

## Review

# Valorization of Fermented Food Wastes and Byproducts: Bioactive and Valuable Compounds, Bioproduct Synthesis, and Applications

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**Abstract:** Significant amounts of fermented food waste are generated worldwide, promoting an abundance of residual biomass that can be used as raw material to extract bioactive peptides, fermentable sugars, polyphenols, and valuable compounds for synthesizing bioproducts. Therefore, generating these high-value-added products reduces the environmental impact caused by waste disposal and increases the industrial economic value of the final products. This review presents opportunities for synthesizing bioproducts and recovering bioactive compounds (employing wastes and byproducts from fermented sources) with several biological properties to support their consumption as dietary supplements that can benefit human health. Herein, the types of fermented food waste and byproducts (i.e., vegetables, bread wastes, dairy products, brewing, and winery sources), pre-treatment processes, the methods of obtaining products, the potential health benefits observed for the bioactive compounds recovered, and other technological applications of bioproducts are discussed. Therefore, there is currently a tendency to use these wastes to boost bioeconomic policies and support a circular bioeconomy approach that is focused on biorefinery concepts, biotechnology, and bioprocesses.

**Keywords:** fermentation; bioactive compounds; bioeconomy; biomass residues; winery wastes; brewing residues; fermented beverages; fermented byproducts; health benefits; phytochemicals; polysaccharides; biorefinery



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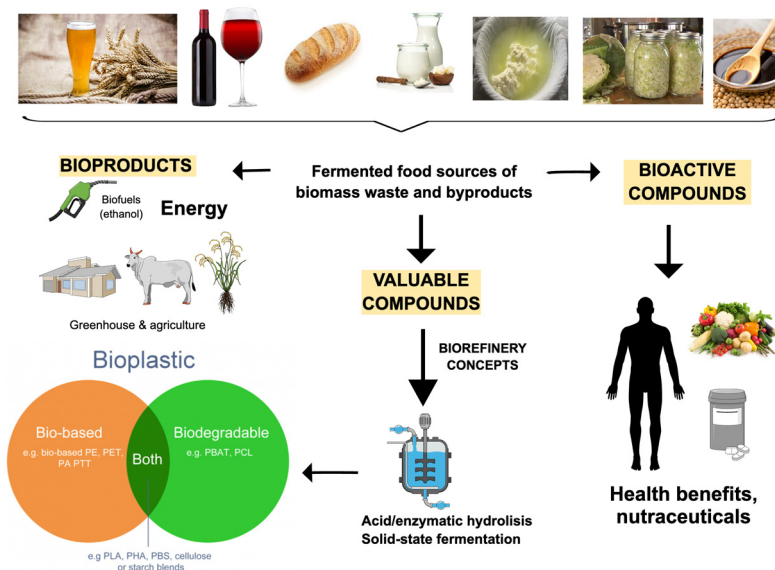
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## 1. Introduction

The increase in the world's population has led to more significant waste generation by society. In addition, the lack of public policies for basic sanitation regarding the disposal and reuse of waste makes low-income countries move toward an increase in waste generation [1]. Figure 1 shows that in 2020, the world production of solid waste was 2.24 billion tonnes, which is approximately 0.79 kg per person per day. It is estimated that in 2050, there will be a growth rate of roughly 73%, which will lead to waste generation around the world of 3.88 billion tonnes [2]. This growth in waste generation is projected to increase rapidly in certain regions due to poor waste disposal practices and management. Thus, without a significant improvement in waste management, there is a trend in waste generation growth and an increase in environmental pollution [3,4]. In this context, using biomass residues in fermentation becomes an excellent alternative for synthesizing bioproducts and extracting bioactive compounds with high industrial added value. In addition, they can be seen as a possible way to increase the circular bioeconomy [5–7].



**Figure 1.** Bioactive compounds and valuable products recovered from several sources of fermented foods and their potential applications.

Agricultural waste and industry byproducts generate leftovers that are discarded in the trash, rejecting a valuable opportunity of environmental and waste management [8,9]. A solution to overcome this challenge is the bioconversion and recovery of these residues in commercial products produced by chemical synthesis or fermentation processes [10]. These residues can be excellent feedstock for biorefinery since residual biomasses are abundant, cheap, readily available, easy to collect from farms or industries, and easy to prepare for their intended use. [11,12]. In this way, two challenges would be solved: the demand for waste disposal sites and the application of these wastes to generate profits [13,14]. World Energy Outlook 2022 reported a truly global energy crisis (higher prices causing painfully high inflation, conflicts, slowing economies, and rising poverty), demanding a larger supply of clean energy sources and technologies [15].

Therefore, biotechnological advances improve synthesis processes, moving toward clean energy, greener bioproducts with high commercial value, clean industrial products (biosources for biodegradable plastics, bio-based solvents, biolubricants, safer food additives, and bioactive compounds with therapeutic and nutraceutical potential) [16–18]. Of these, both bioproducts and bioactive compounds stand out. Although both are derived from biological sources, they serve different purposes and have different characteristics. Bioproducts refer to a wide range of products derived from biological sources such as plants, animals, and microorganisms. These can be categorized into different types, including biofuels, bioplastics, biomaterials, and nanomaterials [19–21]. Bioactive compounds are diverse natural substances that can significantly support human health and body functions [22–24]. These compounds, derived from plants, animals, and microorganisms, gained considerable attention recently due to several biological properties and their potential applications in medicine and healthcare [25–28]. Our research group has been dedicated to the prospection of and discovery of several secondary metabolites drawn from agro-industrial residues (i.e., fruits, vegetables, and plants) [29] and fermented foods (e.g., kefir derived from kefir) [30]. Such bioactive compounds can also be recovered by purposing the final application as food and postharvest additives [31] with antioxidant/antimicrobial effects [29,32], which are valuable for dietary supplements, the food packaging industry [32,33], and health improvement [34,35], and offer promising chemotherapy approaches to treating cancer [36,37].

Fossil-source products are of primary environmental concern since CO<sub>2</sub> emissions have increased dramatically [38]. Therefore, techniques for using supercritical CO<sub>2</sub> in the hydrolysis step of processing lignocellulosic materials are being applied to biomass

residues to facilitate the fermentation and synthesis of bioproducts [38–41]. Fermentation is an ancient process that is widely used in the food industry to produce vinegar, bread, alcoholic beverages (cider, wine, and beers), fermented dairy products (aged cheese, yogurt, and kefir), fermented meats and sausages, fermented fish products, low-alcohol fermented drinks (kombucha, dark tea, and water kefir), fermented soy-based foods (miso, natto, tempeh, soy sauces, and tofu), fermented vegetables (sauerkraut, pickles, kimchi, and other legumes, cereals, and grains that undergo fermentation) [42,43]. Over the years, this process began to be studied in terms of reusing waste from the food and agricultural industry to synthesize products with high added value for industrial commercialization [28,42–44]. Figure 1 shows several sources of fermented foods for recovering valuable and bioactive compounds and producing bioproducts, along with their potential applications related to the fossil sources of CO<sub>2</sub> emissions and the use of biomass residues to obtain bioproducts and bioactive compounds. Biomass residues have a high content of sugars, starch, proteins, cellulose (35–50%), hemicelluloses (25–30%), or lignocellulosic content (15–25%). All these primary metabolites can be used by microorganisms for metabolization, increasing metabolic activity and, consequently, generating fermentation products and byproducts [34,45].

This review article provides insights into the potential capacity of the processes and mechanisms introduced in the biorefinery to synthesize bioproducts with high economic and environmental impact. The analysis of biotechnological products derived from these processes is presented with a critical review based on the results achieved by the authors. In addition, it explores the prospects for biomass and processes that help in the economic and environmental increment of using residues for synthesizing high-added-value products. Finally, the potential use of waste generated by the fermentation process presents a research gap related to identifying the industrial and health applications that enhance the insertion of food and agro-industrial waste in the industrial matrix to improve the circular bioeconomy approach.

## 2. From Industrial Waste to Value-Added Bioproducts

The food and agriculture industries generate enormous amounts of waste with chemical characteristics that make it suitable for use as a raw material to obtain a product with high added value, promoting industrial production sustainability [46–48]. Obtaining bioproducts and bioactive compounds and reducing the loss of resources from waste bioconversion helps save costs, boost productivity, and reduce the environmental impact caused by industrial waste disposal [46,48].

The global biobased chemicals market was valued at USD 61.61 billion in 2022, with a compound annual growth rate (CAGR) of 10.4% during the forecast period [49]. Bio-based products are a class of chemicals derived from renewable biological sources (plants, crops, and biomass), as opposed to the traditional chemicals derived from fossil fuels [7,50], the major sources of which are basic petrochemical feedstocks including naphtha, oil, and gas (i.e., ethane, propane, butane, and methane, which are converted into chemicals such as ethylene, propylene, butadiene, and methanol). Thus, bioproducts draw the market's attention, increasing global demand and the potential to reduce environmental impacts by reducing carbon emissions.

Several bioproducts can be synthesized through the fermentation processes of residual biomass, which is rich in primary and secondary metabolites. These include amino acids, bioplastics made from biopolymers [30], oleochemicals made from natural lipids and fats, biofuels, and food wastes that are rich in bioactive compounds, such as terpenoids and flavonoids [7,49]. Acetone and ethanol, for example, are molecules that can now be synthesized through metabolic engineering, developing a vast range of strategies for synthesizing environmentally friendly compounds [7,48,49].

