

Review

New Frontiers in the Catalytic Synthesis of Levulinic Acid: From Sugars to Raw and Waste Biomass as Starting Feedstock

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Abstract: Levulinic acid (LA) is one of the top bio-based platform molecules that can be converted into many valuable chemicals. It can be produced by acid catalysis from renewable resources, such as sugars, lignocellulosic biomass and waste materials, attractive candidates due to their abundance and environmentally benign nature. The LA transition from niche product to mass-produced chemical, however, requires its production from sustainable biomass feedstocks at low costs, adopting environment-friendly techniques. This review is an up-to-date discussion of the literature on the several catalytic systems that have been developed to produce LA from the different substrates. Special attention has been paid to the recent advancements on starting materials, moving from simple sugars to raw and waste biomasses. This aspect is of paramount importance from a sustainability point of view, transforming wastes needing to be disposed into starting materials for value-added products. This review also discusses the strategies to exploit the solid residues always obtained in the LA production processes, in order to attain a circular economy approach.

Keywords: levulinic acid; acid catalysts; sugars; raw and waste biomass; water; organic solvents

1. Introduction

One of the greatest challenges that industry faces in the 21st century is the transition from a fossil fuel based economy to one based on renewable resources, driving the search of new alternative renewable feedstocks for the production of chemical building blocks [1–6]. In particular, the exploitation of lignocellulosic biomass is receiving an increasing attention due to its renewability, abundance, low value and carbon-neutral balance. Among the target products, levulinic acid (LA) is the main compound of biomass hydrolysis, which has been classified by the United States Department of Energy as one of the top-12 promising building blocks [7]. LA represents a valuable intermediate for the synthesis of several chemicals for application in fuel additives, fragrances, solvents, pharmaceuticals, and plasticizers [8–13]. LA, also known as 3-acetylpropionic acid, 4-oxovaleric acid, or 4-oxopentanoic acid, is a very interesting platform chemical, because of its versatile chemistry, including one carbonyl, one carboxyl and α -H in its inner structure, looking like a short chain and non-volatile fatty acid. Some interesting data about physical properties of LA are reported in Table 1 [14–16].

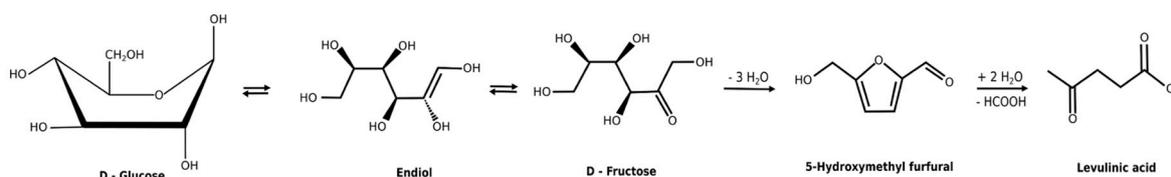
Table 1. Some physical properties of Levulinic Acid (LA).

Molecular Weight (g/mol)	Refractive Index ¹	Density (kg·m ⁻³) ¹	pKa	Melting Point (K)	Boiling Point (K)	Heat of Formation ΔH_f (kJ/mol)	Heat of Vaporization $\Delta_{vap}H_m$ (kJ/mol)
116.2	1.4796	1140	4.5	306–308	518–519	−2417	74.4

¹ Value at 293 K.

By taking into account the chemical structure of LA, carboxylic and then carbonyl groups are very reactive electrophilic centers towards nucleophilic attack. Furthermore, from the point of view of the acidic properties, LA has higher dissociation constant than saturated acids, thus its corresponding acidity is stronger. Lastly, LA can be isomerized into the enolisomer, owing to the existence of a carbonyl group. LA can be produced by three different process routes. The first one is a five-step route from the petrolchemical intermediate maleic anhydride, which was carried out at low scale in the past [17]. Despite the good yields in LA (up to 80 mol %) and even at the low oil price, today this multi-step process is not economically sustainable on large scale.

The second route involves the acid treatment of C₆ sugars, such as glucose, fructose, mannose or galactose, which can also derive from hydrolysis of more complex carbohydrates of the biomass, such as cellulose, hemicellulose or starch [18]. The hydrolysis proceeds via formation of 5-hydroxymethylfurfural (5-HMF) intermediate. Starting from glucose, the main reactions that occur are: (i) glucose isomerization into fructose; (ii) fructose dehydration into 5-HMF; and (iii) 5-HMF rehydration into LA. These reactions are reported in Figure 1.

**Figure 1.** Synthesis of LA starting from D-glucose.

Antal et al. proposed that 5-HMF is produced from fructose via cyclic intermediates [19]. Recent studies have further confirmed that 5-HMF originates from the acid-catalyzed dehydration of C₆-sugars in the furanose form [20,21]. The first step is the formation of 5-HMF by a triple dehydration step. 5-HMF is an unstable molecule and easily condenses, together with sugars and sugar degradation products, into black insoluble charred materials often called “humins” [22–25]. In an extensive review on the 5-HMF formation, Van Putten et al. have demonstrated that the temperature and reaction conditions required for the dehydration of glucose and other aldoses are significantly more severe than those for fructose. This evidence is tentatively explained by the need for glucose to first isomerize to fructose via the enediol form [26]. This isomerization is a Brønsted-base or Lewis-acid catalyzed reaction and thus proceeds very slowly under the strong Brønsted acid conditions generally used for the subsequent dehydration of the fructose. The harsher reaction conditions adopted for aldoses cause the formation of higher amounts of humins. The rehydration of 5-HMF with two molecules of water leads to LA and formic acid [27]. Regarding the thermodynamics of the process, the dehydration of fructose to 5-HMF is highly endothermic (by up to 92.0 kJ/mol), the glucose to fructose isomerization is very weakly endothermic (8.4 kJ/mol), whereas the other steps, including additional water elimination and rehydration to form LA, are exothermic (from 16.7 to 133.9 kJ/mol) [28]. Elevated temperatures and aqueous reaction environment make the dehydration reaction steps thermodynamically more favorable. A proposed rehydration mechanism of 5-HMF into LA in acid environment is reported in Figure 2 [29].

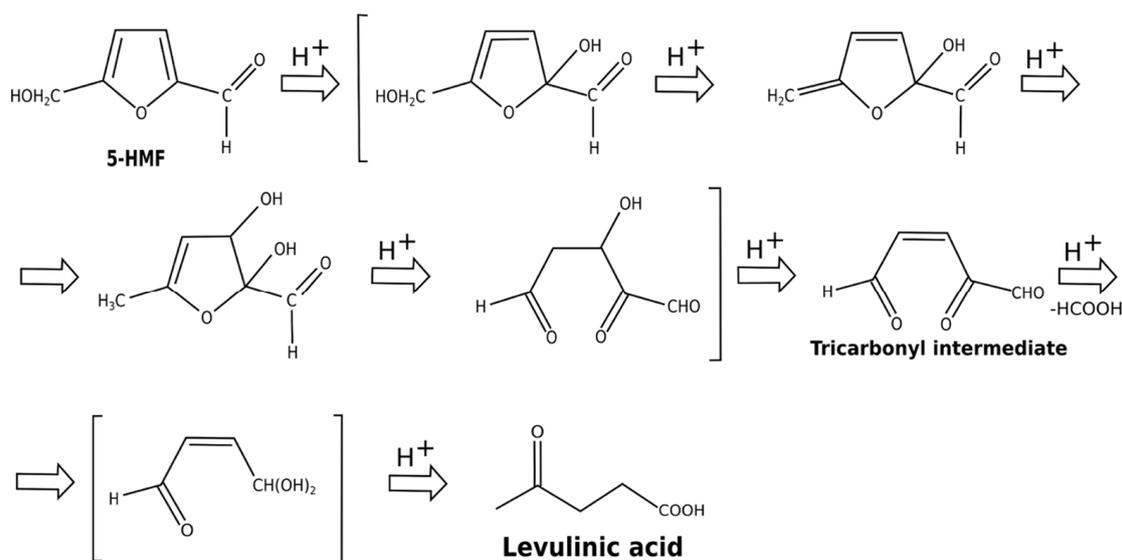


Figure 2. Detailed mechanism for the formation of LA from 5-HMF in acid medium.

Hydration of 5-HMF consists in the addition of a water molecule to the C2–C3 olefinic bond of the furan ring, leading to an unstable tricarbonyl intermediate, which quickly decomposes to LA and formic acid (HCOOH), in stoichiometric amount [22,30]. However, Flannelly et al. have recently reported that formic acid is produced even in excess to LA respect to the stoichiometric amount during the acid hydrolysis of hexose carbohydrates, thus highlighting the potentiality of this co-product coming from LA synthesis [31]. In fact, formic acid is a valuable product in its own right and can be used as a commodity in the chemical and textile industry, as a catalyst, a hydrogen carrier and a road salting component [4,32].

As underlined previously, the major problem during the hydrothermal acid-catalyzed treatments of sugars is the formation of humins, which represent the main solid by-products of the reaction [33,34]. The formation of humins can lead to a considerable loss of the sugar feed, thereby strongly decreasing the efficiency and the economic viability of the entire process [35].

When raw lignocellulosic biomass is employed, acid depolymerization of hemicellulose fraction releases pentoses (xylose and arabinose), which are converted to furfural, while from the different hexoses (glucose, galactose and mannose) of the cellulose fraction, levulinic acid is formed (Figure 3) [36]. In this case, the solid by-product contains humins and also lignin residues.

Two different reaction regimes for the conversion of carbohydrates-containing biomass into LA that differ in the reaction conditions, but not essentially in the reaction pathway, can be distinguished: (i) the dilute acid treatment at high temperature and pressurized atmosphere; and (ii) the treatment with highly concentrated acid at lower temperatures and normal pressure.

The maximum theoretical ponderal yield of LA at complete molar yield is 64.4 wt % from hexose sugars, 71.6 wt % from cellulose and 67.8 wt % from sucrose, with the remaining being formic acid and water. However, the real obtained yields are significantly lower.

A completely different but very interesting route for the synthesis of LA is the direct conversion of furfuryl alcohol, which is obtained by furfural hydrogenation [37]. This third alternative pathway is depicted in Figure 4.

