles (Fig. 6), with slight losses in the yield of 2-furoic acid between reuses but keeping promising conversions and yields after several cycles. The decreasing enzyme activities might be due to the prolonged exposure of the enzymes to hydrogen peroxide (H_2O_2), as reported for similar reactions with CALB [44]. In fact, a possible downside of the proposed approach may be the need of adding H_2O_2, what can force to extra costs and deleterious effects. Herein, the development of more robust and optimized enzymes may add even more value in this field for future biorefineries, enabling also the set-up of continuous processes for furfural selective oxidation to 2-furoic acid.

3.5. Preliminary economic analysis

Integrated processes must show potential to be able to compete in economic terms as well. Despite being still at the lab scale, where many aspects can be susceptible to be improved, a preliminary economic analysis was performed to validate the proposed integrated chemo- and biocatalytic strategy for the production of furfural and 2-furoic acid using RH as starting material. The approach considered the costs associated with rice husks, oxalic acid, sulfuric acid, water, ethyl acetate, *tert*-butanol, hydrogen peroxide (30 % H_2O_2), and immobilized CALB, while costs related to capital expenses and operation costs such as labour and taxation were excluded. The material cost data were adapted from reports by the National Renewable Energy Laboratory (NREL), the Food and Agriculture Organization (FAO), the chemical book website, and various literature sources [45–48]. The cost of raw materials and utilities used in this study are shown in Table 4. From the preliminary, lab-scaled study, a profit margin of 18.50 % (Table 4) was achieved in the production of 2-furoic acid, what results promising given the early stage of the research. It must be noted, though, that considerable further optimization of process efficiency, cost reduction, process integration, and yield improvement is needed to improve the profitability for large-scale 2-FA production.

Table 4
Preliminary economic analysis of for production furfural and 2-furoic acid.

Category	Items	Consumed	Cost per units	Cost$
Raw material	Rice husk	3 g	0.031$/kg	0.0009
	Oxalic Acid	0.4 g	176$/kg	0.07
	tert-butanol	5 mL	56.5$/L	0.263
	Ethyl acetate	7.5 mL	53.3$/L	0.330
	CAL B enzyme	20 mg /mL	[a]227$/10 g	4.54
	30 % H_2O_2 (1.6 eq)	0.5 mL	648$/L	0.258
Utilities	[b] Autoclave	5kWh	[c]$0.086kWh	0.43
	Microwave	600 W 20 min	$0.086kWh	0.0172
Total cost in USD for2-FA				5.90
Selling price of furfural				1$ per g [d]
Selling price of 2-FA				7.24$ per g [e]
Margin profit of 2FA				18.50 %

Calculation for margin profit $= \left(\frac{S-T}{S}\right)$, where s- selling price in $ and T is total cost in $.

[a] Price of CAL B (Purolite) adapted from website of Fischer Scientific.
[b] Energy consumption value in Autoclave adapted from Ogugua et al. [49].
[c] Electricity price adapted from website of Global Petrol Prices.com.
[d] Selling price of furfural- 26$ per 25 g (https://www.tcichemicals.com/US/en/p/F0073).
[e] Selling price of 2furoic acid- 36.20$ per 5 g (https://www.sigmaaldrich.com/US/en/product/aldrich/f20505).

