Innovative biphasic solvent systems for lignocellulosic biorefinery

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Abstract

Bioconversion of lignocellulosics to ethanol is significantly hindered by biomass recalcitrance, therefore often requires a biomass pretreatment step. Furan-based compounds such as furfural and 5-hydroxymethyl furfural are versatile building blocks for fuels and chemicals. However, their production during pretreatment often suffers from low yield and low separation efficiency. Biphasic solvent systems are capable of reducing biomass recalcitrance and extracting furans into the organic phase, thus prevents their degradation, increases their yield, and allows much easier separations. The development of sustainable biphasic solvent system is essential to the furan-driven biorefinery and has drawn significant attention. This review systematically summaries recent advances in development of biphasic solvent systems in lignocellulosic biorefinery for improving the production of liquid fuels and furan-based compounds.

Keywords: Arizona solvent system, Biomass pretreatment, 5-hydroxymethylfurfural, Furfural, Lignin valorization

Worldwide interest in promoting lignocellulosic biorefinery

Biorefinery refers to a sustainable process of producing liquid fuels, biobased chemicals, and materials from lignocellulosic biomass and its components. For example, carbohydrate in the plant cell wall (e.g., cellulose and hemicellulose) could be

converted into liquid fuels such as ethanol via a multi-step bioconversion process including size reduction, **biomass pretreatment**, enzymatic hydrolysis, fermentation, and production purification. Lignin, as the most abundant biopolymer in nature, could be depolymerized to valuable aromatic chemicals and bio-oils. It could be also used in preparing a variety of materials including carbon fibers, adhesives, and bioplastics. Besides the C5/C6 carbohydrates and lignin platform, biomass could be also converted into a mixture of carbon monoxide/hydrogen or methane/carbon dioxide via gasification and digestion, representing the syngas and biogas platform, respectively.

The utilization of lignocellulosic biomass as a renewable, natural carbon resource for the production of biofuels and bio chemicals offers numerous advantage when compared with fossil resources, such as minimizing greenhouse gas emissions and promoting sustainable production practices [1]. It is estimated that the annual global production of renewable biomass, primarily derived from terrestrial plants, amounts to approximately 1.7×10^{11} tons [2]. Billions of tons of forestry and agricultural residues, such as crop straw, are produced around the world each year. For example, it is estimated that China generates approximately ~800 million tons of crop residues annually [3]. Notably, the overall utilization rate of forest biomass resources remains relatively low, which were primarily utilized for the production of solid molding fuel, pellet board and fiberboard, pulp and paper, activated carbon, and compost with low-value.

In 2022, China's National Development and Reform Commission outlined a trajectory for green, low-carbon biomass applications in its 14th Five-Year Plan for Biological Economy Development. This plan emphasized the importance of bio-based materials and an integrated biomass recycling system. The United States also announced by March 2023, a $590 million investment was allocated to optimize four key Bioenergy Research Centers, aiming to enhance energy security, stimulate rural economic opportunities, and reduce greenhouse gas emissions. Moreover, the European Union's Energy Transition framework in 2022 also recognizes the importance of biomass energy, supported by the REPowerEU Energy Guarantee Plan, demonstrating the EU's enduring dedication from 2003 to 2023. Additionally, Japan has emphasized its commitment to biomass energy through the “Biomass Japan Comprehensive Strategy” which includes the innovative “biomass energy town” project. On a global scale, the 2015 United Nations summit catalyzed the adoption of the “2030 Agenda for Sustainable Development” which incorporates 17 Sustainable Development Goals

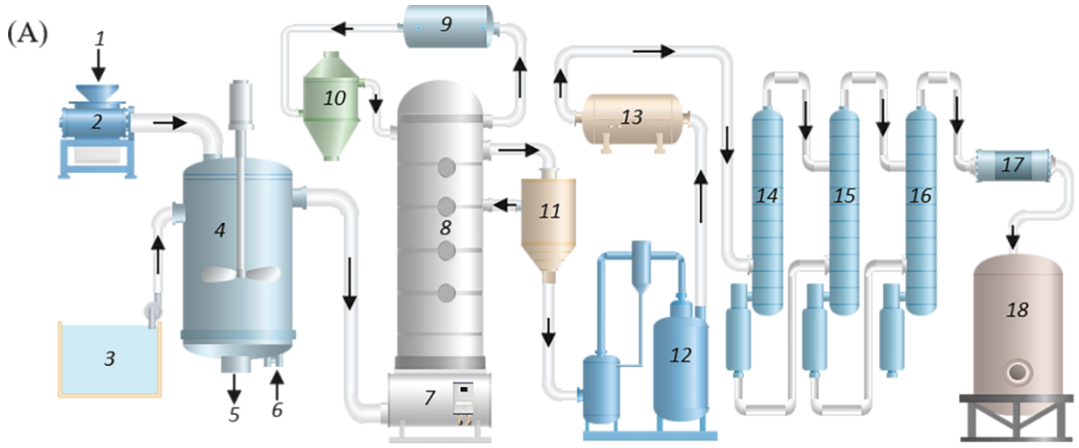
(SDGs) and reflects a collective effort towards achieving sustainable growth.

Given the significance of advancing national strategies such as the Dual carbon target, Bio-economy, and Green manufacturing, it is crucial to investigate the bio-refining of abundant agricultural and forestry residual resources. By deconstructing these lignocellulosic biomass, valuable furan chemicals like furfural (FF) and 5-hydroxymethylfurfural (HMF) can be produced through chemical or biocatalytic process, which could be further converted into functionalized bio-fuels, chemicals, and materials [4]. A variety of heterogeneous catalysts have been developed to successfully convert sugars or biomass to FF and HMF in a homogenous solvent system; however, FF and HMF could be easily depredated or condensed in the reaction media and are often difficult to separate from the solvent system. **Biphasic solvent system** has been developed, aiming to constantly extract the target product such as FF and HMF from the aqueous phase into the organic phase, thus reduce the energy demand associated with the product isolation and purification process.

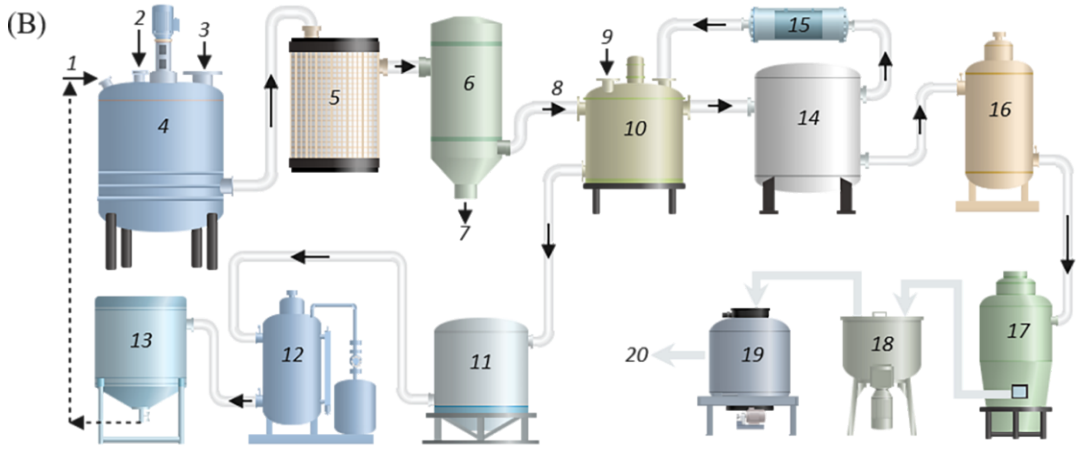
Industrial Production of FF and HMF

Henan Hongye Holdings Group Co., Ltd., Located in Puyang, Henan Province, China, currently holds the largest FF production globally with capacity of 50,000 tons per year. The production process starts with a conventional dilute acid hydrolysis of biomass or cellulose at 140 - 185 ℃ for a duration of 2 to 10 hours (Figure 1(A)). In general, lower reaction temperatures requires extended reaction times in order to achieve comparable FF yield. The final FF products were mainly separated from the liquid phase via steam stripping, and 1 ton of FF requires approximately 12 to 15 tons and 14 to 20 tons of initial biomass (e.g., corn cobs) and steam, respectively. A huge amount of waste residue, acid wastewater, and CO_2 emissions were produced along with the final FF products. On the other hand, Zhejiang Sugar Energy Technology Co., Ltd. serves as the global leader in the production of HMF with an annual manufacturing capacity of 3000 tons (Figure 1(B)). Despite using a novel heterogeneous catalytic negative pressure hydrolysis technology, a relatively low HMF yield (<50%) was achieved using fructose as the initial feedstock. In addition, this process also suffered from high-energy-consumption due to the separation of HMF from the homogenous hydrothermal system which is typically achieved via negative pressure distillation and low-temperature extraction. Other main challenges in the large-scale production of FF

and HMF production include their thermal lability under long-term heating conditions.



