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GC-MS-Based Metabolomics Analysis of Prawn Shell Waste Co-Fermentation by *Lactobacillus plantarum* and *Bacillus subtilis*

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Abstract: GC-MS-based metabolomics were used to investigate metabolic changes in prawn shell waste during fermentation. Microbial strains *Lactobacillus plantarum* and *Bacillus subtilis* were co-fermented in a shake flask comprising of 5% (*w/v*) prawn shell waste and 20% (*w/v*) glucose as a carbon source. Analysis of the prawn shell waste fermentation showed a total of 376 metabolites detected in the culture supernatant, including 14 amino acids, 106 organic acids, and 90 antimicrobial molecules. Results show that the liquid fraction of the co-fermentation is promising for harvesting valuable metabolites for probiotics application.

Keywords: prawn shell waste; *Lactobacillus plantarum*; *Bacillus subtilis*; fermentation; metabolomics

1. Introduction

The industrial seafood processing industry generates more than 1 million metric tons of dry weight of shellfish waste annually [1]. As the heads and exoskeletons of shellfish that comprise about 50–60% of their total weight are not suitable for human consumption, these shellfish residues are discarded as seafood processing waste by ocean dumping, incineration, or disposal in landfills [2]. This has contributed to both land and sea pollution, hence sparking scientific and environmental interest to develop techniques to recover and utilize the biopolymers in shellfish waste [3].

Prawn shell waste is chemically composed of 20–30% chitin, 20–40% protein, 30–60% minerals, and 0–14% lipids [4]. Currently, crustacean waste serves as the largest source of chitin or its deacetylated derivative chitosan [5]. Chitin, a polysaccharide with a similar structure to cellulose, is an *N*-acetyl-glucosamine biopolymer with α-1,4 bonds between each monomeric unit [6]. The isolation of chitin involves deproteinization, demineralization, and bleaching [7]. Traditional chemical methods involve the use of highly concentrated sodium hydroxide to carry out deproteinization and highly corrosive hydrochloric acid to carry out demineralization [8]. Other than the formation of toxic waste, undesired by-products such as irregularly deacetylated polymers result [9]. In addition, the protein and carotenoid components of the prawn shell waste are rendered useless [10].

Research has focused on using environmentally friendly processes such as biological co-fermentation by lactic acid bacteria and protease producing bacteria [11]. The lactic acid produced during fermentation reacts with the calcium carbonate in the prawn shell waste, leading to the formation of calcium lactate, which can be separated from the chitin fraction [12]. Proteolytic enzymatic action also simultaneously hydrolyzes the protein fraction of prawn shells to recover chitin [13]. Much attention has been directed at optimizing the extracellular production of the chitinase enzyme by the selection of appropriate micro-organisms [14]. Various factors such as glucose concentrations, inoculum sizes, pH, temperature, and length of fermentation influence the fermentation process as well as deproteinization and demineralization efficiencies [15].

The remains of shellfish heads and exoskeletons are also rich in lipid soluble carotenoid pigments and the recovery of an astaxanthin-rich carotenoprotein concentrate for its antioxidant properties have been a focal point of scientific study [16]. The extraction of protein hydrolysates from prawn shell waste for use as food flavoring agents or for aquaculture diets has received considerable scientific attention [17]. However, the study of these bioactive compounds in the liquor fraction has posed great challenges due to their inherent instability upon analysis [18].

In this study, GC-MS-based metabolomics profiling was performed on the co-culture supernatant of both microbial strains, lactic acid bacteria *Lactobacillus plantarum* subsp. *plantarum* ATCC 14,917 and protease producing bacteria *Bacillus subtilis* subsp. *subtilis* ATCC 6051, using prawn shell waste as the nitrogen source and 20% glucose in deionized water as the carbon source [19]. *Lactobacillus plantarum* was selected as previous studies found it to be starch-hydrolyzing, heterofermentative, and proteolytic when tested in skim milk agar, which are important properties for the deproteinization and demineralization of prawn shells [20]. *Bacillus subtilis* was chosen as it was affirmed in previous studies to produce a high protease yield, which retained maximum protease activity even in the presence of salt, surfactants, metal ions, and solvents [21].

The composition of totals phenols, polysaccharides, reducing sugars, free amino acids, and organic acids in the culture supernatant were determined by GC-MS analysis after GC derivatization to understand the fermentation characteristics of microbial extraction of chitin from prawn shell waste [22]. The remnants of the prawn shell waste were filtered off from the fermented supernatant, washed with deionized water, and sterilized with 70% (*v/v*) ethanol [23]. After being dried in a vacuum oven at 60°C overnight, chemical analysis was performed and it was found to be chitin [24].

2. Materials and Methods

2.1. Fermentation Conditions and Harvesting of Samples

Single colonies of *Lactobacillus plantarum* on De Man, Rogosa, and Sharpe (MRS) agar plates were picked to 5 mL MRS broth and cultured at 37 °C, 200 rpm, overnight for 12 to 16 h. Similarly, single colonies of *Bacillus subtilis* on Luria-Bertani (LB) agar plates were picked to 5 mL LB broth and cultured at 30 °C, 200 rpm, overnight for 12 to 16 h. The *Lactobacillus plantarum* and *Bacillus subtilis* bacterial cells were collected by centrifuging at 14,500× *g*, 25 °C, for 5 min and their respective supernatants were decanted, leaving the cell pellets behind.

A conical flask containing 5 g of prawn shell waste as well as 20 g of glucose dissolved in 100 mL of deionized water were autoclaved at 121 °C for sterilization [25]. The 100 mL 20% (*w/v*) glucose solution was poured into the sterile conical flask containing 5 g of prawn shell waste. *Lactobacillus plantarum* cells and *Bacillus subtilis* cells were picked up from the centrifuged bacterial cell pellets using inoculating loops and inoculated into the fermentation flask. The fermentation setup procedures were repeated twice and the triplicate flasks were incubated at 30 °C, 200 rpm, for 5 days.

2.2. Samples Preparation for Extracellular Metabolites Analysis

First, 1 mL culture supernatant was collected from each of the three fermentation setups after 5 days. Ten microliters of 2 g/L ribitol dissolved in water was added to 50 µL of each supernatant sample and mixed thoroughly in a fresh Eppendorf tube [26]. The addition of ribitol served as an internal standard to correct for metabolite loss during sample preparation [27]. The samples were lyophilized overnight using a Labconco freeze dryer set at −40 °C and 0.0002 mBar and GC-MS derivatization was performed the next day [28].

2.3. GC-MS Analysis of Extracellular Metabolites

GC derivatization was performed for metabolic profiling on the GC-MS [29]. The lyophilized samples were re-dissolved in 100 µL of 20 mg/mL methoxyamine hydrochloride in pyridine and incubated at 37 °C for 1 h for carbonyls protection [30]. One hundred microliters of *N*-methyl-*N*-(trimethylsilyl)-trifluoroacetamide

(MSTFA) with 1% trimethyl-chlorosilane (TMCS) was added to each sample and silylation was carried out at 70 °C for 30 min [31]. The samples were centrifuged at 14,500× *g* for 15 min and the supernatant was used for GC-MS analysis [32]. Samples of 1 µL were injected into the HP-5MS capillary column (Agilent Technologies, Singapore) by splitless mode using an auto-injector [33]. Helium was used as a carrier gas at 1.1 mL/min [34]. The injector temperature and ion source temperature were set at 250 °C and 230 °C, respectively, on the GC-MS (Agilent Technologies, Singapore) [35]. The oven temperature was kept at 75 °C for 5 min, raised at 4 °C per minute to a final temperature of 280 °C, and held for 2 min [36]. Data were recorded from m/z 50 to 500 with a scan time of 0.1 s [37]. Metabolites were identified using the NIST08 mass spectral library and normalized using the internal standard ribitol before comparison [38].

2.4. Statistical Analysis of Metabolites

The peak area for ribitol from the GC-MS run was recorded and equated to 20 µg/200 µL. The peak areas for detected metabolites were tabulated and their concentrations calculated via multiplying by ribitol concentration 20 µg/200 µL and dividing over peak area for ribitol. Metabolite measurement results from the triplicate fermentation flasks were expressed as mean ± standard deviation.

2.5. Determination of Chitin Yield and Purity

The mass of the crude chitin obtained was weighed after being dried in the vacuum oven overnight to determine its yield. The Lowry's test for residual protein was carried out to ascertain the purity of the recovered chitin. Firstly, 5, 10, 15, 20, 25, and 30 µL of 2 mg/mL bovine serum albumin (BSA) was added to 195, 190, 185, 180, 175, and 170 µL of deionized water respectively to form a range of 200 µL protein standards for the construction of a protein calibration curve. Then, 1 mL of Lowry's solution was added to the protein standards and left to react for 15 min, after which 100 µL of 1 N Folin's Phenol reagent was added and the protein standards were left to react for another 30 min. Absorbance was measured at 750 nm and the values were plotted into a graph of absorbance versus µg protein. Fifty milligrams of the extracted crude chitin was then treated with 10 mL of 1 M aqueous sodium hydroxide solution for 24 h at 70 °C. 1 mL of Lowry's solution and 100 µL of 1 N Folin's Phenol reagent was similarly added to the boiled NaOH supernatant to determine the residual protein content of the recovered chitin [39].

3. Results

3.1. Metabolomics Analysis by GC-MS

A total of 376 metabolites were detected by GC-MS. Fourteen amino acids were detected in the fermentation, with the highest quantity being alanine (4642.67 mg/L), followed by proline (91.76 mg/L), threonine (91.73 mg/L), leucine (63.91 mg/L), norleucine (53.57 mg/L), alanylthreonine (26.39 mg/L), glycine (25.56 mg/L), sarcosine (16.19 mg/L), isoleucine (13.96 mg/L), alloisoleucine (13.86 mg/L), glutamic acid (5.68 mg/L), valine (3.13 mg/L), 1,4-dihydrophenylalanine (2.92 mg/L), and lysine (0.44 mg/L). Ketoisocaproic acid, which is a metabolic intermediate in the metabolic pathway for the amino acid leucine, was detected at 44.06 mg/L; while ketoisovaleric acid, which is a metabolite of the amino acid valine, was detected at 1.2 mg/L.

One hundred and six organic acids were found in the culture supernatant, with the highest quantities being butanoic acid (4399.87 mg/L), mannonic acid (2567.14 mg/L), 2,3-dimethylbutanoic acid (2129.98 mg/L), carbamic acid (1432.07 mg/L), glucopyranuronic acid (1239.42 mg/L), D-glycero-L-manno-heptonic acid (1192.77 mg/L), 3-oxooctanoic acid (1185.00 mg/L), propanoic acid (1184.32 mg/L), and lactic acid (1055.38 mg/L). There were also significant quantities of mandelic acid (443.5 mg/L), gluconic acid (307.05 mg/L), 2-ketobutyric acid (222.57 mg/L), hexanedioic acid (200.31 mg/L), 2-hydroxyisocaproic acid (173.95 mg/L), xylonic acid (156.31 mg/L), butyric acid (153.36 mg/L), hexadecenoic acid (147.85 mg/L), octadecanoic acid (147.83 mg/L), dipropylacetic acid (120.83 mg/L), and 3-deoxy-D-arabino-hexonic acid (112.61 mg/L) detected.

Ninety metabolites were reported in the literature to possess antimicrobial properties, of which 37 metabolites were fatty or organic acids. The remaining 53 reportedly antimicrobial metabolites, which were non-acids, include acetamide (2999.12 mg/L), uridine (1277.01 mg/L), 2-hydroxybenzaldehyde (940.97 mg/L), acethydrazide (366.71 mg/L), 2-propenamide (338.39 mg/L), glycerol (336.23 mg/L), 2-quinolinone (284.36 mg/L), benzenesulfonamide (167.36 mg/L), thymol (68.98 mg/L), quinazoline (66.92 mg/L), sedoheptulose (64.36 mg/L), kaurene (58.27 mg/L), 1,2-benzisothiazole (56.13 mg/L), phenanthroline (49.88 mg/L), ethyl acetate (44.86 mg/L), pyrazine (33.19 mg/L), ethanol (31.01 mg/L), 1,4-benzoquinone (28.12 mg/L), benzoate (24.82 mg/L), benzisothiazolinone (23.64 mg/L), indole (22.32 mg/L), and 2-aminothiadiazole (20.98 mg/L).

Full detailed results for the detected metabolites are shown in Tables 1–4 below.

Table 1. Amino acids detected in culture supernatant of dual *Lactobacillus plantarum* and *Bacillus subtilis* fermentation in prawn shell waste and 20% glucose in deionized water.

