

1 *Review*

2 **New frontiers in the catalytic synthesis of levulinic** 3 **acid: from sugars to raw and waste biomass as starting** 4 **feedstock**

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

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

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31 **1. Introduction**

32 One of the greatest challenges that industry faces in the 21st century is the transition from a
33 fossil-fuel based economy to one based on renewable resources, driving the search ~~of for~~ new
34 alternative renewable feedstocks for the production of chemical building blocks [1-6]. In [particular](#)
35 [this regard](#), the exploitation of lignocellulosic biomass is receiving an increasing attention due to its
36 renewability, abundance, low value and carbon-neutral balance. Among the target products,
37 levulinic acid (LA) is the main compound of biomass hydrolysis which has been classified by the
38 United States Department of Energy as one of the top-12 promising building blocks [7]. ~~and LA~~
39 represents a [valuable promising](#) intermediate for the synthesis of several chemicals for applications
40 in fuel additives, fragrances, solvents, ~~oil additives~~, pharmaceuticals, and plasticizers [8-13]. LA,
41 also known as 3-acetylpropionic acid, 4-oxovaleric acid, or 4-oxopentanoic acid, is a very interesting
42 platform chemical, because of its versatile chemistry, including one carbonyl, one carboxyl and α -H

43 | in its inner structure, [looking like remembering](#) a short chain and non-volatile fatty acid. Some
 44 | interesting data about ~~its~~ physical properties of LA are reported in Table 1 [14-16].

45 | **Table 1.** Some physical properties of 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 $\Delta_{\text{vap}}H_m$ (kJ/mol)
116.2	1.4796	1140	4.5	306-308	518-519	-2417	74.4

¹ Value at 293 °K.

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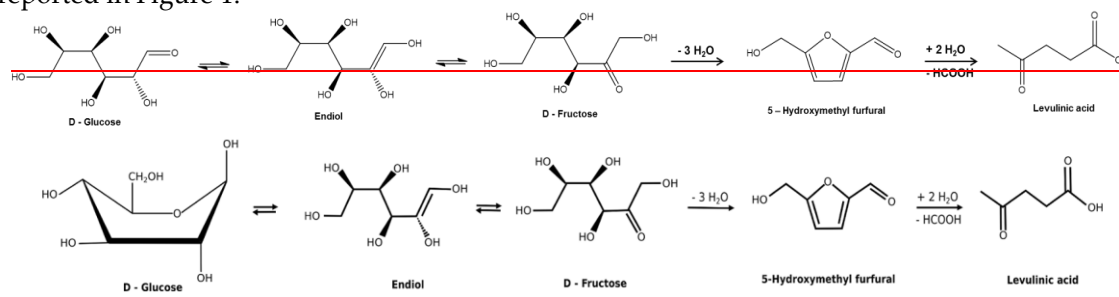
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By taking into account the chemical structure of LA, carboxylic and then carbonyl groups are very reactive electrophilic centers towards nucleophilic attack. Furthermore, from the point of view of the acidity properties, LA has higher dissociation constant than saturated acids, thus its corresponding acidity is stronger. Lastly, LA can be isomerized into the enol isomer, owing to the existence of a carbonyl group. Levulinic acid can be produced ~~by on~~ 3 different process routes. The first one is a 5-step route from the petrochemical 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.

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 ~~as well as from mono and disaccharides~~ [18]. ~~In these cases, the~~ hydrolysis proceeds via formation of 5-hydroxymethylfurfural (5-HMF) intermediate. ~~In more detail, s~~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.



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

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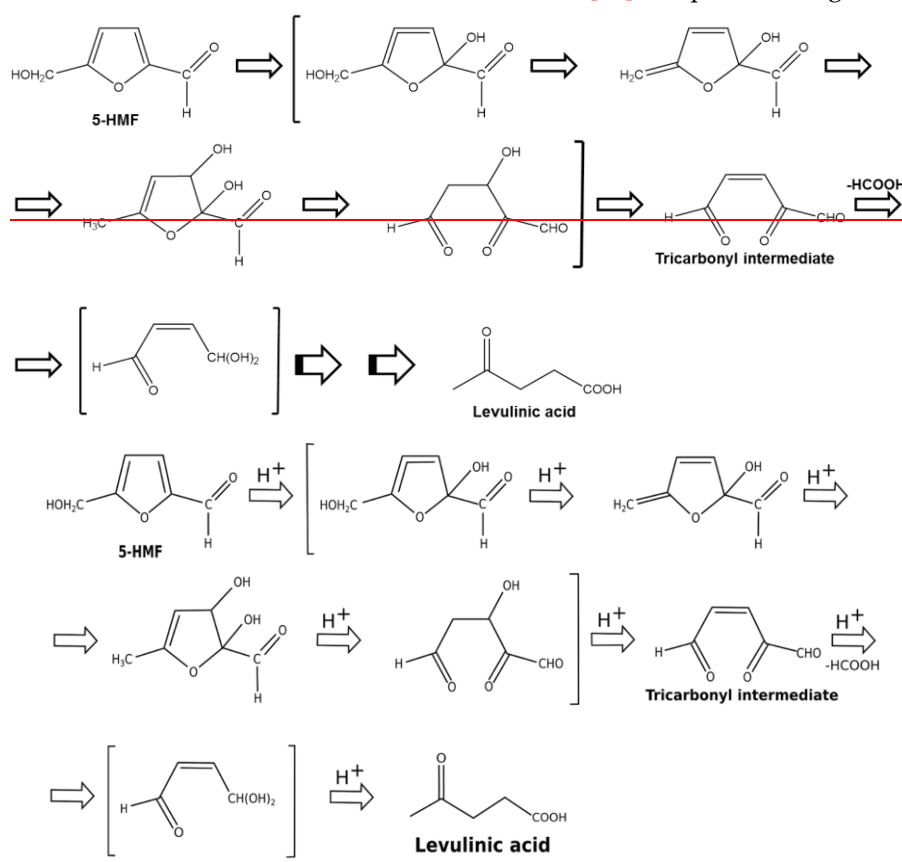
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Antal et al. proposed that 5-HMF is produced from fructose via cyclic intermediates [19]. Recent studies have further confirmed that 5-HMF originates from the acid-catalyzed dehydration of C₆-sugars in the furanose form [20,21]. The first step is the formation of 5-HMF by a triple dehydration step. 5-HMF is an unstable molecule and ~~tends~~ easily ~~to~~ condenses, together with sugars and sugar degradation products, into black insoluble charred materials ~~s~~ often ~~called referred to as~~ "humins" [22-25]. In an extensive review on the 5-HMF formation, Van Putten et al. have ~~shown 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 which~~ is tentatively explained by the need for glucose to first isomerize to fructose via ~~the an~~ 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. ~~As a result of these The~~ harsher reaction conditions ~~adopted~~ for aldoses, ~~cause the formation of~~ higher amounts of humins ~~are formed~~. 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 92.022 kJ/mol), the glucose to fructose ~~isomerisation conversion~~ is very weakly endothermic (8.42 kJ/mol), whereas the other

83 steps, including additional water elimination and rehydration to form LA, are exothermic (from
 84 [16.74](#) to [133.932](#) kJ/mol) [28]. Elevated temperatures and aqueous reaction environments ~~are also~~
 85 ~~predicted to~~ make the dehydration reaction steps thermodynamically more favorable. A proposed
 86 rehydration mechanism of 5-HMF into LA [in acid environment](#)[29] is reported in Figure 2 [29].



89 **Figure 2.** Detailed mechanism for the formation of LA from 5-HMF [in acid medium](#).

90 Hydration of 5-HMF consists in the addition of a water molecule to the C-2–C-3 olefinic bond of
 91 the furan ring, leading to an unstable tricarbonyl intermediate, which quickly decomposes to LA and
 92 formic acid (HCOOH), in stoichiometric amount [22,30]. However, Flannelly et al. have recently
 93 reported that formic acid is produced even in excess to LA respect to the stoichiometric amount
 94 during the acid hydrolysis of hexose carbohydrates, thus highlighting the potentiality of this
 95 co-product coming from LA synthesis [31]. In fact, formic acid is a valuable product in its own right
 96 and can be used as a commodity in the chemical and textile industry, as a catalyst, a hydrogen
 97 carrier and a road salting component [4, 32].

