

Review

Recent Advances in Mechanochemical Pretreatment of Lignocellulosic Biomass

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Abstract: Biorefineries are industrial facilities where biomass is converted into chemicals, fuels and energy. The use of lignocellulose as raw material implies the development of pretreatments to reduce its recalcitrant character prior to the processes that lead to the synthesis of the products of interest. These treatments are based on physico-chemical processes where it is necessary to use acids, bases, oxidants, and high pressure and temperature conditions that lead to the depolymerization of lignocellulose at the expense of generating a series of streams that must be treated later or to the production of by-products. In recent years, mechanochemistry is becoming relevant in the design of processes that help in the depolymerization of lignocellulose. These mechanochemical processes are being used in combination with chemicals and/or enzymes, allowing the use of minor loads of reagents or enzymes. In this review, the advances achieved in the use of mechanochemistry for treating lignocellulosic biomass or cellulose will be presented, with special emphasis on how these mechanochemical processes modify the structure of lignocellulose and help subsequent treatments. It will focus on using ball milling or extrusion, ending with a section dedicated to future work needed to implement these technologies at the industrial level.

Keywords: mechanochemistry; lignocellulose; cellulose; ball milling; extrusion; depolymerization; alkaline treatment; acid treatment



Citation: Pérez-Merchán, A.M.; Rodríguez-Carballo, G.; Torres-Olea, B.; García-Sancho, C.; Maireles-Torres, P.J.; Mérida-Robles, J.; Moreno-Tost, R. Recent Advances in Mechanochemical Pretreatment of Lignocellulosic Biomass. *Energies* **2022**, *15*, 5948. <https://doi.org/10.3390/en15165948>

Academic Editor: Jin Hyung Lee

Received: 11 July 2022

Accepted: 14 August 2022

Published: 17 August 2022

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1. Introduction

Lignocellulosic biomass is considered an exciting raw material from which chemical products and biofuels can be obtained without affecting the food chain. Other natural carbohydrates are those stored in micro and macroalgae [1] and chitin [2]. From these carbohydrates and lignin, it is possible to synthesize molecules with multiple functional groups named building blocks. Due to the high functionalization of these building blocks, 5-hydroxymethylfurfural (5-HMF), furfural (FUR) or levulinic acid (LA) have been proposed as the starting point for the synthesis of a myriad of chemicals, fuels and polymers. The bibliography shows a great number of reviews [3–7] where the processes, reactions and applications of those compounds are revised. However, to reach the final target product, i.e., chemical, biofuel or polymer, from both carbohydrates and lignin, one of the first steps is to subject the lignocellulose to a series of physicochemical treatments. These treatments release the lignin seal and allow access to the polysaccharides (hemicellulose and cellulose). In the literature, numerous works [8–17] describe chemical treatments that require severe conditions of temperature, pressure, mineral acids or strong bases and organic solvents, whereupon it is possible to recover the different fractions of lignocellulose. These chemical treatments generate a series of streams that must be subjected to further treatment prior to their disposal. In addition, they also lead to the appearance of several by-products (FUR, 5-HMF, formic acid) that can be inconvenient for subsequent processes such as those related to enzymatic hydrolysis [18–23] very sensitive to those compounds.

Furthermore, the pretreatment stages constitute about 40% of the overall cost of production of bioethanol [24].

On the other hand, the mechanochemical treatment of biomass is currently attracting the attention of researchers. These physical treatments provide energy in the form of a mechanical action reducing the particle size, crystallinity, and degree of polymerization of lignocellulosic materials, which increases the specific surface area but without generating toxic by-products. The physical forces that cause mechanical and chemical changes in lignocellulose during mechanochemical treatments are impact, compression, friction and shear [25]. According to Lomosky et al., these processes are energy-intensive; therefore, from an economic point of view, mechanical energy is expensive, and it is necessary to use it efficiently [25]. That is why it is frequently used in combination with other pretreatment processes to reduce energy consumption [24].

Despite the potential of mechanochemistry in biomass conversion, mechanochemical pretreatments have the final objective of facilitating the separation of the polymers that constitute lignocellulose and making both polysaccharides and lignin more susceptible to subsequent chemical or enzymatic treatments (Figure 1). This reduces the extreme reaction conditions. The use of mechanochemistry for the direct obtention of products from lignocellulose or for the production of platform molecules is very limited. For example, Furusato et al. [26] used mechanochemistry in the presence of a solid catalyst (layered niobium molybdate) to obtain glucose reaching 72% of water-soluble sugars.

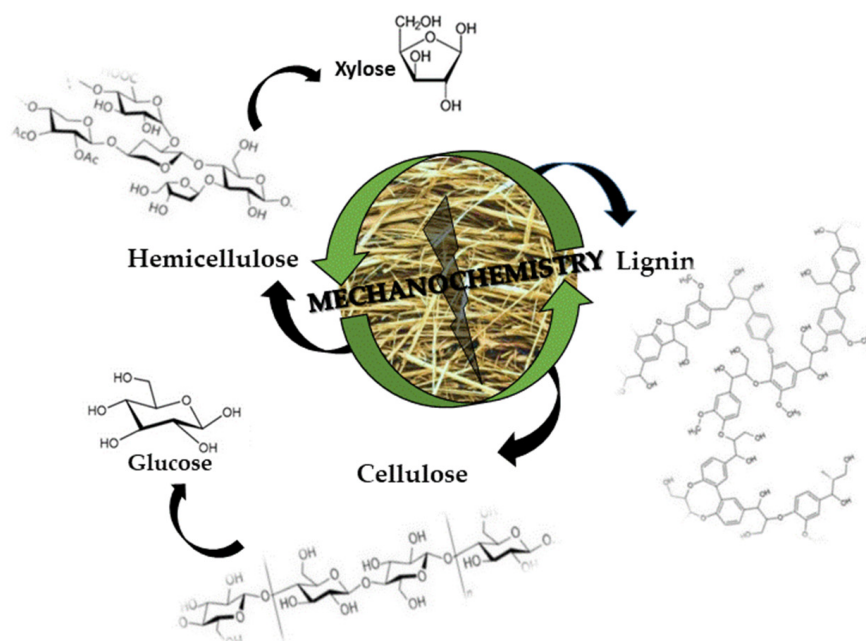


Figure 1. Deconstruction of lignocellulose into their biopolymers by mechanochemical treatment.

The main mechano-physical treatment described in the literature for the deconstruction of lignocellulose is related to ball milling. It is worth mentioning that although there is a whole variety of equipment for treatments or synthesis through mechanochemistry, in the case of biomass, together with milling, the use of extrusion has also been described. We will dedicate a section to the latter in the review. Therefore, this review will present the advantages of these treatments with or without the assistance of chemical coadjuvants such as acids (liquids or solids) and bases. We will present the types of mills used, how they affect the physico-chemical properties of the biomass and how this effect is transferred to the reaction or further processing of the biomass. In this review, we will not focus on the reaction conditions or the reaction mechanisms related to downstream processes but only on how this mechanical treatment favors these processes. Moreover, we do not attempt to describe the technical properties of the mills or what are the physical processes involved.

Excellent reviews about those topics can be found in the literature [25,27,28]. This review will help the readers to understand the challenges and, more importantly, provide insights into designing novel mechanochemical pretreatment strategies for biomass.

2. Ball Milling Pretreatment of Cellulose and Biomass

2.1. Non-Assisted Mechanochemical Pretreatment of Cellulose

One of the main disadvantages of cellulose for its complete utilization by chemical or biological means is its high crystallinity, which makes chemical and/or enzymatic attack difficult. That is why some studies focus on how milling affects its physical properties. The changes that cellulose undergoes have been evaluated by studying different parameters such as its morphology, crystallinity, particle size, and the number of reducing end groups, among others. The aim of studying all these properties is to demonstrate that the milling treatment can weaken the network of hydrogen bonds that hold the cellulose fibers together, fractionating these cellulose fibers and thus reducing their particle size, eventually leading to the amorphization of the crystalline structure.

Table 1 shows some of the published works in which cellulose is the starting biomass material, indicating the type of mill, time and speed of rotation, and the reaction for which the treated cellulose was studied. The cellulose is provided by a commercial company and not extracted from lignocellulosic material. Although this fact makes the research work and the comparison between different works easier, information is also lost on how the cellulose extraction processes can affect the nature of the cellulose. For example, what proportion of amorphous accompanies the sample, what is the cellulose richness of the sample, etc. Table 2 below shows some of the works dealing with real biomass.

Table 1. Pretreatment of cellulose by ball milling.

| Entry | Mill | r.p.m. | Time (h) | Balls/Biomass | Reaction | Reference |
|-------|-------------------------------|------------------|-------------------|--------------------------------------------------------------------|-------------------------------------------------------|-----------|
| 1 | Ball mill | 900 | 1, 4, 7 | ^a Ball (1 Ball; Ø = 15 mm)/2 g | Cellulose hydrolysis in hot compressed water | [29] |
| 2 | Ball Mill | 450 | 2 | ZrO ₂ (900 g of balls; Ø = 3.5 mm)/30 g | Cellulose hydrolysis in water/CO ₂ system | [30] |
| 3 | Planetary ball mill | 600 | 2 | ZrO ₂ (25 balls; Ø = 1 cm)/20 g | Pyrolysis of cellulose | [31] |
| 4 | Ultrafine vibration ball mill | ^b n.p | 1 | ZrO ₂ (Ø = 6–10 mm); Volume ratio 1:2 (cellulose:balls) | Methyl levulinate | [32] |
| 5 | Ultrafine vibration ball mill | ^b n.p | 3–480 min | ZrO ₂ (Ø = 6–10 mm); Volume ratio 1:2 (cellulose:balls) | Methyl levulinate | [33] |
| 6 | Planetary ball mill | 300 | 1 | ZrO ₂ (18 balls; Ø = 1 cm)/3 g | Methyl lactate | [34] |
| 7 | Planetary ball mill | 300, 600, 900 | 4, 8 | Tungsten carbide (70 balls; Ø = 3 mm)/5 g | Hexitols, Ethylene Glycol | [35] |
| 8 | Planetary ball mill | 400 | 8 | Steel Balls/mass ratio balls:sample 100:1 | 5-HMF | [36] |
| 9 | Planetary ball mill | 500 | 0.5, 2, 6, 16, 24 | ZrO ₂ (10 balls; Ø = 1 cm)/3 g | Photoreforming of cellulose to produce H ₂ | [37] |

^a The composition of the ball is not provided ^b n.p.: not provided.

Yun and Wu [29] treated microcellulose by ball milling at different milling times (Entry 1, Table 1). They observed changes in the cellulose microstructure caused by ball milling.

Thus, 1 h of cellulose milling was sufficient to reduce the particle size significantly, but longer times (7 h) led to agglomeration of cellulose particles and hence were ineffective in reducing cellulose particle size. Short cryogenic milling times (2 min) were very effective in reducing the particle size of crystalline cellulose even lower than 4 h of milling, but cellulose crystallinity was merely affected. Although agglomeration did occur, the crystalline peak at 7 h completely vanished, indicating the transformation from a crystalline cellulose structure to an amorphous one. Thus, three factors can be involved in the reactivity of cellulose during the hot-compressed water hydrolysis reaction, i.e., particle size, the degree of polymerization (glucose oligomers) and crystallinity. The first does not seem to have any noticeable influence on the conversion of cellulose since the cellulose conversion of both raw cellulose and the one that underwent the cryogenic milling was very similar. Moreover, the degree of polymerization was closely related to the particle size, so the authors concluded that any reduction in this parameter played a minor role in cellulose reactivity during hydrolysis in HCW. Therefore, the cellulose reactivity was controlled by the crystallinity of cellulose; thereby, the highest specific reactivity was achieved after 7 h of milling. The selectivity of the different oligomers was followed, and the milling time showed that the concentration of each glucose oligomer increased with ball milling time, i.e., the degree of polymerization was decreased to a more complex mixture of glucose oligomers. In conclusion, the authors attributed the highest reactivity of the milled cellulose to the destruction of the hydrogen bonding networks that magnified the accessibility of glycosidic bonds in the glucose chains.

Wu et al. [30] studied the effects of ball milling in the hydrolysis of cellulose in hot water-CO₂ conditions (Table 1, Entry 2). The cellulose milling led to a reduction of crystallinity and particle size of cellulose. In addition, ball-milled cellulose showed a thin layer structure, while original cellulose was much more irregular. The results indicated that ball milling crushed and peeled cellulose into small and thin particles. The authors studied how milling and CO₂ separately or together affected the kinetics of cellulose conversion to glucose and dehydration of glucose to HMF. These changes in the cellulose structure had a crucial effect on cellulose hydrolysis. The ball-milled cellulose conversion without using CO₂ was almost twice that of original cellulose at the same temperature. Dissolved CO₂ in water provided homogeneous H⁺ for cellulose hydrolysis, and cellulose conversion increased when CO₂ was used. However, the effect of CO₂ was more limited because of the low solubility of CO₂ in water and the fact that carbonic acid is a weak acid. Therefore, the enhancement of CO₂ was weaker than ball milling at all temperatures tested. But, when both were used, glucose and HMF yield significantly improved.

Khan et al. [31] studied the effect of ball milling on the calorific properties of crystalline cellulose (Table 1, Entry 3). As mentioned before, they found that the ball milling decreased the crystallinity index determined from the XRD patterns. In addition, the FTIR spectra gave information about the amorphization of cellulose caused by the ball milling treatment since the broad band ascribed to the hydrogen bond network became sharper and shifted to higher wavenumbers. This was assumed to indicate the breakdown of the hydrogen bond network that maintained the crystalline cellulose structure. This milling treatment was beneficial in terms of reducing both the activation energy and thermal stability of the ball-milled cellulose compared to the pristine cellulose. Thus, the activation energy was calculated by different kinetic models, which showed that the activation energy was decreased after the ball milling. This fact was ascribed to a more porous structure and lower crystallinity of the ball-milled cellulose.