Most bioproducts are derived from sucrose, vegetable oil, and starch, known as first-generation (1G) fuels—produced as bioethanol and obtained by fermenting sugarcane juice [51–55]. Second-generation (2G) processes have garnered research attention since they use lignocellulosic biomass residues as a source of sugars for metabolization and

conversion into biofuels [56,57]. The hydrolysis of sugar by microorganisms has been seen as a sustainable alternative to fossil fuels, basic petrochemical feedstocks, and their derivatives. However, the anti-degradation nature of lignocellulosic biomass, the generation of fermentation inhibitors during the hydrolysis step, and the low conversion rates are challenges for large-scale industrial implementation [58–60].

Table 1 presents examples of several fermented food sources, the methods for obtaining bioactive compounds, and other valuable compounds from different biomass resources (natural, byproduct, or waste) along with their potential health benefits to ensure human health or their potential applications in the biotechnology, biorefinery, energy, foods, and biomedical fields. Spent yeast from brewing beer has been subjected to conventional solid–liquid extraction (CSLE) to recover flavor-enhancer nucleotides for the food industry [61]. Previously, spent yeast from brewing was also treated with a high-intensity pulsed electric field (PEF) to recover trehalose, a nonreducing sugar commonly found in natural sources that has bioprotectant properties for foods [62].

**Table 1.** A brief overview of the potential health benefits/application of bioactive compounds and valuable compounds recovered by the valorization of fermented food byproducts and wastes.

| Fermented Food                        | Biomass Resource<br>(Natural,<br>Byproduct, Waste) | Bioactive<br>Compounds/Valuable<br>Compounds                   | Obtaining<br>Method                                                              | Potential Health<br>Benefit/<br>Application | Ref.                              |
|---------------------------------------|----------------------------------------------------|----------------------------------------------------------------|----------------------------------------------------------------------------------|---------------------------------------------|-----------------------------------|
| <b>FERMENTED VEGETABLES</b>           |                                                    |                                                                |                                                                                  |                                             |                                   |
| Kimchi factory                        | Cabbage powder<br>and radish powder                | Dietary fibers                                                 | UAE<br>(H <sub>2</sub> O:acetonitrile)                                           | Functional foods                            | Lee et al.,<br>2016 [63]          |
| Soy sauce                             | Solid waste from<br>soy sauce refuse               | CH <sub>4</sub> , CO <sub>2</sub> and VFAs                     | Anaerobic<br>digestion                                                           | Clean energy<br>(biomethane)                | Nagai et al.,<br>2022 [64]        |
|                                       |                                                    | Protein, insoluble fiber                                       | NaOH treatment                                                                   | Food seasonings<br>and additives            |                                   |
| Fermented<br>soybean food<br>products | Insoluble residue<br>(okara)                       | Phenolic compounds<br>and proteins                             | SSF by <i>Aspergillus<br/>oryzae</i> and<br><i>Aspergillus sojae</i>             | Anti-obesity effects                        | Ichikawa et al.,<br>2022 [65]     |
| Fermented<br>soybean food<br>products | Soybean dregs<br>(okara)                           | Oligosaccharides                                               | Fermentation by<br><i>Neurospora crassa</i>                                      | Prebiotic food                              | Zhou et al.,<br>2019 [66]         |
| Tofu                                  | Wastewater (tofu<br>whey)                          | Peptide lunasin                                                | Ethanol-<br>isoelectric<br>precipitation and<br>gel filtration<br>chromatography | Cancer prevention                           | Nieto-veloza<br>et al., 2021 [67] |
| Fermented<br>cabbage                  | Sauerkraut juice                                   | Phenolic compounds,<br>minerals, vitamins,<br>sugars, and NaCl | Spray-drying to<br>obtain sauerkraut<br>juice powder                             | Salt alternatives<br>in foods               | Janosone et al.,<br>2022 [68]     |
| <b>FERMENTED DAIRY PRODUCTS</b>       |                                                    |                                                                |                                                                                  |                                             |                                   |
| Cheese                                | Wastewater<br>(cheese whey)                        | Lactose                                                        | Biological<br>processes                                                          | Carbon sources for<br>biomolecules          | Bosco et al.,<br>2018 [69]        |
|                                       |                                                    | Lipids and protein                                             | Thermocalcic<br>precipitation                                                    | Bioplastics:<br>polyhydroxyalka-<br>noates  |                                   |
|                                       |                                                    | Protein                                                        | Ultrafiltration                                                                  | WPC for the food<br>industry                |                                   |
| Greek yogurt                          | Acid whey                                          | Calcium phosphate                                              | Liquid–solid<br>hydrocyclone                                                     | Food ingredients,<br>food additive          | Crowley et al.,<br>2019 [70]      |

Table 1. Cont.

| Fermented Food     | Biomass Resource (Natural, Byproduct, Waste) | Bioactive Compounds/Valuable Compounds                                      | Obtaining Method                                                 | Potential Health Benefit/ Application                        | Ref.                                                     |
|--------------------|----------------------------------------------|-----------------------------------------------------------------------------|------------------------------------------------------------------|--------------------------------------------------------------|----------------------------------------------------------|
| Cultured butter    | Buttermilk                                   | MFGM proteins and lipids, minerals, lecithin, lactose                       | Fermentation by LAB                                              | Functional foods; Antihypertensive effects                   | Conway et al., 2014 [71]                                 |
| Milk kefir         | Kefir grains                                 | Polysaccharides, LAB, and yeasts                                            | Milk fermentation: aqueous extraction, lyophilization            | Biopolymer kefiran for food and medical applications         | Jenab et al., 2015 [72]; Piermaria et al., 2015 [73]     |
|                    | Kefir grains                                 | Bioactive polysaccharides and proteins; nisin                               | Immobilized platelet encapsulation on kefiran                    | Biomedical applications—drug delivery and tissue engineering | Jenab et al., 2015 [72]                                  |
|                    | Kefir grains                                 | Bioactive polysaccharides and proteins; lactobacilli                        | Film-forming dispersions                                         | Probiotic delivery                                           | Gagliani et al., 2019 [74]                               |
|                    | Kefir grains                                 | Bioactive polysaccharides and proteins                                      | Polymer solution-casting method                                  | Biodegradable films for food packaging                       | Piermaria et al., 2015 [73]; Montoille et al., 2021 [75] |
|                    | Kefir grains                                 | Bioactive polysaccharides and proteins                                      | Polymer solution-casting method                                  | Biodegradable films for food packaging                       | Piermaria et al., 2015 [73]; Montoille et al., 2021 [75] |
| <b>BREAD WASTE</b> |                                              |                                                                             |                                                                  |                                                              |                                                          |
| Bread              | Bread waste                                  | Organic acids                                                               | Lactic fermentation ( <i>Lactobacillus amylovorus</i> DSM 20532) | Energy recovery—biohydrogen production                       | Adessi et al., 2018 [76]                                 |
|                    | Organic acid from lactic fermentation        | Biohydrogen (H <sub>2</sub> )                                               | Photo-fermentation ( <i>Rhodospseudomonas palustris</i> 42OL)    |                                                              |                                                          |
| Bread              | Out-of-date bread                            | Fermentable sugars—glucose (C <sub>6</sub> H <sub>12</sub> O <sub>6</sub> ) | Acid/enzymatic hydrolysis                                        | Solid-state fermentation                                     | Narisetty, Nagarajan, et al., 2022 [77]                  |
|                    | Bread waste hydrolysate (glucose)            | Bio-based ethanol (C <sub>2</sub> H <sub>6</sub> O)                         | SSF by <i>Saccharomyces cerevisiae</i> KL17                      | Bioethanol production                                        |                                                          |
|                    |                                              | Bio-based methane (CH <sub>4</sub> )                                        | Solid residue of SSF in ethanol production                       | Biomethane production                                        |                                                          |
| Bread              | Bread waste hydrolysate                      | D-2,3-Butanediol                                                            | Fermentation by <i>Bacillus amyloliquefaciens</i>                | Butanediol production                                        | Maina et al., 2021 [78]                                  |
|                    |                                              |                                                                             | Fermentation by <i>Enterobacter ludwigii</i>                     |                                                              | Narisetty et al., 2022 [79]                              |
| Bread              | Bread waste                                  | Fermentable sugars—glucose (C <sub>6</sub> H <sub>12</sub> O <sub>6</sub> ) | Enzymatic hydrolysis                                             | Biosource for microalgae cultivation                         | Jung et al., 2022 [80]                                   |
|                    | Bread waste hydrolysate                      | Paramylon (β(1,3)-glucan)                                                   | Heterotrophic cultivation of microalga <i>Euglena gracilis</i>   | Biosource for bioplastic                                     |                                                          |

Table 1. Cont.

