

Review

# Valorising Agro-industrial Wastes within the Circular Bioeconomy Concept: the Case of Defatted Rice Bran with Emphasis on Bioconversion Strategies

Maria Alexandri \*, José Pablo López-Gómez , Agata Olszewska-Widdrat  and Joachim Venus \* 

Leibniz Institute for Agricultural Engineering and Bioeconomy, Department of Bioengineering, Max-Eyth-Allee 100, 14469 Potsdam, Germany; plopezgomez@atb-potsdam.de (J.P.L.-G.); aolszewska-widdrat@atb-potsdam.de (A.O.-W.)

\* Correspondence: malexandri@atb-potsdam.de (M.A.); jvenus@atb-potsdam.de (J.V.)

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**Abstract:** The numerous environmental problems caused by the extensive use of fossil resources have led to the formation of the circular bioeconomy concept. Renewable resources will constitute the cornerstone of this new, sustainable model, with biomass presenting a huge potential for the production of fuels and chemicals. In this context, waste and by-product streams from the food industry will be treated not as “wastes” but as resources. Rice production generates various by-product streams which currently are highly unexploited, leading to environmental problems especially in the countries that are the main producers. The main by-product streams include the straw, the husks, and the rice bran. Among these streams, rice bran finds applications in the food industry and cosmetics, mainly due to its high oil content. The high demand for rice bran oil generates huge amounts of defatted rice bran (DRB), the main by-product of the oil extraction process. The sustainable utilisation of this by-product has been a topic of research, either as a food additive or via its bioconversion into value-added products and chemicals. This review describes all the processes involved in the efficient bioconversion of DRB into biotechnological products. The detailed description of the production process, yields and productivities, as well as strains used for the production of bioethanol, lactic acid and biobutanol, among others, are discussed.

**Keywords:** pretreatment; bioconversion; bio-based products; fermentation; sustainability; circular economy

## 1. Introduction

The concept of the circular economy drives research into renewable resources, as an alternative to the finite fossil fuels and the negative environmental impact caused by their extensive utilization. Within this concept, renewables would be the key for a sustainable economic growth in respect to the environment and natural resources preservation [1]. Biomass constitutes a promising renewable resource, which—via the biorefinery concept—can be exploited to generate energy and chemicals. In a biorefinery, the conversion of biomass into bioenergy and bioproducts occurs while minimizing the waste generation and the emissions from their production [2].

The European Union has underlined the importance of the circular bioeconomy model with the launch of new campaigns and novel legislations to instigate its implementation [3]. More specifically, the Circular Economy Package (April 2018), recently approved by the European Parliament, has introduced amendments and directives regarding waste recycling as well as landfilling reduction. The amendment of the Landfilling Directive (1999/31/EC) dictates that landfilling should not be the standard measure of

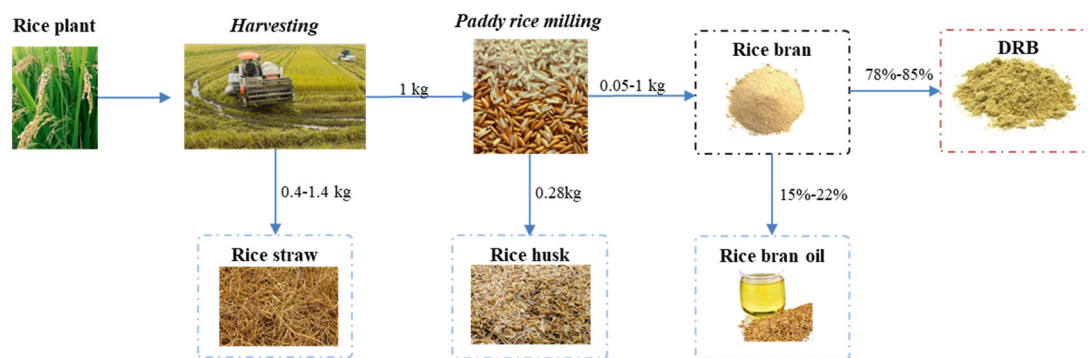
waste handling, and that the member states are required to recycle or recover any suitable waste by 2030. According to the same directive only wastes characterized as “inert waste”, i.e., with a negligible content in pollutants or compounds that could be subjected to physical, chemical or biological transformations, should be landfilled. Thus, member states must develop waste management systems in accordance with Directive 2018/851, in order to establish resource efficiency. In other words, organic wastes are considered a potential resource, and hence should be used instead of disposed.

The new legislations towards a circular economy have pushed research to new limits. It is not enough anymore to find renewable alternatives for the generation of energy and chemicals; additionally, processes should completely exhaust the substrates while generating the minimum amount of wastes. As a result, new investigations into waste materials which were not considered as being of high interest have started to increase in number. It is expected that the number of works into the valorisation of such residues will continue to grow as we transition from fossil fuels to renewables.

*Rice Production and Defatted Rice Bran (DRB). A New Framework Emerges in the Circular Bio-Economy*

Rice (*Oryza sativa* L.) constitutes one of the most important cereal crops worldwide, being a part of the diet of a quarter of the world’s population [4]. Global rice production was estimated at 509.7 million tonnes in 2018, with an expected growth of 52.6 million tonnes by 2027 [5]. Asian countries are the main rice producers, with a production of 459.5 million tonnes in 2018 [5]. China is the most important contributor with an estimated production of 140.8 million tonnes for the same year, followed by India (113.3 million tonnes), Indonesia (47.9 million tonnes) and Thailand (23.3 million tonnes).

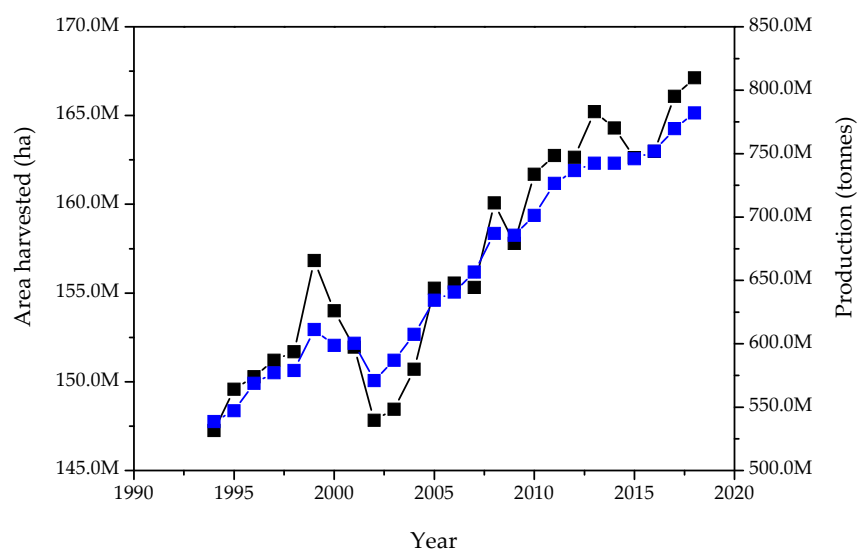
The white rice production process comprises steps of harvesting, cleaning, hulling, whitening, polishing and grading [4]. These steps generate various waste streams with the main ones being the straw, the husks, and the rice bran [6]. Rice straw is the stalk of the plant and it is generated upon harvesting. The husk is the outer layer of the grain and it is removed during the milling process. Rice bran is a by-product of rice milling, derived from the outer layer of brown rice kernel. In general, for every kilogram of milled rice, 0.4–1.4 kg of rice straw (depending on the variety), 0.28 kg of rice husk and 0.05–0.1 kg of rice bran are generated (Figure 1) [7].



