Study of the Potential Use of Fermentation Methods to Increase Antioxidant and Antibacterial Activity of Fruit Peels: A Review

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ABSTRACT
Food industry waste, especially fruit peels, increases every year and their disposal can cause environmental pollution that can affect health. Fruit peels are known to contain antioxidant and antibacterial compounds, and their utilization can provide more value to fruit peel waste. This literature review aims to obtain information about the potential to increase the antioxidant and antibacterial activity of fruit peels through the fermentation method. Based on the literature review, it can be concluded that the fermentation method can increase the antioxidant and antibacterial activity of fruit peels. The solid-state fermentation (SSF) method has more potential to increase the antioxidant activity of fruit peel substrate compared to the submerged fermentation (SmF) method. As for the increase of antibacterial activity, research using the SSF method and fruit peels as the substrate is still limited, and the results cannot be compared to the increase of antibacterial activity using the SmF method. Therefore, there is still scope for research to increase the antibacterial activity of fruit peel substrate using either the SSF or SmF method.

Keywords*: Fruit peels, antioxidant, antibacterial, submerged fermentation, solid state fermentation*

1. INTRODUCTION

The food industry generates increasing amounts of waste each year, including vegetable, fruit, and animal processing waste. If left unmanaged, this waste can cause serious environmental problems and adversely affect human health in the surrounding areas. Fruit peel waste is a type of organic waste that is commonly found in Indonesia. For instance, research has shown that a single pineapple can produce waste ranging from 21.73-24.48%, while a single dragon fruit can produce waste ranging from 30-35% [1], and there are 53.2 tons of cocoa peel waste produced annually [2]. In 2014, China, India, the Philippines, and the United States threw away about 55 million tons of leftover fruit and vegetable peel [3]. Therefore, it is necessary to develop waste management strategies for fruit peel waste to reduce the amount of waste and increase its economic value.

Fruit peel waste can be processed as it contains high levels of macro and micro-nutrients. Fruit peels have many good things in them like vitamins and other chemical compounds such as vitamins C, E, and A, carotenoids, phenolic, tannins, alkaloids, steroids, saponins, terpenoids, thiamine, niacin, pyridoxine, cobalamin, and phytoalbumin [4,5,6,7]. Some of these compounds, such as phenolics and flavonoids, can be used to produce bioplastics, bioabsorbents, and edible films [8].

Antioxidants are compounds that can counteract free radicals by preventing the oxidation process of lipids. Free radicals are constantly produced in the body. When they accumulate in large amounts, they can potentially

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deactivate various enzymes, oxidize fats, and damage DNA in the body, causing mutations that can lead to various diseases [9]. The use of antioxidant compounds is necessary to maintain the health of the body. Research on antioxidant compounds has been widely conducted by extracting flowers, leaves, and fruits, such as antioxidant activity tests on the stem extract of *Alyxia reinwardtii* [10], flower extracts of *Plumeria alba* L. and *Plumeria rubra* L. [11] and leaf extracts of *Lantana camara* using n-hexane, ethyl acetate, and ethanol extraction [12].

Antibacterial compounds are substances that inhibit the growth of pathogenic bacteria and are secondary metabolites in microorganisms. Infectious diseases are caused by the attack of pathogenic bacteria. The mechanism of inhibition of microorganism growth by antibacterial compounds involves the destruction of the cell wall, alteration of membrane permeability, disruption of protein synthesis, and inhibition of enzyme activity. Extracts of *Guazuma ulmifolia* leaves have been reported to have antibacterial activity against Gram-positive *Bacillus cereus* and Gram-negative *Escherichia coli* [13]. Lemon peel can fight germs like *Staphylococcus, Streptococcus, Salmonella*, and *Pseudomonas* [14].

Historically, various parts of plants have been used as medicine. In the past, our ancestors used to crush plant leaves to be used as medicine for humans. Since the 1990s, various studies have been conducted to isolate antioxidant and antibacterial compounds using extraction methods from different parts of plants [15,16,17,18,19]. In recent studies, antioxidant and antibacterial compounds have been isolated because of the fermentation process [20,21,22,23].

The production of antioxidant and antibacterial compounds is commonly achieved through submerged fermentation and solid-state fermentation methods. Fermentation not only affects the nutritional content but also changes the characteristics such as aroma, color, taste, and function of the resulting products. Research has been conducted to produce antioxidant and antibacterial compounds by utilizing microorganisms such as *Aspergillus niger* [20], *Kluyveromyces marxianus* NRRL Y-8281 [24], lactic acid bacteria [26], *Penicillium roqueforti* [26], *Aspergillus saitoi* [22], and *Rhizopus* [23].

In order to learn if using fermentation can make fruit peel waste better at fighting microorganisms, this review highlights the differences in the quality of antioxidant and antibacterial production between the extraction method and the fermentation method. In addition, it examines the efficacy of each method and the potential of the fermentation method to enhance antibacterial and antioxidant activity.

2. METHODOLOGY

This paper used the Systematic Literature Review (SLR) method, including identifying and formulating research questions, exploring, and reviewing various subtopics based on the research questions, finding relevant information based on predetermined subtopics, and processing and synthesizing the data. The final step was discussing the results of the analyzed data.

3. RESULT AND DISCUSSION

3.1. Antioxidant production by non-fermented, solid-state, and submerged fermentation.

There are many sources of free radicals in our lives, including motor vehicle fumes, factory emissions, radiation, food, and the natural oxidation process in the body. When present in excess, free radicals can cause illnesses like cancer and heart disease that get worse over time. To mitigate the harmful effects caused by free radicals, antioxidants are required. Antioxidants function by neutralizing pro-oxidant factor imbalances through the removal or addition of an electron, which stabilizes free radicals. Imbalances in pro-oxidant factors, specifically too many free radicals in the body and not enough antioxidants to control them, can cause oxidative stress. This can damage cells irreversibly, affecting fats, sugars, and DNA. Antioxidants are crucial to the body as a neutralizing agent for free radicals and as a defense mechanism to prevent damage to lipids, proteins, and DNA from occurring [27].

The body creates natural substances called antioxidants, like glutathione reductase, glutathione peroxidase, superoxide dismutase, and catalase, which exhibit enzymatic activity [28]. However, the body's endogenous antioxidants are not sufficient to protect the body from free radicals. Therefore, additional exogenous antioxidants are necessary, which are known as natural or nutrient antioxidants. These antioxidants come from plants and animals, such as flavonoids found in plants, omega-3 and omega-6 from fish, as well as selenium, manganese, zinc, other minerals, and vitamins that can be found in fruits and vegetables [29].

