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Posted Date: 26 December 2025

doi: 10.20944/preprints202512.2086.v1

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Review

Microbial Fermentation: A Sustainable Strategy for Producing High-Value Bioactive Compounds for Agriculture, Animal Feed, and Human Health

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Abstract

Microbial fermentation is a key biotechnological tool for producing bioactive metabolites such as alkaloids, carotenoids, essential oils, and phenolic compounds, among others, with applications in human health, agriculture, and food industries. This review comprehensively reviews recent information on the synthesis of valuable compounds and enzymes through fermentation processes. Here, we discuss the advantages of the different types of fermentation, such as submerged and solid-state fermentation, in optimizing metabolite production by bacteria, fungi, and yeast. The role of microbial metabolism, enzymatic activity, and fermentation conditions in enhancing the bioavailability and functionality of these compounds is discussed. Integrating fermentation with emerging biotechnologies, including metabolic engineering, further enhances yields and specificity. The potential of microbial-derived bioactive compounds in developing functional foods, pharmaceuticals, and eco-friendly agricultural solutions positions fermentation as a pivotal strategy for future biotechnological advancements. Therefore, microbial fermentation is a sustainable tool to obtain high-quality metabolites from different sources that can be used in agriculture, animal, and human health.

Keywords: fermentation; microorganism; bioactive compounds; one-health

1. Introduction

Bioactive compounds are found in plants, fruits, vegetables, and cereals. These compounds, such as alkaloids, antibiotics, mycotoxins, phenolics, pigments, polysaccharides, and vitamins, are among the compounds that microalgae can synthesize or microorganisms can excrete during the fermentation process. These metabolites are linked with promoting benefits for human health, such as antioxidants, anti-tumor, anti-diabetes, cardiovascular protection, and hypoglycemic activities.

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Therefore, metabolites are a target due to the promising ingredients of different nutraceutical, pharmaceutical, and cosmetic products [1-4]. Additionally, plant growth factors, biostimulation, elicitation, and the inhibition of phytopathogenic diseases on plants have been studied, as well as the potential activities of metabolites such as polysaccharides, enzymes, and microorganisms in submerged and solid-state fermentations for agricultural uses [5-7]. Recently, it has been studied the effect of fermentation of food waste to enhance the diet to improve the health and growth of different animals; in this sense, the use of microorganisms as probiotics on animal models, as well as the metabolites obtained by fermentation of food waste as ingredients on animal feed are demonstrated an enhance of health and growth of goats, pig, among other animals; therefore, the use of fermentation of food waste could be a promising alternative to commercial animal products, contributing to a circular economy by enabling waste materials to be reintegrated into the production cycle and continue generating value [8-11]. This study highlights the importance of microbial fermentation as an innovative and sustainable alternative to obtain metabolites related to human health, agricultural, and animal uses.

2. Literature Research Methodology

To collect relevant literature on the subject, we performed literature research using the databases Scopus, Web of Science, and Google Scholar using the following keywords: fermentation, "bioactive compounds", "one-health", "metabolite production", "solid-state fermentation", enzymes, polyphenols, carotenoids, essential oils, polysaccharides, applications, lactic acid bacteria, Lactobacillus, Saccharomyces, Aspergillus, "functional foods", pharmaceuticals. We mainly included literature from 2015-2025 and only reports published in English. At the end, we included 296 articles in this review paper (**Figure 1**).

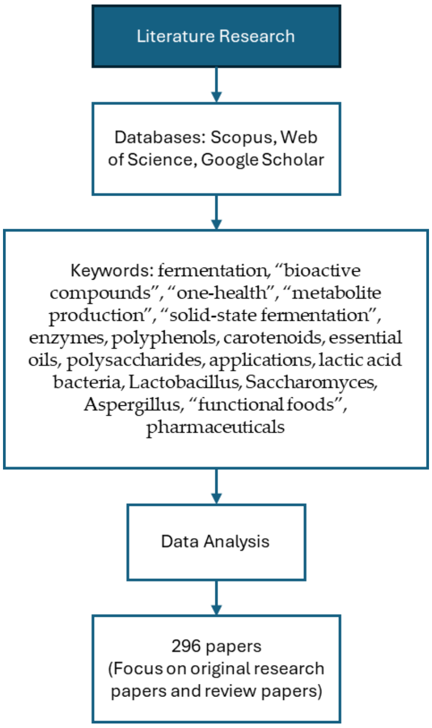

Figure 1. Literature research strategy.

3. Fermentation as a Strategy to Produce Metabolites of Interest

Fermentation is a preservation technique used since ancient times to extend the shelf life of food and improve the bioaccessibility and bioavailability of nutrients from different sources [12]. This process occurs through microorganisms such as bacteria, fungi, and yeast that transform substrates

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into new ingredients such as textures, fragrances, flavors, enzymes, and bioactive compounds[13,14]. The fermented products are affected by several factors, such as temperature, pH, aeration, agitation, and microorganism-to-substrate ratio; these parameters are monitored and studied to control the fermentation process [14,15]. The fermentation process is divided into submerged fermentation (SF) and solid-state fermentation (SFF), which depend on the substrate and nutrient medium based on the cultivation of microorganisms[14]. These fermentation types have some advantages, which are related to the growth of microorganisms, specificity, and adaptation to fermentation conditions (**Figure 2**) [16,17]. In this sense, *Candida*, *Galactomyces*, *Kluyveromyces*, *Monascus*, *Pediococcus*, *Streptococcus*, *Torulaspora*, and *Weisella* microorganisms have been studied on submerged fermentation; while *Lactococcus*, *Lentimus*, *Mucor*, *Thamnidium*, *Trichoderma*, and *Yarrowia* microorganisms have been used on solid-state fermentation [17-22].

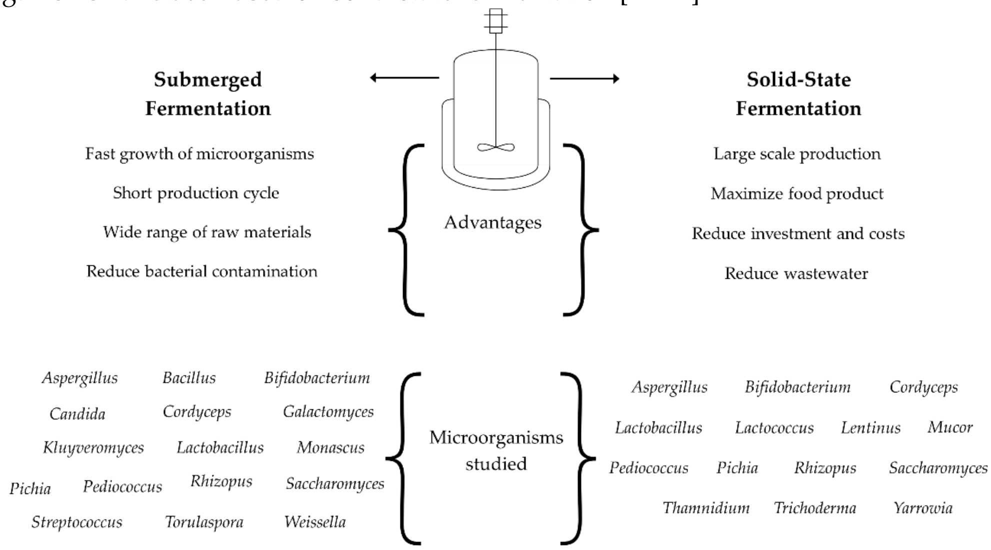

Figure 2. Submerged and solid-state fermentation advantages and microorganisms studied.

3.1. Submerged fermentation

Submerged fermentation is performed in a liquid substrate where microorganisms can adapt to high humidity. This fermentation method is one of the most studied because it is considered technologically easy to scale up to large-scale processes. Less extreme and more economical conditions are required to grow, diffuse, and separate microorganisms and compounds [17,19]. Submerged fermentation can be carried out in various ways, including batch, fed-batch, and continuous fermentation. The fermentation method used needs to be oriented to cover the characteristics of the microorganism and nutrients studied, as well as the infrastructure and separation steps required to obtain product compounds [16,17,23]. This type of fermentation is used in other processes. Also, it has been reported that a wide range of raw materials has been studied to extract different compounds such as flavonoids, antioxidants and antifungal peptides, dietary fibers, volatile compounds, among others of industrial importance [17]. However, submerged fermentation requires a longer fermentation time due to its lower performance. Also, high effluent volumes are produced, and waste needs to be stabilized before being dropped into the environment [24]. The most studied microorganisms on submerged fermentation are bacteria (*Bacillus*, *Bifidobacterium*, *Lactobacillus*, *Pediococcus*, *Streptococcus*), yeast (*saccharomyces*), and some fungi (*Cordyceps*, *Galactomyces*, *kluyveromyces*, *Monascus*, *Picchia*, *Rhizopus*, *Torulaspora*, *Weisella*) that can growth on high humidity and transform the carbohydrates into organic acids, alcohols, other compounds, and new ingredients with health benefits, as well as enzymes that are secreted into the liquid medium [17,25].

3.2. Solid-state fermentation

Solid-state fermentation is a technique in which microorganisms grow in the absence, partially or completely, of water and metabolize the nutrients of the solid substrate to transform carbohydrates

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into other compounds [1]. In recent years, various substrates have been studied for solid-state fermentation. Among these, agricultural biomass is considered an alternative for obtaining metabolites of agricultural, cosmetic, and pharmacological importance using fungi, yeast, and certain bacteria. Also, this solid-state fermentation has been considered cheaper in contrast to submerged fermentation due to processing conditions, simpler equipment, lower sterilization cost, and reduced downstream processing, among others [1,6,20,22]. Likewise, a higher yield of metabolites in shorter times has been obtained under solid-state fermentation compared to submerged fermentation, which could be due to specific growth conditions of microorganisms under stresses conditions, as well as uncompetitive inhibition with other microorganisms to consume the nutrients of substrates [6,12,26].

4. Microbial Metabolism and Fermentation Mechanism

4.1. Metabolic changes in microorganisms

In general, to be considered a "fermentation", microorganisms must produce alcohol, commonly via pyruvate, converted into ethanol and carbon dioxide; this process is frequently related to yeasts, including *Saccharomyces* and non-*Saccharomyces* yeasts [27,28]. Nonetheless, the fermentation process is not exclusive to yeasts; there are several fermentative bacteria, such as Lactic Acid Bacteria, Acetic Acid Bacteria, and native microbiota present in raw materials, which participate in the fermentation of several food and beverage industries [3,29-32]. In this regard, bacterial fermentation holds special interest due to the increasing demand for fermented produce, which serves as a potential source of rich biomass and bioactive compounds, offering consumer benefits [33-35].