**Figure 1.** Production of rice and its by-products. Defatted rice bran (DRB) is the residue after the oil extraction from the rice bran accounting for around 78%–85% (*w/w*) of the bran.

According to FAOSTAT, greenhouse gas emissions attributed to the burning of rice residues accounted for almost 54.634 megatonnes in CO<sub>2</sub> eq. in 2017 [8]. Due to environmental and economic concerns, new studies have focused on the sustainable utilization of the rice production process by-products within a biorefinery concept [9–11]. Specifically, owing to its rich composition in proteins, fibres, vitamins, antioxidants and oil [4], rice bran can find applications as animal feed and in the food and pharmaceutical industries [12–14]. Amongst its components, rice bran oil accounts for approximately 15%–22% *w/w* of rice bran and its high nutritional value has been highlighted in several studies due to its elevated content in sterols, tocopherols, tocotrienols, and  $\gamma$ -oryzanol [4,13]. With a global market estimated at \$1.23 billion for 2018, the increasing demand for rice bran oil has led to the production of large amounts of defatted rice bran (DRB), the main by-product of the oil extraction process.

Figure 2 indicates the global paddy rice production from 1994 to 2020. Rice production was forecasted to increase by approximately  $19.7 \times 10^3$  thousand tonnes by 2020, reflecting the constant demand for this crop [15]. From the overall production, almost 80% is attributed for food, while the rest is distributed for feed, biofuel and other uses [15]. Considering the amounts corresponding for food consumption, it is easy to assess the amounts of by-products co-produced for the same time period. Even though similar data do not exist for DRB, the amounts could be easily calculated when considering that 5%–10% of the overall production corresponds to rice bran generation. A second indicator of the increased DRB quantities is the corresponding expansion in rice bran oil market. In 2016, rice bran oil market registered a sum of 1.5 million tons, growing with a 3% compound annual growth rate (CAGR) during the 2009–2016 period. The rice bran oil market will reach 1.9 million tons by 2022, with a CAGR of 4% for the period between 2017 and 2022 [16]. Thus, an efficient handling of this emerging by-product is crucial, not only to further increase the economic potential of the rice industry, but also to be in line with current environmental policy frameworks and guidelines.



**Figure 2.** World production of paddy rice according to FAOSTAT. Black line: area harvested and blue line: production yields.

Even though DRB is highly nutritional, its application is limited to landfilling or as low-value animal feed [4,17]. Nevertheless, the addition of DRB to the bio-economy chain increases its market value and opens new strategies impacting the economy of the whole process. This approach is consistent with the requirements of a sustainable development and provides advantages not only to the economy but also to the environment. The exploitation of this abundant by-product has been a topic of research, either as a dietary supplement and food additive [18] or for the biotechnological conversion to bulk chemicals like lactic acid [17]. This review aims to provide a complete overview of the potential avenues derived from the biotechnological conversion of DRB. It summarizes the usage of DRB with emphasis on its application into biotechnological products and processes.

## 2. Composition of DRB

DRB contains high amounts of starch (35.3%–47.5%), fibres (about 11%) and proteins (15%–18%), as shown in Table 1. Some residual lipids are still found in its composition, and the concentration depends on the initial content and the extraction process. The dietary fibres of rice bran-and subsequently DRB's- are mainly insoluble [19,20]. Dietary fibres from DRB present high water and oil adsorption capacity, as well as higher antioxidant activity in comparison to other defatted by-products such as sesame husk and flaxseed fibres [19,21].

It is evident from its composition that DRB can be utilized either as additive in foodstuffs, or for the microbial production of value-added products. Sairam et al. studied the nutrient profile and some

physicochemical characteristics of DRB [22]. The sample contained calcium, phosphorous and iron at a concentration of 255, 166 and 290 ppm/100 g DRB, respectively. The water absorption capacity was 240 mL/100 g DRB, whilst the fat absorption capacity was determined at 210 mL/100 g, values rather crucial for its use in bakery products. The authors also found some oryzanol (0.013 g/100g) in hexane extracts of DRB, which is significantly lower in comparison to RB (0.16 g/100 g). Nevertheless, the radical scavenging activity of methanolic extracts from both RB and DRB were quite similar, indicating the existence of phenolic compounds in DRB. The presence of ferulic acid in DRB extracts has already been proven [23].

DRB is also rich in high-quality protein, and given the fact that proteins are generally bound to phenolic compounds, protein hydrolysates from DRB exhibit high antioxidant activities [24–26]. Peptide fractionation from DRB showed 12.5% albumin, 13.9% globulin, 70.8% glutelin and 2.9% prolamine. Albumin peptides exhibited higher antioxidant activity in comparison to the other fractionated ones, due to the presence of hydrophobic amino acids [25].

Since rice starch is much more expensive than other cereal starches, DRB could serve as a cheap alternative source (Table 1). Fabian et al. attempted to isolate starch from DRB via wet-milling [27]. The authors managed to recover approximately 83% of starch, with similar properties of starch isolated from rice endosperm. Their study suggested that DRB starch could be used in food and pharmaceuticals industry.

**Table 1.** Composition (%) of defatted rice bran according to the literature.

Component	Wang et al. [28]	Siepmann et al. [29]	Alexandri et al. [17]	Tanaka et al. [30]	Sairam et al. [22]	Yadav et al. [31]	Daou and Zhang [20]
Protein	15.61	14.89	17.3	18.4	17.2	14.9	16.2
Lipid	0.54	1.67	3.0	1.4	0.66	2.7	2.8
Starch	47.5	-	35.3	46.7 *	-	-	-
Ash	12.44	11.31	-	10.4	14.65	8.2	10.7
Moisture	8.46	11.09	10.1	-	11.1	12.7	8.7
Total dietary fibre	-	-	-	-	11.44	12.7	32.9
Carbohydrates	-	-	-	-	-	48.8	-
Crude fibre	8.42	-	-	-	9.19	-	30.2
Cellulose	-	-	9.8	-	-	-	-
Hemicellulose	-	-	20.6	-	-	-	-
Lignin	-	-	3.9	-	-	-	-

\* And dextrans.