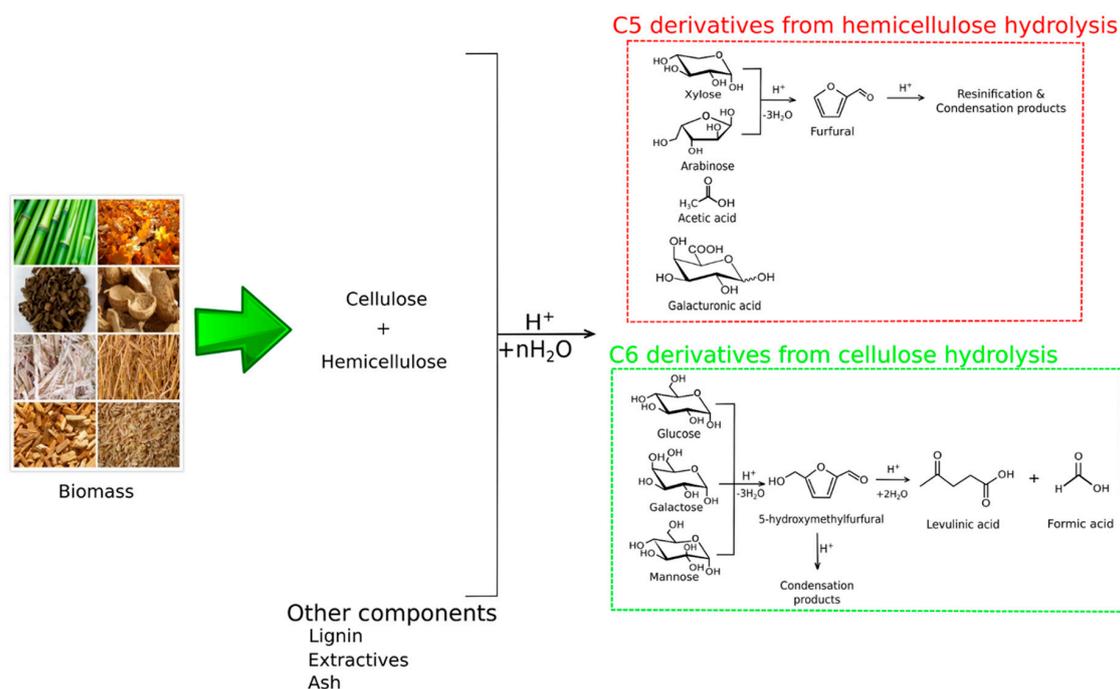


Figure 3. Reaction network of the acid-catalyzed hydrolysis of cellulose and hemicellulose in lignocellulosic biomass.

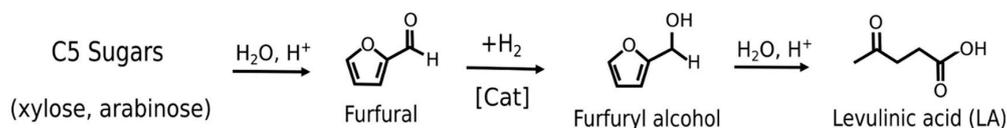


Figure 4. C₅ path to give levulinic acid.

The overall process involves three steps: (i) an acid-catalyzed hydrolysis of hemicellulose polymer and dehydration of the C₅ sugars to furfural [38,39]; (ii) the hydrogenation of furfural to furfuryl alcohol; (iii) the acid-catalyzed hydrolysis of furfuryl alcohol to the desired LA [18,40]. Yields in LA are in the range 83–93 mol % [23]. A modification of the above synthetic strategy employs alcohol instead of water as hydrolyzing agent of the last step furfuryl alcohol-to-levulinic acid, thus directly recovering levulinate esters, with yields in the range 95–98 mol %. The use of an alcoholic solvent can be extended also to the C₆ route, after 5-HMF production, giving also in this case levulinate ester as the main product.

The C₅ pathway is attractive, but still too limited, due to the excessive formation of by-products in the reaction medium [41]. Furthermore, the feasibility of both methods mainly depends on the type and cost of the possible feedstocks. Furfural price is in the range between \$700/t and \$1500/t, whilst furfuryl alcohol is \$1500/t or even higher. The high costs of these precursors make the production of levulinic acid by the C₅ path too expensive compared to that obtained by the C₆ one, the latter being currently the main one developed at industrial scale.

The first researchers to realize the potential of levulinic acid as building block for a wide range of chemicals were Manzer [42,43], Wery and Petersen [7] and Bozell [44]. Further conversion routes of levulinic acid are essential to create new outlet markets. It is eminent that these new routes will be developed in parallel to the realization of efficient levulinic biorefineries. Levulinic acid is considered to be a versatile biobased building block to be further converted in solvents, plasticizers, fuels, value-added chemicals, monomers for polymers, etc. [1,45–50]. Examples of important chemicals from LA and their potential applications are showed in Figure 5. Such valuable chemicals include

γ -valerolactone, levulinate esters and also angelica lactone, ketals, diphenolic acid and δ -amino levulinic acid [13,47,50–52], in addition to the several important compounds obtained from their upgrading, such as 2-methyltetrahydrofuran, hydrocarbon fuels, valerate esters and polymers [49].

The development of new LA-derived products is continuously in progress, alongside LA production at larger scale. In this context, very recently the company GFBiochemicals has announced that the production in their plant of Caserta will be scaled from 1000 t/year up to 10,000 t/year, with a substantial growth in the LA market in the next years.

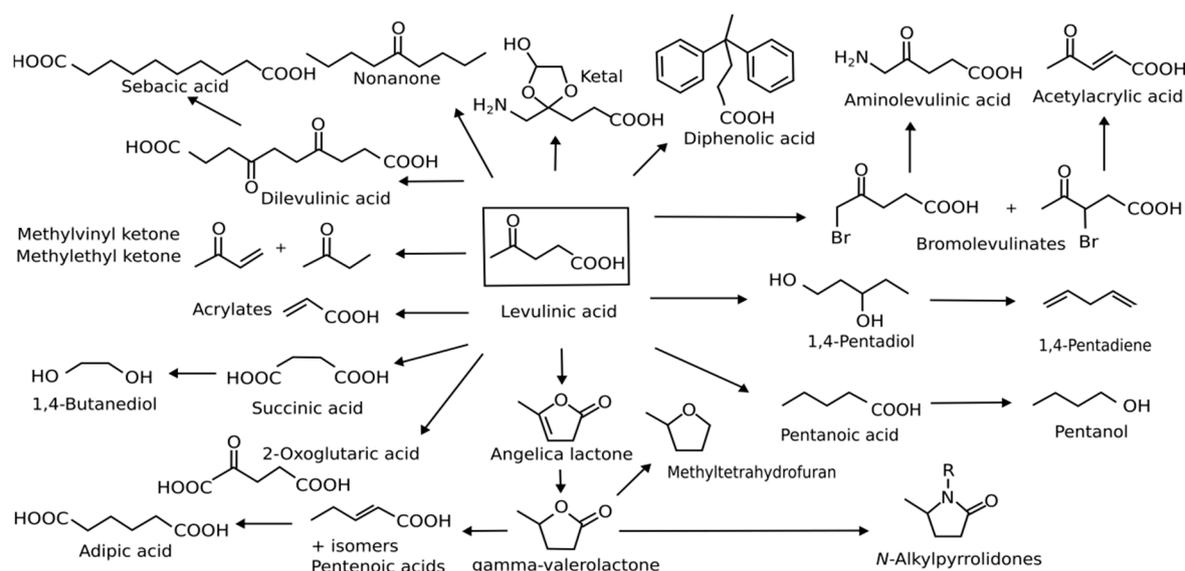


Figure 5. Chemical products derived from levulinic acid.

Important targets for the next commercialization of LA are: (i) the development of a selective dehydration without side reactions, especially the reduction of the tarry humins/char by-products; (ii) the use of cheap or, even better, negative-value biomasses, which significantly reduce the costs of LA production; (iii) the synthesis of new efficient catalysts to replace the traditional inorganic mineral ones, such as H_2SO_4 , HCl , and H_3PO_4 , which are responsible for corrosion problems of the equipment; and (iv) the removal of impurities and other by-products, which must be eliminated from the hydrolysis liquor before the recovery of the pure LA.

This review provides an overview of the more recent and promising trends on the production of LA from various starting substrates using homogeneous or heterogeneous catalyst systems. The different routes are critically commented, underlining the gaps to be filled to attain high level of LA commercialization. Special attention has been paid to the recent advancements in LA production approaches, moving from simple sugars to raw and waste biomasses, also obtained from marine and fungal biomass. This is of paramount importance from a sustainability point of view, transforming wastes needing to be disposed into raw materials for the synthesis of value-added products. In order to make easier the comparison among the different employed methods for LA production, in this review LA yield has been determined on the basis of weight of dry raw biomass as:

$$\text{yield of levulinic acid } (Y_{\text{LA}}) \text{ wt \%} = [\text{Levulinic acid recovered (g)}/\text{dry substrate (g)}] \times 100 \quad (1)$$

The hydrothermal conversion generates a significant amount of solid waste, which is called “hydrochar”. This waste stream is traditionally disposed in landfill, but can be directly exploited for energy recovery within the same levulinic acid plant or, more advantageously, as feedstock to be upgraded into new biochemicals. In this review, some interesting and recent findings and state-of-the-art in biochar exploitation will be introduced and discussed.

2. Catalytic Conversion of Hexoses

2.1. Homogeneous Mineral Acids and Salts in Water

C₆ sugars represent the ideal starting material for LA synthesis due to their water solubility, high purity and simple supply. The most ancient methods for the chemical conversion of aqueous solutions of sugars to LA use homogeneous mineral acid catalysts due to their high catalytic activity. The widely employed mineral acid catalysts, such as HCl, H₂SO₄, HNO₃, H₃PO₄, are selected due to low cost, easy availability and their efficiency towards high LA yields. Their effectiveness depends on concentration, strength of their primary dissociation constant, type and concentration of the employed feedstock and severity of the reaction, in terms of temperature and/or time. All the experiments reported in Table 2 have been carried out in subcritical water, under an external pressure of an inert gas (generally nitrogen) or adopting autogenous pressure, not externally applied, but deriving from high-pressure steam. This last approach clearly involves energy consumption for water vaporization and causes a change of composition of the starting biomass solution. Subcritical water is an environmentally innocuous, non-toxic, and safe solvent. Besides, it has good transport properties (high diffusion coefficient and thermal conductivity, and low viscosity) and the ionic product of subcritical water increases with temperature and is greater by 1 to 2 orders of magnitude than at ambient temperatures, thus promoting acid- and base-catalyzed reactions as biomass conversion [53].

A summary of recent works from the literature employing homogeneous mineral catalysts in water is provided in Table 2.

Table 2. C₆ sugars conversion in water in the presence of homogeneous catalysts: reaction conditions.