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

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

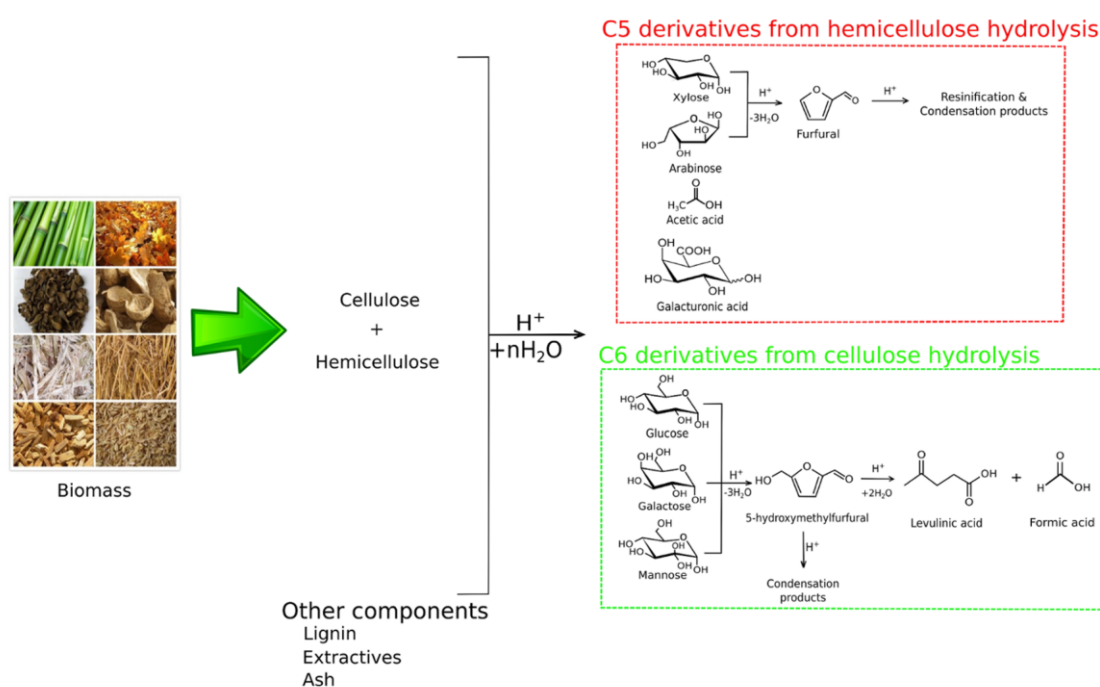


Figure 3: Reaction network of the acid-catalysed hydrolysis of cellulose and hemicellulose in lignocellulosic biomass.

Two different reaction regimes for the conversion of carbohydrates-containing biomass into LA₂ that differ in the reaction conditions, but not essentially in the reaction pathway, can be distinguished ~~as follows~~: (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~~levulinic acid, ~~at complete reached when the molar yield is complete~~, 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, t~~The really obtained yields are significantly lower. ~~The appropriate optimization of the hydrolysis reaction should take into account that the entire feedstock is not available to the conversion into LA, but only the hexose fraction.~~

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:

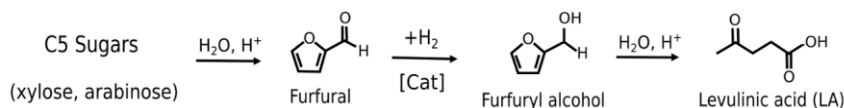


Figure 4. C₅ path to give levulinic acid.

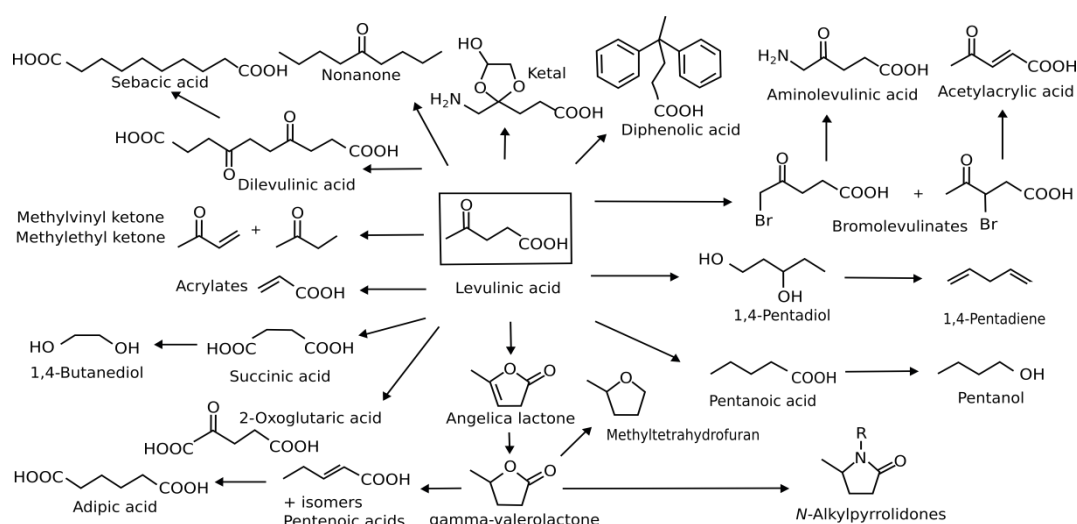
The overall process involves 3-steps: *i*) an acid-catalyzed hydrolysis of hemicellulose polymer and dehydration of the C₅ sugars to furfural [386,397]; *ii*) the hydrogenation of furfural to furfuryl alcohol; *iii*) the acid-catalysed hydrolysis of furfuryl alcohol to the desired LA [18,4038]. Yields in LA are in the range 83–93 mol % [23]. A modification of the above synthetic strategy employs alcohols ~~rather than instead of~~ water as ~~the~~hydrolysing agent ~~of the last step furfuryl alcohol-to-levulinic acid, thus directly recovering levulinate esters, with yields in the range.~~ This gives the corresponding levulinate esters as the final product and yields have been reported to be in the range

137 95-98 mol %. The use of an alcoholic solvent can be extended also to the C₆ route, after 5-HMF
 138 production, giving also in this case levulinate ester as the main product.

139 The C₅ pathway is attractive, but still too limited, due to the excessive formation of by-products
 140 in the reaction medium [41]. The advantage of this route is that the esters have a lower boiling point,
 141 thus allowing distillation as means of purification and more importantly are less prone to give
 142 angelicalactone upon heating. Furthermore This, the method starting both from furfural and
 143 furfuryl alcohol is attractive and its feasibility of both methods mainly depends on the type and cost
 144 of the possible feedstocks. Furfural prices typically is in the range between 700\$/t and 1500\$/t,
 145 whilst and furfuryl alcohol is 1500 \$/t or even higher. The high costs of these precursors This would
 146 make the production of the levulinic acid by the C₅ path too expensive in respect to that the by the
 147 simple hydrolysis route C₆ one, the latter being currently the main one developed at industrial scale.

148 Currently, The first researchers to realize the potential of levulinic acid as building block for a
 149 wide range of chemicals were Manzer [42, 43], Werpy and Petersen [7] and Bozell [44]. levulinic
 150 acid is adopted as specialty chemical in pharmaceutical, cosmetic, and food applications. As already
 151 detailed earlier the market size for levulinic acid is very limited, and it is thus unlikely that these
 152 would be able to absorb large quantities of levulinic acid, which are anticipated to enter the
 153 marketplace. As such, further conversion routes of levulinic acid are essential to create new
 154 outlet markets. It is eminent that these new routes will need to be developed in parallel to the
 155 realization development of efficient levulinic biorefineries. The pioneering researchers to realize the
 156 potential of levulinic acid as building block for a wide range of chemicals were Werpy and Petersen
 157 [7] in 2004 and Bozell in 2010 [39]. Levulinic acid is considered to be a versatile biobased building
 158 block to be further converted in solvents, plasticizers, fuels, value-added chemicals, monomers for
 159 polymers, etc. [1, 45-50]. Examples of important chemicals from LA and their potential applications
 160 are showed in Figure 55. Such valuable chemicals include γ -valerolactone, levulinate esters and also
 161 angelica lactone, ketals, diphenolic acid and δ -amino levulinic acid [13, 47, 50-52], in addition to the
 162 several important compounds obtained from their upgrading, such as 2-methyltetrahydrofuran,
 163 hydrocarbon fuels, valerate esters and polymers [49].

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Figure 54. Chemical products derived from levulinic acid.

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The development of new LA-derived products is continuously in progress, alongside LA
 production at larger scale. In this context, very recently the company GF-Biochemicals 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 next years.

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

175 ~~reduce write-off~~ the costs of ~~LA~~levulinic acid production; iii) the synthesis of new efficient catalysts
 176 ~~which to~~ replace the traditional inorganic mineral ones, such as H₂SO₄, HCl, and H₃PO₄, which ~~are~~
 177 ~~responsible for~~ corrosion problems of the equipment; iv) the removal of impurities and other
 178 by-products, which must be eliminated from the hydrolysis liquor before the recovery of the pure
 179 LA.

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

190 ~~yield of levulinic acid (Y_{LA}) wt % = Levulinic acid recovered (g)/ dry substrate (g) x 100.~~

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

196 ~~The available strategies to enhance the solid residues obtained in the LA production processes~~
 197 ~~will be also outlined, underling as these fractions can be exploited. In order to make easier the~~
 198 ~~comparison between the different employed methods for LA production, in this review LA yield has~~
 199 ~~been determined on the basis of weight of dry raw biomass as: yield of levulinic acid wt % =~~
 200 ~~Levulinic acid recovered (g)/ dry substrate (g) x 100.~~

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202 2. Catalytic conversion of hexoses

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204 2.1 Homogeneous mineral acids and salts in water

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

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

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

Exp.	Substrate and loading (wt %)	Catalyst	Reaction Conditions	Y _{LA}	Ref.
1	fructose 1 wt %	HCl	240°C for 0.03 h	30 wt %	[5442]
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 % *	[5543]
5	fructose 1 wt %	H ₃ PO ₄	240°C for 0.03 h	4.5 wt %	[5442]
6	glucose 1.8 wt %	HCl	141°C for 1 h	29 wt %	[5644]
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 %	[5745]
9	glucose 6.3 wt %	HCl	98°C for 3 h	22 wt %	[5846]
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 %	[5846]
13	glucose 1.8 wt %	H ₂ SO ₄	141°C for 1 h	29 wt %	[5644]
14	glucose 1.8 wt %	H ₂ SO ₄	140°C for 2 h	38 wt %	[5947]
15	glucose 2 wt %	H ₂ SO ₄	180°C for 0.25 h	42 wt %	[6048]
16	glucose 6.3 wt %	H ₃ PO ₄	98°C for 6 h	3.2 wt %	[5846]
17	fructose 2 wt %	TFA	180°C for 1 h	45 wt %	[6149]
18	glucose 1.8 wt %	TFA	180°C for 1 h	37 wt %	[6149]
19	glucose 2 wt %	Methane-sulfonic acid	180°C for 0.25 h	41 wt %	[6048]
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.~~ Not specified.