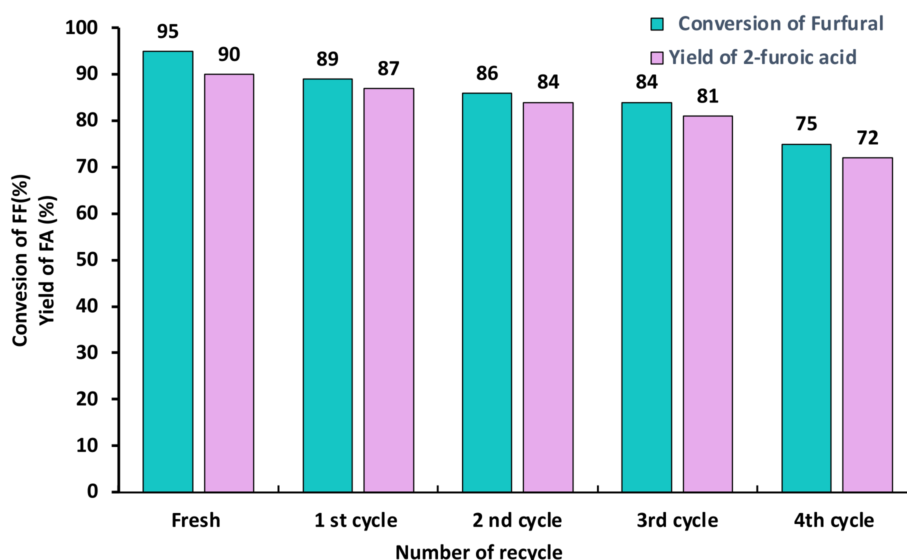

Fig 6. Recyclability of immobilized CALB with bio-based furfural. Reaction conditions: 30 mM of furfural derived from biomass-based xylose, CAL-B (20 mg/mL), 30 % H_2O_2 (6*1.6 eq) were added stepwise at 0, 1,2, 3, 4, and 5 h, respectively. Reaction media: ethyl acetate: *tert*-butanol (1:1 v/v). Conversion and yield were determined by GC-FID analysis of crude reaction sample. Enzyme was recovered by filtration and wash with phosphate buffer.

4. Conclusions

Biocatalysis holds huge potential for biomass valorization within biorefineries, due to the capacity of many enzymes to perform reactions with high efficiency and selectivity in crude effluents containing impurities and catalyst-poisoning compounds. This eliminates the establishment of many intermediate downstream processing units and thus may reduce costs and created wastes significantly. With these premises in mind, this paper has explored a prototypical value chain starting from an agricultural waste (rice husk) to the production of 2-furoic acid. To our knowledge, this is the first time that such a value chain, from rice biomass waste to furoic acid, using lipases and combining also chemical steps, is established. The approach shows promising aspects related to the possibility of integrating chemo- and enzymatic steps, to generate value out of wastes. Furthermore, it allows the future use of the other produced feedstocks (e.g. lignin) in further sequences, since the mild conditions applied avoid the generation of by-product or the raw material (significant) degradation.

The process involved first two chemical steps, namely the organic acid pretreatment of rice husk to render xylose and a solid enriched in cellulose and lignin, and the acidic dehydration of xylose to afford furfural in a biphasic medium (water – ethyl acetate), enabling the *in situ* extraction of the product in the organic media. Connected to that, a lipase-mediated oxidation of furfural to 2-furoic acid was performed in the same ethyl acetate, which was blended with *tert*-butanol to generate a peracid-friendly reaction media. The microwave-assisted acid-catalyzed dehydration of xylose-rich hydrolysate yielded furfural with a 70 % yield, and CALB displayed high tolerance towards furfural and rapidly oxidized it in loadings of up to 400 M furfural. The biocatalyst was effectively recycled for four consecutive cycles. Overall, the proposed path shows that enzymes can be combined with chemical steps within biorefineries, form which value can be created by valorizing side-streams or by-products under conditions in which other chemo-catalysts would be rapidly deactivated. The fact that enzymes can be genetically designed and adapted to processing conditions may open even stronger leads for future biomass upgrading systems.

CRediT authorship contribution statement

Vaibhav Vilas Andhalkar: Writing – original draft, Visualization, Validation, Data curation, Conceptualization. **Pablo Domínguez de María:** Writing – review & editing, Formal analysis, Data curation. **Daniel Montané:** Writing – review & editing, Visualization, Validation, Supervision, Formal analysis. **Francesc Medina:** Writing – review & editing, Visualization, Supervision, Resources, Project administration, Funding acquisition, Formal analysis. **Magda Constantí:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cej.2024.156879.