Metabolite	Molecular Formula	Quantity (mg/L)	Biological Characteristic
Alanine	$C_3H_7NO_2$	4642.67 ± 3.90	Amino acid
Alanylthreonine	$C_7H_{14}N_2O_4$	26.39 ± 0.01	Amino acid
Alloisoleucine	$C_6H_{13}NO_2$	13.86 ± 0.01	Amino acid
1,4-Dihydrophenylalanine	$C_9H_{13}NO_2$	2.92 ± 0.01	Amino acid
Glutamic acid	$C_5H_9NO_4$	5.68 ± 0.01	Amino acid
Glycine	$C_2H_5NO_2$	25.56 ± 0.02	Amino acid
Isoleucine	$C_6H_{13}NO_2$	13.96 ± 0.06	Amino acid
Ketoisocaproic acid	$C_6H_{10}O_3$	44.06 ± 0.13	Leucine ketoacid
Ketoisovaleric acid	$C_5H_8O_3$	1.20 ± 0.01	Valine ketoacid
Leucine	$C_6H_{13}NO_2$	63.91 ± 0.01	Amino acid
Lysine	$C_6H_{14}N_2O_2$	0.44 ± 0.01	Amino acid
Proline	$C_5H_9NO_2$	91.76 ± 1.28	Amino acid
Threonine	$C_4H_9NO_3$	91.73 ± 0.05	Amino acid
Valine	$C_5H_{11}NO_2$	3.13 ± 0.01	Amino acid

Table 2. Antimicrobial Compounds detected in culture supernatant of dual *Lactobacillus plantarum* and *Bacillus subtilis* fermentation in prawn shell waste and 20% glucose in deionized water.

Metabolite	Molecular Formula	Quantity (mg/L)	Biological Characteristic
Acetamide	C_2H_5NO	2999.12 ± 4.06	Antimicrobial [40]
Acethydrazide	$C_2H_6N_2O$	366.71 ± 0.01	Antimicrobial [41]
Acetic acid	$C_2H_4O_2$	71.94 ± 0.17	Antimicrobial [42]
Acridinedione	$C_{13}H_7NO_2$	4.31 ± 0.01	Antimicrobial [43]
Acrylic acid	$C_3H_4O_2$	0.72 ± 0.01	Antimicrobial [44]
Allonic acid	$C_6H_{12}O_7$	18.89 ± 0.08	Anti-tumor
4-Aminobenzoic acid	$C_7H_7NO_2$	7.00 ± 0.01	Antimicrobial [45]
2-Aminothiadiazole	$C_3H_4N_2S$	20.98 ± 0.01	Antimicrobial [46]
Arachidonic acid	$C_{20}H_{32}O_2$	5.92 ± 0.01	Antimicrobial [47]
Azelaic acid	$C_9H_{16}O_4$	0.50 ± 0.01	Antimicrobial [48]
Benzamide	C_7H_7NO	11.18 ± 0.12	Antimicrobial [49]
1,2-Benzenediol	$C_6H_6O_2$	1.31 ± 0.01	Antimicrobial [50]
Benzeneacetic acid	$C_8H_8O_2$	9.04 ± 0.01	Antimicrobial [51]
Benzenepropanoic acid	$C_9H_{10}O_2$	0.84 ± 0.01	Antimicrobial [52]
Benzenesulfonamide	$C_6H_7NO_2S$	167.36 ± 1.56	Antimicrobial [53]
Benzenethiol	C_6H_6S	1.47 ± 0.01	Antimicrobial [54]

Table 2. *Cont.*

Metabolite	Molecular Formula	Quantity (mg/L)	Biological Characteristic
1,2-Benzisothiazole	C_7H_5NS	56.13 ± 0.59	Antimicrobial [55]
Benzisothiazolinone	C_7H_5NOS	23.64 ± 0.01	Antimicrobial [56]
1,2-Benzisoxazole	C_7H_5NO	1.75 ± 0.01	Antimicrobial [57]
Benzoate	$C_7H_5O_2^-$	24.82 ± 0.01	Antimicrobial [58]
1,3-Benzodioxole	$C_7H_6O_2$	6.97 ± 0.01	Antimicrobial [59]
Benzoic acid	$C_7H_6O_2$	27.37 ± 0.38	Antimicrobial [60]
1,4-Benzoquinone	$C_6H_4O_2$	28.12 ± 0.37	Antimicrobial [61]
Benzoxazole	C_7H_5NO	1.26 ± 0.01	Antimicrobial [62]
1-Benzylindole	$C_{15}H_{13}N$	7.92 ± 0.04	Antimicrobial [63]
Butanol	$C_4H_{10}O$	1.81 ± 0.01	Antimicrobial [64]
Butyric acid	$C_4H_8O_2$	153.36 ± 0.26	Antimicrobial [65]
Carbamate	CH_2NO^{2-}	0.92 ± 0.01	Antimicrobial [66]
Carbamic acid	CH_3NO_2	1432.07 ± 4.62	Antimicrobial [67]
Cephaloridine	$C_{19}H_{17}N_3O_4S_2$	6.53 ± 0.01	Antibiotic
Colchicine	$C_{22}H_{25}NO_6$	15.06 ± 0.01	Anti-inflammatory
Decanoic acid	$C_{10}H_{20}O_2$	70.50 ± 0.01	Antimicrobial [68]
Dihydroisosteviol	$C_{20}H_{32}O_3$	5.44 ± 0.01	Antimicrobial [69]
Docosahexaenoic acid	$C_{22}H_{32}O_2$	5.79 ± 0.01	Antimicrobial [70]
Docosanol	$C_{22}H_{46}O$	6.41 ± 0.01	Antimicrobial [71]
Dodecanamide	$C_{12}H_{25}NO$	5.28 ± 0.01	Antimicrobial [72]
Ethanol	C_2H_6O	31.01 ± 0.30	Antimicrobial [73]
Ethyl acetate	$C_4H_8O_2$	44.86 ± 0.48	Antimicrobial [74]
Galacturonic acid	$C_6H_{10}O_7$	5.03 ± 0.05	Antimicrobial [75]
D-gluco-hexodialdodifuranoside	$C_{14}H_{30}O_6$	3.52 ± 0.01	Anticancer
Gluconic acid	$C_6H_{12}O_7$	307.05 ± 0.60	Antimicrobial [76]
Glycerol	$C_3H_8O_3$	336.23 ± 1.94	Antimicrobial [77]
Glyoxylic acid	$C_2H_2O_3$	4.68 ± 0.01	Antimicrobial [78]
Griseoviridin	$C_{22}H_{27}N_3O_7S$	3.14 ± 0.01	Antibiotic
Guaiacol	$C_7H_8O_2$	8.43 ± 0.01	Antimicrobial [79]
Hexadecanoic acid	$C_{16}H_{32}O_2$	147.85 ± 1.49	Antimicrobial [80]
2,4-Hexadienoic acid	$C_6H_8O_2$	0.87 ± 0.01	Antimicrobial [81]
Hexanedioic acid	$C_6H_{10}O_4$	200.31 ± 0.01	Antimicrobial [82]
Hexanoic acid	$C_6H_{12}O_2$	20.24 ± 0.01	Antimicrobial [83]
2-Hydroxybenzaldehyde	$C_7H_6O_2$	940.97 ± 1.64	Antimicrobial [84]
3-Hydroxybutyric acid	$C_4H_8O_3$	18.19 ± 0.24	Antimicrobial [85]
4-Hydroxydiphenylamine	$C_{12}H_{11}NO$	1.77 ± 0.01	Antimicrobial [86]
2-Hydroxyisocaproic acid	$C_6H_{12}O_3$	173.95 ± 2.09	Antimicrobial [87]
3-(4-Hydroxyphenyl)propionic acid	$C_9H_{10}O_3$	1.71 ± 0.01	Anti-inflammatory
Indole	C_8H_7N	22.32 ± 0.27	Antimicrobial [88]
Indole-3-carboxylic acid	$C_9H_7NO_2$	8.27 ± 0.01	Antimicrobial [89]
Isocitric acid	$C_6H_8O_7$	1.30 ± 0.01	Antimicrobial [90]
3-Isoxazolidinone	$C_3H_5NO_2$	3.31 ± 0.01	Antimicrobial [91]
Kaurene	$C_{20}H_{32}$	58.27 ± 0.10	Antimicrobial [92]
2-Keto-D-glucose	$C_6H_{10}O_6$	2.11 ± 0.01	Antibiotic
Lactic acid	$C_3H_6O_3$	1055.38 ± 7.90	Antimicrobial [93]
Linolenic acid	$C_{18}H_{30}O_2$	8.00 ± 0.01	Antimicrobial [94]
Lycopodine	$C_{16}H_{25}NO$	4.13 ± 0.01	Antimicrobial [95]
Malic acid	$C_4H_6O_5$	21.02 ± 0.29	Antimicrobial [96]
Mandelic acid	$C_8H_8O_3$	443.50 ± 6.14	Antimicrobial [97]
Meldrum's acid	$C_6H_8O_4$	1.49 ± 0.01	Antimicrobial [98]
Methanol	CH_4O	10.15 ± 0.01	Antimicrobial [99]
Methylenecyclopropane	C_4H_6	0.18 ± 0.01	Antiviral [100]
Nonadecanoic acid	$C_{19}H_{38}O_2$	2.48 ± 0.01	Anticancer [101]
Nonanoic acid	$C_9H_{18}O_2$	16.07 ± 0.01	Antimicrobial [102]
Octadecanoic acid	$C_{18}H_{36}O_2$	147.83 ± 1.66	Antimicrobial [103]

Table 2. *Cont.*

Metabolite	Molecular Formula	Quantity (mg/L)	Biological Characteristic
Octanoic acid	$C_8H_{16}O_2$	1.38 ± 0.01	Antimicrobial [104]
Octenidine	$C_{36}H_{62}N_4$	1.03 ± 0.01	Antimicrobial [105]
Pentanedioic acid	$C_5H_8O_4$	50.59 ± 0.64	Antimicrobial [106]
Phenanthroline	$C_{12}H_8N_2$	49.88 ± 0.39	Antimicrobial [107]
3-Phenyl-5-isoxazolone	$C_9H_7NO_2$	2.14 ± 0.01	Antimicrobial [108]
Phosphoric acid	H_3PO_4	0.68 ± 0.01	Antimicrobial [109]
Propanamide	C_3H_7NO	6.08 ± 0.01	Antimicrobial [110]
Propanenitrile	C_3H_5N	8.05 ± 0.01	Antimicrobial [111]
Propanoic acid	$C_3H_6O_2$	1184.32 ± 9.56	Antimicrobial [112]
Propionamide	C_3H_7NO	10.84 ± 0.01	Antimicrobial [113]
Pteridine	$C_6H_4N_4$	3.82 ± 0.03	Antimicrobial [114]
Pyranone	$C_5H_4O_2$	7.89 ± 0.07	Antimicrobial [115]
Pyrazine	$C_4H_4N_2$	33.19 ± 0.01	Antimicrobial [116]
Pyridazine	$C_4H_4N_2$	3.29 ± 0.01	Antimicrobial [117]
Pyrrole	C_4H_5N	3.04 ± 0.02	Antimicrobial [118]
Pyrrolopyrimidine	$C_6H_5N_3$	3.33 ± 0.01	Antiviral [119]
Pyruvic acid	$C_3H_4O_3$	56.20 ± 0.02	Antimicrobial [120]
Quinazoline	$C_8H_6N_2$	66.92 ± 0.01	Antimicrobial [121]
Quinoline	C_9H_7N	1.87 ± 0.01	Antimicrobial [122]
2-Quinolinone	C_9H_7NO	284.36 ± 0.01	Antimicrobial [123]
Sedoheptulose	$C_7H_{14}O_7$	64.36 ± 0.01	Antimicrobial [124]
Sesamol	$C_7H_6O_3$	9.33 ± 0.07	Antimicrobial [125]
Tartaric acid	$C_4H_6O_6$	7.94 ± 0.01	Antimicrobial [126]
Thiophene	C_4H_4S	0.93 ± 0.01	Antimicrobial [127]
Thiourea	CH_4N_2S	2.16 ± 0.01	Antimicrobial [128]
Thymol	$C_{10}H_{14}O$	68.98 ± 0.01	Antimicrobial [129]
1,2,4-Triazole-3-carboxylic acid	$C_3H_3N_3O_2$	56.93 ± 0.01	Antimicrobial [130]
Undecanoic acid	$C_{11}H_{22}O_2$	2.09 ± 0.01	Antimicrobial [131]
Urea	CH_4N_2O	0.65 ± 0.01	Antimicrobial [132]
Uridine	$C_9H_{12}N_2O_6$	1277.01 ± 3.34	Antimicrobial [133]

Table 3. Other organic compounds detected in culture supernatant of dual *Lactobacillus plantarum* and *Bacillus subtilis* fermentation in prawn shell waste and 20% glucose in deionized water.