A study by Selawa et al. (2013) showed that foods processed from animals have lower levels of antioxidants than foods processed from plants, especially in fresh and unprocessed foods such as spices, fruits, and vegetables [30]. Research shows that some plants have

proven to be useful in protecting the human body from free radicals due to the antioxidants contained in these plants. Natural antioxidants can be obtained from bark, roots, twigs, stems, leaves, fruits, seeds, and flowers.

Flavonoids are potential antioxidants that scavenge free radicals, chelate metals, and inhibit fat oxidation [31] and abundant in plant tissues. Many research results report that flavonoid compounds have various antioxidant activities in different types of grains, vegetables, and fruits [32,33,34,35]. This is known through the pigments that form yellow, blue, purple, or red in leaves, fruits, bulbs, and flowers.

Fruit peel waste is one of the sources of natural antioxidants. Utilization of natural antioxidants from fruit peel can reduce environmental pollution and increase the value of fruit peel. The antioxidant activity of natural antioxidants is still limited, so it needs to be improved by fermentation [36,37]. Many studies have shown that fruit peels can be used as a natural antioxidant, as shown in Table 1. In the Pure & Pure study (2016), banana peel was fermented with a kombucha culture [38]. The study found that after fermentation, there was more antioxidant activity in the substance. This is shown by the increasing percentage of inhibition. Rahmadi et al (2017) found that spontaneous fermentation of chempedak peel increased antioxidant activity, as the IC_{50} value decreased after fermentation [39]. In the study of Liangkun et al. (2018), pineapple peel fermented by *Bacillus acetus* showed increased antioxidant activity [40]. The same was observed with dragon fruit peel fermented by a mixed culture of *Streptococcus thermophilus*, *Lactobacillus plantarum*, and *Lactobacillus bulgaricus* in a 1:1:1 ratio. Fermentation resulted in an increase in antioxidant activity as indicated by a decrease in the IC_{50} value after fermentation [41]. Based on the data in Table 1, it appears that the fermentation of fruit peels using the submerged fermentation (SmF) method can increase antioxidant activity.

Table 1. Research on the antioxidant activity of compounds derived from fruit peel fermentation.

Fruit Peel Substrate	Microorganism	Fermentation Type and Condition	Antioxidant Test Method	Test Results	Source
Banana peel (pretreatment: boiled for 2 hours, rinsed and dried at 50 °C for 24 hours then grounded)	SCOBY (Symbiotic Culture of. Bacteria and Yeast)	SmF; incubated at room temperature within 21 days.	DPPH	The inhibition ability before fermentation was 73.59%, after fermentation, it was 94.60%.	[38]
Cempedak peel (pretreatment: chopped with size 3-4 cm^3, boiled for 15 min at temperature 80-90 °C)	Spontaneous fermentation	SmF; incubated at 37 °C within 7 days.	DPPH	The IC_{50} values before and after fermentation were 212.6 ppm and 130.8 ppm, respectively.	[39]
Pineapple peel (pretreatment: adjust to 18 °BRIX sugar and pasteurize for 30 min)	*Bacillus aceticus*	SmF; first fermentation temperature was at 28 °C and inoculated with 1% activated yeast, second fermentation temperature was at 30 °C with 3% activated *Bacillus aceticus*.	ABTS	The antioxidant capacities before and 12 days after fermentation were 65.3% and 81.6%, respectively.	[40]
Dragon fruit peel (pretreatment: filtered and	*Lactobacillus plantarum, Lactobacillus*	SmF; fermentation temperature was 42 °C within 14 hours.	DPPH	The IC_{50} value before fermentation was 94.70 × 104	[41]

Fruit Peel Substrate	Microorganism	Fermentation Type and Condition	Antioxidant Test Method	Test Results	Source
pasteurized for 15 min at 80 °C)	*bulgaricus, Streptococcus, Thermophilus* (1:1:1)			mg/l. After fermentation, it was 39.94 × 104 ml/l.	
Pomegranate peel (pretreatment: dried in oven at 50±5 °C then blended)	*Aspergillus niger*	SSF; incubated under constant temperature at 28±2 °C within 4 days.	DPPH	The antioxidant activity on day 1 of fermentation was 16.88% and increased to 43.01% on day 4 of fermentation.	[20]
Orange peel (Pretreatment: autoclave for 15 min at 121 °C)	*Trichoderma V6*	SSF; incubated at 28 °C within 7 days.	DPPH	The IC_{50} values were 9.1 and 8.1 µg GAE before and after fermentation, respectively.	[42]
Watermelon rind (Pretreatment: autoclave for 15 min at 121 °C)	*Trichoderma V6*	SSF; incubated at 28 °C within 7 days.	DPPH	The IC_{50} values were 7.3 and 5.7 µg GAE before and after fermentation, respectively.	[42]
Banana Peel (Pretreatment: autoclave for 15 min at 121 °C)	*Trichoderma V6*	SSF; incubated at 28 °C within 7 days.	DPPH	The IC_{50} values before and after fermentation were 6.4 and 3.8 µg GAE, respectively.	[42]
Lime Peel (Pretreatment: dried in tunnel dryer at 40 °C, crushed and filtered using 20 and 50 mesh)	*Aspergillus saitoi*	SSF; incubated at 30 °C for 7 days with humidity 70%.	DPPH	Antioxidant activity was 5.8 times higher than before fermentation.	[43]
			ABTS	Antioxidant activity was 11 times higher than before fermentation.	

Table 1 shows the results of several studies on fruit peel fermentation using the solid-state fermentation (SSF) method. Pomegranate peels fermented by *Aspergillus niger* showed an increase in antioxidant activity on day 4 of fermentation, which was higher than that on day 1 of fermentation, as indicated by Bind et al. (2014) [20]. In the study by Saleh et al. (2017), orange peel, watermelon peel, and banana peel were fermented using *Trichoderma* V6 [42]. The antioxidant activity of the three types of fruit peels increased after fermentation, as indicated by the decrease in IC_{50} value. Similarly, lime peels were fermented by *Aspergillus saitoi*. The results of the DPPH and ABTS tests showed an increase in antioxidant activity after fermentation, as reported by

Najera (2018). The microorganisms used in SSF belong to functional species, namely *Aspergillus niger*, *Trichoderma* V6, and *Aspergillus saitoi* [43].