### 3. Valorisation Options of Defatted Rice Bran

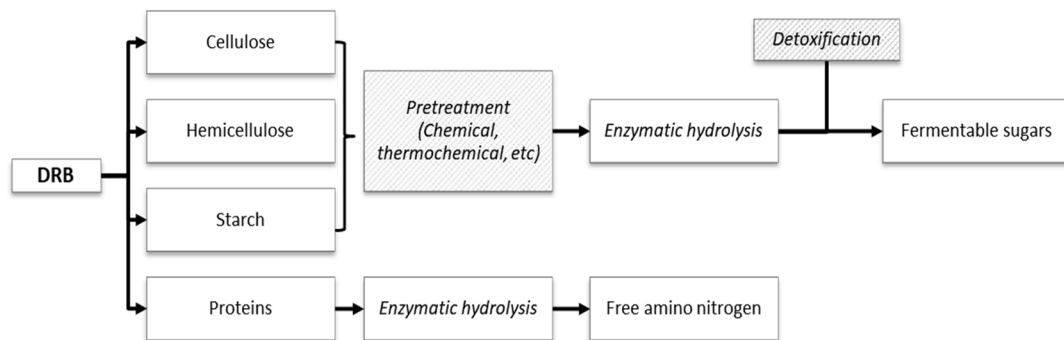
The abundance of DRB together with its high nutritional content attracted the scientific interest in investigating potential valorisation routes. Some studies have focused on its addition in foodstuffs, due to its high protein content and quality of its dietary fibres. DRB proteins, due to their hypoallergenicity, could be added in preparations for infants [17]. Insoluble dietary fibres are beneficial towards human health via assisting the growth of the intestinal microflora [12,13]. Rice starch has the smallest and narrowest size range in comparison to other plant starches, making it suitable for applications in nanotechnology [27]. Another possible route is the utilisation of DRB as a substrate for microbial fermentations. The latter will be discussed in detail in this review. A brief discussion of the utilisation of DRB in food industry will also be carried out.

#### 3.1. Biotechnological Conversion of DRB in Value-added Products

##### 3.1.1. Pretreatment

The effective bioconversion of DRB into value-added products requires—in most cases—a pretreatment step, since most microorganisms are unable to directly use polysaccharides. As shown

in Table 1, DRB is rich in starch and hemicellulose. It also contains proteins and cellulose in smaller quantities. In general, the conversion of DRB to biotechnological products includes the following steps: pretreatment, enzymatic hydrolysis, and fermentation (Figure 3). The hydrolysis steps involve the enzymatic conversion of the polysaccharides (starch, cellulose, hemicellulose) into their corresponding monosaccharides. The pretreatment step is necessary for the efficient enzymatic hydrolysis and therefore fermentable sugar yields. Hydrolysis and fermentation could be carried out separately (SHF-separate hydrolysis and fermentation) or simultaneously, and in this case, it is called simultaneous saccharification and fermentation (SSF). The major advantage of SSF is the minimization of end-product inhibition towards the enzymes. However, SSF could be employed only in cases that the enzymatic reaction conditions are similar to the fermentation's. Table 2 summarizes all the pretreatment methods proposed by the literature for the efficient saccharification of DRB before fermentation.



**Figure 3.** Diagram of the stages for the release of fermentable sugars and free amino nitrogen from defatted rice bran. Striped boxes indicate stages that are not always required.

The selected pretreatment method should efficiently cause structural alterations without damaging the targeted polysaccharides—rendering them more susceptible to enzymatic hydrolysis—or generating inhibitory compounds. This process should also have low energy and chemical demands, and be economical and environmentally benign [32]. Acid hydrolysis is a widely employed chemical pretreatment method, targeting polysaccharide solubilisation, especially hemicellulose. Various acids (organic and inorganic) have been proposed in the literature, such as sulphuric acid, hydrochloric acid, phosphoric acid, and citric acid, as efficient means for hemicellulose solubilisation [33]. Dilute sulphuric acid hydrolysis has been successfully employed in a variety of biomasses, including sugar beet pulp [34], coffee pulp and coffee mucilage [35,36] among others. The main disadvantage of this method is the production of inhibitory compounds (acetic acid, furfural, 5-hydroxymethylfurfural (HMF)) that could hamper the fermentability of the produced hydrolysate. This hydrolysis method has also been employed for sugar release from DRB. In the study of Chandel et al. [37], DRB was subjected to acid hydrolysis at 120 °C for 1 h. Among the different H<sub>2</sub>SO<sub>4</sub> concentrations tested (0.5%–5.5%), the highest total sugar concentration (38.5 g/L) was obtained when 3.5% (*v/v*) H<sub>2</sub>SO<sub>4</sub> was used. Tsigie et al. [38] used acid hydrolysis with H<sub>2</sub>SO<sub>4</sub> for the release of fermentable sugars from DRB. The authors studied the effect of different acid concentrations (1%, 2%, 3%, 4%) and different temperatures (60, 70, 80, 90, 100, and 120 °C) for various hydrolysis times (1–8 h). The results indicated that highest sugar release was achieved when 3% H<sub>2</sub>SO<sub>4</sub> was utilized at 90 °C for 6 h. The hydrolysate contained 43.2 g/L glucose, 4.93 g/L xylose and 2.09 g/L arabinose. Due to the generation of inhibitory compounds (furfural and HMF), detoxification was necessary in order to avoid low product yields during fermentation. Overliming with Ca(OH)<sub>2</sub> led to a reduction of 25% in the concentration of furfural and 24% of the HMF content. Similar conditions were followed in the study of Sutanto et al. [39], in which acid hydrolysis of DRB led to the production of a hydrolysate containing 49.5 g/L reducing sugars and approximately 2.3% furans. Detoxification with overliming resulted in a decrease in the concentration of HMF. Lower H<sub>2</sub>SO<sub>4</sub> concentration (1%) but higher temperature (121 °C) was followed by Al Shorgani et al. [40]. Filtration through activated charcoal was employed as detoxification technique, to reduce the concentration of furfural, HMF,



acetic acid, formic acid and levulinic acid. In another work from the same group, DRB was pretreated with acetyl chloride instead of sulphuric acid [41]. This method released 30.88 g/L fermentable sugars from DRB, however detoxification with activated charcoal was again necessary. A combination of dilute acid pretreatment with enzymatic hydrolysis has also been evaluated in the literature [42,43]. Another approach was proposed by Liu et al. [44], where thermal pretreatment at 120 °C—without addition of chemicals—was followed prior to enzymatic hydrolysis of DRB. The authors highlighted that the temperature and time of the thermal treatment were the important parameters to be optimized. Pretreatment at 120 °C for 1 h significantly improved the subsequent enzymatic hydrolysis’ yields when compared to thermal treatments at 60 and 90 °C. The highest total sugar concentration achieved in this study was 42.88 g/L, a value 8.5 times higher in comparison to untreated DRB. Increasing the time of the process to 1.5 h led to reduced yields, probably due to sugar degradation. Other studies have also shown that thermal treatment renders starch granules more susceptible to enzymatic hydrolysis [45–47].