During fermentation, the process requires that fermentative bacteria start their metabolic activity, which commonly represents entering a new environment, and bacteria must adapt their genetic content in response to the surrounding conditions [36]. In this regard, there are some factors involved in the process, including temperature, pH, as well as the natural composition of the raw material, which induces the metabolic response of microorganisms [37], dealing with changes in the metabolic pathways, such as amino acids production; Liu, *et al.* [30] studied the changes in bacterial communities in fermented foods such as Chinese watermelon-soybean paste, revealing that microbial abundance may vary due to fermentation conditions, dealing with the diversity and richness of metabolites in the fermented food, and showing a positive correlation of *Bacillus* species with the production of all free amino acids and dipeptides, and the presence of 11 major metabolic pathways for the metabolism of tyrosine, arginine and proline, glycerophospholipid, sphingolipid, cofactor biosynthesis, alanine, aspartate, and glutamate; amino sugar and nucleotide sugar metabolism; as well as phenylalanine, tyrosine, and tryptophan biosynthesis. Temperature and time are important factors during of fermentation, which may affect the results and composition of the fermented matrix. Zhao, *et al.* [38] reported that lactic acid bacteria cells increased their levels at low salt fermentation and low temperature, contributing to acid production during the first 45 days of the process, as well as the increase of l-glutamine, l-ornithine, β-D-fructose, d-arabinose, d-gluconic acid, glycine, l-proline, and guanine as a product of the enrichment of 28 metabolic pathways, mainly for Glycine, serine, and threonine metabolism, and aminoacyl-tRNA biosynthesis. As mentioned before, raw material composition plays an important role in the results of fermentation because it represents the "food" for the bacteria; in this regard, it is crucial to understand the presence of essential nutrients, such as carbon sources, which are not necessarily a high diversity contributes to a better response because there are some microorganisms that show a better grow and productive response in the presence of a sole carbon source and specific amino acids [39].

An example of fermentative bacteria is *Lactiplantibacillus plantarum*, which is considered a promising probiotic bacterium, given its potential for fermentation and high adaptability, improving the quality and properties of fermented foods [2]. The versatility of this microorganism resides in its genetic content; *Lactiplantibacillus plantarum* has a genome size of around 3.1 Mbp, which presents diverse genes associated with diverse metabolic functions, such as carbohydrate transport and metabolism, amino acid transport, and metabolism, energy production and conversion, and other genes that contributes to the potential for vitamin production, biotin, alpha- and beta-glucosidase,

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related to probiotic activity [40-42]. The versatility of fermentative bacteria such as *Lactobacillus plantarum* has been evaluated, reporting its ability to redirect around 44% of its gene expression according to each specific growth habitat, particularly by regulation of metabolic activity, including the metabolism of carbohydrates, pyruvate, energy production, and conversion, transport, and metabolism of amino acids, nucleotides, lipids, and inorganic ions. Pyruvate metabolism is essential for fermentative bacteria; in this regard, growth conditions may deal with marked differences in the gene regulation for its utilization, upregulating the expression of the pyruvate dehydrogenase complex, as well as the stress response against antimicrobial compounds produced during fermentation, demonstrating the metabolic versatility of these kinds of microorganisms and their potential for fermentation processes [43,44].

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Table 1. Microbial enzymes application in the food industry **[21,22,45-48]**

Microorganisms	Enzymes	Substrate	Application	Role
A. Niger, P. notatum, B. amyloliquefaciencs, B. stearothermophilus. B. licheniformis, S. cerevisiae, A. awamori, Rhizopus oryzae, Gluconacetobacter, Acetobacter xylinus, Komagataeibacter xylinus, Fusarium sp., B. brevis	α-Amylases	*Grapes, rice, cereals*	Beverages	Juice treatment, low-calorie beer, Clarification of fruit juice.
	Cellulases			Degrade plant cell walls. In wine production is used to increase yield and quality.
	Esterase			Enhancement of flavor and fragrance in fruit juice.
	Glucoamylases			Convert the starch into maltose and fermentable sugar. Use in sake and light beer production.
	Laccases			Modification of color appearance and wine stabilization.
	Pectinases			Clarification of fruit juice
	Proteases			Improves fermentation of beer.
	Xylanases			Release arabinoxylans and lower oligosaccharides, reducing the muddy appearance and viscosity of the beer.
Lactobacillus Acidophilus, B. mesentericus, S. boulardii, S. ellipsoideus, P. Ostreatus, S. diastaticus, L. brevis, L. fermentum, R. oryzae, R. oligosporus, L. plantarum, A. oryzae, A. niger	α-Amylases	*Wheat, maize, sorghum, millet, rice, soybean*	Cereals and legumes	Increase the total starch in barley and peas. Decrease amylose content in rice. Decrease carbohydrates in sorghum.
	Arabinoxylanases			Decrease insoluble fiber.
	Cellulases			Low crude fiber in Pearl millet. Fiber decreases in sorghum and yellow maize.
	Lipases			Decreased fat in mung beans, pigeon peas, red beans, soy and wild *vigna* species, maize, and rice. Increase in fat in pearl millet.
	Polyphenol oxidases			Decrease tannins
	Proteases			Increase in some essential amino acids and IVPD in maize and sorghum. Increase in protein accumulation in pearl millet.
	Tannases			Decreases tannins in beans, oats, and sorghum.
	Xylanases			Decrease fiber in sorghum
Lactobacillus bulgaricus, Lactococcus lactis, L. acidophilus, L. cremoris, L. casei, L. paracasei, L. thermophilus, L. kefiri, L. caucasicus, Penicillium camemberti, P. roqueforti, Acetobacter lovaniensis, Kluyveromyces lactis, S. cerevisiae, A. Niger, A orzyae, B. subtilis, S. boydii, B. subtilis	Catalases	*Milk and casein*	Dairy Products	Removes H_2O_2 and eliminate the effect of volatile sulfhydryl that is responsible for the cooked/off-flavor in ultra-pasteurized milk.
	Lactases			Lactose hydrolysis, whey hydrolysis.
	Lipases			Cheese flavor.
	Proteases			Protein hydrolysis, milk clotting, low-allergenic infant food formulation, enhanced digestibility and utilization, flavor improvement in milk and cheese.

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Bacillus megaterium, Bacillus subtilis	Amine oxidases	Fish proteins	Aquatic products	Inhibit biogenic amine accumulation, which is responsible for decreasing the quality and safety of fish-fermented products
	Decarboxylases			Degrade saturated fatty acids, which influence flavor.
	Esterases			Enhance favorable texture (hardness, gumminess, springiness, and chewiness), flavor, and aroma properties.
	Glucosidases			Release aromatic compounds from flavorless precursors.
	Lipases			Contribute to the development of flavor in the products due to the degradation of lipids to free fatty acids.
	Lyases			Produce flavor substances
	Proteases			Can develop different fermentation outcomes, some of which improve the product, while others may not help and might be detrimental. Generating peptides with antioxidant and antibacterial activities.
	Transferases			Produce flavor substances
L. sakei, L. curvatus, L. plantarum, Leuconostoc carnosum, Leuconostoc gelidium, B. licheniformis, E. faecalis, E. hirae, E. durans, Bacillus subtilis, L. divergens, L. carnis, E. cecorum, B. lentus, T. longibrachiatum, A. niger, A. oryzae, S. aureus	Papain	Meat proteins	Meat	Myofibrillar degradation of as well as collagen proteins helps to tenderize meat
	Polyphenol oxidases			Improve textural characteristics of meat products.
	Proteases			Tendering tough buffalo and sheep meat.
	Transglutaminases			Modify the texture of meat and meat products

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4.2. Enzymes involved in fermentation

Enzymes are considered environmentally friendly biological catalysts, revolutionizing food preparation methods. Their use is widespread across various global food industries, including dairy, brewing, meat, baking, beverages, cereals, legumes, oils, and fats (**Table 1**). Incorporating enzymes and microorganisms in food processing is a well-established traditional practice [18,22]. Microbial enzymes have been utilized in various industries, including fuel[49], human health[50], and soil[51], and are crucial to the food industry due to their greater stability than plant and animal enzymes. They can be produced cost-efficiently through fermentation processes, requiring less time and space [47].

Their high consistency also allows for easy process modifications and optimizations that improve vitamins, essential amino acids, proteins, food appearance, flavors, enhanced aroma, and reduced anti-nutrients [22].

4.3. Enzymes used in the food industry

4.3.1. Amylase and glucoamylase

Amylases are generally categorized into two main types based on their enzymatic class: hydrolases (Enzyme Commission, EC 3) and transferases (EC 2). Within the hydrolase class, they are further divided into two primary groups: endoamylases and exoamylases [52].

Glucoamylases, also called saccharifying enzymes, are within the group of exoamylases due to their ability to hydrolyze α-1,4 glycosidic bonds from the non-reducing starch, malto-oligosaccharides, and related substrates, releasing β-D-glucose [53]. They convert the starch to maltose and fermentable sugars. These enzymes are also produced from Saccharomyces cerevisiae during the fermentation with glucose to obtain ethanol. Also, glucoamylases are essential in brewing's sake and soy sauce and creating light beer. These enzymes break down dextrins, transforming them into fermentable sugars, which result in beer with lower calorie content and reduced alcohol levels [47,53].

On the other hand, α-amylase (EC 3.2.1.1) is part of the family of starch-degrading endoamylase enzymes, which catalyzes the hydrolysis of α-1,4 glycosidic linkages in polysaccharides, producing short-chain dextrins. This enzyme is commonly synthesized by various organisms, including Archaea, fungi, bacteria, and animals [47]. Amylases have diverse applications in food processing, such as brewing, livestock feed, baking, fruit juice production, starch syrups, and starch liquefaction. Specifically, α-amylase breaks starches of flour into fermentable sugars, which are then utilized by yeast during bread production to enhance the bread's taste and quality. This enzyme also helps slow staling when incorporated into bread-making [21].

4.3.2. Proteases

Proteases are crucial in commercial and industrial applications, and catalyse the hydrolysis of peptide bonds of proteins to peptides [54]. They represent a large and diverse group of hydrolytic enzymes classified by their site of action, enzyme active site structure, and specific reaction mechanisms [55]. Proteases are categorized depending on their action sites and along polypeptide chains into exopeptidases and endopeptidases. Exopeptidases target chain ends, while endopeptidases cleave internal bonds. Endopeptidases are further grouped into six types according to the catalytic residue in their active site: serine endopeptidases, aspartic endopeptidases, cysteine endopeptidases, metalloendopeptidases, glutamic endopeptidases, and threonine endopeptidases [47,56].

Proteases are produced by diverse organisms, including plants, Archaea, fungi, bacteria, and animals, and are widely used in various food industry sectors, such as brewing, dairy, baking, food processing, and animal feed [21]. These microbial enzymes perform diverse biochemical,

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physiological, and regulatory roles and have been essential in producing traditional fermented foods [54]. The characteristic flavor of fermented products is highly related to proteolysis due to hydrolysates generated precursor compounds, which are related to some important flavor substances during fermented products [57]. Proteases are produced by diverse organisms, including plants, Archaea, fungi, bacteria, and animals. They are widely used in various food industry sectors, such as brewing, dairy, baking, food processing, and animal feed [21]. These microbial enzymes perform diverse biochemical, physiological, and regulatory roles and have been essential in producing traditional fermented foods [54]. The characteristic flavor of fermented products is highly related to proteolysis due to hydrolysates generated precursor compounds, which are related to some important flavor substances during fermented products [57].

