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Review Article

Advancing the extraction of bioactive compound from fruit by-products through solid-state fermentation: A review

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Abstract: Solid-state fermentation (SSF) is gaining interest for its potential to extract bioactive compounds from agro-industrial by-products, particularly macronutrient-related compounds. This review explored the composition of by-products from processed fruits such as grapes, apples, pomegranates, mangoes, and pineapples with focuses on the SSF technique and key factors influencing this bioprocess. The SSF method has been successfully used to extract phenolic compounds from waste products. However, there is a significant research gap focused on enhancing the carotenoid content in agro-industrial residues or using them as growth substrates for microorganisms that produce carotenoids. Additionally, there is limited research on the use of mango peels as a substrate for SSF to extract phenolic compounds and carotenoids. Addressing these research gaps would significantly contribute to the understanding and application of SSF for the extraction of bioactive compounds from agro-industrial by-products.

Keywords: Agro-waste utilization, Fungal metabolism, Nutraceuticals, Secondary metabolites, Sustainable bioprocessing, Food by-product valorization, Functional compounds

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1. Introduction

The current economic model results in significant waste with one-third of global food production being wasted during post-harvest and processing stages. Improper handling of by-products from the fruit processing industry, such as pomace, shells, and seeds, contributes to 40% of this waste [1-3]. This issue is crucial due to population growth and the need to increase food production [4]. By-products, which comprise 10-60% of fruit, can be costly and pose environmental problems if not properly managed [5-7]. Fruit by-products are a valuable source of bioactive compounds, including phenolic compounds, carotenoids, dietary fibers, pectins, flavonoids, vitamins, minerals, and other essential nutrients, which are used in the production of functional foods, nutraceuticals, cosmetics, and pharmaceuticals due to their health benefits [8]. These compounds possess various health benefits, including anti-cancer, anti-inflammatory, antioxidant, anti-microbial, and anti-viral properties, which help maintain the balance of reactive oxygen species (ROS) in the human body [5, 9]. For example, β-carotene, a precursor of vitamin A and lutein can potentially reduce age-related macular degeneration [10]. Similarly, due to its diverse applications, phlorizin, a phenolic compound found in fruit by-products, is utilized as an oral anti-diabetic drug [11]. Studies have explored various methods for extracting bioactive compounds from by-products, including supercritical fluid extraction (SFE), microwave-assisted extraction (MAE), ultrasound-assisted extraction (UAE), and enzymatic hydrolysis. These methods use solvents such as ionic and eutectic liquids, water, and ethanol [12, 13]. While these methods are effective in extracting bioactive compounds, they also have several limitations, including high equipment and operational costs, high energy consumption, solvent-associated environmental concerns, and process complexity and scalability issues [13, 14] .

In contrast, solid-state fermentation (SSF) is a sustainable and eco-friendly method in which microorganisms such as fungi are used to extract bioactive compounds from processed fruits, such as apples, grapes, pomegranates, and mangoes [15-21]. This cost-effective method enhances profitability and ensures the production of a high-quality extract, making it an ideal alternative to enzyme-assisted extraction in low-income countries with high residue production. However, emerging technologies often face limitations in terms of costs and conditions [5]. This review discussed the composition of by-products from processed fruits, explored the SSF technique, and explained the key factors influencing this bioprocess. In addition, the use of by-products as a substrate in SSF for the extraction of bioactive compounds was investigated.

2. Processed fruit by-products

The fruit processing industry generates significant amounts of agro-industrial waste, which can lead to environmental pollution and underutilization of biomass resources. By-products such as pomace, peel, and seeds are rich in phenolic compounds, carotenoids, dietary fibers, and other biologically active compounds with positive effects on health. For example, pomegranate seeds contain punic acid, which has anti-cancer properties, while green apple peels contain phloridizin, which is used for diabetes treatment [22, 23]. These phytochemicals also have cardioprotective properties, with the antioxidants in grape pomace inhibiting the oxidation of low-density lipoproteins. Phenolics and carotenoids have anti-inflammatory, anti-diabetic, anti-cancer, and anti-viral effects and prevent diseases of the digestive system, osteoporosis, and macular degeneration [24]. The biological potential of utilizing these by-products in a biological context is evident.

2.1 Grape by-products

The wine industry generates significant by-products such as pomace, peel, and seeds, which account for 20% of the weight of the fruit cultivated from 7 million hectares of vineyard land with an annual production of 74.3 million tons of grapes [25]. These by-products are rich in compounds such as anthocyanins, proanthocyanins, stilbenes (resveratrol), catechins, phenolics, and tannins, with diverse biological activity [26, 27]. With higher concentrations of proanthocyanidins, the seeds exhibit excellent antioxidant potential. Grape seeds are rich in unsaturated fatty acids (linoleic and oleic acids) with 8 to 16% oil content, which makes them valuable due to their various benefits for health, including anti-cancer, anti-inflammatory, antioxidant, anti-microbial and anti-viral properties, which help reduce oxidative stress and improve human health.

2.2 Apple by-products

As a kind of globally popular fruit, apples produce by-products such as pomace, shells, and seeds, which comprise 30% of the apples' weight [28]. Apples contain various phenolic compounds, including condensed tannins, flavonoids, chlorogenic acid, and unique phenolics such as quercetin, with 80% concentrated in the peels [29, 30]. Apple pomace, a versatile by-product, can be used as fertilizer or feed. It contains carbohydrates, proteins, sugars, cellulose, ash, acids, calcium, pectin, lignin, vitamins, and pentacyclic triterpenoids [30]. However, the bioactive compounds in apple pomace are often wasted.

2.3 Pomegranate by-products

As the main agro-industrial by-products, the utilization of pomegranate by-products has gained significant attention in recent years, especially in a circular economy [31]. The industrial processing of fruits like pomegranates

produces significant by-products, including peel and seeds, which account for 22% of the fruits' weight [22]. Pomegranate peels contain phenolic compounds such as flavonoids (anthocyanidins), ellagitannins (punicalin and punicalagin), ellagic acid, and other polyphenols [32, 33]. Notably, seeds contain the highest concentration of these bioactive molecules. The by-products of pomegranate also contain lipids, including 12-20% conjugated linolenic acids, polyunsaturated fatty acids, and punicic acids. These phenolic compounds and conjugated linolenic acids have been found to possess antioxidant, anti-tumor, and anti-inflammatory properties. However, existing studies have primarily focused on using this by-product as animal feed for ruminants.