**Table 2.** Pretreatment methods and enzymatic hydrolysis conditions of DRB.

Pretreatment and Hydrolysis Conditions	Sugars Produced (g/L)	Reference
Solid-to-liquid ratio 1:3.5 ( <i>w/w</i> ); 20 µL amylase/kg DRB Protein hydrolysis with 12% residue from starch hydrolysis; 40 mg protease/kg, 1:3 ( <i>w/w</i> ) solid-to-liquid ratio, 50 °C for 10 h	150.0	[28]
Starch and protein hydrolysis with 20% solids Liquefaction: 0.7 mL/kg Termamyl SC at 85 °C, 500 rpm for 2 h; Saccharification: 1 mL/kg Dextrozyme DX 1.5 and 0.5 mL/kg Fermgen, 50 °C for 19 h.	82.3	[17]
Enzymatic hydrolysis with α-amylase (30 µL/g DRB for 2 h), amyloglucosidase (40 µL/g DRB, for 3 h) and protease (15 µL/g DRB) at 200 g/L DRB concentration	68.8	[29]
Acid hydrolysis with 3% H <sub>2</sub> SO <sub>4</sub> , solid-to-liquid ratio 1:8 (g/mL), 90 °C, 6 h; detoxification by neutralization with Ca(OH) <sub>2</sub>	50.2	[38]
Solid-to-liquid ratio 15:120 (g/mL), 3% H <sub>2</sub> SO <sub>4</sub> at 90 °C for 6 h in a waterbath; detoxification with activated carbon or by overliming with Ca(OH) <sub>2</sub>	50.1	[39]
Dilute acid pretreatment with 100 g/L DRB, 3.5% H <sub>2</sub> SO <sub>4</sub> at 120 °C for 1 h and overliming	38.5	[37]
Dilute acid pretreatment with 1% ( <i>v/v</i> ) H <sub>2</sub> SO <sub>4</sub> at 121 °C for 1 h with 12% ( <i>w/v</i> ) DRB; detoxification with activated charcoal	40.2	[40]
Dilute H <sub>2</sub> SO <sub>4</sub> 1% ( <i>v/v</i> ), 121 °C, 15 psi, 1 h with 100 g/L DRB	32.9	[48]
1% ( <i>v/v</i> ) HCl at 80 °C for 3 h; enzymatic hydrolysis with α-amylase (500 µL, 30 °C for 4 h), β-amylase (15 mg) and amyloglucosidase (1 mL) at 37 °C for 4 h, 100 g/L DRB	40.0	[43]
Acid pretreatment with 1% ( <i>v/v</i> ) H <sub>2</sub> SO <sub>4</sub> at 121 °C for 1h using 100 g/L DRB; enzymatic hydrolysis with Celluclast 1.5 L, Novozyme 188, Termamyl 120 L; detoxification by overliming and Amberlite XAD-4 resin	33.4	[42]
Pretreatment with 1% acetyl chloride at 121 °C, 15 psi for 1 h with 10% ( <i>w/v</i> ) DRB; detoxification with charcoal	28.0	[41]
Thermal treatment at 120 °C for 1 h of 100 g/L DRB; enzymatic hydrolysis for 5 h with cellulase (30 FPU/g), xylanase (100 XU/g) and glucoamylase (250 IU/g)	45.6	[44]
Thermal treatment at 135 °C for 5 h with ethanol at pH 8	-	[49]
Microwave treatment at 400 W for 2 min; heating at 100 °C for 20 min at a solid-to-liquid ratio 1:10 ( <i>w/v</i> ); enzymatic hydrolysis with α-amylase (30 U/mL) and glucose-amylase (200 U/mL) at 60 °C for 4 h	0.95 *	[50]

\* g/100 g.

Enzymatic hydrolysis is considered a ‘green’ method, in comparison to thermal and/or chemical pretreatment, since no harmful chemicals are utilized and important amino acids and the vitamins present in DRB are not degraded or damaged [28]. Wang et al. [28] employed enzymatic hydrolysis in

order to produce a hydrolysate rich in glucose and amino acids that would completely support the growth of the lactic acid producing strain *Lactobacillus rhamnosus*. In their study, the authors initially carried out hydrolysis with amylase and glucoamylase for starch degradation. After centrifugation, the supernatant contained almost 150 g/L glucose. The residue from starch hydrolysis was subsequently treated with proteases to produce an amino acid-rich hydrolysate. Analysis of the individual amino acids present in the concentrated rice bran protein hydrolysate (CRBPH) revealed that it could completely substitute yeast extract since 10 g/L CRBPH contained 3014.43 µg/L of amino acids, whereas 15 g/L yeast extract contained 2514.98 µg/L. The complete exploitation as both a carbon and a nitrogen source was also attempted in the study of Alexandri et al. [17]. The authors also targeted starch and protein hydrolysis for the production of a nutrient-rich hydrolysate. Starch hydrolysis occurred in two steps, namely liquefaction and saccharification. During liquefaction, starch was broken into dextrans with the action of thermostable amylases (Table 2). Saccharification was followed by the addition of glucoamylases that further hydrolyse dextrans to glucose. At this step, proteases were also added in order to break down proteins into free amino acids. The total hydrolysis time required was 21 h, and under optimal conditions (20% solid loading), 82.3 g/L of glucose and 234.8 mg/L of free amino nitrogen (FAN) were produced.

### 3.1.2. Production of Bioethanol

Bioethanol is utilized extensively in countries like Brazil and the USA as an alternative fuel for transportation [51]. The worldwide fuel ethanol production reached 26,050 million gallons in 2017; an increase of almost 51% in the last 10 years [52]. For the year 2018, USA produced 16,100 million gallons of ethanol, whereas the corresponding production in Brazil accounted 7950 million gallons [53]. Bioethanol is almost exclusively produced via fermentation of starch or molasses using the yeast *Saccharomyces cerevisiae*, due to its ability to produce high amounts of ethanol [54]. Sucrose from sugarcane and corn starch are the main feedstocks utilized for bioethanol production in Brazil and the USA, respectively [55]. Different renewable feedstocks, such as sorghum juice and bagasse, corn stover and cob, wheat straw and fruit peels have been tested so far for bioethanol production, as alternatives to edible crops [55,56].