Based on the description above, it can be concluded that fermentation has the potential to increase antioxidant activity. Fermentation can induce the degradation of plant cell walls, thereby releasing or inducing the formation of bioactive components [44,45]. Microbial enzymes such as glucosidase, amylase, cellulase, chitinase, inulinase, phytase, xylanase, tannase, esterase, invertase, or lipase, produced during fermentation can hydrolyze glucosides, degrade plant cell walls or starch. These enzymes play a role in breaking down the plant cell wall matrix, thereby facilitating the extraction of phenolic compounds [46]. Bacteria of lactic acid, such as *Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus plantarum, Lactobacillus fermentum, Bifidobacterium animalis subsp. lactis*, and *Bifidobacterium longum*, have been reported to possess β-glucosidase activity [36]. The β-glucosidase enzyme catalyzes the hydrolysis of glycosidic linkages in alkyl and aryl β-D-glucosides, as well as glycosides containing only carbohydrate residues [47]. This enzyme helps to break the bonds between sugars, releasing hydrolyzed glycosides and thus free phenolic or phenolic aglycone groups [48]. Fungi produce several types of enzymes during fermentation, such as glycoside hydrolases, cellulases, xylanases, and esterases [49]. These enzymes can hydrolyze the β-glucoside linkages of various phenolic compounds conjugated to one or more sugar residues via hydroxyl groups. This hydrolytic enzyme can increase the concentration of free phenolics [50].

Phenolic compounds have the ability to scavenge free radicals due to their hydroxyl groups. In general, the higher the total phenolic content, the higher the antioxidant activity of an extract or substrate [51]. According to Wijayanti et al. (2017), antioxidant activity is not only determined by the number of hydroxyl groups, but also by the presence of other functional groups throughout the molecule [52]. Rice et al. (1996) stated that how well the antioxidant works in phenolic acids depends on the amount and position of hydroxyl groups compared to other groups such as CO_2H,CH_2CO_2H, or $(CH)_2CO_2CH$, which withdraw electrons [53]. Therefore, high levels of phenolic compounds do not necessarily result in high antioxidant activity. Other non-phenolic antioxidant compounds may also contribute to an increase in antioxidant activity.

In lactic acid bacterial (LAB) fermentation, the level of antioxidant activity increases with an increase in lactic acid produced. Lactic acid ($CH_3CHOHCOOH$) acts as a proton donor for free radical molecules, making them stable [54]. Moreover, as per Hunaefi et al. (2012), lactic acid bacteria are capable of producing exopolysaccharides, which exhibit potential as antioxidants, as shown by several in vitro antioxidant activity test methods [55].

Table 1 demonstrates that the average increase in antioxidant activity was 30% for fruit peels fermented via the SSF method, while the SmF method resulted in an average increase of 23%. This indicates that the SSF method is more suitable for enhancing antioxidant activity than the SmF method. This difference can also be attributed to the advantages and disadvantages of the SSF and SmF methods. According to Musaalbakri and Colin (2017), the production rate and product concentration are higher in the SSF method than in the SmF method, which may be related to the data in Table 1 [56].

The SSF process comprises three phases: gas, solid, and liquid. The liquid phase involves dissolved nutrients and resulting metabolites; the gas phase predominantly comprises oxygen and carbon dioxide; and the solid phase contains microbial cells and nutrient-rich solid substrates [57]. SSF is an efficient process for producing desired metabolites due to the optimal growth conditions it provides for filamentous fungi. The solid-state environment allows the mycelium to spread on the surface of solid compounds, enabling air to flow and promoting fungi growth and reproduction. Solid-state fermentation using low-humidity culture substrates is particularly suitable for fungi because the growing mycelium reduces viscosity in the growth medium, increasing oxygen solubility, and no agitation minimizes cell tissue disruption, which can increase cell mortality [58].

Microbial growth and product formation in the SSF process occur at low humidity, and the substrate is gradually converted into bioactive compounds that are more readily digested, absorbed, and utilized or stored (bioavailability). SSF is also highly effective in reducing process waste, consuming less energy, and producing less wastewater [59].

Holker et al. (2004) reported several secondary metabolites that were produced in a shorter time and higher yields using the SSF method when compared to the SmF method [60]. These metabolites included 6-pentyl-alpha-pyrone, bafilomycin B1 + C1, tamarind benzoate, benzyl alcohol, cephamycin C, coconut fragrance, ergot alkaloids, gibberellic acid, ochratoxin, oxytetracycline, penicillin, rifamycin-B, and tetracycline. Scientists are interested in fungi because they can make some special enzymes that can be used for

important things. These enzymes can stay strong even in high temperatures. Some of the enzymes are amylase, pectinase, xylanase, cellulase, chitinase, protease, lipase, and β-galactosidases [48].

Several studies using the SSF method have used fungi belonging to the genus *Aspergillus* [20,43,36,61,62]. *Aspergillus* fungi can produce tannase enzymes that can specifically cleave ester bonds, producing gallic acid during tannin enzymatic reactions. Gallic acid can combine with glucose to form hydrolyzed tannins and has antioxidant activity [63]. Depending on the porosity of the substrate, fungi growth can occur on the surface or throughout the substrate. Under such conditions, filamentous fungi produce extracellular hydrolytic enzymes and metabolites. SSF can produce high-potency antioxidant compounds due to the low level of contamination resulting from the low water content of the substrate [64].

The higher antioxidant activity of the results from the SSF method compared to the SmF method (Table 1) does not mean that the SmF method is not useful. The SmF method can be used in combination with bacteria that require high humidity to convert substrates, and it allows the use of free-flowing liquids on the substrate to produce bioactive compounds. By using the SmF method with high water content, bacteria can absorb and convert nutrients in the media more quickly, making it easier to release metabolites. The SmF method, using LAB and *Bacillus*, can produce and increase the antioxidant activity of fruit peels [40,41]. The commonly used LAB are from the genera *Lactobacillus* and *Streptococcus*. This is because LAB produces β-glucosidase enzymes that hydrolyze antioxidant compounds such as flavonoids, phenols, and anthocyanins (glycoside forms) into their aglycone forms, making them more digestible and potentially more effective as antioxidants than their glycoside forms [65]. The SSF can produce antioxidant compounds with high efficacy because the process is easier to control, and the separation and purification of metabolites are more efficient [66]. From the above explanation, it can be concluded that the SSF method is more suitable for producing increased antioxidant activity. However, it does not exclude the possibility of using the SmF method to produce secondary metabolite products if adapted to the advantages and disadvantages of each method.

3.2. Antibacterial production through non-fermented, solid-state, and submerged fermentation.

The use of synthetic antibacterials is a potential way to combat bacterial infections. However, the improper use of synthetic antibacterials can lead to resistance problems and several side effects such as hypersensitivity, drug poisoning, kidney damage, nerve cell damage, and blood cell damage [67]. As a result, many naturally derived antibacterials have been used to treat bacterial infections. According to Dwijayanti and Pamungkas (2016), antibacterials derived from natural ingredients are safer and have milder side effects [68]. The efficacy of plants as antibacterial agents is related to the secondary metabolites they produce. Fruit peels are among the natural ingredients that have been extensively studied for their potential as a source of natural antibacterials. Table 2 illustrates several studies on the production of antibacterials from fruit peels using a fermentation process. Table 2 presents two studies using the submerged fermentation (SmF) method that provides pre-and post-fermentation data. In the study by Kim et al. (2017), spontaneously fermented orange peel showed increased antibacterial activity against the Gram-positive and Gram-negative bacteria compared to pre-fermentation, as confirmed by the increased diameter of the inhibition zone [25].