Experiment	Substrate and Loading	Catalyst	Reaction Conditions	Y _{LA}	Ref.
1	fructose 1 wt %	HCl	240 °C for 0.03 h	30 wt %	[54]
2	fructose 5 wt %	HCl	MW, 170 °C for 0.5 h	31.8 wt %	[34]
3	fructose 5 wt %	H ₂ SO ₄	MW, 170 °C for 0.5 h	27.5 wt %	[34]
4	fructose 5 wt %	H ₂ SO ₄	120 °C for 24 h	62% *	[55]
5	fructose 1 wt %	H ₃ PO ₄	240 °C for 0.03 h	4.5 wt %	[54]
6	glucose 1.8 wt %	HCl	141 °C for 1 h	29 wt %	[56]
7	glucose 10 wt %	HCl	160 °C for 4 h	41 wt %	[27]
8	glucose 15 wt %	HCl	220 °C for 1 h	37.2 wt %	[57]
9	glucose 6.3 wt %	HCl	98 °C for 3 h	22 wt %	[58]
10	glucose 5 wt %	HCl	MW, 170 °C for 0.5 h	31.4 wt %	[34]
11	glucose 5 wt %	H ₂ SO ₄	MW, 170 °C for 0.5 h	26.1 wt %	[34]
12	glucose 6.3 wt %	H ₂ SO ₄	98 °C for 12 h	24.5 wt %	[58]
13	glucose 1.8 wt %	H ₂ SO ₄	141 °C for 1 h	29 wt %	[56]
14	glucose 1.8 wt %	H ₂ SO ₄	140 °C for 2 h	38 wt %	[59]
15	glucose 2 wt %	H ₂ SO ₄	180 °C for 0.25 h	42 wt %	[60]
16	glucose 6.3 wt %	H ₃ PO ₄	98 °C for 6 h	3.2 wt %	[58]
17	fructose 2 wt %	TFA	180 °C for 1 h	45 wt %	[61]
18	glucose 1.8 wt %	TFA	180 °C for 1 h	37 wt %	[61]
19	glucose 2 wt %	Methane-sulfonic acid	180 °C for 0.25 h	41 wt %	[60]
20	glucose 2 wt %	FeCl ₃	180 °C for 2 h	19.3 wt %	[62]
21	glucose 2 wt %	CrCl ₃	180 °C for 2 h	38.7 wt %	[62]
22	glucose 2 wt %	CuCl ₂	180 °C for 2 h	14.8 wt %	[62]
23	glucose 2 wt %	AlCl ₃	180 °C for 2 h	45.8 wt %	[62]
24	glucose 10 wt %	HCl, CrCl ₃	140 °C for 6 h	30 wt %	[63]

* In the paper, the calculation of the reported yield is unclear.

As it is possible to observe from Table 2, HCl and H₂SO₄ are the most widely employed mineral acid catalysts for the conversion of C₆ sugars, allowing high yields to LA (up to 42 wt %), ready availability and low cost. In particular, HCl has been used to produce LA for decades. Thomas and Schuette used HCl as catalyst to produce LA from various carbohydrates already in 1931 [64]. In 1962

Carlson's patent states that HCl is the most preferable catalyst for converting various carbohydrates to LA because it can be easily recovered and recycled and, in addition, LA can be separated using simple vacuum distillation [65]. More recent studies have shown the successful employment of H₂SO₄ when simple sugars, such as fructose and glucose, are employed as starting substrates, leading to comparable LA yields to those obtained with HCl. As an example, Szabolcs et al. studied the degradation of carbohydrates to LA by using microwave energy, reaching yields of 31.8 wt % and 27.5 wt % starting from fructose in the presence of HCl and H₂SO₄, respectively, after a treatment at 170 °C for 30 min (Experiments 2 and 3, Table 2) [34]. When the authors employed glucose as starting substrate in the same reaction conditions, it was possible to obtain yields to LA of 31.4 wt % and 26.1 wt % using HCl and H₂SO₄ respectively (Experiments 10 and 11, Table 2). In this regard, it is interesting to highlight the LA yield achieved by Rackemann et al. about 42 wt %, employing H₂SO₄ at 180 °C for 15 min in water starting from glucose (Experiment 15, Table 2) [60]. Moreover, the same authors compared the results obtained in the presence of H₂SO₄ with those achieved using methanesulfonic acid (Experiment 19, Table 2), reaching similar LA yield under the same experimental reaction conditions.

Another type of catalyst employed for LA production deals with the use of metal salts which show remarkable catalytic activity. This is confirmed by the studies of Peng et al. who investigated the conversion of glucose by different metal chlorides, including FeCl₃, CrCl₃, CuCl₂ and AlCl₃ (Experiments 20–23, Table 2) [62]. Among the investigated metal chlorides, aluminum chloride was found to be the most effective for the conversion of glucose, affording an optimum yield up to 45.8 wt % working in water at 180 °C for 2 h (Experiment 23, Table 2). The catalytic role of these salts can be ascribed to the Lewis acidity of the metal cations, together with the intrinsic Brønsted acidity derived from their hydrolysis. Levulinic acid was produced from glucose in a cascade of reactions using a Lewis acid catalyst (CrCl₃) together with a Brønsted acid (HCl) catalyst (Experiment 24, Table 2). In this study CrCl₃ is an active Lewis acid catalyst in glucose isomerization to fructose, and the combined Lewis and Brønsted acid catalysts perform the isomerization and dehydration/rehydration reactions. A strong interaction between the Cr cation and the glucose molecule enables ring-opening and isomerization of glucose. By combining CrCl₃ and HCl, a real interplay of the two catalysts was ascertained. Even in the absence of HCl, hydrolysis of Cr(III) decreases the solution pH, and this intrinsic Brønsted acidity drives the dehydration and rehydration reactions. Yields of 30 wt % in LA were achieved at moderate temperature (140 °C) [63]. A further confirmation of the cooperative effect of Lewis and Brønsted acids in glucose hydrolysis to LA has been recently reported [66]. The synergistic positive effect on LA yield of coupling CrCl₃ with H₃PO₄ was confirmed compared with single CrCl₃ or H₃PO₄ catalysts. In the hydrolysis of fructose, sucrose and inulin, a strong interaction between the substrate and the Lewis acidic ion Sn⁴⁺ was also evidenced by NMR, suggesting an additional contribution to the catalysis, besides the release of Brønsted acid. This interaction and complex formation promotes the conversion of the substrates to 5-HMF and then to LA and formic acid, underlining an additional function of Lewis acid catalyst Sn⁴⁺, together with the intrinsic Brønsted acidity derived from its hydrolysis [67].

During the production of LA, substantial amounts of soluble and insoluble by-products are produced, even when hexoses are employed as starting feedstock. These compounds may include reaction intermediates, soluble and insoluble humins, polymeric substance and gas-phase components due to thermal degradation of reactants/products. They are generally deeply colored and their complete identification is still a challenge and their removal remains unsolved for most technologies. As an example, when Girisuta studied the acid-catalyzed decomposition of glucose to LA, substantial amounts of insoluble humins were formed, obtained from the acid-catalyzed decomposition of glucose and 5-HMF [56]. The author identified other possible by-products, called reversion products, like levoglucosan or 1,6-anhydro-β-D-glucopyranose, 1,6-anhydro-β-D-glucofuranose, iso-maltose and gentiobiose as shown in Figure 6.

In acidic solutions, the acyclic form of D-glucose (1) exists in equilibrium with its anomeric forms, i.e., α-D-glucopyranose and β-D-glucopyranose. The anomeric forms may be involved in a number of reactions leading to reversion products [68]. Intra-molecular condensation reactions produce anhydro

sugars, mainly levoglucosan and 1,6-anhydro- β -D-glucopyranose. Inter-molecular condensation reactions between two glucose units will give disaccharides such as isomaltose and gentiobiose. Several investigators have also found and isolated other type of disaccharides, i.e., (1-2)-linked and (1-3)-linked ones and/or anhydro sugars, giving low concentration of the reversion products [69]. LA can be reversibly dehydrated to α -angelica lactone (3-penten-4-olide) also in the absence of acid catalyst. In the presence of acid catalysts, under heating, α -angelica lactone can isomerize, thus forming a mixture containing also β -angelica lactone (3-penten-4-olide) and γ -angelica lactone (4-penten-4-olide). Besides, the angelica lactones can also dimerize giving heavier by-products [70].

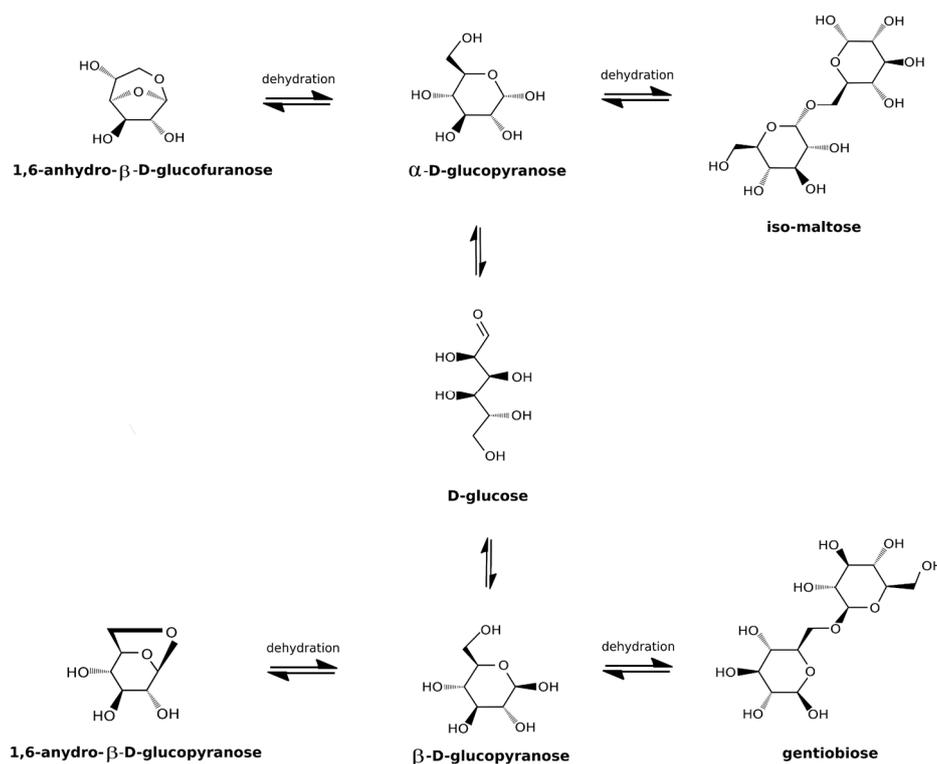


Figure 6. Reversion reactions of glucose in acid solutions [56].

Regarding the heating system, some experiments in Table 2 have been carried out under microwave (MW)-assisted heating, which is considered an effective alternative to the traditional one. MW absorption processes occur uniformly in the dielectric material, resulting in simultaneous heating of the whole volume of the sample, thus allowing better temperature homogeneity. Heat is directly transferred into the sample and the presence of the biomass containing polar oxygenated compounds in the reaction medium further contributes to the dielectric polarization. MW use enables reaching higher heating rate, homogeneous heat distribution, efficient control in the reproducibility of the LA synthesis, and remarkable energy and time saving.

The discussed literature suggests that the MW effect is mainly thermal. There is much debate on the presence of some nonthermal processes, which sometimes are called “microwave specific effects” [71,72]. These last are due to different interactions of the radiation by means of processes that are not inherently thermal, which should reduce the activation energy. These effects are never invoked for the above-discussed homogeneous reactions.

