

Review

Sustainable and Health-Protecting Food Ingredients from Bioprocessed Food by-Products and Wastes

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Abstract: Dietary inadequacy and nutrition-related non-communicable diseases (N-NCDs) represent two main issues for the whole society, urgently requesting solutions from researchers, policy-makers, and other stakeholders involved in the health and food system. Food by-products and wastes (FBPW) represent a global problem of increasing severity, widely recognized as an important unsustainability hotspot, with high socio-economic and environmental costs. Yet, recycling and up-cycling of FBPW to produce functional foods could represent a solution to dietary inadequacy and risk of N-NCDs onset. Bioprocessing of FBPW with selected microorganisms appears to be a relatively cheap strategy to yield molecules (or rather molecules mixtures) that may be used to fortify/enrich food, as well as to formulate dietary supplements. This review, conjugating human health and sustainability in relation to food, describes the state-of-the-art of the use of yeasts, molds, and lactic acid bacteria for producing value-added compounds from FBPW. Challenges related to FBPW bioprocessing prior to their use in food regard will be also discussed: (i) loss of product functionality upon scale-up of recovery process; (ii) finding logistic solutions to the intrinsic perishability of the majority of FBPW; (iii) inserting up-cycling of FBPW in an appropriate legislative framework; (iv) increasing consumer acceptability of food and dietary supplements derived from FBPW.

Keywords: dietary inadequacy; nutrition-related non-communicable diseases (N-NCDs); food by-products and wastes; fiber; antioxidant activity; bioprocessing; yeasts; molds; lactic acid bacteria; novel foods

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1. Introduction

Nowadays, “World food security = sustainable production of food” seems to be a multi-unknown impossible equation. After the Second World War, the demand for affordable, convenient, and easier to cook food has had a continuous increase and the content of highly processed foods in modern diets has been growing, especially in Western Countries [1,2]. However, dietary inadequacy represents an issue for all the World population. This issue regards not only vulnerable groups, such as infants, pregnant and lactating women [3], elderly [4], individuals that must exclude some foods from their diet (i.e., celiac subjects) [5], but also apparently healthy subjects [6]. Among various nutrients, fiber is often not uptaken in sufficient amounts with diet. For instance, a cross-sectional study reported that in 162 Irish adults aged 65 years, fiber deficiency was the most common one after vitamin D [7]. Importance of fiber for human health has been highlighted by the WHO recommendation to intake more than 25 g of fiber per day.

Besides dietary inadequacy, the increasing numbers of deaths due to nutrition-related non-communicable diseases (N-NCDs) such as diabetes, hypertension, cardiovascular and neurodegenerative disorders alert consumers of the relationship between nutrition and health [8–14]. N-NCDs, as well as several other chronic diseases, are triggered by oxidative damage that induces chronic inflammation [13]. The growing awareness of the strict link between nutrition and health stimulates consumers to be curious about healthy eating and the beneficial effects of nutraceuticals and functional food, such as those with high antioxidant activity, on diseases prevention [14,15]. Within this framework, the consumer is viewed as a subject interested in the cultural value of products rather than the value of their function and utility. At the same time, careful consumers are represented as active players within the market, where they exercise their freedom to move in search of natural, sustainable (and possibly organic) food and beverages.

Food wastage represents a global problem of increasing severity, widely recognized as an important ever-growing unsustainability hotspot, gaining rising awareness in recent years [15–18]. The definitions of “food waste” (FW) and “food losses” (FL) within the supply chain have been the subjects of a long debate among related scientist groups and inside institutions. The Food and Agriculture Organization (FAO) “Global Initiative on Food Loss and Waste Reduction” aims to coordinate and enhance the information exchange, collaboration, synergy, harmonization of strategies and methodologies worldwide [19]. Inside this framework, FAO proposed common definitions of FL and FW as global references for any stakeholder and researcher dealing with food by-products and wastes (FBPW) [20]. In particular, FL is intended as “the decrease in edible food mass throughout the part of the supply chain that specifically leads to edible food for human consumption”, while FW is the removal from the food supply chain of food still suitable for consumption left to spoil or expire, in general by the final consumer at household level. In this review, the authors intended as FL the product losses that occur in the upstream phase of the supply chain (agricultural production, postharvest period, manufacturing and retail), and as FW the downstream stages of the Food Supply Chain (FSC) in the hospitality industry (canteens, restaurants, hotels) and households.

FBPW encompasses food by-products or secondary products originally intended for human consumption, but not transformed in their specific supply chains due to technical limitations or market failures. However, food by-products could be a valuable source of bioactive compounds and fibers that, being properly recovered and extracted, may be valorized as high nutritional value food ingredients, supplements and/or nutraceutical formulations [18,19]. These substances can be used primarily in processed or packaged foods for various purposes: to provide compounds that limit the risk of onset of N-NCDs; to improve nutritional content or texture; to prolong shelf life; to control spoilage microorganisms or as substitutes for synthetic additives.

Food industry seeks to reduce the production of FW in relation to the different stages of the supply chain and products. This is fundamental to define both the management strategies for the reduction of FW and the interventions for the recovery of new potentially bioactive compounds [21]. Particular attention has to be devoted to specific FBPW amount, location and transport mode and qualitative aspects strongly affecting costs and quality of bioactive compounds and that will be quite different according to production phases and levels of the supply chain organization [22].

From an environmental perspective, food production has significant environmental impacts such as FL during primary production, processing of raw materials, manufacturing, transportation, storage, distribution and, finally, disposal in landfills [23]. It contributes to the Green House Gasses (GHGs) emissions that negatively affect carbon footprint [16]. Therefore, FL reduction and/or recovery as a source of innovative food ingredients may improve resource use efficiency in a transition towards a circular economy [23,24].

The reduction of FBPW is perfectly consistent with many Sustainable Development Goals (SDGs). In particular, SDG 12 claims to be able to halve per capita global FW at the

retail and consumer levels and reduce food loss along production and supply chains (including postharvest losses) by 2030. In addition, the “Zero Hunger goal” (SDG 2) aims to end hunger, achieve food security and improve nutrition, promoting sustainable agriculture. Reducing FBPW may also contribute to the achievement of SDG 6 (sustainable water management), SDG 13 (climate change), SDG 14 (marine resources), SDG 15 (terrestrial ecosystems, forestry, biodiversity), among other SDGs.

European Waste Framework Directive (WFD) provided the legislative framework for the appropriate management of ranking options in order of priority in a waste hierarchy [25]. This regulatory framework prioritizes the reduction and prevention of FW reducing losses at source or by donations to people in need of food surplus still fit for human consumption. As a second option, actions aimed to repurpose and recycle (e.g., animal feed, industrial use, composting and valorisation as source of high-value bioactive and nutraceutical compounds) are considered [15,19,25].

The overall aim of this review is to analyze the opportunities to obtain ingredients and/or bioactive compounds from microbial processing of FBPW, improving the nutritional aspect of food and/or designing novel functional foods targeted to prevent N-NCDs. An overview on quantification, economic, environmental, and social impact of FBPW will be provided. Besides that, a comprehensive understanding of the potential role of microorganisms in FBPW transformation will certainly open minds, in view of environmental protection and contributing to achievement of sustainable food security.

2. Amounts, Costs, and Environmental Impacts of Disposal

2.1. FW Quantification at European Union (EU) Scale

Despite the increasing interest in the FW problem, there is a lack of knowledge regarding the real consistency of FW, especially concerning values disaggregated per FSC stage and per food groups. A consolidated framework for FW quantification in the EU is still not well defined [21,22,26]. Currently, the amount of food globally lost or wasted is estimated at about 1.3 billion tons per year [18,20,27] and the literature review shows that results for EU waste generation have a wide variability. Corrado and Sala [22] reported a production ranging between 158 and 298 kg/year/capita. The results of FUSIONS project, based on waste data collection and analysis in EU Countries, estimated that in 2012, nearly 20% of the total food produced is wasted, which corresponds to 88 million tonnes (Mt) of FW [28], including edible and inedible food parts and representing a waste of about 173 kg/person/year. This value has been recently used as a reference for policy-making (e.g., in the Farm to Fork Strategy) [29]. Nevertheless, other authors reported significantly higher results: a Mass Flow Analysis estimated a generation of about 129 Mt (fresh weight) of FW along the whole FSC, from an input of around 638 Mt primary food commodities [21,26]. The data variability is due to the different approaches used for the quantifications. The main accounting guidelines are Food Loss and Waste Accounting and Reporting Standard (FLW Protocol), based on a multi-stakeholder partnership (e.g., WRI, FAO, WRAP, UNEP, and WDCSD) [22], and the FUSIONS quantification manual [28]. The different studies and projects about FL in EU [17,19,21,28,30–34] adopted different definitions, system boundaries, and data sources (statistics or direct surveys) differing in scope, aims and methods and including a variable number of Countries with a high variability in food productions and processes. In addition, Country origin of data, supply chain and season in which the estimations have been carried out are further causes of variability.