The crystalline structure of cellulose is a hurdle that must be overcome if the objective is the complete exploitation of glucose both in enzymatic and chemical reactions. Therefore, the mechanical pretreatment of cellulose is an interesting option since it deconstructs the cellulose but without producing by-products (humins, 5-HMF, LA . . .) that consume glucose. The ball milling pretreatment of cellulose was proposed by Chen et al. [32,33] to obtain methyl levulinate (ML) (Table 1, Entry 3). They reported that the yield to ML was increased when the ball milled cellulose reacted with Al₂(SO₄)₃ at all the temperatures

assayed. However, as the reaction proceeded, the yield of ML was slightly decreased [32]. This decrease in yield accounted for a higher reactivity of the ball milled cellulose due to the reaction where intermediate methyl glucoside was formed in a higher amount leading to by-products and giving an overall lower ML yield. The authors showed that ball milling, as previously shown in this review, was an effective method for reducing the crystallinity and particle size of cellulose and increasing reducing-end groups [33]. Among the parameters of milling with the strongest influence on the pretreatment was the milling time. The authors showed that times higher than 120 min did not improve the catalytic performance of $\text{Al}_2(\text{SO}_4)_3$. As ball milling is an energy-consuming process, the authors carried out further catalytic studies after 120 min of milling. The authors found that there was a negative correlation between crystallinity and catalytic activity and a positive correlation with the increase of reducing-end groups; therefore, it is mandatory to reduce the crystallinity so that there is an increase in the reducing-end groups. However, the particle size was not found to be a critical parameter to control.

Other research groups applied this pretreatment of the cellulose to improve the yields of different target compounds obtained from cellulose such as methyl lactate [34], hexitols and ethylene glycol [35], HMF [36] and even H_2 [37].

Lactic acid is a promising platform compound because it is a biodegradable polymer polylactic acid precursor. Therefore, Tominaga et al. [34] proposed a complex catalytic system based on a three-component Lewis acid catalyst comprised of metal triflates, In chloride, and Sn chloride for the direct synthesis of methyl lactate (MeLac) from cellulose in methanol (Table 1, Entry 6). Different metal triflates were assayed, and Sm triflate was the most effective, providing a 45% yield in MeLac. This yield was increased up to 64% when the cellulose was ball-milled in the presence of methanol. They observed that the dry ball milling pretreatment did not positively affect the MeLac yield. Therefore, they studied the particle size of the cellulose after both dry and wet milling and non-treated cellulose. They found that the dry ball milling cellulose particle size was comprised of two kinds of particles with different diameters. The lower average diameter was about 1 μm , and the higher was about 50 μm , the latter being the aggregate of the former. The wet milled cellulose showed a uniform distribution of particle sizes with an average diameter of 7.8 μm after 2 h of milling. The authors attributed the activity differences to the presence or absence of free OH groups, which are more abundant in the dry milled cellulose, leading to undesirable degradation products.

Sorbitol is quite useful as an artificial sweetener, and ethylene glycol is essential in pharmaceuticals, textiles and automobiles. Sorbitol is obtained industrially from the glucose contained in starch; therefore, cellulose could become the feedstock for synthesizing this hexitol. However, it is necessary to overcome its recalcitrant structure for its utilization. In this context, Mankar et al. [35] proposed a catalytic system based on heteropolyacid supported by zirconia and Ru/C catalyst for the hydrolysis–hydrogenation of cellulose (Table 1, Entry 7). They observed that the yield of both hexitols and ethylene glycol was highly improved when the cellulose was ball-milled, reaching 26.2 and 40%, respectively, at 220 °C after 5 h and 100% cellulose conversion. Under the optimized milling conditions (900 rpm for 8 h), it was possible to reduce the crystallinity of the cellulose from 88.9 to 6.5%. Moreover, by FTIR, the band corresponding to the O–H stretching vibration became stronger with the increase in the ball milling intensity ascribed to the cleavage of the hydrogen bonding network. Therefore, the crystallinity of the cellulose decreased. This study shows that the more severe the pretreatment of the cellulose, the better the catalytic performance of the catalysts.

5-HMF, which can be synthesized from biomass-derived carbohydrates such as fructose, glucose and cellulose, is an important platform intermediate for producing fine chemicals, polymeric materials and biofuels [7,38–41]. If cellulose is the chosen feedstock of carbohydrates monomers, Hou et al. [36] showed that cellulose ball milling can enhance the catalytic performance of titanyl sulfate (TiOSO_4) (Table 1, Entry 8). The authors studied the ball milling of cellulose with and without the incorporation of TiOSO_4 . Both situations

resulted in the emergence of cracks in the cellulose compared with the raw microcrystalline cellulose, which had a smoother and denser morphology. The particle size analysis also demonstrated that the particle size decreased when the cellulose was ball milled in the absence of TiOSO_4 , showing an average particle size slightly lower than the pristine cellulose. Still, when the TiOSO_4 was mixed with cellulose and ball milled, the particle size was reduced to 7.3 μm from the initial 35 μm . The authors also showed the beneficial effect of mixing the cellulose and catalyst when the average molecular weight was measured. In this case, it had a remarkable reduction of such parameters, pointing out that the milling resulted in some depolymerization of cellulose, i.e., some glycosidic bonds were broken during the ball milling. Therefore, the cellulose conversion to HMF was studied in a biphasic medium using TiSO_4 as a catalyst. The authors showed that the non-treated cellulose yielded 16.4% after 240 min and at 160 °C. The yield was improved when the cellulose was milled, reaching a 31.6% yield after 120 min, and if the milling was carried out along with the catalyst, the HMF yield was 33.6% after 90 min. The beneficial effect of ball milling in the reaction is obvious by reducing the cellulose fractions' crystallinity and average molecular weight.

Sunlight can convert energy into chemicals and fuels such as CH_4 , alcohol and H_2 . Lan et al. [37] described the enhancement in the photoreforming of cellulose to produce H_2 (Table 1, Entry 9). The milling time affected the degree of polymerization (DP), crystallinity, and amorphization of cellulose. All the ball milled cellulose improved the quantum yield and H_2 production, even after milling times as short as 0.5 h. Although the milling time decreased the DP, this result did not correlate strongly with the H_2 production. Thus, after 0.5 h of milling, the DP was 165.4 and the H_2 production was 10.1 $\mu\text{mol/h}$. It was 13.3 $\mu\text{mol/h}$ after 24 h of milling and a DP of 32.1. However, there was a close relationship between crystallinity and quantum yield and hydrogen production. Based on these findings, the authors claimed that the amorphous cellulose promoted the observed improvement due to the enhancement of accessibility of the internal cellulose structure to the reactant species. Considering that the cellulose was completely amorphous after 2 h of milling, the improvement of photo-reforming activity at higher times of milling does not rely only on the decrease of crystallinity. The authors demonstrated that the recrystallization of the amorphous cellulose to the cellulose II structure was water-induced and the photo-reforming activity was correlated to the emergence of cellulose II. Thus, cellulose II increased from 49.3% to 68.9% when the milling time increased from 0.5 h to 6 h, and the reactivity followed the same trend. Accordingly, the amorphous cellulose produced by ball milling went through recrystallization (to cellulose II) during photo-reforming in the aqueous phase and they found that the proportion of recrystallized cellulose II in the ball milling cellulose correlated well with the H_2 production rate.

2.2. Non-Assisted Mechanochemical Treatment of Lignocellulosic Biomass

To improve the barley straw's acid saccharification, Sidiras et al. [42] treated the straw by ball milling with two kinds of mills, rotatory and vibratory (Table 2, Entry 1). The work aimed to obtain the highest yield of glucose by acid hydrolysis of the pretreated cellulose and develop a model which accounted for the hydrolysis of both kinds of cellulose, amorphous and crystalline. The decrease in cellulose crystallinity rate was more affected by the type of mill than by the type of biomass. The pretreated solid was prehydrolyzed with HCl at 100 °C for 3.5 h. After this treatment, the liquid fraction contained the hemicellulose fraction of the lignocellulose, and the solid fraction comprised cellulose and lignin. Saccharification of straw hemicellulose during prehydrolysis was not affected by milling time. But, on the other hand, due to the formation of amorphous cellulose after milling, the compound was hydrolyzed, even under the comparatively mild conditions of prehydrolysis. Despite the amorphous cellulose being hydrolyzed under mild conditions, at least 10 wt% of cellulose was lost as degradation compounds. Then, 7 min of the solid fraction hydrolysis in a sulfuric acid medium at 175 °C allowed the saccharification of the 50% initial cellulose to water-soluble carbohydrates, with about 90%

as glucose and 10% as mostly cellobiose. Under the same conditions, about 10% of the initial cellulose was converted to glucose degradation products, and the remaining 40% represented non-hydrolyzed cellulose that could be recycled to yield more sugars.

Table 2. Pretreatment of lignocellulosic biomass by ball milling.

| Entry | Biomass | Mill | r.p.m. | Time (h) | Balls/Biomass | Reaction | Reference |
|-------|-------------------------------------------------------|----------------------------------|-------------------|------------|------------------------------------------------------------------------------------------------------|---------------------------------------------------------|-----------|
| 1 | Barley straw | Ball mill/vibratory | 70 | 2–10 | Corundum balls (2.75 kg/30 g) | Acid hydrolysis | [42] |
| 2 | Oil palm empty fruit bunch fibers | Planetary ball mill | 230 | 6–24 | Ceramic balls (40 balls; $\varnothing = 6$ mm)/5 g | Levulinic acid | [43] |
| 3 | Masson pine | Planetary ball Mill | 600 | 0.5–8 | ZrO ₂ (25 balls; $\varnothing = 1$ cm)/4 g | Dissolution of lignocellulose | [44] |
| 4 | Japanese cedar/Used clothing (100% cotton)/Used paper | Ball mill | 60 | 48 | Ceramic balls (1 kg; $\varnothing = 15$ mm)/10 g | 5-HMF | [45] |
| 5 | Corn stover | Planetary ball mill | 300 | 0.3–1 | Al ₂ O ₃ -ZrO ₂ -Steel volume ratio of biomass:balls was set at 1:1 | Enzymatic hydrolysis | [46] |
| 6 | Corn stover | Ultrafine vibration ball milling | ^a n.p. | 5–120 min | ZrO ₂ ($\varnothing = 6$ –10 mm)/Volume ratio biomass:balls 1:2 | Ethyl levulinate | [47] |
| 7 | Corn stover | Vibration grind gill | ^a n.p. | 5–480 min | ZrO ₂ ($\varnothing = 6$ –10 mm)/volume ratio of biomass:balls 1:2 | Alcoholysis of carbohydrate | [48] |
| 8 | Corn stover | Ultrafine vibration ball milling | ^a n.p. | 10–480 min | ZrO ₂ ($\varnothing = 6$ –10 mm)/volume ratio of sample:balls: 1:2 | Enzymatic hydrolysis and alcoholysis (Ethyl levulinate) | [49] |
| 9 | Forestry materials/Agricultural residues/Urban wastes | Mixer-ball mill | 1200 | 4 h | ZrO ₂ (2 balls; $\varnothing = 12$ mm)/1.5 g | Ethylene glycol | [50] |
| 10 | Birch, pine, reed and walnut shell | Planetary ball mill | 450 | 6 h | ZrO ₂ | Enzymatic hydrolysis | [51] |
| 11 | Corn stover | Planetary ball Mill | 220 | 1, 3, 5 | Steel (70 balls; $\varnothing = 10$ mm)/mass of biomass not provide | xylooligosaccharides and glucose | [52] |
| 12 | Bamboo | Vibratory mill | ^a n.p. | 0.5–1 | Steel (3 balls; $\varnothing = 9.5$ and 15.85 mm)/1 g | Enzymatic hydrolysis of carbohydrate | [53] |

^a n.p.: not provided.

In the production of 1 kg of palm oil, approximately 4 kg of dry biomass is generated, from which one-third is oil palm empty fruit bunch (EFB) [43]. This residue is rich in carbohydrates (42.7–65% cellulose, 17.1–33.5% hemicellulose), which makes it an interesting raw material for synthesizing chemicals and fuels. Like all lignocellulosic residues, it is accompanied by lignin, preventing chemical or enzymatic treatments from accessing the carbohydrates. Thus, Chin et al. [43] proposed the ball milling pretreatment of this residue to reduce cellulose crystallinity and particle size (Table 2, Entry 2). They observed that grinding time affected particle size and crystallinity, with times longer than 6 h necessary to achieve a significant reduction of both parameters. Likewise, SEM image analysis showed

that the initial particles were rigid with a smooth surface. In contrast, as they underwent the milling treatment, the surface became rougher, and the size decreased, indicating particle disruption. After this, the solid underwent treatment in a sulfuric acid medium to obtain levulinic acid. It was observed that the ball milling increased the production of levulinic acid when the reaction temperature was maintained under 200 °C for milling times higher than 6 h in accordance with the characterization of the treated residue. The production of levulinic acid was optimized by a response surface morphology design leading to a maximum production of levulinic acid of 10.8 g/L (53.9% based on the total cellulose) at 186 °C and 195.8 min of reaction time with a sulfuric acid concentration of 0.57 N.

The applications of lignocellulose components make it necessary to isolate the different fractions that compose it without substantially modifying its composition or structure. Achieving this objective is not easy due to the difficulty of finding a medium that effectively dissolves the lignocellulose in its totality. There are many approaches for dissolving lignocellulose in organic or inorganic solvent systems, but those methods can dissolve one of the fractions but not others. Zhu et al. [44] developed a method based on an inorganic sodium hydroxide aqueous solution to dissolve ball milled softwood at room temperature (Table 3, Entry 3). The raw material was the Masson pine (*Pinus massoniana*), the most widespread species in the forests of southern China. In this work, 1 wt% of ball-milled solid was treated with solutions of NaOH (2–18 wt%). It was observed that milling times higher than 4 h are necessary to obtain clear solutions, whereas short ball milling times were not effective. The extractable lignin increased from 0 to 8 h of milling yielding 17.4% after 4 h of milling. Longer ball milling time results in greater cleavage of β -aryl ether bonds in lignin. Therefore, although the β -aryl ether structure of lignin changes depending on the milling time, the degree of change was negligible at 4 h of ball milling time. Moreover, the nitrobenzene oxidation method used to check structural changes of lignin's aromatics moieties did not show evidence of such changes after 8 h of milling. The rate of cellulose dissolution was also studied, and it was observed as being faster than lignin when the softwood was milled from 0.5 to 3 h. This fact pointed out that cellulose was solubilized more easily than lignin in this basic medium. The authors ascribed the differences in the solubility to the different structural units, linked types, and distribution of cellulose and lignin in the cell wall components. Finally, the authors studied the regeneration of the solubilized cellulose and lignin, decreasing the solution's pH from 7 to 0 reaching 83% retrieval at pH 0 and 17 wt% of softwood. As the ball milling reduced the molecular weight of lignin and cellulose crystallinity, the recovery of the smallest fractions was difficult to achieve.