| Fermented Food                                        | Biomass Resource (Natural, Byproduct, Waste) | Bioactive Compounds/Valuable Compounds                                                                         | Obtaining Method                                                         | Potential Health Benefit/ Application                | Ref.                             |
|-------------------------------------------------------|----------------------------------------------|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|------------------------------------------------------|----------------------------------|
| Bread                                                 | Remnants of bakery products                  | Sugars and proteins                                                                                            | Bread waste as malt substitute in brewing                                | Beer production                                      | Dymchenko et al., 2021 [81]      |
| Wheat Bread                                           | Stale bread (unsold and returns from shops)  | Fermentable sugars—glucose (C <sub>6</sub> H <sub>12</sub> O <sub>6</sub> )                                    | Enzymatic hydrolysis                                                     | Biosource for xanthan gum biosynthesis               | Demirci et al., 2019 [82]        |
|                                                       | Bread waste hydrolysate                      | Xanthan gum (polysaccharide)                                                                                   | Fermentation by <i>Xanthomonas</i> spp. using glucose as a carbon source | Food additive                                        |                                  |
| Breadcrumbs                                           | Processing bread waste                       | Dietary fiber, starch                                                                                          | Bread crumble extrudates by an extrusion process                         | Wheat flour substitute in extrusion cooking          | Samray et al., 2019 [83]         |
| Bread                                                 | Indian' bakery wastes                        | Reducing sugars                                                                                                | Simultaneous saccharification and SSF by LAB                             | Lactic acid production                               | Sadaf et al., 2021 [84]          |
| <b>FERMENTED BEVERAGES</b>                            |                                              |                                                                                                                |                                                                          |                                                      |                                  |
| Winery                                                | Grape pomace                                 | Phenolic compounds, proanthocyanidins                                                                          | In vitro rumen fermentation                                              | Ruminant feeding with lower CH <sub>4</sub> emission | Suescun-Ospina et al., 2023 [85] |
| Winery                                                | Grape skins from winery waste                | Soluble dietary fibers                                                                                         | High-pressure HTT (autohydrolysis)                                       | Antioxidant effect                                   | Bassani et al., 2020 [86]        |
| Winery                                                | Red grape pomace                             | Anthocyanins, flavan-3-ols, flavonols, procyanidins, galloyl glucose, and gallic acid                          | Aqueous extract drink of red grape pomace (RGPD)                         | Anti-hyperglycemic effect                            | Costabile et al., 2019 [87]      |
| Winery—Noble Muscadine                                | Grape pomace                                 | Anthocyanins, catechin, epicatechin                                                                            | Drying, grounding, and sieving                                           | Anti-hyperlipidemic effect                           | Yu et al., 2017 [88]             |
| Winery—Cabernet Sauvignon ( <i>Vitis vinifera</i> L.) | Grape pomaces (skin and seeds)               | Catechin, epicatechin, rutin, quercetin, kaempferol, transresveratrol, cinnamic and benzoic acid derivatives.  | Dehydration, freeze-drying, and milling to obtain WPF                    | Anti-hyperlipidemic and antioxidant effects          | Ishimoto et al., 2020 [89]       |
| Winery                                                | Grape seed                                   | Proanthocyanidins—monomer, dimer, trimers, oligomers                                                           | -                                                                        | Satiating agent                                      | Serrano et al., 2016 [90]        |
|                                                       |                                              |                                                                                                                |                                                                          | Gut health                                           | Casanova-marti 2018 [91]         |
| Winery—Pinot Noir ( <i>Vitis vinifera</i> L.)         | Grape pomace                                 | Proanthocyanidins, flavan-3-ol monomers, (+)-catechin, (−)-epicatechin, (−)-epicatechin-3-O-gallate, stilbenes | Water-ethanol extraction; freeze-drying; grinding                        | Cardioprotective effect                              | Ballea et al., 2018 [92]         |
| Winery—Fetească Neagră ( <i>Vitis vinifera</i> L.)    | Grape pomace                                 |                                                                                                                |                                                                          |                                                      | Ballea et al., 2018 [93]         |

Table 1. Cont.

| Fermented Food                             | Biomass Resource (Natural, Byproduct, Waste)     | Bioactive Compounds/Valuable Compounds                                                            | Obtaining Method                                                         | Potential Health Benefit/ Application | Ref.                                                                           |
|--------------------------------------------|--------------------------------------------------|---------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|---------------------------------------|--------------------------------------------------------------------------------|
| Winery—Cabernet Sauvignon, Marselan, Syrah | Grape pomace (skins, pulp, seeds, and stem)      | Malvidin, delphinidin, rutin, quercetin, catechin, coumaric acid, kaempferol, trans-cinnamic acid | Solvent extract; spray-drying                                            | Cardioprotective effect               | Chacar et al., 2019 [94]                                                       |
| Winery                                     | Red, white grape pomace/grape seed               | Anthocyanins, flavan-3-ols, flavonols, stilbenes                                                  | Solvent extract; lyophilization                                          | Cancer prevention                     | Pérez-Ortiz et al., 2019 [95]                                                  |
| Winery                                     | Grape seed                                       | Gallic acid, catechin, epicatechin gallate, and epicatechin                                       | Solvent extract; lyophilization                                          | Cancer prevention                     | Leone et al., 2019 [96]                                                        |
| Winery—Merlot, red wine                    | Wine less—liquid                                 | <b>Ethanol</b>                                                                                    | Distillation                                                             | Biofuel production                    | Dimou et al., 2015 [97]                                                        |
|                                            |                                                  | Alcohol-free nutrient-rich liquid                                                                 |                                                                          | Solid-state fermentation              |                                                                                |
|                                            | Wine lees—solids                                 | <b>Phenolic compounds</b>                                                                         | sequential extraction with acetone:H <sub>2</sub> O (after distillation) | Antioxidants                          |                                                                                |
|                                            |                                                  | Residual solids                                                                                   |                                                                          | Food additives                        |                                                                                |
|                                            | Wine lees—Residual solids                        | <b>Tartaric acid</b>                                                                              | Enzymatic hydrolysis                                                     | Food additives                        |                                                                                |
|                                            | Crude nutrient-rich hydrolysate + crude glycerol | Remaining stream (yeast cells)                                                                    |                                                                          | Solid-state fermentation              |                                                                                |
| Brewing                                    | Spent yeast                                      | Poly (3-hydroxybutyrate)                                                                          | SSF by <i>Aspergillus oryzae</i>                                         | Bioplastics                           |                                                                                |
| Brewing                                    | Spent yeast                                      | Peptides (48.3% protein; 86.4% essential amino acids)                                             | Membrane filtration                                                      | Nutraceuticals                        | Oliveira et al., 2022 [98]                                                     |
| Brewing                                    | Spent yeast                                      | Proteins, lipids, and carbohydrates                                                               | Microwave-assisted extraction                                            | Prebiotic/probiotic functional foods  | Cejas et al., 2017 [99]                                                        |
| Brewing                                    | Spent yeast                                      | Trehalose                                                                                         | Pulsed electric field                                                    | Bioprotectant agent                   | Jin 2011 [62]                                                                  |
| Brewing                                    | Spent yeast                                      | Nucleotides                                                                                       | CSLE                                                                     | Flavor enhancer                       | Vieira et al., 2013 [61]                                                       |
| Brewing                                    | Spent yeast                                      | Proteins and phenolic compounds                                                                   | -                                                                        | Food ingredient                       | Vieira et al., 2019 [100]                                                      |
| Brewing                                    | Spent yeast                                      | $\beta$ -glucan                                                                                   | CSLE                                                                     | Immunomodulation                      | Bastos et al., 2015 [101]; Liepins et al., 2015 [102]; Tian et al., 2019 [103] |
| Brewing                                    | Barley malt rootlets                             | Proteins                                                                                          | CSLE                                                                     | Functional foods                      | Mahalingam, 2019 [104]                                                         |
| Brewing                                    | Barley malt rootlets                             | Proteins and phenolic compounds                                                                   | CSLE                                                                     | Antioxidants (functional foods)       | Cheng et al., 2016 [105]; Budaraju et al., 2018 [106]                          |

Table 1. Cont.

| Fermented Food | Biomass Resource (Natural, Byproduct, Waste) | Bioactive Compounds/Valuable Compounds | Obtaining Method | Potential Health Benefit/ Application | Ref.                                                                  |
|----------------|----------------------------------------------|----------------------------------------|------------------|---------------------------------------|-----------------------------------------------------------------------|
| Brewing        | Spent hops                                   | Phenolic compounds                     | UAE (ethanol)    | Antioxidant and antimicrobial effects | Gandolpho et al., 2020; [107] Senna Ferreira Costa et al., 2021 [108] |
| Brewing        | Spent hops                                   | Essential oils; Xanthohumol            | CSLE             | Antioxidant and anticancer activities | Aniol et al., 2007 [109]; 2008 [110]                                  |

SSF: solid-state fermentation; VFAs: volatile fatty acids; RGPD: 9.8 g/100 mL of soluble carbohydrates and 625 mg/100 mL of total polyphenols; WPC: whey protein concentrate; CLSE: conventional solid-liquid extraction; UAE: ultrasound-assisted extraction; HTT: hydrothermal treatment; WPF: wine pomace flour; -: not reported/not specified; MFGM: milk fat globule membrane; LAB: lactic acid bacteria.

### 3. Bioactive and Valuable Compounds

The fermented food industry generates large amounts of residues that are sustainable, providing a rich source of compounds (as primary and secondary metabolites) with valuable nutritional and functional properties, such as proteins, polysaccharides, and polyphenols—from these, bread, brewing, and winery stand out as the most widely fermented sources of byproducts and wastes. They are rich sources of valuable compounds with high potential to ensure human health and to be used as a bioresource in several applications, including the energy, biorefinery, food technology, biomedical, and biotechnology fields. In terms of biorefinery concepts, wine less (the liquid and solid residual fractions, the remaining streams, and alcohol-free nutrient-rich liquid) from Merlot red wine production was employed as a bioresource to produce several added-value products, such as antioxidants, tartrate, ethanol, and bioplastic [97].