Although the hydrolysis of sugars in the presence of homogeneous catalysts are effective, their employment presents relevant disadvantages, such as the difficulty in acid recovery for recycling, the corrosion of equipment and environmental pollution. Moreover, the corrosive conditions demand the use of special material for reactor construction, thereby, increasing the capital investment and

operating costs. These drawbacks can be overcome by replacing homogeneous acid catalysts with heterogeneous solid ones. To date, a cost-effective, environment-friendly process in LA biorefinery employing homogeneous catalysts for simple sugars conversion is still largely needed.

2.2. Heterogeneous Catalysts in Water

As a result of the ever strengthening environmental regulations, solid acids are attractive for replacement of corrosive and harmful traditional mineral acids. These catalysts possess Brønsted and/or Lewis acidic sites. Heterogeneous Brønsted acids include acidic ion-exchange resins (e.g., Nafion-H, Amberlyst, Dowex), heteropoly acids and their derivatives (e.g., $H_{0.5}Cs_{2.5}[PW_{12}O_{40}]$). Solid Lewis acids include metal oxides and their sulfated/phosphated derivatives. Catalysts with mixed Brønsted and Lewis acid centers, including clays and zeolites, may be synthesized in order to have a careful balance of the overall acidity of the system. The use of heterogeneous catalysts for LA synthesis from soluble sugars is also well-established. Regarding their use for LA synthesis starting from simple sugar feedstocks, already in 1956 pioneering studies patented by Redmon underlined the use of the acidic cation exchange resin Amberlite IR-120, in the amount of 18%–19% of the total weight of the reaction mixture, for LA production from aqueous solutions of sugars or sucrose with minimal formation of insoluble humin by-products [73]. Especially in recent years, the range of heterogeneous catalysts studied for LA synthesis has been growing greatly, being an attractive and promising alternative to the homogeneous ones. Generally, solid catalysts can be easily separated from the reaction mixture and recycled, can work at high temperatures and their surface acidity can be tuned to improve selectivity [74]. These properties make solid catalysts suitable candidates for industrial use [27]. Moreover, heterogeneous catalysts are generally selective and do not present corrosion problems. However, the studies on heterogeneous catalysts are still limited if compared to homogeneous ones. This is due to many reasons. First of all, the strong adsorption of the produced LA on the catalyst surface lowers the overall yield to LA which can be obtained from reactions occurring on the bare surface of solid catalyst as well as within the pores of catalyst. Secondly, heterogeneous catalysts can be deactivated when used or recycled over a long period of time, due to the deposition of reaction heavy by-products, such as humins, on the surface of the catalyst or as a consequence of the leaching of the active acid species from the catalyst's surface. A summary of the recent works from the literature employing heterogeneous catalysts in water is provided in Table 3.

Table 3. C₆ sugars conversion in water in the presence of heterogeneous catalysts: reaction conditions.

Experiment	Substrate and Loading	Catalyst	Reaction Conditions	Y _{LA}	Ref.
25	fructose 5 wt %	Amberlyst 15	120 °C for 36 h 140 °C for 8 h	52% * 56% *	[55]
26	fructose 5 wt %	Nafion NR50	120 °C for 24 h	41% *	[55]
27	fructose 5 wt %	SBA-SO ₃ H	120 °C for 24 h	29% *	[55]
28	glucose 1 wt %	Al-Zr oxide	180 °C for 2 h	3.9 wt %	[75]
29	glucose 10 wt %	Zirconium phosphate	160 °C for 3 h	14 wt %	[27]
30	glucose 10 wt %	Amberlyst 70	160 °C for 3 h	21.7 wt %	[27]
31	glucose 1 wt %	CrCl ₃ + HY zeolite hybrid catalyst	145.2 °C for 2.45 h	55.2 wt %	[76]
32	glucose 1 wt %	CrCl ₃ + HY zeolite hybrid catalyst	160 °C for 3 h	40 wt %	[77]
33	glucose 0.5 wt %	FeCl ₃ /HY zeolite catalyst	180 °C for 4.17 h	66% *	[78]
34	glucose 13 wt %	Sulfonated graphene oxide	200 °C for 2 h	50 wt %	[79]
35	glucose 5 wt %	Sulfonated chloromethyl polystyrene resin	170 °C for 10 h	28.5 wt %	[80]

* In the paper the calculation of the reported yield is unclear.

The most traditional heterogeneous acid catalysts, such as the ion exchange sulfonated resins Amberlyst and Zr/Nb phosphates, have been widely employed. Starting from fructose, Son et al.

investigated the use of Amberlyst 15, leading to remarkable LA yield (56%, not specified if LA yield is in mol or wt %) working at 140 °C in water for 8 h (Experiment 25, Table 3) [55]. Weingarten et al. employed Zr phosphate and the resin Amberlyst 70 for the conversion of glucose to LA, achieving in water at 160 °C for 3 h the LA yield of 14 wt % and 21.7 wt %, respectively (Experiments 29 and 30, Table 3) [27]. As above reported for homogeneous metal halides, also for the heterogeneous systems the right balance of both Brønsted and Lewis acidity enhances the LA yield [81]. When the HY zeolite is modified by combining the zeolite with metal halides (such as CrCl₃ or FeCl₃), the resulting hybrid catalysts show an enhanced performance in glucose conversion. Lewis acid sites promote the isomerization of glucose into fructose, while the combination of Brønsted and Lewis acidity favors the dehydration/rehydration reaction to LA. In this regard, Ya'aini et al. studied the performances of hybrid catalysts comprising of CrCl₃ and HY zeolite with different weigh ratios in the production of LA from glucose [77]. The strength and the distribution of the acid sites were studied using NH₃-TPD and resulted markedly influenced by altering the CrCl₃ and HY zeolite ratios in the hybrid catalysts. The hybrid 1:1 catalyst resulted the system with the highest acidity, containing more reactive acid sites on the catalyst surface compared to the other hybrid systems. This system exerts the best catalytic performances, with 40 wt % of LA yield at 160 °C in 3 h (Experiment 32, Table 3). Very interesting performances are also obtained in the presence of graphene oxide-based systems with -SO₃H functional groups. In addition, in this case, the oxygenated and carboxylic groups together with Lewis sites caused by the electron inductive effect of the sulfonic groups enhance adsorption and isomerization of glucose on the catalyst surface. The layered structure of graphene oxide allows an efficient diffusion of reagent and products and the catalyst results thermally stable and recyclable. Finally, promising LA yields were obtained also in the presence of sulfonated systems. Upare et al. employing the sulfonated graphene oxide as catalyst for the conversion of glucose reached a LA yield of 50 wt % in water after 2 h at 200 °C (Experiment 34, Table 3) [79], whereas Zuo et al. studied for the same reaction a sulfonated chloromethyl polystyrene solid acid catalyst, reporting after 10 h in water at 170 °C the LA yield of 28.5 wt % (Experiment 35, Table 3) [80].

However, the majority of substrate loadings reported in Table 3 are under 10 wt %. Many authors have investigated the influence of the substrate loading on the synthesis of LA starting from fructose or glucose and employing homogeneous or heterogeneous catalysts. In all cases, they proved that an increase of the substrate loading beyond a certain level leads to a decrease of LA yield [27,54–56,62], due to a greater by-products formation, in particular humins. The reported concentrations can be interesting for a laboratory scale but are too low in order to be promising for industrial applications. In fact, employing low substrate loading (<10 wt %), the concentration of LA in the stream is low and its recovery difficult and expensive. LA has a high boiling point (245 °C), thus during its recovery through distillation, the solvent, which is the component present in much larger amount, must be evaporated, making the process very energy-intensive. Therefore, in order to scale-up its synthesis from the laboratory to the industrial scale, it is necessary to find an optimum compromise between substrate loading and LA yield/selectivity.

The reported results show that although the LA yields achieved employing heterogeneous catalysts can be, in some cases, promising, these are not yet satisfactory for the use of these systems at the industrial scale. In particular, the study of the life of the catalyst and its reactivation needs further improvement. Therefore, further research is still necessary for developing new catalysts which enhance the LA yield and progressively target towards raw and cheap biomass substrates.

2.3. Homogeneous and Heterogeneous Catalysts in Organic Solvents

Many solvents have been tested for LA production from sugars. Aprotic media have been tested for LA synthesis, such as dimethylsulfoxide (DMSO), dimethylformamide (DMF), dimethylacetamide (DMA), tetrahydrofuran (THF), methyl isobutyl ketone (MIBK), carbon tetrachloride, acetonitrile and ethyl acetate. DMSO is particularly selective towards 5-HMF because it suppresses the subsequent hydrolysis of 5-HMF to LA and formic acid [2,82]. Regarding aprotic solvents, Sanborn

reported the synthesis of LA from fructose sources using a polyethylene glycol and an end capped polyethylene glycol together with an acid catalyst, in the presence of polar aprotic solvents, such as 1-methyl-2-pyrrolidone, dimethylacetamide, dimethylformamide, dimethylsulfoxide, methyl ethyl ketone, methyl isobutylketone, acetonitrile and propionitrile. All the aprotic solvents were found suitable for the investigated reaction [83]. In this regard, another interesting example is that published by Mascal et al. who studied a two-step approach, employing 1,2-dichloroethane as solvent in the first step [84]. In this stage, the conversion of glucose into 5-(chloromethyl)furfural was performed employing concentrated HCl as catalyst in 1,2-dichloroethane heating at 100 °C for 1–3 h [84]. In the second step, the obtained 5-(chloromethyl)furfural was hydrolyzed to LA in water at 190 °C for 20 min [85], allowing a very high LA yield, up to 79 mol % from glucose, corresponding to 51 wt %.

Regarding the use of protic solvents, very few of them have been investigated for the production of LA. Brasholz et al. investigated the conversion of fructose to LA with HCl in the 1:2 mixture of H₂O:CH₃OH achieving after 1.33 h at 140 °C the LA yield of 46.4 wt % [35]. The majority of protic solvents, such as ethanol and butanol or mixtures of them with water, have been tested for the dehydration of fructose to 5-HMF [86,87]. On the other hand, protic solvents and in particular alcohols have been extensively employed for levulinate esters production, through the direct conversion from biomass by alcoholysis under acidic conditions. In fact, carbohydrate compounds can be easily converted into LA via 5-HMF through dehydration and hydration reactions, and LA is then transformed into its esters by esterification reactions [15,88].