(1)Corncob (2)Crusher (3)Acid solution mixing tank (4)Hydrolysis reactor (5)Furfural residue (6)Steam (7)Reboiler (8)Azeotropic primary rectification tower (9)Condenser (10)Flash evaporation tank (11)Separating funnel (12)Vacuum concentration kettle for sodium percarbonate mother liquor (13)Condenser (14)Dehydration Refining Tower 1 (15)Dehydration Refining Tower 2 (16)Dehydration Refining Tower 3 (17)Condenser (18)FAL products



(1)Solvents and catalysts (2)Water (3)Fructose (4)Hydrolysis reactor (5)Filter (6)Centrifugal separators (7)By-product filter cake sold outside (8)Reactive crude product (9)Ethyl acetate (10)Countercurrent extractor (11)Reaction heavy phase buffer tank (12)Vacuum distillation still (13)Solvent recovery and reuse (14)Reaction light phase buffer tank (15)Ethyl acetate condenser (16)Vacuum distillation still (17)Product purification (18)Crusher (19)Centrifuge (20)HMF products

Figure 1. (A) Simplified flowchart of FF industrial production at Henan Hongye. The reaction conditions include a pressure range of 3.5 to 10 atmospheres. Due to the sensitivity of the hydrolysis reaction to temperature conditions, the reaction time range is maintained within a larger temperature range for 2 to 10 hours. (B) Simplified flowchart of HMF industrial production by Zhejiang sugar energy. The process utilizes solid acid resin as a catalyst for the catalytic reaction of fructose raw material. The reaction solution is separated and purified through negative pressure distillation and low-temperature extraction techniques using ethyl acetate as an extraction agent. The isomerization of glucose is hindered by the high activation energy. As a consequence, industrial production typically relies on the use of costlier fructose as the raw material [5].

Overall, the industrial production of furans, as a typical example of lignocellulosic biorefinery, still consumed with unsatisfactory specificity and efficiency due to

uncontrollable conversion and energy-intensive separation in homogeneous solvent system. With a view to scale production of furans and downstream application on value added biofuel, chemicals and materials, a series of research has been conducted to address the issue of low yield and high energy consumption in homogeneous solvent system.

Catalytic conversion of lignocellulosic into FF and HMF

In order to address the key scientific and technological challenge of low yields in furan product synthesis, the majority of current literature focused on effectively controlling the structure-activity relationship of catalysts, particularly in the isomerization and dehydration steps. Several different types of catalysts have been developed, exhibiting high raw material conversion rates, excellent product selectivity, and extended catalyst lifetimes (Table 1). Initially, mineral acid catalysts (e.g., HCl, H_2SO_4) [6, 7] were widely used, which were later replaced by organic acid catalysts [8] and **ionic liquids** [9, 10]. Mineral acid catalysts show great advantages in product yield, while the use of organic acids and ionic liquids helped reduce equipment corrosion, although their catalytic efficiency could be reduced occasionally. Homogeneous metallic salt catalysts [11, 12] were also proposed due to their cost-effectiveness, abundance, and lower corrosiveness. Although ionic liquid and salt catalysts show high catalytic performance for recycling, there is a complex recovery process in homogeneous solution systems. Heterogeneous catalysts have demonstrated favorable catalytic performance and enhanced product yields while allowing for easy catalyst recovery and separation. Heterogeneous catalysts encompass various compositions and structures, including functional polymers [13], functional carbon materials [14], solid salt catalyst [15] and so on. However, further optimization is required in the complex preparation and activation properties of heterogeneous metal salt catalysts.

Table 1 Catalytic conversion of lignocellulosics into FF and HMF

Entry	Catalyst	Sub./Pro.	Con. (%)	yield (%)	Recycle/times	Ref.
1	HCl	xylan/FF	97	93	/	[6]
2	H_2SO_4	beet juice/HMF	/	90	/	[7]
3	Acetic acid	xylose/FF	/	80	/	[8]
4	[BMIM]HSO_4	xylose/FF	99	71	8	[9]

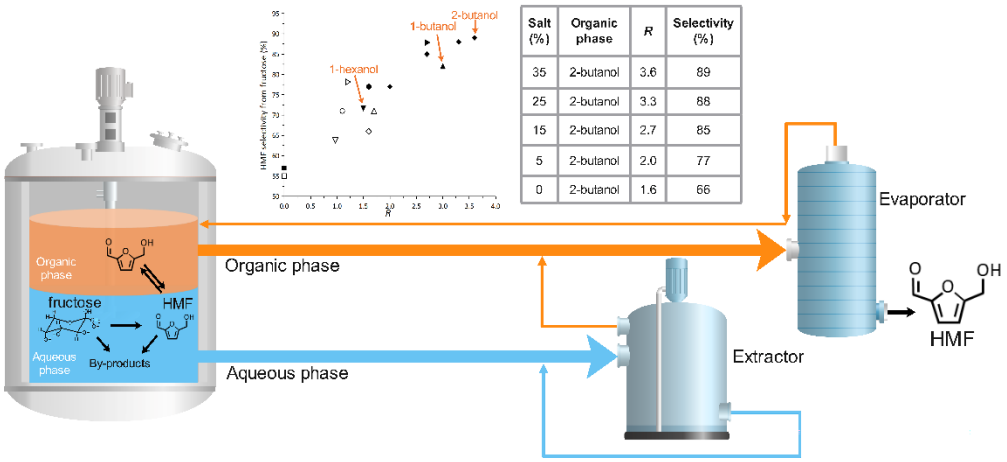
5	[BMIM]Cl	glucose/HMF	/	72	0	[10]
6	$LiCl \cdot 3H_2O$	xylan/FF	100	77	3	[11]
7	$SnCl_4$	xylan/FF	/	78	4	[12]
8	SPAN	Fructose/HMF	99	71	5	[13]
9	Nb/C-50	Glucose/HMF	98	59	8	[14]
10	FeClx/1-D008	xylose/FF	100	96	4	[15]

Recent theoretical and experimental studies has led to the development of inexpensive and efficient catalysts that could enhance the yield of FF and HMF, however, higher energy consumption and unwanted side reaction could still be observed during the separation and purification process (e.g., distillation [16], stripping [17], and membrane separation [18]). For example, the presence of high vacuum and entrainer makes steam distillation and stripping extremely energy-intensive [19]. At the same time, the membrane separation technology with low energy consumption and high product selectivity has high costs associated with the equipment and membrane material. Unlike homogenous co-solvent systems, biphasic solvent systems exploited the differences in the hydrophobicity of the final products and the initial reactants which leads to much higher products yields. They have been proved to be much more effective in suppressing side reactions, improving product yield, and providing better downstream separation [20].

Development of biphasic systems

In 2006, biphasic solvent system consisting of an aqueous phase and methyl isobutyl ketone (MIBK) was firstly used for the dehydration of fructose to HMF (Figure 2) [21]. This study demonstrates for the first time that phase modification can control the selectivity and efficiency of HMF transformation and separation. HMF formed in the aqueous phase is continuously extracted into the MIBK phase, which reduces the side reactions by reducing the residence time of HMF in the aqueous phase. The yield of HMF reached 70% at a fructose concentration of 50%, achieving 80% product selectivity and 90% fructose conversion (Table 2, entry 1). It is worth noting that the ability of organic solvents to extract HMF from the aqueous phase could be quantified using the ratio of HMF concentration in the organic phase to its concentration in the aqueous phase, denoted as *R* [22]. For instance, when 1-hexanol, 1-butanol, and 2-butanol are used to form a biphasic reaction system with water, the corresponding *R* values for HMF are 1.5, 3.0, and 3.6, respectively, suggesting an increase in HMF selectivity (Figure 2) [22]. In addition, by introducing dimethyl sulfoxide (DMSO) and

2-butanol to modify the solvent system, the conversion rate of fructose and xylan can exceed 95%, and the yield of HMF and FF are 85% and 76%, respectively (Table 2, entries 2 and 3) [23]. The enhancement is attributed to the higher affinity of these organic extraction solvents for HMF, which improves the extraction and separation efficiency without impacting the intrinsic reaction process [24].