Metabolite	Molecular Formula	Quantity (mg/L)	Biological Characteristic
Altronic acid	$C_6H_{12}O_7$	0.22 ± 0.01	Organic acid
Amphetamine	$C_9H_{13}N$	1.35 ± 0.01	Stimulant
Aromadendrene	$C_{15}H_{24}$	4.54 ± 0.01	Essential oil
Benzene	C_6H_6	16.07 ± 0.01	Aromatic
Benzocyclobutene	C_8H_8	7.98 ± 0.01	Aromatic
Benzonitrile	C_7H_5N	91.31 ± 0.01	Aromatic
Butanal	C_4H_8O	29.38 ± 0.19	Aldehyde
Butane	C_4H_{10}	543.18 ± 5.86	Alkane
Butanedioic acid	$C_4H_6O_4$	31.11 ± 0.03	Organic acid
Butanediol	$C_4H_{10}O_2$	139.50 ± 0.03	Alcohol
1,2,2,3,4-Butanepentacarbonitrile	$C_9H_5N_5$	0.55 ± 0.01	Aromatic
Butanoic acid	$C_4H_8O_2$	4399.87 ± 6.20	Organic acid
1-Butene	C_4H_8	379.99 ± 5.33	Alkene
1,4-Butenediol	$C_4H_8O_2$	46.28 ± 0.01	Alcohol
2-Butenoic acid	$C_4H_6O_2$	52.41 ± 0.11	Organic acid
3-Buten-1-ol	C_4H_8O	2.31 ± 0.01	Alcohol

Table 3. *Cont.*

Metabolite	Molecular Formula	Quantity (mg/L)	Biological Characteristic
Butylamine	$C_4H_{11}N$	84.67 ± 0.01	Amine
Butyne	C_4H_6	7.46 ± 0.01	Alkyne
Butynol	$C_4H_{10}O$	0.43 ± 0.01	Alcohol
Butyrate	$C_4H_7O^{2-}$	0.72 ± 0.01	Flavoring
Camphoric acid	$C_{10}H_{16}O_4$	0.81 ± 0.01	Organic acid
Carbophenoxon sulfone	$C_{11}H_{16}ClO_5PS_2$	11.46 ± 0.01	Organosulfone
Cholestane	$C_{27}H_{48}$	3.63 ± 0.01	Cholesterol
1-Cholestene	$C_{27}H_{46}$	31.64 ± 0.01	Cholesterol
Cholestenone	$C_{27}H_{44}O$	7.61 ± 0.09	Cholesterol
Cholesterol	$C_{27}H_{46}O$	75.80 ± 0.66	Cholesterol
Chromium	Cr	2.53 ± 0.01	Mineral
Cortisone	$C_{21}H_{28}O_5$	2.09 ± 0.01	Steroid
Cyclobutanemethanol	$C_5H_{10}O$	25.00 ± 0.01	Aromatic
Cyclohexane	C_6H_{12}	4.64 ± 0.03	Aromatic
Cyclohexene	C_6H_{10}	1.31 ± 0.01	Aromatic
3-Cyclohexene-1-methanol	$C_7H_{12}O$	2.78 ± 0.01	Essential oil
1-Cyclohexyl-tetradecane	$C_{20}H_{40}$	5.00 ± 0.01	Aromatic
Cyclopenta[de]naphthalene	$C_{12}H_8$	8.26 ± 0.01	Aromatic
Cyclopentane	C_5H_{10}	4.84 ± 0.01	Aromatic
1,2,4-Cyclopentanetrione	$C_5H_4O_3$	7.93 ± 0.01	Aromatic
Cyclopentene	C_5H_8	0.61 ± 0.01	Aromatic
Cyclopropanecarboxylic acid	$C_4H_6O_2$	3.04 ± 0.01	Organic acid
Decane	$C_{10}H_{22}$	1.98 ± 0.01	Alkane
1-Decanol	$C_{10}H_{22}O$	1.75 ± 0.01	Fatty alcohol
2,6-Diamino-4-hexynoic acid	$C_6H_{10}N_2O_2$	2.10 ± 0.01	Organic acid
1,3-Diazepane-2,4,6-trione	$C_5H_6N_2O_3$	1.09 ± 0.01	Aromatic
3-Dibenzofuranamine	$C_{12}H_9NO$	19.35 ± 0.18	Aromatic
Diethylene glycol	$C_4H_{10}O_3$	67.89 ± 0.68	Solvent
2,3-Dihydroxybutanoic acid	$C_4H_8O_4$	13.75 ± 0.07	Organic acid
1,1-Diisobutoxybutane	$C_{12}H_{26}O_2$	1.72 ± 0.01	Aldehyde
Diisopropyl malonate	$C_9H_{16}O_4$	1.30 ± 0.01	Acid ester
Dimethylbutanedioate	$C_6H_{10}O_4$	0.77 ± 0.01	Flavoring
2,3-Dimethylbutanoic acid	$C_6H_{12}O_2$	2129.98 ± 3.01	Fatty acid
3,3-Dimethyl-1-butanol	$C_6H_{14}O$	18.60 ± 0.01	Alcohol
Dimethylcyclohexanone	$C_8H_{14}O$	89.00 ± 0.01	Aromatic
Dimethyldecahydronaphthalene	$C_{12}H_{22}$	56.95 ± 0.01	Aromatic
Dimethyl malonate	$C_5H_8O_4$	8.30 ± 0.01	Acid ester
Dipropylacetic acid	$C_8H_{16}O_2$	120.83 ± 0.01	Organic acid
13,16-Docasadienoic acid	$C_{22}H_{40}O_2$	51.71 ± 0.35	Fatty acid
Docosanoic acid	$C_{22}H_{44}O_2$	2.40 ± 0.01	Fatty acid
13-Docosenamide	$C_{22}H_{43}NO$	64.20 ± 0.78	Fatty amide
Dodecane	$C_{12}H_{26}$	1462.61 ± 0.01	Alkane
Dodecanedioic acid	$C_{12}H_{22}O_4$	4.84 ± 0.01	Organic acid
5,8,11-Eicosatriynoic acid	$C_{20}H_{28}O_2$	0.97 ± 0.01	Fatty acid
Estratetraenol	$C_{18}H_{22}O$	15.35 ± 0.01	Steroid
Ethane	C_2H_6	37.25 ± 0.01	Alkane
Ethanedioic acid	$C_2H_2O_4$	16.61 ± 0.19	Organic acid
Ethanesulfonic acid	$C_2H_6O_3S$	3.13 ± 0.02	Sulfonic acid
Ethanimidic acid	C_4H_9NO	0.63 ± 0.01	Organic acid
Ethyl butyrate	$C_6H_{12}O_2$	7.25 ± 0.02	Flavoring
Ethylene	C_2H_4	1.99 ± 0.01	Alkene
Ethylene glycol	$C_2H_6O_2$	141.94 ± 0.01	Solvent
3-Furanacetaldehyde	$C_6H_6O_2$	0.75 ± 0.01	Aldehyde

Table 3. *Cont.*

Metabolite	Molecular Formula	Quantity (mg/L)	Biological Characteristic
2-Furancarboxylic acid	$C_5H_4O_3$	1.98 ± 0.01	Organic acid
2-Furanone	$C_4H_4O_2$	3.41 ± 0.02	Flavoring
Glucuronolactone	$C_6H_8O_6$	3.95 ± 0.04	Lactone
Glyceraldehyde acetonide	$C_6H_{10}O_3$	247.79 ± 0.01	Carboxaldehyde
L-gulono-1,4-lactone	$C_6H_{10}O_6$	21.25 ± 0.23	Lactone
Heptadecane	$C_{17}H_{36}$	7.06 ± 0.01	Alkane
Heptadecane-1,2-diol	$C_{17}H_{36}O_2$	54.71 ± 0.01	Fatty alcohol
3-Heptyn-1-ol	$C_7H_{12}O$	10.73 ± 0.01	Fatty alcohol
Heptanamide	$C_7H_{15}NO$	14.97 ± 0.01	Fatty amide
Hexadecanamide	$C_{16}H_{33}NO$	5.81 ± 0.01	Fatty amide
Hexadecane	$C_{16}H_{34}$	97.90 ± 0.01	Alkane
1-Hexene	C_6H_{12}	10.50 ± 0.01	Alkene
3-Hexenedioic acid	$C_6H_8O_4$	11.76 ± 0.01	Fatty acid
3-Hexen-1-ol	$C_6H_{12}O$	3.00 ± 0.01	Fatty alcohol
4-Hexen-1-yne	C_6H_8	2.27 ± 0.01	Alkyne
3-Hydroxy-2-butanone	$C_4H_8O_2$	72.50 ± 0.01	Methyl ketone
2-Hydroxyglutaric acid	$C_5H_8O_5$	2.30 ± 0.01	Organic acid
3-Hydroxypyruvic acid	$C_3H_4O_4$	1.32 ± 0.01	Organic acid
3-Hydroxysebacic acid	$C_{10}H_{18}O_5$	4.09 ± 0.03	Organic acid
Inabenfide	$C_{19}H_{15}ClN_2O_2$	3.19 ± 0.01	Herbicide
Iron	Fe	3.25 ± 0.01	Mineral
2-Ketobutyric acid	$C_4H_6O_3$	222.57 ± 0.02	Organic acid
2-Ketohexanoic acid	$C_6H_{10}O_3$	1.03 ± 0.01	Fatty acid
Ketovaleric acid	$C_5H_8O_3$	17.59 ± 0.01	Ketoacid
Malonic acid	$C_3H_4O_4$	0.25 ± 0.01	Organic acid
Methanaminium	CH_6N	5.93 ± 0.05	Conjugate acid
Methyl butyrate	$C_5H_{10}O_2$	9.83 ± 0.01	Flavoring
Methylcyclopentadiene	C_6H_8	465.49 ± 0.01	Aromatic
6-Methyl-3,5-heptadien-2-one	$C_8H_{12}O$	106.73 ± 0.48	Flavoring
Methyl phenyl sulfoxide	C_7H_8OS	2.38 ± 0.01	Aromatic
2-Methylpropanoic acid	$C_4H_8O_2$	8.21 ± 0.01	Organic acid
2-Methylpropene	C_4H_8	69.91 ± 0.31	Alkene
2-Methyl-4-propyl-1,3-oxathiane	$C_8H_{16}OS$	53.44 ± 0.01	Flavoring
Methyl tetradecanoate	$C_{15}H_{30}O_2$	3.53 ± 0.01	Flavoring
4-Methyl-5-thiazoleethanol	C_6H_9NOS	120.92 ± 0.01	Flavoring
Methyl valerate	$C_6H_{12}O_2$	445.57 ± 0.01	Flavoring
3-Methylvaleric acid	$C_6H_{12}O_2$	5.55 ± 0.01	Fatty acid
Monoethyl malonic acid	$C_5H_8O_4$	13.41 ± 0.16	Organic acid
Monostearin	$C_{21}H_{42}O_4$	35.76 ± 0.31	Emulsifier
Morphine	$C_{17}H_{19}NO_3$	7.05 ± 0.01	Painkiller
N-acetyl-glucosamine	$C_8H_{15}NO_6$	24.93 ± 0.33	Chitosan
Nickel	Ni	6.56 ± 0.01	Mineral
Nonane	C_9H_{20}	2.28 ± 0.01	Alkane
5-Norbornene-2-carboxylic acid	$C_8H_{10}O_2$	0.93 ± 0.01	Organic acid
Octadecanamide	$C_{18}H_{37}NO$	47.22 ± 0.01	Fatty amide
Octadecane	$C_{18}H_{38}$	137.50 ± 0.01	Alkane
Octadecenamide	$C_{18}H_{35}NO$	67.10 ± 0.77	Fatty amide
17-Octadecynoic acid	$C_{18}H_{32}O_2$	18.04 ± 0.01	Fatty acid
Octahydronaphthalene	$C_{10}H_{16}$	3.48 ± 0.01	Aromatic
Octahydronaphthalene-1,4-diol	$C_{10}H_{16}O_2$	57.23 ± 0.01	Alcohol
γ-Octalactone	$C_8H_{14}O_2$	238.91 ± 0.37	Flavoring