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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 the catalyst to produce LA from various carbohydrates already in 1931 [6452]. Carlson's 1962 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 [6553]. 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 minutes (exp. 2 and 3, Table 2). 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 (exp. 10 and 11, Table 2). In this regard, it is

242 interesting to highlight the LA yield achieved by Rackemann et al., about 42 wt %, employing H₂SO₄
243 at 180°C for 15 minutes in water starting from glucose (exp. 15, Table 2). Moreover, the same authors
244 compare the results obtained in the presence of H₂SO₄ with those achieved using methanesulfonic
245 acid (exp. 19, Table 2), reaching similar LA yield under the same experimental reaction conditions.
246 ~~As stated previously, the processes involving homogeneous mineral acids can be carried out~~
247 ~~following two strategies: dilute acid hydrolysis processes working at high temperature and~~
248 ~~concentrated acid hydrolysis processes working at lower reaction temperatures. In both cases,~~
249 ~~shortcomings are present, such as equipment corrosion and harsh operating conditions for dilute~~
250 ~~acid hydrolysis processes, whereas harsher equipment corrosion and the difficult acid recovery are~~
251 ~~the main drawbacks of the concentrated acid hydrolysis route.~~

252 Another type of catalyst employed for LA production deals with the use of metal salts which
253 show a remarkable catalytic activity. This is confirmed by the studies of Peng et al. who investigated
254 the conversion of glucose by different metal chlorides, including FeCl₃, CrCl₃, CuCl₂ and AlCl₃ (exp.
255 20-23, Table 2). Among the investigated metal chlorides, aluminum chloride was found to be the
256 most effective for the conversion of glucose, affording an optimum yield up to 45.8 wt % working in
257 water at 180°C for 2 h (exp. 23, Table 2). The catalytic role of these salts can be ascribed to the Lewis
258 acidity of the metal cations, together with the intrinsic Brønsted acidity derived from their
259 hydrolysis. Levulinic acid was produced from glucose in a cascade of reactions using a Lewis acid
260 catalyst (CrCl₃) together with a Brønsted acid (HCl) catalyst (exp. 24, Table 2). In this study CrCl₃ is
261 an active Lewis acid catalyst in glucose isomerization to fructose, and the combined Lewis and
262 Brønsted acid catalysts perform the isomerization and dehydration/rehydration reactions. A strong
263 interaction between the Cr cation and the glucose molecule enables ring-opening and isomerization
264 of glucose. By combining CrCl₃ and HCl a real interplay of the two catalysts was ascertained. Even in
265 the absence of HCl, hydrolysis of Cr(III) decreases the solution pH, and this intrinsic Brønsted
266 acidity drives the dehydration and rehydration reactions. Yields of 30 wt% in LA were achieved at
267 moderate temperature (140 °C) [63]. A further confirmation of the cooperative effect of Lewis and
268 Brønsted acids in glucose hydrolysis to LA has been recently reported [66]. The synergistic positive
269 effect on LA yield of coupling CrCl₃ with H₃PO₄ was confirmed compared with single CrCl₃ or
270 H₃PO₄ catalysts. In the hydrolysis of fructose, sucrose and inulin, a strong interaction between the
271 substrate and the Lewis acidic ion Sn⁴⁺ was also evidenced by NMR, suggesting an additional
272 contribution to the catalysis, besides the release of Brønsted acid. This interaction and complex
273 formation promotes the conversion of the substrates to 5-HMF and then to LA and formic acid,
274 underlining an additional function of Lewis acid catalyst Sn⁴⁺, together with the intrinsic Brønsted
275 acidity derived from its hydrolysis [67].

276 During the production of LA, substantial amounts of soluble and insoluble by-products are
277 produced, even when hexoses are employed as starting feedstock. These compounds may include
278 reaction intermediates, soluble and insoluble humins, polymeric substance and gas-phase
279 components due to thermal degradation of reactants/products. They are generally deeply colored
280 and their complete identification is still a challenge and their removal remains unsolved for most
281 technologies. As an example, when Girisuta studied the acid-catalysed decomposition of glucose to
282 LA, substantial amounts of insoluble humins were formed, obtained from the acid-catalysed
283 decomposition of glucose and 5-HMF [56]. The author identified other possible by-products, called
284 reversion products, like levoglucosan or 1,6-anhydro-β-D-glucopyranose (4),
285 1,6-anhydro-β-D-glucofuranose (5), iso-maltose (6) and gentiobiose (7), as shown in Figure 6.

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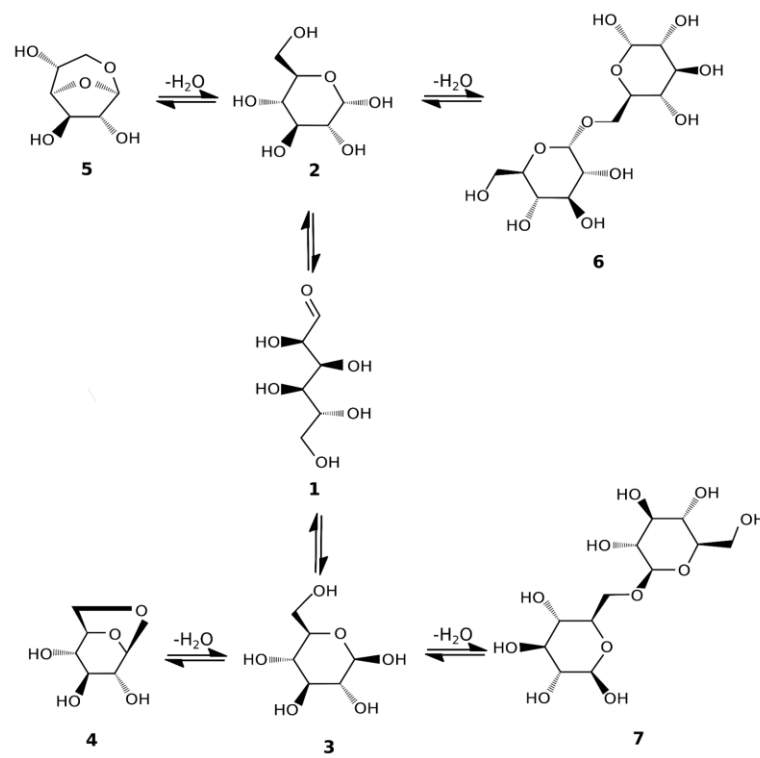


Figure 6. Reversion reactions of glucose in acid solutions [56].

In acidic solutions, the acyclic form of D-glucose (1) exists in equilibrium with its anomeric forms, i.e., α -D-glucopyranose (2) and β -D-glucopyranose (3). 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-glucofuranose. 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].

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 to reach higher heating rate, homogeneous heat distribution, efficient control of 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 and the corrosion of equipment and environmental pollution. Moreover, the corrosive conditions

318 demand the use of special material for reactor construction, thereby, increasing the capital
 319 investment and operating costs. These drawbacks can be overcome by replacing homogeneous acid
 320 catalysts with heterogeneous solid ones. To date, a cost-effective environment-friendly process in LA
 321 biorefinery employing homogeneous catalysts for simple sugars conversion is still largely needed.

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323 2.2 Heterogeneous catalysts in water

324 As a result of the ever strengthening environmental regulations, solid acids are attracting for
 325 replacement of corrosive and harmful traditional mineral acids. These catalysts possess Brønsted
 326 and/or Lewis acidic sites. Heterogeneous Brønsted acids include acidic ion-exchange resins (e.g.,
 327 Nafion-H, Amberlyst, Dowex), heteropoly acids and their derivatives (e.g., $H_{0.5}CS_{2.5}[PW_{12}O_{40}]$). Solid
 328 Lewis acids include metal oxides and their sulfated/phosphated derivatives. Catalysts with mixed
 329 Brønsted and Lewis acid centers, including clays and zeolites, may be synthesised in order to have a
 330 careful balance of the overall acidity of the system. The use of heterogeneous catalysts for LA
 331 synthesis from soluble sugars is also well-established. Regarding their use for LA synthesis starting
 332 from simple sugar feedstocks, already in 1956 pioneering studies patented by Redmon underlined
 333 the use of the acidic cation exchange resin Amberlite IR-120, in the amount of 18-19 % of the total
 334 weight of the reaction mixture, for LA production from aqueous solutions of sugars or sucrose with
 335 minimal formation of insoluble humin by-products [7354]. Especially in recent years, the range of
 336 heterogeneous catalysts studied for LA synthesis has been growing greatly, being an attractive and
 337 promising alternative to the homogeneous ones. Generally, solid catalysts can be easily separated
 338 from the reaction mixture and recycled, can work at high temperatures and their surface acidity can
 339 be adjusted to improve selectivity [7455]. These properties make these solid catalysts suitable
 340 candidates for industrial use [27]. Moreover, heterogeneous catalysts are generally selective and do
 341 not present corrosion problems. However, the studies on heterogeneous catalysts are still limited
 342 if compared to homogeneous ones. This is due to many reasons. First of all, the strong adsorption
 343 of the produced LA levulinic acid on the catalyst surface lowers the overall yield to LA which can be
 344 obtained from reactions occurring on the bare surface of solid catalyst as well as within the pores of
 345 catalyst. Secondly, heterogeneous catalysts can be deactivated when used or recycled over a long
 346 period of time, due to the deposition of reaction heavy by-products, such as humins, on the surface
 347 of the catalyst or as a consequence of the leaching of the active acid species from the catalyst's
 348 surface. A summary of the recent works from the literature employing heterogeneous catalysts in
 349 water is provided in Table 3.