Salt (%)	Organic phase	R	Selectivity (%)
35	2-butanol	3.6	89
25	2-butanol	3.3	88
15	2-butanol	2.7	85
5	2-butanol	2.0	77
0	2-butanol	1.6	66

Figure 2 · Describes the batch process for producing HMF from fructose and investigates the influence of different organic solvent extraction ratios (R) on the selectivity of HMF extraction from fructose.

Classic biphasic solvent systems

In general, classical biphasic systems are defined as two solvents that are immiscible or have extremely low solubility, which causes them to form distinct layer boundaries when mixed with each other [25]. Biorefining using a biphasic solvent system not only enables efficient fractionation of cellulose, hemicellulose, and lignin but also allows solvent recovery and reduced product purification complexity through a simple phase separation operation [26, 27].

H_2O/MIBK —MIBK leveraged the excellent extraction capability of HMF to achieve the selective conversion of a mixture of fructose and glucose to HMF [28, 29]. The kinetic model incorporated the equilibrium extraction of HMF in two phases, considering the volume change resulting from density change and partial miscibility of the biphasic solvent at the reaction temperature. This allowed for an accurate prediction of the reaction network involving fructose and glucose in the biphasic system. Using high fructose corn syrups as the initial feedstock, 96% fructose conversion rate and an 81% HMF yield (Table 2, entry 4) could be achieved in the biphasic mixture of MIBK and water in 16 min, while more than 95% of the glucose remained unreacted. In a separate study, fructose was efficiently converted to HMF in a biphasic solvent system

consisting of H_2O and dimethyl carbonate (DMC) [30]. When both fructose and glucose were used as substrate, a high conversion rate of fructose (90%) and a high yield of HMF (91% based on fructose concentration only) was achieved, with a glucose retention rate of 83% (Table 2, entries 5 and 6). This selective catalytic conversion of fructose in mixed sugars in the biphasic system resulted in lower conversion of glucose and maximized the HMF yield, leading to maximum resource efficiency and economic benefits.

The conversion of xylose to FF using H_2O/MIBK biphasic systems was also reported [29]. It was found that the FF yield achieved in the biphasic system was much higher (~90%) than that in the conventional single-phase solvent system (Table 2, entry 7). Jiang et al. reported that the use of choline chloride (ChCl) as a component of the ChCl/MIBK biphasic solvent system could enhance the formation rate of FF by forming a key intermediate (choline xyloside) with xylose in acid condition (Table 2, entry 8) [31]. The 2-OH position in choline xyloside demonstrates greater affinity towards protons compared to xylose, and consequently, it showcases enhanced reactivity, thus achieving higher FF production. In a novel MIBK-$FeCl_3$ biphasic solvent system, high value end products including FF, glucose, and lignin nanoparticles with high yield could be achieved simultaneously (Table 2, entry 10) [32].

A rapid dehydration of fructose into HMF was conducted using HCl as a catalyst in a MIBK/H_2O biphasic microreactor [33]. Dynamic simulations were performed to quantify the effect of mass transfer on HMF extraction and reactive extraction in order to optimize the HMF yield. In comparison to the monophasic solvent system, the biphasic microreactor exhibited a 22-fold increase in the observed exponential factor and a 2.5~3.3-fold increase in the apparent rate constant for fructose degradation. MIBK exhibits a strong affinity towards FF, allowing for the conversion of hemicellulose to FF. This conversion process occurs in a biphasic system composed of **pre-hydrolysis liquor (PHL)** generated from the pretreatment of lignocellulosic biomass and MIBK. Under conditions of 170°C and 100 minutes, the yield of FF increased from 32.8% in the monophasic system to 60.1% [34]. Furthermore, the biphasic solvent system did not produce any black residues resulting from FF condensation, indicating the absence of side reactions in this system [34, 35]. Collectively, these studies suggest that the use of acid as a catalyst in biphasic systems with a H_2O/MIBK composition is a more economically viable approach for the conversion of cellulose and hemicellulose components in biomass feedstocks into

value-added products such as HMF and FF [36-43].

H_2O/2-MTHF — 2-methyltetrahydrofuran (2-MTHF), a renewable and stable organic solvent with low solubility in water, possesses good extraction capabilities for FF. A high-efficiency conversion of xylan-type hemicelluloses from beech wood to FF is achieved using a biphasic system of 2-MTHF and water (2/5, v/v) [44]. The maximum FF yield obtained using this biphasic system was 78.1%, while the water homogeneous system only yielded 49.3% (Table 2, entry 14) [12]. The addition of water-soluble organic solvents such as DMSO and γ-valerolactone (GVL) further improved the FF yield to 69.4% and 62.4%, respectively. Another study showed that $FePO_4$ could be used as a catalyst to efficiently convert diluted acid-hydrolyzed bagasse into FF in a biphasic system composed of NaCl-modified H_2O/2-MTHF (Table 2, entries 15-18) [45]. The catalytic action of Cl^- in NaCl enhanced the enolization of xylose and the **salting-out effect** of NaCl, leading to improved xylose transformation and the extraction and separation of FF in the organic phase.

H_2O/dichloromethane (DCM) — Biphasic solvent system composed of lithium bromide hydrate solution ($LiBr{\cdot}3H_2O$) and dichloromethane (DCM) enabled a selective separation and depolymerization of the three main components of lignocellulose: cellulose, hemicellulose, and lignin [46]. In the aqueous phase, cellulose and hemicellulose underwent hydrolysis to produce hexose and pentose, which could be further dehydrated or converted into 5-bromomethylfurfural (BMF) and FF before being extracted into the organic phase. Moreover, the lignin component underwent depolymerization and accumulated as a solid residue between the two phases, facilitating its recovery and further utilization. In another study, xylose from a concentrated **pre-hydrolysis liquor** (CPHL) was converted to FF in DCM aqueous biphasic solvent using a sulfonated carbon-based catalyst (SCC) [47]. By optimizing the ratio of organic phase to aqueous phase, the highest xylose conversion rate reached 98%, while the highest FF yield achieved was 81.4% (Table 2, entry 24).

H_2O/toluene, H_2O/p-xylene — Toluene, and p-xylene display immiscibility with water, which confers an advantageous characteristic for their utilization as organic solvents in the extraction of FF from the aqueous phase [48, 49]. It was reported that addition of sulfuric acid into a biphasic system consisting of H_2O/toluene significantly increased the FF yield with 100% FF accumulation in the organic phase [50]. Water-tolerant Lewis acid (e.g., Nb_2O_5) could also be used as catalyst to achieve selective conversion of xylose to FF via dehydration (Table 2, entries 25 and 26) [51]. During the reaction,

an amorphous Nb_2O_5 solid catalyst with hydrophilic properties remains suspended in the water phase. The Lewis acid site on the amorphous Nb_2O_5 catalyst efficiently promotes the selective conversion of xylose to FF through dehydration in the aqueous phase. The amorphous Nb_2O_5 solid catalysts in the biphasic system can be easily recovered and maintain high catalytic activity.

H_2O/n-butanol — Butanol, a renewable solvent that could be produced through the self-hydrolysis of biomass raw materials, could also form a biphasic solvent system with water, and the formed solvent system is more environmentally friendly and holds significant potential for advancing research on biomass conversion and utilization [52]. Promising results were observed in the conversion of cellulose to HMF in a butanol/H_2O biphasic system by using metal chlorides (i.e., $FeCl_3$, $RuCl_3$, VCl_3, $TiCl_3$, $MoCl_3$, and $CrCl_3$, etc.) as catalysts (Table 2, entry 27 and 28) [53] [54]. In another study, an effective solid acid catalyst (Cr-deAL-Y) containing Cr was prepared by dealumination and ion exchange, using H-Y zeolite as the raw material [56]. When the reaction was conducted at 453 K for 30 minutes, both the xylose conversion rate and FF yield reached high levels of 100% and 78%, respectively (Table 2, entry 29) [52].