4.3.3 Lipases

Lipases (EC 3.1.1.3) are a class of enzymes that catalyze the hydrolysis of long-chain triglycerides. They are widely distributed in animals, plants, and microorganisms. However, microbial lipases find an interesting role in biotechnology, as many of them are stable over a wide range of pH, at elevated temperatures, and in organic solvents. They signify the most important group of biocatalysts for industrial applications [58,59]. These enzymes can modify the properties of lipids by altering the location of fatty acid chains in the glyceride and replacing one or more fatty acids with new ones [58,60].

In the food industry, they are applied to enhance flavors in dairy products, particularly by hydrolyzing milk fats to produce desirable cheese flavors. In bread dough, they hydrolyze triglycerides into diglycerides, monoglycerides, and fatty acids, which improve softness, volume, over-fermentation tolerance, and shelf life [60].

4.3.4. Catalase

Catalase (EC 1.11.1.6) is an oxidoreductase enzyme that reduces reactive oxygen species, particularly hydrogen peroxide, produced during aerobic respiration, thereby serving as an antioxidant and protecting cells from oxidative stress [61]. It is widely used in the food industry, often with enzymes like glucose oxidase for food preservation. In milk processing, catalase removes peroxide; in egg whites, it eliminates glucose; and in baking and food packaging, it helps prevent oxidation and reduces perishability. Its application in cheese production is limited [47].

4.3.5. Cellulases and Xylanases

Cellulases are hydrolytic enzymes that catalyze the cleavage of β-1,4 glycosidic bonds in glucose chains, transforming cellulose into cello-oligosaccharides and glucose via chemical or enzymatic hydrolysis. This category includes endoglucanases (EC 3.2.1.4), exoglucanases (EC 3.2.1.91), and β-glucosidases (EC 3.2.1.21) [62]. Similarly, microorganisms produce xylanases to break down xylans, a key hemicellulose component. Three main enzymes—endoxylanases, exoxylanases, and β-xylosidases—work together to degrade the xylan structure. Specifically, endoxylanases (EC 3.2.1.8) cleave β-1,4 bonds within xylan, while exoxylanases (EC 3.2.1.37) act on the non-reducing ends, producing xylooligosaccharides [63].

In the baking industry, cellulase and xylanase, along with amylases, lipases, and oxidases, enhance dough softness and reduce stickiness by breaking down insoluble cellulose and arabinoxylans in wheat flour into simple sugars, thereby improving flavor and texture in products like bread and cookies [47,64].

These enzymes are also widely used in brewing and fruit juice production, often combined with pectinases and amylases. During brewing, grains such as barley, wheat, and corn undergo mashing and malting to activate enzymes that ferment starch into alcohol. In both brewing and juice processing, cellulases and xylanases, along with pectinases, aid in breaking down cell walls and

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releasing sugars, nutrients, pigments, and aromatic compounds. These macerating enzymes are essential for producing fruit juices and wine [18,62,63].

4.3.6. Lactases (β-Galactosidase)

Lactase, a hydrolase enzyme known as β-galactosidase, is sourced from plants, animals, and microorganisms. Microbial β-galactosidases are widely used in food technology to hydrolyze lactose in milk and its by-products, particularly beneficial for individuals with lactose intolerance. These enzymes break down β-galactopyranosides (like lactose) and produce galactooligosaccharides (GOS), which offer prebiotic health benefits. Additionally, β-galactosidase aids in producing lactose-based sweeteners from the high-lactose effluents of cheese production [47,65].

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4.3.7. Tannases

Tannase or tannin acylhydrolase (EC 3.1.1.20) is an extracellular inducible enzyme that catalyzes the hydrolysis of some tannins and gallic acid esters [66]. Tannases are widely applied in the food, brewing, and pharmaceutical industries. They are found across animal, plant, and microbial sources, with microbial tannases preferred for industrial applications. These enzymes hydrolyze tannins by breaking ester and depside bonds, releasing glucose and gallic acid [67]. In the food industry, tannases improve instant tea by enhancing compound extractability and cold-water solubility. Additionally, tannases prevent haze and undesirable phenolic compounds in beer and wine, improving quality. The enzyme also reduces haze and bitterness in fruit juices. In animal feed, tannases degrade anti-nutritional tannins in agro-industrial by-products, enhancing feed quality [66,68].

4.3.8. Esterases

Esterases are hydrolase enzymes that catalyze the formation and breakdown of ester bonds. Their regio-selectivity, stereospecificity, and stability in organic solvents make them highly valuable for various industrial applications [69]. They are essential in food and alcoholic beverages, mainly for modifying oils and fats in fruit juices and creating flavors and fragrances. A key group, feruloyl esterases, breaks the ester bond between ferulic acid and polysaccharides in plant cell walls. By hydrolyzing lignocellulosic biomass, these enzymes are also crucial for waste management [47].

5. Bioactive Compounds Obtained from Microbial Fermentation

5.1. Carotenoids

Carotenoids are a group of compounds related to the pigments yellow, orange, red, and purple, mainly found in fruits, vegetables, and plants [70]. Carotenoids have a 40-carbon structure with double conjugated bonds and a polyene chain end that varies depending on whether or not an oxygen atom is present; in this sense, carotenoids are classified into two groups, carotenes and xanthophylls [70]. Carotene comprises hydrocarbons, carotenoids such as α-carotene, β-carotene, and lycopene.[70,71]. Xanthophylls are carotenoids with an oxygen atom on the end polyene chain that constitutes a hydroxyl, carbonyl, or aldehyde molecule. Some examples of xanthophylls are lutein, astaxanthin, and fucoxanthin [70]. These compounds have been reported to have a high antioxidant activity that can protect the organisms from oxidative stress caused by biotic and abiotic factors; this effect could be associated with their structure of double conjugated bonds. In this sense, it has been reported that carotenoids are related to potential health effects such as UV-protective, antiproliferative, antidiabetic, anti-inflammatory, and antiatherosclerosis responses.

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Microorganisms have gained popularity as an alternative source to plants to obtain multiple bioactive compounds simultaneously, using cheaper raw materials as carbon sources to reduce the cost of biorefinery [75]. Recently, various microorganisms have been studied for their carotenoid production; among these, photosynthetic bacteria, fungi, marine archaea, and yeast have been utilized to obtain lycopene, ketolases, α-carotene, β-carotene, and other carotenoids through biotechnology strategies [70,74,76,77]. The use of microorganisms as carotenoid producers could be due to the controlled cultivation, high efficiency, and target compounds synthesis, and reduced production period by metabolism modifications [78]. Biotechnology strategies such as metabolic engineering tools for the manipulation of biosynthetic pathways for carotenoid production coupled with the fermentation process followed by separation and purification methods have been widely studied to enhance the production and extraction of carotenoids from microorganisms, where the principal factor studied are pH of culture medium, temperature, process time, moisture content, aeration rate, carbon and nitrogen sources, light, carbon/nitrogen ratio, sonication, chemical supplements, among other parameters [74,79,80]. The use of microorganisms as factories for producing carotenoids has been widely studied due to their diverse color tones, the ability to manipulate them, and low equipment requirements [81]. However, some disadvantages, such as the high production costs, have limited their industrial application. As a result, other biotechnological approaches are being explored to enhance carotenoid production and reduce costs using various microorganisms [75,80,82-84].

In this sense, it has been reported that fermentation technology has been used in conjunction with biotechnological manipulations such as metabolic engineering to produce carotenoids with high production yields, efficiency, moderate cost of production, and environmentally friendly in contrast to chemical synthesis and plant or animal sources extraction due to the fast-growing strains and downstream techniques to extract the target products [74,80]. In this sense, microorganisms such as *Blakeslea trispora*, *Chryseobacterium artocarpi* CECT 8497, *Flavobacterium* sp. Cells, *Serratia marcescens*, and *Phaffia rhodozyma*, *Rhodosporidium toruloides*, *Sporobolomyces*, *Sporidioblous*, and *Xanthophyllomyces Dendrorhous* has been used to obtain anthraquinones, astaxanthin, β-carotene, canthaxanthin, flexirubin, lutein, and zeaxanthin by optimized fermentation process [74,77,81,85,86], while other microorganisms as *Escherichia Coli*, *Saccharomyces cerevisiae*, *Pichia pastoris*, and *Yarrowia lipolytica* has been modified throughout biotechnology strategies as well as different extraction process to obtain carotenoids with high yields (**Figure 3**) [15,80,84].

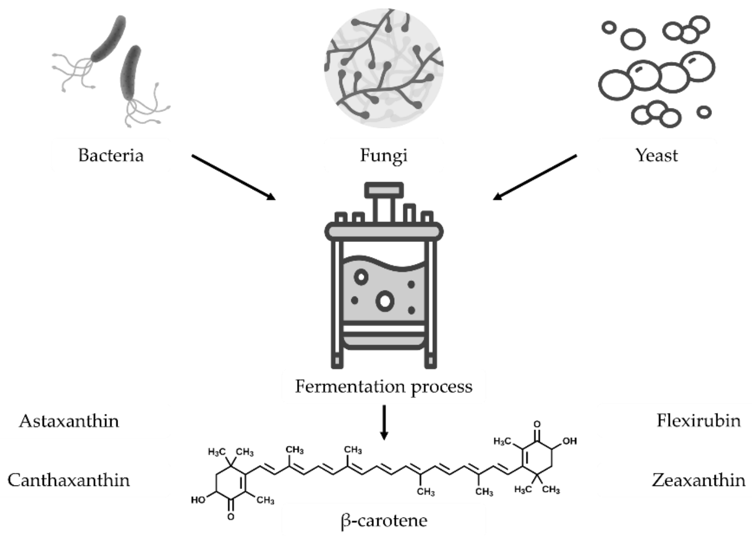

Figure 3. Carotenoids obtained by the fermentation process of microorganisms

On the other hand, the effect of fermentation on carotenoids from different food sources and by-products has been studied [82]. In this sense, orange, sweet potato, carrot, tomato, marigold red

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paper, goji berries, and marine by-products, among other sources, have been studied to obtain astaxanthin, carotenes (α-carotene and β-carotene), lutein, lycopene, and zeaxanthin [75,82,83,87]. Likewise, fermentation factors such as matrix sources, fermentation conditions, as well as the microorganism studied, have been reported to enhance or maintain the carotenoid content; also, the use of some microorganisms could favor the carotenoid extraction and bioavailability by the production of enzymes that separate the carotenoids from the food matrix, and facilitate the extraction with downstream strategies [82,83].