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

Exp.	Substrate and loading (wt %)	Catalyst	Reaction Conditions	Y _{LA}	Ref.
25	fructose 5 wt %	Amberlyst 15	120°C for 36 h 140°C for 8 h	52 % * 56 % *	[5543]
26	fructose 5 wt %	Nafion NR50	120°C for 24 h	41 % *	[5543]
27	fructose 5 wt %	SBA-SO ₃ H	120°C for 24 h	29 % *	[5543]
28	fructose 1.8 wt %	TFA	180°C for 1 h	45.1 wt %	[49]
289	glucose 1 wt %	Al-Zr oxide	180°C for 2 h	3.9 wt %	[7556]
2930	glucose 10 wt %	Zirconium phosphate	160°C for 3 h	14 wt %	[27]
304	glucose 10 wt %	Amberlyst 70	160°C for 3 h	21.7 wt %	[27]
312	glucose 1 wt %	CrCl ₃ + HY zeolite hybrid catalyst	145.2°C for 2.45 h	55.2 wt %	[7657]

323	glucose 1 wt %	CrCl ₃ + HY zeolite hybrid catalyst	160°C for 3 h	40.62 wt-%	[7758]
334	glucose 0.5 wt %	FeCl ₃ /HY zeolite catalyst	180 °C for 4.17 h	66 % *	[7859]
345	glucose 13 wt %	Sulphonated graphene oxide	200°C for 2 h	50 wt %	[7960]
356	glucose 5 wt %	Sulfonated chloromethyl polystyrene resin	170°C for 10 h	28.5 wt %	[8064]

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

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~~The employment of heterogeneous catalysts on simple substrates allows the achievement of lower yields to LA compared to those reached in the presence of homogeneous catalysts.~~ 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 (exp. 25, Table 3). 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 (exp. 2930 and 304, Table 3). 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 (1:1; 1:2 and 2:1 respectively) in the production of LA from glucose. The strength and the distribution of the acid sites were markedly influenced by altering the CrCl₃ and HY zeolite ratios in the hybrid catalysts. The authors found that these systems showed total acidity and acid sites strength in the order: hybrid 1:2 > hybrid 1:1 > hybrid 2:1. However, when the acid sites were considered per unit surface area the hybrid 1:1 catalyst possessed the highest acidity, followed by the hybrid 2:1 system and finally by the hybrid 1:2 catalyst. This indicates that the hybrid 1:1 catalyst contains more reactive acid sites on the catalyst surface compared to the other two hybrid systems. This investigation confirms that the catalytic reaction of the hybrid catalysts is predominantly influenced by the type of acid sites, the amount of the acid sites and their strength, exhibiting the hybrid 1:1 system the highest catalytic performances with 40 wt % of LA yield at 160°C in 3 h (exp. 32, Table 3). Very interesting performances are also obtained in the presence of graphene oxide-based systems with –SO₃H functional groups. Also 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. Regarding the use of heterogeneous catalysts, also zeolite type systems are widely successfully employed. In this regard, it is very interesting the investigation carried out by Ramli et al. who reached the yield to LA of 66 wt % starting from glucose after 4.17 h at 180°C in the presence of Fe/HY zeolite catalyst (exp. 33, Table 3). Finally, promising LA yields were obtained also in the presence of sulfonated systems. Upare et al. employing the sulphonated graphene oxide as catalyst for the conversion of glucose reached a LA yield of 50 wt % in water after 2 h at 200°C (exp. 345, Table 3), 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 yields of 28.5 wt % (exp. 356, Table 3).

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

404 The reported results show that although the LA yields achieved employing heterogeneous
405 catalysts can be, in some cases, promising, the ~~sey~~ are not yet satisfactory for the use of these systems
406 at the industrial scale. In particular the study of the life of the catalyst and its reactivation needs
407 further improvement. So far, the main drawbacks of using heterogeneous catalysts include generally
408 low reaction yields, slow reaction rates and prolonged reaction times to obtain reasonable yields to
409 LA. Therefore, further research is still necessary for developing new catalysts which enhance the LA
410 yield and progressively target towards raw and cheap biomass substrates.

411 2.3 Homogeneous and heterogeneous catalysts in organic solvents

412 Many solvents have been tested for the production of LA from sugars. Aprotic media have been
413 tested for LA synthesis, such as dimethylsulfoxide (DMSO), dimethylformamide (DMF),
414 dimethylacetamide (DMA), tetrahydrofuran (THF), methyl isobutyl ketone (MIBK), carbon
415 tetrachloride, acetonitrile and ethyl acetate. DMSO is particularly selective towards 5-HMF because
416 it suppresses the subsequent hydrolysis of 5-HMF to LA and formic acid [2,8262]. Regarding aprotic
417 solvents, Sanborn reports the synthesis of LA from fructose sources using a polyethylene glycol
418 and an end capped polyethylene glycol together with an acid catalyst, in the presence of polar
419 aprotic solvents such as, 1-methyl-2-pyrrolidone, dimethylacetamide, dimethylformamide,
420 dimethylsulfoxide, methyl ethyl ketone, methyl isobutylketone, acetonitrile and propionitrile. All
421 the aprotic solvents were found, -all of them resulted suitable for the investigated reaction [8363]. In
422 this regard, another interesting example is that published by Mascal et al. who studied a two-step
423 approach, employing 1,2-dichloroethane as solvent in the first step. In this stage, the conversion of
424 glucose into 5-(chloromethyl)furfural was performed employing concentrated HCl as catalyst in
425 1,2-dichloroethane heating at 100°C for 1-3 h [8464]. In the second step, the obtained
426 5-(chloromethyl)furfural was hydrolyzed to LA in water at 190°C for 20 minutes [8565], allowing to
427 reach a very high LA yield, up to 79 mol % from glucose, corresponding to 51 wt %.

428 Regarding the use of protic solvents, very few of them have been investigated for the
429 production of LA. Brasholz et al. investigated the conversion of fructose to LA with HCl in the 1:2
430 mixture of H₂O:CH₃OH achieving after 1.33 h at 140°C the LA yield of 46.4 wt %. The majority of
431 protic solvents, such as ethanol and butanol or mixtures of them with water, have been tested for the
432 dehydration of fructose to 5-hydroxymethylfurfural [86,8766,67]. On the other hand, protic solvents
433 and in particular alcohols have been extensively employed for levulinate esters production, through
434 the direct conversion from biomass by alcoholysis under acidic conditions. In fact, carbohydrate
435 compounds can be easily converted into LA via 5-HMF through dehydration and hydration
436 reactions, into LA which and LA is then transformed into its esters by esterification reactions
437 [15,8868].

438 Generally, the choice of the most suitable organic solvent is critical, due to the great influence of
439 its properties on the reaction. First of all, the solubility of substrate in the solvent is a very important
440 issue. In particular, the polarity plays a key role, because solvent dissolves solutes having similar
441 polarities, thus in the synthesis of LA from sugars it is important employing polar solvents, such as
442 DMSO, DMF, DMA, THF, MIBK etc., which, as said previously, are the main organic solvents
443

444 investigated in this reaction. However, other parameters can influence the solubility, such as solute
 445 size/volume and surface area, polarizability of the molecule and strength of the hydrogen bond
 446 between solvent and solute [89]. Solvents also affect the selectivity of the reaction. DMSO is
 447 particularly selective towards 5-HMF because it suppresses the hydrolysis of 5-HMF to LA and
 448 formic acid and the humins formation [2,62], due to the strong interaction between the C=O group in
 449 5-HMF and DMSO, which limits hydration and intermolecular condensation reactions [90].
 450 However, there are other issues that must be considered during the choice of the solvent, such as the
 451 feasibility of its separation and recycling, its cost and its environmental effects. Regarding the
 452 economic, technological and safety aspects, the majority of organic solvents show remarkable
 453 disadvantages: i) high costs; ii) high boiling points (DMSO, DMF, DMA), which are directly related
 454 to the feasibility of their recycling, traditionally carried out through distillation; iii) reactivity in the
 455 reaction conditions, such as THF that can be hydrolysed in the presence of high amount of water and
 456 acid catalysts; iv) safety problem, such as THF that can be oxidized in air into explosive peroxides; v)
 457 toxicity. For all these reasons, the organic solvents are not used on a large scale. In conclusion, the
 458 best solvent for the sustainable synthesis of levulinic acid from sugars is water, because it is greener,
 459 cheaper and less toxic than the organic solvents. Generally, the choice of the most suitable organic
 460 solvent is critical and the related processes need to be optimized in terms of cost, energy effort and
 461 product recovery because the majority of them show disadvantages of high cost, high boiling points
 462 and adverse environmental effects.