Lignin also has high solubility in n-butanol [55]. Thus, the H_2O/n-butanol biphasic system offers an efficient means of separating and depolymerizing the main components of biomass feedstock especially lignin. In this system, lignin is dissolved and depolymerized in the upper organic phase, while hemicellulose along with a small number of cellulose dissolves in the lower aqueous phase and undergoes depolymerization, forming monosaccharides, oligosaccharides, polyols, and organic acids. Only a small fraction of hemicellulose and the majority of cellulose remain in solid form. A one-pot **reduction catalytic fractionation (RCF)** experiment was conducted on eucalyptus wood chips utilizing a Ru/C catalyst and pressurized hydrogen (30 bar) in a homogeneous phase H_2O/n-butanol system at a temperature of 473 K [56]. The biphasic system is subsequently separated below the upper critical solution temperature (UCST < 398 K). The highest cellulose retention rate achieved was 96 wt%, and the yield of phenolic monomers abundant in the extracted lignin oil from the organic phase was 48.8 wt%. In a study conducted by Schmetz et al., various biomass materials (including eucalyptus wood, sugar cane bagasse, beech wood, Japanese cedar wood, sugar beet pulp, and tall fescue) were subjected to DAP and butanol pretreatment (BUTP) [57]. The results showed that the BUTP method with n-butanol addition yielded cellulose and lignin with higher purity and better quality compared to the DAP.

In a similar process, Brienza et al. utilized a dithionite ($Na_2S_2O_4$)-assisted organic solvent (n-butanol) to separate birch sawdust [58]. After being maintained at 473 K for 3 hours, cellulose pulp with a purity of 76.0% was obtained. The biomass composition demonstrated 91.7% retention of cellulose, 81.9% removal of C5 polysaccharides, and 71.6% removal of acid-insoluble lignin (AIL). Subsequently, a significant yield (>90%) of recovered lignin oil was obtained from the organic phase. Under the optimized conditions, the highest yield of monophenols in acid-insoluble lignin from birch sawdust was approximately 20% [59]. In conclusion, the biphasic system formed by H_2O/n-butanol exhibits promising application potential in biomass pretreatment.

Table 2 Classical biphasic systems for the production of HMF and FF.

Entry	Substrates	Reaction phase	Extractive phase	Con. (%)	FF yield (%)	HMF yield (%)	Ref.
1	Fructose	(H_2O:DMSO) :PVP [a]	MIBK:2-butanol	92	--	71	[21]
2	Fructose	H_2O: DMSO	MIBK:2-butanol	95	--	85	[23]
3	Xylan	H_2O: DMSO	DCM	100	76	--	[23]
4	HFCS-55 [b]	H_2O	MIBK	96 [c]	--	81 [c]	[28]
5	Fructose	H_2O	DMC	97	--	87	[30]
6	Fru. & Glu.	H_2O	DMC	90	--	91	[30]
7	Xylose	H_2O	MIBK	100	90	--	[29]
8	Xylose	H_2O: ChCl	MIBK	100	75	--	[31]
9	D-xylose	H_2O: $FeCl_3$	MIBK	98	76	--	[32]
10	eucalyptus	H_2O: $FeCl_3$	MIBK	--	75 [d]	--	[32]
11	Fructose	H_2O	MIBK	100	--	93	[33]
12	Xylose/Xylan	PHL	MIBK	86	60	--	[34]
13	Xylan	H_2O	2-MTHF [e]	--	54	--	[12]
14	Xylan	H_2O	2-MTHF [f]	--	78	--	[12]
15	Hydrolysate [g]	H_2O	2-MTHF	58	50	--	[45]
16	Hydrolysate [g]	H_2O	Toluene	58	47	--	[45]
17	Hydrolysate [g]	H_2O	MIBK	93	41	--	[45]
18	Hydrolysate [g]	H_2O	CPME	65	47	--	[45]
19	Hydrolysate [g]	H_2O: NaCl	2-MTHF	97	89	--	[45]
20	Corn stover	$LiBr·3H_2O$	DCM	71 [h]	69	--	[46]
21	Poplar	$LiBr·3H_2O$	DCM	72 [h]	62	--	[46]
22	CPHL	CPHL	DCM (2mL)	91	61	--	[47]
23	CPHL	CPHL: NaCl	DCM (2mL)	97	67	--	[47]
24	CPHL	CPHL: NaCl	DCM (4mL)	98	81	--	[47]
25	Xylose	H_2O	Toluene	99	71	--	[51]
26	Xylose	H_2O	p-Xylene	97	63	--	[51]
27	Cellulose	H_2O: NaCl	butanol	95	--	83	[53]
28	Cellulose	H_2O: NaCl	n-butanol	91 [i]	--	49 [i]	[54]

29	Xylose	H_2O: NaCl	n-butanol	100	78	--	[52]

[a] PVP: poly (1-vinyl-2-pyrrolidinone). [b] Fructose-glucose mixture feedstock: 0.26 M fructose and 0.20 M glucose. [c] The conversion of substrate and HMF yield is calculated based on the fructose substrate. [d] Mole yield based on the hemicellulose content. [e] H_2O: 2-MTHF (5/5, v/v). [f] H_2O: 2-MTHF (5/2, v/v). [g] Dilute-oxalic acid pretreated bagasse hydrolysate. [h] The yield of BMF. [i] Mass fraction percentage.

Mechanism of Biphasic System Formation

In order to address the challenge of constructing a green and efficient biphasic system, the Arizona solvent system was utilized to extract and separate the complex mixture of monomers resulting from the oxidative depolymerization of lignin [60]. The construction of a green and efficient biphasic system can be guided by the difference in distribution coefficients between two solutes in different solvents. The Arizona solvent system, initially defined by Margraff [61], consists of four components with significant polarity differences: ethyl acetate (moderately polar), water and methanol (highly polar), and heptane (non-polar). This system includes 23 biphasic liquid systems with varying composition ranges, labeled A to Z (excluding E, I, and O) [62]. Figure 3(A) shows that the optimum material allocation coefficient can be achieved by varying the number of solvent components and their proportions. According to the Arizona system, two kinds of insoluble solvents were selected to form a biphasic system, and the extraction and separation effects of the two solutes were investigated, respectively. When an immiscible solvent II was added into a solvent I that dissolves two different solutes A and B, several possible distribution phenomena that can occur between solute A and B in the biphasic system after being thoroughly mixed and allowed to stand for a period of time, as demonstrated in Figure 3(B) (a), (b), (c), and (d) [60]. When solute A remains completely present in solvent I, its partition coefficient logarithm ($\log(Kp)$) is less than -2. When a small amount of solute B is transferred to solvent II, $-2 < \log(Kp) < 0$. When most or all of solute A is extracted into solvent II, its partition coefficients are expressed as $0 < \log(Kp) < 2$ and $\log(Kp) > 2$, respectively. It is worth noting that the greater the difference in $\log(Kp)$ values between solutes A and B, the higher the separation efficiency. Therefore, measuring the partition coefficient (Kp) of two solutes in a biphasic solvent system provides guidance for constructing an effective biphasic system for extraction and separation.