Soursop peel ferments spontaneously and produces enhanced antibacterial activity against Gram-positive and Gram-negative bacteria. There is no research on fruit peel fermentation using the SSF method that provides data on the antibacterial activity before and after fermentation. Therefore, research on the effect of fermentation on increasing the antibacterial activity of fruit peels is still limited. However, the results of studies by Kim et al. (2017) [25] and Otto et al. (2015) [86] showed that fermentation has the potential to increase the antibacterial activity of fruit peels.

Fermentation can increase the release of phenolic compounds [69], as described previously. Phenolic compounds in plants are known to have antibacterial properties [70]. Phenols can cause hyperacidification, resulting in changes in transmembrane permeability and ion channel proteins, disrupting intercellular signaling pathways [71]. Phytochemicals and their hydrolysis products can block bacterial growth through the bacterial membrane's basic functions [72].

In LAB fermentation, there is another additional mechanism for increasing antibacterial activity. LAB produces organic acids, hydrogen peroxide, diacetyl, and bacteriocins that can inhibit bacterial growth [73,74]. Organic acids such as lactic acid have bactericidal and bacteriostatic effects [75]. The antibacterial activity of organic acids is associated with a decrease in pH [76]. When the environment around microorganisms becomes more acidic, the liquid inside the cell also becomes more acidic. The harmful acids can then pass through the cell

membrane [77]. Undissociated acids act by disrupting electrochemical protein gradients or by altering the permeability of the cell membrane, causing a disruption of the substrate transport system [78]. Hydrogen peroxide has an antibacterial effect due to the oxidation process of sulfhydryl groups, which causes the denaturation of enzymes, starting with membrane lipids peroxidation, which will increase the permeability of the cell membrane [74]. The bacteriocins produced by LAB can increase the cytoplasmic membrane permeability, which triggers the release of cytoplasmic components and causes cell death [79].

Table 2 presents data on the antibacterial activity of fermented fruit peels using both solid-state fermentation (SSF) and submerged fermentation (SmF) methods. In the research conducted by Geetha & Jyothi (2017), the SmF method yielded spontaneously fermented orange peels that exhibited antibacterial activity by forming an inhibition zone against both Gram-negative bacteria (*E. coli, Salmonella typhi*, and *Pseudomonas aeruginosa*) and Gram-positive bacteria (*S. aureus,* and *Streptococcus pyogens*) [14]. Pomegranate peel subjected to fermentation by *Aspergillus niger* using the SSF method demonstrated antibacterial activity by forming an inhibition zone against Gram-negative bacteria such as *E. coli, Klebsiella pneumoniae*, and *P. aeruginosa*, and Gram-positive bacteria, *S. aureus* [20]. Similarly, a combination of banana and orange peels fermented by *Bacillus subtilis* SPB1 (HQ392822) using the SSF method showed antibacterial activity against pathogenic bacteria [87].

Table 2. Research on the antibacterial activity of fermented fruit peel compounds

Fruit peel substrate	Antibacterial compound isolation method	Antibacterial test method	Microorganisms for antibacterial test	Diameter of inhibition zone	Source
Orange peel	Spontaneous SmF; incubated at room temperature for 3 months.	Paper disks; incubated at 37°C within 24 hours for bacteria and room temperature within 48 hours for fungi.	*Escherichia coli*	11 mm	[14]
			Staphylococcus aureus	10 mm	
			Streptococcus pyogenes	10 mm	
			Salmonella typhi	13 mm	
			Pseudomonas aeruginosa	9 mm	
Orange peel	Spontaneous SmF; fermented at 25°C for 15 days.	Agar diffusion; incubated at 37°C for 24 hours.	*Listeria monocytogenes*	9 mm	[25]
			Escherichia coli	11 mm	
Pineapple peel (Pretreatment: rinsed and blended)	SmF by *Acetobacter*; fermented at 37°C for 7 days.	Paper disks; Varies of concentrations are 100%, 75%, 50% and 37%; incubated at 37°C for 24 hours	*Escherichia coli*	16 mm	[85]
			Staphylococcus aureus	20 mm	
			Salmonella paratyphi	19 mm	

Fruit peel substrate	Antibacterial compound isolation method	Antibacterial test method	Microorganisms for antibacterial test	Diameter of inhibition zone	Source
			Pseudomonas aeruginosa	19 mm	
Soursop peel	Spontaneous SmF	Agar diffusion	*Staphylococcus aureus*	30 mm	[86]
			Escherichia coli	22 mm	
Pomegranate peel (Pretreatment: dried with oven at 50±5 °C then grounded)	SSF by *Aspergillus niger;* incubated under constant temperature at 28 ± 2°C within 4 days.	Agar diffusion	*Staphylococcus aureus*	7 mm	[20]
			Escherichia coli	10 mm	
			Klebsiella pneumoniae	15 mm	
			Pseudomonas aeruginosa	8 mm	
Mixed of banana and orange peels	SSF by *Bacillus subtilis* SPB1 (HQ392822); incubated at 18-52°C for 48 hours without shaking.	Agar diffusion; incubated for 24 h	*Escherichia coli*	19 mm	[87]
			Staphylococcus aureus	28 mm	
			Pseudomonas aeruginosa	12 mm	
			Staphylococcus xyloxus	23 mm	

A difference in the diameter of the inhibition zone was also observed between Gram-positive and Gram-negative bacteria. Several tests performed on Gram-negative bacteria resulted in a larger inhibition zone diameter compared to Gram-positive bacteria. However, several studies also showed that test results on Gram-negative bacteria resulted in a smaller inhibition zone diameter compared to Gram-positive bacteria. The cell wall component (teichoic acid) of Gram-positive bacteria is polar or water-soluble and acts as a positive ion transporter to facilitate cellular transport. This water-soluble nature of the Gram-positive cell wall suggests that it is more polar, allowing polar bioactive compounds to easily penetrate and damage the polar peptidoglycan layer [80]. In addition, the diameter of the inhibition zone can be influenced by the concentration of the antibacterial compound and the sensitivity of the test bacteria.

Table 2 shows a lack of evidence that the SSF method can increase the antibacterial activity in fruit peels. This is due to the lack of research on the production of antibacterial compounds in fruit peels using the SSF method. However, based on research conducted on the utilization of other organic materials, it is evident that the SSF method can increase antibacterial activity. For example, the fermentation of candlenut seeds by *Aspergillus oryzae* using the SSF method resulted in an increase in antibacterial activity [81]. Specifically, the antibacterial test for *S. aureus* showed a 158% increase in the diameter of the inhibition zone, while for *P. aeruginosa*, the diameter increased by 134%.