Rice by-products, like rice washing drainage, rice bran, and DRB, have been investigated as interesting alternatives for bioethanol production [54,57]. Utilization of DRB as a carbon source required, in most cases, a pretreatment step, for the release of monosaccharides, which could be easily assimilated by the fermenting microorganisms, as already discussed previously. A concentration of 12.47 g/L ethanol was produced by the strain *Pichia stipitis* NCIM3499, after dilute acid pretreatment of DRB and detoxification [37]. The bioethanol yield had a value of 0.42 g/g and productivity of 0.173 g/L/h. Biological pretreatment with the fungus *Aspergillus niger* increased the ethanol production by *P. kudriavzevii* RCEF4907 in the study of Beliya et al. [58]. Under optimum conditions of temperature (25 °C), pH (6.5) and nutrients (addition of 1% Urea), the strain was able to produce 11.4% ethanol.

A final ethanol concentration of 35.5 g/L (productivity of 1.5 g/L/h) was achieved by *S. cerevisiae* grown on enzymatically treated DRB [29]. The conditions of starch enzymatic hydrolysis were optimized in terms of DRB concentration as well as  $\alpha$ -amylase and amyloglucosidase concentrations (Table 2). The addition of protease before the amylases enhanced the final bioethanol concentration.

### 3.1.3. Production of Lactic Acid

Refined sugars and starch-rich feedstocks are widely used for commercial lactic acid (LA) production. LA has been extensively used in food, cosmetics, pharmaceutical, and chemical industries. Its application for the production of poly-lactic acid (PLA)—a promising alternative to petroleum-based plastics—has boosted its global market [59]. In 2016, the demand for lactic acid amounted to 1220.0 kilotonnes and it was forecasted to reach 1960.1 kilotonnes by 2020 [60]. Together with lactic acid, the PLA market is also growing and expected to reach USD 6.5 billion by 2025 [60]. The price of lactic acid is highly dependent on its application and ranges from \$1.30 to \$2.30 per kg [60]. Fermentation

feedstock comprises a significant part of the overall lactic acid production costs. The utilization of renewable feedstocks is nowadays the most promising alternative for the reduction in costs of many biotechnological products, including LA. Companies like Galactic and NatureWorks have already included agricultural and food wastes in their production line [61]. Among the different renewable feedstocks proposed in the literature for LA production, such as municipal solid wastes [62], coffee byproducts [35,36] and food wastes [63–65], many researchers have also attempted to produce LA from DRB using various microbial strains.

Various *Bacillus coagulans* isolates were able to grow in DRB enzymatic hydrolysates (Table 2) without additional nutrients, with most of them producing final concentrations of LA higher than 65 g/L and yields over 0.85 g/g. Isolates A203 and A107 demonstrated the most promising results. More specifically, strain A107 produced 66.3 g/L of optically pure (99.9%) LA with a yield of total sugars of 0.94 g/g and productivity equal to 2.82 g/L/h. Isolate A203 performed slightly better in terms of LA productivity (2.97 g/L/h), but the obtained yield was lower in comparison to strain A107 (0.88 g/g). Considering that the majority of the strains converted the sugars from the hydrolysate at a yield higher than 70%, DRB could be utilized as a complete substrate for LA fermentation [17].

Two-stage immobilized continuous fermentation was used to maximize the final concentration of L-LA as well as to minimize the residual carbon source concentration. *L. rhamnosus* cells were immobilised on corn stover bagasse, in order to achieve high cell densities and cell viability during the continuous fermentation. Operating under  $0.1 \text{ h}^{-1}$  dilution rate, the L-LA concentration and yield reached their peak values (86 g/L and 0.98 g/g, respectively), with productivities of 6.20 g/L/h in the first stage and 2.18 g/L/h in the second stage [66]. Wang et al. performed fermentations after enzymatic hydrolysis, using supernatant of DRB (DRBSA) together with rice bran protein hydrolysate (CRBPH) as a medium supplement in batch as well as in fed-batch fermentations [28]. The combination of DRBSA and CRBPH resulted in 142 g/L LA concentration, with a productivity of 3.63 g/L/h, similar values to the ones obtained with a yeast extract-based medium (145 g/L and 3.74 g/L/h). A final LA concentration of 210 g/L was achieved in a fed-batch fermentation, in which concentrated DRBSA was added in the bioreactor at a specific fermentation time. The authors concluded that DRB could serve as both carbon and nitrogen source for LA production.

Taniguchi et al. tested the indigenous microorganisms found in DRB for LA production via simultaneous saccharification and fermentation (SSF), under non-sterile conditions [67]. The use of indigenous bacteria would permit the fermentation under non-sterile conditions and lower pH values. Saccharification was carried out using amylase and cellulase at concentrations of 6.7 and 3.3 g/m<sup>3</sup>, respectively. Among the 21 screened strains, two of them were able to produce highly optical pure L-LA, at concentrations ranging from 27 to 29 g/L from 100 g/L DRB, with de Man, Rogosa and Sharpe (MRS) medium at pH 4.5. Replacement of MRS to McIlvaine buffer suppressed the growth of indigenous bacteria and led to 28 g/L LA production from strain No. 16, identified as *L. rhamnosus*. When an elevated initial cell concentration was used as inoculum, the final L-LA optical purity was 95%. The authors also observed that the protein fraction present in DRB favored LA production.

An SSF strategy was also followed for the production of D-LA from DRB by the strain *L. delbrueckii* subsp. *delbrueckii* [30]. A mixture of amylase and cellulase was added prior to fermentation for the production of fermentable sugars. Fermentation at pH 5 suppressed the growth of indigenous LA bacteria that produced racemic mixtures of LA. Under these conditions, 28 g/L D-LA with an optical purity of 95% was achieved from 100 g/L DRB.

The studies of Alexandri et al. and Wang et al. conducted preliminary cost analysis, showing that LA production from DRB could be profitable [17,28]. From these two studies, LA fermentation and hydrolysis costs were USD 0.684/Kg and USD 0.832/Kg for Wang et al. and Alexandri et al., respectively. In both studies, DRB was the main cost contributor with an average price of USD 0.525/kg. However, following the results of Wang et al., LA production from DRB is still more profitable in comparison to corn starch fermentations supplemented with yeast extract or corn steep liquor, by 57.72% and 64%, respectively.



### 3.1.4. Production of Biobutanol

Biobutanol is another environmentally friendly alternative to conventional fuels since it has similar properties to gasoline [40]. Butanol presents many advantages over ethanol, mainly due to its lower miscibility in water and its higher energy content. Thus, butanol can be mixed with gasoline at a higher ratio in comparison to ethanol [43]. The biotechnological production of butanol is based on acetone-butanol-ethanol (ABE) fermentation, catalysed by solventogenic *Clostridium* species [40]. *C. saccharoperbutylacetikum* and *C. saccharoacetobutylicum* have shown great ability in producing bio-butanol in high yields [68]. Agricultural residues such as corn fibre, wheat, barley and rice straw, among others, have been already investigated as potential feedstocks for biobutanol fermentation [51].