5.2. Essential oils

Essential oils are bioactive compounds derived from plants composed mainly of low molecular weight volatile compounds such as terpenes and hydrocarbons [88,89]. These substances have attracted the attention of pharmaceutic and food industries due to their therapeutic [90], anticancer [91], antimicrobial [92], antioxidant [93], and food safety properties [94]. Also, essential oils contain compounds with strong odors, and the fragrance industry has also been interested in the obtention of these materials. The production of essential oils can be carried out by direct plant extraction, plant cell cultures, and microbial fermentation [95]. Specifically, the application of microbial fermentation can be classified into biotransformation (fungi or yeast transform compounds based on certain substrates), methods that use waste residues (food waste), and metabolic pathways followed by genetically modified microorganisms (**Figure 4**).

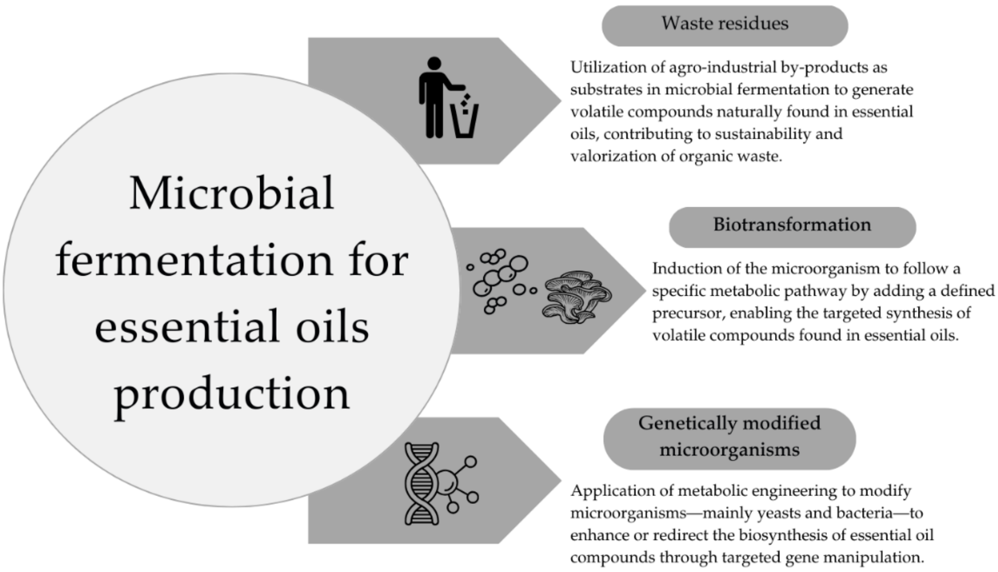

Figure 4. Methods reported in the literature to produce essential oils by microbial fermentation.

Besides these methods, there are a few recent reports regarding the de novo synthesis of essential oils by microorganisms. For example, fungal cultures (13 strains belonging to *Aspergillus* sp., *Ceratocystis* sp., and *Neurospora* sp.) produced interesting volatile compounds that can be found in essential oils from plants such as citral and β-citronellol [96], which have been studied for their antifungal [97] and vasorelaxant properties in rats [98].[98] On the other hand, Sen, *et al.* [99] reported that the interaction of agarwood (*Aquilaria malaccensis*) callus with the associated fungus *Fusarium* produced by fermentation led to a significant accumulation of terpenes such as geranyl isovalerate and tetrapentacontane,1,54, dibromo-. Also, the infection of juvenile *A. malaccensis* plants coupled with associated *Fusarium* registered the presence of sesquiterpenes such as agarospirol, γ-eudesmol, (−)-aristolene, which were exclusive of the fermentation with this fungus. In this sense, the main issue with the de novo synthesis of essential oil compounds by microorganisms is the accumulation of the obtained metabolites that can result in toxic environments for the organisms. This is the case of geraniol and citronellol production by the fungi genus *Ceratocystis*, whose removal procedures

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consisted of integrated bioprocesses that had to be applied to eliminate contaminated substances [100].

Regarding the use of waste residues for obtaining essential oils (or their compounds) through microbial fermentation, [101] proposed a solid-state fermentation process that employs fungi, bacteria, and yeast strains (*Aspergillus*, *Trichoderma*, *Bacillus,* and *Saccharomyces*) to produce volatile compounds from basil leaf and stem waste. Several substances of importance for human health and the food industry were identified, such as ϒ-Bisabolene, isoprenyl cinnamate, diacetyl, and ethyl isovalerate. These compounds are present in natural essential oils from plants, and they have been studied for antioxidant [102], antimicrobial [103], antifungal [104], and food preservation [105] properties. Another therapeutic compound in essential oils is D-limonene, which can be obtained via the fermentation of olive mill waste by Rhizopus oryzae fungus and Candida tropicalis yeast [106]. The quantification of this substance revealed that R. oryzae produced a higher amount of D-limonene than C. tropicalis in controlled conditions: 87.73 µg/kg and 11.95 µg/kg, respectively. Therefore, agro-industrial waste residues are suitable for producing volatile compounds with health benefits. For example, rice bran oil waste is rich in ferulic acid, a vanillin precursor. Zheng, et al. [107] reported a consecutive bioconversion process from ferulic acid of rice bran oil residue fermented by Aspergillus niger to vanillic acid; and then, this broth was fermented by Pycnoporus cinnabarinus to obtain vanillin. A maximum concentration of this compound (2.8 g/L) with a molar yield of 61.9% at 72 h was registered.

In the case of biotransformation as a method for obtaining essential oils from microbial fermentation, this process is defined as the induction of the microbe to follow a specific metabolic pathway from an introduced precursor [108]. For that, geranic acid has been synthesized from geraniol by *Rhodococcus* sp., a group of bacteria isolated from soil. This synthesis was controlled by reaching a maximum conversion (54.6%) of geranic acid after 96 h of incubation at 30 °C as the optimal temperature for the reaction [109]. Besides these bacteria, yeasts have been reported to produce volatile compounds via bioconversion. Oda*, et al.* [110] developed a metabolic pathway by *Hansenula* and *Pichia* yeasts using acetyl-CoA to synthesize citronellol, finding that the accumulation of citronellol in the incubating system could intoxicate yeasts; therefore, sodium acetate was added to control the production rate of citronellyl acetate for all strains. In this sense, yeasts can be affected by their metabolites in the production of the fragrance compound 2-phenylethanol (2-PE) from phenylalanine by *Saccharomyces cerevisiae*, in which the use of hydrophobic polymethylmethacrylate (PMMA) microspheres has been reported to physically remove the accumulation of phenylethanol [111]. This interesting volatile compound has been studied for treating psychiatric disorders such as depression [112].

Based on the above-mentioned, yeasts have been broadly studied to produce compounds of essential oils. However, metabolic engineering has been applied to modify these microorganisms at the genetic level. An increase in geraniol concentration (from 43.19 mg/L to 523.96 mg/L) via synthesis performed by manipulating enzymes GES and Erg20WW in *S. cerevisiae* was reported [113]. Also, this compound's production was enhanced by modifying the site where the geraniol synthesis occurred in *S. cerevisiae* peroxisomes, which improved the geraniol titers by 80% [114]. Therefore, *S. cerevisiae* represents an appropriate "factory" for essential oils generation. Important substances such as limonene have been obtained by orthogonal engineering in which a metabolic pathway was created by genetic modification in this yeast, producing significant amounts of limonene (917.7 mg/L) in fed-batch fermentation [115]. In addition to reported experimental trials, Werner*, et al.* [116] informed through an in-silico study that modifying gene expression of central metabolic enzymes in *S. cerevisiae* can increase β-ionone yields up to 4-fold. Most microorganisms used for essential oil production belonged to the fungi kingdom; however, gene modification has been commonly applied in prokaryotic organisms. One of these microorganisms is *E. coli*, which has been altered to produce volatile compounds such as patchoulol [117], viridiflorol and amorphadiene [118], ionone [119], bisabolol [120], and others.

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5.3. Phenolic compounds

Phenolic compounds are bioactive compounds obtained from plants with a benzene ring with one or more hydroxyl groups. These products can be found in various natural foods, such as cereals, vegetables, fruits, and beverages such as wine, coffee, cocoa, and tea [121,122]. Phenolic compounds, including flavonoids, tannins, lignans, and stilbenes, are abundant plant compounds synthesized via the shikimate pathway using L-phenylalanine and L-tyrosine as precursors [123]. These compounds are present in various foods and beverages, contributing to their health benefits and bioactivity. Cocoa and its derivatives are among the most studied food matrices due to their high polyphenol content. Bacterial fermentation of cocoa beans significantly increases the release of conjugated phenolic compounds, such as caffeoyl aspartic acid and p-coumaroyl tyrosine, within 24 hours of fermentation [124]. Using strains like *Saccharomyces cerevisiae* and *Pichia kudriavzevii* further enhances phenolic content, showcasing their potential for improving food bioactivity [125]. In microbial fermentation, phenolic acids undergo extensive biotransformation by the gut microbiota, producing smaller bioactive metabolites. Microbial fermentation processes significantly influence protocatechuic and vanillic acids derived from cocoa shells. During colonic fermentation, the gut microbiota transforms these compounds into metabolites such as benzoic, phenylpropanoid, and phenylacetic acids. Additionally, fermentation of cocoa by-products generates other phenolic compounds, such as caffeoyl aspartic acid, p-coumaroyl aspartic acid, clovamide, and p-coumaroyl tyrosine. These transformations are heavily influenced by the dietary fiber content in cocoa shells, which modulates the release and microbial accessibility of phenolic acids [126]. Similarly, coffee pulp fermentation enhances the production of phenolic metabolites such as phenylpropanoic acids and phenyl-γ-valerolactones, while reducing the overall concentration of polyphenols [127]. The fermentation process, driven by microbial activity, modulates these phenolic transformations and generates bioactive compounds like benzoic and phenylacetic acids. Additionally, dietary fiber and alkaloid content, such as caffeine and trigonelline, influence the bioavailability and release of phenolic compounds during fermentation [128].