2.4 Mango by-products

As a highly commercialized fruit, mango is produced globally, with an annual production of over 35 million tons. It is consumed freshly or used in various products, such as juices, puree, jam, frozen pulp, and canned slices, resulting in substantial by-products such as shells and seeds. These by-products constitute 30% to 60% of the fruits' weight, equivalent to approximately 228,096 tons annually [34]. Mango peels, which contribute 7% to 24% of the fruit's weight, are rich in dietary fibers and phenolic compounds such as tannins, phenolic acids (ellagic acid, gallic acid, caffeic acid, protocatechuic acid, ferulic acid, 3,4-dihydroxybenzoic acid, 3-C-6-Op-hydrobenzoic acid), flavonoids (quercetin, quercetin O-glycosides, isoquercitrin, quercetin galactosides, and kaempferol), xanthones (mangiferin, isomangiferin, homomangiferin, mangiferin) and triterpenes (lupeol) [35, 36].

Additionally, they contain carotenoids, vitamin C, tocopherols, and sterols (beta-sitosterol, D-avenasterol, campesterol, and stigmasterol) [35]. Moreover, mango seeds are rich in bioactive molecules such as polyphenols, sesquiterpenoids, phytosterols, and tocopherols, enhancing their antioxidant potential. They also have high lipid content and extractable oil, comparable to cocoa butter in profitability, availability, and physio-chemical characteristics. They also possess biologically active compounds with anti-inflammatory, anti-tyrosinase, anti-obesity, and hepatoprotective properties. Notably, mango peels and seeds contain protein (10%), carbohydrates (65-74%), and moisture content (47-71%), varying based on the fruit variety and maturity [37].

2.5 Pineapple by-products

The lignocellulosic content of pineapple by-products and leaves suggests their significant potential as fiber sources, making them valuable for applications to sustainable material. Martínez, and Torres [38] reported that pineapple peel and core contain 75.8% dry fiber, with 75.2% as insoluble fiber and 0.6% as soluble fiber. Similarly. Putra, Or [39], Selani, Shirado [40], and Rodsamran and Sothornvit [41] successfully extracted pectin from pineapple peel, achieving yields ranging from 1.02% to 2.12%, indicating its potential use in film formation and active coating applications. Meanwhile, Anindya, Oktaviani [42] extracted xylan from the pineapple stem, highlighting its potential as an anti-inflammatory agent. As the most abundant hemicellulose, xylan is useful for biofilm production and packaging, where it serves as a barrier for fats and oils [43]. Notably, the hemicellulose content of pineapple peel is higher than other agricultural by-products such as rice straw, wheat, and sugarcane bagasse [44, 45]. Furthermore, Banerjee and Patti [46] demonstrated the potential of pineapple peels in extracting xylooligosaccharides and xylose, which are widely used in the food industry due to their low-calorie content and natural sweetening power.

Besides, pineapple residues are also rich in bioactive compounds, particularly phenolic compounds, which offer various biological benefits. Researchers have extensively studied the extraction of phenolic compounds from agroindustrial waste due to their antioxidant, anti-allergenic, anti-inflammatory, anti-microbial, anti-thrombotic, cardioprotective, and vasodilatory properties [47-49]. These compounds exist in pineapple either in free form or bound to cellular constituents through covalent bonds [50]. The key phenolics identified in pineapple peel are gallic acid, catechin, epicatechin, and ferulic acid [51]. However, the extraction and recovery of phenolic compounds are influenced by various factors including the pineapple variety, fruit part, maturity, environmental factors, genetics, and processing methods. The choice of solvent also plays a significant role in the extraction and recovery of phenolics in pineapple residues [52]. Hossain and Rahman [53] found that methanol (21.50%) was the most effective solvent for phenol extraction, followed by ethyl acetate (4.90%) and water (4.30%).

Moreover, pineapple by-products serve as a valuable source of enzymes, particularly proteolytic enzymes, which have wide-ranging applications in industry. Various parts of pineapple waste, including peels, hearts, and crowns, were studied for enzyme extraction [54]. It was found that the optimal conditions for enzyme activity are a pH between 6-7 and a temperature of 70 °C. Rojas, and Cortés [55] reported the enzyme concentration in pineapple hearts and crowns to be 2,233.50 ± 78.86 U/mg and 36.11 ± 1.62 U/mg, respectively. Ketnawa, and Chaiwut [56] recommend using pineapple peels for enzyme extraction, as they are the largest by-product of pineapple processing. The most significant enzyme in pineapple waste is bromelain, for which there are extensive commercial applications. Additionally, the pineapple stem contains other proteolytic enzymes, including ananain and comosain, while similar proteases have been detected in the peel, core, crown and leaves. The pineapple crown in particular has the highest protein content, making it a particularly valuable source for enzyme extraction. These properties make bromelain highly valuable, with a commercial value of $2,400/kg,

due to its wide range of applications [56].

In short, pineapple residues contain various bioactive compounds such as fibers, hemicelluloses, phenolic compounds, and enzymes, which are valuable for the development of environmentally friendly bio-products. The resourceful application of these by-products can create sustainable biomaterials, functional food constituents, and valuable biochemical compounds and reduce agricultural waste.

3. Solid-state fermentation

Solid-state fermentation (SSF) is a method used to produce high-value products such as soy sauce, tempeh, koji, red fermented rice, and tapai [57, 58]. SSF involves cultivating microorganisms on non-soluble substrates, either natural or artificial, where water is present within the substrate particles [58]. It offers several benefits over submerged fermentation, including lower production costs, higher product concentration, and reduced catabolic repression [5, 26]. Fungi are the primary microorganisms used in the SSF bioprocess; however, yeasts and bacteria have also been studied [59]. For instance, Monosacus spp. (filamentous fungi) and Rhodotorula (yeasts) are used for carotenoid production [9]. The selection of microorganisms is contingent upon the desired final product and the type of substrate used.