Lee et al. were the first to test RB and DRB for butanol fermentation with the strain *C. beijerinckii* NCIMB 8052 [43]. Combined treatment with HCl and enzymes (Table 2) led to sugar release of 41.18 g/L from DRB and 36.2 g/L from RB. In bioreactor fermentations supplemented with nutrients (Table 2), the strain was able to produce 12.24 g/L butanol from DRB hydrolysates and 11.4 g/L butanol from RB hydrolysates. The authors noticed that the strain performed slightly better in DRB hydrolysates and it was also able to grow and produce butanol without any additional supplements. Similar observations were also carried out by Al-Shorgani et al. [42], who also highlighted the influence of the type of pretreatment on ABE and butanol fermentation. Treatment with dilute H<sub>2</sub>SO<sub>4</sub> was proven to be more suitable in comparison to HCl. When combined with enzymatic treatment (Table 2), the strain *C. saccharoperbutylacetonicum* N1-4 produced 7.1 g/L of biobutanol. Detoxification of the hydrolysate with overliming and the non-ionic polymeric resin Amberlite XAD-4 led to a slight increase in final butanol concentration, yield, and productivity (Table 2). The corresponding fermentations with RB led to lower performance (Table 2). A possible explanation proposed by the authors was that the oil content of RB could interfere with the sugar uptake.

In another study by Al-Shorgani et al. [41], acetyl-chloride was evaluated for the pretreatment of DRB prior to fermentation with *C. acetobutylicum* YM1 (Table 2). The proposed method resulted in similar sugar concentrations (30.88 g/L) to the one using H<sub>2</sub>SO<sub>4</sub> (33.5 g/L). Moreover, detoxification with charcoal instead of the resin XAD-4 led to almost 13% higher butanol production (Table 2).

DRB hydrolysates have also been tested in continuous fermentations for ABE production [40]. Pretreatment with dilute H<sub>2</sub>SO<sub>4</sub> was selected for the production of sugar-rich hydrolysates, followed by detoxification with activated carbon. Among the various dilution rates tested (0.01, 0.02, 0.03 and 0.5 h<sup>-1</sup>), 0.02 h<sup>-1</sup> was proven to be adequate for biobutanol production. Economic analysis based on this process and recovery of all products (acetone, butanol, ethanol) via distillation, revealed an estimated cost of butanol production of USD 1.405/kg, considering a price of DRB of USD 50/MT. However, no reference was provided within the text for the DRB cost and the value is lower than in the aforementioned articles [17,28].

### 3.1.5. Production of Bio-Hydrogen

Another alternative to fossil fuels is hydrogen since its burning results only in H<sub>2</sub>O production [69,70]. Another advantage of hydrogen in comparison to fossil fuels is its higher energy content, which presents an estimated value of 112–142 kJ/g, being 2.75-fold higher than conventional fuels [48]. Biotechnological production of bio-hydrogen can be achieved through photo-fermentation, dark fermentation or hybrid processes [71]. Dark fermentation is the most commonly used process for bio-hydrogen production, in which heterotrophic microorganisms are cultivated on carbohydrate-rich substrates under anaerobic conditions and in the absence of light [48]. Bacterial strains belonging to the genera *Enterobacter*, *Bacillus*, *Citrobacter* and *Clostridium* have been mainly studied for hydrogen production in dark fermentation [72]. The use of agro-industrial wastes in dark fermentation has been proven an efficient process due to the high productivities achieved on a wide range of feedstocks [73]. Rice by-products have also been tested for bio-hydrogen production, but the studies dealing with DRB utilization are scarce.

Tandon et al. isolated bacteria from RB and DRB for hydrogen production using the same substrates [74]. The most promising strain was identified as *E. ludwigii* IF2SW-B4. The highest bio-hydrogen production (545 mL/L) was observed when RB was used as substrate, a value almost two-fold greater in comparison to DRB. The strain *C. acetobutylicum* was investigated in the work of Azman et al. for the production of bio-hydrogen from DRB. Prior to fermentation, DRB was pretreated with dilute H<sub>2</sub>SO<sub>4</sub>, resulting in the release of both glucose (29.3 g/L) and xylose (3.55 g/L) [48]. Then, the authors utilized response surface methodology (RSM) in order to determine the optimum fermentation conditions. An incubation temperature of 35.2 °C, pH of 5.5 and inoculum concentration of 11.6% were the best-operating conditions revealed by the model. Under the optimum conditions, 572.5 mL cumulative H<sub>2</sub> production was achieved, a value close to the one defined by the model (574.7 mL).

### 3.1.6. Production of Enzymes

Enzymatic hydrolysis is considered an efficient and eco-friendly process for the release of fermentable sugars from different renewable feedstocks as it is already shown in the previous sections. Enzyme production using cheap substrates would favour the overall cost of the biotechnological processes.

There are some reports in the literature covering the production of enzymes from DRB, mostly utilizing solid-state fermentation (SF) systems. The production of amyloglucosidase, an enzyme mainly used for the saccharification of starch in the food and fermentation industries, by *Aspergillus niger* NRRL 3122 was reported by Manera et al. [75]. In their study, DRB supplemented with urea was added to rice straw (which worked as a solid support) and an SF was carried out. The resulting enzyme mixture was used in further studies targeting the separation of amyloglucosidase from the mixture using ion exchange resins. Although their study did not focus on the optimization of parameters to produce the enzyme, the selection of DRB as a substrate suggests that it could be a good carbon source for the production of amyloglucosidase. Optimization of the co-production of various carbohydrases from steam pretreated DRB with the strain *A. niger* P-19 was also the focus of the study from Chugh et al. [76].

In another study, the simultaneous production of amyloglucosidase and exo-polygalacturonase in a solid-state fermentation was reported [77]. In that case, *A. niger* NRRL 3122 and *A. niger* t0005/007-2 were used to ferment DRB in a rotating drum bioreactor at pilot scale. The authors concluded that the production of each enzyme was heavily influenced by the strain used. The maximum enzymatic activity obtained for amyloglucosidase was 886.25 U, and 84 U for exo-polygalacturonase per gram of dried medium.

The simultaneous production of pectinases (polygalacturonase and polymethylgalacturonase) in SF was also implemented in a bed column bioreactor [78]. In that case, DRB was used as the carbon source for the growth of *A. niger* and *A. oryzae*. The study focused on the determination of the most influential parameters for pectinase production. They concluded that microorganism, aeration, and initial pectin content were the most important parameters affecting the production of enzymes with better performance by *A. niger*.

Finally, DRB was used for the production of phytase, this time in submerged fermentations, by *A. niger* NCIM 563 [79]. They demonstrated that a pre-treatment of the substrate, to remove inorganic phosphate, resulted in a seven-fold enhancement (from 7 U/mL to 48 U/mL) of the enzymatic activity.

