

Review

Advances in Agroindustrial Waste as a Substrate for Obtaining Eco-Friendly Microbial Products

Álvaro Astudillo ¹, Olga Rubilar ^{2,3}, Gabriela Briceño ³, María Cristina Diez ^{2,3} and Heidi Schälchli ^{3,*}

¹ Doctoral Program in Sciences of Natural Resources, University of La Frontera, Temuco 4780000, Chile

² Chemical Engineering Department, University of La Frontera, Av. Francisco Salazar 01145, Temuco 4780000, Chile

³ Biotechnological Research Center Applied to the Environment (CIBAMA-BIOREN), University of La Frontera, Av. Francisco Salazar 01145, Temuco 4780000, Chile

* Correspondence: heidi.schalchli@ufrontera.cl

Abstract: Recycled agroindustrial waste has been of great interest during the last decade as a low-cost and sustainable substrate for fermentation processes. The types of products, yields, and potential applications depend mainly on the waste composition, which varies in terms of proteins, carbohydrates, and/or polyphenolic compounds. The most commonly reported microbial products are enzymes, pigments, biosurfactants, antibiotics, and phenolic compounds for different industrial applications. Advances in research on novel wastes as nutrient sources and the optimization of fermentation processes can help these materials transition from laboratory applications to an industrial level. This review explores reports published in the last five years (2017–2022) on different types of agroindustrial waste and their utilization in the production of useful microbial products. The present scenario and future scope of agroindustrial waste as substrates for submerged and solid-state fermentation processes are also discussed. The information was analyzed considering two main topics: (i) agroindustrial waste as substrates for fermentation processes and (ii) high-added value products obtained by microbial conversion. This review contributes to future research endeavors to discover the key factors that will allow us to reach the market with sustainable microbial products.

Keywords: agroindustrial waste; sustainability; microbial products; biotechnologies



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1. Introduction

Annually, a large amount of waste is generated by the agricultural and food sectors. Some of this waste is used as soil fertilizer or animal feed, while some needs to be treated to avoid environmental problems [1]. FAO [2] estimated that one-third of the food produced for human consumption is lost or wasted, which is equivalent to approximately 1600 million tons per year. In Europe, up to 37 million tons of agroindustrial waste is produced from the food and beverage industry [3]. This situation becomes critical if we consider that agroindustrial waste increases with an increase in human population, which is estimated to increase by 9.3 billion people by 2050 [4]. The literature has shown that most of the waste is rich in nutrients and chemical compounds that can serve as raw materials to obtain various products with high added value through microbial fermentation. Today, the industry appears to be interested but, in many cases, remains fearful of implementing bioprocesses that depend on agroindustrial waste. Despite the above reservations, some companies have made significant investments to build bioproduct production plants from agroindustrial waste, e.g., Raízen S.A. in Brazil and Praj Industries Ltd. in India, who produce 2G ethanol from cane bagasse and rice cane, respectively [5,6]. The latter is already established and will begin to produce 2G ethanol commercially at the end of 2022.

In the last decade, numerous studies have reported on the recycling of agroindustrial waste of various types and origins to obtain useful bioproducts [7–10]. The trend towards the use of less expensive and eco-friendly processes for the production of value-added

products has encouraged research to optimize production and make it profitable at the industrial level. This work aims to review the recent literature, published in the last five years (2017–2022), related to recycling agroindustrial waste as a substrate to produce useful microbial products. Exceptions were made for key articles that were considered of major interest for readers but were outside the established period. Recent advancements in the optimization of fermentation processes are also discussed in this work.

2. Agroindustrial Waste: A Valuable Substrate for Fermentation Processes

Agroindustrial waste can be divided into field and process wastes. Field waste correspond to that generated during the harvesting process (e.g., leaves, stalks, seed pods, and stems), while process waste is generated after the processing of the harvested crop (e.g., molasses, bagasses, and roots) [11]. Of these, the amounts of industrial waste are generally higher than crop waste. For example, Brazil produced 1.5 million tons of açai (*Euterpe oleracea*) in 2018, which is one of the most important crops in the Amazonian region, with an approximate income of USD 1 billion. Of the total production, it is estimated that waste associated with the processing of this fruit corresponds to 85%, with the largest commercial product extracted being the pulp [12]. Sugarcane represents the largest primary crop processed, and together with sugar beet there is a 3.6% production of molasses in the sugar manufacturing process [13]. The reported data indicate that this waste is generated during the harvesting and processing of food, but there are losses throughout the food supply chain that correspond to 30% of all food suitable for human consumption. Of these amounts, 11% to 30% are lost in the harvest and postharvest stages [14].