Agro-industrial waste, which is rich in nutrients such as carbohydrates, proteins, vitamins, and minerals, provides an ideal environment for microbial growth. Depending on the composition of the waste, additional nutrients may be required to meet microbial needs [60, 61]. Factors such as relative and substrate humidity, water activity (Aw), and temperature are important in SSF. Bacteria thrive in media close to pH 7, while fungi and yeasts prefer acidic conditions. On the other hand, actinomycetes prefer alkaline pH values (above pH 7) [12, 57]. Proper temperature control is crucial for limiting microbial growth as it affects enzymes, microorganism growth, and metabolite production due to the heat generated by microbial activity [62]. Maintaining an appropriate particle size also facilitates gas circulation and microorganism invasion [58]. For instance, small particles considerably reduce substrate porosity and rate of gas diffusion, while larger particles restrict moisture retention and thus hinder optimal growth of fungi. Similarly, the presence of lignin in agro-industrial waste can inhibit microbial growth in SSF [63].

3.1 Bioreactors for solid-state fermentation

Solid-state fermentation (SSF) bioreactors are essential to control fermentation conditions and ensure optimal productivity. During the initial fermentation phase, it is imperative to maintain consistent temperature, oxygen levels, and humidity. Given these considerations, the choice of a suitable bioreactor depends on the substrate rigidity, the microorganism type, the desired product, and the process parameters. Bioreactors can be static (tray and packed bed/column) or agitated (horizontal, vertical, and rotating drum), with the latter being the most common. Tray bioreactors and rotating drum bioreactors are commonly used in different configurations [62]. The solid substrate bed in these bioreactors encompasses perforations to improve airflow.

The tray bioreactor is a widely used device consisting of trays placed in a climate chamber with optional perforations (Figure 1). It is a static process that does not require mechanical energy consumption. The bed height directly influences the oxygen level in column-tray bioreactors. The efficiency of the bioreactor in transferring oxygen (O2) to the substrate bed and the removal of carbon dioxide (CO2) from the bed are crucial factors that should be considered [64]. However, the process necessitates manual manipulation, which poses challenges for industrial-scale automation [65].

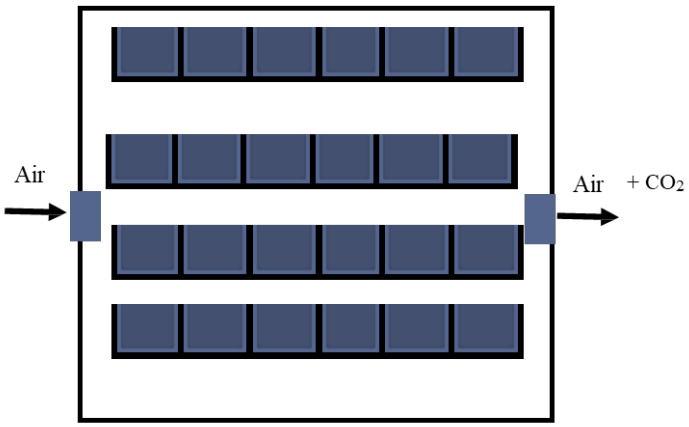

Figure 1. Front-view of a tray bioreactor, with stacked arrangement of trays inside a climate-controlled chamber

The substrate is placed in individual trays to ensure efficient air circulation across the entire surface and to minimize mixing or agitation. Filamentous fungi are primarily used for mycelium growth, but little agitation can cause uneven heat dispersal and heterogeneous accumulation. Similarly, the substrate thickness is also imperative to prevent overheating and maintain an aerobic environment for the microorganisms [66]. Therefore, rotating drum bioreactors are suitable, but excessive agitation can damage the hyphal structures and hinder fungal growth. In tray bioreactors, particle size and relative humidity play a crucial role. A lower relative humidity and a longer mixing time can hinder enzymatic activity, while a higher relative humidity and a shorter mixing time will cause the agglomeration of substrate particles, limiting oxygen transfer between substrate particles [66].

Tray bioreactors, including bubble bioreactors, face challenges such as temperature control in thick beds, uneven water flow due to static processes, and labor requirements. The rotating drum bioreactor (RDB) is a complex system comprising a substrate bed, a gas circulation headspace, and drum walls (Figure 2).

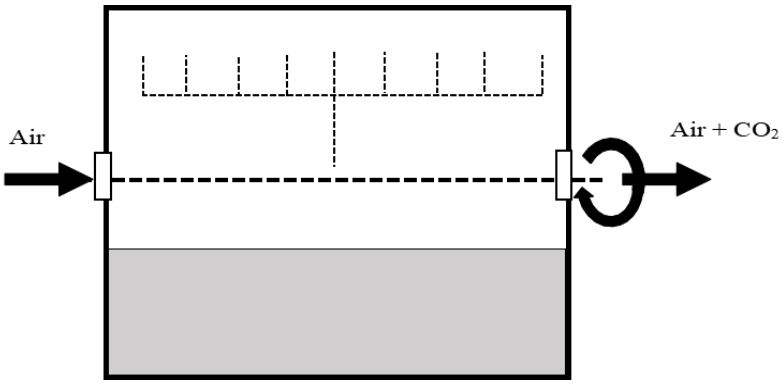

Figure 2. Side-view of a rotating drum bioreactor, showing the cylindrical drum structure, airflow circulation, and agitation mechanism