Generally, the choice of the most suitable organic solvent is critical, due to the great influence of its properties on the reaction. First of all, the solubility of substrate in the solvent is a very important issue. In particular, the polarity plays a key role, because solvent dissolves solutes having similar polarities, thus, in the synthesis of LA from sugars, it is important to employ polar solvents, such as DMSO, DMF, DMA, THF, MIBK etc., which, as said previously, are the main organic solvents investigated for this reaction. However, other parameters can influence the solubility, such as solute size/volume and surface area, polarizability of the molecule and strength of the hydrogen bond between solvent and solute [89]. Solvents also affect the selectivity of the reaction. DMSO is particularly selective towards 5-HMF because it suppresses the hydrolysis of 5-HMF to LA and formic acid and the humins formation [2,62], due to the strong interaction between the C=O group in 5-HMF and DMSO, which limits hydration and intermolecular condensation reactions [90]. However, there are other issues that must be considered during the choice of the solvent, such as the feasibility of its separation and recycling, its cost and its environmental effects. Regarding the economic, technological and safety aspects, the majority of organic solvents show remarkable disadvantages: (i) high costs; (ii) high boiling points (DMSO, DMF, and DMA), which are directly related to the feasibility of their recycling, traditionally carried out through distillation; (iii) reactivity in the reaction conditions, such as THF that can be hydrolyzed in the presence of high amount of water and acid catalysts; (iv) safety problem, such as THF that can be oxidized in air into explosive peroxides; and (v) toxicity. For these reasons, organic solvents are not used on a large scale. In conclusion, the best solvent for the sustainable synthesis of levulinic acid from sugars is water, because it is greener, cheaper and less toxic than the organic solvents.

3. Catalytic Conversion of Cellulose and Raw Biomasses

3.1. Homogeneous Mineral Acids and Salts in Water

Cellulose is an important structural component of the primary cell wall of green plants and many researchers have studied its hydrolysis for the sustainable production of LA and of other value-added chemicals, because it is abundant in nature, non-edible and not competing with the food chain. Regarding raw biomasses, the preferred cheap raw lignocellulose sources include giant reed, switchgrass, miscanthus and poplar as promising examples of fast-growing grasses and trees, whereas sawdust, wheat straw, corn stover, sugarcane bagasse, municipal waste, fruit peels and pulp sludge are promising sources of low-value wastes to be enhanced and exploited. A summary

of the most recent works in the literature employing homogeneous catalysts in water is provided in Table 4. It is remarkable that for many raw and waste biomasses adopted in these experiments the complete composition analysis is not reported and, sometimes, also the total sugar content is unknown. For this reason, the LA ponderal yield is the unique tool to evaluate the effectiveness of the catalytic conversions.

Table 4. Polysaccharides and raw and waste biomasses conversion in water in the presence of homogeneous catalysts: reaction conditions.

Experiment	Substrate and Loading	Catalyst	Reaction Conditions	Y _{LA}	Ref.
36	cellobiose 5 wt %	HCl	MW, 170 °C for 0.5 h	29.9 wt %	[34]
37	cellobiose 5 wt %	H ₂ SO ₄	MW, 170 °C for 0.5 h	28.0 wt %	[34]
38	cellulose 1.6 wt %	HCl	180 °C for 0.33 h	44 wt %	[91]
39	cellulose 10 wt %	HCl	MW, 225 °C for 0.03 h	90% *	[92]
40	cellulose 5 wt %	HCl	MW, 170 °C for 0.83 h	31.0 wt %	[34]
41	cellulose 5 wt %	H ₂ SO ₄	MW, 170 °C for 0.83 h	23.0 wt %	[34]
42	cellulose 1.7 wt %	H ₂ SO ₄	150 °C for 2 h	43 wt %	[93]
43	cellulose 8.7 wt %	H ₂ SO ₄	150 °C for 6 h	40.8 wt %	[94]
44	cellulose 2 wt %	CrCl ₃	200 °C for 3 h	47.3 wt %	[62]
45	cellulose 20 wt %	CuSO ₄	240 °C for 0.5 h	17.5 wt %	[95]
46	waxy corn starch 1 wt %	HCl	MW, 165 °C for 0.58 h 165 °C for 1 h	53 wt % 54 wt %	[96]
47	giant reed 7 wt %	HCl	190 °C for 1 h	24 wt %	[97]
48	giant reed 7 wt %	HCl	200 °C for 1 h	15.8 wt %	[98]
49	giant reed 7 wt %	HCl	2 steps: 1st step: 80 °C for 2 h 2nd step: 190 °C for 1 h	22.8 wt %	[98]
50	giant reed 7 wt %	HCl	MW, 190 °C for 0.33 h	22 wt %	[99]
51	water hyacinth 1 wt %	H ₂ SO ₄	175 °C for 0.5 h	9.2 wt %	[100]
52	corn stalk 10 wt %	FeCl ₃	180 °C for 0.67 h	35 wt %	[101]
53	whole kernel grain sorghum 10 wt %	H ₂ SO ₄	200 °C for 0.67 h	32.6%*	[102]
54	wheat straw 6.4 wt %	H ₂ SO ₄	209.3 °C for 0.63 h	19.9 wt %	[103]
55	wheat straw 7 wt %	HCl	200 °C for 1 h	19.3 wt %	[104]
56	wheat straw 7 wt %	HCl	MW, 200 °C for 0.25 h	20.6 wt %	[104]
57	rice husk 10 wt %	HCl	170 °C for 1 h	59.4 wt %	[105]
58	sugarcane bagasse 11 wt %	H ₂ SO ₄	150 °C for 6 h	19.4 wt %	[106]
59	sugarcane bagasse 10.5 wt %	HCl	220 °C for 0.75 h	22.8 wt %	[107]
60	paddy straw 10.5 wt %	HCl	220 °C for 0.75 h	23.7 wt %	[107]
61	olive tree pruning 7 wt %	HCl	200 °C for 1 h	18.6 wt %	[104]
62	olive tree pruning 7 wt %	HCl	MW, 200 °C for 0.25 h	20.1 wt %	[104]
63	poplar sawdust 7 wt %	HCl	200 °C for 1 h	21.3 wt %	[104]
64	poplar sawdust 7 wt %	HCl	MW, 200 °C for 0.25 h	26.4 wt %	[104]
65	tobacco chops 7 wt %	HCl	200 °C for 1 h	5.2 wt %	[104]
66	post-harvest tomato plants 10 wt %	HCl	MW, 225 °C for 0.03 h	63%*	[92]
67	paper sludge 7 wt %	HCl	200 °C for 1 h	31.4 wt %	[104]
68	paper sludge 7 wt %	HCl	MW, 200 °C for 0.25 h	31.7 wt %	[104]
69	screen rejects 7 wt %	HCl	MW, 190 °C for 0.33 h	7 wt %	[108]
70	red alga <i>Gracilaria verrucosa</i> 6.7 wt %	H ₂ SO ₄	175 °C for 0.58 h	22.6 wt %	[109]
71	red alga <i>Gelidium amansii</i> 16.7 wt %	H ₂ SO ₄	2 steps: 1st step: 76 °C for 49.5 h 2nd step: 180 °C for 0.8 h	20.6 wt %	[110]
72	macroalga <i>Kappaphycus alvarezii</i> 6.7 wt %	H ₂ SO ₄	178 °C for 0.65 h	18 wt %	[111]
73	chitosan 10 wt %	HCl	MW, 225 °C for 0.03 h	95% *	[92]
74	chitosan 25 wt %	SnCl ₄	MW, 210 °C for 0.5 h	27 wt %	[112]
75	chitin 2.5 wt %	HCl	MW, 190 °C for 0.5 h	18.7 wt %	[34]
76	chitin 2.5 wt %	H ₂ SO ₄	MW, 190 °C for 0.5 h	21.6 wt %	[34]

* In the paper, the calculation of the reported yield is unclear.

When cellobiose is employed as starting substrate for LA production, yields of 29.9 wt % and 28.0 wt % were reached in the presence of HCl and H₂SO₄, respectively, after a treatment of 30 min at 170 °C under MW irradiation (Experiments 36 and 37, Table 4). Comparable yields were achieved when cellulose was used as starting substrate: LA yields of 31 wt % and 23 wt % in the presence of the homogeneous mineral acids, HCl and H₂SO₄, respectively, were obtained at 170 °C for 50 min under MW irradiation (Experiments 40 and 41, Table 4). Adopting traditional heating, Shen et al. obtained 44 wt % of LA yield starting from cellulose working in water at 180 °C for 20 min employing the mineral acid HCl (Experiment 38, Table 4) [91], whereas Girisuta et al. achieved the same LA yield (43 wt %) again starting from cellulose in water at 150 °C for 2 h in the presence of H₂SO₄ (Experiment 42, Table 4) [93], highlighting the efficiency of these homogeneous acid catalysts in the production of LA from cellulose. Generally, a low solid concentration results in a higher yield of LA. Peng et al. observed that the optimal concentration of substrate is very important in terms of the efficient use of cellulose and the final reached LA concentration [62]. Higher LA yield was achieved at lower substrate concentrations, but a higher LA concentration in the product stream is extremely favorable since it results in lower energy consumption upon purification of LA and also reduces the amount of wastewater produced [62]. However, it is not possible to increase infinitely the substrate loading due to the product feedback inhibition. In addition, too much or too little water inhibits the hydrolysis process, thus again underlining the importance to select the right substrate loading [107].

When raw lignocellulosic feedstocks are used, mineral acids are the most widely employed catalysts [2,3,113,114]. Licursi et al. used HCl in the conversion of giant reed to LA at 190 °C. After 1 h of reaction, LA yield of 24 wt % was reached (Experiment 47, Table 4) [97]. The same authors report similar LA yields in a two-step procedure carrying out the first stage at 80 °C for 2 h, followed by the second step at 190 °C for 1 h (Experiment 49, Table 4). When MW irradiation was employed, a comparable LA yield of 22 wt % was obtained from giant reed in water at 190 °C in the presence of HCl in only 20 min, thus confirming the great efficiency of MW energy (Experiment 50, Table 4) [99]. Wheat straw is another promising feedstock and many studies have adopted this substrate. Chang et al. studied the effects of temperature, acid concentration, liquid/solid ratio and reaction time on LA production from wheat straw in the presence of H₂SO₄, obtaining under the best experimental conditions of 209.3 °C for 37.6 min the LA yield of 19.9 wt % (Experiment 54, Table 4) [103]. The same yields (around 20 wt %) were achieved from wheat straw in the presence of HCl at 200 °C after 1 h when the reaction was performed in the autoclave and after only 15 min under MW irradiation (Experiments 55 and 56, Table 4).

The employment of renewable raw complex lignocellulosic feedstocks, from which mixtures of sugars are obtained, appears as an attractive alternative compared to the use of the pure monomeric sugars for the production of LA because it provides a sustainable cheap solution to the existing environmental problem, at the same time increasing the agribusiness and employment in rural sector, alongside the development of rural areas. However, there are still some drawbacks, which can affect the process economics, such as the irregularity of the biomass availability (the supply of biomass is not constant round-the-year), the variability in its composition and the logistics cost which results in the biggest bottleneck in the conversion of raw biomasses to LA. The transportation cost is not only influenced by the distance traveled, but also by the type of biomass and by the form in which it is transported. In this context, the integration of preprocessing of raw material and transport along with a careful supply chain planning might overcome many logistics issue. In addition, LA yields obtained from renewable inexpensive feedstocks are low, making imperative a proper optimization of the process which may result in higher LA yields. The complexity and heterogeneity of lignocellulosic biomass make pretreatment a mandatory step in its conversion to sugars and subsequently to LA in order to improve yield and reaction rates. On the other hand, the choice of pretreatment is of paramount importance and its severity depends on the complexity of the raw starting compounds [115,116].