Numerous agroindustrial wastes are composed of complexes of polysaccharides and proteins, carbohydrates, and polyphenolic constituents, among others [15]. Therefore, it is possible to use these wastes as sustainable and low-cost sources of nutrients for obtaining value-added products through fermentation processes, thus generating mass and energy balances derived from cultivation, extraction, processing, and disposal [12]. The availability and low-cost of agroindustrial waste are key factors in the cost-effective production of microbial products, since the nutritional components of a culture medium represent between 38% and 72% of the total production cost [16]. Along with reducing production costs, the use of agro-industrial residues as raw material can encourage innovation in agribusiness [17].

The composition of agroindustrial waste varies according to its origin, but such waste mainly presents complex carbohydrates and proteins, so it is possible to use it as a food carrier for microorganisms [18]. Table 1 details the composition of different types of agroindustrial waste.

Although different compounds can be extracted directly from agroindustrial waste, the reuse and transformation of this nutrient-rich waste through fermentation processes opens a range of possibilities to obtain useful and novel microbial products. In general, the transformation of agroindustrial waste into bioproducts by microorganisms can be achieved through submerged fermentation (SmF) or solid-state fermentation (SSF), which largely depend on the type of waste and the producing microorganism [19]. For example, an increase in bioproducts obtained by fermentation processes (e.g., phenolic compounds) can be increased ~13 fold compared to unfermented waste through SSF [20]. On the other hand, SmF is considered an interesting solution to treat liquid waste such as olive-oil mill wastewater and, at the same time, obtain enzymes and compounds with anti-tyrosinase activities via *Pleurotus citrinopileatus* [21].

Thus, the metabolic activity and great versatility of microorganisms offer more inexpensive and environmentally friendly strategies to produce valuable bioactive microbial compounds and achieve bioremediation.

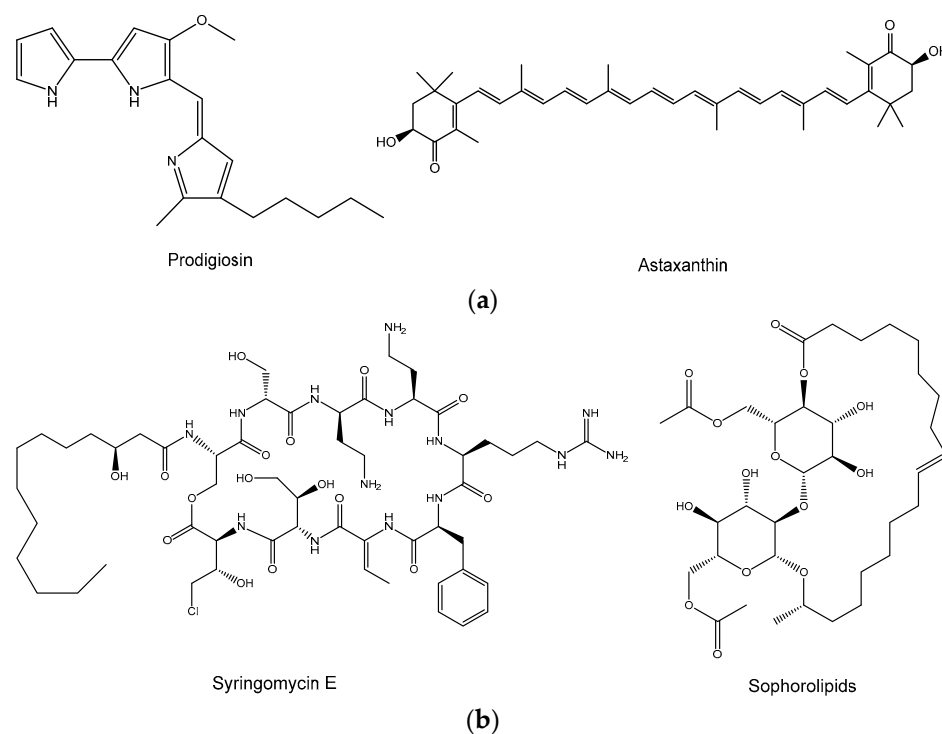
Table 1. Components of agroindustrial waste used to obtain bioactive compounds.