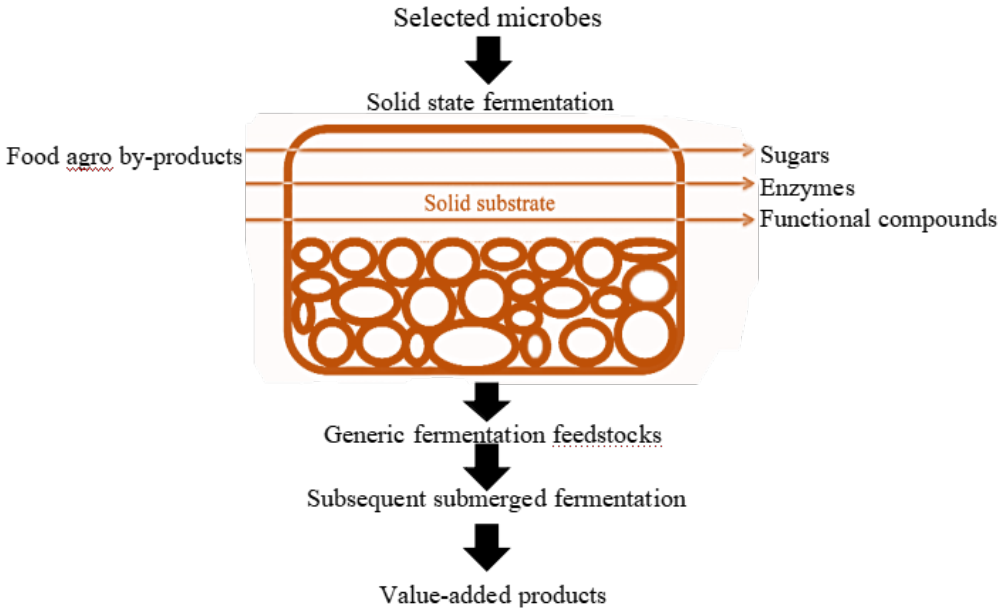

Figure 3. Extraction of bioactive compounds through solid-state fermentation

The substrate bed, which accounts for 10-40% of the bioreactor's volumetric capacity, is crucial for homogeneity and temperature control. The RDB offers enhanced humidity and temperature control through agitation, but its intensity depends on the substrate rigidity and the microorganism's shear force sensitivity. Shear forces significantly impact the hyphal structure of filamentous fungi [62]. The RDB demonstrates improved mixing and cooling capabilities compared to tray bioreactors, as noted by Kruthi Doriya [64].

In the bioreactor, mixing or agitation is used to prevent compaction of the bed and to increase the substrate area for air entry, based on the microorganisms and other factors. For instance, the injection of humid air can regulate temperature, humidity, substrate, and O_2 rate, making it a promising bioreactor for large-scale compound production [65]. However, further studies are needed to determine the specific microorganisms used, as SSF is primarily associated with fungi and bacteria to a lesser extent.

3.2 Extracting bioactive compounds through solid-state fermentation

Fruit by-products such as pomace, peels, and seeds are rich in biologically active compounds such as phenolics and carotenoids [67, 68]. However, the conjugated nature of bioactive molecules such as sugar groups, organic acids, amines, and lipids decreases their overall antioxidant activity in by-products [60]. Conventional solid-liquid extraction focuses primarily on the recovery of the free fraction of bioactive compounds present in the plant matrix. Therefore, alkaline or acid hydrolysis is commonly used but often leads to compound degradation. In response to these challenges, researchers are exploring new technologies to improve extraction yields. Various extraction techniques, including supercritical CO_2 extraction [69], pressurized liquids [69], UAE and MAE [6, 36], and electrical pulses, have shown promise in removing impurities from various materials. However, factors such as energy consumption, equipment costs, and the value of the extracted compounds influence the choice of extraction methods. Some techniques may have limitations for industrial use and can be expensive, particularly in underdeveloped countries where large amounts of fruit by-products are generated (Figure 3).

SSF has emerged as an efficient and cost-effective method, as microorganisms, particularly fungi, secrete enzymes that hydrolyze lignocellulosic structures, releasing bioactive compounds. This process makes the compounds free and readily dissolved in solid-liquid extraction phases. Using agro-industrial by-products as a substrate in SSF significantly enhances economic viability [64]. Notably, SSF yields higher product concentrations, compared to submerged fermentation. Similarly, enzyme-assisted extraction is also a widely used method for extracting bioactive compounds from plant wall matrices; however, it is subject to limitations such as process instability and high costs. Researchers are exploring the use of agro-industrial by-products as substrates in SSF to extract high-value enzymes, thereby reducing these costs [61, 64].

3.2.1 Extracting bioactive compounds from grape by-products through SSF

Grape by-products are rich in bioactive compounds, necessitating efficient and cost-effective extraction methods. Previous studies have explored the use of SSF to extract phenolic compounds from plant matrices [27, 29]. Pertuzatti, Mendonça [25] utilized the strain Rhizomucor miehei NRRL 5282, which yielded a total polyphenol content of 1956 mg gallic acid equivalent (GAE)/100 g of dry matter (DM) after fermentation at 37 ºC for 7 days. The results were 30% higher than that of non-fermented grape pomace. The phenolic compounds of the fermented grape by-product include flavonols, stilbenes, proanthocyanidins, gallic acid, epicatechin, and catechin. Zambrano, and Kotogán [27] reported that the enzyme β-glucosidase secreted by Rhizomucor miehei (NRRL 5282) is closely linked to the polyphenol content of grape pomace extract. SSF allows for the enrichment of by-products with 378.85 mg of γ-linolenic acid/100g DM when fermented with Umbelopsis isabellina [29]. In contrast, the fermentation of grape pomace with Actinomucor elegans produces lutein and β-carotene contents of 60.15 mg and 55.75 mg/100g DM, respectively [29]. These results are achieved without adding nutrients to the grape pomace, specifically by reducing the nitrogen source of the substrate. In addition, Teles, Chávez [26] obtained 910.56 mg of total phenolics/100 g of DM and 5.76 mg of proanthocyanidins/100g of DM by using wheat bran and grape pomace as a substrate (1:1) in SSF with Aspergillus niger 3T5B8. The study aimed to produce hydrolytic enzymes (xilaxa, β-glucosidase, polygalacturonase, and tannase) from grape pomace at 37 ºC and 60% humidity, which were then used to release phenolic compounds. However, the high lignin content in grape pomace limits microbial growth. In this context, grape pomace has the potential for extracting bioactive compounds, particularly phenolics, through SSF. Factors such as temperature, moisture content, and lignin influence the growth of microorganisms. Spore concentrations ranging from 106 to 108/ml are typically used in investigations, with positive results observed after 96 hours of fermentation [26, 29]. However, the use of regulators to control the release or production of specific metabolites is an interesting area that requires further research.