463

464 3. Catalytic conversion of cellulose and raw biomasses

465

466 3.1 Homogeneous mineral acids and salts in water

467

468 Cellulose is an important structural component of the primary cell wall of green plants and
 469 many researchers have studied its hydrolysis for the sustainable production of LA levulinic acid and
 470 of other value-added chemicals, because it is abundant in nature, non-edible and not competing with
 471 the food chain. ~~On the other hand, r~~Regarding raw biomasses, the preferred cheap raw
 472 lignocellulose sources of ~~lignocellulose~~ include giant reed, switchgrass, miscanthus and poplar as
 473 promising examples of fast-growing grasses and trees, whereas sawdust, wheat straw, corn stover,
 474 sugarcane bagasse, municipal waste, fruit peels and pulp sludge are promising sources of as
 475 low-value wastes to be enhanced and exploited. A summary of the most recent works in the
 476 literature employing homogeneous catalysts in water is provided in Table 4. It is remarkable that for
 477 many raw and waste biomasses adopted in these experiments the complete composition analysis is
 478 not reported and, sometimes, also the total sugar content is unknown. For this reason, the LA
 479 ponderal yield is the unique tool to evaluate the effectiveness of the catalytic conversions.

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

Exp.	Substrate and loading (wt %)	Catalyst	Reaction Conditions	Y _{LA}	Ref.
367	cellobiose 5 wt %	HCl	MW, 170°C for 0.5 h	29.9 wt %	[34]
378	cellobiose 5 wt %	H ₂ SO ₄	MW, 170°C for 0.5 h	28.0 wt %	[34]
389	cellulose 1.6 wt %	HCl	180°C for 0.33 h	44 wt %	[9169]
3940	cellulose 10 wt %	HCl	MW, 225°C for 0.03 h	90 % *	[9270]
404	cellulose 5 wt %	HCl	MW, 170°C for 0.83 h	31.0 wt %	[34]
412	cellulose 5 wt %	H ₂ SO ₄	MW, 170°C for 0.83 h	23.0 wt %	[34]
423	cellulose 1.7 wt %	H ₂ SO ₄	150°C for 2 h	43 wt %	[9374]
43	cellulose 8.7 wt %	H ₂ SO ₄	150°C for 6 h	40.8 wt %	[9472]
445	cellulose 2 wt %	CrCl ₃	200°C for 3 h	47.3 wt %	[6250]
45	cellulose 20 wt %	CuSO ₄	240°C for 0.5 h	17.5 wt %	[9573]

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 %	[9774]
48	giant reed 7 wt %	HCl	200°C for 1 h	15.8 wt %	[9875]
49	giant reed 7 wt %	HCl	2 steps: 1 st step: 80°C for 2 h; 2 nd step: 190°C for 1 h	22.8 wt %	[9875]
50	giant reed 7 wt %	HCl	MW, 190°C for 0.33 h	22 wt %	[9976]
51	water hyacinth 1 wt %	H ₂ SO ₄	175°C for 0.5 h	9.2 wt %	[10077]
52	corn stalk 10 wt %	FeCl ₃	180°C for 0.67 h	35 wt %	[10178]
53	whole kernel grain sorghum 10 wt %	H ₂ SO ₄	200°C for 0.67 h	32.6 %*	[10279]
54	wheat straw 6.4 wt %	H ₂ SO ₄	209.3°C for 0.63 h	19.9 wt %	[10380]
55	wheat straw 7 wt %	HCl	200°C for 1 h	19.3 wt %	[10481]
56	wheat straw 7 wt %	HCl	MW, 200°C for 0.25 h	20.6 wt %	[10481]
57	rice husk 10 wt %	HCl	170°C for 1 h	59.4 wt %	[10582]
58	sugarcane bagasse 11 wt %	H ₂ SO ₄	150°C for 6 h	19.4 wt %	[10683]
59	sugarcane bagasse 10.5 wt %	HCl	220°C for 0.75 h	22.8 wt %	[10784]
60	paddy straw 10.5 wt %	HCl	220°C for 0.75 h	23.7 wt %	[10784]
61	olive tree pruning 7 wt %	HCl	200°C for 1 h	18.6 wt %	[10481]
62	olive tree pruning 7 wt %	HCl	MW, 200°C for 0.25 h	20.1 wt %	[10481]
63	poplar sawdust 7 wt %	HCl	200°C for 1 h	21.3 wt %	[10481]
64	poplar sawdust 7 wt %	HCl	MW, 200°C for 0.25 h	26.4 wt %	[10481]
65	tobacco chops 7 wt %	HCl	200°C for 1 h	5.2 wt %	[10481]
66	post-harvest tomato plants 10 wt %	HCl	MW, 225°C for 0.03 h	63 %*	[9270]
67	paper sludge 7 wt %	HCl	200°C for 1 h	31.4 wt %	[10481]
68	paper sludge 7 wt %	HCl	MW, 200°C for 0.25 h	31.7 wt %	[10481]
69	screen rejects 7 wt %	HCl	MW, 190°C for 0.33 h	7 wt %	[10885]
70	red alga Gracilaria verrucosa 6.7 wt %	H ₂ SO ₄	175°C for 0.58 h	22.6 wt %	[10986]
71	red alga Gelidium amansii 16.7 wt %	H ₂ SO ₄	2 steps: 1 st step: 76°C for 49.5 h; 2 nd step: 180°C for 0.8 h	20.6 wt %	[11087]
72	macroalga Kappaphycus alvarezii 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 % *	[9270]
74	chitosan 25 wt %	SnCl ₄	MW, 210°C for 0.5 h	27 wt %	[11288]
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]

483 |
484 | When cellobiose is employed as starting substrate for LA production, yields of 29.9 wt % and
485 | 28.0 wt % were reached in the presence of HCl and H₂SO₄ respectively after a treatment of 30
486 | minutes at 170°C under MW irradiation (exp. 367 and 378, Table 4). Analogous yields were achieved
487 | when cellulose was used as starting substrate: LA yields of 31 wt % and 23 wt % in the presence of
488 | the homogeneous mineral acids, HCl and H₂SO₄ respectively were obtained at 170°C for 50 minutes
489 | under MW irradiation (exp. 404 and 412, Table 4). Adopting traditional heating, Shen et al. obtained
490 | 44 wt % of LA yield starting from cellulose working in water at 180°C for 20 minutes employing the
491 | mineral acid HCl (exp. 389, Table 4), whereas Girisuta et al. achieved the same LA yield (43 wt %)
492 | again starting from cellulose in water at 150°C for 2 h in the presence of H₂SO₄ (exp. 423, Table 4),
493 | highlighting the efficiency of these homogeneous acid catalysts in the production of LA from
494 | cellulose. Generally, a low solid concentration results in a higher yield of LAlevulinic acid. Peng et
495 | al. observed that the optimal concentration of substrate is very important in terms of the efficient use
496 | of cellulose and the final reached LA concentration. Higher LA yield was achieved at lower substrate
497 | concentrations, but a higher LA concentration in the product stream is extremely favorable since it
498 | results in lower energy consumption upon purification of LA and also reduces the amount of waste
499 | water produced [6250]. However, it is not possible to increase infinitely the substrate loading due to
500 | the product feedback inhibition. In addition, too much or too little water inhibits the hydrolysis
501 | process, thus again underlining the importance to select the right substrate loading [10784].

502 | When raw lignocellulosic feedstocks are used, mineral acids are the most widely employed
503 | catalysts [2,3,113,11489,90]. Licursi et al. used HCl in the conversion of giant reed to LA at 190°C.
504 | After 1 h of reaction, LA yield of 24 wt % was reached. The same authors report similar LA yields in
505 | a two-step procedure carrying out the first stage at 80°C for 2 h, followed by the second step at 190°C
506 | for 1 h (exp. 49, Table 4). When MW irradiation was employed, a comparable LA yield of 22 wt %
507 | was obtained from giant reed in water at 190°C in the presence of HCl in only 20 minutes, thus
508 | confirming the great efficiency of microwave MW energy (exp. 50, Table 4). Wheat straw is another
509 | promising feedstock and many studies have adopted this substrate. Chang et al. studied the effects
510 | of temperature, acid concentration, liquid/solid ratio and reaction time on LA-levulinic acid
511 | production from wheat straw in the presence of H₂SO₄, obtaining under the best experimental
512 | conditions of 209.3 °C for 37.6 minutes the LA yield of 19.9 wt % (exp. 54, Table 4). The same yields
513 | (around 20 wt %) were achieved from wheat straw in the presence of HCl at 200°C after 1h when the
514 | reaction was performed in the autoclave and after only 15 minutes under MW irradiation (exp. 55
515 | and 56, Table 4).

516 | The employment of renewable raw complex lignocellulosic feedstocks, from which mixtures of
517 | sugars are obtained, –appears as an attractive alternative in respect to the use of the pure monomeric
518 | sugars for the production of LA because it provides a sustainable cheap solution to the existing
519 | environmental problem, at the same time increasing the agribusiness and employment in rural
520 | sector, alongside with the development of the rural areas. However, there are still some drawbacks,
521 | which can affect the process economics, such as the irregularity of the biomass availability (the
522 | supply of biomass is not constant round-the-year), the variability in its composition and the logistics
523 | cost which results in the biggest bottleneck in the conversion of raw biomasses to LA. The
524 | transportation cost is not only influenced by the distance traveled, but also by the type of biomass
525 | and by the form in which it is transported. In this context, the integration of preprocessing of raw
526 | material and transport along with a careful supply chain planning might overcome many logistics
527 | issue. In addition, LA yields obtained from renewable inexpensive feedstocks are low, making
528 | imperative a proper optimization of the process which may result in higher LA yields. The
529 | complexity and heterogeneity of lignocellulosic biomass make pretreatment a mandatory step in its
530 | conversion to sugars and subsequently to LA in order to improve yield and reaction rates. On the
531 | other hand, the choice of pretreatment is of paramount importance and its severity depends on the
532 | complexity of the raw starting compounds [115,11691,92].