In addition to the increased productivity and activity of antibacterial compounds compared to the SmF method, the use of the SSF method can also reduce costs by utilizing agro-industrial solid waste substrates. The low water volume of the SSF method further contributes to the economic process, primarily because the fermenter is smaller, and the steps after making the product are easier and cheaper. There is also less stirring and cleaning needed due [82,83,84]. Although the SmF method can produce many bioactive compounds, new studies show that scientists who are using SSF to make useful substances work better than the SmF method [83].

Although the use of the SSF method resulted in higher antibacterial activity compared to the SmF method, the latter should not be considered unusable. In particular, the use of specific bacteria, such as LAB, has been shown to enhance the antibacterial activity of the SmF method. This is due to the ability of LAB to produce potent antimicrobial compounds in the form of lactic acid, acetic acid, diacetyl, fatty acids, and bacteriocins during the fermentation process [73]. Therefore, while the SSF method is superior in terms of increasing antimicrobial activity, the SmF method is still viable for the production of highly active secondary metabolites, provided that the appropriate bacteria and optimized fermentation conditions are used.

In conclusion, fruit peel waste has the potential to be of high value. In particular, fruit peels are widely recognized as a rich source of antioxidants and antibacterials and are believed to provide various health benefits. The activity of antioxidant and antibacterial compounds in fruit peels can be enhanced by using the fermentation method. Based on existing research, solid-state fermentation (SSF) has been shown to increase antioxidant activity in fruit peels more effectively than submerged fermentation (SmF), especially when fungi group microorganisms are used. Regarding the enhancement of antibacterial activity in fruit peels, a direct comparison between SmF and SSF methods is not yet possible due to the limited research conducted on the latter. However, research on organic materials other than fruit peels suggests that the SSF method produces a greater increase in antibacterial activity than the SmF method when using fungi group microorganisms.

AUTHORS' CONTRIBUTIONS

MMM formulated the research questions, performed the data analysis, and drafted the manuscript. NRH and HGM identified relevant literature and extracted information and data. AM contributed to the data analysis and revised the manuscript.

REFERENCES

[1] M. Marjenah, W. Kustiawan, I. Nurhiftiani, K.H.M. Sembiring, R.P. Ediyono, Pemanfaatan limbah kulit buah-buahan sebagai bahan baku pembuatan pupuk organik cair, in: Jurnal Hutan Tropis 1(2), 2017, pp. 120-127. eISSN 25991183.

[2] M. Kamelia, Fathurohman, Pemanfaatan kulit buah kakao fermentasi sebagai alternatif bahan pakan nabati serta pengaruhnya terhadap pertumbuhan ternak entok (*Cairina muschata*), in: Jurnal Tadris Pendidikan Biologi 8(1), 2017, pp.66-77.

[3] A.S. Narashans, P. Sunil, S. Sunil, M.Y. Elhadi, G.L. Maria, Fruit and vegetable waste: bioactive compounds, their extraction, and possible utilization, in: Comprehensive Reviews in Food Science and Food Safety 17(1), 2018, pp. 512-532.

[4] I.N. Muhammad, Y. Evi, Zulfalina, Identifikasi kandungan ekstrak kulit buah naga merah menggunakan fourier transform infrared (FTIR) dan fitokimia, in: Journal of Aceh Physics Society (JAcPS) 5(1), 2016, pp. 14-16.

[5] M.S. Alfrida, Aktivitas ekstrak kulit buah nanas (*Ananas comosus* L.) terhadap pertumbuhan

Pseudomonas aeruginosa, in: Jurnal Farmasi 13 (2), 2017, pp. 1-5.

[6] A. Harni, A.H. Fakhrurrazi, Uji antibakterial ekstrak kulit buah naga putih (*Hylocereus undatus*) terhadap bakteri *Staphylococcus epidermis*, in: Jurnal Ilmiah Mahasiswa Veteriner 1(3), 2017, pp. 416-423.

[7] I. Maulana, Uji antibakterial ekstrak kulit buah naga merah (*Hylocereus polyrhizus*) terhadap bakteri *Salmonella pullorum*, in: Skripsi, Universitas Syiah Kuala, Banda Aceh.

[8] H.R. Nurhilmi, Potensi limbah kulit buah sebagai bahan baku dalam pembuatan edible film, in: Jurnal Teknologi Pangan, 2019, pp.92-98.

[9] S. Astuti, Isoflavon kedelai dan potensinya sebagai penangkap radikal bebas, in: Jurnal Teknologi Industri dan Hasil Pertanian, 13(2),2008, pp. 126-136.

[10] J. Rattanapan, S, Jirapast, T. Santi, Chemical constituents and antioxidant activity from the stems of *Alyxia reinwardtii*, in: Academy of Chemistry of Globe Publications, 6(3), 2012, pp.288-291.

[11] H. Rahman, V.B. Reddy, S. Ghosh, S.K., Mistry, G. Pant, G. Sibi, Antioxidant, cytotoxic, and hypolipidemic activities of *Plumeria alba* L. and *Plumeria rubra* L., in: American Journal of Life Science, 2(1), 2014, pp. 11-15.

[12] M. Oktavian, R. Ahmad, Musafira, Kajian aktivitas antioksidan ekstrak daun tembelekan (*Lantana camara* L.) berdasarkan tingkat kepolaran pelarut, in: Jurnal Riset Kimia, 2(3),2016, pp. 16-23.

[13] Rahmawati, Uji aktivitas antibakteri ekstrak etanol daun jati belanda (*Guazuma ulmifolia* Lamk.) terhadap bakteri penyebab diare (*Bacillus cereus* dan *Escherichia coli*), in: Skripsi, FMIPA, Universitas Islam Bandung, 2014.

[14] S. Geetha, K. Jyothi, Antimicrobial activity of fermented citrus fruit peel extract, in: Int. Journal of Engineering Research and Application, 7(11),2017, pp. 25-28.

[15] R.L. Prior, G. Cao, A. Martin, E. Sofic, J.McEwen, C. O'Brien, N. Lischner, M. Ehlenfeldt, W. Kalt, G. Krewer, C.M. Mainland, Antioxidant capacity as influenced by total phenolic and anthocyanin content, maturity, and variety of *Vaccinium* species, in: J. Agric. Food Chem., 46(7), 1998, pp. 2686-2693.

[16] H.E. Miller, F. Rigelhof, L. Marquart, A.Prakash, M. Kanter, Antioxidant content of whole grain breakfast cereal, fruits, and vegetables, in: Journal of Nutrition, 84(1), 2000, pp. 95-135.