Cereals naturally contain phenolic compounds predominantly in bound forms, which limits their bioavailability [129,130]. Specific processing techniques, such as microbial fermentation, are required to enhance the release of these antioxidant compounds and increase their free-form levels. Fermentation with ragi tape effectively enhances phenolic content in black glutinous rice. Over 72 hours, free phenolics increased by 49%, and free-conjugated phenolics peaked at 48 hours with an 8% rise. This process significantly improved antioxidant activity, as indicated by reduced IC50 values. Key phenolic compounds, including caffeic and ferulic acids, showed notable increases, highlighting the potential of ragi tape fermentation to boost the antioxidant properties of this rice variety [131]. Solid-state fermentation (SSF) of sorghum grain (SG) enhances sensory characteristics by modifying its polyphenol content. Various microbial strains (*Lactiplantibacillus plantarum*, *Saccharomyces cerevisiae*, *Rhizopus oryzae*, *Aspergillus oryzae*, and *Neurospora sitophila*) were used to assess their impact on polyphenols. After SSF, tannin and free phenolic contents were reduced by 56.36% and 23.48%, respectively. Cellulase played a crucial role in degrading tannins and phenolic compounds, while xylanase initially released flavonoids, although microbial consumption altered this effect over time. These findings highlight the potential of SSF to modify the polyphenolic profile and improve SG bioactivity and processing characteristics *[132]*. In a study on rye flour fermentation, the microbial community of germinated rye was enriched during lactic acid fermentation with increased terpenoid and phenolic compounds. Metabolomic analysis revealed notable changes in phenolic compound profiles, including the accumulation of bioactive polyphenols. Specifically, compounds such as ferulic acid, caffeic acid, and p-coumaric acid were identified post-fermentation, suggesting that sourdough fermentation can enhance the content of bioactive polyphenols, contributing to the health-promoting potential of fermented rye flour *[133]*. Studies consistently demonstrate that microbial fermentation significantly enhances the phenolic profile and antioxidant activity of cereals. While cereals naturally contain phenolics, a substantial portion exists in bound forms, limiting their bioavailability *[134]*. Fermentation releases these bound phenolics, as observed in black glutinous

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rice with ragi tape, sorghum, and sourdough-fermented rye, where free phenolics like caffeic, ferulic, and p-coumaric acids increased, boosting antioxidant activity. This process is attributed to microbial enzymes like feruloyl esterases, which hydrolyze bonds linking phenolic acids to cell walls [135].

Microbial fermentation is a crucial bioprocess for preserving fruits and vegetables. This biological method reduces the risk of contamination by producing antimicrobial compounds like organic acids, ethanol, and bacteriocins. Beyond preservation, fermentation enhances these foods' nutritional value and creates new and desirable tastes and textures[136]. Citrus fruits, including their peels, are abundant sources of bioactive compounds such as phenolic acids, flavanones, and polymethoxylated flavones, alongside carotenoids and ascorbic acid [137,138]. Microbial fermentation of citrus peels, including orange, lemon, and grapefruit, was conducted using *Lactobacillus plantarum* and *Lactobacillus acidophilus* as fermentation agents. This process significantly enhanced the phenolic profile by transforming bound phenolics into more bioavailable forms. Key phenolic acids such as ferulic acid, caffeic acid, and p-coumaric acid were notably increased. Additionally, flavonoids like naringenin and hesperidin showed considerable elevation, improving antioxidant activity [139]. In the case of orange peel, SSF significantly increased the release of phenolic compounds. The fermentation process primarily resulted in the formation of flavonoid aglycones, such as naringenin, hesperetin, and nobiletin, replacing the glycoside hesperidin found in unfermented peels. Additionally, the fermented peel showed enhanced antioxidant activity [140].

In chili peppers, microbial fermentation increases both the quantity and diversity of phenolic compounds [141]. Lactic acid bacteria secrete enzymes like amylase, β-glucosidase, and phenolic acid decarboxylase, facilitating the release of bound polyphenols and enhancing antioxidant activity [142]. Caffeic acid, a key phenolic, rises during early fermentation stages but degrades into compounds like vinyl catechol and ethyl catechol as fermentation progresses [143]. Ferulic acid, another significant phenolic found in chili pepper and carrots, can be metabolized into vanillic acid and protocatechuic acid, highlighting the transformative potential of fermentation on polyphenolic profiles [144]. In chili peppers, microbial fermentation increases both the quantity and diversity of phenolic compounds *[141]*. Lactic acid bacteria secrete enzymes like amylase, β-glucosidase, and phenolic acid decarboxylase, facilitating the release of bound polyphenols and enhancing antioxidant activity *[142]*. Caffeic acid, a key phenolic, rises during early fermentation stages but degrades into compounds like vinyl catechol and ethyl catechol as fermentation progresses *[143]*. Ferulic acid, another significant phenolic found in chili pepper and carrots, can be metabolized into vanillic acid and protocatechuic acid, highlighting the transformative potential of fermentation on polyphenolic profiles *[144]*.

Onion by-products are abundant in fiber and bioactive compounds, offering a valuable source for developing various bioproducts, including polyphenols [145]. A study assessed the potential of onion skins for polyphenol release through fermentation by different microorganisms, including bacterial and yeast strains. Results showed that fermentation with specific strains like Lactiplantibacillus plantarum and Saccharomyces cerevisiae increased the content of bioactive compounds, particularly quercetin aglycone, by up to 60% in yellow onion skins [146].

Wild herbs and plants are rich in phenolic compounds, particularly flavonoids [147]. Fermentation with microorganisms such as bacteria is known to increase the bioactive compounds in plants, particularly those with antioxidant and antibacterial properties [148]. For example, a study investigated the fermentation of *Dendrobium officinale* using brewer's yeast (*Saccharomyces cerevisiae*) to enhance its bioactive compounds, particularly phenolics. By optimizing fermentation conditions through single-factor and orthogonal experiments, the researchers produced a fermentation broth enriched in these valuable compounds. Notably, the fermentation process yielded four key phenolic acids: gallic acid, protocatechuic acid, catechol, and pentosidine B sesil [149]. *Achillea millefolium* L. (yarrow) and *Origanum majorana* L. were studied as sources of phenolic-rich extracts, focusing on their impact on human gut microbiota and microbial metabolism. SSF enhanced the bioavailability of phenolic compounds like rosmarinic acid and caffeoylquinic acids. The microbial metabolism yielded significant metabolites, including phloroglucinol and 3,4-dimethoxyphenylacetic acid [150]. Beverages such as wine, beer, coffee, and tea are substantial sources of polyphenols, the most

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abundant antioxidants in the human diet [151]. Fermentation is an emerging method used to enhance the phenolic content in beverages, thereby improving their antioxidant properties. For instance, microbial fermentation of tea extracts using *Trichoderma reesei*, *Aspergillus niger*, and lactic acid bacteria (LAB) transformed pivotal bioactive compounds. Galloylated catechins were hydrolyzed, and organic acids were decarboxylated, increasing phenolic bioavailability. Additionally, alcohols and ketones accumulated, enhancing the aroma profile [152]. This highlights fermentation as a promising tool for improving both the phenolic composition and sensory qualities of tea beverages. Blueberry pomace, a by-product of juice processing, has shown significant potential as a matrix for phenolic enrichment through SSF. In a recent study, various fungal and LAB strains, including *Aspergillus niger* (AN), *Lactobacillus acidophilus* (LA), and *Lactobacillus plantarum* (LP), were utilized to enhance its polyphenol profile. Fermentation increased the content of key phenolic acids such as gallic acid, caffeic acid, and chlorogenic acid, as well as flavonoids like quercetin. Notably, anthocyanin levels decreased overall, except in pomace fermented by AN, where anthocyanidins showed an upward trend. Enhanced antioxidant activities were observed, with ABTS, DPPH, and FRAP radical scavenging capacities rising by 33.56%, 59.89%, and 87.82%, respectively. Additionally, simulated gastrointestinal digestion revealed improved bioaccessibility of polyphenols, underscoring SSF as an effective method for value-added utilization of blueberry pomace in functional food development [153]. Albino bilberry (*Vaccinium myrtillus* L.) juice [154] and Chinese rice wine [155] exemplify the impact of fermentation on enhancing phenolic composition and flavor complexity. In albino bilberry juice, fermentation with non-Saccharomyces yeasts resulted in increased phenolic acids (21.8%–42.5%), flavonols (26.8%–47.2%), and flavan-3-ols (4.9%–74.5%), with novel flavonols synthesized during the process. *Hanseniaspora uvarum* yielded the highest phenolic enhancements, showcasing yeast metabolism's role in antioxidant enrichment. Similarly, in Chinese rice wine brewed from five raw materials, liquid-state fermentation and grain liquefaction influenced flavor compounds and microbial diversity. Buckwheat-fermented wine stood out with the highest ester (27.39 mg/L), amino acid (1.47 mg/mL), and phenolic acid (904.29 mg/L) contents, contributing to its complex sensory profile characterized by honey, floral, and umami notes. Metagenomic sequencing revealed variations in microbial communities, with dominant genera including Saccharomyces, Aspergillus, and Bacillus. Together, these studies emphasize the importance of fermentation parameters and raw material selection in tailoring phenolic profiles, microbial ecology, and sensory attributes in functional beverages.

Fermentation can generate the synthesis of phenolic compounds, further increasing their content and antioxidant capacity [156]. However, the lack of standardized methodologies for analyzing phenolic compounds, the use of various microorganisms, and different extraction methods present opportunities to further improve the understanding and application of microbial fermentation in enhancing phenolic profiles *[157-159]*. Standardizing analytical techniques, selecting the appropriate microorganisms, and extraction methods are essential to maximizing the benefits of fermentation for food quality improvement.

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Table 2. Summary of phenolic compounds enhanced through fermentation in recent studies.

Food Matrix	Fermentation Treatment	Phenolic Compounds Increased	
Cocoa shells	In vitro colonic fermentation	Caffeoyl aspartic acid, p-coumaroyl aspartic acid, clovamide, p-coumaroyl tyrosine	[126]
Coffee pulp	In vitro colonic fermentation	Phenylpropanoic acids, phenyl-γ-valerolactones	[127]
Black glutinous rice	Ragi tape fermentation	Caffeic acid, ferulic acid	[131]
Sorghum grain	SSF with various microbial strains	Tannins, free phenolics (caffeic, ferulic, p-coumaric acids)	[132]
Rye flour	Lactic acid fermentation	Ferulic acid, caffeic acid, p-coumaric acid	[133]
Citrus peels (orange, lemon, grapefruit)	*Lactobacillus plantarum, Lactobacillus acidophilus*	Ferulic acid, caffeic acid, p-coumaric acid, naringenin, hesperidin and nobiletin	[139,140]
Chili peppers	Lactic acid bacteria	Caffeic acid, ferulic acid	[141]
Onion skins	*Lactiplantibacillus plantarum, Saccharomyces cerevisiae*	Quercetin aglycone	[146]
Dendrobium officinale	*Saccharomyces cerevisiae*	Gallic acid, protocatechuic acid, catechol, pentosidine B sesil	[149]
Achillea millefolium L. and *Origanum majorana* L.	SSF with various microbial strains	Rosmarinic acid, caffeoylquinic acids, phloroglucinol and 3,4-dimethoxyphenylacetic acid	[150]
Tea extracts	*Trichoderma reesei*, *Aspergillus niger*, Lactic acid bacteria	Galloylated catechins, organic acids	[152]
Blueberry pomace	Various fungal and LAB strains (*Aspergillus niger, Lactobacillus acidophilus, Lactobacillus plantarum*)	Gallic acid, caffeic acid, chlorogenic acid, quercetin	[153]
Albino bilberry juice	Non-Saccharomyces yeasts	Phenolic acids, flavonols, flavan-3-ols	[154]
Chinese rice wine	*Saccharomyces, Aspergillus, Bacillus*	Phenolic acids	[155]

[1] Summary of microbial fermentation treatments applied to various food matrices. The table highlights the phenolic compounds that were enhanced as result of fermentation, showcasing the potential of microbial processes in improving the bioavailability and antioxidant properties of phenolic compounds in food.