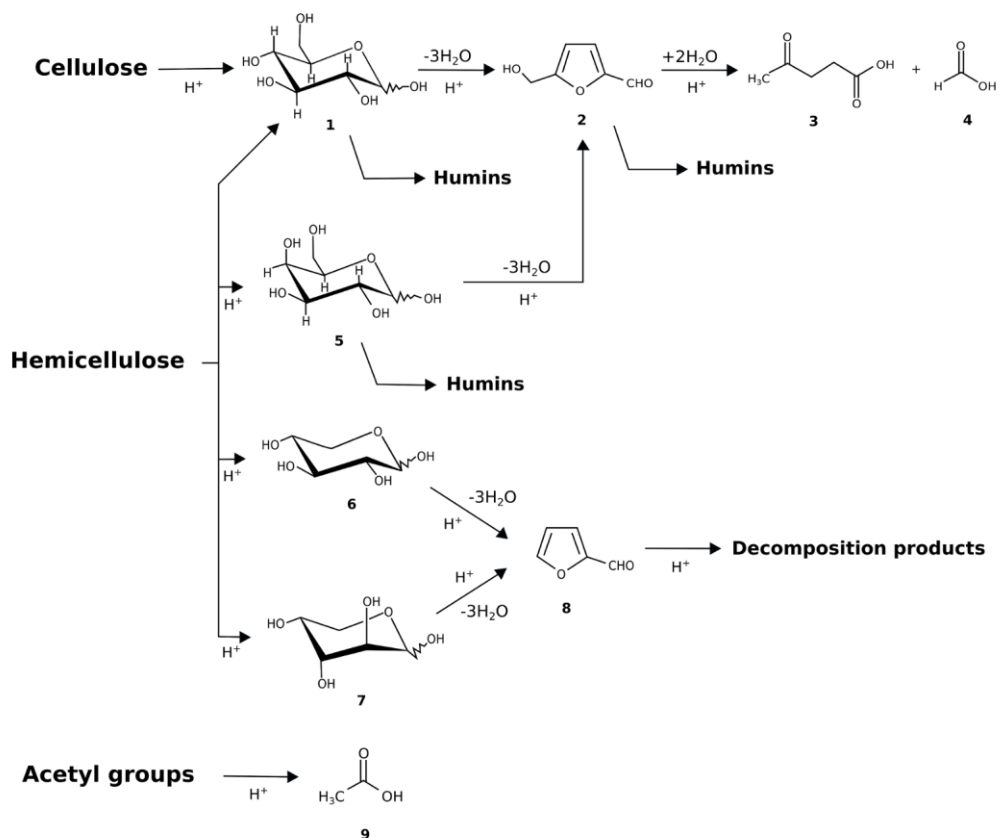
533 | In addition to these feedstocks, many low-value agricultural or algae wastes have been
534 | employed for the production of LA, thus enhancing and exploiting them to give an added-value

535 compound. In this case, HCl is the most widely employed acid catalyst, allowing promising results,
536 as evidenced by the LA yields shown in Table 4. Bevilaqua et al. investigated the production of LA
537 from rice husks using HCl as acid catalyst. Rice husks ~~is a very are the most~~ abundant agricultural
538 crop residue ~~in southern Brazil (2.4 Mton, 2011)~~ and approximately 1 ton of rice husks is left over for
539 each 4 ton of rice produced. Taking into account that rice husks show a content of polysaccharides
540 higher than 50 wt % (w/w), ~~it they~~ can be ~~employed as feedstock in for~~ the ~~green and sustainable~~
541 production of LA, having this ~~waste feedstock no other noble use no added value at all~~. Working at
542 170°C for 1 h in the presence of HCl, it is possible to reach a LA yield of 19.3 wt % (exp. 567, Table 4).
543 Yan et al. studied the production of LA from sugarcane bagasse and paddy straw in the presence of
544 HCl at 220°C for 45 minutes. Sugarcane and paddy grow in southern China in very large quantities:
545 the first one is mainly utilized to produce sucrose, whereas the second one is used as feed and raw
546 material in the food industry. However, million of tons of sugarcane bagasse and paddy straw are
547 discarded or incinerated. As a consequence, the possibility of using these biomass wastes directly for
548 the production of ~~LA levulinic acid~~ represents an important step toward sustainability and green
549 chemistry. ~~Under In~~ the adopted reaction conditions the LA yields of 22.8 wt % and 23.7 wt % from
550 sugarcane bagasse and paddy straw were reached respectively (exp. 59 and 60, Table 4). Other
551 interesting waste biomass sources for LA production are olive tree pruning and poplar sawdust.
552 When olive tree pruning ~~washas been~~ employed, working in water at 200°C in the presence of HCl,
553 LA yields of 18.6 wt % and 20.1 wt % were achieved, in the absence and in the presence of MW after
554 1 h and 15 minutes respectively (exp. 61 and 62, Table 4), highlighting the positive effect of MW
555 energy. In the case of poplar sawdust, the beneficial effect of MW irradiation is even higher:
556 adopting the same reaction conditions, already used for the conversion of olive tree pruning (water,
557 200°C in the presence of HCl), LA yields of 21.3 wt % and 26.4 wt % were achieved, in the absence
558 and in the presence of MW irradiation after 1 h and 15 minutes respectively (exp. 63 and 64, Table 4).
559 In addition, the positive MW effect was also confirmed in the conversion of paper sludge as raw
560 starting substrate to LA, obtaining under the same reaction conditions adopted for olive tree
561 pruning and poplar sawdust (water, 200°C in the presence of HCl), LA yields of 31.4 wt % and 31.7
562 wt %, in the absence and in the presence of MW after 1 h and 15 minutes respectively (exp. 67 and 68,
563 Table 4). Finally, some considerable rejected waste fractions called “screen rejects” obtained from the
564 papermaking process including both cellulose fibers and non-fibrous organic contaminants have
565 been exploited by means of the hydrothermal route to give LA in agreement with the integrated
566 recycled paper mill approach. Under MW irradiation, it was possible to reach the LA yield of 7 wt %
567 working at 190°C for 20 minutes (exp. 69, Table 4). These examples ~~are promising because~~
568 highlight the real possibility to upgrade and exploit these wastes, otherwise allocated to disposal.

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

580 A deep investigation on by-products was carried out for the acid-catalysed hydrolysis of the
581 water hyacinth plant to LA [100]. The authors found in solution organic acids, such as acetic acid and
582 propionic together with the co-product formic acid, a big number of intermediate products arising
583 from the cellulose and hemicellulose fraction of the water hyacinth leaves identified as monomeric
584 sugars, glucose and arabinose, as well as furan derivatives, 5-HMF and furfural. The dark-brown
585 solid was formed by a mixture of humin type by-products deriving from the acid-catalysed
586 decomposition of glucose and 5-HMF [59], as well as products of condensation reactions of

587 C₅-sugars and furfural [119], residual insoluble lignin and ash. On the basis of the product
 588 composition and literature precedents for other biomass sources [120, 121], the authors proposed a
 589 simplified reaction pathway for the acid-catalysed hydrolysis of the cellulose and hemi-cellulose
 590 fraction of the water hyacinth, as shown in Figure 7.
 591



592
 593 **Figure 7.** Simplified reaction network for the acid-catalysed hydrolysis reaction of the water hyacinth plant (1:
 594 Glucose, 2: 5-Hydroxymethylfurfural, 3: Levulinic acid, 4: Formic acid, 5: Galactose, 6: Xylose, 7: Arabinose, 8:
 595 Furfural, 9: Acetic acid) [100].
 596

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

608 It is remarkable that LA can be also obtained from chitosan and chitin with good yields which
 609 surely can be further improved (exp. 73-76, Table 4). These unexplored raw materials are the second
 610 most abundant polysaccharides after cellulose, being obtained as industrial waste materials from
 611 seafood industry and fisheries. Also the exploitation of a chitin-containing fungal biomass and the
 612 purification of the obtained LA from unconverted glucosamine have been patented [122]. Their
 613 optimized exploitation of all these innovative starting materials can represent a turning point for LA
 614 production.