Waste	MC	Cel	Hem	Lig	CH	Pro	Phe	RS	Reference
Banana leaf	-	55 ^a	20 ^a	25 ^a	-	-	-	-	[22]
Bean Husk	-	-	-	-	-	262 ^c	-	327 ^c	[23]
Brewer's spent grain	64 ^b	210 ^b	243 ^b	144 ^b	-	-	0.55 ^b	47.4 ^b	[20]
Coffee husk	91 ^a	-	-	-	14 ^a	14 ^a	1 ^d	14 ^a	[24]
Coffee pulp	12 ^a	33 ^a	29 ^a	26 ^a	-	11 ^a	-	97 ^c	[25]
Grape marc	-	14 ^a	10 ^a	67 ^a	-	14 ^a	0.22 ^a	0.4 ^a	[26]
Grape stalk	570 ^b	288 ^b	133 ^b	435 ^b	-	-	4.4 ^b	57 ^b	[20]
Mango seed	40 ^a	3 ^a	14 ^a	2 ^a	82 ^a	7 ^a	-	14 ^c	[27]
Olive pomace	-	13 ^a	30 ^a	55 ^a	-	6 ^a	0.7 ^a	3 ^a	[26]
Pea pods	-	-	-	-	-	414 ^c	-	144 ^c	[23]
Peanut cake	9 ^a	-	-	-	-	44 ^a	-	-	[9]
Potato skin	-	-	-	-	-	165 ^c	-	845 ^c	[23]
Sorghum waste	7 ^a	2 ^a	82 ^a	12 ^a	-	13 ^a	-	56 ^c	[25]

MC = Moisture Content; Cel = Cellulose; Hem = Hemicellulose; Lig = Lignin; CH = Carbohydrates; Pro = Protein; Phe = Total Phenols; RS = Reducing Sugars. ^a = % (db); ^b = g/kg; ^c = mg/g; ^d = g/100 g.

3. Current Studies on High-Value-Added Microbial Compounds

Bioactive microbial compounds can be produced by various microorganisms using different agroindustrial wastes [28–30]. Studies reported in the last five years on microbial products obtained through fermentation processes are highlighted in this section. The compounds that can be obtained vary in terms of their activities, as well as the complexity of their structures (e.g., pigments, biosurfactants, and phenolic compounds). Figure 1 shows some examples of the chemical structures of microbial products obtained through fermentation using agroindustrial waste as a substrate. These examples are outlined in the following sections.

**Figure 1.** Cont.

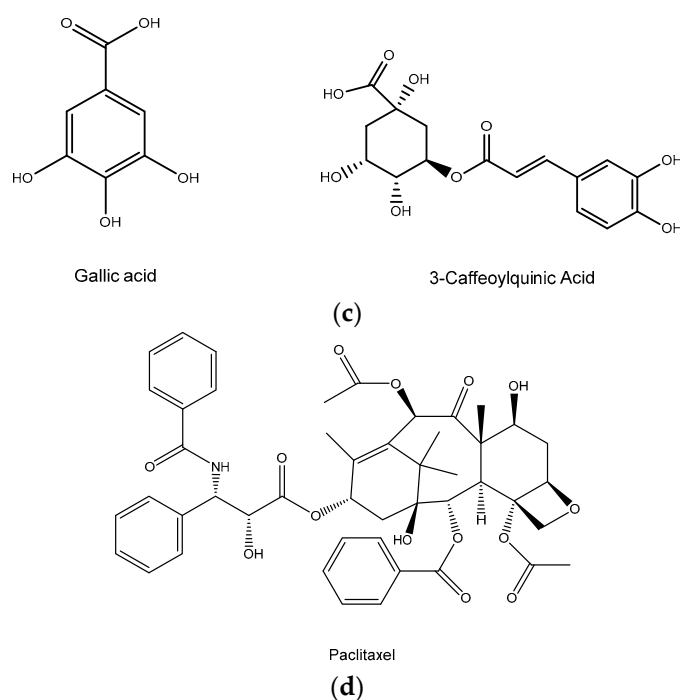


Figure 1. The chemical structures of some bioactive compounds produced by microorganisms using agroindustrial waste. The molecules correspond to (a) pigments, (b) biosurfactants, (c) phenolic compounds, and (d) other compounds.

At present, it is estimated that 60% of approved small-molecule drugs are related to natural products [31], demonstrating the importance of natural resources and underscoring the need to make sustainable use of the resources provided by nature. This section reviews current studies (in the last five years) that demonstrate the great interest in giving added value to microbial products while looking for more economical and eco-friendly industrial processes.

3.1. Enzymes

Hydrolases are the most commonly reported class of hydrolytic enzymes produced through microbial fermentation using agroindustrial waste (Table 2). Among the enzyme-producing fungi, the genus *Aspergillus* stands out for its production of cellulase-type enzymes, xylanases, and glucosidases through lignocellulosic waste [20,26,28]. The fungus *Aspergillus flavipes* has also been reported for its protease production using wheat bran through SSF [10]. Although fungal proteases predominate in industrial processes due to their high production rate [32], this enzyme can also be produced by bacteria. The bacterium *Anoxybacillus rupiensis* uses potato peel powder for producing protease and amylase through SmF [33].