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5.4. Polysaccharides

The fermentation process induces the production of several types of polysaccharides by microorganisms. Some of these compounds possess properties which are beneficial for human health, such as antioxidant, antitumor, and anti-inflammatory activities [160,161]. Also, they are considered biocompatible and biodegradable materials with high yield and reproducible production [160].

In this sense, a high amount of research can be found in the literature reporting that lactic acid fermentation by bacterial strains (*Lactobacillus*, *Leuconostoc*, among others) produces exopolysaccharides. Exopolysaccharides are a specific type of extracellular biopolymers synthesized by bacteria and some fungi, having several health and physicochemical properties [162,163]. For that, **Table 3** summarizes different exopolysaccharides with biological activities produced by microbial fermentation.

One of these substances is dextran, a long-chain glycopolymer reported as a functional molecule for medical purposes such as plasma volume expander, wall material for encapsulation, and an alternative to tomography markers [164]. Schmid*, et al.* [165] stated that the properties of dextran are dependent on its molecular weight (i.e. length of the polymer chain). In that report, dextran polymers with high molecular weights (1.09×10^8 – 1.86×10^8 Da) produced by *Liquorilactobacillus hordei* exhibited different rheological properties, indicating that the dextran with the longest chain had the best capacity to form films and gels.

Similarly, Esmaeilnejad-Moghadam*, et al.* [164] found that dextran synthesized by *Leuconostoc mesenteroides* in milk permeate culture media possessed the lowest molecular weight and increased solubility as compared to dextran produced in broth medium. Besides its techno-functional properties, an appropriate antioxidant activity has been detected (by ABTS and DPPH analyses) in dextran obtained by the fermentation with *Leuconostoc pseudomesenteroides* isolated from the Juçara palm tree [166]. However, some bacteria cannot produce exopolysaccharides in fermentation conditions. As an example, *Lactobacillus fermentum* was investigated during the fermentation of longan pulp, finding that the polysaccharides of the fruit changed in composition and chemical structure because of the action of the bacteria. The polysaccharides from the fermented pulp were composed mainly of arabinose (49%), galactose (23%), glucose (14%), and other monosaccharides (~14%), in which immunomodulatory and prebiotic activities were detected [167].

Also, the prebiotic activity has been attributed to fructooligosaccharides that can be synthesized by the enzymes inulosucrase and endoinulinase present in bacteria such as *Leuconostoc citreum* and *Aspergillus niger*, respectively. In this study, sucrose was more effective than inulin as a substrate for the chain reaction to produce these prebiotic compounds [168]. On the other hand, the production of functional polysaccharides by fungi has been commonly studied in fermentation conditions involving *Tremella* spp. The basidiospore fermentation by *Tremella aurantialba* in tofu wastewater has been proposed as a method for obtaining adequate yields of polysaccharides (~15.02 g/L) whose composition was based on monosaccharides such as glucose and mannose [169]. Similarly, Ge*, et al.* [170] examined *Tremella fuciformis* in fermentation conditions, finding that this fungus produced macromolecular polysaccharides (yield ≈ 9.0 g/L) which were composed of xylose, mannose and galactose residues and having antioxidant properties determined by the scavenging capacity of superoxide anions and hydroxyl radicals analyses. Besides the antioxidant activity, neuroprotective [171], immunomodulatory [172], and antitumor [173] activities have been reported for polysaccharides produced by *Tremella* spp.

Regarding the fermentation by yeasts, Chen*, et al.* [174] addressed the biological properties of polysaccharides obtained by the fermentation of a flower *Dendrobium officinale* carried out by *Saccharomyces cerevisiae* and *Wickerhamomyces anomalous*. Both yeasts produced four polysaccharides (comprised of mannose and glucose, having the following ratios 3.31:1, 5.56:1, 2.40:1, and 3.29:1) that were isolated, possessing an enhanced antioxidant property; however, the anti-inflammatory activity was inadequate for the proposed experimental conditions.

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Also, the production of endopolysaccharides by yeast has been reported for the fermentation of biodiesel-derived crude glycerol, in which yeast strains belonging to *Debaryomyces* sp., *Naganishia uzbekistanensis*, *Rhodotorula* sp., and *Yarrowia lipolytica* generated biopolymers with potential for pharmaceutical applications [175].

Furthermore, bacteria can produce polysaccharides of interest alongside other microorganisms. In this sense, the fermentation of okara (residue from soybean) by lactic acid bacteria *Lactobacillus bulgaricus* and fungi *Neurospora crassa* produced polysaccharides (composed mainly of galacturonic acid, galactose, and arabinose) with sugar blood regulation, glucose adsorption delaying and prebiotic properties [176]. In another study, yeast *Saccharomyces cerevisiae* and bacteria *Bacillus subtilis* enhanced the polysaccharides obtained by the fermentation of wheat bran, indicating that the isolated products (composed mostly of galactose, xylose, and galacturonic acid) possessed suitable antioxidant properties (measured by DPPH test) [177]. Therefore, the combination of bacteria with other microorganisms, such as fungi and yeasts can result in the enhancement of polysaccharides produced by fermentation of different sources.

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Table 3. Exopolysaccharides synthesized by microbial fermentation and their health properties

Microorganism	Specie	Exopolysaccharide	Health properties	Ref.
Bacteria	*Acetobacter xylinum*	Levan	Antioxidant, anti-inflammatory	[178]
Bacteria	*Lactobacillus plantarum*	Glucose and galactose residues	Antioxidant	[179]
Bacteria	*Paenibacillus polymyxa*	Heteroglycan formed by (1→4) and (1→6) hexose residues	Antioxidant, immunomodulatory, mitogenic, allergenic, anti-inflammatory	[180]
Bacteria	*Escherichia coli* (modified with a *Leuconostoc citreum* gene)	Alternan	Encapsulation capability	[181]
Bacteria	*Bacillus* sp. isolated from fermented pickles	Glucose and galactose residues	Antioxidant	[182]
Fungi	*Polyporus umbellatus*	3 polysaccharides composed by mannose, galactose and glucose (molar ratios: 43.6:2.5:1.0; 17.7:3.1:1.0 and 4.6:2.6:1.0)	Antioxidant, immunological, cellular aging delaying, DNA damage protecting	[183]

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6. Applications of Bioactive compounds obtained from microbial fermentation

6.1. Animal feed

The use of fermented feed is gaining attention as a sustainable approach to improving livestock health while addressing environmental concerns. Fermented feed is a biologically modified product resulting from microbial fermentation that transforms feed components into microbial proteins, bioactive peptides, amino acids, and beneficial probiotics [184]. This process enhances the digestibility of complex carbohydrates, proteins, and fibers, improving nutrient availability and reducing the impact of anti-nutritional factors such as phytates and protease inhibitors [185,186]. Fermented feed is gaining attention as a sustainable approach to improving livestock health while addressing environmental concerns. Fermented feed is a biologically modified product resulting from microbial fermentation that transforms feed components into microbial proteins, bioactive peptides, amino acids, and beneficial probiotics [184]. This process enhances the digestibility of complex carbohydrates, proteins, and fibers, improving nutrient availability and reducing the impact of anti-nutritional factors such as phytates and protease inhibitors [185,186].

Gut microbiota *is crucial* in livestock health and productivity [187]. Fermented feed has been shown to positively modulate gut microbiota composition by increasing the abundance and diversity of beneficial microorganisms. This promotes optimal nutrient absorption, gastrointestinal health, and immune function while reducing disease incidence and oxidative stress *[188,189]*. This modulation of gut microbiota through fermented feed is increasingly recognized as a sustainable alternative to antibiotics, improving animal welfare and production efficiency [190].*[190]*. It also mitigates oxidative stress by protecting the gastrointestinal tract, aiding recovery, and boosting stress resilience, supporting efficient and sustainable livestock production [188].

The growing interest in fermented feed stems from its demonstrated benefits across various livestock species. For example, in Bamei piglets, the inclusion of *Lactobacillus plantarum* and *Bacillus subtilis*-fermented feed led to higher weight gain, better feed efficiency, and improved immunity, as evidenced by elevated levels of immunoglobulins and reduced inflammatory markers. The fermented feed also positively impacted the gut microbiota, enhancing the diversity of beneficial bacteria such as *Lactobacillus* and *Prevotellaceae*, which are crucial for maintaining intestinal health and optimizing nutrient absorption *[191]*. Similarly, fermenting the plant-based fraction of their feed with *Lactobacillus* and *Bacillus subtilis* significantly improved growth performance, meat quality, and nutrient utilization in broiler chickens. Additional benefits included reduced cholesterol content and better feed conversion ratios, showcasing its potential to enhance poultry production efficiency and product quality *[184]*. Similar benefits have been observed in aquaculture, where fermented feeds improve nutrient digestibility, enhance immune responses, and promote growth. These feeds support metabolic and digestive enzyme activity by providing proteins and micronutrients while reducing anti-nutritional factors, contributing to healthier and more sustainable aquaculture production *[192]*. Furthermore, the microbial fermentation of *Psophocarpus tetragonolobus* (winged bean tubers) has shown promising results in ruminant diets, enhancing their nutritional value, improving feed degradability, and optimizing volatile fatty acid profiles, with increased propionic acid levels and energy efficiency. This highlights the potential of fermented tuber pellets as a sustainable alternative to traditional feed ingredients like corn meal, supporting both animal health and productivity *[193]*. In poultry, a study on Xuefeng black-bone chickens demonstrated that the combination of microbial fermented feed and ginseng polysaccharides using (*Saccharomyces cerevisiae*, *Bacillus subtilis*, *Lactobacillus plantarum*, and *Enterococcus faecium*) further enhanced growth performance, feed efficiency, and immune function *[194]*. These studies demonstrate the broad applicability of microbial fermentation in improving livestock health and productivity across species such as swine, poultry, ruminants, and fish. By supporting sustainable and efficient production systems, fermented feeds represent a vital tool in advancing eco-friendly livestock management.

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6.2. Agricultural use

Microbial products offer a sustainable alternative to traditional agricultural chemicals and fertilizers by enhancing crop yields and improving soil health. Companies increasingly use microorganisms as biocontrol agents and biofertilizers through carrier-based inoculants, which enrich the soil by producing essential nutrients through their metabolic activities. Building upon these benefits, recent studies have highlighted the critical role of microbial metabolites in promoting plant growth and enhancing disease resistance. This supports plant growth by enhancing nutrient availability, such as nitrogen, phosphorus, and potassium, while improving soil properties and boosting beneficial bacteria. These applications not only decrease reliance on chemical inputs but also contribute to soil biodiversity and health, which is crucial for maintaining long-term agricultural sustainability *[195-197]*.