3.2.2 Extracting bioactive compounds from apple by-products through SSF

Apple by-products contain bioactive molecules, particularly phenolic compounds, which have been extensively studied. SSF offers a novel approach to improve extraction performance by fermenting apple peels

Table 1. Solid-state fermentation of agricultural by-products, conditions, enzymatic reactions and bioactive yields

Sample	Microorganism	Condition	Enzymatic Reaction	Bioactive yield	References
Grape pomace	Rhizomucor miehei NRRL 5282	37 °C, 7 d	β-glucosidase hydrolysis of phenolics	1956 mg GAE/100g DM (30% increase)	[25, 27]
	Umbelopsis isabellina		γ-linolenic acid and β-carotene biosynthesis	378.85 mg of γ-linolenic acid/100g DM	[29]
	Actinomucor elegans		Lutein and β-carotene	Lutein: 60.15 mgβ-carotene: 55.75 mg/100g DM	
	Aspergillus niger 3T5B8		Polygalacturonase	Proanthocyanidins: 5.76 mg/100g DM	[26]
Apple peels	Aspergillus niger ZDM2	30 °C, 7 d	Polyphenol release β-glucosidase	1440 mg polyphenols/100g DM, and 382 mg flavonoids	[28]
	A. niger ZDM2, A. aculeatus ZGM6, A. tubingensis ZDM1, and A. japonices ZGM4		Pectinase-assisted flavonoid extraction	Higher antioxidant activity (3x increase)	
Apple pomace	Phanerocheate chrysosporium	37 °C, 14 d	Laccase and tannase hydrolysis	16.12 mg GAE/g DM	[60]
	Mucor circinelloides	30 ºC, 5.8 d	Inulinase enzymes	411.3 UI/GDS inulinase enzymes	[30]
Pomegranate peels	Aspergillus niger GH1	30 °C, 5.8 d	Ellagitannin hydrolysis	47 mg polyphenols/g DM	[3]
Mango seeds	Aspergillus niger PHS	37 °C, 7 d	Ellagic acid biosynthesis Ellagitannase enzyme biosynthesis	132.63 mg ellagic acid/g DM 938.8 U of ellagitannase enzyme/gE	[3, 70]
	Aspergillus niger	0.27 mL/min flow rate for 70 min	Ellagitannins hydrolysis	1.09g of ellagic acid/L	[1]
	Aspergillus niger GH1	30 °C 20 h	Phenolic compound solubilization	948 to 3288 mg GAE/100g DM (500% increase)	[34, 6, 71]
Mango peels	Lactobacillus plantarum, Saccharomyces boulardii, Rhodotorula glutinis	30 °C, 7 d	Carotenoid accumulation	125 ppm of β-carotene, 340 mg lycopene/L)	[59, 9]
Pineapple pulp, heart, and crown	Kluyveromyces marxianus	30 C, 3 d	Phenolic content	112 mg GAE/100 g to 120 mg EAG/100 g	[48]
Pineapple peels	Trichoderma viride ATCC 36316	30° C , 96 h	Crude protein extraction	4.53% to 14.89% crude protein	[72]
	Ralsthonia eutropha	30 °C , 24 h	Polyhydroxyalkanoates production	44 mg/100g polyhydroxyalkanoates	[73]
	Aspergillus oryzae	30 °C , 36 h	Fructooligosaccharides (FOS) production	4.15 g/L fructooligosaccharides (FOS)	[75]
	Saccharomyces cerevisiae	36 °C , 30 h	Ethanol production	30.77 g/L ethanol	[77]
	Lactobacillus rhamnosus GG	37 °C ,10 h	Lactic acid production	2.63 g/L lactic acid	[78]
Pineapple flesh, heart, peels, and crown	Rhizopus oligosporus	20 -22 °C , 12 d	Phenolic content	3.00 mg GAE/g to 5.20 mg GAE/g	[52]
	Rhizopus oryzae, NRRL 395	32.2 °C , 3 d	Lactic acid production	103.69 mg/g lactic acid	[74]
	Lactobacillus delbrueckii	37 °C , 72 h	Lactic acid production	13.10 g/L lactic acid	[79]
Pineapple leaves	Saccharomyces cerevisiae	38 °C , 2 d	Second-generation ethanol production	15.24 g/L ethanol	[76]
Pineapple shell and heart	Chromobacterium violaceum	30 °C, 16 h	Polyhydroxybutyrate (PHB) production	57.2 ± 1.0 g/L Polyhydroxybutyrate	[80]

with four Aspergillus species, including A. aculeatus ZGM6, A. japonicus ZGM4, A. niger ZDM2 and A. tubingensis ZDM1). A. niger ZMD2 A yielded 1440 mg of polyphenols and 382 mg of flavonoids per 100 g DM at 30 °C for 7 days, with a threefold increase in antioxidant activity compared to the unfermented peel [28]. In addition, Ajila, and Brar [60] reported a slightly higher yield of total phenolic content (16.12 mg GAE/g DM) when fermenting apple pomace with Phanerocheate chrysosporium at 37 ºC for 14 days. However, the study does not provide evidence of the formation of other metabolites, such as taxifolin, eridictyol, and catechin isomers. These compounds are typically found in apple peels fermented with A. niger ZDM2, A. aculeatus ZGM6, A. tubingensis ZDM1, and A. japonices ZGM4 [28]. The discrepancy in the extraction of phenolic compounds from fermented apple pomace can be ascribed to various factors such as microbial strains, fermentation conditions, and post-fermentation extraction methods. Table 1 presents the studies conducted using fruit by-products as substrates for SSF.