Lipases can be synthesized by fungi and bacteria using solid or liquid agroindustrial waste [34,35]. The ability of some bacteria to use agroindustrial effluents as a source of nutrients for the production of lipases or other value-added products also offers an interesting alternative for water decontamination.

Other enzymes produced by microorganisms using agroindustrial waste are L-asparaginase [36] and n-demethylases [25]. L-asparaginase is a key chemotherapeutic agent in acute lymphoblastic leukemia, and its production has been mostly studied in bacteria rather than fungi [37]. Therefore, the production of L-asparaginase by *Bacillus aryabhattai* using olive mill wastewater as a substrate for growth and enzyme production [36] could have enormous biotechnological potential due to its double applications in both environmental and pharmaceutical areas. Peña-Lucio et al. [25] reported the production of n-demethylase by *Rhizopus oryzae* using coffee pulp and sorghum as a substrate. The production of n-demethylase has special interest due to its potential to produce biofuels and pharmaceuticals from coffee waste.

Table 2. Enzyme and peptide-producing microorganisms using agroindustrial waste as a nutrient source.

Microorganism	Enzyme	Fermentation	Agroindustrial Waste	Reference
Bacteria				
<i>Anoxybacillus rupiensis</i>	Amylase Protease	SmF	Potato peel powder	[33]
<i>Bacillus</i> sp.	α -amylase	SmF	Potato peels, mango peels and lemon peels	[38]
<i>Bacillus subtilis</i>	Milk clotting enzyme	SmF	Orange peel and rice straw	[39]
<i>Bacillus aryabhattai</i>	L-asparaginase	SmF	Olive mill wastewater	[36]
<i>Bacillus tequilensis</i>	α -amylase	SmF	Rice bran	[40]
<i>Pseudomonas Aeruginosa</i>	Lipase	SmF	Palm oil mill effluent	[34]
<i>Bacillus amyloliquefaciens</i>	α -amylase	SSF	Wheat bran with potato peel	[41]
Fungi				
<i>Aspergillus heteromorphus</i>	Cellulase Exoglucanase	SmF	Anaerobically treated distillery spent wash and rice straw	[42]
<i>Aspergillus flavipes</i>	Xylanase Proteases	SSF	Wheat bran	[10]
<i>Aspergillus flavus</i>	Cellulase Xylanase	SSF	Rice straw	[28]
<i>Aspergillus ibericus</i>	Cellulase Xylanase β -Glucosidase	SSF	Brewer's spent grain	[20]
<i>Aspergillus niger</i>	Lipase	SSF	Rice bran with Jathropa seed cake	[35]
<i>Aspergillus oryzae</i>	Proteases	SSF	Wheat bran	[10]
<i>Rhizopus oryzae</i>	n-Demethylases	SSF	Coffee pulp and sorghum	[25]

3.2. Pigments

Microbial pigments with a wide spectrum of colors can be produced by bacteria and fungi. The most commonly reported microbial pigments are carotenoids, melanins, flavins, phenazines, quinones, monascins, violacein, and indigo [43]. The literature reported similarities in the type of pigment produced by bacterial and fungal species using traditional culture media [44]. However, most of the studies on microbial pigment production using agroindustrial waste are focused on fungal species (Table 3). Two of the most commonly reported pigment-producing microorganisms are *Monascus* sp. and *Rhodotorula* sp. The fungus *Monascus purpureus* is able to synthesize red and yellow pigments using different agroindustrial wastes as substrates, such as potato pomace and soybean meal [8,45]. In [46], the genus *Rhodotorula* was highlighted for its carotenoid production using a mixture of agroindustrial wastes obtained from local markets in India. This study reported that carotenoids can be produced in similar amounts by *Rhodotorula* spp., which is affected by the waste composition used as a substrate. Schallchli et al. [30] reported the production of reddish-purple pigments by *Streptomyces* sp. in bacteria using potato solid waste as a basal substrate through SmF. Interestingly, the authors indicated that the actinobacteria strain was not able to produce the pigments when a traditional medium was used.

The interest in pigments from natural sources has been increasing due to the safety problems presented by artificial pigments [47]. Therefore, studies on alternatives for producing low-cost pigments and enhancing pigment yields are required [48].

Table 3. Pigment-producing microorganisms using agroindustrial waste as a nutrient source.