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

618 When MW heating is adopted, generally an increase of LA yield respect to traditional heating is
 619 observed (compare exp. 61 with 62 and 63 with 64, Table 4), adopting shorter reaction time. The
 620 considered experiments have been generally carried out adopting constant temperature mode. As
 621 previously observed for the hydrolysis of simple sugars, also in the case of homogeneous catalysis
 622 on raw biomasses the MW beneficial role is described as thermal effect.-

623

624 3.2 Heterogeneous catalysts in water

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

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

Exp.	Substrate and loading (wt %)	Catalyst	Reaction Conditions	Y _{LA}	Ref.
77	cellobiose 5 wt %	Sulfonated chloromethyl polystyrene resin	170°C for 5 h	12.9 wt %	[8064]
78	sucrose 5 wt %	Sulfonated chloromethyl polystyrene resin	170°C for 10 h	16.5 wt %	[8064]
79	cellulose 5 wt %	Sulfonated chloromethyl polystyrene resin	170°C for 10 h	24 wt %	[8064]
80	cellulose 5 wt %	Al-NbOPO ₄	180°C for 24 h	38 wt %	[12393]
81	cellulose 2.5 wt %	Sulfonated carbon	190°C for 24 h	1.8 wt %	[12494]
82	cellulose 2 wt %	ZrO ₂	180°C for 3 h	39 wt %	[12595]
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 %	[10484]
85	wheat straw 6 wt %	Niobium Phosphate	MW, 200°C for 0.25 h	10.1 wt %	[10484]
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 %	[12696]
			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 %	

			^a 6.6% acid concentration		
			^b 13.3% acid concentration		
87	empty fruit bunch 1 wt %	CrCl ₃ + HY zeolite hybrid catalyst	145.2 °C for 2.45 h	15.5 wt %	[7657]
88	kenaf 1 wt %	CrCl ₃ + HY zeolite hybrid catalyst	145.2 °C for 2.45 h	15.0 wt %	[7657]
89	kiwifruit waste residue 6.7 wt %	20% Nb/Al oxide	190°C for 0.17 h 190°C for 0.25 h	13.8 wt % 14.7 wt %	[12797]

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The employment of solid heterogeneous catalysts for LA synthesis starting from insoluble polysaccharides and raw biomasses ~~represents is~~ still a challenge, ~~but and~~ appears more difficult in comparison to the use of homogeneous ones. ~~In fact, because in a solid-insoluble-substrate/solid-catalyst system the of the difficulty of~~ mass transport ~~applied to solid insoluble substrate/solid catalyst system is very troubled~~ and ~~the heterogeneous catalysts have not due to~~ the ability, ~~characteristic of the of~~ homogeneous ~~one systems,~~ to deliver the active species into the solid or swelled biomass [12898]. ~~For all these reasons, making more suitable~~ 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 (exp. 79, Table 5). The authors employed the same catalytic system at 170° 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 (exp. 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. After 3 h of reaction, total conversion of cellulose was achieved together with a remarkably high yield to LA, equal to 39 wt % (exp. 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 % (exp. 83, Table 5). A similar catalyst, niobium phosphate, ~~doped with several amount of aluminium was employed in the synthesis of LA from cellulose (exp. 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. In fact, 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%, highlighting as a tunable acid strength is a fundamental parameter in order to obtain high LA yields.~~

~~Niobium phosphate was also successfully employed tested also~~ in the catalytic hydrothermal conversion of inulin and wheat straw to LA under MW irradiation. After 15 minutes 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 (exp. 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~~

673 | heated, but also in this case the positive role of MW is due to simple thermal effects. In addition,
 674 | Aamong the acid catalysts listed above, it is considerable to highlight the use of the heterogeneous
 675 | super-acid catalyst named $S_2O_8^{2-}/ZrO_2-SiO_2-Sm_2O_3$ employed by Chen et al. in the conversion of rice
 676 | straw to LA, achieving LA yields around 10 wt % working in the temperature range of 150-200°C for
 677 | 10 minutes in water (exp. 86, Table 5). Finally, another interesting example showing the employment
 678 | of heterogeneous catalysts to waste residues is reported by Wang et al. (exp. 89, Table 5). Today, the
 679 | kiwifruit industry is booming worldwide. Kiwifruit is widely cultivated in southern China and the
 680 | total production was over 1.17 million tons in 2014. About 37% of the fruit was processed into juice
 681 | and chips, with residual peels accounting for 3–5 wt % of the fruit. In almost all the kiwifruit
 682 | genotypes cultivated, the levels of fructose and glucose are very high, making them a promising
 683 | candidate for the production of LA. At the moment, the kiwifruit waste residues, containing
 684 | monosaccharides, are discarded. In this regard, the authors have studied the catalytic conversion of
 685 | kiwifruit waste residues to LA in water at 190°C in the presence of 20 % Nb/Al oxide as catalyst,
 686 | achieving after 15 minutes of reaction the LA yield of 14.7 wt % (exp. 89, Table 5). The achieved
 687 | result is remarkable and the catalyst ~~remain resulted~~ active up to five recycles. The promising
 688 | performance is due to the particular properties of the catalyst, such as robust water-tolerance, high
 689 | surface area and acidity. Regarding the latter, the authors investigated different Nb loading of Nb/Al
 690 | oxides-, proving that the total acid content decreases with the increase of Nb/Al ratio, instead the
 691 | concentration of strong acid sites increases. Therefore, 20% Nb/Al oxide is the most promising
 692 | catalyst, showing the best compromise between the amount of strong acid sites and total acidity and
 693 | a suitable Brønsted to Lewis acid site ratio, which allowed to achieve the highest LA yield.

694 | ~~The robust water tolerance, high special surface area, acidity, and Brønsted acid concentration~~
 695 | ~~of the Nb/Al oxide catalyst are considered to be responsible for this promising performance.~~

696 | As previously underlined for LA synthesis from sugars, the substrate loadings reported in the
 697 | literature are generally lower than 10 wt% also starting from polysaccharides and raw biomasses
 698 | (Table 4 and Table 5). This is justified not only by the high amount of by-products formed when high
 699 | feedstock loadings are adopted, but also by mechanical mixing problems in the reactor, due to the
 700 | high solid substrate/solvent ratio [27]. Therefore, the consequent drawbacks previously reported for
 701 | sugars are more serious.

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

711

712 | 3.3 Monophasic organic solvents

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

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

Exp.	Substrate and loading (wt %)	Catalyst	Reaction Conditions	Y _{LA}	Ref.
90	cellulose	$[C_4H_6N_2(CH_2)_3SO_3H]_{3-n}$	140 °C for 12 h in	63.1 wt %	[13099]

	2 wt %	H _n PW ₁₂ O ₄₀ , n = 1, 2 3]	H ₂ O/MIBK (1/10 v/v)		
<u>91</u>	cellulose	Sulfonated	170°C for 10 h in	47 wt %	[13099]
	4 wt %	chloromethyl polystyrene resin	H ₂ O-GVL (10/90 wt %)		
<u>92</u>	cellulose	Amberlyst 70	160°C for 16 h in	49.469 wt %	[13100]
	2 wt %		H ₂ O-GVL (10/90 wt %)	%*	
<u>93</u>	corn stover	Amberlyst 70	160°C for 16 h in	38.7 wt %	[13200]
	6 wt %		H ₂ O-GVL (10/90 wt %)	%*	

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

Zuo et al. investigated the conversion of microcrystalline cellulose into LA catalyzed by a sulfonated chloromethyl polystyrene resin (CP-SO₃H-1.69), obtaining at 170°C yields to LA up to 65.5 mol % (which corresponds to 47 wt %) at complete substrate conversion. The authors attributed the high yield of LA to the fact that GVL can solubilize cellulose and, therefore, improve the interactions between cellulose and the solid acid catalyst (exp. 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 %⁶⁹, not specified if LA yield is in mol or wt %) compared to the low yield (13.6 wt %¹⁹, not specified if LA yield is in mol or wt %) achieved in 100 % water (exp. 92, Table 6). 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 %⁵⁴, not specified if LA yield is in mol or wt %), at 160°C after 16 h (exp. 93, Table 6). According to the authors, the good performances extraordinary behavior of Amberlyst 70 in the H₂O/GVL solvent are due as previously reported by Zuo, to the capacity of GVL of solubilizing the cellulose, which increases the accessibility of the sugar oligomers to the acid sites where the dehydration reactions take place. In addition, GVL swells the Amberlyst 70 resin, thereby improving the diffusivity through the pores and increasing its the catalytic activity of Amberlyst 70.

The employment of fluorinated solvents like perfluorohexane tri-fluoroacetic acid has also been also studied for biomass conversion to LA [13201]. However, tri-fluoroacetic acid forms azeotrope with water, making very difficult its recovery and reuse. 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, another 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, which is a renewable and sustainable liquid resource for energy, is very often employed as component in biphasic systems for the conversion of biomasses to LA, because its use eliminates the need for any pretreatment method, converting simultaneously cellulose and hemicelluloses to LA, not requiring, therefore, any separation of hexose and pentose sugars. A biphasic system, consisting of GVL and an aqueous solution of HCl (0.1–1.25 M) containing NaCl and a solute, such as sugar or salt, has been reported by Wettstein et al. for LA production. The reaction was carried out at 155 °C and was found that majority of LA was extracted by GVL solvent, achieving yields from cellulose after 1.5 h to LA of 72 mol %, which corresponds to 51.6 wt % [13302].

A biphasic reactor system consisting of an aqueous layer containing the acid catalyst, such as 1M H₂SO₄ or zeolite (ZSM-5), and an organic layer consisting of organic solvent, such as

760 2-sec-butylphenol (SBP), 4-n-hexylphenol (NHP) or 4-propylguaiacol, have been developed by
761 Dumesic et al. for the production of LA through the conversion of corn stover to furfural carried out
762 at 170°C, followed by the reduction of furfural to furfuryl alcohol which is further hydrolyzed to LA
763 at 125°C [13403].