Recent studies have highlighted the pivotal role of microbial metabolites in plant growth promotion and disease resistance. Plant growth-promoting rhizobacteria produce metabolites such as auxins, cytokinins, and gibberellins, which enhance nutrient uptake, stimulate plant growth, and improve disease resistance by inhibiting pathogens and inducing systemic resistance *[198,199]*. Plants further influence their microbiomes by secreting specific compounds that recruit beneficial microbes to suppress pathogens and enhance plant immunity *[200]*. These insights demonstrate the potential of microbial metabolites to support resilient cropping systems while reducing dependency on chemical inputs.

In addition to promoting disease resistance, microbial metabolites also play a key role in helping plants cope with environmental stresses such as drought, salinity, and temperature extremes by enhancing plant physiology, boosting antioxidants, and improving water retention, ultimately increasing productivity under stress *[201,202]*. Exopolysaccharides secreted by soil bacteria improve soil aggregation and water retention, promoting plant hydration during drought by enhancing water infiltration *[203]*. Under salinity stress, osmoprotectants like trehalose and proline produced by microbes accumulate in plant cells to maintain osmotic balance and protect cellular components from salt-induced damage *[204]*. Microbial compounds also enhance plant antioxidant systems, scavenging reactive oxygen species to prevent oxidative damage and preserve cellular integrity *[205]*. In addition, some metabolites induce the expression of stress-responsive genes, enabling better adaptation and tolerance to abiotic stresses *[206]*.

Given their benefits, the adoption of microbial metabolites in agriculture represents a sustainable shift from traditional chemical fertilizers and pesticides, promoting eco-friendly farming practices. Microbial inoculants derived from beneficial bacteria and fungi, combined with renewable feedstocks in microbial fermentation, enhance soil fertility, support plant health, and reduce reliance on chemical inputs, contributing to sustainability by minimizing dependence on non-renewable resources *[207]*. Furthermore, microbial biotechnology bolsters soil biodiversity and health, with managed soil microbiomes significantly improving crop productivity and resilience *[208]*.

Recent advancements in biotechnology, including the development of engineered microbes, have enhanced the production of microbial metabolites, providing sustainable alternatives to traditional fertilizers and pesticides by efficiently converting renewable feedstocks into biofertilizers and biopesticides *[209]*. These biotechnological advancements not only enhance microbial metabolite production but also significantly contribute to improving agricultural efficiency. By optimizing fermentation conditions and selecting suitable microorganisms, the yield and effectiveness of these metabolites have been enhanced. For example, engineered microbes are capable of converting renewable feedstocks into high-value biofertilizers and biopesticides, which support eco-friendly agricultural practices *[210]*. Additionally, the use of genetic engineering techniques has led to the development of tailored microbial strains that produce specific metabolites at higher concentrations, improving agricultural efficiency *[211]*. Microorganisms significantly important in agriculture have long been recognized as an effective and eco-friendly alternative in modern farming, reducing the dependence on synthetic fertilizers and pesticides *[212]*. Furthermore, biotechnological advancements in microbial applications support sustainable agriculture by minimizing reliance on

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non-renewable resources, as they utilize renewable feedstocks in fermentation processes. As these technological advances continue to evolve, they further drive the adoption of microbial-based practices, ultimately ensuring a more sustainable and productive agricultural system *[213]*.

6.3 Human health

The fermentations stand out as a promising alternative for improving health due to its content of bioactive compounds, which are linked to the metabolic and biotransformation activities carried out by microorganisms [214]. The transformation of the natural components of the raw material during fermentation results in the production of enzymes that cause the transformation of complex compounds into simple biomolecules, giving rise to compounds with biological activity beneficial to human health (Figure 5) [136,215].

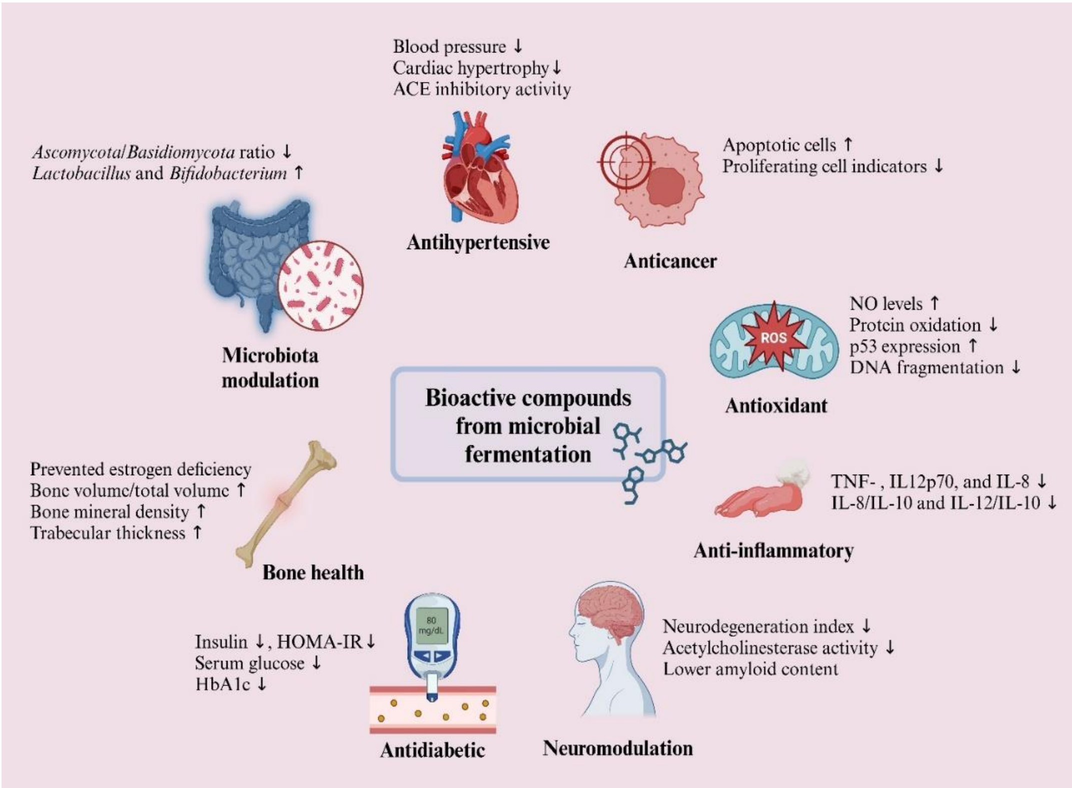

Figure 5. Principal human health applications of bioactive compounds from microbial fermentation. Created by Biorender.com.

Dairy fermentations such as milk, yogurts, cheeses, creams, and ice creams contain probiotic bacteria, and some meats, sausages, bread, and cereal products [216]. The necessary amount of these viable microorganisms in a food to exert health benefits varies between 10^8 and 10^9 colony-forming units (CFU) per day. Their effectiveness depends on the type of microorganism and the physiological conditions of the consumer [217]. The mechanisms of action associated with the health effects of these microorganisms include competitive inhibition of pathogenic bacteria proliferation (through alterations in pH levels and a reduction in oxygen availability) and non-competitive inhibition via the production of bacteriocins [218]; synthesis of essential micronutrients (vitamins, amino acids and enzymes) enhance the bioavailability of compounds [219]; stimulation of the host immune system by promoting the production of interleukin-10 (IL-10) and immunoglobulin A (IgA) antibodies [220]. They also play a crucial role in protecting intestinal epithelial cells against inflammation and associated disorders by regulating the production of antibodies, lymphocytes, interleukins, cytokines, and chemokines [221]. Additionally, probiotic microorganisms present in fermented foods

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have been reported to produce the enzymes β-galactosidase and lactase, which help combat lactose intolerance by converting glucose and galactose into short-chain fatty acids [222].

On the other hand, the fermentation of whey protein has gained significant attention in recent years, as it enables the enzymatic hydrolysis of peptides that can act as bioactive compounds. This process is made possible by the activity of proteases, which generate low molecular weight peptides (<10 kDa) with specific compositions that allow them to enter the cell nucleus and interact directly with DNA-associated proteins regulating gene expression [223,224]. These bioactive peptides have been linked to the positive regulation of cell proliferation in human cell cultures and the inhibition of growth in various types of cancer cells. Additionally, they have demonstrated immune system-like functions, such as promoting lymphocyte proliferation, antibody production, and cytokine regulation [225]. Furthermore, they stimulate the phagocytic capacity of macrophages and inhibit the secretion of specific cytokines. Antidiabetic, antihypertensive, and xanthine oxidase inhibitor activities are also reported by these bioactive molecules [226].

Following this, kefir is a fermented lactic acid derivative with characteristics similar to yogurt. Its main components, such as lactic acid bacteria, organic acids, polysaccharides, and bioactive peptides, have significant health benefits [227].[227]. Several studies have demonstrated its antioxidant, anti-inflammatory, anti-hypertensive, anticancer, and antidiabetic properties. Additionally, kefir has been associated with therapeutic effects on bone health, the immune system, cognitive function, and the gut microbiota [228-232].

Continuing with lactic fermentations, but now in solid-state form, bioactive peptides from various cheese varieties have been shown to provide health benefits by acting as antioxidants, antihypertensives, and antidiabetics [233]. For example, in a study where individuals with hypertension consumed 30 g/day of Italian cheese (Grana Padano), a significant reduction in blood pressure (both systolic and diastolic) was observed after two months [234]. In another study, six different types of cheese were evaluated, including Gouda, which showed the best results in antioxidant activity, ECA inhibitory activity, and DPP-IV enzyme inhibition. The study concluded that consuming 10–20 g of Gouda cheese, as part of a balanced diet, could be sufficient to obtain health benefits [235]. Another important compound in this type of lactic fermentation is conjugated linoleic acid. Reports have shown an increase in these bioactive levels during cheese maturation, which could enhance its potential health benefits, including antidiabetic, anticancer, anti-atherosclerotic, and antihypertensive effects [236].

On the other hand, soy fermentation is an important source of bioactive peptides with significant health benefits. For example, peptides obtained from tempeh fermentation have demonstrated antioxidant, anti-inflammatory, and antihypertensive effects [237,238]. Saponins and phytosterols, which are bioactive compounds naturally found in soy, have gained interest due to their medicinal properties [239]; regarding to[239]; regarding saponins, the presence of these compounds in some fermented foods has been associated with obesity prevention, positive regulation of the immune system, antiviral effects, and antitumor properties [240]. At the same time, sterols can inhibit cholesterol absorption in the intestine, potentially reducing the risk of cardiovascular diseases [241]. Another important compound in soy is gamma-aminobutyric acid (GABA), which acts as a neurotransmitter in the central nervous system; its health benefits include lowering blood pressure, promoting relaxation, and improving mood [241]. Fermented food soy has been reported to be a rich source of GABA due to the production of enzymes during fermentation, which facilitates its transformation through the action of glutamic acid decarboxylase [241]. Soy is also naturally rich in vitamins, minerals, and fiber, which are crucial for human growth and proper metabolism [238]. In addition to this, another important aspect of soy is its high content of allergenic proteins and other allergens, such as Gly m 1, P28, and P34, which, during fermentation processes (particularly those involving *Rhizopus* spp., *Aspergillus oryzae*, and *Bacillus subtilis*), can reduce the allergenicity of these proteins, decreasing the symptoms associated with their reactivity [242]. Also, bioactive compounds such as phenolic acids, flavonoids, and isoflavones have been identified in soy-derived fermentations [243]. Some of these fermented products originate from *Meju*, a dry soybean block fermented with

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fungi and *Bacillus sp.*, which has been attributed with anticancer potential due to the presence of trypsin inhibitors, isoflavones, vitamin E, and unsaturated fatty acids [244,245]. Additionally, *Doenjang* extracts have been linked to the activation of the enzyme glutathione S-transferase and the increased activity of natural killer cells [246].