Microorganism	Pigment	Fermentation	Agroindustrial Waste	Reference
Bacteria				
<i>Streptomyces</i> sp.	Reddish-purple pigment	SmF	Discarded potato	[30]
<i>Serratia nematodiphilia</i>	Prodigiosin	SSF	Wheat bran	[49]
<i>Rhodopseudomonas faecalis</i>	Lycopene	SmF	Soybean meal	[50]
Fungus				
<i>Monascus purpureus</i>	Red pigments	SSF	Potato pomace	[8]
	Yellow pigments			
<i>Monascus purpureus</i>	Red pigments	SmF	Soybean meal	[45]
<i>Monascus sanguineus</i>	Red pigments	SSF	Broken rice	[51]
<i>Rhodotorula mucilaginosa</i>	Carotenoids	SmF	Onion peels and mung bean husk	[23]
<i>Sporidiobolus pararoseus</i>	β -cryptoxanthin β -carotene	SmF	Parboiled rice water and sugar cane molasses	[52]
<i>Xanthophyllomyces dendrorhous</i>	Astaxanthin	SmF	Pineapple waste, orange waste and pomegranate waste	[53]
<i>Xanthophyllomyces dendrorhou</i>	Carotenoids	SmF	Mesquite pods	[54]

3.3. Biosurfactants

Biosurfactants are surface-active biomolecules produced by microorganisms with a wide range of applications. Although there are a few studies on biosurfactant production with fungi, some evidence indicates that fungal species have the potential to yield good amounts of biosurfactants compared to bacteria [55]. On the other hand, fungi can also be used to produce biosurfactants through SSF, which would reduce energy costs associated with their production. Rodríguez et al. [29] reported sophorolipid production with *Starmerella bombicola* ATCC 22214 using nine types of agroindustrial waste through SSF. Of the studied waste types, wheat straw, rice husk, and coconut fiber offered the best results (Table 4).

Table 4. Biosurfactant-producing microorganisms using agroindustrial waste as a nutrient source.

Microorganism	Biosurfactant	Fermentation	Agroindustrial Waste	Reference
Bacteria				
<i>Bacillus subtilis</i>	Lipopeptide	SmF	Molasses	[56]
<i>Lactococcus lactis</i>	Glycolipopeptide	SmF	Vinasse	[57]
<i>Pseudomonas aeruginosa</i>	Octadecanoic acid Lipopeptide	SmF	Sugar cane molasses	[58]
<i>Bacillus haynesii</i>	Cyclododecanol Lipopeptide	SmF	Orange peel	[59]
Fungus				
<i>Starmerella bombicola</i> ATCC 22214	Sophorolipids	SSF	Wheat straw, rice husk and coconut fiber	[29]

The biosurfactants produced by bacteria using agroindustrial waste through SSF have not been fully explored, possibly due to the difficulties of growing in environments with low water availability. However, the literature indicates that some bacterial species are able to produce lipopeptides using agroindustrial waste through SmF, including molasses, vinasse, sugar cane molasses, and orange peel (Table 4). Although agroindustrial waste can

be used as the only substrate, it can also be supplemented with salts or other nutrients to improve biosurfactant production yields. For example, *Bacillus subtilis* ANR 88 was able to produce lipopeptides using molasses as the main substrate supplemented with ammonium ferric citrate, enhancing 0.25% of biosurfactant production [56].

3.4. Phenolic Compounds

Phenolic compounds are natural bioactive molecules that have interesting bioactivities (e.g., antioxidant, antimicrobial, and anti-inflammatory properties), which have great interest in technological and medicinal areas [60]. The extraction of phenolic compounds from agroindustrial waste could be improved by enzymatic processes involved in microbial metabolism during the fermentation process [61]. For example, studies reported that total phenols could increase by 78% in cultures of *Rhizopus oligosporus* with apricot pomace under SSF [62]. The same effect was observed in the fermentation of peanut press cake using *Aspergillus oryzae*, where a gradual increase in the concentration of gallic acid, chlorogenic acid, 4-hydroxy butyric acid, and p-Coumeric acid was observed after different days of fermentation [9]. Similar results were observed in rice bran with *Lactobacillus lactic* and *Lactobacillus plantarum*. The inoculation of rice bran with the previous *Lactobacillus* species increased the content of total phenols by 10% compared to unfermented rice bran [63]. Table 5 shows the types of phenolic compounds obtained via the fermentation of agroindustrial waste.

Table 5. Phenolic compounds released by microbial fermentation in agroindustrial waste.