### 3.1.7. Production of Other Biotechnological Products

In addition to the previously described products, which cover most of the investigation for the biotechnological conversion of DRB, other value-added chemicals have also been studied, though, in a lesser extent.

Another alternative that has been investigated is the protein enrichment of the DRB by the fermentation of the material using filamentous fungi. In another study [80], the fungi *A. niger* MTCC 1842, *A. oryzae* MTCC 1846 and *Trichoderma viride* NRRL 1186 were used in SF of the DRB. Protein content increased by around 13% in all the cases evaluated with the best performance in terms of growth rate for *A. oryzae*. The fungus *Rhizopus oryzae* was used in SF targeting the enhancement of

protein digestibility of the DRB [81]. A positive effect on the n-6 fatty acid profile (increment by 6.19%) and a significant reduction in phytate and trypsin content were observed. However, the in vitro protein digestibility was decreased, indicating that the microorganism was not suitable for the process.

Acid-pretreated DRB has been employed as fermentation substrate for microbial oil production with the strain *Y. lipolytica*, resulting in about 3.8 g/L lipid titers [38,39]. The effective production of nisin- an antimicrobial peptide- from DRB enzymatic hydrolysates was presented from Liu et al., using a genetically engineered *L. lactis* strain [44]. The authors reported a final nisin titer of 3824.53 IU/mL, a value 1.37 times higher of the one obtained from sucrose medium.

Ferulic acid, a phenolic compound with antioxidant and anti-inflammatory properties, has been also the targeted product using DRB as substrate. Uraji et al. evaluated the enzymatic production of ferulic acid using different commercial enzymes [82]. They concluded that the most efficient cocktail was Cellulosin HC100 which contains  $\alpha$ -L-arabinofuranosidase, multiple xylanases, and an acetyl xylan esterase. Ferulic acid obtained from DRB can also be converted to vanillin, which is a commonly used compound in the food industry [49]. Fermentation of DRB with *B. subtilis* subsp. *subtilis* aided the release of the bound phenolic compounds to cell walls of DRB, resulting in a higher phenolic release [83]. The produced phenolic extract exhibited also a higher antioxidant activity in comparison to the unfermented DRB extracts.

Gamma-amino butyric acid (GABA) is another example of an organic acid which can be obtained from DRB. In their report, Tuan et al. [84] used lactic acid bacteria for the production of this acid. As the authors described, one of the main problems in the case of GABA production from DRB was the low purity and concentration in the fermentation broth. Thus, they investigated the application of cation exchange resins (Purolite C100). After purification optimization, they achieved a concentration of 743.8 ppm, a purity of 44.0% and a yield of 84.2%.

Finally, the production of xanthan gum from DRB by fermentation has also been investigated. After enzymatic hydrolysis, *Xanthomonas campestris* NRRL B-1459 and *X.campestris* pv. *campestris* were used for the fermentations resulting in productivities of 21.87 and 17.10 g/L, respectively [85].

### 3.2. Use of Defatted Rice Bran in Foodstuffs

The addition of DRB as a supplement in various foodstuffs, such as bread, cakes and other baked goods has been evaluated, mainly for the increment of the dietary fibre content or for improving their sensory characteristics or health benefits. In the study of Yadav et al., wheat flour was enriched with DRB for the preparation of chapati, a baked product highly popular in India [31]. The addition of 20% fine DRB in wheat flour led to a final product with higher ash and dietary fibre content, presenting also acceptable organoleptic properties. An increase in both dietary fibre content and antioxidant activity of bread supplemented with 10% DRB was observed by Sairam et al [22]. The resulting bread also presented longer shelf life. In the recent publication of Prestes et al., DRB was added in craft, rice beers for the improvement of both nitrogen content and sensory properties of the final product [86]. Higher nitrogen and flavonoid content was achieved, as well as increased concentration of  $\gamma$ -aminobutyric acid, which is considered beneficial to human health. DRB also contributed in foam formation and colour, resulting in a full-bodied beer.

DRB-derived proteins have also been evaluated as functional ingredients. Foong et al. investigated the iron-binding capacity of DRB peptides for the improvement of iron uptake from the human body [87]. The authors conducted enzymatic hydrolysis with commercial protease-rich preparations (Alcalase and Flavourzyme) and then tested the bioavailability in vitro using a digestion and absorption model (Caco-2 cells). Their results corroborate the high potential of DRB protein hydrolysates as iron-fortified supplements.

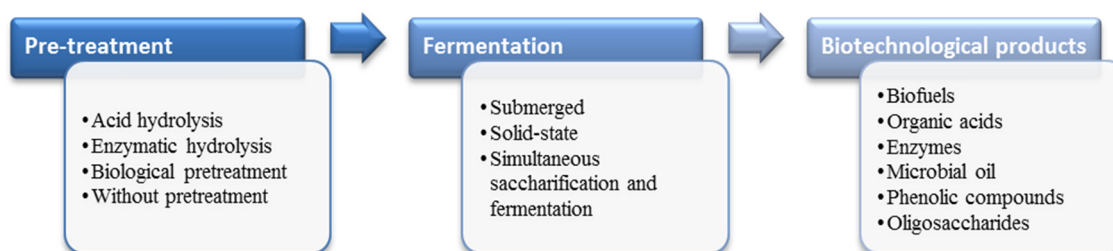
The oligosaccharides present in DRB could also serve as additives for functional food preparations according to the studies of Kurdi and Hansawasdi [88] and Liu et al [50]. Mixtures of oligosaccharides, mainly containing glucose, galactose and mannose, were initially produced via acidic hydrolysis. These oligosaccharides were able to support the growth or probiotic bacteria such as *Lactobacillus* sp. and

*Bifidobacterium* sp. Liu et al. utilized the fungus *Grifola frondosa* in order to modify rich in polysaccharides DRB water extracts [50]. The fermented extracts exhibited higher antioxidant activity and the decrease in molecular weight indicated that the extracts contained both polysaccharides and oligosaccharides, but no monosaccharides. Water unextractable arabinoxylans (WUAX) were also proven to possess antioxidant activities, not only because they were bound to phenolic compounds, but also because of their molecular structure [23]. Ethanol extracts of WUAX were rich in hydroxybenzoic acids and hydroxycinnamic acids. Ferulic acid was the major bound phenolic compound, followed by *p*-coumaric.

#### 4. Discussion and Future Prospects

The increasing interest towards bioeconomy and sustainability has directed research into developing bioprocesses based on renewable substrates and the efficient management of waste and by-product streams. This search has been encouraged by the creation of new legislations and policies. It is evident that governments have realised that without an effective exploitation of the substrates, which encompasses a complete utilisation of the wastes generated, the chances of success are reduced. Therefore, the criteria to evaluate bioprocesses have become more demanding and currently, a truly sustainable process must incorporate waste management.