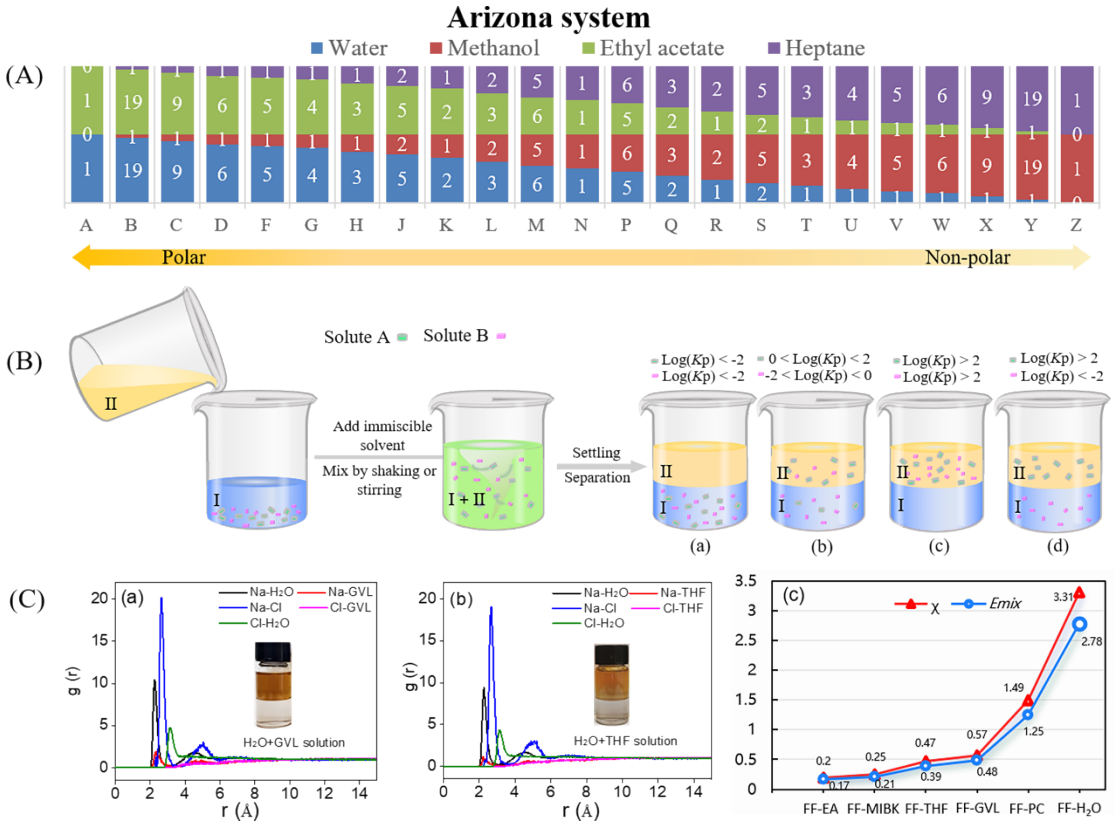


Figure 3. (A) The 23 Arizona solvent composition rendering shows the distribution of solvent components in different quantities and proportions in the system. (B) Partition coefficients of different solutes in immiscible solvent. (C) (a) and (b) respectively show the radial distribution functions (RDF) of the solvent center of mass for GVL and THF in NaCl aqueous solution. g(r) represents the quantity, while r(Å) represents the distance. (c) Weak interactions between solute FF and solvent molecules. In the Flory-Huggins lattice theory, the interaction parameter χ is utilized to signify the solvent capacity within a solvent system. The smaller the χ value, the stronger the weak intermolecular forces between molecules. Abbreviations: EA, ethyl acetate; THF, tetrahydrofuran; PC, propylene carbonate.

Lin and colleagues conducted molecular dynamics simulations to investigate the interactions between molecules and predicted the moving trajectories of the reactant (xylose) and product (FF) in the biphasic system during the reaction process [20]. The research aimed to establish a green and efficient biphasic system using insoluble or slightly soluble organic phases and water, based on classical biphasic system theory. Commonly used solvents for FF preparation include toluene, MIBK, 2-butanol, cyclopentyl methyl ether (CPME), 2-MTHF, and DCM. The solvation free energy of FF ($\Delta G_{sol\text{-}ff}$) in organic solvents was calculated using GROMACS, revealing the following order: DCM < 2-butanol < 2-MTHF ≈ CPME < MIBK < toluene. The order of xylose conversion efficiency was found to be: DCM/H_2O > 2-MTHF/H_2O > 2-

butanol/H_2O ≈ MIBK/H_2O > CPME/H_2O > toluene/H_2O, which aligns with the solvation free energy order. This indicates that the solvation free energy in the organic solvent significantly affects FF formation as lower solvation free energy leads to higher FF selectivity [63]. However, FF degradation in the aqueous phase and partition coefficient of the organic phase also impact FF yield and separation efficiency. Prof. Ren's research provides a theoretical foundation for furan chemical conversion within the classical biphasic system framework. On the other hand, it was also reported that the use of more polar solvents initially immiscible with water (such as toluene, MIBK, CPME, and DCM) can enhance product yield [20]. Similarly, in the studies conducted by Professor Dumesic, it was found that the addition of polar aprotic solvents like GVL, THF, DMSO, and dioxane to the solvent system, which possess solvation effects on solute molecules, can improve the yield of HMF products [64]. During our previous study, we also observed that compared to low polar or non-polar solvents, certain polar aprotic solvents with strong polarity [65] (such as GVL, THF, DMSO, and sulfolane) were more favorable for the formation of FF and HMF. However, these polar solvents are miscible with water and cannot form a classic biphasic system. And then, we investigated the mechanism of phase separation after adding salt to homogeneous systems formed by strongly polar aprotic solvents and water. By using molecular dynamics simulations to assess weak intermolecular interactions, which provided new insights into the formation of the phasic system shown as Figure 3(C). Both (a) and (b) demonstrate that the quantities of Na^+ and Cl^- interacting with water molecules are notably higher than those of the organic solvent molecules GVL and THF, revealing the localized arrangement of solvent molecules around NaCl [66]. The χ values for FF with organic solvents in (c) are smaller than the χ value for FF with H_2O, indicating stronger intermolecular forces between FF and organic solvent molecules compared to FF and H_2O molecules [66]. This result provides strong evidence for the ability of organic solvents to extract FF from H_2O."

Non-classical biphasic systems

In order to settle the dispute of dissolution and separation in classical biphasic system, our previous works [11] showed that obvious layer boundaries could be easily formed in the originally miscible polar aprotic solvent and water system by adding a certain amount of inorganic salt, inspired by the **Hofmeister effect** and the salting out effect. This kind of biphasic solvent system is defined as a non-classical biphasic system.

As a green bio-based polar aprotic solvent, GVL has been widely applied in biorefinery of lignocellulosic biomass. Our group previously reported a non-classical GVL-based biphasic system solvent for efficient pretreatment of bamboo [67, 68]. After pretreatment, NaCl could be added into the homogeneous pretreatment liquid and change it into a biphasic solvent system. It should be noted that hemicellulose and its derivatives are mainly present in the aqueous phase of the newly formed biphasic system, while lignin and its derivatives are retained in the GVL phase. This significantly reduces the complexity of product separation. Moreover, our team innovatively designed another non-classical biphasic system (GVL/$LiCl{\cdot}3H_2O$) combining molten salt hydrate with GVL for catalytic conversion of xylan to FF [11]. More than 99.9% of xylan conversion could be obtained with 77.22 mol% yield of FF at 413 K for 2 h (Table 3, entry1), which confirmed that the metal salt LiCl not only promote the conversion of transition state intermediates but also conduct the formation of biphasic system. Similar works have also been reported by other research groups. Prof. Pan's team added the metal salt $Al_2(SO_4)_3$ into the GVL/H_2O co-solvent system and achieved a high conversion rate of xylan to FF under microwave heating conditions (88%) [69]. The effect of different organic solvents on xylan conversion efficiency to FF was also investigated (Table 3, entry 2), which demonstrated that GVL showed a more significant solvent effect compared with other solvents.

It is worth noting that the THF/H_2O biphasic system is also beneficial to the transformation and separation of carbohydrates as shown in Table 3 (entries 10-16)[70]. The yields of FF in THF/H_2O-NaCl biphasic system using xylose and xylan as substrates was 75% and 66%, respectively (Table 3, entries 17 and 18) [71]. Similarly, in the NaCl-H_2O/THF catalytic system, reaction at 200℃ for 2 h with $InCl_3$ as catalyst, the yield of HMF converted from microcrystalline cellulose (MCC) was 39.7% [72]. Interestingly, a simple and efficient biphasic solvent system consisting of THF and concentrated seawater (ca. 30 wt% salts) has been proposed to effectively convert cellulose and hemicellulose into HMF and FF without using acid catalyst (Table 3, entries 20 to 22) [73]. Moreover, various lignocellulosic biomass feedstocks, including corn stover, pine, grass, and poplar, were liquified in this biphasic system with low HMF yield (20-35%) and relatively high FF yield (51-66%) (Table 3, entries 23 to 26) [74].

Table 3 Non-classical biphasic systems for the production of HMF and FF.