Microorganism	Antioxidant Compound	Fermentation	Agroindustrial Waste	Reference
Bacteria				
<i>Lactobacillus lactic</i> <i>Lactobacillus plantarum</i>	Total phenols	SSF	Rice bran	[63]
Fungus				
<i>Aspergillus awamori</i>	Phenolic compounds	SSF	Peanut press cake	[64]
<i>Aspergillus niger</i>	Procyanidin B2 monomers	SSF	Hass avocado seeds	[65]
<i>Aspergillus niger</i>	Pentagalloylglucose	SSF	Mango seed waste	[27]
<i>Aspergillus oryzae</i>	Ellagic acid	SSF	Peanut press cake	[9]
	Gallic acid			
	Chlorogenic acid			
	4-hydroxy butyric acid			
	p-Coumeric acid			
<i>Rhizopus oligosporus</i>	3-caffeoylquinic acid	SSF	Apricot pomace	[62]
	5-caffeoylquinic acid			
	Quercetin-3-rutino-side			
<i>Rhizopus oryzae</i>	Quercetin-3(6''acetyl-glucoside)	SSF	Olive mill waste	[20]
<i>Aspergillus fumigatus</i>	Hydroxycinnamic acids	SSF	Orange peel waste	[66]
	Ellagic acid	SmF		

3.5. Others Bioactive Compounds

Apart from the products already mentioned, it is possible to obtain other microbial products using agroindustrial waste (Table 6). Natamycin can be produced by *Streptomyces gilvosporeus* using a mixture of wheat bran, rapeseed cake, rice hull, and crude glycerol as substrates through SSF [67]. Other compounds such as paclitaxel [68] and ergosterol [26] can also be produced through the bioconversion of agroindustrial waste, such as *A. fumigatus* and *A. niger*, respectively, using sugarcane bagasse, wheat bran, and olive mill waste.

Table 6. Other compounds produced by microorganisms using agroindustrial waste as a nutrient source.

Microorganism	Product	Fermentation	Agroindustrial Waste	Reference
Bacteria				
Bacterial consortium	Volatile fatty acids	Anaerobic fermentation	Cucumber, tomato and lettuce waste	[69]
<i>Saccharopolyspora erythraea</i>	Erythromycin	SSF	Sugarcane bagasse, beet sugar root and oatmeal	[70]
<i>Streptomyces rimosus</i>	Paromomycin	SSF	Corn bran	[71]
<i>Streptomyces gilvosporeus</i>	Natamycin	SSF	Wheat bran, rapeseed cake, rice hull and crude glycerol	[67]
Fungi				
<i>Aspergillus fumigatus</i>	Paclitaxel	SSF	Sugarcane bagasse Wheat bran	[68]
<i>Aspergillus niger</i> <i>Aspergillus ibericus</i>	Ergosterol Lignocellulolytic enzymes	SSF	Olive mill waste with winery waste	[26]
<i>Fusarium</i> sp. (Recombinant)	Lovastatin	SSF	Groundnut oil and soybean oil cakes	[72]
<i>Pleurotus citrinopileatus</i>	Antityrosinase compounds	SmF	Olive-oil mill wastewater	[21]
<i>Rhizopus oryzae</i>	2-pentanone d-limonene 2-phenylethanol	SmF	Olive mill waste	[73]
<i>Candida tropicalis</i>	d-limonene methyl butanoate	SmF	Olive mill waste	[73]
<i>Pichia kudriavzevii</i>	2-phenylethanol	SSF	Sugarcane bagasse	[74]

Food additives (e.g., flavor-related compounds) produced by microorganisms using agroindustrial waste as substrates have also been reported [75]. Olive mill waste, which represents an important environmental problem in Mediterranean areas, can be used by *Rhizopus oryzae* to produce 2-pentanone, d-limonene, and 2-phenylethanol through SmF [73]. Other types of waste, such as sugarcane bagasse, can be supplemented with L-phenylalanine and used as a substrate for *Pichia kudriavzevii* under SSF conditions for producing 2-phenylethanol [74]. Martínez-Avila et al. [74] also indicated that 2-phenylethanol production using *P. kudriavzevii* can be optimized using an adequate temperature and initial humidity for the substrate, reaching up to a 70% increase compared to the non-optimized process. Furthermore, aroma production can be obtained not only from microbial fermentation using agroindustrial waste but also from precursor compounds involved in the synthesis of flavors, such as ferulic acid [76,77]. Ferulic acid is a precursor in the synthesis of biovanillin, one of the most widely used flavors in the food, beverage, and pharmaceutical industries, which can be produced by *Enterobacter hormaechei* through SmF using some fruit peels as a substrate [76,77].