The production of 5-HMF is a key process in biomass valorization in a biorefinery. Although the 5-HMF yields are higher when the starting point is a sugar such as glucose or fructose, fructose being preferred, the conversion of cellulose to HMF is more difficult due to the insolubility of cellulose in water. Minura et al. [45] applied a catalytic method to produce HMF from glucose or fructose to cellulose and other raw lignocellulosic materials such as natural wood, cotton clothing, or paper (Table 2, Entry 4). The lignocellulosic material was 48 h ball-milled before reaction, and the yield of 5-HMF was markedly increased after ball milling. Following the reaction products as a function of the reaction time, the authors showed that the glucose appeared first and then was converted into 5-HMF. The increase of the 5-HMF yield was attributed to both the reduction of cellulose particle size and crystallinity of cellulose since the amorphous cellulose was more reactive than the crystalline cellulose prior to milling. When other solids were selected to prove the concept of this work, the authors again showed that milling the lignocellulosic solids increased the 5-HMF yield. Thus, the yield of 5-HMF from natural wood was over 35%, as calculated based on the glucose content in the wood.

The effect of milling provokes changes in the structure of lignin and carbohydrates, along with an improvement in the accessibility to cellulose and hemicellulose. This effect depends on the milling time and other conditions, such as the ball mill model, ball material, and operation frequency [44]. Although many works have optimized milling parameters

such as time and frequency, among others, Lee et al. [46] studied how the balls' properties influenced the enzymatic digestibility of sugars of corn stover (Table 2, Entry 5). They selected three commercially available kinds of balls made of alumina, zirconia and steel. The authors evaluated the influence of the surface morphology and specific gravity on their performance. The balls had different properties; for example, the balls made of steel had 1.9 higher specific gravity than those made of alumina. On the other hand, the alumina and zirconia balls were rougher and with higher non-uniformity than steel ones. The corn stover after milling did not result in solid loss or significant composition changes irrespective of the ball used, which could be useful in biorefining operations compared to other chemical pretreatment processes such as organosolv. The particle size was drastically decreased after milling—the type of ball affected the particle size at the lowest milling times. Thus, when steel balls were used, 73% of particles had sizes $<100\ \mu\text{m}$, but when the time was increased to 60 min, the fraction of particles with sizes $<100\ \mu\text{m}$ was very similar regardless of the nature of the balls. However, the zirconia balls yielded the lowest proportion of particles with $<100\ \mu\text{m}$ sizes, probably due to the compaction of individual fibrils. Steel balls were the most effective at reducing the biomass size. As other authors have shown, planetary ball mills also reduce cellulose crystallinity. After 20 min, no significant reduction in the crystallinity was observed, regardless of the ball material. Alumina balls were the least effective in reducing the cellulose crystallinity; after 60 min of milling, the reduction was 69, 76 and 77% for alumina, zirconia and steel balls, respectively. The enzymatic digestibility of the $<100\ \mu\text{m}$ particle sizes was studied to determine the accessibility of cellulose after physical treatments. For all types of balls and for all milling times, glucose production was higher than in the case of untreated biomass. The authors attributed these differences to the fact that cellulose in the untreated corn stover was not sufficiently exposed to cellulase, which obstructed enzyme accessibility to cellulose. For the 20 min milling treatments, steel balls were more effective than the rest. However, when the milling time increased, the treatment with alumina balls produced the most glucose. However, when zirconia and steel balls were used, an improvement was not observed if the treatment was increased from 40 to 60 min. After 60 min of pretreatment, the glucose yield was 91.9, 66.6 and 79.9% when alumina, zirconia and steel balls were used. The glucan yield was 80% for all pretreatment conditions after 12 h of enzymatic hydrolysis. This fact means that ball milling mitigates the mass transfer limitation in the enzymatic reactions. It was observed that the enzymatic digestibility decreased if the particle size of the biomass increased. The authors used the astra blue staining to test the exposition level of cellulose and hemicellulose after the treatments. The authors observed that the alumina balls were the most effective in the adsorption of astra blue. Although the steel balls achieved the highest reduction in particle size after 60 min of treatment, they did not produce the highest glucose yield or achieve the highest astra blue adsorption. This is because the biomass treated with the alumina balls presented a higher surface area. Thus, after 60 min of milling, the surface area was 896, 531 and $395\ \text{m}^2/\text{kg}$ for the alumina, zirconia and steel balls. The authors attributed the biomass digestibility to the particle morphology after the milling treatments. The particles were initially reduced to very fine sizes, but after a certain milling time, there are no decreases in size, and the surface area increases. Steel balls have the highest specific gravity, while alumina balls have the highest textural roughness. Steel balls are the most suitable for reducing the particle size at short times, but if the aim is to increase the action of the enzymes, alumina balls are the most suitable, but with pre-treatments at longer times.

Liu et al. [47] studied the ball milling pretreatment to promote the conversion of corn stover to ethyl levulinate (EL) under microwave irradiation (Table 2, Entry 6). The alcoholysis reaction was carried out in the presence of ethanol and sulfuric acid for 30 min. At 160 and 170 °C, ball milling pretreatment remarkably enhanced the EL yield, from 15.6 and 36.2 mol% (non-treated) to 20.5 and 44.6 mol% (after 120 min of milling), respectively, clearly demonstrating that the mechanical pretreatment was a very effective pretreatment for corn stover. The characterization of the ball-milled biomass indicated that the pretreatment sharply reduced the particle size. After 20 min of milling, the average particle size

was $<30\ \mu\text{m}$, and longer times did not significantly decrease. In addition, the untreated biomass showed a smooth surface modified to a more open and porous structure. Specifically, with increasing ball milling time, the proportion of the intact structure decreased due to fiber fragmentation, indicating that the network structure of the corn stover was destroyed by ball milling. The authors concluded that the ball milling led to a breakage of the fibers, resulting in a porous structure that left the cellulose exposed to catalysts and chemicals. The cellulose crystallinity was also characterized, and the XRD patterns showed the amorphization of cellulose after 60 min of milling. This amorphous state contributed to the increase in the reactivity of cellulose. Finally, the concentration of reducing-end groups increased steadily with the milling time, being a track of the breakage of the glycosidic bonds, reducing the degree of polymerization of cellulose. This treated corn stover was tested in the alcoholysis reaction. The authors identified three ways of acting of the mechanical treatment: firstly, the reduction in particle size with augmented surface increased the reaction accessibility of cellulose; secondly, the destruction of compact cellulose crystal structure resulted in the reduction of alcoholysis energy barrier; and finally, the depolymerized polysaccharides provoked an increase of the reaction sites, which further improved the reaction activity and promoted EL conversion.

The same research group [48] studied the alcoholysis of ball milled corn stover in the presence of a Brønsted acid derived from an ionic liquid ($\text{HSO}_3\text{-IL}$) and aluminum sulfate, observing that prolonging the milling time can contribute to ethyl levulinate production (Table 2, Entry 7). As the ball milling proceeded, ethyl levulinate formation increased gradually, from a yield of 18.1 mol% (non-treated) to 22.2 mol% (after 60). However, longer milling times did not improve the EL yield. It should be pointed out that ball milling is an energy-consuming process, so the energy requirement for mechanical fragmentation also needs to be considered. As a result, 60 min was selected as the ball-milled sample for further studies, and they observed a total carbohydrate conversion of 88.1 mol% after 20 min of reaction. The main products were EL, FUR and ethyl-D-glycopyranoside (EDGP). Other compounds detected with yields lower than 5 mol% were 5-ethoxymethylfurfural, glucose, levoglucosenone and 5-methoxymethylfurfural. FUR is derived from the xylose contained in hemicellulose that reached a yield of 44.5 mol% compared to 28.1 mol% for the non-treated corn stover. Therefore, the milling treatment greatly promoted the production of FUR. We can conclude that ball milling effectively uses pentoses and hexoses in lignocellulose to produce added-value chemicals.

Moreover, these authors have tested ball milled corn stover in the enzymatic saccharification [49] (Table 2, Entry 8). The ball-milled corn stover showed a drastic reduction of crystallinity, disappearing the peaks ascribed to crystalline cellulose after 60 min of milling. In addition, the morphology was severely modified by the milling. The apparition of cracks was noticeable after 10 min of milling, and the particles became small irregular particles. Longer milling times resulted in honeycomb structures with a porous structure. The increase of reducing-end moieties with the ball milling was a track of the breakage of the glycosidic bonds. The digestibility of the ball milled corn stover was studied, and the untreated biomass resulted in 24.6% glucans and 11.8% xylans being saccharified to glucose and xylose. Nevertheless, the saccharification was enhanced after ball milling, releasing more than 60% glucose and 35% xylose after 60 min of ball milling. The authors associated this enhancement with the modification of the physicochemical properties of corn stover. The glucosidic bonds are more accessible to the enzymes and are readily hydrolyzed.

Other research has shown that milling is beneficial in promoting the conversion of lignocellulosic carbohydrates into value-added chemicals, such as ethylene glycol (EG) [50]. In this study (Table 2, Entry 9), the authors study a myriad of agro-forestry residues along with other residues such as cotton wool, printing paper, tissue paper and spent coffee grounds. These residues were ball-milled and then treated to isolate the holocellulose (cellulose plus hemicellulose) from lignin. The residues before and after lignin removal were tested in the catalytic hydrogenation with ruthenium and tungsten supported on carbon nanotubes. The XRD peaks of the crystalline cellulose, after ball milling almost disappeared,

indicating the destruction of cellulose structure and a reduction of the crystallite sizes. As the hemicellulose and lignin displayed an amorphous structure and therefore could not be evaluated by XRD analysis, the samples were treated to remove the lignin fraction of the lignocellulosic. Thus, comparing the XRD patterns before and after lignin removal, the crystallinity indexes were observed for all the samples. The lignin-free samples presented values between 26–62%, while for the ball-milled samples, the values oscillated between 10–48%. Regardless of the different morphological structures of each waste, ball milling samples resulted in a similar morphology with narrower structures and fine size particles. The surface became more irregular and rougher than the raw materials, and the fiber structure disappeared after milling. No differences in the morphological structure were observed after the lignin removal by SEM images. When the holocelluloses were tested in the catalytic reaction, they were converted into ethylene glycol and other polyols. The conversions ranged between 39.2% and 93%, corresponding to cork and Australia wood holocelluloses. Based on the holocellulose content of the biomass, an EG yield of 40% was achieved from eucalyptus wood and cotton wool. The reaction was carried out with the ball-milled materials after the lignin removal to develop a greener process. In this case, the EG yields varied between 10–20% for the raw materials without milling treatment, and these yields were increased up to 24–41% when the residues were milled.

Wang et al. [51] proposed a multi-step process (Table 2, Entry 10) to isolate lignin from various biomass raw materials without modifying structure and composition. Thus, it would be used for novel high-end applications such as biopolymers or phenolic resins [52]. In this process, the biomass is treated sequentially by periods of ball milling and then enzymatic digestion. The biomass was milled for 6 h, and the enzymatic treatment was applied. The cocktail of enzymes was more specific for cellulose than hemicellulose hydrolysis. The second cycle was conducted on the recovered solid residue from the first enzymatic digestion by 6 h of milling, and then the second enzymatic hydrolysis was carried out. This process was repeated up to three times. This method was selected to avoid the lignin degradation that impairs the intense ball milling. For the same volume:mass ratio (enzyme:biomass), if a single milling treatment of 24 h was selected, the number of carbohydrates on the solid residue was lower than in the first cycle of the multi-step process. In this first cycle, the amount of hemicellulose was higher than cellulose due to the nature of the enzymatic cocktail. The second cycle reduced the number of carbohydrates to the level of a single procedure with milling times of 24 h. Among the selected biomass feedstocks, nutshells were more likely to be used in a single 24 h ball milling procedure since the carbohydrate reductions after 3 cycles were similar to that obtained in a single 24 h ball milling. As this work aimed to evaluate the obtained lignin, its properties were analyzed. Thus, no significant differences were observed in terms of the proportion of main linkage content and S/G (Syringyl/Guaiacyl units) ratios, indicating the limited influence of ball milling on the structure of lignin. Moreover, a slight decrease of β -O-4 linkages was found for birch (<3%) after 48 h of milling, indicating the ball milling time might have a slightly negative effect on β -O-4 linkages. In contrast, the other linkages content, such as β -5 and β - β , relatively increased for samples of birch and pine, indicating that these are more recalcitrant. The analysis of the molecular weight of the recovered lignin showed that 48 h of milling dramatically decreased the MW of the recovered lignin, particularly for the reed sample. As the number of β -O-4 linkages of the lignin between the samples milling 24 h and 48 h was almost the same, this indicated that the polymer is cleaved to produce small fragments during the milling process. This can be important when the lignin use requires high molecular weight lignin and the measurement of β -O-4 linkage content shows it would not be an adequate measure of degradation.

Fulong et al. [53] developed a method to produce xylooligosaccharides (XOS) and glucose (G) from corn stover by combining ball milling, ultrasound and hydrothermal treatment (Table 2, Entry 11). The biomass was then subjected to subsequent enzymatic treatment. Under the optimal conditions, the highest yield of XOS was 80.4%. The enzymatic hydrolysis of the hydrothermally treated biomass yielded 92.6% of glucose, and

66.8% of the lignin was recovered. Ball milling reduced the corn stover's particle size and crystallinity index. Thus, the average particle diameter and CrI decreased from 396.87 μm to 51.66 μm and from 41% to 28% after 1 h ball milling. Increasing the ball milling time provoked larger particles (400–800 μm) to transform into smaller particles (<25 μm). The decrease in crystallinity was attributed to the destruction of the crystalline region of cellulose due to the forces exerted by the milling. Moreover, the reduction of the crystallinity had a beneficial effect on the following hydrothermal and enzymatic treatments due to the higher accessibility to carbohydrates. When the ball milling time increased from 1 h to 5 h, the yield of xylose increased because more acetyl groups were released and promoted the hydrolysis of xylan. Thus, the amount of xylose plus XOS increased from 43.5 to 70.3%. However, glucose yield during the enzymatic hydrolysis did not increase (from 83 to 87%) as much as that of the xylose. This was ascribed to the lower decrease of both the particle size and crystallinity of the substrate when the milling time was 5 h.