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

775 In recent years, research on ionic liquids has gained great attention due to their wide
776 employment of them as solvents as well as catalysts. Ionic liquids are salts consisting of ions which
777 are liquid at ambient temperatures or below 100 °C [13504]. The stability, the low vapour pressure,
778 the easy separation and recyclability of ionic liquids, coupled with the fact that their physical and
779 chemical properties can be easily tuned by varying the ions, are some of the important reasons for
780 the intense interest for the use of researchers in these solvents which have been used to convert
781 raw biomass into added-value products [13605-14211]. In detail, catalytic conversion of biomass to
782 LA in the ionic liquid [EMIM][Cl] using a hybrid catalyst (CrCl₃ and HY-zeolite) has shown to yield
783 46 wt % of LA from cellulose working at 61.8°C for 14.2 minutes, whereas 20 wt % yield was
784 obtained from empty fruit bunch compared to 15.5 wt % yield achieved in the absence of the ionic
785 liquid [110]. Some attempts have also been made to selectively convert cellulose into LA using
786 MW microwave-assisted synthesis in SO₃H-functionalized ionic liquids; which resulted after 30
787 minutes at 160 °C in the LA yield of 39.4 wt % was reached [14211]. Nevertheless, ionic liquids also
788 show important drawbacks. First of all, their status as 'green solvents' has been questioned: the fact
789 that their properties can be tuned by changing the involved ions leads to an enormous diversity in
790 both the number and properties of ionic liquids, making both the method of production of the ionic
791 liquid and its properties (toxicity, explosivity, biodegradability, etc.) not completely
792 environment-friendly [14312]. Another disadvantage of ionic liquids is their high viscosity which
793 reduces mass transfer in the liquid, leading to only a small fraction of the liquid to be in contact with
794 the substrates. Moreover, the low vapour pressure of ionic liquids, which is considered one of their
795 'green' characteristics, prevents an easy recovery of used ionic liquids via distillation, requiring
796 alternative methods for separating the reacting species and recovering the ionic liquid [14413].
797 Moreover, the effect of moisture in the feedstock on the performance of ionic liquids is another
798 aspect that needs to be considered, because some chemical properties, such as anionic basicity, can
799 be adversely affected by the presence of water [14514], whereas physical properties, such as viscosity,
800 can actually be improved by the addition of water [14413]. Furthermore, ionic liquids can also lead
801 to severe corrosion in numerous metals, especially in the presence of water, leading to process
802 equipment damage and additional cost [14615]. As a consequence, the need to purify them after
803 recycling, together with their potential sensitivity to moisture and oxide impurities represent
804 additional challenges, not already solved. Finally, another limitation in the employment of ionic
805 liquids is their high cost, typically between two and one hundred times that of organic solvents
806 [14716]. At the moment, all these elements have limited their perspectives for use at industrial
807 scale.

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812 4. Biochar recovery and exploitation possibilities

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814 The hydrothermal conversion of ~~any~~ biomass feedstock produces a carbonaceous charred solid
815 by-product, named “hydrochar”, which is separated from the hydrolysate solution by filtration. This
816 solid includes mainly humins deriving from the degradation of furanic intermediates of C₅ and C₆
817 sugars source, which have undergone aldol addition/condensation reactions [22,14817].
818 Furthermore, the ~~influence contribute~~ of the degraded lignin fraction should be considered, if
819 lignocellulosics are used as starting feedstock, thus further contributing to the increase of
820 aromaticity degree of the final hydrochar [14918]. In addition, the chemical composition of the
821 hydrochar may be even more complex, if the starting feedstock is a waste material, such as
822 bio-solids, municipal wastes, paper mill sludge, and so on. On this basis, it is noticeable that the
823 yield and properties of the char strongly depend on the composition of the starting feedstock and ~~the~~
824 adopted process conditions, ~~these last including temperature, residence time, substrate~~
825 ~~concentration and pH~~ [15019,15120].

826 The hydrochar recovered after LA production could be ~~immediately~~ used as solid bio-fuel
827 within the same biorefinery plant, having a heating value which is typical of that of the traditional
828 lignite coal [9774,15221] or as a storable solid fuel for energy generation (via cocombustion or use in
829 carbon fuel cells). ~~In detail, t~~The higher heating value (HHV) of the hydrochar is always higher than
830 that of the starting untreated biomass [25], because of the predominant dehydration route which has
831 occurred during the hydrothermal treatment, having released furans (e.g. furfural and
832 5-hydroxymethyl furfural) and organic acids (levulinic acid, formic acid) into the liquid phase. The
833 hydrothermal treatment of a carbohydrate feedstock is not limited to the production of ~~LA levulinic~~
834 ~~acid~~ but can be applied for the production of other organic acids [15322] and, from the perspective of
835 the solid residue, different kinds of hydrochar can be obtained. However, the available information
836 on hydrochar are limited and, therefore, many works are incomplete and most of them report low
837 yields towards LA without explaining the amount and the nature of by-products. ~~Definitely, passing~~
838 ~~to raw and waste starting materials, T~~he amount of ~~the~~ generated ~~byproduct~~ wastes ~~increases when~~
839 ~~moving from raw to waste starting materials is increasing~~ and therefore new exploitation
840 possibilities of these biowastes, in addition to the traditional energy recovery must be evaluated and
841 developed, thus ensuring the sustainability of the entire process. In the field of the hydrothermal
842 route, the state of the art on hydrochar suggests that it is certainly a valuable resource, having a
843 chemistry which is typical of carbon materials. The main proposed alternative use of the hydrochar
844 is for the synthesis of porous activated carbons, by suitable physical and chemical activation
845 procedures [15423, 155]. However, from a different perspective, new applications have been studied,
846 ~~that is~~ for environmental applications, such as a soil amendment for the increase of soil fertility,
847 while providing a long-term carbon sink [15624,15725] and as an efficient adsorbent in
848 environmental remediation processes [15826,15927]. Furthermore, hydrochar is suitable for a wide
849 range of other important applications in modern nanotechnology, ~~including going from~~ catalysis
850 ~~and to~~ energy storage and generation [16028].

851 ~~The above reported exploitation possibilities provides the direct use of the hydrochar, despite~~
852 ~~some chemical modification of the same.~~ Recently, different and smart approaches for hydrochar
853 exploitation have been proposed, which involve the use of the “humins-like” hydrochar as starting
854 feedstock for new upgrading reactions. Hoang et al. have studied the exploitation of humins via dry
855 reforming. The volatile organic components released during heating are mainly phenols, aromatic
856 hydrocarbons, and furans, which can be used as a source of potential chemicals or further reformed
857 to syngas/H₂ in the second stage, thereby converting the whole humin feedstock. Due to the
858 recalcitrant behaviour of this thermally stable bio-material, its non-catalytic dry reforming is very
859 difficult, but the authors have significantly improved the kinetics by adopting Na₂CO₃ as alkali
860 catalyst [16129]. In another research, Wang et al. have recently studied the catalytic hydrotreatment
861 of C₆-derived humins, by using ~~a~~ formic acid as hydrogen donor in isopropanol or hydrogen gas,
862 achieving promising results (humins conversion about 70 %) with Ru/C catalyst. The authors have
863 partially depolymerized the carbonaceous humins, ~~producing identifying mainly~~ substituted

864 alkylphenolics, naphthalenes, and cyclic alkanes, which can be used as liquid biofuels or as a source
865 for interesting bulk chemicals after fractionation [16230].

866 These new applications of the hydrochar add value to this waste material and provide a
867 synergistic and holistic approach that could advantageously be integrated into future biorefinery
868 schemes beyond its direct use as a solid fuel, ~~but the effective utilization of hydrochar would~~
869 ~~requires~~ further experimental research and investigation in terms of relationships among feedstocks
870 compositions, physico-chemical properties and process conditions ~~and development of a diverse~~
871 ~~range of processing options~~ to produce hydrochar with characteristics required for various industry
872 applications. ~~This approach will have a positive effect on the techno-economic viability of~~
873 ~~biorefinery schemes involving the conversion of biomass into bio-based chemicals such as LA and~~
874 ~~HMF.~~

875 5. Conclusions and future perspectives

876 The synthesis of LA from biomasses can be achieved from C₅-sugars in hemicellulose and
877 C₆-sugars in cellulose, starting from simple sugars to real raw and waste biomasses. A closer
878 inspection of the described results reveals that although monosaccharides like fructose and glucose
879 offer the highest product yields, the use of polysaccharides and in particular raw and waste
880 biomasses is required for industrial-scale production to be viable from ~~the~~ sustainability and ~~the~~
881 economical viewpoints. In order to achieve these goals, improvements are needed in the catalyst and
882 solvent selection. ~~Homogeneous systems are used widely in laboratory scale syntheses, but in larger~~
883 ~~scale processes, there are still drawbacks in separating the product with high purity and without~~
884 ~~degradation, in recovering and recycling the catalyst and in tackling ecological and safety hurdles.~~
885 ~~On the other hand, heterogeneous catalysts are easier to recover and recycle, but they give lower~~
886 LA yields than homogeneous systems and need to be regenerated after consecutive runs. ~~The~~
887 ~~industrial scale adoption of heterogeneous catalysts is not still feasible, mainly due to their difficult~~
888 ~~reactivation/recycling, caused by the formation of solid humin by-products, which are found to be~~
889 ~~very thermally-stable. This drawback is particularly relevant for raw lignocellulosic biomasses, due~~
890 ~~to the presence of the degraded lignin fraction in the final hydrochar. At the current state of the art,~~
891 ~~heterogeneous catalysts are employed only at laboratory scale with simple sugars as starting~~
892 ~~feedstocks. In this case, the production of humins is better controlled, but the problem of higher cost~~
893 ~~of these "ideal" feedstocks (respect to the lignocellulosic ones) strongly limits the scale-up on larger~~
894 ~~scale. Further research is surely necessary to solve these problems and develop new cheaper,~~
895 ~~thermally-stable and easily recyclable heterogeneous catalysts.~~

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

902 The ~~use exploitation~~ of raw and waste biomass is attracting increasing interest and the use of novel
903 non terrestrial resources ~~such~~ as algae and chitin/chitosan can represent a significant turning point.
904 In addition, ~~also~~ the recovery and ~~the~~ exploitation of the solid residues obtained in ~~the~~ LA
905 production processes is another important aspect to be addressed from a sustainable biorefinery
906 perspective.

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

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