Entry	Substrates	Reaction phase	Extractive phase	HMF yield (%)	FF yield (%)	Ref.
1	Xylan	$LiCl{\cdot}3H_2O$	GVL	--	77	[11]
2	Xylan	H_2O: $Al_2(SO_4)_3$	GVL	--	88	[69]
3	MCC [a]	[BMIM]Cl	GVL	20	--	[75]
4	Fructose	[BMIM]Cl	GVL	90	--	[75]
5	Glucose	[BMIM]Cl	GVL	79	--	[75]
6	Inulin	[BMIM]Cl	GVL	41	--	[75]
7	Xylan	H_2O: NaCl	GVL	--	80	[76]
8	Xylan	H_2O: NaCl	THF	--	41	[76]
9	Xylan	H_2O: $Al_2(SO_4)_3$	THF	--	33	[69]
10	Glucose	H_2O: NaCl	THF	85	--	[70]
11	Sucrose	H_2O: NaCl	THF	81	--	[70]
12	Starch	H_2O: NaCl	THF	65	--	[70]
13	Maltose	H_2O: NaCl	THF	65	--	[70]
14	Glucan	H_2O: NaCl	THF	60	--	[70]
15	Moso bamboo	H_2O: NaCl	THF	22	16	[70]
16	Cellulose	H_2O: NaCl	THF	53	--	[70]
17	Xylose	H_2O: NaCl	THF	--	75	[71]
18	Xylan	H_2O: NaCl	THF	--	66	[71]
19	MCC	H_2O: NaCl	THF	40	--	[72]
20	Beech wood	Seawater [a]	THF	44	41	[73]
21	Corn stalks	Seawater [a]	THF	50	42	[73]
22	Pine wood	Seawater [a]	THF	46	37	[73]
23	Corn stover	H_2O: NaCl	THF	19	56	[74]
24	Pine wood	H_2O: NaCl	THF	35	62	[74]
25	Grass	H_2O: NaCl	THF	23	66	[74]
26	Poplar	H_2O: NaCl	THF	26	51	[74]
27	Glucose	H_2O: NaCl	THF	84	--	[76]
28	Glucose	H_2O: NaCl	THF	78	--	[77]

[a] Concentrated seawater.

Notably, the non-classical biphasic system effectively solves the problems of difficult product separation, complicated purification process, and high energy consumption in traditional biorefineries. Technically, according to our previous research, the construction of non-classical biphasic systems serves a dual purpose for stratifying the miscible cosolvent system and increasing the distribution coefficient of furan products in THF or GVL. With a view to efficient construction and effective application of non-classical biphasic system, the mechanism of non-classical biphasic system formation at the molecular scale should be further clarified.

Other than classical biphasic system theory, the construction of non-classical biphasic system is based on the theoretical combination of the Hofmeister effect and

the salting out effect. The Hofmeister effect explains the formation reason of non-classical biphasic systems on a macro scale, where differences in partition coefficients lead to phase delamination. Furthermore, the salting out effect explains the formation mechanism of non-classical biphasic systems at the mesoscopic scale, that is, the metal salt changes the distribution of hydration in the solvent system. Based on our reported experimental and molecular simulated results, our group proposes the mechanism[66] for the formation of non-classical biphasic systems at the molecular scale as follows: first, the addition of metal salts changes the spatial distribution of weak intermolecular interactions in the solvent system, and then the hydration of water molecules around the solute the distribution changes accordingly, eventually leading to differences in distribution coefficients and the formation of a biphasic system. Future work will study the composition of weak interactions study in non-classical biphasic systems in detail and the deep-seated mechanisms that form non-classical biphasic systems.

Based on the theoretical innovation of non-classical biphasic systems, we further investigated key technologies for its application on green and effective biorefinery process, including of controlled depolymerization of lignocellulose [78, 79], directed conversion of furan chemicals [66], and full component utilization of lignocellulosic biomass [80, 81]. Notably, the separation efficiency of hemicellulose and lignin exceeded 98%, while maintaining a cellulose retention rate of over 91.5%, which is beyond what have been reported in homogeneous system and classic biphasic system. Moreover, the yield of glucose from enzymatic hydrolysis increased by 50% when compared to a homogeneous system, following with the yield of phenolic monomers and oligomers surpassed 70%, which could be attributed to the solvation of furan and lignin units from solvent molecules [67, 78]. Furthermore, we preliminarily integrated Na^+ ions into the initial mixture of polar aprotic solvent and water in order to investigate the weak interactions between solvent molecules via molecular dynamics simulations, which will provide a novel perspective and solid evidence to comprehensively explain the formation of non-classical biphasic system. In considering of the industrial application of non-classical biphasic system, we also conducted the mass and energy balance calculation [80, 81]. Significantly, more than 80% of the initial mass of lignocellulose could be converted for the production of materials and high value-added chemicals, resulting in a revenue exceeding 4393 USD per ton of treated lignocellulosic raw material. Moreover, the energy consumption for product separation in non-classical biphasic system has been reduced to below 44% of the overall process cost, which

highlights the potential for large-scale application of non-classical system.

Concluding Remarks and prospects

Biomass pretreatment technologies have advanced tremendously over the past few decades for both carbohydrate-centered and lignin-first biorefinery processes. Novel solvents such as organosolv, ionic liquid and **deep eutectic solvent** all proved to be effective solvents that could be used in pretreating biomass to increase cellulose accessibility for biofuel production or fractionating lignin for its valorization in homogenous solvent system. Biphasic solvent system plays an essential role in the furan type of compound-driven biorefinery approach due to its ability to extract FF/HMF from the reactive phase and consequently increases their yield and saving energy by providing better downstream separations. By selecting appropriate solvents, biphasic solvent system is capable of achieving high yield of furans while simultaneously perform *in-situ* extraction of hemicellulose and lignin, enabling integrated fractionation and utilization of biomass components.

The formation mechanism of biphasic systems and their advantages in biomass fractionation have been fully demonstrated in literature. However, there are still some unresolved problems in the application of biphasic solvent systems in future integrated biorefinery especially in the industry. For example, some of the organic solvents being used in biphasic solvent system occasionally have undesired physical properties, and others may contain potential hazardous substances and low biodegradability, which could all limit their large-scale application in industry. For example, GVL has been used as an effective extractive phase in the non-classical biphasic system for the production of FF and HMF; however, it has an extremely high boiling point (>200 ℃) thus could potentially cause the product separation process energy intensive and complicated. Renewable solvent like cellulose-derived Cyrene has high viscosity, while solvent like THF is a toxic and carcinogenic compound. Deep eutectic solvent and ionic liquid as emerging effective homogeneous pretreatment solvents have yet to be widely utilized in biphasic solvent system. They could offer excellent properties such as high thermal stability, non-volatility, and high lignin solubility, but are costly to produce on a large scale.

The mechanism by which miscible solvents form non-classical biphasic systems is still unclear at the molecular scale. Computational technologies such as quantum chemical calculations and molecular dynamics simulations can help guide the selection

of solvent by analyzing various interactions between solvent in those non-classical biphasic systems in detail. Computational solvent screen techniques such as Conductor-like screening model for real solvents (COSMO-RS) should be used to screen novel solvent such as ionic liquid and deep eutectic solvent for their ability to form non-classical biphasic solvent system with other organic solvent as well as their ability for extracting furans and dissolving hemicellulose/lignin.

In addition, flow-through pretreatment could constantly remove the undesired degraded or condensed product from the solvent system, thus potentially could be much more economically feasible than conventional batch reactors. Future study could be directed toward the development of biphasic solvent system in a continuous reactor. Last but not least, techno-economic assessments and life cycle analysis of biphasic solvent system in modern integrated biorefinery has not been appropriately addressed, and these work needs to be performed in order to building a case for pilot scale utilization of this novel solvent system.

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Declaration of interests

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.