Table 3. *Cont.*

Metabolite	Molecular Formula	Quantity (mg/L)	Biological Characteristic
Octane	C_8H_{18}	25.30 ± 0.01	Alkane
1-Octene	C_8H_{16}	10.56 ± 0.01	Alkene
Oleic acid	$C_{18}H_{34}O_2$	17.59 ± 0.01	Fatty acid
3-Oxooctanoic acid	$C_8H_{14}O_3$	1185.00 ± 0.01	Fatty acid
2-Oxovaleric acid	$C_5H_8O_3$	4.12 ± 0.01	Ketoacid
Para-methoxy-*N*-methylamphetamine	$C_{11}H_{17}NO$	145.28 ± 0.01	Stimulant
Pentadecanoic acid	$C_{15}H_{30}O_2$	11.42 ± 0.01	Fatty acid
Pentaethylene glycol	$C_{22}H_{46}O_6$	6.10 ± 0.01	Solvent
Pentadecane	$C_{15}H_{32}$	2.32 ± 0.01	Alkane
Pentanamide	$C_5H_{11}NO$	1.41 ± 0.01	Acid amide
Pentane	C_5H_{12}	7.22 ± 0.09	Alkane
Pentanoic acid	$C_5H_{10}O_2$	26.12 ± 0.20	Flavoring
Pentaoxacyclopentadecane	$C_{10}H_{20}O_5$	1.60 ± 0.01	Crown ether
Pentenedioate	$C_5H_6O_4^{2-}$	2.88 ± 0.01	Organic acid
Pentenedioic acid	$C_5H_6O_4$	7.41 ± 0.07	Organic acid
2-Pentenoic acid	$C_5H_8O_2$	70.15 ± 0.95	Organic acid
9-O-pivaloyl-*N*-acetylcolchinol	$C_{25}H_{31}NO_6$	24.44 ± 0.17	Aromatic
Pregnenolone	$C_{21}H_{32}O_2$	3.80 ± 0.01	Steroid
Propanal	C_3H_6O	2.77 ± 0.02	Aldehyde
Propane	C_3H_8	6.39 ± 0.02	Alkane
Propanedioic acid	$C_3H_4O_4$	10.46 ± 0.01	Organic acid
1,3-Propanediol	$C_3H_8O_2$	3.03 ± 0.01	Alcohol
1,2,3-Propanetriol	$C_3H_8O_3$	1595.72 ± 0.02	Polyol
Propanone	C_3H_6O	114.26 ± 1.34	Ketone
2-Propenamide	C_3H_5NO	338.39 ± 4.16	Fatty amide
2-Propenoic acid	$C_3H_4O_2$	15.90 ± 0.01	Organic acid
Propylamine	C_3H_9N	3.25 ± 0.01	Fatty amine
Propylene glycol	$C_3H_8O_2$	2458.09 ± 1.26	Solvent
Pseudoephedrine	$C_{10}H_{15}NO$	24.34 ± 0.01	Decongestant
Pseudouridine	$C_9H_{12}N_2O_6$	2.99 ± 0.01	Nucleoside
Pyrandiol	$C_5H_6O_3$	40.72 ± 0.01	Alcohol
Pyruvate oxime	$C_3H_5NO_3$	14.13 ± 0.09	Acid amine
Scopolin	$C_{16}H_{18}O_9$	179.76 ± 2.08	Phytochemical
Sebacic acid	$C_{10}H_{18}O_4$	3.53 ± 0.01	Fatty acid
Succinate	$C_4H_4O_4^{2-}$	0.78 ± 0.01	Flavoring
Succinonitrile	$C_4H_4N_2$	0.16 ± 0.01	Nitrile
Talonic acid	$C_6H_{12}O_7$	5.55 ± 0.01	Organic acid
Tetradecane	$C_{14}H_{30}$	14.12 ± 0.01	Alkane
Tetradecanoic acid	$C_{14}H_{28}O_2$	7.86 ± 0.03	Fatty acid
1-Tetradecanol	$C_{14}H_{30}O$	1.24 ± 0.01	Fatty alcohol
Tetraethylene glycol	$C_8H_{18}O_5$	0.53 ± 0.01	Solvent
1,2,4,5-Tetramethylbenzene	$C_{10}H_{14}$	650.91 ± 0.01	Aromatic
Thiodiglycol	$C_4H_{10}O_2S$	12.39 ± 0.14	Alcohol
Tricyclodecenyl propionate	$C_{13}H_{18}O_2$	2.31 ± 0.01	Fragrance
Tridecane	$C_{13}H_{28}$	207.98 ± 0.01	Alkane
Tridecanoic acid	$C_{13}H_{26}O_2$	15.33 ± 0.01	Fatty acid
Triethylene glycol	$C_6H_{14}O_4$	120.91 ± 0.04	Solvent
2,3,4-Trihydroxybutanoic acid	$C_4H_8O_5$	41.02 ± 0.31	Organic acid
2,4,5-Trihydroxypentanoic acid	$C_5H_{10}O_5$	18.61 ± 0.01	Organic acid
1,2,4-Trimethylbenzene	C_9H_{12}	16.28 ± 0.01	Aromatic
1-Undecene	$C_{11}H_{22}$	7.66 ± 0.03	Alkene
Vitamin C	$C_6H_8O_6$	9.22 ± 0.01	Ascorbic acid

Table 4. Sugar derivatives detected in culture supernatant of dual *Lactobacillus plantarum* and *Bacillus subtilis* fermentation in prawn shell waste and 20% glucose in deionized water.

Metabolite	Molecular Formula	Quantity (mg/L)	Biological Characteristic
Altro-heptulose	$C_7H_{14}O_7$	6.79 ± 0.01	Sugar substitute
Arabinitol	$C_5H_{15}O_5$	115.06 ± 0.03	Sugar alcohol
Arabinofuranose	$C_5H_{10}O_5$	1714.08 ± 2.23	Sugar substitute
Arabinofuranoside	$C_5H_9O_5$	592.25 ± 0.06	Sugar substitute
D-arabino-3-hexulose	$C_6H_{12}O_6$	17.21 ± 0.01	Sugar substitute
Arabinonic acid	$C_5H_{10}O_6$	81.43 ± 1.14	Sugar acid
Arabinopyranose	$C_5H_{10}O_5$	2350.31 ± 1.98	Sugar substitute
Arabinose	$C_5H_{10}O_5$	912.65 ± 2.11	Sugar substitute
Arabitol	$C_5H_{10}O_5$	1456.58 ± 0.56	Sugar alcohol
3-Deoxy-D-arabino-hexonic acid	$C_6H_{12}O_6$	112.61 ± 0.11	Sugar acid
2-Deoxy-erythro-pentofuranose	$C_5H_{10}O_4$	596.47 ± 8.29	Sugar substitute
3-Deoxy-erythro-pentonic acid	$C_5H_{10}O_5$	43.20 ± 0.03	Sugar acid
2-Deoxy-erythro-pentopyranose	$C_5H_{10}O_4$	2.50 ± 0.01	Sugar substitute
2-Deoxy-erythro-pentose	$C_5H_{10}O_4$	42.49 ± 0.36	Sugar substitute
2-Deoxy-D-galactopyranose	$C_6H_{12}O_5$	281.36 ± 2.07	Sugar substitute
2-Deoxy-D-glucose	$C_6H_{12}O_5$	677.13 ± 0.01	Sugar substitute
Deoxy-ribose	$C_5H_{10}O_4$	19.08 ± 0.01	Sugar substitute
3-Deoxy-D-ribohexonic acid	$C_6H_{12}O$	20.71 ± 0.01	Sugar acid
Dihydroxyacetone	$C_3H_6O_3$	21.99 ± 0.01	Sugar substitute
Dulcitol	$C_6H_{14}O_6$	3323.48 ± 4.53	Sugar alcohol
Erythritol	$C_4H_{10}O_4$	0.26 ± 0.01	Sugar alcohol
Erythro-pentitol	$C_5H_{12}O$	29.50 ± 0.03	Sugar alcohol
Erythrose	$C_4H_8O_4$	522.45 ± 5.06	Sugar substitute
Erythro-tetrofuranose	$C_5H_{10}O_5$	22.65 ± 0.01	Sugar substitute
Fructopyranose	$C_6H_{12}O_6$	6.94 ± 0.01	Sugar substitute
Fructose	$C_6H_{12}O_6$	2462.43 ± 1.42	Sugar substitute
Fructose oxime	$C_6H_{13}NO_6$	2421.99 ± 0.01	Sugar substitute
Galactofuranose	$C_6H_{12}O_6$	1076.99 ± 0.78	Sugar substitute
Galactoheptulose	$C_7H_{14}O_7$	2.20 ± 0.01	Sugar substitute
Galactopyranose	$C_6H_{12}O_6$	943.28 ± 2.36	Sugar substitute
Galactose	$C_6H_{12}O_6$	8909.55 ± 1.18	Sugar substitute
Galactose oxime	$C_6H_{13}NO_6$	369.21 ± 0.39	Sugar substitute
Glucaric acid	$C_6H_{10}O_8$	0.08 ± 0.01	Sugar acid
Glucitol	$C_6H_{14}O_6$	601.89 ± 7.85	Sugar alcohol
Glucofuranose	$C_6H_{12}O_6$	2035.95 ± 1.10	Sugar substitute
Glucopyranose	$C_6H_{12}O_6$	7024.77 ± 8.40	Sugar substitute
Glucopyranuronic acid	$C_6H_{10}O_7$	1239.42 ± 0.13	Sugar acid
Glucose	$C_6H_{12}O_6$	2010.62 ± 1.31	Sugar substitute
Glucose oxime	$C_6H_{13}NO_6$	610.91 ± 0.23	Sugar substitute
Glucuronic acid	$C_6H_{10}O_7$	7.58 ± 0.07	Sugar acid
Glutaconic acid	$C_5H_6O_4$	0.77 ± 0.01	Sugar acid
Glyceraldehyde	$C_3H_6O_3$	422.51 ± 1.30	Sugar substitute
D-glycero-D-galacto-heptose	$C_7H_{14}O_7$	91.04 ± 0.01	Sugar substitute
D-glycero-D-gluco-heptose	$C_7H_{14}O_7$	129.78 ± 1.66	Sugar substitute
D-glycero-D-gulo-heptonic acid	$C_7H_{14}O_8$	40.26 ± 0.14	Sugar acid
D-glycero-L-manno-heptonic acid	$C_7H_{14}O_8$	1192.77 ± 2.99	Sugar acid
Gulonic acid	$C_6H_{12}O_7$	14.17 ± 0.10	Sugar acid
Gulose	$C_6H_{12}O_6$	361.01 ± 2.59	Sugar substitute
Lactose	$C_{12}H_{22}O_{11}$	125.72 ± 0.01	Sugar substitute
Levoglucosan	$C_6H_{10}O_5$	1.32 ± 0.01	Sugar substitute
Lyxopyranose	$C_5H_{10}O_5$	1654.75 ± 1.82	Sugar substitute