One of the advantages of lignocellulose is that it is distributed worldwide. Each region has its own biomass available for valorization, so developing countries can choose their own biomass that does not compete with arable land or water for food crops. In this context, Ekwe et al. [54] studied the effect of ball milling (Table 2, Entry 12) on bamboo (*Bambusa Vulgaris*) to obtain fermentable sugars such as xylose and glucose after enzymatic hydrolysis. This biomass grows in marginal lands and does not need fertilization or abundant water inputs. It is rich in cellulose and hemicellulose and has low ashes content. The bamboo samples were subjected to two times of milling, 30 and 60 min, respectively. Sugar yields of the ball-milled treated samples noticeably increased. Thus, after 30 min of milling, an eightfold increase in total sugar yield was observed (total sugar recovery, 40%), and, after 60 min of milling, the sugar yield increased by 50% relative to the sample milled for 30 min (total sugar recovery, 62%). After the enzymatic hydrolysis, 45% of lignin was recovered. The authors claimed that the ball milling was an effective activation treatment of the bamboo biomass. The untreated and ball milled samples were characterized to understand the above results. Thus, the FESEM images showed that the ball milling reduced particle size to irregularly shaped and rough particles. On the other hand, the cellulose crystallinity was drastically decreased even after 30 min of milling. The authors also demonstrated that the ball milling did not provoke the exfoliation of lignin from the cellulose fraction using the NMR relaxation experiment. FESEM, XRD, and NMR analysis confirmed that the main effect of ball milling was to expose and amorphize the cellulose to improve enzyme access and activity. As this pretreatment seems promising for treating bamboo biomass, the authors attempted to evaluate the energy consumption for large-scale application of ball milling. Starting from the laboratory vessel, full of biomass (2 g) and for 60 min of milling, the power required for treating 1 kg of bamboo was 5.6 MJ. The reduction of particle size is key to knowing the energy consumption; thus, the authors assumed an energy consumption of 2.9 MJ/kg, considering a reduction of 96% in the particle size. Moreover, the type of mill influences the energy consumed. Assuming the extremes (ball mill and knife mill) and accounting for the amount of size reduction required here (96%), the estimated energy requirements ranged from 0.5 to 3.5 MJ/kg, so the amount of energy required for mechanochemical pretreatment ranged from 0.5 to 5.6 MJ/kg. This work is one of the scarce that informs about the energy consumption by the ball milling method. These energy requirements are in the order of the acid diluted hydrolysis pretreatment of biomass. However, extrapolation is risky since energy consumption depends on numerous factors. Among them, the degree of particle size reduction and crystallinity necessary for subsequent treatments to be effective, such as hydrothermal or enzymatic processes (the most studied), the type of mill to be used, and the grinding time, among others. The same biomass can affect all of the above parameters, so a study must be carried out for each case.

Chitin is considered the second most abundant polysaccharide (after cellulose) on Earth. It is present in crab, shrimp, insect shells, and fungal cell walls as ordered microfibrils. Chitin is a poly(β -(1-4)-N-acetyl-D-glucosamine) with β (1 \rightarrow 4) linkages, and its structure resembles that of cellulose [55]. Each polymer chain strongly interacts with the adjacent

through hydrogen bonds, which provide high thermochemical stability, as well as high insolubility and crystallinity. Thus, chitin is a highly insoluble polymer, making it poorly biodegradable. The oligomers and monomers (N-acetylglucosamine) of chitin have attracted attention because of their versatility and many applications in different fields such as antitumoral and cosmetic [56]. Nakagawa et al. [56] reported a new mechanochemical method to cause the amorphization of chitin and improve the enzymatic hydrolysis of the polymer. The milling resulted in a reduction of the particle size and crystallinity. Thus, the crab shell showed the smallest average diameter (10.1 μm), and the XRD patterns of materials ground with the mill became smaller and smoother until no obvious peaks were present, especially under severe conditions. These changes dramatically improved the enzymatic hydrolysis of the chitin. For example, the enzymatic hydrolysis of crab chitin and crab shell was 7-fold and 3.5-fold increased by mechanochemical grinding.

The amorphization of chitin using the mechanochemical treatment was also studied by Margoutidis et al. [57]. In this study, the authors used kaolinite to promote the depolymerization of α -chitin. In the absence of kaolinite, the authors showed that, for the same volume occupied by stainless steel balls, the crystallinity index decreased from 91% to 35% with balls of 0.64 cm and to 51% with balls of 1.27 cm in diameter after 120 min of milling. By FTIR and MALDI-ToF analysis, the authors demonstrated that the ball milling caused a reduction of the crystallinity through glycosidic bonds breaking along with the disruption of the intermolecular hydrogen bonds. When kaolinite was added during the milling process, it was observed that the solid became more amorphous. Still, no conclusive results could be drawn about the loss of chitin crystallinity from these kaolinite/chitin mixtures. However, the analysis of the soluble products when kaolinite was present increased from 36%, in its absence, to 76%, after 6 h of milling. The degree of depolymerization was also followed by analyzing the soluble products by MALDI-ToF. These results showed the presence of monomers in pentamers, increasing the peak intensity of the monomers and dimers with the milling time.

2.3. Base-Assisted Mechanochemical Treatment of Lignocellulosic Biomass

The high-pH conditions have been proposed as an efficient method to remove the lignin and partially the hemicellulose. This is so because alkaline conditions promote breaking the ester bonds between lignin and hemicellulose. The bonds that intertwine lignin and hemicellulose are lost and increase the porosity of the material, releasing the hemicellulose, and preventing its fragmentation [58]. This alkaline pretreatment has also been successfully applied in combination with the mechanical treatment to increase the accessibility of enzymes to cellulose. Those results are shown in Table 3.

For wet treatments, 30 mL of distilled water was added to the biomass to attain a solid to liquid ratio of 1:10. Endo et al. treated Eucalyptus wood chips using their hydrothermal method [59], developed to increase the enzyme accessibility to the sugars contained in the cell walls, but adding solutions of NaOH [60] and $\text{Ca}(\text{OH})_2$ [61] during the hydrothermal treatment to subsequently subject the wet solid fraction to ball milling (Table 3, Entry 1). They attempted to increase the digestibility of sugars. The enzymatic results showed that regardless of the temperature of hydrothermal treatment, those samples treated with NaOH dissolutions gave higher glucose yields than those NaOH-free samples. Thus, if the hydrothermal treatment was carried out at 170 $^\circ\text{C}$ in the presence of 20 wt% of NaOH, the glucose yield was 99%, i.e., full digestibility of cellulose. When it was carried out in the absence of NaOH, the glucose yield was 64%. As the cellulose was unaffected by the hydrothermal treatment, lignin and hemicellulose decreased as the temperature and NaOH concentration increased, lignin being the most affected. The lignin and hemicellulose remained a third and half of the initial values. The delignification improved the milling by weakening the wood structure. This was measured by analyzing the surface area of the samples before and after the treatments. Before any treatment, the surface area was 11 m^2/g . When the samples were autoclaved at 170 $^\circ\text{C}$ and milled, the surface area increased up to 132 m^2/g , and when the substrate was treated with NaOH (without autoclaving) and milled,

the surface increased up to 128 m²/g. Finally, the combination of the three treatments: NaOH, autoclaving and wet ball milling, resulted in a surface area of 232 m²/g, revealing that the bundles of cellulose microfibrils were unraveled. Therefore, the alkaline treatment broke the ester bonds, and lignin and hemicellulose were partially removed, leading to the softening of cell woods, favoring the fibrillation by the ball milling. In the case of adding Ca(OH)₂, the results were similar to the former [60]. However, the glucose yield after hydrothermal treatment with Ca(OH)₂ (20 wt%) and wet-ball milling was 90% at 170 °C. The cellulose amount in the solid fraction was not affected by the alkaline-milling treatment, and more than 60% of the initial lignin content was retained. This was explained by the fact that the Ca²⁺ might form complexes with the ionizable groups of lignin such as carboxylate, methoxy and hydroxyl groups, weakening the solubility of lignin. This chemical modification of the lignin could have an undesirable effect on the saccharification of cellulose, leading to lower glucose yields than the NaOH-modified substrates.

Table 3. Pretreatment of biomass assisted by alkaline conditions.

| Entry | Biomass | ^a Base (w/d) | Mill | r.p.m. | Time (h) | Balls/Biomass | Reaction | Reference |
|-------|-------------------------|-------------------------------|-------------------------------|-------------------|----------|-----------------------------------------------------------------------------|-----------------------------------|-----------|
| 1 | Eucalyptus wood chips | NaOH, Ca(OH) ₂ (w) | Planetary ball mill | 450 | 4 | ^b ZrO ₂ (30 balls, Ø = 10 mm) | Enzymatic hydrolysis | [60,61] |
| 2 | Organosolv lignin | NaOH (d) | Planetary ball mill | 798 | 12 | ZrO ₂ (30 balls, Ø = 5 mm)/100 mg | Cleavage β-O-4 bonds | [62] |
| 3 | Kraft lignin | KOH (w, toluene) | Vibratory mill | 1500 | 3 days | Stainless steel (1 ball, Ø = 5 mm) | Depolymerization of lignin | [63] |
| 4 | Organosolv lignin | ^c NaOH (d) | Ball mill | 800 | 0–8 | Stainless steel (3 balls, Ø = 12 mm)/1.5 g | Depolymerization of lignin | [64] |
| 5 | Bagasse and Pen-nisetum | NaOH (w) | Planetary ball mill | 400 | 2 | ^d Not informed/1 g | Enzymatic saccharification | [65] |
| 6 | Corn stover | NaOH (w) | Ultrafine vibration ball mill | ^e n.p. | 0–0.5 | ^f ZrO ₂ /(2:1 volume ratio balls:biomass solution) | Enzymatic hydrolysis | [18] |
| 7 | Wheat straw | NaOH/citric acid/NaCl (d) | Planetary ball mill | 450 | 1–4 | ZrO ₂ (35 balls, Ø = 10 mm)/5 g (volume ratio balls:biomass 1:1) | Saccharification of carbohydrates | [66] |
| 8 | Enset fibers | ^g NaOH (w/d) | Planetary ball mill | 200, 350, 500 | 0.25–2 | ZrO ₂ (25 balls, Ø = 10 mm)/ ^f 3 g | Enzymatic hydrolysis | [67] |

^a w = wet conditions; d = dry conditions. ^b Mass of biomass before mechanical treatment was 3 g suspended in 40 mL of water. ^c MeOH was added as a scavenger, but its volume was so low that we considered the process dry. ^d The material and number of balls were not informed. The biomass was suspended in 1 mL of NaOH solution. ^e n.p.: not provided. ^f The number and diameter of the balls were not informed. The balls occupied 35% of the jar volume. ^g Dry and wet treatments were alternated.

As in the previous work, the ball milling was carried out in the presence of alkaline solutions, Kleine et al. [62] proposed a solvent-free milling process (Table 3, Entry 2) in which organosolv lignin was mixed with an alkaline solid and a grinding auxiliary (Na₂SO₄) to cleave the β-O-4 linkages of the lignin. Before this study, the authors optimized the milling conditions using a model compound, dilignol erythro-1a, showing that the hydroxides of alkaline metals were more effective than sodium carbonate or calcium hydroxide in degrading the model compound. The products of the reaction were 2-methoxyphenol and

phenyl propane. Among the hydrides and hydroxides tested, the authors chose NaOH as the best candidate to continue with the study, finding that the best conditions were achieved when the milling was carried out during 720 min and with 10 eq. of NaOH (94% of yield). The authors also studied different milling parameters that affected the milling efficiency, such as the grinding bowl topology, the number of balls, and the grinding speed. The best result was achieved when the reaction was performed in the grinding bowl with a diameter of 4.8 cm using 30 balls and a rotational speed of 13.3 Hz. The authors claimed that the reaction degradation needed both mechanical stress/pressure (represented by the kinetic energy in the system) and a specific temperature range (resulting from friction). The former depended on bowl size, which guaranteed high motional freedom of the grinding balls. The rotational speed modulated the latter, which promoted particle interactions and frictions, leading to a process temperature of 50 °C. This methodology was applied to the organosolv lignin, one purified before milling and another without the purification step. The purification step was carried out to eliminate the carbohydrate residues on the lignin. The purified sample showed that the most abundant linkage was β -O-4 above the resinol and phenylcoumaran motifs. After the milling treatment, 76% of β -O-4 motifs were cleaved during the process, and the resinol binding motifs appeared to remain unaffected by the treatment. The non-purified sample showed that 55% of the β -O-4 motifs were broken after the grinding, as well as the glycosidic bonds. Therefore, the treatment was able to depolymerize the carbohydrate content of this sample.

In another work [63], THF was used as a solvent to prevent the adhesion of Kraft lignin on the surface of the steel balls of the mill (Table 3, Entry 3). In this work, Yao et al. mixed Kraft lignin with KOH and toluene to use it as a pretreatment for the depolymerization of the lignin. Using both FTIR and HSQC NMR experiments, the authors showed that the mechanochemical treatment led to the oxidation of the hydroxyl groups into carbonyl. Thus, the analysis of the aromatic region of the HSQC NMR experiments demonstrated that the cross-peaks associated with oxidized guaiacyl were nearly absent. However, after the milling, the oxidized motifs were notably present. Then, both lignin and milled lignin were subjected to a two-step oxidative depolymerization process by oxidation of the benzylic hydroxyl groups to carbonyl groups using a TPPFeCl (porphyrin)/t-BuOOH catalyst system. This was followed by Baeyer–Villiger (BV) oxidation of ketones to esters with HCOOH/H₂O₂, followed by in situ hydrolyses of the esters to carboxylic acids and phenols. After methylation, the authors proved that the BV reaction produced methyl vanillate and methyl 5-carbomethoxyvanillate (minor compound) with a total yield of 10%. These compounds were formed from the oxidized lignin when the lignin was milled and treated with porphyrin. Therefore, this method can effectively depolymerize the lignin into monomers, finding a synergetic effect between both treatments (milling and oxidation with porphyrin) since both methods produced a lower yield separately of monomers, and their sum did not reach 10%.