References

1. Mariscal, R., *et al.* (2016) Furfural: a renewable and versatile platform molecule for the synthesis of chemicals and fuels. *Energy Environ. Sci.* 9, 1144-1189
2. Gerardy, R., *et al.* (2020) Continuous Flow Upgrading of Selected C2-C6 Platform Chemicals Derived from Biomass. *Chem. Rev.* 120, 7219-7347
3. Jiang, D., *et al.* (2012) Bioenergy potential from crop residues in China: Availability and distribution. *Renewable Sustainable Energy Rev.* 16, 1377-1382
4. Xu, C., *et al.* (2020) Recent catalytic routes for the preparation and the upgrading of biomass derived furfural and 5-hydroxymethylfurfural. *Chem. Soc. Rev.* 49, 4273-4306
5. Liang, J., *et al.* (2023) Advances in selective conversion of carbohydrates into 5-hydroxymethylfurfural. *Green Energy Environ.* DOI: 10.1016/j.gee.2023.11.005
6. Sener, C., *et al.* (2018) Enhanced Furfural Yields from Xylose Dehydration in the gamma-

Valerolactone/Water Solvent System at Elevated Temperatures. *ChemSusChem* 11, 2321-2331
7. Abdilla-Santes, R.M.*, et al.* (2019) High-Yield 5-Hydroxymethylfurfural Synthesis from Crude Sugar Beet Juice in a Biphasic Microreactor. *ChemSusChem* 12, 4304-4312
8. Wang, Q.*, et al.* (2018) Rapid and simultaneous production of furfural and cellulose-rich residue from sugarcane bagasse using a pressurized phosphoric acid-acetone-water system. *Chem. Eng. J.* 334, 698-706
9. Peleteiro, S.*, et al.* (2016) Furfural production in biphasic media using an acidic ionic liquid as a catalyst. *Carbohydr. Polym.* 153, 421-428
10. Chiappe, C.*, et al.* (2017) Recycle and Extraction: Cornerstones for an Efficient Conversion of Cellulose into 5-Hydroxymethylfurfural in Ionic Liquids. *ACS Sustainable Chem. Eng.* 5, 5529-5536
11. Liu, C.*, et al.* (2021) Synthesis of furfural from xylan in γ-valerolactone/molten salt hydrate biphasic system. *Chem. Eng. J.* 425, 130608
12. Wang, W.*, et al.* (2015) Direct transformation of xylan-type hemicelluloses to furfural via SnCl(4) catalysts in aqueous and biphasic systems. *Bioresour. Technol.* 183, 188-194
13. Dai, J.*, et al.* (2017) Sulfonated polyaniline as a solid organocatalyst for dehydration of fructose into 5-hydroxymethylfurfural. *Green Chem.* 19, 1932-1939
14. Li, X.*, et al.* (2018) Efficient conversion of cellulose into 5-hydroxymethylfurfural over niobia/carbon composites. *Chem. Eng. J.* 332, 528-536
15. Sun, K.*, et al.* (2021) A solid iron salt catalyst for selective conversion of biomass-derived C5 sugars to furfural. *Fuel* 300, 120990
16. Metkar, P.S.*, et al.* (2015) Reactive distillation process for the production of furfural using solid acid catalysts. *Green Chem.* 17, 1453-1466
17. Shi, N.*, et al.* (2014) One-Pot Degradation of Cellulose into Furfural Compounds in Hot Compressed Steam with Dihydric Phosphates. *Acs Sustain Chem Eng* 2, 637-642
18. Qin, F.*, et al.* (2014) A PDMS membrane with high pervaporation performance for the separation of furfural and its potential in industrial application. *Green Chem.* 16, 1262-1273
19. Slak, J.*, et al.* (2022) A review of bio-refining process intensification in catalytic conversion reactions, separations and purifications of hydroxymethylfurfural (HMF) and furfural. *Chem. Eng. J.* 429, 132325
20. Lin, Q.*, et al.* (2021) Solvent effect on xylose-to-furfural reaction in biphasic systems: combined experiments with theoretical calculations. *Green Chem.* 23, 8510-8518
21. Roman-Leshkov, Y.*, et al.* (2006) Phase modifiers promote efficient production of hydroxymethylfurfural from fructose. *Science* 312, 1933-1937
22. Roman-Leshkov, Y.*, et al.* (2007) Production of dimethylfuran for liquid fuels from biomass-derived carbohydrates. *Nature* 447, 982-985
23. Chheda, J.N.*, et al.* (2007) Production of 5-hydroxymethylfurfural and furfural by dehydration of biomass-derived mono- and poly-saccharides. *Green Chem.* 9, 342-350
24. Gurbuz, E.I.*, et al.* (2012) Conversion of hemicellulose to furfural and levulinic acid using biphasic reactors with alkylphenol solvents. *ChemSusChem* 5, 383-387
25. Khoo, K.S.*, et al.* (2020) Liquid Biphasic System: A Recent Bioseparation Technology. *Processes* 8, 2
26. Ma, C.*, et al.* (2021) Acid-Catalyzed Conversion of Cellulose Into Levulinic Acid With Biphasic Solvent System. *Front. Plant Sci.* 12, 630807

27. Chen, Z., *et al.* (2022) Lignin-based solid acid catalyst for cellulose residue conversion into levulinic acid in biphasic system. *Ind. Crops Prod.* 178, 114523
28. Guo, W., *et al.* (2021) Selective fructose dehydration to 5-hydroxymethylfurfural from a fructose-glucose mixture over a sulfuric acid catalyst in a biphasic system: Experimental study and kinetic modelling. *Chem. Eng. J.* 409, 128182
29. Guo, W., *et al.* (2023) Insights into the reaction network and kinetics of xylose conversion over combined Lewis/Brønsted acid catalysts in a flow microreactor. *Green Chem.* DOI: 10.1039/d3gc00153a
30. Sayed, M., *et al.* (2020) 5-Hydroxymethylfurfural from fructose: an efficient continuous process in a water-dimethyl carbonate biphasic system with high yield product recovery. *Green Chem.* 22, 5402-5413
31. Jiang, S., *et al.* (2018) Unveiling the role of choline chloride in furfural synthesis from highly concentrated feeds of xylose. *Green Chem.* 20, 5104-5110
32. Zhang, Q., *et al.* (2021) A sustainable biorefinery strategy: Conversion and fractionation in a facile biphasic system towards integrated lignocellulose valorizations. *Renewable Energy* 179, 351-358
33. Desir, P. and Vlachos, D.G. (2022) Intensified reactive extraction for the acid-catalyzed conversion of fructose to 5-hydroxymethyl furfural. *Chem. Eng. J.* 428, 132556
34. Liu, H., *et al.* (2013) Furfural formation from the pre-hydrolysis liquor of a hardwood kraft-based dissolving pulp production process. *Bioresour. Technol.* 131, 315-320
35. Lai, F., *et al.* (2020) Highly efficient conversion of cellulose into 5-hydroxymethylfurfural using temperature-responsive ChnH5-nCeW12O40 (n = 1–5) catalysts. *Chem. Eng. J.* 396, 125282
36. Sweygers, N., *et al.* (2020) Simultaneous production of 5-hydroxymethylfurfural and furfural from bamboo (Phyllostachys nigra “Boryana”) in a biphasic reaction system. *Chem. Eng. J.* 386, 123957
37. Kaur, I. and Ni, Y. (2015) A process to produce furfural and acetic acid from pre-hydrolysis liquor of kraft based dissolving pulp process. *Sep. Purif. Technol.* 146, 121-126
38. Mittal, A., *et al.* (2017) Production of Furfural from Process-Relevant Biomass-Derived Pentoses in a Biphasic Reaction System. *ACS Sustainable Chem. Eng.* 5, 5694-5701
39. Feng, Y., *et al.* (2019) Development of Betaine-Based Sustainable Catalysts for Green Conversion of Carbohydrates and Biomass into 5-Hydroxymethylfurfural. *ChemSusChem* 12, 495-502
40. Zhang, X., *et al.* (2016) Highly efficient preparation of HMF from cellulose using temperature-responsive heteropolyacid catalysts in cascade reaction. *Appl. Catal., B* 196, 50-56
41. Faba, L., *et al.* (2019) Carbon Materials as Phase-Transfer Promoters for Obtaining 5-Hydroxymethylfurfural from Cellulose in a Biphasic System. *ChemSusChem* 12, 3769-3777
42. Wang, A., *et al.* (2021) Plasmon-Enhanced 5-Hydroxymethylfurfural Production from the Photothermal Conversion of Cellulose in a Biphasic Medium. *ACS Sustainable Chem. Eng.* 9, 16115-16122
43. Wu, P., *et al.* (2023) Facile synthesis of SAPO-34 nanocrystallites with excellent performance for the dehydration of carbohydrates to 5-hydroxymethylfurfural. *Green Chem.* 25, 1395-1405
44. Zhou, N., *et al.* (2021) Conversion of xylose into furfural over MC-SnOx and NaCl catalysts in a biphasic system. *J. Cleaner Prod.* 311, 127780
45. Wang, X., *et al.* (2019) Efficient catalytic conversion of dilute-oxalic acid pretreated bagasse hydrolysate to furfural using recyclable ironic phosphates catalysts. *Bioresour. Technol.* 290, 121764
46. Yoo, C.G., *et al.* (2017) Effective conversion of biomass into bromomethylfurfural, furfural, and

depolymerized lignin in lithium bromide molten salt hydrate of a biphasic system. *RSC Advances* 7(1), 300-308