It is important to mention that isoflavones are the main compounds responsible for the anticancer potential of fermented soy products, as they have demonstrated beneficial therapeutic effects in cell lines of various types of cancer, including stomach, colon, lymphoma, pancreas, prostate, breast, and neuroblastoma [245]. Furthermore, these compounds have been associated with cardiovascular health benefits, increasing HDL cholesterol levels while reducing LDL cholesterol and triglyceride levels [247]. On the other hand, the anti-inflammatory effects of soy fermentation have been widely studied. It has been found that consuming foods such as miso and soy sauce reduces serum levels of IL-6 and IL-18 and inflammatory markers, including high-sensitivity C-reactive protein (hs-CRP) [248]. Some studies have also linked isoflavones to neuroprotection, promoting neuronal regeneration and enhancing existing neuronal functions. Therefore, soy fermentations represent an important source of bioactive compounds, particularly genistein, with great potential in preventing various diseases [249].

Fermentation has also been used to develop natural cosmetics with potential benefits for skin health. In this regard, studies on *Camellia sinensis* var. *Assamica* has shown that the activity of enzymes produced during the fermentation process can promote the release of bioactive compounds with moisturizing properties (such as amino acids and sugars); these compounds may help improve skin hydration and support its barrier function [250]. Additionally, an increase in the content of compounds like gallic acid and epigallocatechin gallate (EGCG) has been observed in the extract of *Camellia sinensis* tea, which could enhance its antioxidant and anti-inflammatory properties, which may help protect the skin from damage caused by free radicals and UV radiation, delaying skin aging and contributing to cancer prevention [251].

On the other hand, solid-state fermentation of phenols has been reported to improve the nutritional quality and antioxidant properties of various legumes and cereals (rice, wheat bran, corn, oats, rye, and millet). This process involves enzymes such as amylases, proteases, and lipases, which hydrolyze polysaccharides, proteins, and lipids into products with lower toxicity, improved texture, flavor, and aroma, as well as a reduction in antinutritional compounds such as phytic acid, tannins, and gas-producing compounds [237].

According to several studies, a wide variety of phenolic compounds have also been identified in liquid fermentation, such as wine, including catechins, p-coumaric acid, resveratrol, rutin, quercetin, myricetin, anthocyanins, tannins, and flavan-3-ols, as well as several phenolic acids such as caffeic, ellagic, syringic, vanillic, and ferulic acids [252]. Additionally, the fermentation process of red wine leads to the formation of compounds like melatonin and hydroxytyrosol, which have been strongly associated with the numerous health benefits of this beverage [253,254]. The bioactive compounds in red wine have been extensively studied in both *in vitro* and *in vivo* investigations, demonstrating a wide range of health benefits, including antioxidant, antibacterial, anti-inflammatory, anticancer, and antidiabetic properties [255-259]. Other notable effects include antithrombotic, antidepressant, and neuroprotective activities, microbiota regulation, and anti-obesity effects, as they influence adipose tissue metabolism, hypocholesterolemia, and endothelial function [260-263].

Vinegar is a highly valued fermented product obtained from fruits such as grapes, apples, pomegranates, and cranberries through a fermentation process that can occur via two different pathways: alcoholic and acetic [264]. The microorganisms commonly used in this process belong to the Acetobacter and Komagataeibacter species, which have been associated with increased bioactive compounds such as polyphenols and organic acids [3]. Among these, acetic acid is considered the most important component of vinegar. In this context, apple cider vinegar has been shown to provide various health benefits, including improvements in cognitive, liver, and reproductive function, and therapeutic effects in diabetes [265-269]. It also exhibits antioxidant, antimicrobial, anti-inflammatory, and anti-obesity properties. Another significant effect studied is its ability to combat

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hypercholesterolemia by improving total cholesterol levels, triglycerides, LDL cholesterol, total cholesterol/HDL-C ratio, and LDL-C/HDL-C ratio [270]. These effects have been linked to bioactive compounds such as catechins, p-hydroxybenzoic acid, gallic acid, caffeic acid, p-coumaric acid, and chlorogenic acid [271].

Kombucha is a liquid fermented that is notable for its potential health benefits, including antioxidant, antitumor, hepatoprotective, and antidiabetic properties. It is prepared by fermenting black or green tea (derived from the *Camellia sinensis* plant) using a symbiotic culture of yeasts, acetic acid bacteria, and lactic acid bacteria [272,273]. This product contains bioactive compounds such as catechins, theaflavins, thearubigins, and vitamins B1, B6, B12, and C, which are associated with its reported health benefits [274,275]. In this context, *in vivo* studies have demonstrated the antidiabetic potential of kombucha, showing effects such as reduced blood glucose levels, increased plasma insulin, and modulation of gluconeogenic and glycolytic enzyme activity in experimentally induced diabetic rats [276]. Additionally, this beverage has been shown to inhibit the activity of enzymes like α-amylase and α-glucosidase, leading to a slower rate of blood glucose absorption [277]. The antiproliferative activity of kombucha has also been evaluated in various cancer cell lines, including MCF-7 (breast cancer), A549 (lung cancer), and HCT8, HCT 116, and CACO-2 (colon cancer) [272,278]. Furthermore, studies suggest it may exhibit selectivity toward cancer cells while sparing normal lung cells [279]. On the other hand, this type of fermentation has also been shown to reduce the levels of pro-inflammatory markers, including nitric oxide (NO), tumor necrosis factor (TNF), and interleukin-6 (IL-6) in macrophages activated by LPS. Additionally, it has been found to inhibit the enzyme 15-lipoxygenase (15-LOX), a key mediator in inflammatory processes [278,280].

Another important liquid fermentation is black tea, made by a unique microbial fermentation process involving some basic functional microorganisms of the genera Aspergillus, Bacillus, Candida, Cyberlindnera, Klebsiella, Lactobacillus, Penicillium, Rasamsonia, among others. Compounds such as alkaloids, polyphenols, polysaccharides, and volatile compounds have been identified in this beverage, where caffeine stands out as one of the most abundant alkaloids and catechin in the group of polyphenols [281,282]. Multiple in vivo studies have shown that black tea has health benefits, for example, by reducing blood glucose levels and lowering the risk of diabetes by up to 45% in people with regular consumption of black tea (2-3 g per day) [283]. It has also been associated with significant weight and fat loss, improving the lipid profile and reducing hyperlipidemia in humans [284]. It has also been shown to ameliorate chemically induced colitis in mice by modulating the gut microbiota, to decrease insulin resistance and chronic kidney disease in rats by modulating insulin signaling and increasing Nrf2 expression [285], and to exert a hepatoprotective effect by modulating hepatic oxidative stress, inflammatory response and gut microbiota dysfunction in mice [286], and that it possesses potent lipid-lowering activity in high-fat zebrafish model [287].[287]. Additionally, in some in vitro and in vivo studies, it showed potential to prevent the onset of cardio and neurodegenerative diseases associated with its interaction with proteins of the signaling pathways of these diseases, so this fermentation has potential for the prevention and treatment of chronic diseases [288,289].

5. Perspectives

The use of microorganisms as potential biofactories of bioactive compounds using biotechnological strategies such as fermentation, coupled with other techniques such as metabolic engineering tools, is on the rise due to advantages such as reduced use of chemicals and water, and ease of cultivation and separation of compounds. Also, bioactive compounds obtained from microorganisms are considered to have a natural origin, and the commercial market has become more popular in contrast to chemical synthesis [15,31,75,81]. Likewise, the bioactive compounds such as carotenoids, essential oils, phenolic compounds, and polysaccharides, among others, obtained through microbial fermentation have been used for nutraceutical enrichment of animal feed [290], as well as the production of protein-rich animal feed using different sources such as agro-industrial and food wastes [291]. In recent years, microbial fermentation has been explored as an alternative to using

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agrochemicals to protect crops and reduce plant diseases caused by bacteria, fungi, nematodes, and yeast. Biostimulants have been developed to enhance the growth, yield, and defense of various crops [292,293]. In human health, microbial fermentation has been studied for the extraction of bioactive compounds as an alternative to traditional chemical extraction for the enrichment of food or for use as a nutraceutical because these compounds have been linked to the proper functioning of the organism and the reduction of non-communicable diseases [294-296].

Despite the use of microorganisms to obtain bioactive compounds using biotechnology strategies, research needs to continue developing efficient processes to release and enhance the extraction of the bioactive compounds because fermentation parameters such as fermentation time, solid-to-liquid ratio, temperature, pH, microorganism used, carbon source, a downstream technique to separate the molecules of interest need to be optimized to reduce the high cost of the technologies, to guarantee an appropriate bioprocess to high yield, selectivity, and avoid microbial contamination during fermentation process [1,22,81,160].

6. Conclusions

Bioactive compounds, including alkaloids, phenolic compounds, pigments, vitamins, and others, are of interest in many industries for their potential as chemopreventive agents against many chronic diseases, such as cancer, cardiovascular diseases, and diabetes. They can also prevent aging-related diseases. These metabolites are mainly found in plants, and for their use, the extraction techniques often produce high quantities of toxic waste from solvents such as hexane, methanol, and acetonitrile, among others. Microbial fermentation is a sustainable tool for obtaining high-quality metabolites from various plant and animal matrices and producing them through biotechnology to achieve a higher yield of these compounds. These metabolites can be used in agriculture, as well as in animal and human health. The potential use of these metabolites nowadays relies on the biotechnological techniques implemented to produce each group of metabolites.

Author Contributions: Conceptualization, Supervision, Writing – Original draft, Writing – Review & Editing, E.P.G.-G., L.A.C.B.; Investigation, Writing – Original draft, V.E.Z.-S.; Writing – Original draft, E.G.A., M.S.C.M., J.A.M.F., A.H.A.G.; Writing – Review & Editing, J.B.H. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Acknowledgments: V.E.Z.-S. would like to thank the Secretaría de Ciencia, Humanidades, Tecnología e Innovación (SECIHTI) for the doctoral scholarship.

Conflicts of Interest: The authors declare no conflicts of interest.

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