One of the drawbacks of the depolymerization of lignin is that related to the repolymerization reactions that can form new bonds from reactive intermediates, resulting in products more recalcitrant to depolymerization than the original one. For depolymerization to be successful and to obtain the highest proportion of monomers, it is necessary to isolate or deactivate such intermediates. This is what Brittain et al. [64] developed for the depolymerization of organosolv lignin (Table 3, Entry 4). The lignin, pellets of NaOH and methanol, when it was required as a scavenger, were charged in a ball mill and milled at different times. The authors were interested in what happened at short times of milling. In this study, as common in previous studies, NaOH was effective in depolymerizing lignin under mechanochemical conditions. Thus, the average molecular weight of the milled lignin was half the initial value within the first 30 min of milling, and then the depolymerization was slowed. By LC-MS analysis, those compounds were basically dimers. The maximum yield of monomers was obtained during the first 5 min and then dropped sharply. This was attributed to the accessibility of certain regions of the lignin and the presence of loosely bound water in these 5 initial minutes. Then, when

water was consumed, repolymerization was favored, and some of the formed monomers were consumed. After that, the monomers increased again between 10 min and 5 h of milling because more water was accessible in the lignin, pushing the hydrolysis reactions. Moreover, the authors did not discard those condensation reactions because the β -O-4 linkages were not reduced after 2 h of milling. Finally, between 5 and 8 h, the production of the monomers decreased, given the marked increase of trimers and higher oligomers after 8 h. When methanol (0.4 mL/1.5 g lignin) was added during the milling as a scavenger, it was observed that the initial rate of depolymerization was higher and an additional 40% reduced the final average molecular weight compared to the samples milled with NaOH. In addition, the monomer yield was increased by 70%, and the fraction of β -O-4 linkages broken after 2 h of milling increased from 15% to 65%. All that evidence led the authors to conclude that a reduction of repolymerization reactions occurred when methanol was added. The authors found that methanol could potentially have two roles. First, the methanol could donate a proton to the carbanion intermediates formed in the reaction. In this case, the role of methanol would be as a substitute for the small amount of water in the system. The second role is related to its contribution to the solvolysis reaction as a complement to the hydrolysis reaction. Another parameter analyzed in this study was the amount of water. As base-catalyzed depolymerization is basically a hydrolysis reaction, it was interesting to analyze the role of the amount of water. The water had the inconvenience that it could act as a plasticizer due to the formation of hydrogen bonds. This behavior prevents efficient mixing and grinding. Although the theoretical amount of water needed to hydrolyze the ether bonds was 6 wt%, the highest monomer yield was achieved when the amount of water was 14 wt%. Interestingly, the maximum yield of monomers was not correlated with the minimum average molecular weight. This suggests that the water increased the reactivity of the intermediates leading to an increase in the yield of higher-length chains. The highest amounts of water resulted in the plasticization of the system, impeding the grinding of the samples.

Huang et al. [65] considered a mechanochemical alkaline pretreatment of biomass (bagasse and Pennisetum) but using very low concentrations of NaOH (Table 3, Entry 5). The lignocellulose was suspended in a dilute NaOH solution and milled for 2 h. Then, the solid residue was hydrothermally treated at different times and temperatures under alkaline conditions. Finally, the enzymatic saccharification was carried out, and the concentration of reducing sugars was evaluated. This work did not focus on the changes resulting from the mechanochemical treatment, so the severity of such treatment was not analyzed. Still, the authors showed that the combination of the alkaline mechanochemical and hydrothermal treatment was efficient in disrupting the lignocellulose structure and leaving a solid mainly rich in cellulose and to a lesser extent in hemicellulose. The nature of the lignin affected the final concentration of cellulose, showing that the lignin coming from the Pennisetum was more degraded than bagasse. Finally, the results showed that the glucose yields increased with the increment of NaOH concentration and severity factor.

Yang et al. [18] outlined the wet-alkaline mechanochemical pretreatment of lignocellulose for saccharification purposes (Table 3, Entry 6). In this work, the biomass and NaOH solutions were mixed thoroughly and then milled for short times (10–30 min) compared with previously published works. The concentration of NaOH varied between 1 and 3 wt%. Separately, both the milling and NaOH treatment yielded higher sugar values than the control experiment. However, the NaOH treatment was able to yield more glucose than milling. When the lignocellulosic sample was suspended in the NaOH solution and milled, the sugar yield was boosted, reaching 91% of glucose after 10 min of milling and a NaOH concentration of 3 wt%.

The saccharification of carbohydrates of wheat straw biomass (Table 3, Entry 7) was studied by Liu et al. [66]. These authors depicted a method of pretreatment of the biomass by mixing solid bases (NaOH), acids (citric acid) and salts (NaCl) with the biomass and then milling the mixture at different times (1–4 h). The solid was washed with water at 100 °C. The composition of the pretreated biomass with the different chemicals varied

as a function of the chemical used compared with the raw material. The ball milling in the absence of chemicals did not change the biomass composition, but for the same time of milling, the cellulose content was increased when chemicals were added, being more noticeable in the case of the NaOH. This was ascribed to eliminating the non-cellulosic fraction of the biomass as lignin. Thus, the milling process favored the NaOH melting and coalescence, enhancing the contact between the biomass and NaOH and increasing wheat straw's delignification degree. These composition changes led to a higher saccharification of the biomass when the samples were milled with NaOH than in the other situations. For example, the ball milled sample for 4 h led to a glucose yield of 60.1%, the same result that the sample ball milled with NaOH for 1 h. When the milling was increased to 4 h with NaOH, the glucose yield increased to 82.4%. The authors attribute the best performance of the ball milling assisted by the presence of solid chemicals to the fact that the physical process associated with the ball milling could destroy and open up the complex fiber structure allowing the solid particles to penetrate the loose fiber structure. On the other hand, the high temperatures caused by milling favored the melting of chemicals, accelerating the reaction. The samples were analyzed after the pretreatment showing that the ball milling provoked the reduction in both the particle size and the crystallinity of the cellulose in the absence or presence of chemicals, the reduction more pronounced when the NaOH was used. The reduction of crystallinity was ascribed to the transformation of the cellulose I structure into the amorphous cellulose II. On the other hand, the specific surface area and the reducing-end groups increased after the milling. Therefore, the long cellulose fibers were decomposed into microfibrils by ball milling coupled with solid NaOH particles, improving cellulose hydrolysis.

As it is well known, a biorefinery's viability requires using local biomass. In this context, Sitotaw et al. [67] valorized Enset fibers (Table 3, Entry 8) from a local farm in Ethiopia for yielding glucose. The authors compared four different pretreatments: the first was an alkaline treatment of the biomass with solutions of NaOH (0.5 wt%) at 43 °C, the temperature inside the ball milling jars. The second treatment was dry and wet ball milling. The third method was a combination of the two previous treatments, i.e., first the alkaline treatment and then the ball milling or vice versa. The fourth method was based on adjusting the humidity of the biomass to 20% with a solution of NaOH (10 and 20% w(NaOH)/w(biomass)), and it can be considered a dry mechanochemical method. The solids after each treatment were characterized to know the crystallinity, particle size and morphology. The authors firstly evaluated the effect of the wet and dry milling, concluding that the latter was more efficient in decreasing the crystallinity. Thus, the crystallinity index reduction was marginal when wet conditions were used. Under dry conditions, it was possible to transform the crystalline material into an amorphous one after 30 min and 500 rpm. A sharp decrease in the particle size was observed after 15 min of milling at 500 rpm, but longer periods of milling did not decrease the particle size anymore. This was attributed to the agglomeration of the fine particles due to the compression effect exerted by the impacts of the balls. The SEM images showed that the rod-like particle structure was destroyed at 350 rpm and 60 min of milling, and the particles acquired a spherical and flaky shape. However, the wet ball milling only caused defibrillation without breaking the particles. Water acts as a plasticizer; thus, when mechanical forces were applied to the swelled cellulose, molecular chain slippage would occur, reducing the extent of morphology and crystallinity changes. The glucose yield was higher when dry ball milling was carried out. This was attributed to the presence of liquid during milling, which swelled the biomass particles, causing damping of the mechanical forces during impacts (lowering the impact energy). However, the presence of lignin and hemicellulose impeded the complete cellulose hydrolysis (71% of the theoretical value). Therefore, the alkaline treatments were then studied. The authors concluded that the dry mechanochemical treatment was more efficient than the others because it achieved higher glucose yields at shorter times and used a lower number of process steps (grinding plus reaction). This was attributed to the synergistic effects of NaOH and the various impact and attrition forces generated in the ball mill,

which continuously enables the lignin removal and size reduction process. As a result, new surfaces were continuously created to improve cellulose accessibility. But also, the dry mechanochemical treatment was the most efficient in terms of energy consumption because the energy efficiency was 1.3, 5.3, and 7.8 times higher than the energy efficiency of dry ball milling, sequential and alkaline pretreatment, respectively.

As shown above, under certain conditions, the base was used in the solid phase, but the forces and pressures exerted by the balls during the impacts might melt the solid, improving the contact between the lignocellulose and the base. Therefore, favoring the delignification of the biomass. However, the actual solid-solid reaction between biomass and a solid catalyst must overcome numerous drawbacks, such as the mass transfer that the action of the mechanochemical approach could improve.

2.4. Acid-Assisted Mechanochemical Treatment of Lignocellulosic Biomass

Using chemical treatments with acids, bases or ionic liquids has proven to be effective for treating lignocellulosic biomass, but they are costly and environmentally harmful methods. A simpler and less harsh way of treating lignocellulose is to use mechanical methods combined with mineral or organic acids, which allows lignocellulose to be converted into oligosaccharides that can be more easily hydrolyzed under milder conditions. Therefore, mechanocatalytic depolymerization of lignocellulosic biomass impregnated with strong acids is a promising process to produce sugars and lignin for the sustainable manufacture of chemicals and biofuels. Although the simple description of the grinding conditions can result insufficient to comparatively analyze the results, a review of acid-assisted mechanical treatment of lignocellulosic biomass has been carried out in this section to have an overview of state of the art on this attractive research area. The main results are presented in Table 4.

Ruppert et al. [68] (Table 4, entry 1) used different surface techniques to investigate the effect of several treatments for biomass depolymerization: ball milling, impregnation with sulfuric acid and impregnation combined with ball milling. Cellulose impregnation was carried out by dispersing 1 g of α -cellulose in a solution of sulfuric acid in diethyl ether. Cellulose or pretreated cellulose was then subjected to hydrolysis in a stainless-steel autoclave from Parr at 170 °C for 5 h. The highest hydrolysis activity was obtained for the material impregnated with sulfuric acid (90% conversion) and for the material first ball milled and impregnated later (86% conversion). In addition, the main product yields were similar for these two materials (32–35% levulinic acid, 33% formic acid and 2.3% glucose). A slightly lower conversion (78%) was obtained when cellulose was firstly impregnated and then milled. Using time-of-flight (ToF)-SIMS, the authors determined the changes occurring at the uppermost layer of the materials. They concluded that samples impregnated in the last step showed the highest activity in the hydrolysis due to the highest accessibility of sulfonic groups on the cellulose surface. The lower activity for cellulose milled after impregnation was due to a possible encapsulation of sulfonic groups inside the structure when cellulose was milled during impregnation.

The combination of ball milling and chemical swelling by phosphoric acid (Table 4, entry 2) enhanced enzyme saccharification and ethanol production from paper sludge [69]. Maximum values of cellulose hydrolysis rate (97.1%) and glucose productivity (30.0 mg/g/h) were obtained for this pretreated paper sludge compared to untreated samples [69]. The authors associated this improvement with the reduction of particle size of paper sludge, which favored enzyme accessibility and cellulose digestibility. Moreover, for the simultaneous saccharification and fermentation, the ethanol productivity using pretreated paper sludge was 3-fold compared to that obtained for untreated paper sludge.

Yu et al. [70] (Table 4, entry 3) achieved near-complete recovery of sugar monomers (~94%) from biomass via a two-step hydrolysis process. The depolymerization of biomass into sugar oligomers was achieved by mechanochemical hydrolysis of acid-impregnated biomass. Monomers were obtained in a second step by hydrolysis at a low acid concentration and a low temperature. Cellulose (or wood biomass) was firstly impregnated with strong acids via wet [71–73] or dry impregnation with gaseous HCl [73] to obtain

acid-loading of 0.25–1 mmol g⁻¹ and then was ball milled. After 20 min ball milling of the acid-impregnated sample with acid-loading of 0.25 mmol g⁻¹, the XRD patterns, the FTIR results and the SEM images clearly showed that mechanochemical hydrolysis converted crystalline cellulose into amorphous cellulose. A complete cellulose conversion into water-soluble products during mechanochemical hydrolysis was obtained [71,72]. Ball milling time optimization is important to achieve energy savings; increasing the time from 20 to 60 min involved tripling energy consumption and only represented an increase of the water-soluble products by 17%. An additional acid hydrolysis step was carried out to convert glucose oligomers into glucose. Studies revealed that longer ball milling time reduced the hydrolysis time required to achieve maximum sugar recovery, but longer hydrolysis time led to more glucose degradation. The authors concluded that this two-step hydrolysis could effectively replace enzymatic hydrolysis.

Lin et al. [74] compared dilute chemical wet milling of corn stover with conventional methods of dry ball milling and water milling pretreatment with a planetary ball mill for enzymatic hydrolysis of carbohydrates (Table 4, Entry 4). Dilute chemical wet milling was carried out with solutions of H₂SO₄, HCl, HNO₃, CH₃COOH, HCOOH, H₃PO₄, and NaOH, KOH, Ca(OH)₂, NH₃. The pretreatment by wet milling was better than that of dry milling. Dry milling pretreatment resulted in lower amounts of sugars with the enzymatic hydrolysis of the solid fraction, while the diluted alkali milling pretreated materials exhibited the best enzymatic hydrolysis efficiency. The optimal milling parameters were ball speed of 350 rpm, solid/liquid ratio of 1:10, the raw material particle size of 0.5 mm, and the number of balls of 20 (steel ball, Φ = 10 mm), grinding for 30 min.