Many authors performed analysis of a FSC system, highlighting the way the generation of waste material (FL, organic waste, or FW) may affect the different phases of the production, distribution, and consumption of food [16,30,35–37]. According to the stage of the FSC, different characteristics are shown [38]: in general, FL from the upstream phases of the supply chain (i.e., production and processing) contain large quantities of raw waste of a few different types; on the contrary, those referred to the lower stages (e.g.,

distribution and retailing) contain lower quantities of residues, very differentiated by type [39].

In general, in low-income Countries, FL are higher at the upstream production phases (farming, postharvest and processing stages), whereas in high-income Countries, FL are higher at the end, namely at retail and consumer levels [16]. Estimated losses in farming and postharvest phases vary between 8.4% and 25% [21,28,30,40]. In the postharvest phase, the distinction between perishable and non-perishable foodstuffs is crucial [35]. In industrialized Countries, non-perishable food crops (e.g., maize, wheat, rice, sorghum and millet) losses are very low; oppositely, postharvest loss rates for perishable crops are higher and mainly due to quality and size standard inadequacy. Food loss and waste during manufacturing and industrial processing, varying between 12% and 39%, may be generated throughout the entire processing phase. The losses usually occur during transport and storage, washing, peeling, slicing, boiling operations, or may be due to process interruptions, contamination, inappropriate packaging or by sorted-out crops [16,36,37]. FW at distribution stage, ranging from 5% to 19%, are mainly generated by inappropriate transportation methods, unsuitable packaging, ineffective scheduling and agreements for the purchase and receipt of goods [32–34]. At the retail stage, waste generation may be related to a scarce ability to foresee the demand, mismanagement of inventories and warehouses, inappropriate conditions during transport, disposal of unsold food, inappropriate packaging, food policies and their interpretation, misunderstanding of labeling by consumers. The higher number of losses (33–65%) is related to consumption behaviors. Although the majority of waste is generated at retail level, it would be more logical to identify the manufacturing step as the best step for the optimal waste management, especially in view of the possibility of adopting circular economy strategies and/or obtaining high value compounds. In fact, the composition of the waste generated in the transformation phase is generally more homogeneous from the point of view of its chemical composition [41] and has a greater spatial concentration that facilitates the collection operations in view of subsequent treatments.

Some knowledge gaps emerged regarding the total waste breakdown per food product or product group. More discarded products (cereals, fresh fruits, and vegetables) are considered, and extra data are available with respect to animal-derived products [42]. On average, vegetables mostly contribute to the total waste amount (about 24%), followed by fruits (about 22%), cereals (about 12%), meat (about 11%), roots and tubers (about 11%) and oil crops (10%). Animal origin food, namely dairy, fish and eggs, represent the smallest part in volume of the total food consumption and contribute, respectively, to the total waste amount about 5%, 3% and 1%, respectively [21,22].

2.2. FW Economic Assessment and Costs

Economic estimation of FBPW follows two main approaches focusing on: (i) the production cost of the food wasted or (ii) its market price [42]. According to the results of the Waste and Resources Action Programme (WRAP), the costs for producers related to FW for EU Countries in 2012 were nearly 45 billion euros at production stage, about 35 billion euros at postharvest, processing and distribution phases and nearly 40 billion euros at the consumption phase [16,42]. In the absence of more up-to-date data reported in the literature, it is possible (starting from Eurostat statistics on the amount of waste for 2020) to estimate, by default, a total value for the FW of 155 billion euros, 110 billion euros being attributed to the household consumption, 43 billion euros to the postharvest, processing and distribution phases, and 2 billion euros to the primary phase. According to the FUSION Project, the estimated value of FBPW was around 143 billion euros [43]. The main part of this value depends on the consumption phase: household waste value has been assessed to be about 98 billion euros; postharvest, processing and distribution phases accounted for 43 billion euros; production loss costs have been estimated at 1.8 billion euros.

Studies dealing with management costs of food recovery or reporting attempts of modeling economic profitability of food recovery are still scarce [39,41]. Often, costs of FL are underestimated, despite it is generally recognized that good waste management may be crucial to improve profits and enhance the sustainability of FL reduction policies. Economic value of food waste and losses depends on volumes of products, on their location in market space, on transport action, and on the time which the evaluation is referred to [44]. Really, as many authors underlined [44–46], the economic importance of FL must be considered and evaluated in comparison to the cost linked to the loss-abating actions.

Profitability of all food chain members may be strongly influenced by two effective waste management actions: (i) the appropriate management of materials and energy involved in production that can effectively reduce production costs and environmental impacts; (ii) the recovery and the valorization of materials otherwise thrown away [47]. An efficient recovery, valorising and recycling of FBPW and wastewater may allow the production of high-value compounds which can be used in food, pharmaceuticals and cosmetics industries, as natural antioxidants, preservatives, and supplements to help prevent N-NCDs and dietary inadequacy [18,47].

2.3. FBPW Environmental Aspects

The environmental impact of FW has been mainly assessed using Life Cycle Assessment (LCA) approaches, applying top-down, (e.g., through input–output tables and related figures) or bottom–up approaches and using more detailed product databases from national statistics and/or surveys on consumption patterns to determine the waste global warming potential [48–50]. For Europe, relying on FAO Food Balance Sheets data, it was estimated that 31% of the total use of freshwater resources, 24% of cropland, and 25% of fertilizers for food production converge in losses [51]. Cereals make the greatest contribution in determining this impact, since for this crop the FSC losses correspond to almost 45% of the cultivated area. Fruits and vegetables contribute to losses of 19%, while pulses and oilseeds represent 30% and roots and tubers account for 6% [51].

In 2013, FAO defined food loss and waste carbon footprint as the total amount of GHGs that the products emit throughout their life cycle expressed in kg of CO₂ equivalents (eq) [52]. In terms of GHG, Europe contributes 15% for this impact, corresponding to an approximate carbon footprint of 495 million tons CO₂ eq and 700–900 kg CO₂ eq per capita and per year [17]. LCA allows to estimate carbon footprint in terms of GHG, defining the contribution of each phase of the FSC to the carbon footprint. For Europe, FAO estimated 18% contribution to the total emission from primary production, 18% from postharvest handling and storage, 15% from processing and manufacturing, 14% from retail and distribution and, finally, 35% from consumption. Regarding commodities, cereals, meat, and vegetable waste provides the highest contribution to the carbon footprint, accounting together for more than 60% of the carbon footprint. Cereals, meat, and horticultural product waste mostly contribute to the impact, as each group generates an emission of about 100 Mt CO₂ eq. The emissions linked to milk and dairy waste amount approximately to 40 Mt CO₂ eq. Lost and wasted roots and fruits each provide a contribution of about 30 Mt CO₂ eq.; oil crops and pulses, as well as fish and seafood, provide each an emission of about 20 Mt CO₂. Low emissions are related to pulses, with very low nutritive needs due to their capability to fix nitrogen from the air, and to roots and tubers, since their high yield per area shows low emissions of GHG per kg of product [17,52,53].

2.4. Social Issues

The impact of FBPW generated along the food production–consumption chain results from complex interactions between the individual sphere and external elements [54]. Among individual factors, some authors [16] stressed the difficulties of farmers and food processors to manage production, marketing and logistics, especially in small-scale enterprises with limited investment in infrastructure. In the agricultural phase, large quantities of losses may be generated by overproduction due to overestimation of market demand, unexpected market price fluctuations, and by the technical inefficiency of harvesting techniques, making the harvesting uneconomic. Moreover, the inadequacy of storage, cooling and packaging facilities may negatively affect the agricultural and processing phases. Other authors [36,55–57] underlined the role of socio-demographic factors, perceptions and understandings of FW, concerns about financial loss and environmental and social implications of FW. Household food-related practices and routines such as the frequency of purchase, the tendency to buy products on offer and the proper understanding of storage methods and expiry dates on the label are factors playing a key role in the generation of FW. In particular, the possibility of selling products beyond the date defined by the words “best before” could contribute to reducing waste. However, in many European Countries, a gap in legislation regarding this area still exists and the subject is still debated among lawyers. In addition, initiatives are multiplying to promote the purchase of products, often at a lower price, that, exclusively because of their external characteristics (such as size, shape, imperfect packaging, etc.), do not meet high quality standards, but retain their hygienic and nutritional properties.