Some agroindustrial waste has also been determined to produce biopesticides to control agricultural pests. Ndao et al. [78] reported the use of industrial starch wastewater for *Bacillus thuringiensis* to produce endotoxins (Cry IAb) to control larvae of *Choristoneura fumiferana*. This study concluded that substrates pre-treated at pH 2 provided significant organic matter solubilization for *B. thuringiensis*, which resulted in larvicidal potency equivalent to that of the commercial biopesticide Foray 76B. Another use of agroindustrial

waste is as a growth substrate for biological control agents—e.g., the entomopathogenic fungus *Metarhizium anisopliae* for controlling gram pod-borer (*Helicoverpa armigera*) [79] and the fungus *Trichoderma* sp. for controlling banana vascular wilt caused by *Fusarium oxysporum* [80].

4. Improving Fermentation Processes and Sustainability

In general, two different types of fermentation can be used for the bioconversion of agroindustrial waste into high value-added microbial products: SSF and SmF. The advantages and disadvantages of both fermentation types (Table 7) must be considered before establishing a process and studying the best culture conditions to produce microbial products. A key factor for selecting an adequate fermentation process is the type of agroindustrial waste. Most microorganisms are strongly dependent on the amount of water present in the substrate or the adjustment of some culture conditions during the fermentation period, such as pH or metal ions [81]. The water content of a solid mash in SSF depends on the used microorganisms but often varies between 40 and 80%, with there being more than 95% in a typical SmF [82]. Bacteria usually cannot tolerate low moisture levels. Consequently, most reports on the production of bacterial products using agroindustrial waste employed SmF.

Table 7. Some advantages and disadvantages reported for Solid State Fermentation (SSF) and Submerged Fermentation (SmF) using agroindustrial waste as the main substrate.

	SSF	SmF
Advantages	<ul style="list-style-type: none"> - Higher bioproduct yields - Low energy consumption - Easy processing with minimal or no pretreatment of waste - Less generation of wastewater - No foam generation - Low capital investment—use of simplified bioreactors (scale-up) 	<ul style="list-style-type: none"> - Requires lower fermentation periods - Easy control of parameters - Substrates are consumed very rapidly (possibility to implement fed batch or continuous culture)
Disadvantages	<ul style="list-style-type: none"> - Requires longer fermentation periods - Need for supplementation in some cases (low nutrient availability) - Low amenability of the process to regulation - Heterologous fermentation conditions - Low reproducibility of yields - Unfeasible determination of growth kinetics (scale-up) 	<ul style="list-style-type: none"> - Lower bioproduct yields - High energy consumption - High generation of wastewater - Need to control foam generation - High capital investment—stirred bioreactors (scale-up)

[48,67,83–85].

SmF is a fermentation process in the presence of excess free water. This technology is the most commonly reported for producing industrial microbial products due to the ease of controlling culture parameters on a large scale [86] and shorter production periods [55] compared to SSF. Indeed, numerous microbial products created through SmF have been recently reported. Here, we highlight the genus *Bacillus* as one of the most commonly reported bacterial sources of diverse enzymes and biosurfactants produced through SmF using agroindustrial waste. Rice bran, fruit peels, rice straw, molasses, and olive mill wastewater are some of the agroindustrial wastes reported to be adequate substrates for producing bioproducts via *Bacillus* spp. However, specific culture conditions such as temperature, pH, incubation period, and the addition of nutritional compounds must be studied to obtain high amounts of products [40]. Another important aspect to consider is the low nutrient availability shown by some agroindustrial waste, making it necessary to study the pre-treatment process before using waste as a substrate. For example, the

pre-treatment of fruit peels with 0.8% sulfuric acid can lead to an increase in amylase production using *Bacillus* sp. [38]. Sugarcane bagasse can also be pre-treated using alkaline conditions and enzymatic hydrolysis to produce high value-added microbial products such as reddish pigments with *Monascus ruber* through SSF [87]. Pretreatment methods for the recovery of fermentable sugars from agroindustrial waste were reviewed recently by Kumar et al. [88], including microwave radiation, ultrasound, steam explosion, liquid hot water, ammonia fiber explosion, pyrolysis, and microfluidics.

SSF is a fermentation process in an environment with low free water content or the total absence of free water [89]. In recent years, SSF has become the most commonly reported technology for producing high value-added products via fungi and some bacteria. The success of this process is because SSF resembles the natural habitat of diverse microorganisms [85]. Nevertheless, as with SmF, to improve the production of microbial products using agroindustrial waste it is necessary to study the best growing conditions [90]. Some of the key parameters are the particle size of the waste, inoculum size, pH, and moisture content [28]. The moisture content has special relevance because it can directly limit microbial growth [8]. For example, Yepes-Betancur et al. [65] reported that avocado seeds with a relative humidity of 60% are an adequate substrate to obtain high antioxidant activity of compounds produced by *A. niger*. On the other hand, it is possible to obtain a nutrient-rich substrate for producing microbial products through SSF by mixing waste with different nutrient contents. Studies in this area were carried out by Zeng et al. [67], who reported the use of a mixture of wheat bran, rapeseed cake, rice hull, and crude glycerol to produce natamycin with *S. gilvosporeus* through SSF under moisture content and an inoculum size of 70% and 15%, respectively. In addition, a reduction in raw material cost can be achieved by using agroindustrial waste, reaching 50% in some cases (e.g., natamycin production) [67].