Eucalyptus urophydis was efficiently deconstructed by a diluted acidic short-time ball milling process (Table 4, Entry 5). The subsequent enzymatic hydrolysis provided high yields (>90%) of fermentable sugars (glucose and xylose) [75]. The crystallinity indexes of the substrates, determined by solid-state CP/MAS ¹³C NMR, decreased dramatically after the mechanical treatment, especially for that impregnated with an acetic acid aqueous solution, which suggested that effective decrystallization of cellulose occurred during the impregnation and mechanical treatment. This treatment also proved effective in significantly lowering the degree of polymerization of the substrates as determined by the NMR technique. After acetic acid impregnation and ball milling treatment, the deconstruction of raw material favored subsequent enzymatic hydrolysis with glucose and xylose yields up to 95.7 and 91.0%, respectively.

Another important factor to remember is that side reactions occur during acid hydrolysis. Thus, hexoses dehydrate to form HMF that can further be degraded to levulinic and formic acid. These products, among other compounds, are formed during acid treatment and have inhibitory effects, lowering the efficiency of the hydrolysis process [76,77]. Mechanocatalytic pretreatment is a promising method to prevent the formation of these by-products. In this sense, Lempiäinen et al. [78] (Table 4, entry 6) studied the effect of mechanochemical pretreatment on the structure of depolymerized willow. A one-step and solvent-free mechanocatalytic process were performed with a planetary ball mill by direct acid catalysis with sulfuric acid. When the acid load was 3.0 mmol/g, the willow would agglomerate on the milling equipment due to the acid-catalyzed intermolecular surface dehydration of microfibrils [79]. Increasing the amount of acid in the mechanocatalytic pretreatment, a decrease in the intensity of the diffraction peaks in the XRD patterns was observed. Likewise, a drop in the crystallinity index of cellulose from 59% to 14% was observed for the willow sawdust sample when the acid load was 1 mmol/g. From the study of the effect of mechanocatalytic treatment parameters on sugar release, the highest total reducing sugars yield (17.1%) was achieved with 0.5 mmol/g acid load after 45 min of milling. The monosaccharide yield increased with the time of milling achieving 24.2 g/kg and 11.6 g/kg of glucose and xylose, respectively. The amount of fructose decreased to a non-detectable level after milling for 30 min. Small amounts of HMF (0.8–1.1 g/kg) were also detected, it could have reacted into levulinic acid and formic acid, but these compounds were not analyzed in this study. The total reducing sugars yields were higher when

the mechanocatalytically pretreated willow sample was hydrolyzed (60 min at 100 °C). After milling for 45 min, glucose, xylose and arabinose yields were 25.9 g/kg, 15.5 g/kg and 3.8 g/kg, respectively. Total monosaccharide yield reached its maximum with 1.0 mmol/g acid load. Fructose and sucrose were not detected when the acid load was increased, probably due to their degradation into HMF that was not detected due to its degradation into levulinic acid and formic acid. The authors concluded that the composition of the sugar solution produced could be optimized by varying parameters such as the ratio of the sulfuric acid catalyst to willow, the milling time and the rotation speed. Thus, the crystallinity and size of cellulose decreased with a longer ball milling duration, which increased sugar yield. The same conclusions were obtained when this mechanocatalytic treatment was applied to a forest industry side stream, birch sawdust [80] (Table 4, entry 7). The highest glucose yield (23.8 g/kg) was achieved after 60 min of milling with an acid catalyst load of 1.5 mmol/g. Moreover, birch was more sensitive to this mechanocatalytic treatment than willow. The total reducing sugars yield was slightly better for birch when the pretreatment was done in similar conditions.

Table 4. Pretreatment of biomass assisted by acid conditions.

| Entry | Biomass | ^a Acid (w/d) | Mill | r.p.m. | Time (h) | Balls/Biomass | Reaction | Reference |
|-------|-------------------------|-----------------------------------------------------------------------------------------------------------------------|--------------------------------------------|-------------------|--------------|--------------------------------------------------|----------------------|-----------|
| 1 | Cellulose | H ₂ SO ₄ (d) | Ball mill | - | 1 | ^b Agate (Ø = 20 mm)/3 g | Hydrolysis | [68] |
| 2 | Paper sludge | H ₃ PO ₄ (d) | Vibration ball mill | 3600 | 2 min | ^c 20 g | Ethanol production | [69] |
| 3 | Cellulose, wood biomass | H ₂ SO ₄ (d) | Ball mill | 1800 | 0.3–1 | WC (Ø = 15 mm)/15:1 ratio weight ball:sample | Acid hydrolysis | [70] |
| 4 | Corn stover | H ₂ SO ₄ , HCl, HNO ₃ , acetic and formic acid, H ₃ PO ₄ (d,w) | Planetary ball mill | 250, 300, 350 | 0.5 | Steel (10, 15 and 20 balls, Ø = 10 mm)/3 g | Enzymatic hydrolysis | [74] |
| 5 | Eucalyptus wood | HCl, Acetic acid (d) | Planetary ball mill | 450 | 2 | ^d n.p. | Enzymatic hydrolysis | [75] |
| 6 | Willow sawdust | H ₂ SO ₄ (d) | Planetary ball mill | 800 | 0.7–5 | ZrO ₂ (16 balls, Ø = 10 mm)/2 g | Acid hydrolysis | [78] |
| 7 | Birch sawdust | H ₂ SO ₄ (d) | Planetary ball mill | 800 | 0.7–5 | ZrO ₂ (16 balls, Ø = 10 mm)/2 g | Acid hydrolysis | [80] |
| 8 | Beechwood | H ₂ SO ₄ (d) | Planetary ball mill, high-energy ball mill | 400–800, 800–1500 | 0.5–8, 0.3–3 | stainless steel balls (Ø = 4–20 mm); Ø = 2–10 mm | Depolymerization | [81,82] |

^a w = wet conditions; d = dry conditions. ^b Number of balls or the volume occupied by them is not informed. ^c The material and number of balls are not informed. ^d n.p.: not provided.

It is common knowledge that mechanochemistry uses mechanical forces to activate chemical bonds. However, knowing how ball mill setup and experimental parameters influence kinetic energy transfer to a chemical reaction is currently a challenge. Kessler et al. [81,82] (Table 4, Entry 8) found linear correlations between the yield of water-soluble products and the energy dose used in the mechanocatalytic depolymerization of beech wood acidified with H₂SO₄. Two ball mills functioning under distinct working principles were used. A planetary ball mill and a high-energy ball mill. An experimental

set was generated by varying rotational speed (800–1500 rpm), milling time (0.3–3 h), ball count (16–2061 units per jar) and size (2–10 mm). In the experiments performed in the planetary mill, a linear regime was observed when performing the mechanocatalytic depolymerization experiments employing a grinding medium composed of balls of a diameter equal to or higher than 10 mm, because the ball-ball friction was reduced, ensuring a dominant energy transfer through the impact of balls against the jar wall. No linear correlation was found when balls of 4 or 5 mm were used, which appears to be associated with forming a solid deposit with different mechanical properties from wood chips or sawdust. When mechanocatalytic depolymerization was carried out in the high-energy ball mill, the water-soluble product yield also increased with the energy dose (from 14% to 99% at 3.3 kJ/g and 81.5 kJ/g, respectively), but the productivity was 20% lower than that found for the planetary mill.

2.5. Solid Acid-Assisted Mechanochemical Treatment of Lignocellulosic Biomass

The recovery of homogeneous acid catalysts imposes great challenges to the feasibility of conventional hydrolysis processes. Solid acid catalysts are readily recyclable, easy to separate from the reaction medium, and more economical and environmentally friendly. Still, they are usually not as effective as mineral acids due to the mass-transfer limitations. A strategy to overcome this problem is using mechanocatalytic treatment, which offers many advantages such as less waste, insensitivity of feedstock, multiple product pathways and scalability. It is currently a challenge to achieve effective mechanocatalysts that are mechanically robust with sites physically accessible and chemically active. Some grinding techniques like pebble (or rolling) mills, shaker mills, attrition mills, and planetary mills effectively contact the catalyst with the biomass. Pre-treatment ball milling of biomass and a solid catalyst has proven to improve solid-solid reactions. Thus, for example, the rate constant of hydrolysis of cellulose to oligomers using this mix-milling method was 13-fold higher than when individual milling was carried out [83].

Although mechanocatalysis with metal-oxides [26,84] or resins [83,85] have shown to overcome substrate-catalyst contact restrictions, some catalysts are not recyclable after milling. They suffer structural degradation and deactivation as a consequence of mechanochemical treatment. On the other hand, most of the studies in the bibliography have focused on the mechanocatalytic formation of oligosaccharides from model substrates rather than real lignocellulosic biomass. In Table 5, some of the published works about this topic are gathered, indicating the type of mill, time and rotation speed, among other technical parameters. In these cases, the solid acid is mixed with, mainly cellulose, the biomass, and then they are milled together.

Blair et al. [84] (Table 5, entry 1) used three milling technologies for mechanocatalytic depolymerization of cellulose: rolling, shaking and attrition mills. Pure microcrystalline cellulose and natural cellulose from different sources were treated with different solid catalysts. The most effective catalyst was kaolinite; after 3 h of treatment in a shaker mill, 84% of the cellulose was converted to water-soluble compounds. Layered compounds such as natural clays can be effective mechanocatalysts because the hydrogen bonds that hold the layers together can be broken by mechanical processing [86]. In a shaker mill after 2 h of treatment a ratio of 9:1:4.3 of levoglucosan:fructose:glucose was obtained. Similar product distribution was achieved in an attrition mill. In a rolling mill at 100 rpm resulted in 13% solubilization after 96 h of treatment. The levoglucosan was transformed into 5-HMF and FUR in a shaker mill with prolonged treatment.

Several solid acid catalysts combined with a commercial 5 wt% Ru/C were studied in hydrolytic hydrogenation of ball-milled cellulose using a planetary ball mill at room temperature [87] (Table 5, Entry 2). Cellulose conversions were higher when a solid acid catalyst was added along with the Ru/C catalyst. Cellulose conversion increased with the acidity of the catalysts. Thus, less than 40% cellulose conversion was achieved with kaolinite, ZrO₂, and SiO₂-ZrO₂, but when HMOR (Si/Al = 10), H β (Si/Al = 25), HZSM-5 (Si/Al = 38) and amorphous zirconium phosphate (ZPA) were used, 75–78% of conversion

was obtained. Particularly, using ZPA, cellulose was completely converted after 2 h ball milling, and the yield of sugar alcohols reached 90.3%. Concentrations of sugar alcohols up to 67 mg/mL were obtained by increasing the cellulose/catalyst mass ratio.

On the other hand, it is known that metal-oxide, zeolite or polymer-based catalysts are long-term unstable under hydrothermal conditions of lignocellulose hydrolysis processes [88–91]. That is why recent research has focused on using acid functionalized carbons that display higher stability because polyaromatic systems do not undergo hydrolytic attack. Carboxylic or sulfonic acid functionalized carbons have emerged as useful catalysts for renewable hydrolysis polysaccharides such as cellulose and hemicellulose. Kobayashi et al. [92] showed that although the ball milling treatment (Table 5, Entry 3) of cellulose with carboxylic acid functionalized carbon did not lead to mechanocatalytic depolymerization, it enhanced its propensity to undergo hydrolysis in the presence of strong homogeneous Brønsted acids. Thus, when cellulose was ball milled with the catalyst (substrate/catalyst = 6.5, 60 rpm, 48 h), it could be hydrolyzed at 180 °C to yield 21.3% and 70% oligosaccharides, respectively. The same research group obtained carbon catalysts with a high density of carboxylic groups by mechanochemical oxidation with persulfate salts [93] (Table 5, entry 4). Microcrystalline cellulose was milled with the catalyst. This solid-solid mixture resulted in a 13-fold increase in the hydrolysis rate compared to the process where the components were individually milled. The vicinal carboxyl groups work synergistically by forming hydrogen bonds with the glucan chain, followed by the hydrolysis of glycosidic bonds in cellulose and hemicellulose [94]. When cellulose was milled with the catalyst in the presence of a trace amount of HCl, glucose was obtained in 85% yield after 20 min of reaction. The high efficiency of the simultaneous mechanochemical treatment of the cellulose and the catalyst was associated with the amorphization of cellulose, which increases the accessibility of the cellulose hydrolysis, and with the good solid-solid contact, that overcomes the mass-transfer resistance between the solids [83].

Similar results were obtained using carbonaceous solid acid catalysts with carboxylic and phenolic groups prepared from the forestry and agricultural residues of rice straw, corn straw, sawdust and cow dung [95] (Table 5, entry 5). Only 3.6% glucose yield was obtained for the hydrolysis of raw cellulose in water. However, 59.3% glucose yield in water was found when cellulose was pretreated by mixing with the carbonaceous catalyst in a planetary ball mill. Glucose yield increased to 74% when the hydrolysis was carried out in 0.015 wt% HCl aqueous solution. This research group proposed another carbonaceous material bearing -Cl and -SO₃H groups, synthesized by solvent-free carbonization of sucralose and p-toluenesulfonic acid, as catalysts for the hydrolysis of cellulose in water. SEM and XRD of the ball-milled mixture of the catalyst and cellulose showed that microcrystalline cellulose was reduced to small particles with good contact with the catalyst. The XPS and FTIR spectroscopy results demonstrated good stability of the catalysts in the heating and mixed ball milling processes. From the hydrolysis studies, the authors concluded that ball milling pretreatment mixing the cellulose and the catalyst was much more effective for producing glucose (52.8% yield) than cellulose ball-milled individually and then hydrolyzed by the catalyst in water (35.6% yield). The highest glucose yield (88%) was obtained when the ball-milled mixture of catalyst and cellulose was hydrolyzed in a 0.02 wt% HCl aqueous solution after 1 h at 200 °C. By-products such as levulinic acid, HMF and humic acid were formed for longer reaction times and at the higher reaction temperature. The recycling study demonstrated relatively good stability of the sucralose-derived catalyst in a 0.02 wt% H₂SO₄ solution which showed a glucose yield decrease from 71.9% to 55.4% after five cycles of reaction.