The solid waste from soy sauce refuse, when chemically treated with alkali, provides high contents of insoluble fibers and proteins, with the potential for use as food seasoning and food additives [64]. Conversely, when the waste was biologically treated, Nagai et al. (2022) reported its potential as an energy source in methane gas production due to the CH<sub>4</sub>, CO<sub>2</sub>, and volatile fatty acids (VCAs) obtained after anaerobic digestion [64].

A circular fermented food waste management system could combine baking and brewing to produce alcoholic beverages from bakery leftovers. One author's idea was to reduce the waste from the bakery by employing sugars and proteins (from bread wastes and the remnants of bakery products) as malt substitutes in the brewing of lager beer [81]. However, the results indicated a lower amount of malt in the bread-waste samples and a lower number of extracted enzymes from the malt, making the resulting beer's body weaker and decreasing its level of acceptance in terms of sensory evaluation. The bread alone could not provide the requisite number of enzymes to achieve the fullness of flavor needed for beer [81].

Another study proposed a new way to reduce bread waste, using breadcrumbs as a relatively inexpensive raw material. Breadcrumb extrudates were considered by the authors as promising raw materials in extrusion cooking due to their potential functional properties and higher total dietary fiber content than traditional wheat flour extrudate [83].

#### *Biological Activities, Functional Foods, and Health Benefits*

Residual biomass from vegetable-based fermented foods and fermented dairy products have also been highlighted as strong candidates for recovering interesting compounds with several health benefits and potential applications as nutraceuticals in functional foods [104] and dietary supplements [111]. For example, cabbage/radish powder [63] and soybean dregs (okara) [66]—byproducts from kimchi and fermented soybean factories,

respectively—were used to successfully recover prebiotic dietary fibers (i.e., oligosaccharides) and proteins, which are valuable for functional foods. Okara is the residual byproduct generated when processing fermented soybean food products such as miso, natto, and tempeh. Likewise, Ichikawa et al. (2022) recently reported the *in vivo* anti-obesity effects of phenolic compounds and proteins recovered from insoluble residuals derived from okara [65]. Oliveira et al. (2022) recently reported the use of yeast peptide extracts in a circular economy concept, employing membrane filtration to recover peptide fractions (48.3% proteins and 86.4% essential amino acids) [98].

An innovative and sustainable approach to valorizing bioactive compounds and the nutrients of soybean combined ethanolic-isoelectric precipitation and gel filtration chromatography to obtain the naturally occurring bioactive peptide lunasin from tofu whey wastewater [67]. Moreover, the anticancer potential of the bioactive peptide that was recovered was also confirmed as reducing nitric oxide and pro-inflammatory cytokines (TNF- $\alpha$  and IL-6) with lipopolysaccharide-activated murine macrophages [67]. Sauerkraut juice from fermented cabbage was valorized in sauerkraut juice powder (SJP) as a strong candidate for replacing NaCl salt in foods since it is rich in phenols, minerals, vitamins, sugars, and NaCl. Moreover, Janosone et al. (2022) showed that SJP conserved the organoleptic properties of foods and the sensory aspects of food when tested. Fermented dairy products also showed potential as functional foods and food additives. For example, deproteinized acid whey from Greek yogurt [70] was subjected to liquid–solid hydrocyclone technology to precipitate calcium phosphate and recover calcium and phosphorous minerals for milk fortification. Calcium phosphate is a food additive that is commonly employed as a baking ingredient, bread enhancer, and acidulant.

Fermented beverage residues generated from wineries and brewing beer are a source of flavonoids and other phenolic compounds, proteins, insoluble and soluble dietary fibers, and other phytochemicals, which have shown biological properties that are essential to ensuring human health, including (1) antioxidant activity [86,89,97,108–110]; (2) anti-hyperglycemic [87], anti-hyperlipidemic [88,89], and cardioprotective [92–94] effects; (3) anticancer potential [95,96]; (4) immunomodulatory activity [101–103]; (5) an *in vivo* satiating effect provided by grape-seed proanthocyanidin extract (a byproduct from wineries) [90]; (6) gut health balance [91]; (7) prebiotic/probiotic agents [99] for functional foods; and (8) antimicrobial effects [107,108] inhibiting Gram-negative and Gram-positive pathogenic bacterial activity, which is responsible for the most prevalent global foodborne diseases.

Acutely administered grape seed-proanthocyanidins were suggested as a beneficial satiating agent under the conditions defined in the study by Serrano et al. (2016). This study reported quite interesting findings, stating that proanthocyanidins without galloyl forms, such as those derived from cocoa extract, were not as effective as grape-seed-derived forms in stimulating the active glucagon-like peptide 1 (GLP-1), the most potent stimulator of glucose-induced insulin secretion [90].

Buttermilk, a byproduct obtained in the processing of cultured butter, was chemically characterized as a milk fat globule membrane (MFGM) rich in bioactive proteins and lipids, minerals, lecithin, and lactose [71]. Its consumption by normotensive individuals showed its potential as a functional food, due to an anti-hypertensive effect manifesting in moderately hypercholesterolemic men and women [71].

#### 4. Methods of Obtaining Products

Among the various extraction methods, high temperatures can cause the degradation of these phenolic compounds, generating a loss of bioactive activity, such as antioxidant or antibiotic activities [112]. Thus, to overcome such limitations, solid-state fermentation (SSF) has been shown as an alternative method capable of producing and facilitating the extraction of these compounds from residues and the wastes from several sources of fermented foods [65,77,97]. Such fermented waste can be used as a source of carbohydrates for various microorganisms, which go through the fermentation process and generate metabolites and products that can be extracted and employed in the food industry for

human health [113]. There are different methods of extracting bioactive compounds, with conventional methods such as maceration and decoction being replaced by green solvents (i.e., ionic liquids), supercritical fluids, and deep eutectic solvents. In addition, unconventional extraction methods, such as ultrasound-assisted extraction [63,107,108], pulsed electric fields [62], enzymes, autohydrolysis [86], hydrocyclone technology [70], thermocatalytic precipitation [69], and microwaves [99], are increasing. These advanced methods allow more efficient and sustainable extraction, reducing time and solvent usage. Extraction with supercritical fluids uses supercritical CO<sub>2</sub> as a solvent to extract bioactive compounds. Supercritical CO<sub>2</sub> has unique properties, combining the characteristics of a gas and a liquid, which allows the selective and efficient extraction of the desired compounds. Furthermore, supercritical CO<sub>2</sub> is considered a green solvent as it is non-toxic, non-flammable, and easily recoverable [114]. Green solvents, such as ionic liquids and deep eutectic solvents, are more sustainable alternatives to traditional organic solvents. These solvents have low toxicity and are biodegradable, which makes them more environmentally friendly. Furthermore, they can also improve the extraction efficiency and the quality of the obtained compounds. Table 1 displays the different sources of bioactive compounds and the extraction methods used to improve the yield of the extracted product.

Using efficient and sustainable extraction techniques, understanding the mechanisms of action, and ensuring the quality of the compounds will allow the development of more effective and safer products. Therefore, it is essential to continue investing in research and development in this area to explore the full potential of bioactive compounds in improving human health and well-being.

Ultrafiltration and membrane filtration technology has been widely reported for the separation and concentration of cheese whey protein [69], spent yeast protein, and bioactive peptides since it can be operated under gentle conditions, with low energy consumption, and without compromising the molecular structures and biological activities [98]. Spent yeast, the most frequent fermentation byproduct in brewing, can supply several bioactive compounds and ingredients: mannans and  $\beta$ -glucans. Oliveira et al. (2022) recently described a scalable and low-cost process to obtain yeast peptide extracts within a circular economy concept, using membrane filtration to recover peptide fractions (48.3% proteins and 86.4% essential amino acids) with high potential for nutraceutical applications as dietary supplements and functional foods.

#### *Waste Fermentation: Steps and Optimization Factors*

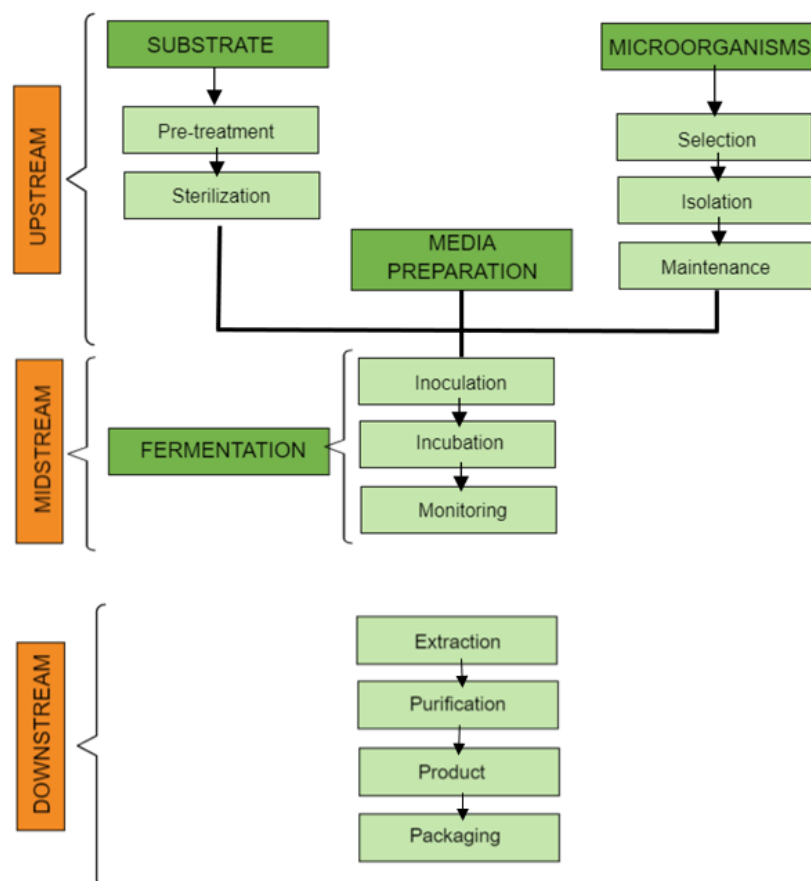
Fermentation is the process by which biomass residues are used as substrates for the metabolism of various microorganisms [115]. Figure 2 outlines the stages of this process and the monitoring and follow-up needed to obtain better results.