Among external factors, national and local policies play an important role in supporting strategies implementing collection and recycling of FBPW, preventing landfilling and incineration, and facilitating the recovery and valorization of functional substances from waste in a circular economy approach [57]. Specific strategies are mainly represented by landfill and incineration taxes, economic incentives for FW reduction, re-design of municipal waste collection systems and awareness campaigns. Moreover, the regulatory framework [25] defines the conditions for the exploitation of waste for the extraction of high value-added compounds, ensuring traceability, safety, and sustainability.

The development of virtuous practices for reduction and valorisation of FBPW can considerably contribute to the rural, coastal and industrialized areas sustainable development. In particular, the creation of innovative supply chains for food residues, by-products and waste may represent investment and employment opportunities, fostering local development and supporting small-to-medium enterprises [58]. Nevertheless, consumers’ knowledge about nutritional and environmental advantages of foods enriched with by-products is still scarce, and their acceptability of foods supplemented with these new bioactive compounds and/or nutrients may be still low [59].

3. Microorganisms for Bioprocessing Food by-Products and Wastes

In the last decades, the demand to valorize and reuse FBPW for different fields increased all over the World. Traditionally, food by-products are reused for feed manufacturing or incorporated in agricultural soils. Nevertheless, their richness in bioactive compounds and nutrients alert the scientific community to their real value in different (e.g., cosmetic, nutraceutical or even pharmaceutical) fields. However, the recovery of bioactive compounds and nutrients from FBPW, applying safe, eco-friendly, and cost-effective extraction techniques that meet the social, economic, and environmental issues is a challenge. Although natural extracts are usually regarded as healthy, it is imperative to evaluate their safety, ensuring consumer acceptance and assessing the legislation compliance. Despite the fact that consumers are now more conscious of the effects of their habits on the planet, sustainability and circular economy concepts need to be more rooted in industries and even governments, alerting for the importance of

upcycling (the concept of reuse discarded material with the aim to create a product of higher quality or value than the original). Figure 1, a SWOT diagram, summarizes the strengths (S), weaknesses (W), opportunities (O) and threats (T) of the current management of FBPW. As it is possible to observe, topics such as sustainability, richness in bioactive compounds, biological properties, health impact or addition of value to residues are clearly the strength aspects that should be considered regarding the management of FBPW. The circular economy, coupled with the valorization concept, generation of new health claims and respective products and profit generation (not only for food and nutraceutical industry but also producers where the residues are generated) are the main opportunities identified. Nevertheless, this management is associated with several weaknesses, mainly safety concerns, absence of specific legislation at European level, consumer doubts (especially concerning safety and efficacy), reduced industry interest (clearly linked to consumer interests) and low reproducibility among different batches produced. Therefore, the actual threats are represented by the difficulty to develop new extraction techniques that ensure the obtainment of bioactive compounds, the demonstration of safety and efficacy of the final products, the scale-up processes to ensure reproducibility of the final products and, finally, the industry investment in equipment as well as the market to convince consumers of the efficacy of these products.



Figure 1. SWOT analysis for management of food by-products and wastes.

Presently, microbial processing of FBPW offers a good opportunity for both environmental protection and sustainability. Microorganisms, which have been routinely consumed as a part of fermented foods and more recently as probiotic dietary supplements, have the potential to provide a variety of solutions through different products and procedures. Compared with animals and plants, microorganisms double their biomass very rapidly, with short doubling time (e.g., 20–30 min for *Escherichia coli* and *Bacillus subtilis*, and about 90 min for *Saccharomyces cerevisiae*). In addition, cultivation of microorganisms requires less water/land and generates smaller carbon footprints to produce a unit amount of biomass, compared to crop/livestock farms. Another attractive point of valorizing FBPW with microorganisms is the lesser, if not absent, ethical issues compared with contemporary livestock farming. Therefore, microorganisms can be a promising food resource in the process toward making our food system more sustainable [60].

Nowadays, fermentation *sensu lato* is a well-designed biotechnology for manufacturing functional foods and dietary supplements. Fermentation, or rather bioprocessing, is highly dependent on the reciprocal interactions among microorganisms, but can result in a huge range of derivatives and/or enhance the availability of bioactive or nutritionally valuable compounds. Microorganisms and their enzymes cause changes in the chemical and physical properties of the material subjected to bioprocessing, be it high-quality raw matter or wasted food or food by-products. The selection of starters is

an imperative criterion for bioprocessing of FBPW to ensure that microorganisms efficiently use FBPW as growth substrate, without negatively impacting the safety of the fermented substrate [61]. With no reference to geographical origin, allochthonous are defined as the starters, isolated from specific raw matrices with the purpose of fermenting different types of products. Autochthonous starter cultures are defined as the starters isolated from specific types of raw materials to ferment the same raw matrix. Autochthonous starters showed higher performance compared to allochthonous starters, but not all the strains may guarantee the same performance during bioprocess [62]. Selection of starters for FBPW bioprocessing should be based mainly on their fitness for environmental (not rarely hostile) conditions [63]. For instance, tolerance to high concentrations of phenols represents an additional criterion for selecting robust starter candidates that could ferment by-products and waste of vegetable origin, particularly rich in phenols [63]. Overall, the starters must be adapted to large-scale cultivation in relatively inexpensive substrates.

Industrial applications of yeasts, molds and lactic acid bacteria (LAB) to produce biologically active compounds from FBPW will be treated in this section. Table 1 serves as an appetizer and summarizes the main metabolic pathways and enzymes involved during the fermentation of FBPW and their relevant outcomes.

Table 1. Main metabolic pathway and enzymes involved during bioprocessing of food wastes and by-products and their corresponding outcomes.

Food Waste/by-Product	Microorganisms	Metabolic Pathway/Enzymes	Effects	Ref.
Apple by-product	<i>Lactiplantibacillus plantarum</i> , <i>Lactiplantibacillus fabifermentans</i> , <i>Saccharomyces cerevisiae</i>	Phenolic compound metabolism (phenolic acid carboxylase and reductase)	Phenolic acids ↑, DPPH scavenging activity ↑, Antiradical and anti-inflammatory features in Caco-2 cell ↑	[18]
Apple pomace	<i>Phanerochaete chrysosporium</i>	Hydrolytic enzymes	Phenolic compound production ↑	[64]
Coconut water	<i>Rhodotorula rubra</i> <i>Xanthophyllomyces dendrorhous</i>		Levels of carotenoids ↑	[65,66]
Cocoa pod husk, cassava peel and palm kernel cake	<i>Rhizopus stolonifer</i>	Ligno-cellulolytic enzymes	Fiber and cyanide contents ↓, protein content ↑, radical scavenging activities	[67]
Papaya fruit waste	<i>Yarrowia lipolytica</i>	Lipases and proteases	Recombinant therapeutic proteins ↑, enzymes ↑ and antibodies	[68]
Olive Mill Wastewater (OMW)	<i>Magnusiomyces capitatus</i> <i>Yarrowia lipolytica</i>	Extracellular lipolytic activity Phenols degradation	Lipase activity ↑, olive oil concentration ↑ Citric and oleic acid production	[69,70]
Plum by-products	<i>Aspergillus niger</i> <i>Rhizopus oligosporus</i>	Cholesterol and fatty acid metabolism	Sterol esters and polar lipids ↑, Stimulator antioxidants ↑	[71]