Although carboxylic and sulfonic acid surface functionalities into carbons have shown to be effective in cellulose conversion, hydrolysis with sulfonic acid functionalized materials typically requires lower temperatures. However, a problem to be aware of is the propensity of sulfonic acid groups to leach in hydrothermal conditions and to undergo deactivation via ion exchange-induced proton leaching that can be overcome by the addition of complexation agents [96]. Vogel et al. [97] (Table 5, entry 6) designed a catalytic

process based on the hydrolysis in a semi-batch reactor or a mechanocatalytically pretreated cellulose using a high stable sulfonated carbon catalyst. When cellulose was individual ball milling and then hydrolyzed in the presence and the absence of EDTA and sulfonated carbon catalyst, the authors concluded that the substrate had a higher tendency to undergo homogeneously catalyzed reactions rather than heterogeneous reactions with the solid acid. However, when ball milling was performed in the presence of the solid catalyst, a truly heterogeneously catalyzed hydrolysis occurred, leading to the formation of up to 64% soluble oligosaccharides. The stability of the sulfonated carbon catalysts was studied by repeated ball milling treatment and hydrolysis cycles. Despite the initial leaching of $-SO_3H$ groups and the reduction in the catalyst particle size, the catalytic activity remained stable over four cycles.

Table 5. Pretreatment of lignocellulosic biomass assisted by solid acid catalysts.

| Entry | Biomass | Catalyst | Mill | r.p.m. | Time (h) | Biomass/Catalyst | Balls/Biomass | Reaction | Reference |
|-------|-------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|------------------|-------------------|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|-----------|
| 1 | Cellulose | Kaolinite, delaminated kaolinite, aluminum phosphate, aluminum oxide, talc, Y-type zeolite, bentonite, vermiculite, quartz, muscovite mica, silicon carbide, graphite, aluminum sulfate | Rolling mill, mixer mill, attrition mill | ^a 350 | 0.5–3 | ^{a,b,c} 1:1 (wt:wt) | ^b 316 stainless steel (25 balls, $\varnothing = 1.27$ cm)/2 g; ^c 440C steel (3 balls, $\varnothing = 1.27$ cm)/2 g; ^a chrome steel (18 kg of balls; $\varnothing = 0.64$ cm)/1200 g | Cellulose solubilization | [84] |
| 2 | Cellulose | Amorphous zirconium phosphate | Planetary ball mill | 500 | 2–4 | 1 g/0.9 g | ZrO ₂ (15 balls; $\varnothing = 7$ mm) | Sugar alcohols production | [87] |
| 3 | Cellulose | Activated carbon | Ball mill | 60 | 48 | 10 g/1.24 g | Al ₂ O ₃ (2 kg, $\varnothing = 0.5$ cm) | Cellulose hydrolysis | [92] |
| 4 | Cellulose | Carboxylated carbon | Planetary ball mill | 500 | 2 | 4 g/0.616 g | Al ₂ O ₃ (200 g, $\varnothing = 0.5$ cm)/4 g | Cellulose hydrolysis | [93] |
| 5 | Cellulose | Activated carbon | Planetary ball mill | 300 | 4 | ^d 0.1 g/- | ZrO ₂ (60 g, $\varnothing = 0.8$ cm)/1 g | Cellulose hydrolysis | [95] |
| 6 | Cellulose and spruce-fir wood | Sulfonated carbon | Ball mill | 300 | ^e n.p. | 1:1 (wt:wt) | Sialon balls (25, $\varnothing = 1$ cm)/9 g | Cellulose hydrolysis | [97] |
| 7 | Cellulose, lignocellulose | Al ₂ (SO ₄) ₃ | Planetary ball mill | 350 | 4 | 0.972 g/0.342 g | Stainless steel balls (100 g, $\varnothing = 1$ cm)/1 g | 5-HMF and FUR | [98] |

^a Revolutions of the attrition mill. ^b Rolling Mill. ^c Mixer mill. ^d The mass of catalyst is not provided. ^e n.p.: not provided.

A green and efficient mechanochemical method has been recently proposed to obtain 5-HMF and FUR from cellulose and several lignocellulosic biomasses [98] (Table 5, entry 7). Biomass and Al₂(SO₄)₃ were pretreated in a planetary ball mill. The mixture was directly used in the conversion reaction performed in a water/ γ -valerolactone (GVL) biphasic system (by addition of NaCl), in which the formed 5-HMF in an aqueous solution was extracted to the GVL phase, thereby reducing its decomposition. The 5-HMF yield was 33.4% for the untreated cellulose after 70 min. When cellulose was firstly ball milling pretreated, 5-HMF yield increased to 39.8%. The maximum 5-HMF yield (44.6%) was obtained at 50 min when cellulose was first pretreated by Al₂(SO₄)₃-assisted ball milling, which turned out to be a more effective treatment to destroy the rigid structure of cellulose. Besides, with the assistance of ball milling, the catalyst has better contact with cellulose ensuring high efficiency of the catalyst even with high loading of the substrate. When the

method was applied to a real waste biomass (corn straw, rice straw, cow dung and poplar sawdust) in addition to HMF, high FUR yields (>50%) were obtained.

3. Extrusion Pretreatments of Lignocellulosic Biomass

Although ball mills in the bibliography are the most commonly used for the pretreatment of lignocellulose biomass, other equipment such as extruders have also proven to be efficient in disrupting lignocellulose. It produces a high shear, rapid heat transfer, and effective and rapid mixing, in a continuous operation, with good modulation of treatment steps [99]. The extruders have different configurations, and the screws can rotate inside a control temperature barrel. Key processing variables related to biomass pre-treatment include temperature, screw speed, screw configuration, and screw compression ratio (channel depth at the feed to channel depth at discharge ratio) [99]. Temperature control converts biomass treatment into a thermomechanical process similar to hot-compressed water treatment. Moreover, extrusion is a very versatile technique since the solid biomass can be mixed with water, acid or basic solution, oxidant or organic solvents to improve the recovery of each fraction of the lignocellulose. Here, we will show some examples of using extruders as grinding methods.

Lamsal et al. [100] applied two usual physical biomass treatments, particle size reduction by grinding and thermomechanical extrusion, to wheat bran and soybean hull. They evaluated different technical parameters for the extrusion method, varying the screw speed and temperature of the barrel. A laboratory hammer mill was used for particle size reduction. The extrusion resulted in a higher reducing sugar yield than particle size reduction. The best combination of extrusion screw speed and maximum barrel temperature was low residence time and high temperatures (7 Hz/150 °C) and high residence time and low temperature (3.7 Hz/r6). In both cases, the specific mechanical energy (SME) input was approximately 1500 kJ/kg. The authors hypothesized that the combined effect of temperature and shear might lead to greater surface area exposure. Reduction in cellulose crystallinity might not play a significant role since the reduction of particle size by hammer mill and extrusion resulted in a similar crystallinity index.

Razumovskii et al. [101] used a twin-screw extruder to treat birch wood. This treatment showed that the simple passage of the wood through the extruder did not produce changes in the chemical composition of the material. Thus, whether the working temperature was 20 °C without adding water or 90 °C with 15% water and a single passage through the extruder (2 min), the composition of sugars extracted in water at 100 °C was similar. Still, it showed a positive effect on the subsequent enzymatic hydrolysis, increasing the percentage of glucose extracted after enzymatic hydrolysis. If the number of steps was increased to 3 and in the conditions of 90 °C and 15% water, the content of extracted sugars would slightly increase, and so would the enzymatic hydrolysis. Therefore, the sole physical treatment of lignocellulose did not produce significant changes in the composition of the material, but it enhanced enzymatic hydrolysis.

Similar results were also found by Vandenbossche et al. [102] when treated in a twin-screw extruder wheat straw. The extrusion was performed for 30 min, and the solid material was fed with water. Each section of the extruder was thermostatized at a fixed temperature. This thermomechanical method aimed to induce a deconstruction of material but without producing inhibitors to the following enzymatic treatments. These authors also showed that the mechanical treatment gave a strong straw defibration, but the enzymatic digestibility only achieved 35%, whereas the ground straw yielded 22%.

Choi et al. [103] developed a mechanochemical method for the continuous fractionation of biomass with a continuous twin screw-driven reactor (CTSR). The extruder provided the mechanical shear to reduce the biomass's size effectively, enabling enzymatic hydrolysis. In the CTSR method, an acid solution is continuously supplied, so the cumulative effect of temperature and acid concentration had a profound effect on the recovery of free sugars and sugar decomposition products. This result was ascribed to the fact that the high mechanical shear disrupted lignocellulose, promoting a more effective mixing between

the biomass and the acid catalyst. Particularly, in this study, they fractionated yellow poplar sawdust (YPS) with diluted sulfuric acid using a CTSR to achieve a high hemicellulosic sugar recovery, limiting the cellulose degradation and the formation of by-products such as FUR or formic acid. The analysis of the hemicellulosic sugars (xmg) in the liquid fraction showed that the yield was maximized at 61.5% when the YPS was fractionated at 133 °C with 0.8 wt% H₂SO₄. This maximum was sharply decreased (32.1%) even with a slight increase in temperature (6 °C). This was attributed to the partial xylose conversion to FUR and formic acid. As the temperature greatly influenced sugar recovery, the authors studied the optimal reaction temperature within a narrower temperature range (between 121 °C and 136 °C). The xmg yield increased from 24.2% (121 °C), 55.2% (124 °C), and 74.8% (127 °C) and after reaching an optimum, the xmg yield decreased drastically to 66.9% (130 °C) and 28.1% (136 °C). This was attributed to the high rate of xylose decomposition due to the increased reaction temperature. It also evaluated the effect of the sulfuric acid concentration. They observed that as the acid concentration was above 0.8 wt%, the xmg yield decreased sharply due to the decomposition of xmg using more severe reaction conditions. The degradation of cellulose was followed by its concentration in the liquid fraction during the CTSR fractionation process. Increasing the acid concentration and temperature caused the glucose concentration to gradually increase, i.e., using more aggressive reaction conditions promoting cellulose hydrolysis. The maximum glucose released was 10%, attained by an acid concentration of 1.3 wt%. Since the main goal of fractionation is the clean separation of the hemicellulosic sugar, it is important to minimize glucose release from YPS. Thus, the cellulose and hemicellulose recoveries in the solid residue and the hydrolysate were calculated to be 87.6% and 98.4%, respectively, at the optimal conditions.

Gu et al. [104] studied the influence of different parameters on the extrusion of Douglas-fir wood residues. Before extrusion, the solid was hydrated at different moisture contents (30, 40 and 50%), and after the solid underwent a saccharification process to evaluate the yield of sugars. Motor torque strongly correlates with specific mechanical energy (SME), glucose and xylose/mannose yields. The maximum torque value was observed with the sample with 30% moisture and at 25 °C. This value was attributed to the fact that low temperatures and moisture content resulted in lower mobility of the solid, and much higher motor power is required to force the solid out of the extruder. At the same time, this fact resulted in high residence times in the extruder under high mechanical stress leading to a high yield of sugars. As EMS is directly related to torque, EMS also showed a strong correlation with sugar yield because mechanical energy favored the deconstruction of the lignocellulose structure by modifying the outer layers of the cell wall structure and improved enzyme accessibility to cellulose and hemicellulose. The SME value was 0.3 kWh/kg to achieve a 40.5% glucose yield and 18.3% xylose/mannose yield, lower than the 7-min ball milling [105], which consumed 0.97 kWh/kg to achieve similar glucose and xylose/mannose yields. However, the correlation between SME and torque with the crystallinity index was strongly negative. This means that the higher the mechanical energy, the lower the crystallinity due to the alteration of the cellulose structure. Regardless of the moisture content of the wood and the temperature of the barrel of the extruder, the crystallinity did not show great differences when it was compared to the control analysis. Although the control and extruded samples showed similar crystallinity indexes, the sugar yield was always higher for the extruded samples. This is because extrusion caused changes in the structure of the wood samples, such as delignification, alteration of the lignin and hemicellulose structure, removal of hemicellulose, etc. All these factors can enhance enzymatic hydrolysis due to improved enzyme accessibility. Other samples showed a higher index crystallinity than the control sample. This could be considered evidence of the recrystallization of the cellulose. This was observed when the barrel temperature was high (100 and 150 °C). Moisture during the heating process can lead to the recrystallization of cellulose because of the rearrangement of the hydrogen bonds. Another analyzed property was the particle size of the extruded solid, observing that high barrel temperatures caused an increase of the particle size regardless of the level of moisture. This was ascribed to

the agglomeration of the solid particles when water was evaporated. Barrel temperature negatively influenced sugar yields, as residual woods after extrusion could have a more recalcitrant structure than the control sample.

Gao et al. [106] obtained defibrillated cellulose from pea wastes comprised of leaves, vines and stems. To achieve this goal, the fresh biomass was passed through a twin-screw press juicer, and the extruder was subjected to a microwave hydrothermal treatment. The highest yield was obtained when the biomass was extruded for all temperatures tested. This fact was due to the breakage of the ordered structure of lignocellulose, removing some hemicellulose and amorphous cellulose, yielding a more cellulosic material with less hydrolyzable content. They analyzed the properties of the microfibrillated cellulose after the extrusion, followed by the hydrothermal treatment. This was corroborated by XRD analysis in which the cellulose microfibrils were more crystalline after the extrusion and hydrothermal treatment than those not extruded. These microfibrils showed higher crystallinity and thermal stability and were more cellulosic in nature with reduced hemicellulose and lignin content.

Li et al. [107] studied the defibrillation of lignocellulose material (wood pulp) using a twin-screw extruder. They prepared different samples varying the water content, ranging between 30 and 80 wt% of water. The samples were run through the extruder 1, 3, 5 and 7 times. The main goal of this work was to ensure that the mechanical extrusion method was able to increase the chemical accessibility of the lignocellulose. The results showed that the samples after seven passes through the extruder lost the most moisture content; for example, the sample with a content of 70 wt% of solids lost 8.25% of the initial water. Water loss was ascribed to the heat released during the friction between pulp fibers. The water retention value (WRV) is a measurement of the fibers' micro and nano fibrillation. More than three passes through the extruder caused a reduction of WRV when the solids content was above 50 wt%. The sample with 60 wt% of solids and after five passes exceeded the WRV of the raw material by 2.1 times. The SEM analysis of this sample showed a fine powder morphology, which explains the great water absorption and the high surface area. Moreover, the light microscopy showed that the fibers were reduced in length, observing the formation of microfibrils separated from the pulp, so the microfibrillation was the dominant process during the extrusion treatment. However, when more severe conditions of extrusion were applied or the amount of solid increased, some agglomeration of the extruded pulp was observed. The SME values were calculated as a function of the number of extrusions and the solid contents, being those data of 198 Wh/kg per pass when the solid content was 60 wt%. This value increased up to 249 Wh/kg per pass when the solid concentration was 70 wt%. The acetylation reaction studied the evaluation of the micro-fibrillation of the lignocellulose. The extrusion increased the degree of grafted acetyl groups but also affected the rate of acetylation, and 96% of the maximum acetylation was achieved after 12 min. In contrast, the raw material needed twice as long.