[17] T.D. Roach, K.J. Sufka, Characterization of the chick carrageenan response, in: Brain Research,994(2), 2003, pp. 216-225.

[18] F. Abas, N.H. Lajis, D.A. Israf, S. Khozirah, Y.U.Kalsom, Antioxidant and nitric oxide inhibition activities of selected Malay traditional vegetables, in: Food Chemistry, 95(4), 2006, pp.566-573.

[19] M.N. Rahman, Aktivitas antibakteri senyawa hasil biotransformasi kurkumin oleh mikroba endofit asal kunyit, in: Skripsi, FMIPA, IPB, Bogor, 2009.

[20] A. Bind, S.K. Singh, V. Prakash, M. Kumar, Evaluation of antioxidants through solid state fermentation from pomegranate peels using *Aspergillus niger* and its antibacterial properties, in: International Journal of Pharmacy and Biological Science, 4(1), 2014, pp. 104-111.

[21] S.A. Mohamed, R.M. Saleh, S.A. Kabli, G.M. Al-Garni, Influence of solid-state fermentation by *Trichoderma* spp. on solubility, phenolic content, antioxidant, and antimicrobial activities of commercial turmeric, in: Biosci. Biotechnol. Biochem., 80(5), 2016, pp. 920-928.

[22] M.C.I. Parez, C.J. Guillen, R.G. Guevara, N.E.Rocha, A. Mercado, Effect of nitrogen privation on the phenolic contents, antioxidant and antibacterial activities in *Moringa oleifera* leaves, in: Industrial Crops and Products, 114(1), 2018, pp. 45-51.

[23] D. Permadi, A. Dzolqornaen, Optimization on antioxidant yield from banana (*Musa sapientum* L.) peel waste through fermentation method, in: Proceeding 6th Asian Academic Society International Conference (AASIC), 2018, pp. 605-610.

[24] M.M. Rashad, E.M. Abeer, M.A. Mamdouh, U.N. Mohamed, Antioxidant and anticancer agents produced from pineapple waste by solid-state fermentation, in: International Journal of Toxicology and Pharmacological Research, 7(6), 2015, pp. 287-296.

[25] S.S. Kim, K.J. Park, H.J. An, Y.H. Choi, Phytochemical, antioxidant, and antibacterial activities of fermented *Citrus unshiu* byproduct, in: Food Sci. Biotechnol., 26(2), 2017, pp. 461-466.

[26] Lessa, A. Ozana, D.S.R. Nadabe, G.F.L. Selma, L.E.G. Mellisa, O.S. Alexilda, Effect of the solid-state fermentation of cocoa shell on the secondary metabolites, antioxidant activity, and fatty acids, in: Journal of Biotechnology, 2017.

[27] W. Asri, Peran antioksidan bagi kesehatan, in: Jurnal Biotek Medisiana Indonesia, 3(2), 2014, pp. 59-68.

[28] R.K. Murray, D.K. Granner, P.A. Mayes, Rodwll, Harper's Illustrated Biochemistry, 26th ed., Lange Medical Books/McGraw-Hill, New York, 2003.

[29] S.P. Mahantesh, A.K. Gangawane, C.S. Patil, Free radicals, antioxidants, disease and phytomedicines in human health: future perspectives, in: World Research Journal of Medicinal & Aromatic Plants, 1(1), 2012, pp. 6-10.

[30] W. Selawa, M.R.J. Runtuwene, G. Citraningtyas, Kandungan flavonoid dan kapasitas antioksidan total ekstrak etanol daun binahong (*Anredera cordifolia* (ten) Steenis.), in: Jurnal Ilmiah Farmasi, 2(1), 2013, pp. 18-22.

[31] N.C. Cook, S. Samman, Review flavonoids-chemistry, metabolism, cardioprotective effect, and dietary sources, in: Journal of Nutrition Biochemical, 7(2), 1996, pp. 66-76.

[32] A. Redha, Flavonoid: struktur, sifat antioksidatif dan peranannya dalam sistem biologis, in: Jurnal Belian, 9(2), 2010, pp. 196-202.

[33] S. Sen, R. Chakraborty, The role of antioxidants in human health, in: ACS Symposium Series, 2011, pp. 1-37.

[34] R. Venkatesh, D. Sood, A review of the physiological implication of antioxidants in food, in: Skripsi, Worchester Polytechnic Institute.

[35] J.S. Dias, Nutritional quality and health benefits of vegetables: a review, in: Food and Nutrition Sciences, 3(10), 2012, pp. 1354-1374. doi:10.4236/fns.2012.310179.

[36] Sulasiyah, P.R. Sarjono, A.L. Aminin, Antioxidant from tumeric fermentation products (*Curcuma longa*) by *Aspergillus oryzae*, in: Jurnal Kimia Sains dan Aplikasi, 21(1), 2018, pp.13-18. doi: 10.14710/jksa.21.1.13-18.

[37] E.D. Wijayanti, L.J. Yustin, Aktivitas antioksidan sari rimpang temu giring (*Curcuma heyneana*) terfermentasi *Lactobacillus bulgaricus*, in: Journal Cis-Trans, 2(1), 2018, pp. 1-5. doi:10.17977/ um026v2i12018p001.

[38] A.E. Pure, M.E. Pure, Antioxidant and antibacterial activity of kombucha beverages prepared using banana peel, common nettles and black tea infusions, in: Applied Food Biotechnology, 3(2), 2016, pp. 125-130. doi:10.22037/afb.v3i2.11138.

[39] A. Rahmadi, K. Sari, S. Sitohang, N. Khairiyah, F. Handayani, A. Emmawati, Profil perubahan populasi BAL, pH, kadar flavonoid, dan potensi aktivitas antioksidan pada fermentasi mandai cempedak higienis tanpa garam, in: Seminar Nasional Perhimpunan Ahli Teknologi Pangan Indonesia, Bandar Lampung, 2017, pp. 2-8.

[40] L. Liangkun, H. Hui, Y. Yuan, W. Xiaoyi, L.Lijing, G. Xiao, Evaluation of antioxidant activity and flavor profile change of pineapple peel vinegar during fermentation, in: 3rd International Conference on Materials Science, Machinery and Energy Engineering (MSMEE 2018) Zhanjiang: CSP, 2018, pp. 380-387.

[41] Eveline & Audina, Utilization of super red dragon fruit peel (*Hylocereus costaricensis* (F.A.C weber) briton & rose) in the making of fermented beverage, in: International Conference on Food Science & Technology, 292, 2019, pp. 1-9. doi:10.1088/1755-1315/292/1/012037.