Data availability

Data will be made available on request.

References

[1] V.V. Andhalkar, R. Ahorsu, P. Domínguez De María, J. Winterburn, F. Medina, M. Constantí, Valorization of lignocellulose by producing polyhydroxyalkanoates under circular bioeconomy premises: facts and challenges, ACS Sustain. Chem. Eng. 10 (50) (2022) 16459–16472, https://doi.org/10.1021/acssuschemeng.2c04925.

[2] A. Pintor, I. Lavandera, A. Volkov, V. Gotor-Fernández, Chemoselective lipase-catalyzed synthesis of Amido derivatives from 5-hydroxymethylfurfurylamine, ACS Sustain. Chem. Eng. 11 (2023) 10284–10292, https://doi.org/10.1021/acssuschemeng.3c00775.

[3] P. Domínguez De María, Industrial biorenewables: a practical viewpoint, John Wiley & Sons, 2016.

[4] V.V. Andhalkar, D. Montané, F. Medina, M. Constantí, Biorefinery design with combined deacetylation and microwave pretreatment for enhanced production of polyhydroxyalkanoates and efficient carbon utilization from lignocellulose, Chem. Eng. J. 486 (2024) 149754, https://doi.org/10.1016/j.cej.2024.149754.

[5] S. Kar, Q.Q. Zhou, Y. Ben-David, D. Milstein, Catalytic furfural/5- Hydroxymethyl furfural oxidation to Furoic acid/furan-2,5-dicarboxylic acid with H2 production using alkaline water as the formal oxidant, J. Am. Chem. Soc. 144 (2022) 1288–1295, https://doi.org/10.1021/jacs.1c10908.

[6] A. Jaswal, P.P. Singh, T. Mondal, Furfural-a versatile, biomass-derived platform chemical for the production of renewable chemicals, Green Chem. 24 (2022) 510–551, https://doi.org/10.1039/d1gc03278j.

[7] N.K. Gupta, A. Fukuoka, K. Nakajima, Metal-free and selective oxidation of furfural to Furoic acid with an N-heterocyclic Carbene catalyst, ACS Sustain. Chem. Eng. 6 (2018) 3434–3442, https://doi.org/10.1021/acssuschemeng.7b0368.

[8] N. Li, M.H. Zong, (Chemo)biocatalytic upgrading of Biobased Furanic platforms to chemicals fuels, and materials: a comprehensive review, ACS Catal. 12 (2022) 10080–10114, https://doi.org/10.1021/acscatal.2c02912.

[9] X. Zhang, S. Xu, Q. Li, G. Zhou, H. Xia, Recent advances in the conversion of furfural into bio-chemicals through chemo- and bio-catalysis, RSC Adv. (2021) 27042–27058, https://doi.org/10.1039/d1ra04633k.

[10] P. Lokhande, P.L. Dhepe, Selective and robust Ru catalyst for the aqueous phase aerobic oxidation of furfural to 2-furoic acid, ACS Appl. Mater. Interfaces 15 (2023) 47004–47015, https://doi.org/10.1021/acsami.3c09965.

[11] G. Bharath, K. Rambabu, A. Hai, N. Ponpandian, J.E. Schmidt, D.D. Dionysiou, M. Abu Haija, F. Banat, Dual-functional paired photoelectrocatalytic system for the photocathodic reduction of CO_2 to fuels and the anodic oxidation of furfural to value-added chemicals, Appl Catal B 298 (2021) 120520, https://doi.org/10.1016/j.apcatb.2021.120520.

[12] P. Rapado, L. Faba, S. Ordóñez, Role of the different catalytic sites in the H_2O_2-mediated aqueous-phase furfural partial oxidation, J. Environ. Chem. Eng. 11 (6) (2023), https://doi.org/10.1016/j.jece.2023.111466.