The upstream phase comprises the preparation of the substrate and the pre-treatment and sterilization processes, wherein the application of chemical, physical, biological, and combined methods have the purpose of hydrolyzing and separating the components of the lignocellulosic material to facilitate metabolism by microorganisms [115–117]. In addition, the choice of the reaction medium and the microorganisms to be used depends on the chosen substrate and the type of final product required [118,119].

In the midstream phase, the fermentation process occurs, and the treated substrate is inserted into the reaction medium, where the inoculum of microorganisms is introduced. From that moment on, the parameters of temperature, rotation, pH, time, and the presence or absence of oxygen are employed to synthesize products with high added value [118,120,121]. The microorganisms then metabolize the substrate by producing intracellular and extracellular enzymes that serve as catalysts for the growth and formation of intermediate compounds and specific products [120,122–124].

The growth of microorganisms within this reaction medium initially occurs through a “lag phase” of adaptation to the medium and parameters, followed by an “exponential phase” where the most significant growth and metabolization of biomass residues occur [125,126]. Afterward, there is a “stationary phase” where the synthesis and metab-

olization are stabilized and, finally, the “decay phase” of the process, where there is a decrease in the production of enzymes and, consequently, in the metabolization of the substrate and the reduced synthesis of products [126,127]. Finally, after the synthesis of products via fermentation, the downstream phase begins, which covers the extraction of the final product from the reaction medium. The purification and packaging of this product would be the final phase in the industry following commercialization [126,127].



**Figure 2.** Process steps of fermentation of residual biomass.

The pre-treatment processes of biomass residues aim at the structural breakdown of lignin and hemicelluloses, decrease the crystallinity present in cellulose to facilitate the action of hydrolyzing agents, for example, acids and enzymes, and increase the surface area by increasing the porosity of the structure [77]. They must also provide for the formation of sugar, avoid the deterioration of carbohydrates, avoid the formation of inhibitory products for the subsequent conversion processes that the biomass will undergo, such as fermentation, and lastly, which is of paramount importance for all the production chain, should have an excellent cost–benefit ratio [128–130].

Drying is the process of evaporating off the moisture present in the biomass, which can be carried out either at room temperature (in the open air) or by using a heat source to accelerate the process [88,89,92–94]. In some cases, this method is also used to separate cellulose from hemicelluloses and lignin because when lignocellulosic biomass is subjected to a temperature range of between 150 and 180 °C, the partial solubilization of these two components occurs, facilitating the separation of cellulose [52]. As an alternative to the heat source, the use of lyophilization also removes moisture from the sample, converting water into ice without passing through the liquid phase [72,73,95,96]. Grinding [88,92,93] reduces the particle size of biomass residues, increasing the surface area and permeability of the agents that will act as part of the conversion process into bioproducts.

Dilute acid hydrolysis [77] uses a dilute acid as a solvent, usually sulfuric acid, nitric acid, phosphoric acid, hydrochloric acid, and carbonic acid, under controlled temperature and concentration conditions for a predetermined time. This pre-treatment is intended to increase the enzymatic digestibility of cellulose, facilitating the conversion of, for example, glycans into sugars to facilitate fermentation and bioproduct synthesis [45,131,132]. In turn, hemicellulose is practically hydrolyzed, and cellulose remains practically solid, meaning that the method hydrolyzes hemicelluloses more easily than cellulose [133–136].

The biological method encompasses enzymes and microorganisms, working together to degrade the cell wall fiber and increase access to the substrate for fermentation. This technique is widely studied because it is less expensive and more environmentally friendly as it uses mild temperature and pressure conditions and does not include chemicals that could generate toxic compounds. On the other hand, it needs continuous monitoring and process optimization, due to the specificity of microbiological metabolism, which makes the process slower than other techniques [51,81,129,137–140].

In addition to all the methods mentioned above, there is the possibility of combining different techniques to improve the biomass hydrolysis step [141]. For example, a physical (grinding) method coupled with a chemical (acid) method, as adopted by Quintero, Rincón, and Cardona (2011) [52], since the acid would be more likely to catalyze hydrolysis in the already crushed sample, lowering the temperature of the reaction medium. The growth of the microorganism and, consequently, the increase in metabolism due to the greater surface area of the substrate occurred with greater intensity when using an alkaline pretreatment [64], followed by alkaline combined with ozone pretreatment, ozone pretreatment, and, finally, pre-treatment with high-temperature water. Thus, the highest level of cellulose degradation (35.38%) was observed in the alkaline pretreatment group ( $p < 0.05$ ), while the maximum lignin loss of 28.10% was achieved in the pretreatment group with ozone, which shows the importance of combining processes to achieve higher fermentation yields.

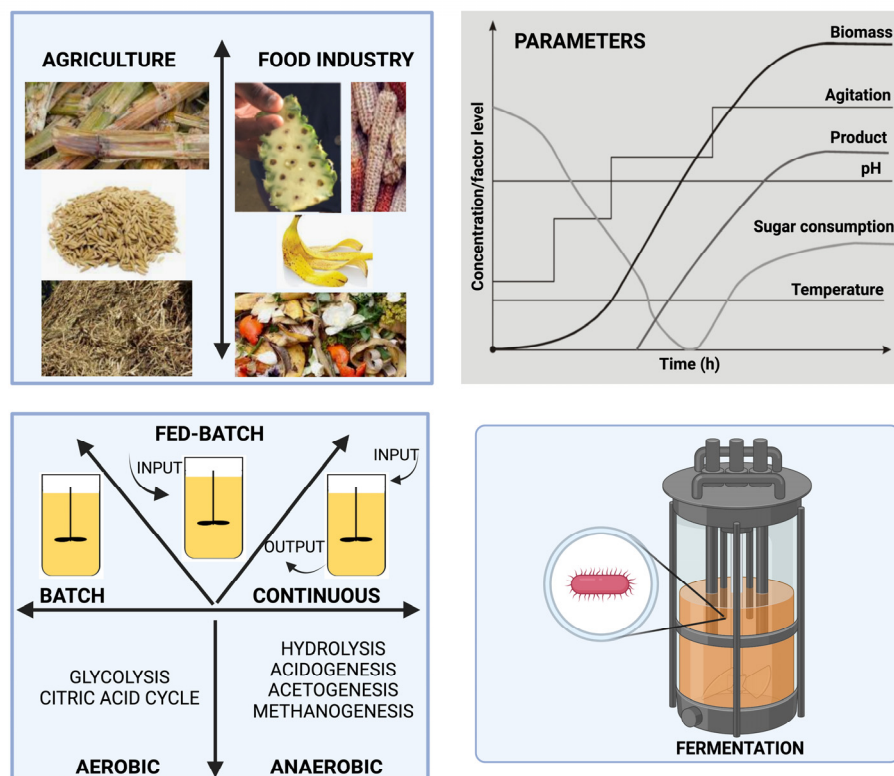
Biomass already has a high market value due to its use in the food industry. Several byproducts and wastes from certain fermented foods have been highlighted as valuable sources of fermentable sugars, such as insoluble residues and dregs (okara) from fermented soybean products, bread wastes, grape pomace (pulp, skins, seeds, and stems), and wine lees from winery byproducts, along with brewing residues (spent yeast, spent hops, and barley malt rootlets) and buttermilk from cultured butter.

In this way, the fermentation of residues from fermented foods emerges as a new technique to manage and take advantage of this biomass. Therefore, biomass residues from fermented dairy products have been widely studied and employed as a substrate to synthesize high-value-added products such as biofuels, antioxidants, biopolymers, and polyphenols.

Lignocellulosic residues have a high content of carbohydrates, proteins, lipids, cellulose, lignin, hemicelluloses, and lipids, among other substances and minerals that can be metabolized by various microorganisms [65,66,82,84,86,97]. Figure 3 represents some sources of residues, the culture medium parameters, and the types of fermentation that can be used to generate several commercial products. Thus, understanding the different chemical characteristics of the biomass and the target product is essential for the biorefinery process and, consequently, for synthesizing a product with high added value.