47. Deng, A.*, et al.* (2016) A feasible process for furfural production from the pre-hydrolysis liquor of corncob via biochar catalysts in a new biphasic system. *Bioresour. Technol.* 216, 754-760
48. Sahu, R. and Dhepe, P.L. (2012) A one-pot method for the selective conversion of hemicellulose from crop waste into C5 sugars and furfural by using solid acid catalysts. *ChemSusChem* 5, 751-761
49. Tran, T.T.V.*, et al.* (2019) Highly productive xylose dehydration using a sulfonic acid functionalized KIT-6 catalyst. *Fuel* 236, 1156-1163
50. Wang, Q.*, et al.* (2019) Production of furfural with high yields from corncob under extremely low water/solid ratios. *Renewable Energy* 144, 139-146
51. Gupta, N.K.*, et al.* (2017) Amorphous Nb2O5 as a Selective and Reusable Catalyst for Furfural Production from Xylose in Biphasic Water and Toluene. *ACS Catal.* 7, 2430-2436
52. Wang, Y.*, et al.* (2022) Efficient conversion of xylose to furfural over modified zeolite in the recyclable water/n-butanol system. *Fuel Process. Technol.* 237, 107472
53. Yan, L.*, et al.* (2019) Ruthenium trichloride catalyzed conversion of cellulose into 5-hydroxymethylfurfural in biphasic system. *Bioresour. Technol.* 279, 84-91
54. Zhang, L.*, et al.* (2021) Enhanced conversion of α-cellulose to 5-HMF in aqueous biphasic system catalyzed by FeCl3-CuCl2. *Chin. Chem. Lett.* 32, 2233-2238
55. Schmetz, Q.*, et al.* (2020) Monitoring technical lignin partition in aqueous/alcohol biphasic systems according to pH: influences of the molecular structure and solvent characteristics. *Green Chem.* 22, 7031-7046
56. Renders, T.*, et al.* (2018) Catalytic lignocellulose biorefining in n-butanol/water: a one-pot approach toward phenolics, polyols, and cellulose. *Green Chem.* 20, 4607-4619
57. Schmetz, Q.*, et al.* (2019) Versatility of a Dilute Acid/Butanol Pretreatment Investigated on Various Lignocellulosic Biomasses to Produce Lignin, Monosaccharides and Cellulose in Distinct Phases. *ACS Sustainable Chem. Eng.* 7, 11069-11079
58. Brienza, F.*, et al.* (2021) Enhancing lignin depolymerization via a dithionite-assisted organosolv fractionation of birch sawdust. *Green Chem.* 23, 3268-3276
59. Brienza, F.*, et al.* (2022) Unleashing lignin potential through the dithionite-assisted organosolv fractionation of lignocellulosic biomass. *Chem. Eng. J.* 450, 138179
60. Alherech, M.*, et al.* (2021) From Lignin to Valuable Aromatic Chemicals: Lignin Depolymerization and Monomer Separation via Centrifugal Partition Chromatography. *ACS Cent. Sci.* 7, 1831-1837
61. Margraff, Foucault, R. (1994) *Centrifugal Partition Chromatography*. Db Marcel Dekker
62. Berthod, A.*, et al.* (2005) Alkane effect in the Arizona liquid systems used in countercurrent chromatography. *Anal. Bioanal. Chem.* 383, 327-340
63. Lin, Q.*, et al.* (2020) Solvent effect on xylose conversion under catalyst-free conditions: insights from molecular dynamics simulation and experiments. *Green Chem.* 22, 532-539
64. Mellmer, M.A.*, et al.* (2019) Effects of chloride ions in acid-catalyzed biomass dehydration reactions in polar aprotic solvents. *Nat. Commun.* 10, 1132
65. Liu, C.*, et al.* (2020) Facile Directional Conversion of Cellulose and Bamboo Meal Wastes over Low-Cost Sulfate and Polar Aprotic Solvent. *ACS Sustainable Chem. Eng.* 8, 5776-5786
66. Cai, T.*, et al.* (2023) The weak interaction between polar aprotic solvent and saline water enables

efficient production of furans from lignocellulosic biomass. *Green Chem.* 25, 375-383
67. Yin, X.*, et al.* (2022) A mild biomass pretreatment process with efficiency and specificity in co-solvent of γ-valerolactone and aqueous p-toluenesulfonic acid. *Chem. Eng. J.* 437, 135408
68. Yin, X.*, et al.* (2021) The Pretreatment of Lignocelluloses With Green Solvent as Biorefinery Preprocess: A Minor Review. *Front. Plant Sci.* 12
69. Yang, T.*, et al.* (2017) Insight into Aluminum Sulfate-Catalyzed Xylan Conversion into Furfural in a gamma-Valerolactone/Water Biphasic Solvent under Microwave Conditions. *ChemSusChem* 10, 4066-4079
70. Xing, X.*, et al.* (2022) Hf-beta zeolites as highly efficient catalysts for the production of 5-hydroxymethylfurfural from cellulose in biphasic system. *Int. J. Biol. Macromol.* 222, 3014-3023
71. Yang, Y.*, et al.* (2012) Synthesis of furfural from xylose, xylan, and biomass using AlCl3.6H2O in biphasic media via xylose isomerization to xylulose. *ChemSusChem* 5, 405-410
72. Shen, Y.*, et al.* (2014) InCl3-catalyzed conversion of carbohydrates into 5-hydroxymethylfurfural in biphasic system. *Bioresour. Technol.* 172, 457-460
73. Guo, T.*, et al.* (2018) Catalytic Transformation of Lignocellulosic Biomass into Arenes, 5-Hydroxymethylfurfural, and Furfural. *ChemSusChem* 11, 2758-2765
74. Yang, Y.*, et al.* (2012) Conversion of carbohydrates and lignocellulosic biomass into 5-hydroxymethylfurfural using AlCl3·6H2O catalyst in a biphasic solvent system. *Green Chem.* 14, 509-513
75. Yin, Y.*, et al.* (2022) Insights into Shape Selectivity and Acidity Control in NiO-Loaded Mesoporous SBA-15 Nanoreactors for Catalytic Conversion of Cellulose to 5-Hydroxymethylfurfural. *ACS Sustainable Chem. Eng.* 10, 17081-17093
76. Wang, K.*, et al.* (2021) Highly Efficient 5-Hydroxymethylfurfural Production from Glucose over Bifunctional SnOx/C catalyst. *ACS Sustainable Chem. Eng.* 9, 11351-11360
77. Rezayan, A.*, et al.* (2022) Synthesis of bifunctional tin-based silica–carbon catalysts, Sn/KIT-1/C, with tunable acid sites for the catalytic transformation of glucose into 5-hydroxymethylfurfural. *Chem. Eng. J.* 429, 132261
78. Yin, X.*, et al.* (2022) A novel solvothermal biorefinery for production of lignocellulosic xylooligosaccharides, fermentable sugars and lignin nano-particles in biphasic system. *Carbohydr. Polym.* 295, 119901
79. Liang, J.*, et al.* (2023) Facile biphasic system of γ-valerolactone/saline water for effective lignocellulose fractionation. *Ind. Crops Prod.* 195, 116481
80. Liu, C.*, et al.* (2022) A sustainable and profitable biorefinery strategy for efficiently converting lignocellulose to furfural, glucose and phenolic compounds. *Green Chem.* 24, 8494-8502
81. Liu, C.*, et al.* (2023) Integrated lignocellulosic biorefinery for efficient production of furans and photothermal materials. *Chem. Eng. J.* 453, 139688