In addition to these feedstocks, many low-value agricultural or algae wastes have been employed for the production of LA, thus enhancing and exploiting them to give an added-value compound.

In this case, HCl is the most widely employed acid catalyst, allowing promising results, as evidenced by the LA yields shown in Table 4. Bevilaqua et al. investigated the production of LA from rice husk using HCl as acid catalyst (Experiment 57, Table 4) [105]. Rice husk is a very abundant agricultural crop residue and approximately one ton of rice husk is left over for each four tons of rice produced. Taking into account that rice husk shows a content of polysaccharides higher than 50 wt %, it can be employed as feedstock in the production of LA, having this waste no other noble use. Yan et al. studied the production of LA from sugarcane bagasse and paddy straw in the presence of HCl at 220 °C for 45 min [107]. Sugarcane and paddy grow in southern China in very large quantities: the first one is mainly utilized to produce sucrose; whereas the second one is used as feed and raw material in the food industry. However, million of tons of sugarcane bagasse and paddy straw are discarded or incinerated. As a consequence, the possibility of using these biomass wastes directly for the production of LA represents an important step toward sustainability and green chemistry. Under the adopted reaction conditions the LA yields of 22.8 wt % and 23.7 wt % from sugarcane bagasse and paddy straw were reached respectively (Experiments 59 and 60, Table 4) [107]. Other interesting waste biomass sources for LA production are olive tree pruning and poplar sawdust. When olive tree pruning was employed, working in water at 200 °C in the presence of HCl, LA yields of 18.6 wt % and 20.1 wt % were achieved, in the absence and in the presence of MW after 1 h and 15 min respectively (Experiments 61 and 62, Table 4), highlighting the positive effect of MW energy. In the case of poplar sawdust, the beneficial effect of MW irradiation is even higher: adopting the same reaction conditions, already used for the conversion of olive tree pruning (water, 200 °C in the presence of HCl), LA yields of 21.3 wt % and 26.4 wt % were achieved, in the absence and in the presence of MW irradiation after 1 h and 15 min respectively (Experiments 63 and 64, Table 4). In addition, the positive MW effect was also confirmed in the conversion of paper sludge as raw starting substrate to LA, obtaining under the same reaction conditions adopted for olive tree pruning and poplar sawdust (water, 200 °C in the presence of HCl), LA yields of 31.4 wt % and 31.7 wt %, in the absence and in the presence of MW after 1 h and 15 min respectively (Experiments 67 and 68, Table 4). Finally, some considerable rejected waste fractions called “screen rejects” obtained from the papermaking process including both cellulose fibers and non-fibrous organic contaminants have been exploited by means of the hydrothermal route to give LA in agreement with the integrated recycled paper mill approach. Under MW irradiation, it was possible to reach the LA yield of 7 wt % working at 190 °C for 20 min (Experiment 69, Table 4). These examples highlight the real possibility to upgrade and exploit these wastes, otherwise allocated to disposal.

LA production process from raw or waste lignocellulosic biomass produces LA, furfural, and formic acid as main products, together with many other organic substances (e.g., acetic acid, amino acids, soluble lignins, extractives, and polymeric contaminants) and inorganic salts. The precipitation of mineral salts and sticky organics represents a severe risk because they might interfere with the conversion or separation steps by fouling and eventual clogging of the process units. Moreover, the release of basic components can neutralize part of the acid catalyst, thus requiring an increased concentration. Recently, the coproduced furfural has been used as an extraction solvent in the purification of LA itself, to extract LA and formic acid from the acidic hydrolysis reaction of biomass. Lee et al. have proposed a hybrid purification process with high energy efficiency combining liquid–liquid extraction of LA and formic acid with furfural and distillation [117,118].

A deep investigation on by-products was carried out for the acid-catalyzed hydrolysis of the water hyacinth plant to LA [100]. The authors found in solution organic acids, such as acetic acid and propionic together with the co-product formic acid, a big number of intermediate products arising from the cellulose and hemicellulose fraction of the water hyacinth leaves identified as monomeric sugars, glucose and arabinose, as well as furan derivatives, 5-HMF and furfural. The dark-brown solid was formed by a mixture of humin type by-products deriving from the acid-catalyzed decomposition of glucose and 5-HMF [59], as well as products of condensation reactions of C₅-sugars and furfural [119], residual insoluble lignin and ash. On the basis of the product composition and literature precedents for other biomass sources [120,121], the authors proposed a simplified reaction pathway for the

acid-catalyzed hydrolysis of the cellulose and hemi-cellulose fraction of the water hyacinth, as shown in Figure 7.

Another yet almost unexplored biomass for the production of LA is represented by algae. Preliminary studies have been reported on their exploitation, performing one-step or two-step acid hydrolysis, and promising yields, up to 22 wt %, were ascertained (Experiments 70 and 71, Table 4). When red macroalga *Kappaphycus alvarezii* was hydrolyzed at different temperatures, preliminary depolymerization of sugars to the main carbohydrate component galactose and lower amount of glucose was ascertained. The successive conversion to LA showed a similar reactivity for the two different C₆ sugars (Experiment 72, Table 4). This topic is particularly interesting for the future, also considering the possibility of extending it to the relevant amount of naturally-grown algae biomass collected from eutrophic water. Besides, algal biomass exhibits higher growth rates than many terrestrial plants, does not require soil, and, last but not least, has been proved less recalcitrant to hydrolysis, at least, into simple sugars for bioethanol production.

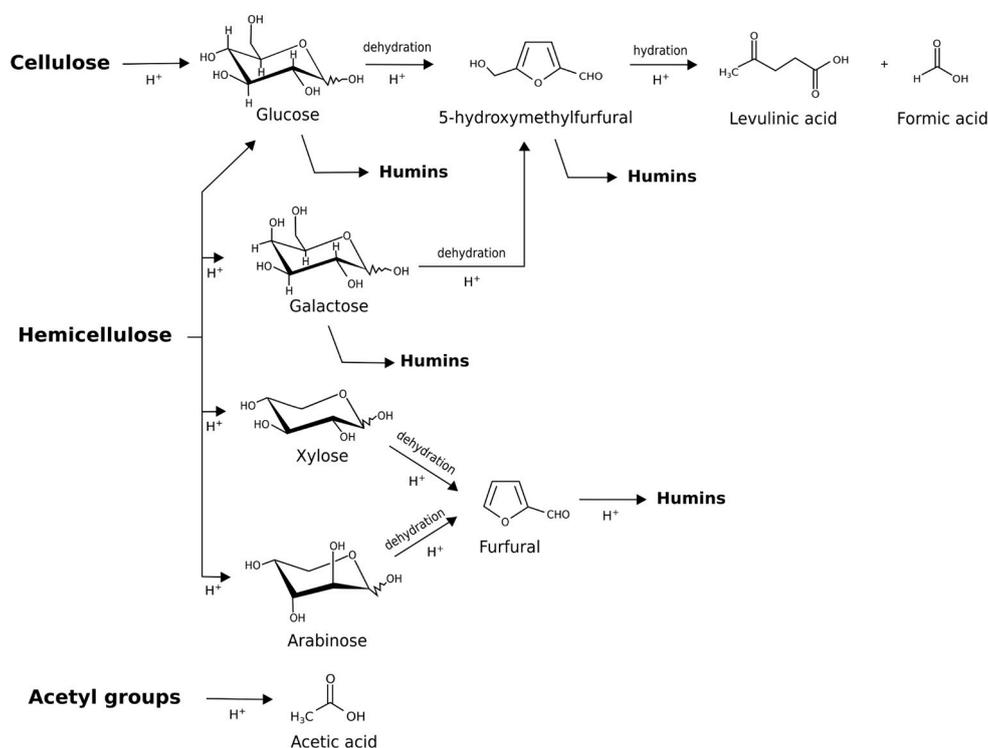


Figure 7. Simplified reaction network for the acid-catalyzed hydrolysis reaction of the water hyacinth plant [100].

It is remarkable that LA can be also obtained from chitosan and chitin with good yields that can surely be further improved (Experiments 73–76, Table 4). These unexplored raw materials are the second most abundant polysaccharide after cellulose, being obtained as industrial waste materials from seafood industry and fisheries. In addition, the exploitation of a chitin-containing fungal biomass and the purification of the obtained LA from unconverted glucosamine have been patented [122]. The optimized exploitation of all these innovative starting materials can represent a turning point for LA production.

Although many raw feedstocks have been investigated for LA production, there are several other potential raw materials that still remain almost unexplored for LA synthesis. These include municipal solid waste, domestic organic waste, cotton straw, reeds, seaweeds, etc.

When MW heating is adopted, generally an increase of LA yield respect to traditional heating is observed (compare Experiment 61 with 62 and 63 with 64, Table 4), adopting shorter reaction time.

The considered experiments have been generally carried out adopting constant temperature mode. As previously observed for the hydrolysis of simple sugars, also in the case of homogeneous catalysis on raw biomasses the MW beneficial role is described as thermal effect.

3.2. Heterogeneous Catalysts in Water

The sustainable production of LA from insoluble polysaccharides and raw biomasses in water slurry in the presence of heterogeneous catalysts is one of the greatest challenges that industry faces in the 21st century, moving towards a bio-based society. Although its importance, successful investigations are scarce due to the achieved low LA yields and further efforts are required to improve the related process, such as to increase the reaction rates, to shorten the reaction time and to make easier the recycle of the catalyst. The main reason of the generally low activity is related to the very difficult solid–solid interaction between the substrate and the catalyst itself. Besides, the deposition of solid by-products, such as humins and lignin-derived residues, can deactivate the catalyst surface. A summary of recent works from the literature employing heterogeneous catalysts in water is provided in Table 5.

Table 5. Polysaccharides and raw and waste biomasses conversion in water in the presence of heterogeneous catalysts: reaction conditions.