Table 4. *Cont.*

Metabolite	Molecular Formula	Quantity (mg/L)	Biological Characteristic
Lyxose	$C_5H_{10}O_5$	603.81 ± 2.35	Sugar substitute
Maltose	$C_{12}H_{22}O_{11}$	5653.05 ± 5.87	Sugar substitute
Mannitol	$C_6H_{14}O_6$	177.42 ± 0.80	Sugar alcohol
Mannofuranose	$C_6H_{12}O_6$	1009.76 ± 5.57	Sugar substitute
Mannofuranuronic acid	$C_6H_8O_6$	51.35 ± 0.01	Sugar acid
Mannonic acid	$C_6H_{12}O_7$	2567.14 ± 1.67	Sugar acid
Mannopyranose	$C_6H_{12}O$	358.11 ± 0.21	Sugar substitute
Mannose	$C_6H_{12}O_6$	5744.85 ± 7.73	Sugar substitute
Melibiose	$C_{12}H_{22}O_{11}$	0.69 ± 0.01	Sugar substitute
2,5-Methylene-D,L-rhamnitol	$C_7H_{14}O_5$	1.33 ± 0.01	Sugar substitute
Methyl-D-galactofuranoside	$C_7H_{14}O_6$	481.33 ± 1.13	Sugar substitute
Methyl-D-glucopyranoside	$C_7H_{14}O_6$	4908.57 ± 6.54	Sugar substitute
Methyl-D-lyxofuranoside	$C_6H_{12}O_5$	499.24 ± 4.75	Sugar substitute
Methyl-D-mannopyranoside	$C_7H_{14}O_6$	131.27 ± 0.01	Sugar substitute
Methyl-D-ribofuranoside	$C_6H_{12}O$	120.28 ± 0.01	Sugar substitute
Methyl-D-xylopyranoside	$C_6H_{12}O_5$	1.23 ± 0.01	Sugar substitute
Myo-inositol	$C_6H_{12}O_6$	130.33 ± 0.50	Sugar substitute
Pentitol	$C_5H_{12}O_5$	185.84 ± 0.01	Sugar Alcohol
Phenyl-D-galactopyranoside	$C_{12}H_{16}O_6$	9584.87 ± 0.01	Sugar substitute
D-ribo-2-hexulose	$C_6H_{12}O_6$	5.77 ± 0.03	Sugar substitute
Ribonic acid	$C_5H_{10}O_6$	89.50 ± 0.70	Sugar acid
Ribopyranose	$C_5H_{10}O_5$	1427.89 ± 7.29	Sugar substitute
Ribose	$C_5H_{10}O_5$	249.45 ± 3.50	Sugar substitute
Sorbopyranose	$C_6H_{12}O_6$	39.12 ± 0.11	Sugar substitute
Talose	$C_6H_{12}O_6$	800.65 ± 2.15	Sugar substitute
Threitol	$C_4H_{10}O_4$	121.12 ± 1.66	Sugar alcohol
Threonic acid	$C_4H_8O_5$	30.15 ± 0.01	Sugar acid
Turanose	$C_{12}H_{22}O_{11}$	66.04 ± 0.40	Sugar substitute
Xylitol	$C_5H_{12}O_5$	508.27 ± 0.44	Sugar alcohol
Xylofuranose	$C_5H_{10}O_5$	88.69 ± 0.01	Sugar substitute
D-xylo-hexulose	$C_6H_{12}O_6$	2.66 ± 0.02	Sugar substitute
Xylonic acid	$C_5H_{10}O_6$	156.31 ± 1.43	Sugar acid
Xylofuranose	$C_5H_{10}O_5$	88.69 ± 0.01	Sugar substitute
Xylopyranose	$C_5H_{10}O_5$	915.86 ± 0.30	Sugar substitute
Xylose	$C_5H_{10}O_5$	1417.45 ± 1.36	Sugar substitute
Xylulose	$C_5H_{10}O_5$	7.30 ± 0.01	Sugar substitute

3.2. Chitin Yield and Purity Calculations

From 5.0 g of prawn shell waste, 20 g of glucose, and 100 g of deionized water, the dry weight of crude extracted chitin was found to be 0.50 ± 0.01 g, translating to an overall fermentation yield of 0.50/125.0 × 100% = 0.4%.

Lowry's test was performed on 1 mL of supernatant extracted from 50 mg chitin heated in 10 mL NaOH and its absorbance was found to be 0.213, corresponding to 20 μg of protein when compared against the protein calibration curve (Figure 1). This translates to a residual protein of 200 μg per 50 mg chitin, which is a residual protein content of 200/50,000 × 100% = 0.4%.

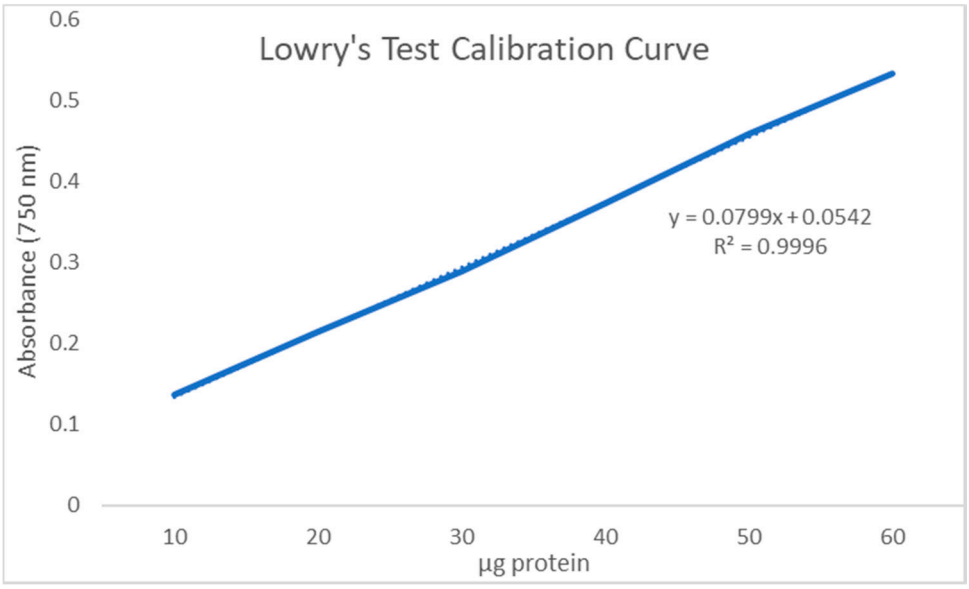

Figure 1. Lowry's test calibration curve (absorbance vs. µg protein).

4. Discussion

Bacteria species coexist with neighboring microorganisms in a dynamic community by producing small metabolites in response to environmental changes such as biotic and abiotic stresses. These volatile organic and inorganic compounds are released during interspecies bacteria interactions due to competition and cooperation, forming soluble metabolites in the supernatant [134]. Detection and quantification of these bacteria volatile compounds have always been of great interest in the food, cosmetic, flavor, and fragrance bioprocessing industry as well as in the clinical and medical field. However, analysis of bacteria volatile compounds has remained challenging due to the wide abundance of metabolites and the complexity of the culture medium from where they are extracted.

The co-fermentation of prawn shell waste and 20% glucose by *Lactobacillus plantarum* and *Bacillus subtilis* for chitin extraction produced bacteria volatile metabolites of various chemical classes. Fatty acid derivatives such as hydrocarbons, ketones and alcohols, organic acids, as well as sulphur and nitrogen-containing compounds were detected in the culture supernatant. These metabolites were generally produced by different catabolic pathways such as glycolysis, proteolysis, and lipolysis to break down the proteins, fats, and minerals residual in the prawn shell waste [135]. Linear-chained hydrocarbons detected were most probably derived from products of the fatty acid biosynthetic pathway. Both short-chain alkanes and longer-chain hydrocarbons were found in the culture supernatant, testifying to the ability of the microbial strains to synthesize branched hydrocarbons.

Methyl ketones detected were probably produced from the decarboxylation of fatty acids [136]. For example, 3-hydroxy-2-butanone (72.50 mg/L) or acetoin detected might have been derived from pyruvate fermentation. Long-chain aliphatic alcohols such as 1-decanol (1.75 mg/L) were probably produced through the oxidation of fatty acid derivatives. Significant production of butanediol (139.50 mg/L) was detected due to the presence of glucose as the main nutrient in the growth medium. Short-chain branched alcohols such as 3,3-dimethyl-1-butanol (18.60 mg/L) detected might have been produced from the enzymatic conversion of branched chain amino acids such as leucine.

Several short-chain fatty acids were detected in the culture supernatant such as acetic acid (71.94 mg/L), propanoic acid (1184.32 mg/L), and butanoic acid (4399.87 mg/L). These saturated aliphatic organics acids most probably resulted from bacteria fermentation of carbohydrates. Glyoxylic acid (4.68 mg/L) detected could either have been produced in the tricarboxylic acid cycle or generated during amino acid metabolism, for example during the degradation of glycine (25.56 mg/L),

threonine (91.73 mg/L), and proline (91.76 mg/L). Indole (22.32 mg/L) biosynthesis, another by-product of amino acid catabolism, was also detected in the fermentation supernatant [137].

An oxidative deamination of many amino acids might have also led to the production of aldehydes, ketones, or alcohols detected. For example, the degradation of 1,4-dihydrophenyalanine (2.92 mg/L) might have served as the first step of aromatic volatile compounds synthesis, producing benzene, its carbohydrate derivatives, as well as other benzenoid volatiles. Many volatile organic compounds produced by *Lactobacillus plantarum* and *Bacillus subtilis* have been reported to display antimicrobial activity. Among these known antimicrobial metabolites, benzenoids are the most represented in quantity compared to alkanes, aldehydes, ketones, acids, and alcohols. While a huge majority of antimicrobial benzenoid volatiles have a benzene core linked to a fatty acids derivative, benzenoids are very diverse and can be linked with carbohydrate chains containing nitrogen and sulphur [138].

The antimicrobial mode of action of these bacteria volatile organic compounds might arise from their lipophilic nature, which enables them to destabilize the cell membrane integrity of antagonistic pathogens, inhibiting their growth [139]. Besides benzenoids, nitrogen-containing volatile organic compounds are another important group of antimicrobial metabolites, consisting of non-cyclic amides and amines as well as cyclic azoles, pyrazines, pyridazines, and pyrimidines. Pyrazine (33.19 mg/L), pyridazine (3.29 mg/L), and pyrrolopyrimidine (3.33 mg/L) were detected in the *Lactobacillus plantarum* and *Bacillus subtilis* co-fermentation supernatant. Pyrazine, which is the most strongly represented in antimicrobial activity among them, is either formed from the non-enzymatic animation of acyloins or derived from aminoketone intermediates produced from amino acid catabolism. This testifies to the successful breakdown of amino acids from the prawn shell waste.

Antimicrobial active metabolites may have potential use as natural preservatives to control the growth and inactivate undesired microorganisms in food [140]. For example, lactic acid (1055.39 mg/L) and acetic acid (71.94 mg/L) are produced by *Lactobacillus plantarum* in probiotics to compete for nutrients with other foodborne pathogens. Other organic acids such as propanoic acid (1184.32 mg/L) and butanoic acid (4399.87 mg/L) are also produced, which further reduce the pH of the culture medium. The production of other substances such as ethanol (31.01 mg/L), fatty acids such as 3-hydroxybutyric acid (18.19 mg/L), 3-hydroxysebacic acid (4.09 mg/L), and 3-hydroxpyruvic acid (1.32 mg/L), as well as 3-hydroxy-2-butanone (72.5 mg/L) further intensify its antimicrobial activity. The metabolomics results show that *Lactobacillus plantarum* is more heterofermentative than homofermentative as a variety of metabolites are generated from the degradation of hexoses.

5. Conclusions

Many useful metabolites are produced when *Lactobacillus plantarum* and *Bacillus subtilis* are fermented with prawn shell waste together with 20% glucose as a carbon source. Besides lactic acid, a variety of organic acids such as fatty acids and amino acids as well as several antimicrobial molecules were detected in the culture supernatant. This shows that protease-mediated protein hydrolysis of the prawn shells is successful in removing proteins, minerals, and fats from the prawn shells. While harnessing the solid fraction of the fermentation as chitin, the nutrient-rich liquid fraction may be used for probiotics applications.