[42] R.M. Saleh, S.A. Kabli, S.M. Al-Garni, S.A. Mohamed, Y.Q. Almulaiky, Enhancement of the total phenolic and flavonoid contents and antioxidant activity of some fruit peels by solid-state fermentation of Trichoderma V6, in: JKAU: Sci., 29(2), 2017, pp. 13-20. doi: 10.4197/Sci.29-2.3.

[43] V.C. Najera, E.L. Cervantes, L.A. Flores, C.L.Sanchez, Biotransformation of hesperidin from lime peel (*Citrus limetta* Risso) in solid fermentation by *Aspergillus saitoi*, in: CyTA-Journal of Food, 16(1), 2018, pp. 537-543. doi:10.1080/19476337. 2018.1430707.

[44] K. Katina, A. Laitila, R. Juvonen, K. Liukkonen, S. Kariluoto, V. Piironen, Bran fermentation as a means to enhance technological properties and bioactivity of rye, in: Food Microbiology, 24,2007, pp. 175-186.

[45] T.M. Dordevic, S.S. Marinkovic, D. Brankovic, Effect of fermentation on antioxidant properties of some cereals and pseudo cereals, in: Food Chemistry, 119, 2010, pp. 957-963. doi:10.1016/j.foodchem.2009.07.049.

[46] S.J. Hur, S.Y. Lee, Y.C. Kim, I. Choi, G.B. Kim, Effect of fermentation on the antioxidant activity in plant-based foods, in: Food Chemistry, 160, 2014, pp. 346-356. doi: 10.1016/j.foodchem.2014.03.112.

[47] D.A. Vattem, K. Shetty, Ellagic acid production and phenolic antioxidant activity in cranberry pomace (*Vaccinium macrocarpon*) mediated by *Lentinus edodes* a using solid-state system, in: Process Biochemistry, 39, 2003, pp. 367-379. doi: 10.1016/S0032-9592(03)00089-X.

[48] S. Martins, S.I. Mussatto, G.M. Avila, J.M. Saenz, C.N. Aguilar, J.A. Teixeira, Bioactive phenolic compounds: production and extraction by solid-state fermentation. A review, in:

Biotechnology Advances, 29, 2011, pp. 365-373. doi: 10.1016/j.biotechadv.2011.01.008.

[49] S. Cai, O. Wang, W. Wu, S. Zhu, F. Zhou, B. Ji, Comparative study of the effects of solid-state fermentation with three filamentous fungi on the total phenolic content (TPC), flavonoids, and antioxidant activities of subfractions from oats (*Avena sativa* L.), in: Journal of Agricultural and Food Chemistry, 60, 2012, pp. 507-513. doi:10.1021/jf204163a.

[50] S. Georgetti, F. Vincentini, C. Yokoyama, M.Borin, A. Spadaro, M. Fonseca, Enhanced in vitro and in vivo antioxidant activity and mobilization of free phenolic compounds of soybean flour fermented with different beta-glucosidase- producing fungi, in: Journal of Applied Microbiology, 106, 2009, pp. 459-466. doi:10.1111/j.1365-2672.2008.03978.x.

[51] M. Tosun, S. Ercisli, M. Sengul, H. Ozer, T. Polat, E. Ozturk, Antioxidant properties and total phenolic content of eight salvia species from Turkey, in: Biol Res, 42, 2009, pp. 175-181. doi:10.4067/S0716-97602009000200005.

[52] E.D. Wijayanti, N.C. Setiawan, J.P. Christi, Effect of lactic acid fermentation on total phenolic content and antioxidant activity of fig fruit juice (*Ficus carica*), in: Advances in Health Science Research (AHSR), 2, 2017, pp. 282-289. doi: 10.2991/hsic-17.2017.44.

[53] C.A. Rice-Evans, N.J. Miller, G. Paganga, Structure-antioxidant activity relationships of flavonoids and phenolic acids, in: Free Radical Biology & Medicine, 20(7), 1996, pp. 933-956.

[54] E.P. Oktaviani, Kualitas dan aktivitas antioksidan minuman probiotik dengan variasi konsentrasi ekstrak kulit buah naga merah (*Hylocereus polyrhizus*), Skripsi, Universitas Atma Jaya Yogyakarta, 2014.

[55] D. Hunaefi, D.N. Akumo, H. Riedel, I.Smetanska, The effect of *Lactobacillus plantarum* ATCC 8014 and *Lactobacillus acidophilus* NCFM fermentation on antioxidant properties of selected in vitro sprout culture of *Orthosiphon aristatus* (java tea) as a model study, in: Antioxidants, 1, 2012, pp. 4-32. Doi: 10.3390/antiox101004.

[56] A.M. Musaalbakri, W. Colin, (2017). Design aspects of solid-state fermentation as applied to microbial bioprocessing, in: Journal of Applied Biotechnology & Bioengineering, 4(1), 2017, pp.1-25. doi: 10.15406/jabb.2017.04.00094.

[57] S.R. Couto, M. A. Sanromán, Application of solid-state fermentation to food industry, in: Journal of Food Engineering, 76(3), 2006, pp.291–302. doi:10.1016/j.jfoodeng.2005.05.022.

[58] M.K. Gowthaman, C. Krishna, M. Moo-Young, Fungal solid state fermentation. Applied Mycology and Biotechnology, 2001, pp. 305–352. doi:10.1016/s1874-5334(01)80014-9.

[59] C.G. Schmidt, L.M. Gonçalves, L. Prietto, H.S.Hackbart, E.B. Furlong, Antioxidant activity and enzyme inhibition of phenolic acids from fermented rice bran with fungus *Rhizopus oryzae*, in: Food Chemistry, 146, 2014, pp. 371–377. doi:10.1016/j.foodchem.2013.09.101.

[60] U. Holker, M. Hofer, J. Lenz, Biotechnological advantages of laboratory-scale solid-state fermentation with fungi, in: Applied Microbiology and Biotechnology, 64(2), 2004, pp. 175-186. doi:10.1007/s00253-003-1504-3.

[61] F.V. Dulf, D.C. Vodnar, E.H. Dulf, M.I. Tosa, Total phenolic contents, antioxidant activities, and lipid fractions from berry pomaces obtained by solid-state fermentation of two *Sambucus* species with *Aspergillus niger*, in: Agricultural and Food Chemistry, 2015, pp. A-L. doi:10.1021/acs.jafc.5b00520.

[62] F.V. Dulf, D.C. Vodnar, E.H. Dulf, A. Pintea, Phenolic compounds, flavonoids, lipids and antioxidant potential of apricot (*Prunus armeniaca* L.) pomace fermented by two filamentous fungi strains in solid state system, in: Chemistry Central Jurnal, 11(92), 2017, pp. 1-10. doi: 10.1186/s13065-017-0323-z.