Ajila, and Brar [60] demonstrated that the microwave-assisted method (MEA) is more efficient than ultrasound-assisted extraction (UAE) when considering the factors of solvent, temperature, and time. Furthermore, apple pomace fermented with Mucor circinelloides, produced inulinase enzymes with 411.3 UI/GDS under optimal conditions of 83.5% moisture content, pH 6.4, and 30ºC temperature for 5.8 days [30]. This suggests that apple by-products can potentially promote the growth of microorganisms but may require specific mineral media depending on the strain and intended product. The problem can be solved by partially combining them with other by-products to ensure the economic viability of the process. The researchers used a specific microorganism with an inoculum concentration of 107/ml and a pH range of 4.5 to 7 [28].

3.2.3 Extracting bioactive compounds from pomegranate by-products through SSF

Pomegranate by-products are rich in polyphenols and have a high antioxidant activity [32]. Fermenting pomegranate peels with A. niger GH1 yielded 47 mg of polyphenols/g DM, with ellagic acid being the most abundant. Size exclusion chromatography was used to separate and purify the extract. In another study, ellagic acid production was reported to be 6.3 mg/g DM when using A. niger GH1 and 4.6 mg/g DM when using A. niger PHS. However, under optimal conditions, yields increased significantly from 8.48 to 132.63 mg/g of DM. Key factors of SSF include temperature, humidity, concentrations of MgSO4 and KCl, fruit variety, and the method used for the extraction of bioactive compounds. In addition, the researcher efficiently produced 938.8 U of ellagitannase enzyme/gE by using A. niger as a carbon source and ellagitannin solution. The bioprocess performance was directly influenced by varying concentrations of ellagitannins, KCl, and MgSO4 [70].

The pomegranate peels, rich in ellagitannins, can be used as a substrate for producing ellagic acid through ellagitannin metabolization by A. niger [81]. Combining pomegranate by-products with sugarcane bagasse or corn by-products could improve production yields. Additionally, using the ellagitannase enzyme as a biocatalyst in a continuous packed-bed reactor has shown significant efficacy in the hydrolysis of ellagitannins from pomegranate by-products. The process yielded 1.09g of ellagic acid/L after 70 minutes, at a flow rate of 0.27 mL/min of the ellagitannin solution (0.1 %, w/v) produced by SSF [1]. The efficiency of this enzymatic process indicates the potential of pomegranate by-products as valuable substrates for producing important commercial metabolites, explicitly ellagic acid [82].

3.2.4 Extracting bioactive compounds from mango by-products through SSF

Mango by-products, including peels and seeds, contain biologically active compounds such as carotenoids and phenolic compounds. The potential of these compounds in by-products has led to more studies focusing on their extraction [34]. Fermentation has emerged as a desirable technique to enhance the content of recoverable compounds in extracts. The fermentation of mango seeds with A. niger GH1 aims to solubilize the bound fraction of phenolic compounds, increasing phenolics from 948 to 3288 mg GAE/100g DM after a 20-hour fermentation period when ethanol was used for post-fermentation extraction [71]. However, further optimization of the SSF process could improve these values. The matrix-solvent ratio, interaction time, cycles, and extraction temperature greatly influence post-fermentation extraction. Notably, the SSF technique yielded up to 500 % more polyphenols than extraction without SSF pretreatment [66].

While conventional techniques have been used to extract polyphenols (55-110 mg/g DM) and carotenoids (365-3945 µg/g DM) from mango peels, their potential use as a substrate for SSF to obtain bioactive compounds has not yet been explored [60]. Torres-León, and Ramírez-Guzmán [5] found that fermentation of mango peels with Lactobacillus plantarum and Saccharomyces boulardii improved the content of proteins, fats, and minerals. This was attributed to the use of carbohydrates as a carbon source [59]. Some microorganisms, such as Rhodotorula glutinis YB-252, produced carotenoids through SSF and accumulated 125 ppm of β-carotene and 340 mg of lycopene/L, using imidazole as a regulator to prevent catalase enzyme synthesis [9]. Given that mango peels are rich in macronutrients and bioactive compounds such as carotenoids and polyphenols, they offer a promising avenue for future research due to the lack of such studies in current scientific literature.

3.2.5 Extracting bioactive compounds from pineapple through SSF

Pineapple by-products have been identified as potential

raw materials for SSF and offer a sustainable approach to producing valuable bio-based compounds. Studies have shown that SSF enhances the biochemical properties of different parts of the pineapple, including the flesh, heart, peel, crown, and stem, leading to increased yields of phenolic compounds, proteins, organic acids, enzymes, and biopolymers. Rashad, Mahmoud [48] found that using Kluyveromyces marxianus for pineapple fermentation at 30°C for 3 days increased the yield of phenolic compounds from 112 mg GAE/g to 120 mg GAE/g. Similarly, Correia and McCue [52] demonstrated that fermentation with Rhizopus oligosporus incubated at 20–22°C for 12 days substantially enhanced the phenolic content from 3.00 mg GAE/g to 5.20 mg GAE/g.

In addition to the phenolic compounds, SSF has been found to enhance the protein content of pineapple by-products. In a study by Aruna [72], fermentation of pineapple peels with Trichoderma viride ATCC 36316 at 30°C for 96 hours was found to significantly increase crude protein content from 4.53% to 14.89%, suggesting the potential use of fermented pineapple residues as a protein-rich ingredient in animal feed formulations. Likewise, pineapple residues have been extensively studied for their potential in the production of biopolymers. Vega-Castro, Contreras-Calderon [73] found that Ralstonia eutropha cultured at 30°C for 24 hours efficiently metabolized pineapple peels to produce 44 mg/100g of polyhydroxyalkanoates (PHAs), a biodegradable polymer used in eco-friendly packaging and medical biomaterials. Alternatively, Sukruansuwan and Napathorn [80] explored the fermentation of pineapple shell and heart using Cupriavidus necator strain A-04, which yielded 57.20 g/L of polyhydroxybutyrate (PHB), highlighting the potential use of pineapple residues as a cost-effective substrate for a sustainable production of biopolymers.