Cellulose substrate	<i>Lactiplantibacillus plantarum</i>	Proteolysis	GABA production ↑	[72]
Maize by-products	<i>Lactiplantibacillus plantarum</i> , <i>Weissella confusa</i>	Cellular process/ Lipase activity	Phytic acid ↓, radical scavenging activity ↑, stability ↑, oxidative processes ↓	[73]
Barley by-products	<i>Pediococcus acidilactici</i>	Fatty acid metabolism (Hydratase)	Oleic, arachidic, eicosadienoic, behenic, and lignoceric fatty acids ↑, health-promoting features ↑	[74]
Wheat bran and cornmeal	<i>Mucor</i> spp.	Biosynthesis of secondary metabolites	γ-linolenic acid and β-carotene ↑	[75,76]
Wheat bran	<i>Saccharomyces cerevisiae</i>	Xylanase activity	Folate content	[77]
Wheat bran	<i>Kazachstania exigua</i>	Phenolic compound metabolism and hydrolytic activity	Level of folates ↑, free phenolic acids ↑, and soluble arabinoxylans ↑	[78]
Rice bran	<i>Issatchenkia orientalis</i>	Glycolysis	↑ Free phenolic content	[79]
Rice pasta	<i>Monascus purpureus</i>	Cellular process	Natural pigments ↑, Monacolin K ↑, citrinin ↓	[80]
Black rice bran	<i>Aspergillus awamori</i>	Glycoside hydrolase, polysaccharides degrading enzymes and esterase	Phenolic compound production ↑	[81]
Cheese whey	<i>Kluyveromyces marxianus</i> , <i>Kluyveromyces fragilis</i> , <i>Candida pseudotropicalis</i> , <i>Candida versatilis</i>	Lipolytic activity	Microbial mass production ↑	[82]
Whey	<i>Lactiplantibacillus plantarum</i>	Cellular processes	Bacteriocins ↑, shelf life ↑, growth of <i>Penicillium expansum</i> and <i>Penicillium brevicompactum</i> ↓	[83]
Yogurt whey	<i>Lactocaseibacillus casei</i>	Emden–Meyerhof–Parnas pathway for glycolysis	Lactic acid production ↑	[84]
Whey	<i>Leuconostoc mesenteroides</i> , <i>Lactobacillus jensenii</i> , <i>Lactobacillus acidophilus</i>	Proteolysis	Bioactive peptides ↑, ABTS+ antioxidant activity ↑	[85]
Dairy waste water	<i>Candida bombicola</i>	Cellular process	Level of sophorolipids ↑	[86]

Dairy whey	<i>Kluyveromyces fragilis</i> <i>Candida bombicola</i>	Acidogenic fermentation	Bioenergy, organic acids, bioactive peptides Surfactants	[87]
Dairy wastewater	<i>C. tropicalis</i> , <i>C. rugosa</i> , <i>C. lipolytica</i> , <i>Y. lipolytica</i>	Fats and esters utilization	Microbial mass production ↑	[88]
Chicken egg shell membrane	<i>Lactiplantibacillus plantarum</i>	Proteolysis	Bioactive peptides ↑, Radical scavenging activity ↑	[89]
Fish head	<i>Pediococcus acidilactici</i> and <i>Enterococcus faecium</i>	Proteolysis	Antimicrobial peptides ↑	[90]
Slaughterhouse wastewater	<i>Yarrowia lipolytica</i>	Lipolytic activity	Level of lipids ↑ (palmitic, stearic and oleic acids), biodiesel recovery	[91,92]
Brewers' spent grain (BSG)	<i>Pichia stipitis</i> <i>Kluyveromyces marxianus</i>	Fermentation pathways	Phenol compounds	[93]

3.1. Involvement of Yeasts during FBPW Valorization

Yeasts have been known to humans for thousands of years as they have been used for wine-, beer- and bread-making. In fermented foods, yeasts produce alcohol and other organic molecules, improve flavor, aroma and texture of the final product, enhance the nutritional properties and may reduce anti-nutritional factors and toxins. Over the years, yeast strains, isolated and characterized from several naturally fermented foods, have been successfully applied as starter/co-starter to produce both conventional and functional foods at industrial level [94,95].

Nowadays, the concept of yeast utilization was reevaluated, and yeasts are also considered as alternative sources of various bioactive compounds (e.g., antimicrobials), enzymes and vitamins. Thus, yeasts are increasingly involved in food industry as additives, source of pigments, conditioners and flavoring agents. Modern scientific advances allow the cultivation of yeasts also starting from FW, to respect the goal of circular economy. Different food-grade yeasts, FBPW, and industrial processes may be used to produce functional foods and/or bioactive compounds [96]. Indeed, yeasts, by virtue of their high resistance to abiotic stress factors such as low pH, presence of salt and high concentrations of ethanol have great potential for valorizing FBPW [94,95].

3.1.1. Dietary Fiber

Dietary fibers are heterogenous nutrients classified into two main groups: water soluble (e.g., pectin) and water insoluble (e.g., cellulose and lignin) dietary fibers. These fibers are naturally found in whole grains, such as oats and barley, and fruits, such as apples. Dietary fibers stimulate metabolic interactions among bacterial species colonizing the gastrointestinal tract and their regular consumption can promote the indirect stimulation of the growth of other microbes within the bacterial community [97]. Lack of dietary fiber in the human diet is considered as a risk factor in the development of colon cancer and N-NCDs (e.g., bowel disease, hyperlipidemia, diabetes, obesity) [98]. Generally, major fiber sources for adults are vegetables and fruits and other food ingredients, such as grain mixtures and yeast breads/rolls, which contributed 72% of the total intake [99].

Fiber naturally present or added to foods has several positive influences on consumer health, including cardioprotective action [100]. Among them, the hypotensive action of dietary fiber may be attributed to reduction in insulin resistance and the compensatory

hyperinsulinemia [101,102]. Furthermore, the reduction in cholesterol has been attributed to the high fiber content of whole grains and oleaginous seeds (e.g., flax seeds) [103]. Therefore, functional foods enriched with fibers certainly represent a driving force in the World food market, because they improve nutrition. Fortification of bakery products (e.g., biscuits, cookies, cake, bread) based on refined flour with dietary fiber represents an outstanding example. Health effects of oat are mainly due to its content in total dietary fiber and β -glucan. β -glucans are considered immune-modulating compounds that may activate the host immune system and initiate inflammatory processes and, thereby, provide resistance against infections and cancer development. They also have cholesterol-lowering effects and antioxidant activity [104]. In addition, they can help lowering blood glucose and insulin concentrations [105]. In the Western World, dietary supplements containing β -glucans are mostly derived from baker's yeast, *S. cerevisiae*. Indeed, yeast's cell wall is rich in linear (β -1,3) and branched (β -1,6) glucans.

Yeasts may be quickly cultured in a variety of different growth conditions and the biomass of food-grade yeasts could be produced using by-products of the sugar industry. Additionally, starch, distiller's wash, whey, together with fruit and vegetable wastes, can also be used [106]. Potato juice and glycerol are by-products of the manufacturing of potato starch and biodiesel, respectively [107,108]. These two by-products were used in research by Bzducha-Wróbel et al. [106] to produce yeast biomass with altered cell wall structure with increased amounts of β -glucans. The main by-products of beer manufacturing are the brewers' spent grain, trub removed after wort boiling, and spent yeast. The production of brewing by-products is very similar globally, with possible differences in their composition depending on the location. These materials are currently often unutilized and present hardly any market value.

Recently, Chotigavin et al. [109] studied the effects of tannic acid on *Saccharomyces carlsbergensis*, a brewer's yeast. Indeed, a lot of waste produced during beer fermentation (exhausted barley grains) are rich in tannins that interact with the yeast cell wall to form polysaccharides or to cause stress that results in an inhibitory or lethal effect. Tannins have been extensively studied as harmful or sensory quality-decreasing factors, primarily in animal nutrition, but little is known about their contaminating effects on the environment. Tannins inhibit the growth of many microorganisms, resist microbial attack and are recalcitrant to biodegradation. Their toxic effect is mainly due to the inhibition of enzymes, the action on membranes, and the deprivation of metal and substrate ions. These compounds have the capacity to participate in non-reversible reactions with proteins due to the presence of a large number of phenolic hydroxyl groups [110]. During beer production, tannic acid coming from tannin degradation increases the thickness of the β -glucan-chitin layer, while decreasing the mannoprotein layer. Thicker cell walls correspond to higher carbohydrate and β -glucan levels. The addition of 0.1% *w/v* tannic acid boosted β -glucan synthesis and content by 42.23% [111].

A mixture of apple pulp and peel residuals was fermented by *S. cerevisiae* in combination with *Weissella cibaria*. The content of total and insoluble dietary fibers markedly increased. These fermented apple by-products were used as ingredients to prepare wheat bread fortified with fiber, without altering bread rheology and color [112]. Patented application (Table 2) of selected strains of *S. cerevisiae* SPC-SNU 70-1, *Lactilactobacillus curvatus* (formerly *Lactobacillus curvatus*) SPC-SNU 70-3, *Lactiplantibacillus plantarum* (*Lactobacillus plantarum*) SPC-SNU 72-1, *Levilactobacillus brevis* (*Lactobacillus brevis*) SPC-SNU 70-2 and *Fructilactobacillus sanfranciscensis* (*Lactobacillus sanfranciscensis*) SPC-SNU 70-4 have been individually tested as starters of wheat bran for producing a high dietary fiber bread, with staling-delay effect and an excellent texture improvement [113].