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References

1. Kandra, P.; Challa, M.M.; Jyothi, H.K.P. Efficient use of shrimp waste: Present and future trends. *Appl. Microbiol. Biotechnol.* **2012**, *93*, 17–29. [CrossRef]
2. Ferrer, J.; Paez, G.; Marmol, Z.; Ramones, E.; Garcia, H.; Forster, C.F. Acid hydrolysis of shrimp-shell wastes and the production of single cell protein from the hydrolysate. *Bioresour. Technol.* **1996**, *57*, 55–60. [CrossRef]
3. Gomez-Rios, D.; Barrera-Zapata, R.; Rios-Estepa, R. Comparison of process technologies for chitosan production from shrimp shell waste: A techno-economic approach using Aspen Plus. *Food Bioprod. Process.* **2017**, *103*, 49–57. [CrossRef]
4. Manni, L.; Ghorbel-Bellaaj, O.; Jellouli, K.; Younes, I.; Nasri, M. Extraction and Characterization of Chitin, Chitosan, and Protein Hydrolysates Prepared from Shrimp Waste by Treatment with Crude Protease from *Bacillus cereus* SV1. *Appl. Biochem. Biotechnol.* **2010**, *162*, 345–357. [CrossRef] [PubMed]
5. Arancibia, M.Y.; Aleman, A.; Calvo, M.M.; Lopez-Caballero, M.E.; Montero, P.; Gomez-Guillen, M.C. Antimicrobial and antioxidant chitosan solutions enriched with active shrimp (*Litopenaeus vannamei*) waste materials. *Food Hydrocoll.* **2014**, *35*, 710–717. [CrossRef]
6. Mao, X.; Liu, P.; He, S.; Xie, J.; Kan, F.; Yu, C.; Li, Z.; Xue, C.; Lin, H. Antioxidant Properties of Bio-active Substances from Shrimp Head Fermented by *Bacillus licheniformis* OPL-007. *Appl. Biochem. Biotechnol.* **2013**, *171*, 1240–1252. [CrossRef] [PubMed]
7. Benhabiles, M.S.; Abdi, N.; Drouiche, N.; Lounici, H.; Pauss, A.; Goosen, M.F.A.; Mameri, N. Protein recovery by ultrafiltration during isolation of chitin from shrimp shells *Parapenaeus longirostris*. *Food Hydrocoll.* **2013**, *32*, 28–34. [CrossRef]
8. El-Beltagy, A.E.; El-Sayed, S.M. Functional and nutritional characteristics of protein recovered during isolation of chitin from shrimp waste. *Food Bioprod. Process.* **2012**, *90*, 633–638. [CrossRef]
9. Prameela, K.; Venkatesh, K.; Immandi, S.B.; Katsuri, A.P.K.; Krishna, C.R.; Mohan, C.M. Next generation nutraceutical from shrimp waste: The convergence of applications with extraction methods. *Food Chem.* **2017**, *237*, 121–132. [CrossRef]
10. Robert, M.; Zatylyn-Gaudin, C.; Fournier, V.; Corre, E.; Corguille, G.L.; Bernay, B.; Henry, J. Transcriptomic and peptidomic analysis of protein hydrolysates from the white shrimp (*L. vannamei*). *J. Biotechnol.* **2014**, *186*, 30–37. [CrossRef]
11. Bueno-Solano, C.; Lopez-Cervantes, J.; Campas-Baypoli, O.N.; Lauterio-Garcia, R.; Adan-Bante, N.P.; Sanchez-Machado, D.I. Chemical and biological characteristics of protein hydrolysates from fermented shrimp by-products. *Food Chem.* **2009**, *112*, 671–675. [CrossRef]
12. Sila, A.; Nasri, M.; Bougatef, A. Isolation and characterization of carotenoproteins from deep-water pink shrimp processing waste. *Int. J. Biol. Macromol.* **2012**, *51*, 953–959. [CrossRef] [PubMed]
13. Narayan, B.; Velappan, S.P.; Zituji, S.P.; Manjabhatta, S.N.; Gowda, L.R. Yield and chemical composition of fractions from fermented shrimp biowaste. *Waste Manag. Res.* **2010**, *28*, 64–70. [CrossRef]
14. Perez-Santin, E.; Calvo, M.M.; Lopez-Caballero, M.E.; Montero, P.; Gomez-Guillen, M.C. Compositional properties and bioactive potential of waste material from shrimp cooking juice. *LWT Food Sci. Technol.* **2013**, *54*, 87–94. [CrossRef]
15. Sachindra, N.M.; Bhaskar, N. In vitro antioxidant activity of liquor from fermented shrimp biowaste. *Bioresour. Technol.* **2008**, *99*, 9013–9016. [CrossRef]
16. Armenta-Lopez, R.; Guerrero, L.I.; Huerta, S. Astaxanthin Extraction from Shrimp Waste by Lactic Acid Fermentation and Enzymatic Hydrolysis of the Carotenoprotein Complex. *Food Chem. Toxicol.* **2002**, *67*, 1002–1006.
17. Gomez-Estaca, J.; Calvo, M.M.; Alvarez-Acero, I.; Montero, P.; Gomez-Guillen, M.C. Characterization and storage stability of astaxanthin esters, fatty acid profile and α-tocopherol of lipid extract from shrimp (*L. vannamei*) waste with potential applications as food ingredient. *Food Chem.* **2017**, *216*, 37–44. [CrossRef]
18. Sila, A.; Sayari, N.; Balti, R.; Martinez-Alvarez, O.; Nedjar-Arroume, N.; Moncef, N.; Bougatef, A. Biochemical and antioxidant properties of peptidic fraction of carotenoproteins generated from shrimp by-products by enzymatic hydrolysis. *Food Chem.* **2014**, *148*, 445–452. [CrossRef]
19. Mao, X.; Zhang, J.; Kan, F.; Gao, Y.; Lan, J.; Zhang, X.; Hu, Z.; Li, Y.; Lin, H. Antioxidant Production and Chitin Recovery from Shrimp Head Fermentation with *Streptococcus thermophilus*. *Food Sci. Biotechnol.* **2013**, *22*, 1023–1032. [CrossRef]

20. Francisco, F.C.; Simora, R.M.C.; Nunal, S.N. Deproteination and demineralization of shrimp waste using lactic acid bacteria for the production of crude chitin and chitosan. *Aquac. Bioflux* **2015**, *8*, 107–115.
21. Maruthiah, T.; Somanath, B.; Immanuel, G.; Palavesam, A. Deproteinization potential and antioxidant property of haloalkalophilic organic solvent protease from marine *Bacillus* sp. APCMST-RS3 using marine shell wastes. *Biotechnol. Rep.* **2015**, *8*, 124–132. [CrossRef] [PubMed]
22. Armenta, R.E.; Guerrero-Legarreta, I. Amino acid profile and enhancement of the enzymatic hydrolysis of fermented shrimp carotenoproteins. *Food Chem.* **2009**, *112*, 310–315. [CrossRef]
23. Jung, W.J.; Jo, G.H.; Kuk, J.H.; Kim, K.Y.; Park, R.D. Extraction of chitin from red crab shell waste by cofermentation with *Lactobacillus paracasei* subsp. *tolerans* KCTC-3074 and *Serratia marcescens* FS-3. *Appl. Microbiol. Biotechnol.* **2006**, *71*, 234–237. [CrossRef] [PubMed]
24. Aytekin, O.; Elibol, M. Cocultivation of *Lactococcus lactis* and *Teredinobacter turnirae* for biological chitin extraction from prawn waste. *Bioprocess. Biosyst. Eng.* **2010**, *33*, 393–399. [CrossRef] [PubMed]
25. Phuong, P.T.D.; Minh, N.C.; Cuong, H.N.; Minh, N.V.; Han, N.T.; Hoa, N.V.; Yen, H.T.H.; Trung, T.S. Recovery of protein hydrolysate and chitosan from black tiger shrimp (*Penaeus monodon*) heads: Approaching a zero waste process. *J. Food Sci. Technol.* **2017**, *54*, 1850–1856. [CrossRef] [PubMed]
26. Fernando, R.; Munasinghe, D.M.S.; Gunasena, A.R.C.; Abeynayake, P. Determination of nitrofuran metabolites in shrimp muscle by liquid chromatography-photo diode array detection. *Food Control* **2017**, *72*, 300–305. [CrossRef]
27. Chen, D.; Ye, Y.; Chen, J.; Yan, X. Evolution of metabolomics profile of crab paste during fermentation. *Food Chem.* **2016**, *192*, 886–892. [CrossRef]
28. Xiao, M.; Qian, K.; Wang, Y.; Bao, F. GC-MS metabolomics reveals metabolic differences of the farmed Mandarin fish *Siniperca chuatsi* in recirculating ponds aquaculture system and pond. *Sci. Rep.* **2020**, *10*, 6090. [CrossRef]
29. Ma, Q.Q.; Wang, X.D.; Cui, Y.Y.; Zhang, N.N.; Qin, J.G.; Du, Z.Y.; Chen, L.Q. Untargeted GC-MS metabolomics reveals metabolic differences in the Chinese mitten-hand crab (*Eriocheir sinensis*) fed with dietary palm oil or olive oil. *Aquacult. Nutr.* **2018**, *24*, 1623–1637. [CrossRef]
30. Zang, J.; Xu, Y.; Xia, W.; Jiang, Q.; Yang, F.; Wang, B. Phospholipid molecular species composition of Chinese traditional low-salt fermented fish inoculated with different starter cultures. *Food Res. Int.* **2018**, *111*, 87–96. [CrossRef]
31. Ming, T.; Han, J.; Li, Y.; Lu, C.; Qiu, D.; Li, Y.; Zhou, J.; Su, X. A metabolomics and proteomics study of the *Lactobacillus plantarum* in the grass carp fermentation. *BMC Microbiol.* **2018**, *18*, 216. [CrossRef] [PubMed]
32. Lopez-Cervantes, J.; Sanchez-Machado, D.I.; Rosas-Rodriguez, J.A. Analysis of free amino acids in fermented shrimp waste by high-performance liquid chromatography. *J. Chromatogr. A* **2005**, *1105*, 106–110. [CrossRef] [PubMed]
33. Lopez-Cervantes, J.; Sanchez-Machado, D.I.; Rosas-Rodriguez, J.A. High-performance liquid chromatography method for the simultaneous quantification of retinol, α-tocopherol, and cholesterol in shrimp waste hydrolysate. *J. Chromatogr. A* **2006**, *1105*, 135–139. [CrossRef] [PubMed]
34. Park, S.E.; Yoo, S.A.; Seo, S.H.; Lee, K.I.; Na, C.S.; Son, H.S. GC-MS based metabolomics approach of Kimchi for the understanding of *Lactobacillus plantarum* fermentation characteristics. *LWT Food Sci. Technol.* **2016**, *68*, 313–321. [CrossRef]
35. Yang, X.; Hu, W.; Xiu, Z.; Jiang, A.; Yang, X.; Sarengaowa; Ji, Y.; Guan, Y.; Feng, K. Microbial dynamics and volatilome profiles during the fermentation of Chinese northeast sauerkraut by *Leuconostoc mesenteroides* ORC 2 and *Lactobacillus plantarum* HBUAS 51041 under different salt concentrations. *Food Res. Int.* **2020**, *130*, 108926. [CrossRef] [PubMed]
36. Li, Q.; Kang, J.; Ma, Z.; Li, X.; Liu, L.; Hu, X. Microbial succession and metabolite changes during traditional serofluid dish fermentation. *LWT Food Sci. Technol.* **2017**, *84*, 771–779. [CrossRef]
37. Li, P.; Tang, H.; Shi, C.; Xie, Y.; Zhou, H.; Xia, B.; Zhang, C.; Chen, L.; Jiang, L. Untargeted metabolomics analysis of *Mucor racemosus* Douchi fermentation by gas chromatography with time-of-flight mass spectrometry. *Food Sci. Nutr.* **2019**, *7*, 1865–1874. [CrossRef]
38. Srivastava, S.; Kumar, P.R.; Mishra, S.K. Identification of Metabolites through GC/LC-MS Processed Data using Different Reference Libraries and Their Comparison. *J. Pharm. Biomed. Sci.* **2016**, *6*, 363–368.
39. Devi, R.; Dhamodharan, R. Pretreatment in Hot Glycerol for Facile and Green Separation of Chitin from Prawn Shell Waste. *ACS Sustain. Chem. Eng.* **2018**, *6*, 846–853. [CrossRef]