Some studies have shown that pineapple by-products can be used to produce lactic acid, a crucial precursor for biodegradable plastics and food preservation. Zain, and Aziman [74] demonstrated that pineapple flesh, heart, peel, and crown can be used as a substrate for Rhizopus oryzae NRRL 395 to produce lactic acid at a concentration of 103.69 mg/g. de la Rosa, Múñiz-Marquez [75] observed that Aspergillus oryzae grown at 30°C for 36 hours facilitates the production of fructooligosaccharides (FOS) at a concentration of 4.15 g/L. Other organic acids were also obtained from pineapple by-products using SSF. On the other hand, studies by Silva, Bronzato [76] and Casabar, Unpaprom [77], showed that fermentation of pineapple leaves and peels with Saccharomyces cerevisiae at 38°C for 2 days resulted in bioethanol yields of 15.24 g/L and 30.77 g/L, respectively, highlighting the potential of pineapple by-products in biofuel production for sustainable energy solutions. Diaz-Vela, Totosaus [78] utilized SSF with the Pediococcus pentosaceus UAM22 strain at 37°C for 10 hours to extract acetic acid (0.49 g/L) and propionic acid (0.15 g/L) from pineapple peels, which have various industrial applications, including food preservation and pharmaceuticals. Similarly, pineapple by-products have shown potential for microbial enzyme production.

Furthermore, Idris and Suzana [79] found that Lactobacillus delbrueckii grown at 37°C for 72 hours produced 13.10 g/L of lactic acid. Finally, Sukruansuwan and Napathorn [81] demonstrated that pineapple flesh, heart, peels, and crown fermented with Chromobacterium violaceum at 30°C for 16 hours facilitated polyhydroxybutyrate (PHB) production, yielding 57.2 ± 1.0 g/L. These studies highlight the potential of SSF in transforming pineapple by-products into valuable bio-based compounds, such as phenolic compounds, proteins, organic acids, enzymes, biopolymers, bioethanol and bioactive pigments.

4. Application of bioactive compounds from SSF

SSF is a sustainable and cost-effective bioprocess that utilizes microorganisms such as fungi, bacteria, and yeast to improve the bioavailability and bioactivity of natural compounds [83]. The fermentation process of agricultural and industrial by-products is a significant source of bioactive compounds, including polyphenols, flavonoids, peptides, and enzymes with potent antioxidant, anti-inflammatory, anti-microbial, and metabolic regulatory properties [84]. These compounds have been widely used in functional foods, nutraceuticals, cosmetics, and pharmaceuticals to improve human health and well-being. This study explored the functional applications of bioactive compounds extracted through SSF, particularly applications in functional foods, nutraceuticals, cosmetics, and pharmaceuticals.

4.1 Functional foods and nutraceuticals

Antioxidants play a crucial role in protecting the body from oxidative stress, which is associated with chronic diseases such as cardiovascular disorders, neurodegenerative conditions, and cancer [85]. SSF-derived bioactive compounds including phenolic acids, flavonoids, and peptides, exhibit potent antioxidant activity and have been widely explored for use in dietary supplements [86]. The SSF process enhances the bioavailability of these compounds and increases their effectiveness in neutralizing free radicals and reducing cellular damage. One of the key advantages of SSF-derived antioxidants is their ability to modulate cellular redox balance and inhibit lipid peroxidation [87]. Studies have shown that SSF of food waste, such as fruit peels, leads to the production of bioactive peptides with potent antioxidant activity [88]. These peptides not only scavenge reactive oxygen species (ROS) but also upregulate endogenous antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPx), thereby enhancing the body's defense mechanisms against oxidative damage [89]. Similarly,

phenolic compounds produced through SSF have superior stability and bioactivity compared to naturally occurring counterparts [90].

Fermented extracts rich in catechins, ferulic acid, and quercetin are commonly incorporated into dietary supplements due to their proven ability to reduce inflammation, improve cardiovascular health, and protect against age-related oxidative stress. In addition, the controlled biotransformation of polyphenols during SSF enhances their solubility and absorption in the gastrointestinal tract, making them more bioavailable in the human body. Another promising aspect of SSF-derived antioxidants is their potential use in functional beverages and fortified foods such as fermented tea extracts and fermented cereals. These products enriched with polyphenols and peptides have been used in nutrition bars and breakfast products to support overall health [91].

4.2 Role in gut health and metabolic regulation

The human gut microbiota plays a crucial role in digestion, immune function, and metabolic regulation [92]. Bioactive compounds derived from SSF have been extensively studied for their prebiotic and probiotic properties, which contribute to gut health by promoting the balance of beneficial microorganisms and enhancing nutrient absorption [93]. Fermented foods enriched with bioactive peptides, polysaccharides, and organic acids have been shown to improve the integrity of the gut barrier, modulate inflammatory responses, and support the growth of beneficial bacteria such as Lactobacillus and Bifidobacterium [94]. Short-chain fatty acids (SCFAs) such as butyrate, propionate, and acetate are major bioactive compounds produced through SSF and play a crucial role in maintaining intestinal homeostasis.

Studies demonstrated that SSF of dietary fibers from fruits enhances SCFA production and supports colon health by reducing inflammation and protecting against colorectal cancer [95]. In addition to SCFAs, SSF-derived bioactive peptides exhibit anti-inflammatory and anti-microbial properties that contribute to gut health. These peptides inhibit pathogenic bacteria and stimulate the growth of commensal microbiota, prevent infections, and promote a balanced gut environment. Additionally, SSF-derived peptides regulate appetite hormones, improve metabolic function, and reduce the risk of obesity-related diseases.