In the current scenario of increasing consumption of foods of vegetable origin, especially those ready-to-eat, discarded fruits, peel/skin, seeds or stones are more and more available. Yeasts could be used to ferment these fiber-rich FBPW to produce prebiotic compounds such as arabinoxylan-oligosaccharides, xylose, and fructo-

oligosaccharides, as already shown for brewer's spent grain, rice husks, soybean hulls or grape pomaces [114–116], sugar cane bagasse, or banana peel and/or leaves [79,80]. Xylose is a reducing sugar, first isolated from wood and deriving from hemicellulose. Recent results published by Khummanee et al. [117] showed that the xylose-based oligosaccharide XG1, synthesized by yeasts, could be classified as prebiotic because it selectively promoted the growth and metabolic activity of only bacteria with health benefits.

3.1.2. Enzymes

Yeasts cultured on FBPW may be used as sources of enzymes. Solid-state fermentation (SSF) is a process that occurs in the absence or near absence of water. According to Bhanja et al. [118], SSF is superior to submerged fermentation due to higher productivity, lower water and energy requirement, easy aeration, lower demand for sterility, resemblance to the natural habitat of microorganisms and simplified downstream processing. SSF has been used for the production of enzymes that can enhance the release of phenolics from cereal matrices (e.g., rye bran, wheat germ, and barley wastes) or other vegetables such as soybean and buckwheat [119]. These enzymes are able to cut bran phenolic bonds, increasing their bio-accessibility and biological activity. Many fungal species, including yeasts, can be used in SSF because of their low requirements of water and O₂. Among the possible microorganisms involved in SSF, *S. cerevisiae* has high potential, for example in producing enzymes like β -glucosidases, carboxylesterases, and possibly feruloyl esterases [120]. During SSF, plant-based wastes rich in soluble and insoluble fiber are utilized by lignocellulolytic fungi that have enzymes, such as lignases, cellulases or hemicellulases, that break fiber hard structure [121]. Besides the release of phenolics, fungi also synthesize bioactive compounds, such as mycophenolic acid, dicerandrol C, phenylacetates, anthraquinones, benzofurans and alkenyl phenols, that have antitumoral, antimicrobial, antioxidant and antiviral activities (Table 2). Another important group of compounds synthesized by fungi during SSF are polysaccharides that also have important health-promoting properties.

Table 2. Patented technological processes and applications for valorising food waste and by-products through microbial fermentations.

Patent ID	Food/Plant by-Product	Microorganisms	Effect/Outcome	Application	Ref.
CN-103627645-A	Bean curd yellow water	Yeasts	Carotenoid production	Carotenoid-enriched protein—food supplement	[122]
CN-107937234-A	Grape seed	Yeasts	Polyphenols	Procyanidin- and polyphenol-enriched grape vinegar	[123]
KR-101990582-B1	Wheat bran	<i>Saccharomyces cerevisiae</i> SPC-SNU 70-1, <i>Latilactobacillus curvatus</i> SPC-SNU 70-3, <i>Lactiplantibacillus plantarum</i>	High fiber content, improvement of taste and reduced firmness	High dietary fiber bread	[113]

		SPC-SNU 72-1, <i>Levilactobacillus brevis</i> SPC-SNU 70-2 <i>Fructilactobacillus</i> <i>sanfranciscensis</i> SPC- SNU 70-4			
CN-106722835-B	By-product chili juice	<i>Saccharomyces</i> <i>cerevisiae</i>	Taste improvement	Novel flavor pepper sauce	[124]
CN-105695340-B	Orange peel	<i>Aspergillus oryzae</i>	Health promoting effects, production of naringinase	Food supplement	[125]
CN-106819352-B	Orange peel	<i>Bifidobacterium longum</i> <i>Trichoderma viride</i> <i>Aspergillus niger</i>	Appetite improvement and beauty preservation	Fruitcake	[126]
CN-106858552-B	Olive pomace	<i>Aspergillus niger</i> <i>Rhodotorula glutinis</i> CICC 31229	Improved fragrance and digestibility	Food applications	[127]
KR-101955775-B1	Grape or cereal by-products	<i>Bacillus subtilis</i> <i>Bacillus thuringiensis</i> Lactic acid bacteria Photosynthetic bacteria Yeast Bacteria Gram-positive actinomycetes Fungi	Antioxidant and immunostimulatory effect	Functional foods or ingredients	[104]
KR-101922961-B1	Citron residues	<i>Lactiplantibacillus</i> <i>plantarum</i> GAVOL-07	Production of polysaccharides with antioxidant and anti- browning activity	Novel beverage	[128]
CN-105961586-B	Banana peel	<i>Lactobacillus</i> <i>delbrueckii</i> subsp. <i>bulgaricus</i> , <i>Streptococcus</i> <i>thermophilus</i>	Increased content of dietary fibers and trace elements, improved flavor	Fermented beverage	[129]
CN-107259271-B	Fruit and vegetable residues	<i>Lactiplantibacillus</i> <i>plantarum</i> <i>Lactobacillus</i> <i>acidophilus</i> <i>Lacticaseibacillus</i> <i>rhamnosus</i>	Free radical scavenging activity, alpha-glucosidase inhibition	Fermented fruit and vegetable juice	[130]

KR-102214532-B1	Garcinia cambogia fruit peel	<i>Lactobacillus acidophilus</i> <i>Lactiplantibacillus plantarum</i> <i>Limosilactobacillus fermentum</i>	Anti-obesity and anti-inflammatory effect	Food ingredient	[131]
JP-6539400-B1	Grape pomace	Bacteria and yeasts	Production of LPS	Functional ingredient	[132]
FI-127240-B	Berry by-products	<i>Lactococcus</i> sp. <i>Lactobacillus</i> sp. <i>Pediococcus</i> sp. <i>Oenococcus</i> sp.	Production of antimicrobials	Cosmetics, hygiene products, food supplements, food products, feeds, pharmaceutical products	[133]
CN-107006606-B	Red bean dregs	<i>Lactobacillus delbrueckii</i> subsp. <i>bulgaricus</i> <i>Streptococcus thermophilus</i> <i>Lactiplantibacillus plantarum</i> <i>Levilactobacillus brevis</i>	Antioxidant, antifatigue and immunoregulatory effects	Functional yogurt	[134]
RU-2734461-C2	Cereal bran or crushed cereal grains	<i>Lactobacillus acidophilus</i> LA-5 <i>Bifidobacterium animalis</i> subsp. <i>lactis</i> BB-12 <i>Streptococcus thermophilus</i> <i>Lactobacillus delbrueckii</i> subsp. <i>bulgaricus</i>	Antidiabetic effect	Antidiabetic yogurt	[135]
US-10645954-B2	Yogurt whey	<i>Lactobacillus</i> sp. <i>Streptococcus thermophilus</i>	Increased content of calcium, potassium, phosphorous and fatty acids	Beverage/food ingredient	[136]

3.1.3. Pigments

The color of food is a critical factor influencing the general acceptance. Pigment-producing microorganisms are quite common in nature, although there is a long way from the laboratory to the marketplace [137]. The processes use fungi, bacteria, or microalgae to provide pigments such as carotenoids or phycocyanin. Compared to synthetic pigments, microbial pigments have higher biodegradability and compatibility with the environment and numerous applications from food to cosmetics have been described [138]. In addition, due to an increasing feeling of mistrust among consumers, current research is aimed at producing natural and healthy food colorants from microbial sources. Indeed, several studies have emphasized the significance of microorganisms in exploiting the primary carbon sources found in agricultural wastes, such as glucose and sucrose, which might contribute to a better efficiency in the specific production of carotenoids (classified as xanthophylls and carotenes) [139–141]. These carotenoids may be used as natural pigments during food processing. For many years, they have been considered beneficial for eye health and it was the only positive aspect of carotenoids discussed in humans. Over time, other health-promoting effects, such as protection against degenerative diseases and cancer, were attributed to the carotenoids consumption [142].

Yeast fermentation of bean curd yellow water, leading to the production of carotenoid-enriched protein, was patented (patent number CN-103627645-A) [122] (Table 2). *Rhodotorula rubra* and *Xanthophyllomyces dendrorhous* were studied for pigment production on various residues as sole substrates. Kaur et al. [65] demonstrated that submerged fermentation of whey or coconut water had a stimulatory effect on growth and yields of intracellular pigments of *R. rubra* [66].