[63] Y.A.S. Anwar, Burhanuddin, Pengaruh komposisi media terhadap aktivitas dan karakter enzim tanin asil hidrolase dari *Aspergillus niger*, in: Jurnal Ilmu Kefarmasian Indonesia, 10(2), 2012, pp. 87-92.

[64] P. Gervais, P. Molin, The role of water in solid-state fermentation, in: Biochemical Engineering Journal, 13(2-3), 2003, pp. 85-101. Doi:10.1016/s1369-703x(02)00122-5.

[65] H. Michlmayr, W. Kneifel, (2013). β-Glucosidase activities of lactic acid bacteria: mechanisms, impact on fermented food and human health, in: FEMS Microbiology Letters, 352(1), 2013, pp.1–10. doi:10.1111/1574-6968.12348.

[66] R.R. Singhania, R.K. Sukumaran, A.K. Patel, C.Larroche, A. Pandey, Advancement and comparative profiles in the production technologies using solid-state and submerged fermentation for microbial cellulases, in: Enzyme and Microbial Technology,46(7),2010,pp.541-549. doi:10.1016/j.enzmictec.2010.03.010.

[67] R.M. Putri, V.E. Diana, K. Fitri, Perbandingan uji aktivitas antibakteri dari ekstrak etanol bunga, daun dan akar tumbuhan rosella (*Hibiscus sabdariffa* L.) terhadap bakteri *Staphylococcus aureus*, in: Jurnal Dunia Farmasi, 3(3), 2019, pp.131-143.

[68] S.I. Dwijayanti, G.S. Pamungkas, Uji aktivitas antibakteri ekstrak daun tapak darah (*Catharantus roseus* (L.) G. Don.) terhadap bakteri *Staphylococcus aureus* dan *Pseudomonas aeruginosa*, in: Biomedika, 9(2), 2016, pp.11-20.

[69] T. Bhanja, A. Kumari, R. Banerjee, (2009).Enrichment of phenolics and free radical scavenging property of wheat koji prepared with two filamentous fungi, in: Bioresource Technology, 100(11), 2009, pp. 2861-2866. doi:10.1016/ j.biortech.2008.12.055.

[70] K.M. Cho, S.Y. Hong, R.K. Math, J.H. Lee, D.M.Kambiranda, J.M. Kim, (2009). Biotransformation of phenolics (isoflavones, flavanols and phenolic acids) during the fermentation of cheonggukjang by *Bacillus pumilus* HY1, in: Food Chemistry, 114, 2009, pp. 413-419. doi: 10.1016/j.foodchem. 2008.09.056.

[71] I. Mantzourani, C.A. Bontsidis, S. Plessas, A.Alexopoulos, E. Theodoridou, C. Tsigalou, Comparative susceptibility study against pathogens using fermented cranberry juice and antibiotics, in: Frontiers in Microbiology, 10,2019, pp. 1-10.

[72] M. Majeed, K. Nagabhushanam, S. Arumugam, S. Natarajan, S. Majeed, A., Pandey, Cranberry seed fiber: a promising prebiotic fiber and its fermentation by the probiotic *Bacillus coagulans* MTCC 5856, in: International Journal of Food Science and Technology 2018, pp. 1-8. doi:10.1111/ijfs.13747.

[73] H.J. Lawalata, L. Sembiring, E.S. Rahayu, Molecular identification of lactic acid bacteria producing antimicrobial agents from bakasang, an Indonesian traditional fermented fish product, in: Indonesian Journal of Biotechnology, 16(2), 2011, pp. 93-99.

[74] I.F. Gonzales, A.C. Guerrero, G. Quijano, The benefit of probiotics on human health, in: Journal of Microbial & Biochemical Technology, 2011, pp. 1-6. doi: 10.4172/1948-5948.S1-003.

[75] R. Agrawal, Probiotics: an emerging food supplement with health benefits, in: Food Biotechnology, 19, 2005, pp. 227-246. doi:10.1080/08905430500316474.

[76] R.K. Podolak, J.F. Zafas, C. Kastner, D. Fung, Inhibition of *Listeria monocytogenes* and *Escherichia coli* O157:H7 of beef application of organic acids, in: Journal of Food Protection, 59(4), 1996, pp. 370-373.

[77] E.R. Kashket, Bioenergetics of lactic acid bacteria: cytoplasmic pH and osmotolerance, in: FEMS Microbiology Reviews, 46, 1987, pp. 233-244.

[78] J. Snijders, J.V. Logtestijn, D. Mossel, F.Smulderst, Lactic acid as a decontaminant in slaughter and processing procedures, in: Veterinary Quarterly, 7(4), 1985, pp. 277-282.

[79]E. Simova, D.Beshkova, Z. Dimitrov, Characterization and antimicrobial spectrum of bacteriocins produced by lactic acid bacteria isolated from traditional bulgarian dairy products, in: Journal of Applied Microbiology, 106, 2009, pp. 692-701. doi: 10.1111/j.13652672.2008.04052.x.

[80] F.K. Dewi, Aktivitas antibakteri ekstrak etanol buah mengkudu (*Morinda citrifolia* L.) terhadap bakteri pembusuk daging segar, Tesis, Universitas Sebelas Maret, Solo, 2010.

[81] G.D. Limbong, L.N. Nababan, A. Manurung, M.M. Martgrita, Antioxidant and antibacterial activities enhancement of solid-state fermented candlenut kernels by *Aspergillus oryzae*, in: Journal of Microbiology. 13(2), 2019, pp. 50-55. doi: 10.5454/mi.13.2.2.

[82] U. Holker, J. Lenz, Solid-state fermentation, are there any biotechnological advantages?, in: Current Opinion in Microbiology, 8(3), 2005, pp. 301–306. doi:10.1016/j.mib.2005.04.006.

[83] P.S. Nigam, A. Pandey, Production of bioactive secondary metabolites, in: Biotechnology for agro-industrial residues utilization, 1st ed., Springer, Netherlands, 2009.

[84] A. Pandey, (2003). Solid-state fermentation, in: Biochemical Engineering Journal, 13(1), 2003, pp. 81-84.

[85] P.M. Tumane, S. Sarkar, D.D. Wasnik, N.A.Kolte, Production of vinegar from pineapple peels using *Acetobacter* species isolated from soil sample and its antibacterial activity, in: International Journal of Life Science 6(4), 2018, pp. 948-956. ISSN: 2320-964X.

[86]R.B.D. Otto, M. Nankwanga, D. Sesaazi, Comparison of antibacterial activities of fermented with those of unfermented *Annona muricata* (L) fruit extracts, in: Int. J. Curr. Microbiol. App. Sci. 4(6), 2015, pp. 696-707. ISSN: 2319-7706.