[13] G. Papanikolaou, P. Lanzafame, S. Perathoner, G. Centi, D. Cozza, G. Giorgianni, M. Migliori, G. Giordano, High performance of Au / ZTC based catalysts for the selective oxidation of bio-derivative furfural to 2-furoic acid 1, Catal. Commun. 149 (2021) 106234, https://doi.org/10.1016/j.catcom.2020.106234.

[14] P. Domínguez de María, N. Guajardo, Biocatalytic valorization of furans: opportunities for inherently unstable substrates, ChemSusChem 10 (2017) 4123–4134, https://doi.org/10.1002/cssc.201701583.

[15] C. Wu, C. Ma, Q. Li, H. Chai, Y.C. He, Efficient production of hydroxymethyl-2-furfurylamine by chemoenzymatic cascade catalysis of bread waste in a sustainable approach, Bioresour. Technol. 385 (2023) 129454, https://doi.org/10.1016/j.biortech.2023.129454.

[16] J. Di, X. Liao, Q. Li, Y.C. He, C. Ma, Significantly enhanced bioconversion of high titer biomass-derived furfural to furfuryl alcohol by robust endogenous aldehyde reductase in a sustainable way, Green Chem. 25 (2023) 9194–9202, https://doi.org/10.1039/d3gc01417g.

[17] Q. Li, C.-L. Ma, Y.-C. He, Effective one-pot chemoenzymatic cascade catalysis of biobased feedstock for synthesizing 2, 5-diformylfuran in a sustainable reaction system, Bioresour. Technol. 378 (2023) 128965, https://doi.org/10.1016/j.biortech.2023.128965.

[18] M. Krystof, M. Pérez-Sánchez, P. Domínguez De María, Lipase-mediated selective oxidation of furfural and 5-hydroxymethylfurfural, ChemSusChem 6 (2013) 826–830, https://doi.org/10.1002/cssc.201200954.

[19] X. Lopez-Lorenzo, H. Asem, A. Stamm, S. Subramaniyan, M. Hakkarainen, P. O. Syrén, Whole-cell mediated carboxylation of 2-furoic acid towards the production of renewable platform chemicals and biomaterials, ChemCatChem 15 (2023) e202201483.

[20] Y. Zhang, X. Di, W. Wang, M. Song, Q. Yu, Z. Wang, Z. Yuan, X. Chen, H. Xu, Y. Guo, Kinetic study of lipase-catalyzed esterification of furoic acid to methyl-2-furoate, Biochem. Eng. J. 161 (2020) 107587, https://doi.org/10.1016/j.bej.2020.107587.

[21] Z.W. Wang, C.J. Gong, Y.C. He, Improved biosynthesis of 5- hydroxymethyl-2-furancarboxylic acid and furoic acid from biomass- derived furans with high substrate tolerance of recombinant Escherichia coli HMFOMUT whole-cells, Bioresour. Technol. 303 (2020) 122930, https://doi.org/10.1016/j.biortech.2020.122930.

[22] A. Di Cheng, S.S. Shi, Y. Li, M.H. Zong, N. Li, Biocatalytic oxidation of biobased furan aldehydes: comparison of toxicity and inhibition of furans toward a whole-cell biocatalyst, ACS Sustain. Chem. Eng. 8 (2020) 1437–1444, https://doi.org/10.1021/acssuschemeng.9b05621.

[23] Z. Zheng, Q. Xu, H. Tan, F. Zhou, J. Ouyang, Selective biosynthesis of furoic acid from furfural by pseudomonas putida and identification of molybdate transporter involvement in furfural oxidation, Front. Chem. 8 (2020) 587456, https://doi.org/10.3389/fchem.2020.587456.

[24] Z. Ma, Z. Liao, C. Ma, Y.C. He, C. Gong, X. Yu, Chemoenzymatic conversion of Sorghum durra stalk into furoic acid by a sequential microwave-assisted solid acid conversion and immobilized whole-cells biocatalysis, Bioresour. Technol. 311 (2020) 123474, https://doi.org/10.1016/j.biortech.2020.123474.