3.1.4. Other Bioactive Compounds

The numerous biotechnological approaches that aim to use yeast-driven fermentation in the recovery of dairy waste led to the production of various bioactive compounds. Bioactive peptides are protein fragments that exhibit different functionalities once released from the original proteins. They could display antihypertensive, antioxidant, antimicrobial, opioid, mineral binding, antithrombotic, or immunomodulatory activities. So far, 4283 bioactive peptides have been registered on the BIOPEP database [141]. They can be released from the precursor protein either by single or mixed proteolytic enzymes, fermentation or after gastrointestinal digestion. Yeast extract is the soluble fraction of yeast cells widely used in the food industry, but also in animal feed and microbial culture media. It can affect peptides and protein recovery values, the downstream unit operations, the economy of the process, and bioactivity of yeast extract. Spent brewer's yeast (SBY) is one of the major by-products produced during the brewing process. SBY is an abundant source of β -glucans, vitamins, minerals, fiber, and bioactive peptides. Although it has been widely used in animal feed, over the last decades considerable efforts have been devoted to exploiting bioprocessed SBY as an additional ingredient for functional food [143].

Biosurfactants are surface-active molecules, usually extracellularly produced by bacteria, yeast or fungi, that represent other bioactive compounds with possible benefits to health [144]. Research on biosurfactants production has grown significantly due to the advantages they present over synthetic compounds such as biodegradability, low toxicity, diversity of applications and functionality under extreme conditions. Although the majority of microbial surfactants have been reported in bacteria, the pathogenic nature of some producers restricts the wide application of these compounds. A growing number of aspects related to the production of biosurfactants from yeasts have been the topic of research during the last decade; thus, the industrial importance of yeasts and their potential to biosurfactant production is relevant. Yeasts can produce biosurfactants starting from industrial production waste such as those of the brewing industry.

Furthermore, bioprocessing wastewater with *Candida bombicola* yielded biosurfactants [145].

Several patents providing solutions for obtaining bioactive compounds and nutrients from FBPW through a controlled fermentation process are available (Table 2). Among others, yeasts have been also used in combination with bacteria to bioprocess grape pomace, for efficiently obtaining lipopolysaccharides (LPS), which are extremely efficient as immunostimulatory compounds [132]. A novel chili sauce was produced through fermenting the by-products from chili processing by a *S. cerevisiae* strain able to produce methyl salicylate, the major flavor component in wintergreen oil commonly used as food additives, and form a novel flavor [124].

3.2. Involvement of Molds in FBPW Management

Molds are multicellular filamentous fungi that are plenteous and ubiquitously distributed in nature. Compared to yeasts and bacteria, molds are more easily manageable, highly resistant to wide variations in environmental conditions, and able to produce enzymes that degrade plant cell walls, which leads to an improvement of the biochemical composition and bioactivity of the substrates [146,147].

In general, foods showing the presence of molds are considered inadequate for human consumption. However, some special molds can be regarded as potential starters to manufacture certain foods or food supplements. Most molds show better performance on solid materials with low water activity and in the presence of oxygen [148,149].

Molds can be involved in biological processes that bring to the production and release of bioactive compounds with a positive impact on human health. Bioactive compounds (e.g., polyphenols, carotenoids, β -glucans) and nutrients (e.g., vitamins, amino acids) can be recovered from by-products and wastes through mold-driven bioprocesses and then used for the fortification and enrichment of foods with health-beneficial properties.

Molds secrete extracellular enzymes that can break down organic compounds and synthesize the essential compounds for their growth [150]. The recovery of enzymes could be a valuable strategy to obtain bioactive compounds in a subsequent step, avoiding the use of solvents [151]. Enzymes may be used as co-adjuvants for conventional foods or for producing or facilitating the release of bioactive compounds. For instance, using their extracellular lignocellulolytic enzymes and with the help of rhizoids, molds can penetrate deeply into the recalcitrant components of plant cells, hydrolyse cell wall and degrade the less accessible lignocellulosic materials [152]. Indeed, *Rhizopus* spp. have been used for wide applications in food industry by-products' valorization, for example, in lignocellulose wood-based substrates [153,154].

Molds produce amylase, pectinase, cellulase, protease, xylanase, glucose-oxidase, catalase, alkaline phosphatase, acid phosphatase, and phytase [155]. Fungal amylases are employed in bread-making, to clarify beer, wines, and fruit juices and to hydrolyze starch in fruit extracts [156]. Amylases and proteases produced by the genus *Aspergillus* are used to enhance the consistency and gas retention of dough [157]. In addition, molds can convert starch and non-starch polysaccharides to monosaccharides [158]. Pectinases, cellulases, tannase, and β -glucosidase have been widely used for the hydrolysis and, consequently, the recovery of phenolic compounds from grape pomace. These enzymes can be synthesized by the strain *Aspergillus niger* 3T5B8 using as substrate a mixture of grape pomace and wheat bran [159]. Pectinase and cellulase, synthesized by *A. niger* and *Aspergillus flavus*, are used in the preparation of easily digestible foods [160]. Fungal lipases and proteases are produced by *A. niger* and *Aspergillus oryzae* to accelerate cheese ripening. Indeed, several volatile organic compounds, such as methylketones, are generated after fatty acid milk hydrolysis by lipases [160]. *A. niger* releases certain proteases that are used in cheese-making as an alternative to rennet [160].

Rhizopus spp. are used in submerged fermentation to reduce the chemical oxygen demand of wastewaters [161], converting the organic substances into readily harvestable

fungal biomass, rich in chitosan and proteins [162], which can be used in human diet or as animal feed. This would help the EU to gain partial independence from imported corn, wheat, barley, and soya, which are the main components of animal feed [163].

Lateef et al. [67] demonstrated that the inoculation of cocoa pod husk, cassava peel and palm kernel cake with *Rhizopus stolonifer* increased the protein content and radical scavenging activity. These bioprocesses also decreased the crude fiber and cyanide contents, thus increasing fiber bioavailability and decreasing the toxicity of those by-products. The breakage of cell wall components favored the release of free phenolic compounds, mainly ferulic acid, chlorogenic acid, hydroxybenzoic acid [164]. Phenolics are well-known bioactive chemicals with significant antioxidant activity that are used to combat oxidative damage disorders (e.g., cardiovascular disease, cancer) after their intake. The intake of plant-based foods with a natural content of antioxidants can be associated with a reduced risk of these chronic diseases. Molds impact antioxidant activity either directly or indirectly. Several research studies confirmed that filamentous fungi contain antioxidant enzymes, ascorbic acid, γ -linolenic acid, β -carotene, and tocopherols [151,160,165]. Strains of *Mucor* spp. showed high potential for producing γ -linolenic acid and β -carotene during wheat bran and cornmeal fermentation [166]. *A. niger* and *Rhizopus oligosporus* modified phenolics composition and antioxidant activity of plum pomaces deriving from the juice industry and brandy distillery wastes, including spent fruit pulp and peels [71]. The total phenolic contents markedly increased after fermentation with *R. oligosporus* and *A. niger* by over 30% and 21%, respectively [41]. The antioxidant activity increased significantly. The increased production of fumaric, ferulic, *p*-coumaric, sinapic, vanillic and synergic acids was also observed through fermentation of apple pomace, pulp and paper waste and rice bran using *Aspergillus* spp. and *Rhizopus* spp. [167–169]. Lai et al. [64] described the use of *Phanerochaete chrysosporium* to enhance the phenolic production in apple pomace. Fermentation by *Aspergillus awamori* of peanut press cakes (PPC), representing one of the major by-products generated in India, released bound phenolics as well as increased antioxidant activity [170]. PPC fermented by *A. awamori* could be used for fortification of sweetened yogurt cheese with polyphenols and proteins [86]. Shin et al. [81] reported high recovery of polyphenols using black rice bran fermented with *A. awamori*. According to Cai et al. [171], the increased density of mycelium in the bran oat substrates bioprocessed by *A. oryzae* and *A. niger* was accompanied with a high release and increase in phenolic compounds and flavonoids.

Molds may be exploited as a source of pigments. *Monascus* red color is used in Asia as an additive for wine, candy, cooked meat, bean curd, ice cream, popsicles, biscuits, jelly, puffed food, seasoning, canned pickles, pastries, and ham coloring. Bioprocessing of rice pasta with *Monascus purpureus* proved to be a successful technology for producing coloring agents [80]. Arpink Red (industrial name: natural red) from *Penicillium oxalicum* and β -carotene from *Blakeslea trispora* are already used in the food industry as colorants [138].