40. Toche, R.B.; Janrao, R.A. Synthesis and characterization and antimicrobial evaluation of novel urea, sulfonamide and acetamide 3,4-dihydropyrazinol[1,2-*a*]indol-1(2*H*)-one derivates. *Arab. J. Chem.* **2019**, *12*, 3406–3416. [CrossRef]
41. Popiolek, L.; Biernasiuk, A. Design, synthesis, and in vitro antimicrobial activity of hydrazide-hydrazones of 2-substituted acetic acid. *Chem. Bio. Drug Des.* **2016**, *88*, 873–883. [CrossRef] [PubMed]
42. Fraise, A.P.; Wilkinson, M.A.C.; Bradley, C.R.; Oppenheim, B.; Moiemen, N. The antibacterial activity and stability of acetic acid. *J. Hosp. Infect.* **2013**, *84*, 329–331. [CrossRef] [PubMed]
43. Josephrajan, T.; Ramakrishnan, V.T.; Kathiravan, G.; Muthumary, J. Synthesis and antimicrobial studies of some acridinediones and their thiourea derivatives. *Arkivoc* **2005**, *11*, 124–136.
44. Gratzl, G.; Paulik, C.; Hild, S.; Guggenbichler, J.P.; Lackner, M. Antimicrobial activity of poly(acrylic acid) block copolymers. *Mater. Sci. Eng. C* **2014**, *38*, 94–100. [CrossRef]
45. Meeta, M.; Kumar, P.; Narasimhan, B. Synthesis, antimicrobial evaluation and QSAR studies of *p*-amino benzoic acid derivatives. *J. Pharm. Technol. Res. Manag.* **2014**, *2*, 339–356.
46. Sariguney, A.B.; Kocabas, E.; Erci, F.; Torlak, E.; Coskun, A. Synthesis and Antimicrobial Activity of Some 2-aminothiazole and 2-aminothiadiazine Derivatives. *J. Heterocycl. Chem.* **2018**, *55*, 2107–2110. [CrossRef]
47. Das, U.N. Arachidonic acid and other unsaturated fatty acids and some of their metabolites function as endogenous antimicrobial molecules: A review. *J. Adv. Res.* **2018**, *11*, 57–66. [CrossRef]
48. Leong, H.J.; Oh, S.G. Preparation of antibacterial TiO_2 particles by hybridization with azelaic acid for applications in cosmetics. *J. Ind. Eng. Chem.* **2018**, *66*, 242–247. [CrossRef]
49. Nuta, D.C.; Chifiriuc, M.C.; Draghici, C.; Limban, C.; Missir, A.V.; Morusciag, L. Synthesis, characterization and antimicrobial activity evaluation of new agents from benzamides class. *Farmacia* **2013**, *61*, 966–974.
50. Kim, M.G.; Lee, H.S. 1,2-benzenediol isolated from persimmon roots and its structural analogues show antimicrobial activities against food-borne bacteria. *J. Korean Soc. Appl. Biol. Chem.* **2014**, *57*, 429–433. [CrossRef]
51. Abdelkader, M.S.A.; Rateb, M.E.; Mohamed, G.A.; Jaspars, M. Harpulliasides A and B: Two new benzeneacetic acid derivatives from *Harpullia pendula*. *Phytochem. Lett.* **2016**, *15*, 131–135. [CrossRef]
52. Li, J.; Duan, M.; Yao, X.; Tian, D.; Tang, J. Prenylated benzenepropanoic acid analogues from the *Citrus grandis* (L.) Osbeck and their anti-neuroinflammatory activity. *Fitoterapia* **2019**, *139*, 104410. [CrossRef] [PubMed]
53. Igwe, C.N.; Okoro, U.C. Synthesis, Characterization and Evaluation for Antibacterial and Antifungal Activites of *N*-Heteroaryl Substituted Benzene Sulphonamides. *Org. Chem. Int.* **2014**. [CrossRef]
54. Ambala, A.; Lincoln, C.A. Synthesis, characterization, antimicrobial activity and DNA cleavage study of (E)-2-(((2-(P-Tolyloxy)Quinolin-3-Yl)Methylene)Amino)Benzenethiol Schiff base metal complexes. *Chem. Data Collect.* **2020**, *27*. [CrossRef]
55. Vicini, P.; Zani, F.; Cozzini, P.; Doytchinova, I. Hydrazones of 1,2-benzisothiazole hydrazides: Synthesis, antimicrobial activity and QSAR investigations. *Eur. J. Med. Chem.* **2002**, *37*, 553–564. [CrossRef]
56. Alex, D.; Gay-Andrieu, F.; May, J.; Thampi, L.; Dou, D.; Mooney, A.; Groutas, W.; Calderone, R. Amino Acid-Derived 1,2-Benzisothiazolinone Derivatives as Novel Small-Molecule Antifungal Inhibitors: Identification of Potential Genetic Targets. *Antimicrob. Agents Chemother.* **2012**, *56*, 4630–4639. [CrossRef]
57. Rakesh, K.P.; Shantharam, C.S.; Sridhara, M.B.; Manukumar, H.M.; Qin, H.L. Benzisoxazole: A privileged scaffold for medicinal chemistry. *Med. Chem. Commun.* **2017**, *8*, 2023–2039. [CrossRef]
58. Chen, H.; Zhong, Q. Antibacterial activity of acidified sodium benzoate against *Escherichia coli* O157:H7, *Salmonella enterica*, and *Listeria monocytogenes* in tryptic soy broth and on cherry tomatoes. *Int. J. Food Microbiol.* **2018**, *274*, 38–44. [CrossRef]
59. Leite, A.C.L.; da Silva, K.P.; de Souza, I.A.; de Araujo, J.M.; Brondani, D.J. Synthesis, antitumour and antimicrobial activities of new peptidyl derivatives containing the 1,3-benzodioxole system. *Eur. J. Med. Chem.* **2004**, *39*, 1059–1065. [CrossRef]
60. Park, E.S.; Moon, W.S.; Song, M.J.; Kim, M.N.; Chung, K.H.; Yoon, J.S. Antimicrobial activity of phenol and benzoic acid derivatives. *Int. Biodeterior. Biodegrad.* **2001**, *47*, 209–214. [CrossRef]
61. Carcamo-Noriega, E.N.; Sathyamoorthi, S.; Banerjee, S.; Gnanamani, E.; Mendoza-Trujillo, M.; Mata-Espinosa, D.; Hernandez-Pando, R.; Veytia-Bucheli, J.I.; Possani, L.D.; Zare, R.N. 1,4-Benzoquinone antimicrobial agents against *Staphylococcus aureus* and *Mycobacterium tuberculosis* derived from scorpion venom. *Proc. Natl. Acad. Sci. USA* **2019**, *116*, 12642–12647. [CrossRef] [PubMed]

62. Rida, S.M.; Ashour, F.A.; El-Hawash, S.A.M.; El-Semary, M.M.; Badr, M.H.; Shalaby, M.A. Synthesis of some novel benzoxazole derivatives as anticancer, anti-HIV-1 and antimicrobial agents. *Eur. J. Med. Chem.* **2005**, *40*, 949–959. [CrossRef] [PubMed]
63. Kashid, A.M.; Dube, P.N.; Alkutkar, P.G.; Bothara, K.G.; Mokale, S.N.; Dhawale, S.C. Synthesis, biological screening and ADME prediction of benzylindole derivatives as novel anti-HIV-1, anti-fungal and anti-bacterial agents. *Med. Chem. Res.* **2013**, *22*, 4633–4640. [CrossRef]
64. Gouda, K.G.M.; Kavitha, M.D.; Sarada, R. Antihyperglycemic, antioxidant and antimicrobial activities of the butanol extract from *Spirulina Platensis*. *J. Food Biochem.* **2015**, *39*, 594–602. [CrossRef]
65. Namkung, H.; Yu, H.; Gong, J.; Leeson, S. Antimicrobial activity of butyrate glycerides towards *Salmonella Typhimurium* and *Clostridium perfringens*. *Poultr. Sci.* **2011**, *90*, 2217–2222. [CrossRef]
66. Kratky, M.; Vinsova, J. Salicylanilide *N*-monosubstituted carbamates: Synthesis and in vitro antimicrobial activity. *Bioorg. Med. Chem.* **2016**, *24*, 1322–1330. [CrossRef]
67. Zanatta, N.; Borchhardt, D.M.; Alves, S.H.; Coelho, H.S.; Squizani, A.M.C.; Marchi, T.M.; Bonacorso, H.G.; Martins, M.A.P. Synthesis and antimicrobial activity of new (4,4,4-trihalo-3-oxo-but-1-enyl)-carbamic acid ethyl esters, (4,4,4-trihalo-3-hydroxy-butyl)-carbamic acid ethyl esters, and 2-oxo-6-trihalomethyl-[1,3]oxazinane-3-carboxylic acid ethyl esters. *Bioorg. Med. Chem.* **2006**, *14*, 3174–3184. [CrossRef]
68. Kumar, A.; Singh, S.; Jain, S.; Kumar, G. Synthesis, antimicrobial evaluation, QSAR and in silico ADMET studies of decanoic acid derivatives. *Pol. Pharm. Soc. Drug Res.* **2011**, *68*, 191–204.
69. Al-Dhabi, N.A.; Arasu, M.V.; Rejiniemon, T.S. In Vitro Antibacterial, Antifungal, Antibiofilm, Antioxidant, and Anticancer Properties of Isosteviol Isolated from Endangered Medicinal Plant *Pittosporum tetraspermum*. *Evid.-Based Complem. Altern. Med.* **2015**, *2015*, 164261. [CrossRef]
70. Shin, S.Y.; Bajpai, V.K.; Kim, H.R.; Kang, S.C. Antibacterial activity of bioconverted eicosapentaenoic (EPA) and docosahexaenoic acid (DHA) against foodborne pathogenic bacteria. *Int. J. Food Microbiol.* **2007**, *113*, 233–236. [CrossRef]
71. Lakshmi, S.A.; Bhaskar, J.P.; Krishnan, V.; Sethupathy, S.; Pandipriya, S.; Aruni, W.; Pandian, S.K. Inhibition of biofilm and biofilm-associated virulence factor production in methicillin-resistant *Staphylococcus aureus* by docosanol. *J. Biotechnol.* **2020**, *317*, 59–69. [CrossRef] [PubMed]
72. Abdalha, A.A.; Mekawey, A.A.I. Antimicrobial Susceptibility of Certain Fungal and Bacterial Strains to Dodecanamide and Quinazolinone Derivatives. *World Appl. Sci. J.* **2013**, *24*, 312–319.
73. Oh, D.H.; Marshall, D.L. Antimicrobial activity of ethanol, glycerol monolaurate or lactic acid against *List*. *Monocytogenes*. *Int. J. Food Microbiol.* **1993**, *20*, 239–246. [CrossRef]
74. Tamokou, J.D.D.; Mpetga, D.J.S.; Lunga, P.K.; Tene, M.; Tane, P.; Kuiate, J.R. Antioxidant and antimicrobial activities of ethyl acetate extract, fractions and compounds from stem bark of *Albizia adianthifolia* (Mimosoideae). *Bmc Complem. Altern. Med.* **2012**, *12*. [CrossRef]
75. Huisjes, E.H.; de Hulster, E.; van Dam, J.C.; Pronk, J.T.; van Maris, A.J.A. Galacturonic Acid Inhibits the Growth of *Saccharomyces cerevisiae* on Galactose, Xylose, and Arabinose. *Appl. Environ. Microbiol.* **2012**, *78*, 5052–5059. [CrossRef]
76. Nieto-Penalver, C.G.; Savino, M.J.; Bertini, E.V.; Sanchez, L.A.; de Figueroa, L.I.C. Gluconic acid produced by *Gluconacetobacter diazotrophicus* Pal5 possesses antimicrobial properties. *Res. Microbiol.* **2014**, *165*, 549–558. [CrossRef]
77. Berger, F.M.; Hubbard, C.V.; Ludwig, B.J. The Antimicrobial Action of Certain Glycerol Ethers and Related Compounds. *Appl. Microbiol.* **1953**, *1*, 146–149. [CrossRef] [PubMed]
78. Nurullaeva, M.K.; Azizov, U.M.; Mikhlina, E.E.; Turchin, K.F.; Silin, V.A.; Yakhontov, L.N. Synthesis of (3-pyridyl)glyoxylic acid derivatives and their antimicrobial properties. *Pharmaceut. Chem. J.* **1987**, *20*, 563–567. [CrossRef]
79. Liu, H.; Lepoittevin, B.; Roddier, C.; Guerineau, V.; Bech, L.; Herry, J.M.; Bellon-Fontaine, M.N.; Roger, P. Facile synthesis and promising antibacterial properties of a new guaiacol-based polymer. *Polymer* **2011**, *52*, 1908–1916. [CrossRef]
80. Vasudevan, A.; Vijayan, D.; Mandal, P.; Haridas, M. Anti-inflammatory Property of n-Hexadecanoic Acid: Structural Evidence and Kinetic Assessment. *Chem. Biol. Drug Des.* **2010**, *9*, 1236–1240.
81. Narasimhan, B.; Judge, V.; Narang, R.; Ohlan, R.; Ohlan, S. Quantitative structure-activity relationship studies for prediction of antimicrobial activity of synthesized 2,4-hexadienoic acid derivatives. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5835–5845. [CrossRef] [PubMed]