According to the reviewed literature, the use of agroindustrial waste as a raw material can not only help lower the production costs of microbial products, but also improve the sustainability of such products [91]. In general, SSF processes have gained special interest in terms of sustainability since they entail lower energy and water consumption, require less wastewater generation, and allow the efficient use of agroindustrial waste as raw material [67,84]. However, there are important challenges that threaten the sustainability of many microbial high-value-added products, such as the development of pre-treatments with low energy costs and extraction techniques based on green solvents. Thus, with the concept of sustainability arises the need to study not only the optimization of fermentation processes using agroindustrial waste, but also sustainability through all stages of the production process and final disposal—for example, through a life cycle assessment [92].

5. Advances for Scaling up Fermentation Processes

Most of the reported studies on the use of agroindustrial waste as nutrient-rich substrates for obtaining microbial products through fermentation processes were assessed at the flask level. Evaluation in larger scale reactors is necessary to realize production at an industrial level and to obtain scalable prototypes. According to Crater and Lievense [93], the fermentation process on a lab scale uses bioreactors with volumes between 0.5 and 10 L. Instead, a pilot plant considers bioreactors with volumes between 100 and 10,000 L, which entails a higher investment.

The literature on the evaluation of microbial products using agroindustrial waste in pilot plants is scarce. Deljou et al. [94] reported the synthesis of α -amylase by *Bacillus licheniformis* using rice husks through SmF in a shake flask (100 mL working volume) and stirred reactor (1 L working volume), obtaining 3-fold enzyme production in the reactor (723 U/L/h). Similar studies in lab-scale reactors indicated that the aeration rate and agitation speed are two key parameters that influence enzyme production. Although similar yields of some enzymes (e.g., xylanase) can be achieved using agroindustrial waste in flasks or lab-scale reactors, changes in aeration and the speed of agitation can significantly decrease production by up to 75% [95].

One advantage observed in scaling-up using reactors is the recovery of the same amount of microbial product with less fermentation time. For example, Nguyen et al. [96] reported

prodigiosin production with *Serratia marcescens* using groundnut oil processing (1%) as a substrate in shake flasks and a 14 L reactor. The authors reported a yield of 5380 mg/L of prodigiosin after 48 h of fermentation in the shake flasks and 6886 mg/L after 10 h in the bioreactor. Similar results for prodigiosin production were reported by Tran et al. [97] in a 14 L reactor after 14 h of fermentation using cassava wastewater, obtaining 6150 mg/L. To obtain the reported prodigiosin values, the authors also indicated that cassava wastewater must be supplemented with 0.25% casein, 0.05% MgSO₄, and 0.1% K₂HPO₄.

SSF has greater scaling challenges than SmF, largely due to the availability of reactors for pilot-scale implementation [98]. Some recent studies have reported the optimization of culture conditions in flasks and their scaling-up in especially designed and/or adapted reactors for SSF using agroindustrial waste—for example, the scaling up of α -amylase production with *A. oryzae* through SSF using groundnut oil cake under optimized conditions in a pilot-scale fermenter (600 L of capacity). The initial moisture content (64%), pH (4.5), incubation period (108 h), and temperature (32.5 °C) were previously optimized in flask assays [99].

Despite recent advances, more studies at larger scales should explore technologies for waste pretreatment, the optimization of fermentation processes, and the downstream steps involved in product recovery to advance towards the industrial production of sustainable microbial high added-value products.

6. Conclusions

The environmental problems related to agroindustrial waste can be reduced through bioconversion of this waste into bioactive compounds in an eco-friendly way, thereby recycling nutrients using microorganisms. Together with a reduction in production costs, the use of agroindustrial waste in the production of microbial products could contribute to improving sustainability associated with industrial processes. The reviewed reports have focused on optimizing the culture conditions in fermentation processes to maximize the production of bioactive compounds and proposing new types of agroindustrial waste as suitable substrates. However, there are important challenges to scaling up fermentation processes that open up interesting lines of research with innumerable possibilities in the valorization of agroindustrial waste. Thus, it is necessary to focus research efforts on pretreatment alternatives and downstream steps for product recovery that can generate efficient technologies for the industrial production of sustainable microbial products that are safe for humans and the environment.

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