There are two main types of fermentation, namely, aerobic and anaerobic fermentation. These can also be divided according to the reactor's substrate feed type: batch, fed-batch, and continuous. Batch fermentation occurs when there is no addition of substrates or removal of a product during the process until fermentation is finished, causing an accumulation of byproducts that can increase the toxicity of the fermentation medium [79,142,143]. The fed-batch type of fermentation is one in which a specific feed is introduced during the fermentation process, thus allowing a greater concentration of cells, and is the form of processing most widely used by industries [77,97]. Adding substrates to the fermentation medium allows microorganisms to continue metabolizing and generating products [64,69,80,82]. Continuous fermentation, in turn, occurs when there is the continuous

addition of substrate and a continuous removal of products from the medium, resulting in a steady-state operation where the rate of cell growth and the concentrations of metabolites remain constant. However, due to the constant entry and exit of substances from the fermentation broth, the chance of contamination is very high, which leads to a decrease in the reaction yield.



**Figure 3.** Sources of residues and wastes, the associated parameters, and the types of fermentation according to its valorization in commercial products.

In addition, all processes have specific reaction parameters, such as pH, temperature, agitation, microorganisms, cell density, and the presence or absence of aeration, which define whether the process will comprise aerobic or anaerobic fermentation [64]. As a result, we accept that numerous factors can and will influence the final yield of the fermentation product, making process optimization and the analysis of its variables crucial for the success of the process in laboratory and industrial applications.

## 5. Applications of Valuable Compounds from Fermented Residues

The fermentation process favors the synthesis of products with high added value. However, the use of fermentation also leads to the production of fermentative residues containing metabolites, extracellular enzymes, and other byproducts generated by microbiological metabolism. In addition to presenting the novelties found in bioproducts, this article aims to show the possibility of processes where the waste that is generated throughout the various stages can be reused to produce outstanding products in the industry, both environmentally and economically. Thus, several studies delve into the reuse of these fermentative residues, their physicochemical characteristics, and the various applications for which they can be reused.

### 5.1. Animal Feeding

Very recently, phenolic compounds from rich-grape marc (or pomace) from the País winery, an abundant resource suggested as having a possible in animal feed, were considered for potential positive environmental effects on enteric CH<sub>4</sub> emissions in Chile by

Suescupun-Ospina et al. (2023) [85]. The authors evaluated the effect of the oven- and freeze-drying process and showed that oven-dried grape marc had the highest proanthocyanidin content and lower CH<sub>4</sub> production [83].

## 5.2. Biofuels

The production of cleaner fuels can be accomplished by improving the refining of environmentally friendly technologies and by adding synthetic fuels or ethanol [48]. Within environmentally friendly technologies, we use residual biomass to synthesize bioethanol through the fermentation process of substrates with a high carbohydrate content for degradation. The use of sugarcane juice to synthesize bioethanol is already a reality. However, this substrate competes with the food industry [144]. To resolve this problem, other biomass resources, such as byproducts and wastes from fermented food factories, stand out as substrates since they are also rich in the carbohydrates needed for fermentation [77,79,97].

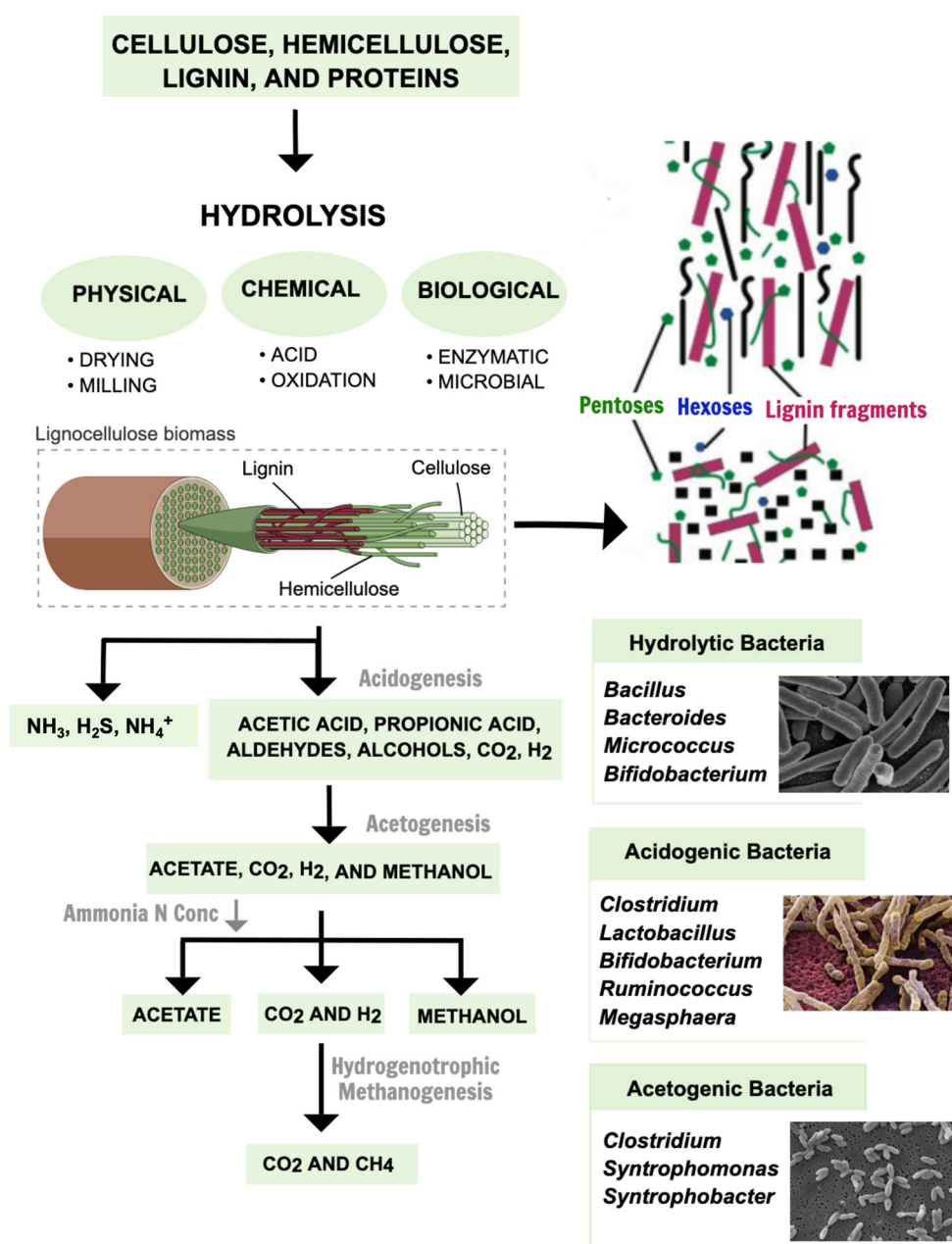
The cellulose and hemicellulose in lignocellulosic biomass can be chemically or enzymatically degraded, generating hydrolyzed sugars that provide raw materials for microorganisms to act upon during fermentation [145]. Lignin, the third component, is formed by aromatic polymers, and its catabolism generates a mixture of aromatic components that can be enzymatically converted into a set of organic molecules in the form of D-3,2-butanediol [79,143], methane [64], poly(3-hydroxybutyrate) (PHB) [97] and PHA [69], and tartrate or tartaric acid [97].

Unlike bread waste, which is rich in fermentable sugars for H<sub>2</sub>, ethanol, methane, and recovery, some biomass residues, such as wood bark, are not easily converted into biofuels through the application of microorganisms. The use of the gasification process with these residues produces a synthesis gas (syngas) that offers a solution to this problem, such as the conversion of CO and H<sub>2</sub> (which are present in the syngas) into multicarbon compounds [146]. Such an approach may be extended to other fermented biomass residues.

The production of fuels covers the use of various residues, both from agriculture and the food industry. Food waste occurs in large quantities worldwide; thus, anaerobic digestion can be employed, including H<sub>2</sub> in the fermentation stage [76] and CH<sub>4</sub> in the methanogenesis stage [77]. This process, also called dark fermentation, uses an environmentally friendly approach to solve the problem of food waste and delivery residue to synthesize industrial products. Several microorganisms can be used, including hydrolytic, acidogenic, and acetogenic bacteria, to form VACs, metabolites, CO<sub>2</sub>, CH<sub>4</sub> [64] alcohols [77], and H<sub>2</sub> [76]. The use of residues for H<sub>2</sub> synthesis is still being optimized for use on an industrial scale, which brings other possibilities for study and evaluation regarding the topic [147,148].

Moreover, it has already been proven that dual-stage H<sub>2</sub> production achieves 20% more biogas than single-stage production [149]. In the methanogenic phase, the VACs thus produced are transformed into CH<sub>4</sub> and are recovered as biofuel, whereby part of the methane remains dissolved and can be treated for application in biofertilizers [150]. Dark fermentation encompasses the use of waste to synthesize environmentally friendly products for industrial commercialization. Thus, its optimization is essential for food and agro-industrial waste re-usage [151]. Figure 4 exemplifies the synthesis steps of some biofuels via dark fermentation.

To produce a range of compounds such as acetate, ethanol, butyrate, and butanol, fermentation by microorganisms depends on acetyl coenzyme A (acetyl-CoA). The oxidation of H<sub>2</sub> to 2H<sup>+</sup> with H<sub>2</sub>O, or of CO with H<sub>2</sub>O to 2H<sup>+</sup>, provides the reducing equivalents for the reduction of CO<sub>2</sub> to form methanoic acid (HCOOH), from methylene tetrahydrofolate (CH-THF) to methenyl tetrahydrofolate (CH<sub>2</sub>-THF), from CH<sub>2</sub>-THF to methyltetrahydrofolate (CH<sub>3</sub>-THF), and from CO<sub>2</sub> to CO. Acetyl-CoA synthase/CO dehydrogenase catalyzes the formation of acetyl-CoA from methyl group bonding, CO group bonding, and coenzyme A (CoA). The metabolic pathways of acetyl-CoA reduction, which are involved in the fermentation of biomass conversion into a range of biofuel compounds, are displayed in Figure 5 [151–153].