Experiment	Substrate and Loading	Catalyst	Reaction Conditions	Y _{LA}	Ref.
77	cellobiose 5 wt %	Sulfonated chloromethyl polystyrene resin	170 °C for 5 h	12.9 wt %	[80]
78	sucrose 5 wt %	Sulfonated chloromethyl polystyrene resin	170 °C for 10 h	16.5 wt %	[80]
79	cellulose 5 wt %	Sulfonated chloromethyl polystyrene resin	170 °C for 10 h	24 wt %	[80]
80	cellulose 5 wt %	Al-NbOPO ₄	180 °C for 24 h	38 wt %	[123]
81	cellulose 2.5 wt %	Sulfonated carbon	190 °C for 24 h	1.8 wt %	[124]
82	cellulose 2 wt %	ZrO ₂	180 °C for 3 h	39 wt %	[125]
83	cellulose 4 wt %	Zirconium phosphate	220 °C for 2 h	12 wt %	[27]
84	inulin 6 wt %	Niobium Phosphate	MW, 200 °C for 0.25 h	28.1 wt %	[104]
85	wheat straw 6 wt %	Niobium Phosphate	MW, 200 °C for 0.25 h	10.1 wt %	[104]
86	rice straw 6.6 wt %	S ₂ O ₈ ²⁻ /ZrO ₂ -SiO ₂ -Sm ₂ O ₃	150 °C for 0.17 h ^a	2.2 wt %	[126]
			180 °C for 0.17 h ^a	6.1 wt %	
			200 °C for 0.17 h ^a	9.3 wt %	
			240 °C for 0.17 h ^a	6.7 wt %	
			200 °C for 0.17 h ^b	14.2 wt %	
87	empty fruit bunch 1 wt %	CrCl ₃ + HY zeolite hybrid catalyst	145.2 °C for 2.45 h	15.5 wt %	[76]
88	kenaf 1 wt %	CrCl ₃ + HY zeolite hybrid catalyst	145.2 °C for 2.45 h	15.0 wt %	[76]
89	kiwifruit waste residue 6.7 wt %	20% Nb/Al oxide	190 °C for 0.17 h	13.8 wt %	[127]
			190 °C for 0.25 h	14.7 wt %	

^a 6.6 wt % acid concentration; ^b 13.3 wt % acid concentration.

The employment of solid heterogeneous catalysts for LA synthesis starting from insoluble polysaccharides and raw biomasses represents still a challenge, but appears more difficult in comparison to the use of homogeneous ones. In fact, in a solid-insoluble-substrate/solid-catalyst system the mass transport is very troubled and the heterogeneous catalysts have not the ability, characteristic of the homogeneous one, to deliver the active species into the solid or swelled biomass [128]. For these reasons, the heterogeneous systems result more suitable when water-soluble carbohydrates are processed. However, interesting examples of heterogeneous catalysts applied to insoluble polysaccharides and raw biomasses are reported in the literature. Recently, Zuo et al.

studied a sulfonated chloromethyl polystyrene solid acid catalyst for the catalytic conversion of cellulose into LA, obtaining 24 wt % LA yield performing the reaction at 170 °C for 10 h in water (Experiment 79, Table 5) [80]. The authors employed the same catalytic system at 170 °C in water also for the conversion of the disaccharides cellobiose and sucrose to LA, achieving the LA yields of 12.9 wt % and 16.5 wt % after 5 and 10 h, respectively (Experiments 77 and 78, Table 5). Another promising catalyst is zirconium dioxide, as reported by Joshi et al. who used this system for the conversion of cellulose to LA at 180 °C [125]. After 3 h of reaction, total conversion of cellulose was achieved together with a remarkably high yield to LA, equal to 39 wt % (Experiment 82, Table 5). Weingarten et al. investigated the possibility to use zirconium phosphate as heterogeneous catalyst in the same reaction, again starting from cellulose, reaching in this case at 220 °C for 2 h the LA yield of 12 wt % (Experiment 83, Table 5) [27]. A similar catalyst, niobium phosphate doped with several amount of aluminum, was employed in the synthesis of LA from cellulose (Experiment 80, Table 5). The authors investigated the influence of the modification of the acid properties of the catalyst on the selectivity and yield to LA. An appropriate acid strength is crucial for the conversion of carbohydrates to LA, especially in the rate-determining opening of the H-bonded cellulose structure. The authors found that the strength of Brønsted acid sites, but especially that of Lewis ones, increased with the increasing of Al amount and LA yield resulted correspondingly enhanced, reaching the highest value (38 wt %) for an Al content of 2.49%. This result highlights as a tunable strength of the two types of acid sites results a fundamental parameter in order to obtain high LA yields.

Niobium phosphate was also employed in the catalytic hydrothermal conversion of inulin and wheat straw to LA under MW irradiation. After 15 min at 200 °C the LA yield of 28.1 wt % and 10.1 wt % starting from inulin and wheat straw respectively were obtained without appreciable formation of solid by-products (Experiments 84 and 85, Table 5).

These heterogeneous acid catalysts, due to their significant polar character, generally are strong microwave absorbers which can strongly interact with the MW field [129]. By this way, not only the liquid phase but also the solid component, including the catalytic species, are efficiently and quickly heated, but also in this case the positive role of MW is due to simple thermal effects. Among the acid catalysts listed above, it is considerable to highlight the use of the heterogeneous super-acid catalyst named $\text{S}_2\text{O}_8^{2-}/\text{ZrO}_2\text{-SiO}_2\text{-Sm}_2\text{O}_3$ employed by Chen et al. in the conversion of rice straw to LA, achieving LA yields around 10 wt % working in the temperature range of 150–200 °C for 10 min in water (Experiment 86, Table 5) [126]. Finally, another interesting example showing the employment of heterogeneous catalysts to waste residues is reported by Wang et al. (Experiment 89, Table 5) [127]. Today, the kiwifruit industry is booming worldwide. Kiwifruit is widely cultivated in southern China and the total production was over 1.17 million tons in 2014. About 37% of the fruit was processed into juice and chips, with residual peels accounting for 3–5 wt % of the fruit. In almost all kiwifruit genotypes cultivated, the levels of fructose and glucose are very high, making them a promising candidate for the production of LA. At the moment, the kiwifruit waste residues, containing monosaccharides, are discarded. In this regard, the authors have studied the catalytic conversion of kiwifruit waste residues to LA in water at 190 °C in the presence of 20% Nb/Al oxide as catalyst, achieving after 15 min of reaction the LA yield of 14.7 wt % (Experiment 89, Table 5). The achieved result is remarkable and the catalyst remains active up to five recycles. The promising performance is due to the particular properties of the catalyst, such as robust water-tolerance, high surface area and acidity. Regarding the latter, the authors investigated different Nb loading of Nb/Al oxides, proving that the total acid content decreases with the increase of Nb/Al ratio, instead the concentration of strong acid sites increases. Therefore, 20% Nb/Al oxide is the most promising catalyst, showing the best compromise between the amount of strong acid sites and total acidity and a suitable Brønsted to Lewis acid site ratio, which allowed to achieve the highest LA yield.

As previously underlined for LA synthesis from sugars, the substrate loadings reported in the literature are generally lower than 10 wt % also starting from polysaccharides and raw biomasses (Tables 4 and 5). This is justified not only by the high amount of by-products formed when high

feedstock loadings are adopted, but also by mechanical mixing problems in the reactor, due to the high solid substrate/solvent ratio [27]. Therefore, the consequent drawbacks previously reported for sugars are more serious.

The reported results show that the LA yields achieved using heterogeneous catalysts are not yet satisfactory for the use of these systems at industrial scale and further investigations are needed. In this regard, an extensive investigation of the surface characteristics, density of acid sites, shape, selectivity, porosity and mechanical and physicochemical properties of the catalysts appears necessary to gain a proper understanding of the catalyst role and thereby allow increased LA yields to be achieved. It is also important to mention that the toxicity of heavy metals limits its application for LA production. However, considering these drawbacks, heterogeneous catalysts are desirable in the future for industrial uses, due to their easier recovery and recyclability than homogeneous ones.

3.3. Monophasic Organic Solvents

When cellulose and raw biomasses are employed as starting substrates, monophasic systems employed for the production of LA are mainly those made of two completely miscible solvents, such as the system composed of H₂O (10 wt %) and GVL (90 wt %) which is the most widely adopted. Table 6 shows some interesting examples (Experiments 90–93, Table 6).

Table 6. Polysaccharides and raw and waste biomasses conversion in monophasic organic solvents: reaction conditions.

Experiment	Substrate and Loading	Catalyst	Reaction Conditions	Y _{LA}	Ref.
90	cellulose 2 wt %	[C ₄ H ₆ N ₂ (CH ₂) ₃ SO ₃ H] _{3–n} H _n PW ₁₂ O ₄₀ , n = 1, 2, 3	140 °C for 12 h in H ₂ O/MIBK (1/10 v/v)	63.1 wt %	[130]
91	cellulose 4 wt %	Sulfonated chloromethyl polystyrene resin	170 °C for 10 h in H ₂ O-GVL (10/90 wt %)	47 wt %	[80]
92	cellulose 2 wt %	Amberlyst 70	160 °C for 16 h in H ₂ O-GVL (10/90 wt %)	49.4 wt %	[131]
93	corn stover 6 wt %	Amberlyst 70	160 °C for 16 h in H ₂ O-GVL (10/90 wt %)	38.7 wt %	[132]

Zuo et al. investigated the conversion of microcrystalline cellulose into LA catalyzed by a sulfonated chloromethyl polystyrene resin, obtaining at 170 °C yields to LA up to 65.5 mol % (which corresponds to 47 wt %) at complete substrate conversion [80]. The authors attributed the high yield of LA to the fact that GVL can solubilize cellulose and, therefore, improves the interactions between cellulose and the solid acid catalyst (Experiment 91, Table 6). Alonso et al. converted cellulose to LA after 16 h of reaction at 160 °C using the sulfonated resin Amberlyst 70 as catalyst in a solution of 90 wt % GVL and 10 wt % H₂O as solvent obtaining promising LA yield (49.4 wt %) compared to the low yield (13.6 wt %) achieved in 100% water (Experiment 92, Table 6) [131]. The authors also studied in the H₂O-GVL solvent the conversion of the real biomass corn stover to LA, achieving a remarkable LA yield (38.7 wt %), at 160 °C after 16 h (Experiment 93, Table 6). According to the authors, the good performances of Amberlyst 70 in the H₂O/GVL solvent are due, as previously reported by Zuo, to the capacity of GVL of solubilizing the cellulose. In addition, GVL swells the Amberlyst 70 resin, thereby improving the diffusivity through the pores and increasing its catalytic activity.

The employment of fluorinated solvents like perfluorohexane has been also studied for biomass conversion to LA [132]. However, the harmful properties and the high cost of this class of solvents preclude them from an extensive use. It is clear that the choice of the most suitable organic solvent is critical and in addition to the suitability of solvents in terms of substrate conversion, product selectivity and yields, other important factors to be taken into consideration are their environmental impact and separation and recycling efficiency.

3.4. Biphasic Systems and Ionic Liquids

In the synthesis of LA, biphasic solvent systems are used when an organic phase is immiscible with the aqueous phase and the first one has a significantly higher partition coefficient for LA with respect to water, thus allowing easier recovery.