[25] M. Milić, E. Byström, P. Domínguez de María, S. Kara, Enzymatic cascade for the synthesis of 2, 5-furandicarboxylic acid in biphasic and microaqueous conditions: 'Media-Agnostic'Biocatalysts for Biorefineries, ChemSusChem 15 (9) (2022), https://doi.org/10.1002/cssc.202102704.

[26] X. Zhu, C. Ma, J. Xu, J. Xu, Y.C. He, Sulfonated vermiculite-mediated catalysis of reed (Phragmites communis) into furfural for enhancing the biosynthesis of 2-furoic acid with a dehydrogenase biocatalyst in a one- pot manner, Energy Fuel 34 (2020) 14573–14580, https://doi.org/10.1021/acs.energyfuels.0c02707.

[27] X.Y. Zhang, X. Wang, N.W. Li, Z.W. Guo, M.H. Zong, N. Li, Furan carboxylic acids production with high productivity by cofactor- engineered whole-cell biocatalysts, ChemCatChem 12 (2020) 3257–3264, https://doi.org/10.1002/cctc.202000259.

[28] D. Yang, C. Ma, B. Peng, J. Xu, Y.C. He, Synthesis of furoic acid from biomass via tandem pretreatment and biocatalysis, Ind. Crop. Prod. 153 (2020) 112580, https://doi.org/10.1016/j.indcrop.2020.112580.

[29] Q. Wu, M.H. Zong, N. Li, One-pot chemobiocatalytic production of 2,5- Bis (hydroxymethyl)furan and its diester from biomass in aqueous media, ACS Catal. 13 (2023) 9404–9414, https://doi.org/10.1021/acscatal.3c01216.

[30] R. Kourist, J. González-Sabín, Non-conventional media as strategy to overcome the solvent dilemma in chemoenzymatic tandem catalysis, ChemCatChem 12 (2020) 1903–1912, https://doi.org/10.1002/cctc.201902192.

[31] P.M. Grande, J. Viell, N. Theyssen, W. Marquardt, P. Domínguez De María, W. Leitner, Fractionation of lignocellulosic biomass using the OrganoCat process, Green Chem. 17 (2015) 3533–3539, https://doi.org/10.1039/c4gc02534b.

[32] D. Weidener, H. Klose, W. Leitner, U. Schurr, B. Usadel, P. Domínguez De María, P. M. Grande, One-step lignocellulose fractionation by using 2,5- furandicarboxylic acid as a biogenic and recyclable catalyst, ChemSusChem 11 (2018) 2051–2056, https://doi.org/10.1002/cssc.201800653.

[33] T. vom Stein, P.M. Grande, H. Kayser, F. Sibilla, W. Leitner, P. Domínguez de María, From biomass to feedstock: one-step fractionation of lignocellulose components by the selective organic acid-catalyzed depolymerization of hemicellulose in a biphasic system, Green Chem. 13 (2011) 1772–1777, https://doi.org/10.1039/c1gc00002k.

[34] A. Sluiter, B. Hames, R.O. Ruiz, C. Scarlata, J. Sluiter, D. Templeton, D. Crocker, D. of Energy, Determination of structural carbohydrates and lignin in biomass. National Renewable Energy Laboratory (NREL) Laboratory Analytical Procedures (LAP) for standard biomass analysis, Biomass Analysis Technology Team Laboratory Analytical Procedure 2011 (2007) 1–14. https://doi.org/NREL/TP-510-42618.

[35] A. Mittal, S.K. Black, T.B. Vinzant, M. O'Brien, M.P. Tucker, D.K. Johnson, Production of furfural from process-relevant biomass-derived Pentoses in a biphasic reaction system, ACS Sustain. Chem. Eng. 5 (2017) 5694–5701, https://doi.org/10.1021/acssuschemeng.7b00215.