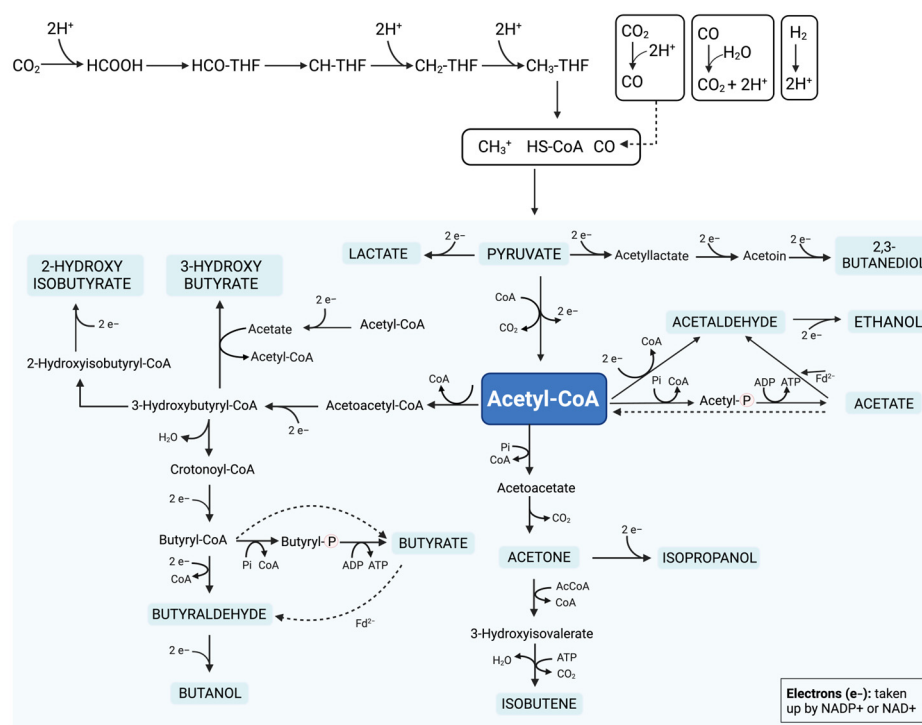


**Figure 4.** Synthesis steps for some of the biofuels obtained via dark fermentation.

Hydrogenogenic carboxydophilic microorganisms (HCM) conserve energy by synthesizing  $\text{H}_2$ , in which a monofunctional CO dehydrogenase oxidizes CO. The electrons from the oxidation process undergo the reduction of protons in hydrogen molecules through an energy-converting hydrogenase (ECH). Furthermore, ECH couples  $\text{H}_2$  to the membrane translocation of protons/sodium ions, which generates an ion gradient, driving ATP synthesis. HCM use is independent of the acetyl-CoA pathway [151–153].

Bread and bakery product wastes have an interesting composition (up to 70% of carbohydrates, mainly starch), which is attractive as a nutrient source for microorganisms and can improve the circular economy by reusing energy-rich food wastes for gas production [77] and energy recovery [76]. Bread waste was employed to produce organic acids by lactic fermentation (*Lactobacillus amylovorus* DSM 20532) and was sequentially employed for hydrogen ( $\text{H}_2$ ) production ( $3.1 \text{ mol H}_2 \text{ mol}^{-1} \text{ glucose}$ ) and energy recovery ( $54 \text{ MJ t}^{-1} \text{ dry waste}$ ) by photo-fermentation (*Rhodospirillum rubrum* 42OL) [76]. Using biorefinery concepts and a circular economic approach, bread waste was employed to

produce bioethanol [77], butanediol [78,79], and biomethane [77]. The fermentable sugars from out-of-date bread supplied by local supermarkets in the United Kingdom were first submitted to acid/enzymatic saccharification to recover glucose-rich hydrolysates, which were sequentially fermented with *Saccharomyces cerevisiae* KL17 to produce ethanol with higher efficiency, using the fed-batch mode of cultivation [77]. In further experiments, Narisetty et al. (2022) [77] employed solid residues (from acid/enzymatic hydrolysis, along with the respective SSF residues after ethanol production) under anaerobic digestion to yield biomethane, revealing a biochemical methanation potential of up to 379 mL CH<sub>4</sub>/g. Likewise, other studies have previously reported glucose-rich enzymatic hydrolysate from bread waste being submitted for fermentative production by *Bacillus amyloliquefaciens* [78] and by *Enterobacter ludwigii* [79] to accumulate D-2,3-butanediol.



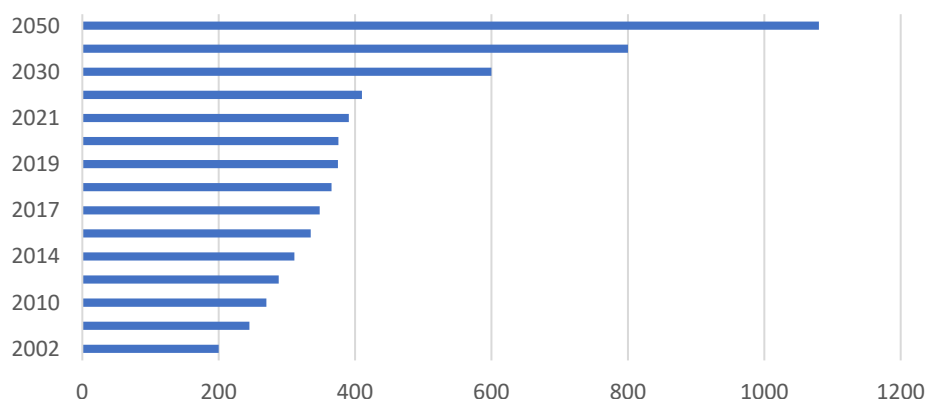
**Figure 5.** Metabolic pathways of acetyl coenzyme A (acetyl-CoA) reduction, involving the fermentation of biomass conversion into a range of biofuel compounds.

### 5.3. Biopolymers and Bioplastics

The continuous production of plastics from the petrochemical industry has generated an exorbitant amount of waste for disposal. Such waste is part of approximately 140 million tons of plastics produced in 2022, and an estimate of plastic waste in the ocean has reached a level of 150 million tons [154,155]. Figure 6 shows a forecast for global plastics generation from 2002 to 2050 [156,157].

This challenging scenario has motivated researchers to evaluate biodegradable plastics produced by the fermentation of microorganisms to replace petroleum-based plastics [158–161]. The production of biopolymers from microbial fermentation is a less expensive, adaptable, and environmentally harmless process when compared to producing plastics made from fossil fuels. However, bioplastics are susceptible to water hydrolysis, which reduces their strength and durability [161,162]. The synthesis of bioplastics, such as polylactic acid (PLA) and polyhydroxyalkanoates (PHAs), derives from renewable sources such as food waste, lignocellulose residues, and vegetable oils [161,162]. The purpose of studies concerning bioplastic production through microbial fermentation is to create plastic with mechanical, physical-chemical, and thermal properties to match the performance of fossil-based plastics.

On the other hand, the high biodegradability of bioplastic makes it environmentally friendly, reducing plastic waste due to its shorter product lifetime [162,163].



**Figure 6.** Forecast of plastics use generated worldwide from 2002 to 2050.

Although it is possible to produce synthetic biodegradable polymers from petrochemical byproducts such as polycaprolactone (PCL) [164,165], several methods of bioplastic synthesis from renewable resources use natural polysaccharides (lignin, cellulose, and starch), proteins, and lipids. Other examples include polyhydroxyalkanoates (PHA) [154,166], polyhydroxy butyrate (PHB) [155], and poly(3-hydroxybutyrate-co 3-hydroxy valerate) (PHBV) [158,167]. The third alternative uses microbiological fermentation, whereby lactic acid is synthesized and polymerized to form a PLA-biobased product [14].

Under biorefinery concepts, wine lees (the liquid and solid residual fractions, remaining streams, and alcohol-free nutrient-rich liquid) from producing Merlot red wine were employed as a bioresource to produce bioplastic poly(3-hydroxybutyrate) (PHB) synthesis. This included the production of generic fermentation feedstock (ethanol, phenolic compounds, and tartaric acid) [97]. Thus, the crude nutrient-rich hydrolysate from enzymatic hydrolysis was used to initiate PHB production with high efficiency using the strain *Cupriavidus necator* DSM 7237, while the hydrolysis of pretreated lees was performed using crude enzyme consortia via solid-state fermentation with *Aspergillus oryzae* [97].

Demirci et al. (2019) and Jung et al. (2022) produced paramylon and xanthan gum biopolymers from fermentable sugars obtained and extracted from bread waste (stale bread that remained unsold and returned goods from shops). After the enzymatic hydrolysis step, the glucose thus obtained was employed in both studies as a bioresource: i) as a carbon substrate for the heterotrophic cultivation of the microalgae *Euryglana gracilis* to produce the carbohydrate paramylon [80]; ii) as a carbon source in the fermentation of *Xanthomonas* spp. to obtain the xanthan gum polysaccharide [82]. Xanthan gum is widely used in the food industry as a common additive to stabilize and emulsify food products.