Interestingly, molds are utilized to produce β -glucans, organic acids, vitamins, and amino acids. Kim et al. provided a method for mass production of β -glucan from *Schizophyllum commune*, culturing this fungal species in a broth supplemented with a synthetic adsorbent [172]. *Aspergillus clavatus*, *Aspergillus wentii*, *Penicillium luteum*, *Penicillium citrinum*, and *Mucor pyriformis* are widely used to produce citric acid from oxalic acid [160]. The latter is considered an antinutritional factor, because it can inhibit the absorption of essential nutrients [173].

Molds are the object of extremely innovative patents (Table 2). *Aspergillus* spp., cultured on orange peel, produces naringenin by the action of naringinase, a flavonoid-type enzyme with blood pressure lowering activity, removing toxic substances and promoting urination. In addition, when fermenting dried orange peels and wax apples mixed to fruit juice, *A. niger* contributes to the production of fruit cakes, which increase appetite [126]. Another substrate for *A. niger* is olive pomace, which can be valorized by sequential bioprocessing with *Rhodotorula glutinis* to improve the digestibility of the

product. The first fermentation causes the enzymatic lysis of starch, protein, cellulose, and hydrolysis of tannins, which cause the heavy astringent taste of olive, improving the fragrance of the product, whereas the second fermentation increases the content of carotenoids [127]. A mixture of microorganisms including LAB, photosynthetic bacteria, Gram-positive actinomycetes, yeasts and molds has been exploited to produce a food additive through fermentation of grape or cereal by-products. Photosynthetic bacteria including cyanobacteria, actinomycetes including *Streptomyces* spp., and molds including *Aspergillus* spp. and *Penicillium* spp. that hydrolyse carbohydrates and fibers, produce high amounts of β -glucan [[104] in Table 2].

3.3. Involvement of Lactic Acid Bacteria in FBPW Management

LAB genera, highly involved in food fermentation, include mainly *Lactobacillus* (and related, newly re-classified genera), *Leuconostoc*, *Pediococcus*, *Enterococcus* and *Streptococcus* [174]. Within the LAB, fructophilic lactic acid bacteria (FLAB) are heterofermentative lactobacilli that prefer fructose instead of glucose as carbon source, although additional electron acceptor substrates (e.g., oxygen) remarkably enhance their growth on glucose. FLAB are found in fructose-rich habitats such as flowers, fruits, and the gastrointestinal tract of honeybee [175]. FLAB might be successfully exploited in FBPW management.

LAB can be involved in bioprocesses that bring to the production of bioactive compounds, enzymes and pigments [74]. The presence of carbon source makes FBPW inhabitable to a wide variety of LAB [164]. Meat and seafood by-products are rich in proteins (e.g., collagen, gelatine) and vitamins. Whey by-products contain lactose, proteins, and minerals [164]. Lactic acid fermentation of FBPW relies on the capability of LAB to rapidly metabolize the available nutrients. Adaptation to ecosystems is species- and strain-specific, and highly dependent on inherent chemical and physical parameters. The adaptive growth and survival strategies of LAB during fermentation cause down-regulation of central metabolism genes, induction of alternative substrates transport and metabolism, and stimulation of specific responses functionally related to the inherent features of food matrices [176,177].

Fermentation by LAB can increase the total amount of phenolic compounds through biotransformation between soluble phenolics and the release of bound phenolics controlled by different enzymes [178]. Species- or strain-specific metabolic features of LAB include the capacity to metabolize phenolic acids into the corresponding reduced or vinyl derivatives, which may exert higher biological activities than the precursors. Specific glycosyl hydrolases of *L. plantarum* and *Lactocaseibacillus rhamnosus* (formerly *Lactobacillus rhamnosus*) are involved in the metabolism of flavonoid glycosides to the corresponding aglycones, which display high antioxidant and anti-inflammatory effects [18]. High polyphenol bioavailability enhances *in situ* radical scavenging potential through the synthesis of detoxification enzymes such as NADPH oxidase, catalase, and superoxide dismutase [179]. LAB-bioprocessed FBPW could yield additional ingredients that confer or increase antioxidant activity of foods. Biotechnological recycling of apple by-products using *L. plantarum* or *Lactiplantibacillus fabifermentans* (formerly *Lactobacillus fabifermentans*) increased the bioavailability of phenolic compounds, which was likely responsible for the increased radical scavenging capacity [180]. *Taralli*, traditional Italian baked goods, were enriched with olive paste previously fermented by *S. cerevisiae* and *Leuconostoc mesenteroides*, resulting in higher levels of polyphenols, triterpenic acids, tocopherols and carotenoids than conventional *taralli* [181]. *L. brevis* and *Candida humilis* were successfully used to ferment wheat bran, enabling the release of phenolic compounds due to the activity of their cell wall-degrading enzymes [182].

LAB bioprocessing of FBPW may lead to an increase in dietary fiber [183]. *Enterococcus faecalis* was used to ferment wheat bran, causing an increase in soluble dietary fiber, phenols (ferulic acid), flavonoids, and alkylresorcinols, compared to raw material [184]. On the other hand, FBPW may contain anti-nutritional compounds such as phytic and oxalic acids, saponins, lectins, and alkaloids. Several LAB strains, isolated from ethnic

fermented vegetables of the Himalayas, showed high capacity to degrade anti-nutritional factors [185]. Fermentation of *Portulaca oleracea* with *Apilactobacillus kunkeei* and *L. plantarum* decreased (ca. 30%) the accumulation of oxalic acid [173]. Furthermore, using maize milling by-products fermented with *L. plantarum* and *Weissella confusa* as a flour ingredient improved the nutritional, textural and sensory properties of wheat bread, which was characterized by a higher concentration of dietary fiber and proteins, protein digestibility, reduced content of phytic acid and increased radical scavenging activity [73].

The potential of LAB and their enzymes for producing/releasing bioactive compounds mainly present in FBPW has been also thoroughly researched. Fatty acid hydratases bring out hydration of polyunsaturated fatty acids to hydroxy-fatty and conjugated-fatty acids with recognized immunomodulatory and antioxidant activity in humans [186]. According to Bartkiene et al. [74], *Pediococcus acidilactici* enriches barley by-products with oleic, arachidic, eicosadienoic, behenic, and lignoceric fatty acids, with high health-promoting properties. Strains of *Latilactobacillus sakei* subsp. *sakei* (formerly *Lactobacillus sakei*), *L. curvatus*, and *L. plantarum* showed high efficiency in producing bacteriocins (e.g., plantaricin), which were active towards food spoilage and pathogens [61]. The use of bacteriocins is a promising alternative to the use and addition of chemical preservatives in foods. The *L. plantarum*-fermented whey increased the shelf-life of bread and inhibited the growth of *Penicillium expansum* and *Penicillium brevicompactum* [83]. Yogurt whey was an excellent industrial source for lactic acid production by *L. casei* [84]. This application found high relevance because lactic acid is widely used both in food and pharmaceutical industries due to its positive impact on nutrient absorption, gut health, and protection against cell damage and chronic diseases [187]. LAB can produce exopolysaccharides (EPS), some of which stimulate the growth of probiotic bacteria. In addition, EPS are suggested to have immunomodulatory effects, antioxidant activity and cancer-preventive activity [188].

Moreover, LAB have a potential role in enrichment of FBPW in bioactive peptides and γ -amino butyric acid (GABA), a non-protein amino acid which exhibits several functionalities in humans [189]. Sharma et al. [72] demonstrated that *L. plantarum* LP-9 was capable of strongly increasing the GABA concentration in bran from wheat, rice, and corn. Chicken eggshell membrane fermented with *L. plantarum* yielded protein hydrolysates with strong radical scavenging activity [89]. LAB-bioprocessed whey generated bioactive peptides and amino acids of prominent antioxidant activity [85]. Fish head fermented with LAB resulted in high levels of antimicrobial peptides [90]. The oxidation of the NADH accumulated during sugar catabolism makes LAB efficient cell factories for polyols synthesis [190]. Polyols such as xylitol, erythritol, and mannitol have attracted interest due to their low caloric, glycemic, and insulinemic indices and their anti-cariogenic and prebiotic features [190]. *Lactobacillus florum* and *Fructobacillus tropaeoli* produced high-quality mannitol and erythritol [191,192]. Astaxanthin is a carotenoid used as an antioxidant supplement and can be recovered successfully from FBPW, especially seafood by-products. Shrimp processing wastes are very cheap raw materials for recovering astaxanthin. Fermentation of shrimp processing wastes by *Lactobacillus acidophilus* and *Streptococcus thermophilus* was successfully used for edible oil extraction and astaxanthin recovery [193].