Due to the cellulose derivatives' high cost, Lu et al. [108] developed a method to produce lignocellulose nanofibrils (LCNF) from waste residues from wood and agriculture. The raw materials (bamboo logs, poplar and pine chips, wheat straw) were soaked with glycerol and heated at 120 °C for 2 h. The lignocellulose materials were twice extruded with a single-screw device to obtain crushed lignocellulose in glycerol (CLC). The CLC solid was diluted in glycerol, then treated with sulfuric acid (0.15%) at 100 °C for 1 h, then neutralized with NaOH to pH 7 and milled. This treatment decreased the hemicellulose fraction of the raw material, and the cellulose and lignin were barely modified after this mechanical and chemical treatment. In fact, for each raw material, it was observed an increase in the cellulose amount in the LCNF. The energy consumption for each kind of lignocellulose material was lower than the required for the conventional nanocellulose technology; thus, the kWh/ton of LCNF produced varied from 13,000 to 15,100. The LCNF yield also depended on the raw material, the highest being obtained with poplar (75.3%) and the lowest with wheat straw (62.3%), the latter being the raw material with the highest amount of hemicellulose and the former having the highest cellulose content

and the lowest hemicellulose mass percentage. Different analytical techniques analyzed the LNCF samples. The SEM images showed that the lignocellulose fibers were cut into individual micro-sized fibers (about 10 μm). By AFM images, the length of the micro-fibers was measured. They were about several microns in length and less than 100 nm in diameter after the mechanical and chemical treatment. The crystallinity was also analyzed, showing that the extrusion treatment decreased the crystalline structure of the cellulose. Still, the acid treatment increased it due to the dissolution of the amorphous phases of cellulose and lignin. Finally, the mass balance for the poplar raw material was calculated by obtaining 75.3 g of LNCF and a liquor fraction comprised of high purity lignin 2.3 g, byproducts 14.5 g (lignin, acetyl groups, xylooligosaccharides and glucose and 7.9 g of others (ashes and extractives). Similar compositions were found for the rest of the raw materials.

Endo et al. [61] developed a method for the fibrillation of lignocellulose biomass (eucalyptus wood chips) to increase the accessibility to the enzymatic saccharification. This method was based on the HCW at mild conditions (140–180 °C and 30 min), followed by disk milling of the solid residue. Optimizing the HCW process allowed minimizing the amount of water (1:5, biomass:water weight ratio) and the temperature. The liquid phase after the HCW treatment recovered the xylooligosaccharides and the water-soluble lignin fraction, but the latter recovered in the solid was almost the initial amount contained in the biomass. The amount of xylose and glucose in the liquid fraction was also very low, indicating that both monomers were in their respective polymers. The solid residue was disk milled, and the saccharification was evaluated, concluding that the highest glucose yield (42.8%) was obtained after 3-pass disk milling after HCW treatment at 180 °C. The authors noted that this glucose amount corresponds to the total glucose contained in the cellulose. SEM analyzed the morphology of the residue solid after disk milling. Fibers of 20 μm in size formed the solid residue after HCW treatment. A close view of the fibers showed that a nanospace separated the microfibrils exposed on the surface. The presence of such nanospace (although it was not measured because of the scale of the image) was ascribed to the elimination of hemicellulose and partially the lignin. However, the microfibrils were not completely fibrillated, which hinders the action of the enzymes for the complete saccharification of the solid. But, when the solid residue was passed 10 times over the disk mill, the degree of fibrillation was increased, generating more space between the microfibrils, and increasing the surface area of the cellulose. When the lignin was removed from the microfibrils, pure cellulose microfibrils of 20 nm were observed, although the presence of lignin did not affect the saccharification of the solid residue. The energy consumption of the HCW plus disk milling was evaluated. The energy per kg of biomass was 0.89 MJ for the HCW process at 180 °C and 30 min when thermal recycling was achieved at temperatures above 65 °C. Although increasing the number of passes through the mill provoked an increase in the viscosity of the solid and the energy consumption, with only three passes, this consumption was as low as 0.6 MJ/kg. Therefore, 1.49 MJ/kg was consumed to achieve the complete saccharification of the cellulose.

Cardoso Coimbra et al. [109] showed that extrusion assisted by alkaline conditions was an efficient method for the pretreatment of wheat straw for enzymatic hydrolysis of biomass (Table 3, Entry 9). The solution of NaOH (10% *w/v*) and the biomass were fed continuously to the extruder using two pumps. The residence time of the extrudate in the reactor was 2 min. After extrusion, the pH was adjusted with phosphoric acid and washed with distillate water. The filtrates and solid residue were collected and analyzed. The alkaline extruded biomass's composition was different from that of the untreated biomass. The main differences were related to the cellulose content, which notably increased after treatment with the concomitant reduction of the lignin and the complete solubilization of acetyl groups. These effects were expected since the alkaline treatment of lignocellulose is an efficient method for lignin and hemicellulose removal. In this study, the combination of the mechanical extrusion method, which impairs the energy for the reduction in particle size and the energy for mixing the solution with the biomass, with the alkaline treatment led to a reduction of lignin, 22% of lignin removal, even at very short times. On the other

hand, the percentage of glucan + xylan after treatment increased to 75.6% in comparison with the initial 66.1%, and the glucose content in the filtrates was equivalent to 2.2% of the glucan contained in the raw material, indicating that there was a little loss of glucose. In the case of xylan, it was found in the filtrate that 4.4% of the contained in the raw material. It is important to note that most solubilized glucose and xylose were in the filtrate's oligomeric form. The authors also claimed that this alkaline-extrusion method did not produce enzymatic inhibitors such as FUR or 5-HMF. This method developed by the authors increased 13 times for glucan and 11 times for xylan hydrolysis over the untreated material.

Ismail et al. [110] studied the effect of the hydrothermal process with dilute acid on extruded Napier grass, followed by enzymatic saccharification prior to simultaneous saccharification and co-fermentation for bioethanol production. Extrusion of Napier grass significantly decreased the water content in the biomass and 30.2% of lignin removal, compared to 58% [8] and 84% [111], when both acid and alkaline were utilized, and alkaline only. The extruded material was mixed with aerosolized dilute sulfuric acid prior to the steam explosion. Longer retention times resulted in higher total sugars, regardless of the steam temperature. The highest glucose and total sugar production (33 g/L) were obtained after treatment at 190 °C and 3% sulfuric acid for 30 min. To minimize the production of inhibitors (acetate, formate, 5-HMF and FUR) without compromising the sugar production, the best conditions were 200 °C and 3% sulfuric acid for 5 min. The ethanol yield of 0.26 g ethanol/g biomass was achieved based on 76% carbohydrate content.

Disc refining is a well-known technique applied in the paper industry for decades. Ma et al. reported a mechanochemical pretreatment based on a disc refining device to enhance biomethane production from corn straw [112]. This device was a household disc refining machine in which a shearing force was generated between the disc gaps, and energy transfer took place in the friction forces inside the lignocellulosic biomass. The corn straw was impregnated with different kinds and concentrations of acidic solutions of organic (acetic, propionic, and butyric acid) and minerals acids (sulfuric and phosphoric acid). A disc refiner milled the impregnated corn straw eight times (2800 rpm). Using mineral acids generated inhibition byproducts, e.g., FUR and 5-HMF, during biomass pretreatments that significantly inhibited the anaerobic digestion process [9,113]. Maximum biomethane yield (239 mL/g-total solid, 47.13%) was obtained when the corn straw was pretreated by acid impregnation and disc refining. This is because acids absorbed on the surface of the corn straw induced a mechanochemical process that destroyed the corn straw-resistant structure of lignocellulose. The authors performed an economic analysis of the anaerobic digestion process. They concluded that the mechanochemical pretreatment of acid-impregnated biomass had a higher net profit (ton^{-1}) than the process without pretreatment.

Mild mechanical refining has also been proposed as a simple, scalable and mature technology for the coproduction of xylooligosaccharides and fermentable monosaccharides from the hydrolysis of the cellulose of poplar [114]. Xylooligosaccharides are short-chain sugar oligomers of β -1,4-linked xylose units with a degree of polymerization from two to six residues that can be used as prebiotics [115]. Poplar sawdust was pretreated with an acetic acid solution. After vacuum filtration, the solid was subjected to mechanical refining using a Papir Forsknings Institutet refiner. Then, enzymatic hydrolysis of pretreated poplar sawdust was carried out. Fermentable glucose production from pretreated residue increased by 2.3 folds when the pretreated solids with acetic acid were mechanically refined prior to cellulolytic hydrolysis. Moreover, a remarkable increase in glucose yield was achieved (from 67.1 to 84.9%) as the revolutions of PFI milling increased. This high enhancement in the enzymatic hydrolysis was due to the altered physicochemical characteristics after milling [116]. For a mass balance, 100 g poplar sawdust can be converted into 48.0 g monosaccharides (40.5 g glucose and 7.5 g xylose), 7.2 g xylooligosaccharides, and 2.7 g low degree of polymerization xylans. From these results, the combination of acetic acid pretreatment, PFI refining and post-enzymatic hydrolysis has been demonstrated to be a viable method for recovering wood carbohydrates.

4. Future Outlooks

Since 1894, when Ostwald defined mechanochemistry as one of the disciplines of chemistry, along with thermochemistry, electrochemistry and photochemistry [117], mechanochemistry has progressed, finding applications in numerous fields such as inorganic material synthesis, organic reactions, and so on. In this review, mechanochemistry has the potential to be a useful tool for lignocellulose treatment since it reduces the crystallinity and the degree of polymerization of cellulose and the particle size of lignocellulose. In combination with other treatments, it achieves, to a greater or lesser extent, the hydrolysis of the constituent polymers of lignocellulose. The two most widely studied methods at the laboratory level are those based on ball mills and extrusion, with extrusion showing greater versatility due to it allowing different treatments along the length of the screws. Even so, it is still necessary to delve into different aspects of applying this technique to the pretreatment of lignocellulose. Firstly, considering that these techniques consume a lot of energy per kg of material treated, it is necessary to carry out more in-depth techno-economic studies on their impact on the final cost of the product to be obtained. This also implies having information on how the nature of the lignocellulose changes throughout the treatment and studying these changes in the initial stages of the treatment.

Future research should be focused on understanding the impact of mechanical treatment on lignocellulosic biomass at the molecular level, which will help to optimize the operational parameters for applications and large-scale production. In the literature, we have only found one study [118] that addresses this issue but from model compounds such as cellobiose.

It has been shown above that the combination of mechanical milling with a catalyst can depolymerize lignocellulosic biomass using lower amounts of mineral acids and/or solid acid catalysts and strong bases. This is due to a synergistic effect between the action of the acid catalyst and mechanical forces, which not only provide energy to the catalytic system but, in the case of cellulose, also prompt the conformational change of the pyranic ring. This enables the protonation and cleavage of the β -1,4 glycosidic bond. If solid catalysts are used to accelerate the deconstruction of lignocellulose during the mechanochemical process, it is necessary to prepare catalysts that are capable of withstanding all the forces involved in the process without altering their activity. Mechanochemistry is a suitable strategy to overcome the solid-solid mass transfer barrier, but the challenge is to achieve recyclable catalysts after milling, avoiding its structural degradation and deactivation. In this regard, if adequate solid catalysts are designed, the use of strong acids and bases could be avoided, as well as the use of water during treatment could be reduced. Water's role should be considered and studied during the mechanochemical process since it has been seen that depending on the conditions, its use can be favorable or unfavorable.

On the other hand, the simple description of the milling conditions is insufficient to conduct a comparative analysis of the results in the literature because the energy dose the different systems provides depends on their design. In this sense, applying theoretical models that relate the energy provided by the mills with the process parameters will help to compare the results obtained by different mechanical systems. Achieving an understanding of the complex mechanism of mechanical biomass treatment will reduce the number of steps and the number of chemicals in the process.

5. Conclusions

To fully utilize the monomers that form lignin and the sugars that form lignocellulose to synthesize a myriad of compounds, it is necessary to separate lignin from cellulose and hemicellulose. In this review, it has been shown that mechanochemistry has a place in the pretreatment of lignocellulose, given it generates fewer wastes due to the minimum consumption of water and/or chemical products. On the other hand, it can deconstruct the lignocellulose favoring the subsequent processes.

The mechanochemical treatment of lignocellulose by ball milling causes a reduction in the crystallinity of the cellulose, achieving significant amorphization and a considerable

reduction in particle size. In the works reviewed, it is highlighted that these changes are responsible for the improvements observed in the enzymatic or chemical processes of the subsequent treatments of lignocellulose. It is also true that the best results are obtained when ball milling is done in the presence of different acids or bases. This is because synergy is produced between the mechanical energy exerted by the impacts of the balls and the chemical reactions that these acids or bases catalyze.

Finally, extrusion is another mechanochemical treatment route for lignocellulosic biomass, presenting advantages that make it very interesting to implement at an industrial level. The advantages include the possibility of modifying the different sections of the extruder screws, the possibility of thermostating the extruder, simultaneous deconstruction of lignocellulose and the synthesis or production of a compound of interest, and to supply the necessary raw material and reagents continuously.

Author Contributions: Conceptualization, R.M.-T. and J.M.-R.; writing—original draft preparation, A.M.P.-M., G.R.-C. and B.T.-O.; writing—review and editing, R.M.-T. and J.M.-R.; visualization, C.G.-S. and B.T.-O.; project administration, P.J.M.-T.; funding acquisition, P.J.M.-T. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Spanish Ministry of Science and Innovation (PID2021-122736OB-C42), FEDER (European Union) funds (PID2021-122736OB-C42, P20-00375, UMA20-FEDERJA88) and B.T.O. acknowledges Ministerio de Universidades for his predoctoral contract.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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