A suitable example is the DRB, which has experienced an increase in production due to the exploitation of rice bran oil. As in many other cases with organic residues, the chemical composition of DRB makes it a substrate of interest for biotechnological processes (Figure 4). Pretreatment methods are, in most cases, necessary for the release of sugars when DRB is used as the carbon source in fermentation processes. Such pre-treatment can be chemical or biological by the action of enzymes either obtained commercially or produced in-situ.



**Figure 4.** Conversion steps of DRB into biotechnological products.

Fermentation studies have been developed for the bioconversion of DRB mainly into bioethanol, biobutanol, bio-hydrogen and lactic acid with relative success. The formation of each product (stated in Table 3), with respect to conditions used, required different amounts of DRB ranging from 1% to 25% *w/v*. In particular, high productivities of LA have been achieved with fed-batch and continuous fermentation by *Bacillus* and *Lactobacillus* strains, with preliminary economic evaluation placing DRB as a more competitive substrate than commercial substrates. As shown in Table 3, LA production yield from DRB can range from 30% to 50%. Additionally, the production of enzymes from DRB has also been investigated, mainly in SF fermentations involving filamentous fungi. Amongst them, amyloglucosidase, used in the hydrolysis of starch, is the more investigated enzyme. In 2019, the global enzymes market accounted for USD 9.9 billion and is estimated to increase at a CAGR of 7.1% between 2020 and 2027 [89]. Enzymes are a profitable market presenting an interesting valorisation approach for DRB, after process optimisation and cost analysis. Production of microbial oil, ferulic acid, GABA and xanthan gum has also been explored in the literature, but in a lesser extent.

**Table 3.** Production of various biotechnological products from DRB.

Product	Strain	Conditions	Titer (g/L)	Yield (g <sub>P</sub> /g <sub>DRB</sub> )	P (g/L/h)	Ref.
Bioethanol	<i>P. stipitis</i> NCIM3499	Batch	12.47	0.12	0.173	[37]
	<i>P. kudriavzevii</i> RCEF4907	Batch	11.4 <sup>a</sup>	-	1.58	[58]
	<i>S. cerevisiae</i>	Batch	35.5	0.18	1.5	[29]
L-Lactic acid	<i>B. coagulans</i>	Batch	66.3	0.33	2.82	[17]
	<i>B. coagulans</i>	Batch	71.2	0.35	2.97	
	<i>L. rhamnosus</i>	Single-stage continuous	88	-	5.2	[66]
		Two-stage continuous	86	-	6.20/2.18	
	<i>L. rhamnosus</i> LA-04-1	Batch	142	0.50	3.63	[28]
	Different LAB isolates	fed-batch	21	-	2.56	
		SSF	31.1	0.31	-	[67]
D-Lactic acid	<i>L. delbrueckii</i> subsp. <i>delbrueckii</i>	SSF	28	0.28	0.78	[30]
Biobutanol	<i>C. beijerinckii</i> NCIMB	Batch	12.24	0.12	0.26	[43]
	<i>C. saccharoperbutylacetium</i> N1-4	Batch	7.1	0.07	0.059	[42]
		Duran bottles	7.22	0.08	0.060	
		Batch	6.48	-	0.09	[41]
	<i>C. acetobutylicum</i> YM1	Batch (supplemented with TYA <sup>b</sup> )	5.64	-	0.08	
		Continuous	5.89	-	0.118	[40]
			6.87	-	0.136	
Bio-hydrogen	<i>E. ludwigii</i> IF2SW-B4	Batch	295 <sup>c</sup>	-	1.82 <sup>e</sup>	[74]
	<i>C. acetobutylicum</i> YM1	Batch (Supplemented with TYA)	572.5 <sup>d</sup>	-	-	[48]
Amyloglucosidase	<i>A. niger</i> NRRL 3122	SF (supplemented with urea)	-	-	-	[75]
	<i>A. niger</i> NRRL 3122 and t0005/007-2	SF, rotating drum, pilot scale	Enzyme activity of 84 U per gram of dried medium	-	-	[77]
Exo-polygalacturonase	<i>A. niger</i> NRRL 3122 and t0005/007-2	SF, rotating drum, pilot scale	Enzyme activity of 84 U per gram of dried medium	-	-	[77]
Xantan gum	<i>X. campestris</i> NRRL B-1459	Batch	21.87	0.43	-	[85]
	<i>X. campestris</i> pv. <i>campestris</i>		17.10	0.34	-	
Nisin	Engineered <i>L. lactis</i>	Batch	3824.53 IU/mL	-	-	[44]
Vanillin	<i>A. niger</i> and <i>P. cinnabarinus</i>	Batch	2.8	-	-	[49]
Microbial oil	<i>Y. lipolytica</i>	Batch	5.16	0.04	-	[38]
			3.80	0.03	1.52 g/L/day	[39]
Phenolic-rich extracts	<i>B. subtilis</i> subsp. <i>subtilis</i>	Batch	67.64 mg/100g fermented extract	0.68 <sup>f</sup>	-	[83]

<sup>a</sup> result expressed in %; <sup>b</sup> TYA—tryptone-yeast extract-acetate medium; <sup>c</sup> mL/L; <sup>d</sup> mL; <sup>e</sup> mL/g substrate/h (3rd day); 1.02 mL/g/h (6th day); <sup>f</sup> mg/g.



Since DRB production is following the increasing demand for rice bran oil, the number of investigations targeting the biotechnological conversion of DRB will also continue growing. However, it is not clear at this point which product would be the most profitable, and thus further efforts are necessary in order to enhance the overall value of the current processes and also to develop new methods and to test new processes for the bioconversion of DRB. On top of that, techno-economic analysis coupled with life cycle analysis should be also carried out for the proposed products. Gathering all this information would lead to safer analysis on which biotechnological route is more suitable for the effective utilisation of DRB.

## 5. Conclusions

The present review demonstrated the recent advances in the biological conversion of DRB into value-added products and biofuels. The abundance of this by-product stream will definitely lead to more intensive works, which would attempt to provide a more holistic approach for its valorisation. Strategies targeting the production of more than one product from DRB would be a possible suggestion for further investigation. Nevertheless, the successful implementation of the circular bioeconomy concept relies not only on technology development, but also on an adequate policy framework in which by-product streams like DBR can be fully exploited in these new applications. The existence of 224 bio-based industries operating using difference feedstocks (including biowastes, lignocellulosic biomass and waste oils/fats) is indicative of the slow yet steady transition to the bioeconomy [90]. The cascade utilisation of more byproduct streams is sure to follow as the technological maturity approaches. Furthermore, policy frameworks and incentive schemes should coordinate with researchers and create relations with the respective private sectors. As highlighted by D'Amato et al. [91], the new policies will need to target more integrated solutions for an increased effectiveness to attain the appointed sustainability goals.

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