Although up to 50% of residual whey from cheesemaking is being valorized as a source of high-added-value compounds in food/pharmaceutical factories, mainly as proteins with high levels of biological properties, lactose, lactic acid (LA), and minerals, there is still a high proportion of this whey that is discarded, thus promoting environmental pollution [168]. An integrated cheese whey valorization process [69] utilized the wastewater from cheesemaking to produce several added-value products, including lipid recovery via thermocalcic precipitation, protein recovery via ultrafiltration, and lactose valorization through biological processes to obtain polyhydroxyalkanoates (PHA). Therefore, this circular economic approach can provide lactose as a carbon source for biomolecules, lipids, and proteins to produce bioplastic PHA for use as a flame retardant, along with whey protein concentrates for the food industry. It can also potentially obtain lactic acid (LA), a monomer of PLA derived from natural sources. Thus, LA is produced using the bacterial fermentation of fermentable biomass. Likewise, reducing sugars from bread wastes drawn from Indian bakery wastes were simultaneously submitted to saccharification and SSF by

LAB, suggesting bread wastes as potential candidates for lactic acid production [84]. Those findings are interesting because PLA ( $C_3H_4O_2$ )<sub>n</sub> is a biodegradable thermoplastic that can be synthesized using residues such as sugarcane bagasse, corn cobs, starch, and food waste [42,169]. PLA is a well-known biopolymer with many applications and properties, such as biodegradability, biocompatibility, elasticity, moldability, and rigidity. In addition, it is the first polymer produced from renewable sources to be marketed for various applications, such as for grocery bags and food packaging [42]. PLA synthesis has, as an initial step, the production of LA by the fermentation process. Lactic acid comes in the form of a white powder or yellow liquid. Its structural formula incorporates chiral carbon, which leads to the formation of a left-handed ( $L^+$ ) and a right-handed ( $D^-$ ) structure. The chemical activity of the LA molecule depends on the acidity in an aqueous medium and the functional activities of groups present in the chemical structure, such as the carboxyl and hydroxyl groups, which promote a wide variety of chemical reactions [13,169]. The global market for PLA is constantly expanding, which causes an increase in its demand due to its widespread use in the packaging, agriculture, and transportation industries. Therefore, an efficient manufacturing method with reduced production costs is needed so as to evaluate other methods that can be employed when using agricultural and food waste [161].

#### 5.4. Nanomaterials

Nanotechnology is being applied in several areas and sectors of industry, such as food, cosmetics, and chemistry. Some studies have demonstrated the importance of nanomaterials based on fermented food residues or byproducts and several applications on health and food. A nanocomposite based on kefir films has garnered research attention due to the electrospinning and film-forming abilities of the kefir polysaccharides recovered from kefir grains. Kefiran, an exopolysaccharide, derived from the microflora of kefir grains, which are used to produce fermented milk beverages, has recently attracted research attention due to its biological properties and its potential for use in the nanomedicine and food packaging industries [30]. Recent investigations reported a kefir biopolymer, manufactured via electrospinning, to produce kefir nanofiber [170,171]. Kefiran nanofibers are potentially valuable for encapsulating bioactive ingredients in food [172], as matrix for probiotic/drug delivery [72–74,173,174], and scaffolds for regenerative medicine and tissue engineering [170].

#### 5.5. Other Applications Using Fermentative Residues

Fermentation residues from Ca/Fe-rich antibiotics, for example, can be considered very hazardous but, at the same time, can be recycled and applied in adsorption resources by using biochar [175]. Despite the possibilities, such hazardous wastes have seldom been explored and require several stages of waste preparation. In one study, residual vancomycin and antibiotic-resistant genes were fully exposed during pyrolysis. The process showed fast kinetics and a maximum adsorption rate of 102 mg *p*/g. Ca and Fe represented active sites that helped in the adsorption process. Therefore, the use of biochar produced from fermentative residues can be used in the treatment of wastewater to absorb contaminants. Furthermore, biochar can be used as a phosphate fertilizer, as it promotes seed germination (germination rate: 96.7% vs. 80.0% in the control group,  $p < 0.01$ ) and seedling growth (shoot length was increased by 57.9%,  $p < 0.01$ ) due to the slow release of the available phosphate. Consequently, hazardous waste was turned into phosphate fertilizer, adding to the benefits of biomass reutilization, and recovering phosphate from wastewater. Biochar from spiramycin (SPI) fermentation residues (SFR) in China, which are dangerous, can also be cited here. The pyrolysis method was adopted to convert SFR to biochar to remove SPI from wastewater, and the results showed no residual SPI, indicating the achievement of SFR detoxification. Furthermore, after recycling 5 times, the SPI removal efficiency was still greater than 80.0%, indicating a promising method for SFR disposal [176].

Lipstatin, a fermentative residue (LFR) from the pharmaceutical industry, can be discarded in the soil after the composting stage due to its high content of organic matter.

Generally, residues from such fermentation processes are composed of a high amount of organic matter, which is of high importance in fertilization. The pH value of soil fertilized with composted LFR slightly decreased, without the accumulation of lipstatin. Soil nutrients, including the available phosphorus, potassium, organic matter, and soluble organic matter, increased significantly in soil fertilized with composted LFR, providing excellent application as a biofertilizer [177]. Likewise, the synthesis of doramectin offers another interesting example of the use of fermentative residue from the pharmaceutical industry, which generates a high rate of residues with a large amount of organic matter, resulting in their applicability in agricultural fertilization [178].

## 6. Challenges and Future Perspectives

Although bioactive compounds and bioproducts have shown great potential in the pharmaceutical and food industries, there are still challenges to be faced. These challenges include the efficient and sustainable sourcing of compounds, the standardization and quality control of products, understanding the mechanisms of action, and ensuring the safety of compounds.

**Reduced Greenhouse Gas Emissions:** Biofuels derived from biosources can reduce greenhouse gas emissions, compared to products derived from fossil fuels. For instance, biofuels and bioplastics have the potential to lower carbon emissions. **Circular Economy:** Bioproducts based on biorefinery concepts can improve the circular economy by promoting the reuse and recycling of materials. Biodegradable bioplastics, for example, can replace traditional plastics and reduce plastic pollution, also producing safer food packaging materials. **Health and Wellness:** Several valuable compounds from fermented food wastes and byproducts with antimicrobial/antioxidant activity can be used in the production of functional foods and dietary supplements, to ensure human health by means of cancer prevention and the management of several endocrine/metabolic disorders (i.e., hypertension, type 2 diabetes, hypercholesterolemia, and cardiovascular diseases), employing novel drug delivery systems for pharmaceutical and cosmetics purposes. For example, probiotics and vegetable fermentation-based ingredients have gained popularity in the food and beauty industries. Bioactive compounds have various health benefits, including antioxidant, anti-inflammatory, and antimicrobial properties. The producers are interested in developing functional foods, dietary supplements, and nutraceuticals. **Biopharmaceuticals:** The biopharmaceutical industry continues to grow, with bioproducts playing a significant role in developing vaccines, monoclonal antibodies, and other therapeutic agents. In this context, kefir-based nanomaterials are promising candidates for biomedical applications and tissue engineering. **Research and Innovation:** Advances in biotechnology, synthetic biology, and genetic engineering are opening up new possibilities for synthesizing and producing bioproducts. Researchers are exploring novel techniques to improve yields, reduce production costs, and expand the range of bioproducts. **Pharmaceuticals:** bioactive compounds are valuable in terms of drug discovery. They serve as the basis for many pharmaceuticals, including antibiotics, anticancer agents, and drugs to manage various diseases. Research in this area can lead to the discovery of new therapeutic agents. **Natural Product Chemistry:** The study of active compounds involves natural product chemistry, a rich source of chemical diversity that is of great importance for drug discovery. Advances in analytical techniques and compound isolation methods contribute to discovering new bioactive molecules. **Agriculture and Crop Protection:** Bioactive compounds can be used for pest control, disease management, and improving crop yields. This can reduce the reliance on synthetic chemicals and promote sustainable agriculture. **Biotechnology and Genetic Engineering:** Advances in biotechnology, including genetic engineering and synthetic biology, offer the potential to enhance the production of active compounds through microbial fermentation or plant engineering. **Regulatory Support:** Regulatory agencies in many countries recognize the great value of active compounds and provide guidelines and support for their development and use.

The advancement of extraction technologies, such as supercritical fluids and green solvents, will allow a more efficient and sustainable recovery of bioactive and other valuable compounds. Furthermore, developing more advanced analysis methods and understanding the compounds' mechanisms of action will open up new opportunities for using these substances in industry.

## 7. Conclusions

In summary, the search for agro-industrial and fermented food residues as sources of bioproducts and bioactive compounds is growing; studying different fermentation processes and mechanisms has proved to be very effective in terms of costs and industrial yields. The fermentation process is very complex and needs specific optimization methods for each type of bioproduct analyzed. Therefore, searching and studying these diverse methods has become fundamental for industrial and technological expansion. The generation of waste is a matter of worldwide concern. Thus, making applications available for such sources enables remarkable commercial growth, generating products with high-added value for industry and society. Since kefir, a coproduct obtained from the kefir grains used to produce milk-fermented beverages, has demonstrated enormous potential to be applied in nanomedicine, other residual biomass derived from fermented foods is also expected to be investigated as a potential source for developing new bioproducts for health and food purposes.

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