The application of LAB has been patented to produce a beverage rich in polysaccharides from fermented citron pomace and peel [128], and a health-promoting beverage from fermented banana peel [129] (Table 2). Polysaccharide-enriched foods and beverages can be used as potent activators of the immune system, especially the adaptive system. In addition, these biopolymers exert antioxidant, anti-inflammatory and antiviral activities, are biocompatible, non-toxic and biodegradable [194]. Fermentation greatly improved the original flavor of banana peel, boosted the immunity system, enhanced the phagocytosis of macrophages, and improved the resistance of human body to pathogenic bacteria [129] (Table 2). A mixture of *L. plantarum*, *L. acidophilus*, *L. rhamnosus* and *Limosilactobacillus fermentum* (formerly *Lactobacillus fermentum*) was patented for the

fermentation of fruit and vegetable residues (e.g., blueberries, apples, pears, dragon fruits, kiwi fruits, bitter gourds, carrots, pumpkins, pomegranate extract and garcinia cambogia fruit peel). The fermented matrices showed the ability to reduce blood sugar and displayed anti-obesity and anti-inflammatory effects [130,131] (Table 2). In addition, cloudberry by-products fermented by *Lactococcus* sp., *Pediococcus* sp. and *Oenococcus* sp. stimulated the production of ellagic acid, ellagitannins and/or derivatives, phenolic compounds showing antimicrobial action against *Staphylococcus aureus*, which is one of the major pathogenic and antibiotic-resistant bacteria causing infection of superficial skin and soft tissue, sepsis, pneumonia, and endocarditis [195]. The same fermentation process can be applied to different by-products, such as pomace, press cake, berry cake and fruit cake [133,195]. In addition, red bean sprout pulp fermentation processes using *Lactobacillus delbrueckii* subsp. *bulgaricus*, *S. thermophilus*, *L. plantarum* and *L. brevis* have been optimized and patented to produce a yogurt containing bioactive polysaccharides, flavone, GABA and dietary fiber [134] (Table 2). A sugar-free and antidiabetic yogurt was developed by fermenting a mix of milk, cereal bran or crushed cereal grains, and water [186]. A method of producing a beverage rich in fatty acids, calcium, phosphorus, and potassium has been developed by recycling the residual (and highly nutritious) whey from the production of Greek yogurt [136] (Table 2).

4. Concluding Remarks

This review conjugates human health and sustainability through discussion about recycling FBPW in the food chain. FBPW is a key area in the circular economy, being considered as an under-utilized resource that can be brought into use. The circular economy creates more employment with fewer resources [196] and is strongly related to sustainable consumption and production, i.e., with SDG 12 of the United Nations 2030 Agenda for Sustainable Development. The bio-economy policy and the circular economic model represent great opportunities for tackling the FBPW issue, especially in medium-high income Countries where the bulk of the problem is associated with deplorable consumption behaviors occurring at the end of the FSC. However, the transition needs to be accompanied by adequate policies. Demand and supply side policies are crucial for pushing out emerging sectors such as the bioeconomy.

As analyzed in Paragraph 3, the enormous potential of using microorganisms for valorizing FBPW emerges. Due to the huge available microbial diversity, it is possible to think that every kind of FBPW can be turned into food ingredients and dietary supplements targeted to decrease the risk of onset N-NCDs and/or to remedy nutrient inadequacy. The “simplest” challenge is to reproduce, under controlled conditions (selected microbial strains, temperature, oxygen concentration, etc.), the breakdown processes naturally occurring, just exploiting the high reproductive potential of properly selected molds, yeasts, and especially bacteria. Given that different microbial populations co-exist and/or follow one another in natural breakdown processes, the set-up of processes based on sequential biotransformation of FBPW appears as the most profitable (from an economical and environmental point of view) way to recover the highest possible potential from those matrices.

Another challenge to be faced is the fact that microbial-based processes for increasing the value of FBPW are often conceived and tested at laboratory level. However, their use at industrial level remains essential in view of managing the huge amounts of waste and by-products. Testing the process at pilot plant scale represents the essential link between laboratory research and industrialization, which would ensure the sustainability of the process, the economic benefit for the involved food industry, and the perpetual establishment of the derived products in the market [47]. A scale-up process should be conducted without diminishing the functional properties of the target compounds and, at the same time, should result in a product that meets consumer expectations in terms of high-quality organoleptic standards [197]. Scale-up of recovery processes meets the same limitations as any food manufacture procedure. Transition from laboratory to

industrialized processes is usually accompanied by extension of time, heavier handling, increased air incorporation, and higher degree of scrutiny. All these parameters may generate loss of product functionality. Subsequently, process cost could increase, as industrially recovered compounds are used in food formulations at higher concentrations compared with laboratory-recovered compounds [47].

It is expected that the existing technologies for valorizing FBPW will be flanked by several new technologies and their quality will improve. However, researchers and industries involved in the field shall consider the intrinsic perishability of the majority of FBPW. Possible solutions are represented by cooling/freezing FBPW, thus slowing microbial growth, or sterilization using high temperatures. However, these solutions would increase the carbon footprint of the process [39,41]. To locate the plants where FBPW are treated immediately near to the industries generating FBPW would represent the ideal solution, because it would allow the treatment of FBPW at the right time and with very limited transport costs.

Technological advancements shall be flanked by public (at political and administrative levels) interventions focused on (i) mapping and tracing FBPW; (ii) framing the materials deriving from microbe-driven processes in an appropriate legislative framework; (iii) educating consumers to use materials derived from waste. FBPW from primary production and food processing are often very heterogeneous and their availability typically varies depending on the season (especially for FBPW of vegetable origin). Therefore, it becomes essential to map those resources, not only in terms of geographical location but also availability over time. This mapping of FBPW will boost the set-up of plants that shall be capable of treating heterogeneous material, without stopping because of the lack of feedstock. Safety aspects and the related legislative framework seem to be not yet adequately developed. Regulations and guidelines about employment of FBPW for applications such as food ingredients, dietary supplements, and animal feed are still scarce. In Europe, the production of bioactive compounds extracted from FBPW is regulated by the general food law, and particularly by European Community (EC) Regulation No. 178/2002, Article 2 and *Codex Alimentarius* guidelines. Some compounds may fall into the regulatory framework of Regulation (EU) No. 2015/2283 on Novel Foods, intended as foods that have not been consumed to a significant degree by humans in the EU before 15 May 1997. This framework aims to ensure an efficient level of consumer safety and a smooth functioning of the market in food and feed. In the EU, this also represents the regulatory framework within which the European Food Safety Authority underpins all European legislation and policies about the food and feed safety aspects [198,199]. From this point of view, it is worth envisaging the fate of those microorganisms used to convert FBPW into food ingredients/dietary supplements. In case of microorganisms labeled as Generally Recognized As Safe/Qualified Presumption of Safety, their removal after fermentation would not be mandatory, although advisable for increasing the yields of processes based on liquid feedstocks. However, the question remains: how to deal with technologically relevant microorganisms that are not food-grade? Indeed, thermal treatment would be sufficient to exclude the risk of infection originating from some of them, but not in case of microorganisms producing toxins or other health noxious compounds. Besides microbiological risks, it will be necessary to evaluate the (residual) presence of anti-nutritional factors in the materials derived from FBPW.

Finally, for food/dietary supplement applications of materials coming from FBPW, a slow but targeted cultural revolution should be implemented. The assessment of impact of novel foods containing FBPW and targeted to improve nutrition and decrease the risk of N-NCDs requires a comprehensive knowledge of their acceptance and adoption in different population groups by geographical area, age, class, gender, and socio-economic status and legal framework. Research studies focusing on the inclusion of extracts from FBPW should consider consumer acceptability both from a sensory point of view [200–204] and in regard to overcoming cultural constraints [204]. Acceptability could be

increased through providing consumers with simple but detailed information about the flow generating a given product and the way in which it can be beneficial for protecting the environment on the planet Earth.

The future trend regarding waste management is the utilization of waste as raw material in cascade processes leading to the generation of various products with diversified market applications. This approach, coupled with minimization of waste generation, will lead to the development of no-waste production processes. This can only be achieved through appropriate legislation enforcement in different Countries, consumer awareness of the benefits that could be provided by such an approach, and the creation of market outlets for the new products. Transdisciplinary research projects, such as the SYSTEMIC project (an integrated approach to the challenge of sustainable food systems: adaptive and mitigatory strategies to address climate change and malnutrition) (<https://systemic-hub.eu/coordination/>), (accessed on 15th November 2022) focusing, among various facets, on valorization of FBPW and assessment of consumer acceptance of sustainable novel food, will provide the adequate scientific knowledge for establishing appropriate legislation that regulates market of novel products, contributing to achievement of food security.

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