[36] P. Domínguez de María, Recent developments in the biotechnological production of hydrocarbons: paving the way for bio-based platform chemicals, ChemSusChem 4 (2011) 327–329, https://doi.org/10.1002/cssc.201000306.

[37] K. Watanabe, N. Yamagiwa, Y. Torisawa, Cyclopentyl methyl ether as a new and alternative process solvent, Org. Process Res. Dev. 11 (2007) 251–258, https://doi.org/10.1021/op0680136.

[38] P. Domínguez de María, On the need for gate-to-gate environmental metrics in biocatalysis: fatty acid hydration catalyzed by oleate hydratases as a case study, Green Chem. 24 (2022) 9620–9628, https://doi.org/10.1039/d2gc03419k.

[39] P. Domínguez de María, S. Kara, F. Gallou, Biocatalysis in water or in non-conventional media? adding the CO_2 production for the debate, Molecules 28 (2023), https://doi.org/10.3390/molecules28186452.

[40] X.K. Li, Z. Fang, J. Luo, T.C. Su, Coproduction of furfural and easily hydrolyzable residue from sugar cane bagasse in the MTHF/aqueous biphasic system: influence of acid species NaCl addition, and MTHF, ACS Sustain. Chem. Eng. 4 (2016) 5804–5813, https://doi.org/10.1021/acssuschemeng.6b01847.

[41] Y. Yang, C.W. Hu, M.M. Abu-Omar, Synthesis of furfural from xylose, xylan, and biomass using $AlCl_3 \cdot 6H_2O$ in biphasic media via xylose isomerization to xylulose, ChemSusChem 5 (2012) 405–410, https://doi.org/10.1002/cssc.201100688.

[42] T. Vomstein, P.M. Grande, W. Leitner, P. Domínguezdemaría, Iron-catalyzed furfural production in biobased biphasic systems: from pure sugars to direct use of crude xylose effluents as feedstock, ChemSusChem 4 (2011) 1592–1594, https://doi.org/10.1002/cssc.201100259.

[43] P. Domínguez de María, Biocatalysis, sustainability, and industrial applications: show me the metrics, Curr Opin Green Sustain Chem 31 (2021) 100514, https://doi.org/10.1016/j.cogsc.2021.100514.

[44] M. Markiton, S. Boncel, D. Janas, A. Chrobok, Highly active nanobiocatalyst from lipase noncovalently immobilized on multiwalled carbon nanotubes for Baeyer-Villiger synthesis of lactones, ACS Sustain. Chem. Eng. 5 (2017) 1685–1691, https://doi.org/10.1021/acssuschemeng.6b02433.

[45] A.T.O. Ramírez, M.R. Tovar, O. Silva-Marrufo, Rice husk reuse as a sustainable energy alternative in Tolima, Colombia, Sci. Rep. 14 (2024), https://doi.org/10.1038/s41598-024-60115-5.

[46] X. Song, Y. Zhang, C. Chang, Novel method for preparing activated carbons with high specific surface area from rice husk, Ind. Eng. Chem. Res. 51 (2012) 15075–15081, https://doi.org/10.1021/ie3012853.

[47] G. Zang, A. Shah, C. Wan, Techno-economic analysis of an integrated biorefinery strategy based on one-pot biomass fractionation and furfural production, J. Clean. Prod. 260 (2020) 120837, https://doi.org/10.1016/j.jclepro.2020.120837.

[48] C. of Renewable Energy Development, E. Research Institute, N. Development, R. Commission, Biomass Support for the China Renewable Energy Law: Feasibility Report – Agricultural and Forestry Solid Wastes Power Generation Demonstration, (2005). http://www.osti.gov/bridge.

[49] C.J. Ogugua, S.V. Anton, A.P. Tripathi, M.D. Larrabeiti, S.O. van Hees, J. Sinke, C. A. Dransfeld, Energy analysis of autoclave CFRP manufacturing using thermodynamics based models, Compos. A Appl. Sci. Manuf. 166 (2023), https://doi.org/10.1016/j.compositesa.2022.107365.