4.3 Cosmetic and pharmaceutical applications

Bioactive compounds derived from SSF are increasingly used in the cosmetic and pharmaceutical industries due to their potent anti-aging, skin-protective, and wound-healing properties [89]. These compounds (antioxidants, peptides, and polysaccharides) maintain skin health by reducing oxidative stress, preventing collagen degradation, and enhancing cellular regeneration. They neutralize reactive oxygen species (ROS), which contribute to premature skin aging. Fermented extracts rich in polyphenols such as resveratrol and catechins are used in anti-aging formulations to protect against UV-induced damage, improve skin elasticity, and reduce the appearance of wrinkles. In addition, SSF-derived bioactive compounds, including flavonoids and carotenoids, are crucial for protecting the skin from environmental stressors. They absorb harmful UV radiation and inhibit matrix metalloproteinases (MMPs), which degrade collagen and contribute to skin aging [91]. SSF-derived bioactive compounds also have anti-inflammatory and anti-microbial properties that effectively combat inflammatory skin conditions such as acne, eczema, and psoriasis. SSF-derived extracts containing gallic acid and ferulic acid, inhibit pro-inflammatory cytokines and reduce oxidative stress, thereby improving skin inflammation [93].

In short, SSF-derived bioactive compounds offer health benefits in various industries, including functional foods, nutraceuticals, cosmetics, and pharmaceuticals. They have antioxidant, anti-inflammatory, and anti-microbial properties that make them effective in dietary supplements, gut health improvement, anti-aging skincare, and wound healing. As the demand for natural, sustainable ingredients increases, SSF-based products will play a vital role in health and wellness applications. Future research and advances in SSF technology will further enhance the efficacy and commercial viability of these bioactive compounds.

5. Conclusions

SSF has emerged as a sustainable and efficient bioprocess for extracting bioactive compounds from by-products of agro-industrial fruits. This review highlights the potential of SSF in enhancing the bioavailability and antioxidant properties of phenolic compounds, carotenoids, and other valuable metabolites from fruit by-products such as grapes, apples, pomegranates, mangoes, and pineapples. By utilizing microbial metabolism, SSF offers an eco-friendly alternative to conventional extraction methods, reducing processing costs while maximizing yield and functional benefits. Despite its advantages, SSF faces several challenges, particularly in large-scale industrial applications. Issues such as substrate heterogeneity, moisture control, and heat management of the metabolism require further research and optimization. Additionally, the role of specific microbial strains and enzyme activity in the extraction of bioactive compounds needs to be further investigated. Future studies should focus on improving fermentation efficiency, optimizing bioreactor designs, and exploring novel microbial consortia to enhance the recovery of high-value functional compounds. With increasing global interest in sustainability and circular economy practices, SSF presents a promising strategy for valorizing fruit-processing by-products. The integration of SSF with emerging technologies such as green extraction methods, nanotechnology, and bioengineering could further

enhance its industrial applicability. Addressing the current limitations will be key to unlocking the full potential of SSF in the development of functional foods, nutraceuticals, pharmaceuticals, and biopolymers, ultimately contributing to a more sustainable and resource-efficient food industry.

6. Future perspectives and challenges

SSF is a sustainable bioprocessing technology that can be used to extract bioactive compounds from fruit by-products for potential applications in the food, pharmaceutical, and cosmetic industries. This fermentation process utilizes microorganisms such as fungi, bacteria, and yeasts to enhance the bioavailability and bioactivity of natural compounds, including polyphenols, flavonoids, peptides, and enzymes. SSF-based extraction offers numerous advantages, including reduced water usage, lower energy consumption, and improved bioactivity. However, its application on an industrial scale remains a major challenge [96]. The complex nature of SSF requires precise control of factors such as substrate selection, microbial strain optimization, aeration, and moisture content to ensure a consistent yield of bioactive compounds. Unlike submerged fermentation (SF), which allows for easier scaling up through bioreactors, there are no well-established bioreactor models for SSF, making it difficult to achieve uniform fermentation conditions on a large scale.

Substrate heterogeneity is another key challenge in SSF, as its solid agricultural residues such as fruit peels or wheat bran serve as growth media for microorganisms. Maintaining uniform moisture levels and oxygen (O_2) distribution within solid substrates is complex and affects microbial activity and metabolite production [97]. Additionally, temperature control is more challenging in SSF because metabolic heat accumulation in solid substrates can create temperature gradients that potentially limit microbial growth. Continuous processing is another limitation of SSF, as it is typically performed in batch or semi-batch processes, which limits scalability and increases production costs [98]. Addressing these technical challenges is critical to making SSF a viable industrial process.

The implementation of smart monitoring technologies such as artificial intelligence (AI) and sensors for temperature, humidity, and oxygen levels can optimize fermentation conditions in real-time, enhancing precise control and scalability. Similarly, pretreatment of substrates, such as enzymatic hydrolysis or optimization of particle size, can also improve homogeneity and microbial access to nutrients and thus increase the yield of metabolites. In addition, developing genetically modified (GM) microbial strains with enhanced SSF efficiency can improve extract yields and the production of bioactive compounds. Combining SSF with SF could enhance production efficiency by leveraging the advantages of both processes [98].

The growing demand for sustainable and eco-friendly processes has led to research into green chemistry approaches for extracting bioactive compounds from SSF [98]. Traditional solvent-based extraction methods often use toxic chemicals that can compromise the safety and purity of bioactive compounds. Therefore, green extraction methods are essential for sustainable production. For example, supercritical CO_2 can be effectively utilized as a solvent in SFE for the efficient extraction of bioactive compounds from plant-based sources while eliminating toxic residues. In addition, the integration of ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), and enzyme-assisted extraction (EAE) with SSF can significantly improve the extraction and production of bioactive compounds from fruit-based sources. Furthermore, nanotechnology using lipid or polymer-based carriers can protect bioactive compounds from degradation and improve absorption in the human body [99]. Nanoemulsions can also enhance the solubility of hydrophobic bioactive compounds such as flavonoids and polyphenols, making them more effective in pharmaceutical and nutraceutical formulations. The combination of SSF with nanotechnology could therefore revolutionize the production and application of bioactive compounds in various industries.

Overall, SSF is a promising method for the sustainable production of bioactive compounds, but its full potential is hindered by challenges in large-scale implementation and process optimization. Integrating SSF with green technologies such as supercritical CO_2 extraction, UAE, MAE, EAE and nanotechnology can improve efficiency and bioavailability. Technological advancements are expected to significantly impact the future of bioactive compound production, with SSF playing a vital role in addressing these challenges.

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Conflicts of interest

The authors declare no conflicts of interest.

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