GVL is very often employed as component in biphasic systems for the conversion of biomasses to LA. A biphasic system, consisting of GVL and an aqueous solution of HCl (0.1–1.25 M) containing NaCl, has been reported by Wettstein et al. for LA production [133]. The reaction was carried out at 155 °C and was found that majority of LA was extracted by GVL solvent, achieving after 1.5 h yields from cellulose to LA of 72 mol %, which corresponds to 51.6 wt % [133].

A biphasic reactor system consisting of an aqueous layer containing the acid catalyst, such as 1 M H₂SO₄ or zeolite (ZSM-5), and an organic layer consisting of organic solvent, such as 2-*sec*-butylphenol (SBP), 4-*n*-hexylphenol (NHP) or 4-propylguaiacol, have been developed by Gürbüz et al. for the production of LA through the conversion of corn stover to furfural carried out at 170 °C, followed by the reduction of furfural to furfuryl alcohol which is further hydrolyzed to LA at 125 °C [134].

The choice of the most appropriate organic solvents is very difficult due to the limitation of biphasic solvent systems. In fact, small amounts of product are left in the aqueous phase reducing yields especially when the partitioning is inadequate. In order to overcome the problem of low partitioning, large amounts of solvent have to be used, making the process high energy demanding in the subsequent product and solvent recovery step. Moreover, these multi-solvent processes require a relatively complex plant design, unavoidably increasing capital costs. As a consequence, only the organic solvents with high partition coefficient for LA with respect to water can be used because they reduce the required volume, lowering the energy input for the recovery of LA. This opens the way to novel solvents to be explored which promise an increase in the product yield and which can be used at larger scale with low economic charge.

In recent years, research on ionic liquids has gained great attention due to their wide employment as solvents as well as catalysts. Ionic liquids are salts consisting of ions which are liquid at ambient temperatures or below 100 °C [135]. The stability, the low vapor pressure, the easy separation and recyclability of ionic liquids, coupled with the fact that their physical and chemical properties can be easily tuned by varying the ions, are some of the important reasons for the intense interest for the use of these solvents to convert raw biomass into added-value products [136–142]. Catalytic conversion of biomass to LA in the ionic liquid [EMIM][Cl] using a hybrid catalyst (CrCl₃ and HY-zeolite) has shown to yield 46 wt % of LA from cellulose working at 61.8 °C for 14.2 min. Under these conditions 20 wt % yield was obtained from empty fruit bunch compared to 15.5 wt % yield achieved in the absence of the ionic liquid [110]. Some attempts have also been made to selectively convert cellulose into LA using MW-assisted synthesis in SO₃H-functionalized ionic liquids: after 30 min at 160 °C a LA yield of 39.4 wt % was reached [142]. Nevertheless, ionic liquids also show important drawbacks. First of all, their status as “green solvents” has been questioned: the fact that their properties can be tuned by changing the involved ions leads to an enormous diversity in both the number and properties of ionic liquids, making both the method of production of the ionic liquid and its properties (toxicity, explosivity, biodegradability, etc.) not completely environment-friendly [143]. Another disadvantage of ionic liquids is their high viscosity which reduces mass transfer in the liquid, leading to only a small fraction of the liquid to be in contact with the biomass. Moreover, the low vapor pressure of ionic liquids, which is considered one of their ‘green’ characteristics, prevents an easy recovery of used ionic liquids via distillation, requiring alternative methods for separating the reacting species and recovering the ionic liquid [144]. Moreover, the effect of moisture in the feedstock on the performance of ionic liquids is another aspect that needs to be considered, because some chemical properties, such as anionic basicity, can be adversely affected by the presence of water [145], whereas physical properties, such as viscosity, can actually be improved by the addition of water [144]. Furthermore, ionic liquids can also lead to severe corrosion of numerous metals, especially in the presence of water, leading

to process equipment damage and additional cost [146]. As a consequence, the need to purify them after recycling, together with their potential sensitivity to moisture and oxide impurities represent additional challenges, not already solved. Finally, another limitation in the employment of ionic liquids is their high cost, typically between two and one hundred times that of organic solvents [147]. At the moment, all these elements have limited their perspectives for use at industrial scale.

4. Biochar Recovery and Exploitation Possibilities

The hydrothermal conversion of biomass feedstock produces a carbonaceous charred solid by-product, named “hydrochar”, which is separated from the hydrolysate solution by filtration. This solid includes mainly humins deriving from the degradation of furanic intermediates of C₅ and C₆ sugars source, which have undergone aldol addition/condensation reactions [22,148]. Furthermore, the influence of the degraded lignin fraction should be considered, if lignocellulosics are used as starting feedstock, thus further contributing to the increase of aromaticity degree of the final hydrochar [149]. In addition, the chemical composition of the hydrochar may be even more complex, if the starting feedstock is a waste material, such as bio-solids, municipal wastes, paper mill sludge, and so on. On this basis, it is noticeable that the yield and properties of the char strongly depend on the composition of the starting feedstock and the adopted process conditions [150,151].

The hydrochar recovered after LA production could be used as solid bio-fuel within the same biorefinery plant, having a heating value which is typical of that of the traditional lignite coal [97,152] or as a storable solid fuel for energy generation (via co-combustion or use in carbon fuel cells). The higher heating value (HHV) of the hydrochar is always higher than that of the starting untreated biomass [25], because of the predominant dehydration route which has occurred during the hydrothermal treatment, having released furans (e.g., furfural and 5-hydroxymethyl furfural) and organic acids (levulinic acid, formic acid) into the liquid phase. The hydrothermal treatment of a carbohydrate feedstock is not limited to the production of LA but can be applied for the production of other organic acids [153] and, from the perspective of the solid residue, different kinds of hydrochar can be obtained. However, the available information on hydrochar are limited and, therefore, many works are incomplete and most of them report low yields towards LA without explaining the amount and the nature of by-products. The amount of generated byproduct wastes increases when moving from raw to waste starting materials and therefore new exploitation possibilities of these biowastes, in addition to the traditional energy recovery must be evaluated and developed, thus ensuring the sustainability of the entire process. In the field of the hydrothermal route, the state of the art on hydrochar suggests that it is certainly a valuable resource, having a chemistry which is typical of carbon materials. The main proposed alternative use of the hydrochar is for the synthesis of porous activated carbons, by suitable physical and chemical activation procedures [149,154]. However, from a different perspective, new applications have been studied for environmental applications, such as a soil amendment for the increase of soil fertility, while providing a long-term carbon sink [155,156] and as an efficient adsorbent in environmental remediation processes [157,158]. Furthermore, hydrochar is suitable for a wide range of other important applications in modern nanotechnology, including catalysis and energy storage and generation [159].

Recently, different and smart approaches for hydrochar exploitation have been proposed, which involve the use of the “humin-like” hydrochar as starting feedstock for new upgrading reactions. Hoang et al. have studied the exploitation of humins via dry reforming [160]. The volatile organic components released during heating are mainly phenols, aromatic hydrocarbons, and furans, which can be used as a source of potential chemicals or further reformed to syngas/H₂ in the second stage, thereby converting the whole humin feedstock. Due to the recalcitrant behavior of this thermally stable bio-material, its non-catalytic dry reforming is very difficult, but the authors have significantly improved the kinetics by adopting Na₂CO₃ as alkali catalyst [160]. In another research, Wang et al. have recently studied the catalytic hydrotreatment of C₆-derived humins, by using formic acid as hydrogen donor in isopropanol or hydrogen gas, achieving promising results (humin conversion

about 70%) with Ru/C catalyst. The authors have partially depolymerized the carbonaceous humins, producing substituted alkylphenolics, naphthalenes, and cyclic alkanes, which can be used as liquid biofuels or as a source for interesting bulk chemicals after fractionation [161].

These new applications of the hydrochar add value to this waste material and provide a synergistic and holistic approach that could advantageously be integrated into future biorefinery schemes beyond its direct use as a solid fuel. The effective utilization of hydrochar requires further experimental research and investigation in terms of relationships among feedstock composition, physico-chemical properties and process conditions to produce hydrochar with characteristics required for industrial applications.

5. Conclusions and Future Perspectives

The synthesis of LA from renewables can be achieved from C₆-monosaccharides, employed moving from monomeric sugars up to the cellulose component of real raw and waste biomass. A closer inspection of the described results reveals that, although monosaccharides like fructose and glucose offer the highest product yields, the use of polysaccharides and in particular of raw and waste biomasses is required for the industrial-scale production sustainability. In order to achieve these goals, improvements are needed in the catalyst and solvent selection. In the recent years the positive cooperative effect of Lewis and Brønsted acid sites has been evidenced both for homogeneous catalysts and for heterogeneous ones and their right combination enhances the yield to LA. Heterogeneous catalysts are easier to recover and recycle, but they give lower LA yields than homogeneous systems and need to be regenerated after consecutive runs. The industrial scale adoption of heterogeneous catalysts is not still feasible, mainly due to their difficult reactivation/recycling, caused by the formation of solid humin by-products, which are found to be very thermally-stable. This drawback is particularly relevant for raw lignocellulosic biomasses, due to the presence of the degraded lignin fraction in the final hydrochar. At the current state of the art, heterogeneous catalysts are employed only at laboratory scale with simple sugars as starting feedstocks. In this case, the production of humins is better controlled, but the problem of higher cost of these “ideal” feedstocks (respect to the lignocellulosic ones) strongly limits the scale-up on larger scale. Further research is surely necessary to solve these problems and develop new cheaper, thermally-stable and easily recyclable heterogeneous catalysts.

On the other hand, the use of homogeneous catalysts, in particular HCl and H₂SO₄, offers greater flexibility, being recovered quite easily from the reaction medium by distillation and re-used. Anyway, the problem of corrosion of the equipment is only partially solved by the use of acid-resistant materials, which are currently used mainly at laboratory scale, given their high cost. The combined use of dilute mineral acids and high temperature/long reaction time actually represents the best compromise for LA production, reducing the corrosion of the equipment.

The use of raw and waste biomass is attracting increasing interest and the use of novel non terrestrial resources such as algae and chitin/chitosan can represent a significant turning point. For many promising but less common raw and waste biomasses the complete composition analysis is not reported and, sometimes, also the total sugar content is unknown. For this reason, the LA ponderal yield is the unique tool to preliminarily evaluate the effectiveness of the catalytic conversion, but further investigation is necessary.

In addition, the recovery and exploitation of the solid residue obtained in LA production process is another important aspect to be addressed from a sustainable biorefinery perspective.

In conclusion, the main challenges that have to be tackled in the near future can be summarized into the following points: (i) improve the design and the use of efficient heterogeneous catalysts with high recyclability; (ii) enhance their selectivity and the catalyst lifetime; (iii) develop new strategies to obtain LA from raw and waste biomasses; (iv) optimize the exploitation of the solid residues obtained in the LA production processes; (v) upgrade the current technologies to produce pure LA through more sustainable approaches; and (vi) scale up the process going beyond the economic and technological barriers.

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