82. Choi, W.H.; Jiang, M.H. Evaluation of antibacterial activity of hexanedioic acid isolated from *Hermetia illucens* larvae. *J. Appl. Biomed.* **2014**, *12*, 179–189. [CrossRef]
83. Alva-Murillo, N.; Ochoa-Zarzosa, A.; Lopez-Meza, J.E. Short chain fatty acids (propionic and hexanoic) decrease *Staphylococcus aureus* internalization into bovine mammary epithelial cells and modulate antimicrobial peptide expression. *Vet. Microbiol.* **2012**, *155*, 324–331. [CrossRef] [PubMed]
84. Kratky, M.; Vinsova, J.; Volkova, M.; Buchta, V.; Trejtnar, F.; Stolarikova, J. Antimicrobial activity of sulfonamides containing 5-chloro-2-hydroxybenzaldehyde and 5-chloro-2-hydroxybenzoic acid scaffold. *Eur. J. Med. Chem.* **2012**, *50*, 433–440. [CrossRef] [PubMed]
85. Ma, L.; Zhang, Z.; Li, J.; Yang, X.; Fei, B.; Leung, P.H.M.; Tao, X. A New Antimicrobial Agent: Poly (3-hydroxybutyric acid) Oligomer. *Macromol. Biosci.* **2019**, *19*. [CrossRef]
86. Kumar, A.; Mishra, A.K. Synthesis and antimicrobial activity of some new diphenylamine derivatives. *J. Pharm. Bioallied Sci.* **2015**, *7*, 81–85. [CrossRef]
87. Sakko, M.; Moore, C.; Novak-Fraser, L.; Rautemaa, V.; Sorsa, T.; Hietala, P.; Jarvinen, A.; Bowyer, P.; Tjaderhane, L.; Rautemaa, R. 2-hydroxyisocaproic acid is fungicidal for *Candida* and *Aspergillus* species. *Mycoses* **2014**, *57*, 214–221. [CrossRef]
88. Sundar, L.; Chang, F.N. Antimicrobial activity and biosynthesis of indole antibiotics produced by *Xenorhabdus nematophilus*. *J. Gen. Microbiol.* **1993**, *139*, 3139–3148. [CrossRef]
89. Himaja, M.; Jose, T.; Ramana, M.V.; Anand, R.; Munirajasekhar, D. Synthesis and biological evaluation of indole-3-carboxylic acid derivatives of amino acids and peptides. *Int. Res. J. Pharm.* **2010**, *1*, 436–440.
90. In, Y.W.; Kim, J.J.; Kim, H.J.; Oh, S.W. Antimicrobial activities of acetic acid, citric acid and lactic acid against *Shigella* species. *J. Food Saf.* **2013**, *33*, 79–85. [CrossRef]
91. Ferrazzano, L.; Viola, A.; Lonati, E.; Bulbarelli, A.; Musumeci, R.; Cocuzza, C.; Lombardo, M.; Tolomelli, A. New isoxazolidinone and 3,4-dehydro-β-proline derivatives as antibacterial agents as MAO-inhibitors: A complex balance between two activities. *Eur. J. Med. Chem.* **2010**, *124*, 906–919. [CrossRef] [PubMed]
92. Velikova, M.; Bankova, V.; Tsvetkova, I.; Kujumgiev, A.; Marcucci, M.C. Antibacterial *ent*-kaurene from Brazilian propolis of native stingless bees. *Fitoterapia* **2000**, *71*, 693–696. [CrossRef]
93. Wang, C.; Chang, T.; Yang, H.; Cui, M. Antibacterial mechanism of lactic acid on physiological and morphological properties of *Salmonella Enteritidis*, *Escherichia coli* and *Listeria monocytogenes*. *Food Control* **2015**, *47*, 231–236. [CrossRef]
94. Lee, J.Y.; Kim, Y.S.; Shin, D.H. Antimicrobial Synergistic Effect of Linolenic Acid and Monoglyceride against *Bacillus cereus* and *Staphylococcus aureus*. *J. Agric. Food Chem.* **2002**, *50*, 2193–2199. [CrossRef]
95. Orhan, I.; Ozeelik, B.; Aslan, S.; Kartal, M.; Karaoglu, T.; Sener, B.; Terzioglu, S.; Choudhary, M.I. Antioxidant and antimicrobial actions of the clubmoss *Lycopodium clavatum* L. *Phytochem. Rev.* **2007**, *6*, 189–196. [CrossRef]
96. Raybaudi-Massilia, R.M.; Mosqueda-Melgar, J.; Martin-Belloso, O. Antimicrobial activity of malic acid against *Listeria monocytogenes*, *Salmonella Enteritidis* and *Escherichia coli* O157:H7 in apple, pear and melon juices. *Food Control* **2009**, *20*, 105–112. [CrossRef]
97. Motamedifar, M.; Bazargani, A.; Namazi, M.R.; Sarai, H.S.E. Antimicrobial Activity of Mandelic Acid Against Methicillin-Resistant *Staphylococcus aureus*: A Novel Finding with Important Practical Implications. *World Appl. Sci. J.* **2014**, *31*, 925–929.
98. Ristovski, J.T.; Jankovic, N.; Borcic, V.; Jain, S.; Bugarcic, Z.; Mikov, M. Evaluation of antimicrobial activity and retention behavior of newly synthesized vanilidene derivatives of Meldrum's acids using QSRR approach. *J. Pharm. Biomed. Anal.* **2018**, *155*, 42–49. [CrossRef]
99. Karaman, I.; Sahin, F.; Gulluce, M.; Ogutcu, H.; Sengul, M.; Adiguzel, A. Antimicrobial activity of aqueous and methanol extracts of *Juniperus oxycedrus* L. *J. Ethnopharmacol.* **2003**, *85*, 231–235. [CrossRef]
100. Kern, E.R.; Kushner, N.L.; Hartline, C.B.; Williams-Aziz, S.L.; Harden, E.A.; Zhou, S.; Zemlicka, J.; Prichard, M.N. In Vitro Activity and Mechanism of Action of Methylenecyclopropane Analogs of Nucleosides against Herpesvirus Replication. *Antimicrob. Agents Chemother.* **2005**, *49*, 1039–1045. [CrossRef]
101. Yoo, J.C.; Han, J.M.; Nam, S.K.; Ko, O.H.; Choi, C.H.; Kee, K.H.; Sohng, J.K.; Jo, J.S.; Seong, C.N. Characterization and Cytotoxic Activities of Nonadecanoic Acid Produced by *Streptomyces scabiei* subsp. *chosunensi* M0137 (KCTC 9927). *J. Microbiol.* **2002**, *40*, 331–334.
102. Sahin, N.; Kula, I.; Erdogan, Y. Investigation of Antimicrobial Activities of Nonanoic Acid Derivatives. *Fresenius Environ. Bull.* **2006**, *15*, 141–143.

103. Pu, Z.H.; Zhang, Y.Q.; Yin, Z.Q.; Xu, J.; Jia, R.Y.; Lu, Y.; Yang, F. Antibacterial Activity of 9-Octadecanoic Acid-Hexadecanoic Acid-Tetrahydrofuran-3,4-Diyl Ester from Neem Oil. *Agric. Sci. China* **2010**, *9*, 1236–1240. [CrossRef]
104. Hilgren, J.D.; Salverda, J.A. Antimicrobial Efficacy of a Peroxyacetic/Octanoic Acid Mixture in Fresh-Cut-Vegetable Process Waters. *J. Food Sci.* **2000**, *65*, 1376–1379. [CrossRef]
105. De Lucena, J.M.V.M.; Decker, E.M.; Walter, C.; Boeira, L.S.; Lost, C.; Weiger, R. Antimicrobial effectiveness of intracanal medicaments on *Enterococcus faecalis*: Chlorhexidine versus octenidine. *Int. Endod. J.* **2013**, *46*, 53–61. [CrossRef]
106. Kuhrt, M.F.; Fancher, M.J.; McKinlay, M.A.; Lennert, S.D. Virucidal Activity of Glutaric Acid and Evidence for Dual Mechanism of Action. *Antimicrob. Agents Chemother.* **1984**, *26*, 924–927. [CrossRef]
107. Roy, S.; Hagen, K.D.; Maheswari, P.U.; Lutz, M.; Spek, A.L.; Reedijk, J.; van Wezel, G.P. Phenanthroline Derivatives with Improved Selectivity as DNA-Targeting Anticancer or Antimicrobial Drugs. *ChemMedChem* **2008**, *3*, 1427–1434. [CrossRef]
108. Mazimba, O.; Wale, K.; Loeto, D.; Kwape, T. Antioxidant and antimicrobial studies on fused-ring pyrazolones and isoxazolones. *Bioorg. Med. Chem.* **2014**, *22*, 6564–6569. [CrossRef]
109. Arias-Moliz, M.T.; Ferrer-Luque, C.M.; Espigares-Rodriguez, E.; Liebana-Urena, J.; Espigares-Garcia, M. Bactericidal activity of phosphoric acid, citric acid, and EDTA solutions against *Enterococcus faecalis*. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* **2008**, *106*, 84–89. [CrossRef]
110. Evren, A.E.; Yurttas, L.; Yilmaz-Cankilic, M. Synthesis of novel *N*-(naphthalen-1-yl)propanamide derivatives and evaluation of their antimicrobial activity. *Phosphorussulfur Silicon Relat. Elem.* **2020**, *195*, 158–164. [CrossRef]
111. Desai, N.C.; Pandya, D.; Vaja, D. Synthesis, characterization and antimicrobial studies on 3-((4-(4-nitrophenyl)-6-aryl-1,6-dihydropyrimindin-2-yl)thio)propanenitriles and their derivatives. *Med. Chem. Res.* **2017**, *26*, 1089–1097. [CrossRef]
112. Zhang, W.; Liu, W.; Jiang, X.; Jiang, F.; Zhuang, H.; Fu, L. Design, synthesis and antimicrobial activity of chiral 2-(substituted-hydroxyl)-3-(benzo[d]oxazol-5-yl)propanoic acid derivates. *Eur. J. Med. Chem.* **2011**, *46*, 3639–3650. [CrossRef] [PubMed]
113. Helal, M.H.; Abbas, S.Y.; Salem, M.H.; Farag, A.A.; Ammar, Y.A. Synthesis and characterization of new types of 2-(6-methoxy-2-naphthyl)propionamide derivatives as potential antibacterial and antifungal agents. *Med. Chem. Res.* **2013**, *22*, 5598–5609. [CrossRef]
114. El Azab, I.H.; Khalifa, M.E.; Gobouri, A.A.; Altalhi, T.A. Synthesis, Characterization and Pharmacological Evaluation of Some New Pteridine-Based Heterocycles as Antimicrobial Agents. *J. Heterocycl. Chem.* **2019**, *56*, 1352–1361. [CrossRef]
115. Elaasser, M.M.; Abdel-Aziz, M.M.; El-Kassas, R.A. Antioxidant, antimicrobial, antiviral and antitumour activities of pyranone derivative obtained from *Aspergillus candidus*. *J. Microbiol. Biotech. Res.* **2011**, *1*, 5–17.
116. Premkumar, T.; Govindarajan, S. Antimicrobial study of pyrazine, pyrazole and imidazole carboxylic acids and their hydrazinium salts. *World J. Microbiol. Biotechnol.* **2005**, *21*, 479–480. [CrossRef]
117. Kandile, N.G.; Mohamed, M.I.; Zaky, H.; Mohamed, H.M. Novel pyridazine derivatives: Synthesis and antimicrobial activity evaluation. *Eur. J. Med. Chem.* **2009**, *44*, 1989–1996. [CrossRef]
118. Yurttas, L.; Ozkay, Y.; Kaplancikli, Z.A.; Tunali, Y.; Karaca, H. Synthesis and antimicrobial activity of some new hydrazone-bridged thiazole-pyrrole derivatives. *J. Enzym. Inhib. Med. Chem.* **2013**, *28*, 830–835. [CrossRef]
119. Jacobson, J.G.; Renau, T.E.; Nassiri, M.R.; Sweier, D.G.; Breitenbach, J.M.; Townsend, L.B.; Drach, J.C. Nonnucleoside Pyrrolopyrimidines with a Unique Mechanism of Action against Human Cytomegalovirus. *Antimicrob. Agents Chemother.* **1999**, *43*, 1888–1894. [CrossRef]
120. Purohit, A.; Mohan, A. Antimicrobial effects of pyruvic and succinic acids on Salmonella survival in ground chicken. *LWT Food Sci. Technol.* **2019**, *116*, 108596. [CrossRef]
121. Jafari, E.; Khajouei, M.R.; Hassanzadeh, F.; Hakimelahi, G.H.; Khodarahmi, G.A. Quinazolinone and quinazoline derivatives: Recent structures with potent antimicrobial and cytotoxic activities. *Res. Pharm. Sci.* **2016**, *11*, 1–14. [PubMed]
122. Eswaran, S.; Adhikari, A.V.; Shetty, N.S. Synthesis and antimicrobial activities of novel quinoline derivatives carrying 1,2,4-triazole moiety. *Eur. J. Med. Chem.* **2009**, *44*, 4637–4647. [CrossRef] [PubMed]
123. Peterson, L.R. Quinolone Molecular Structure-Activity Relationships: What We Have Learned about improving Antimicrobial Activity. *Clin. Infect. Dis.* **2001**, *33*, S180–S186. [CrossRef]

124. Brilisauer, K.; Rapp, J.; Rath, P.; Schollhorn, A.; Bleul, L.; Weiβ, E.; Stahl, M.; Grond, S.; Forchhammer, K. Cyanobacterial antimetabolite 7-deoxy-sedoheptulose blocks the shikimate pathway to inhibit the growth of prototrophic organisms. *Nat. Commun.* **2019**, *10*, 545. [CrossRef] [PubMed]
125. Hans, S.; Sharma, S.; Hameed, S.; Fatima, Z. Sesamol exhibits potent antimycobacterial activity: Underlying mechanisms and impact on virulence traits. *J. Glob. Antimicrob. Resist.* **2017**, *10*, 228–237. [CrossRef]
126. Kenawy, E.R.; Abdel-Hay, F.I.; Shahada, L.; El-Shanshoury, A.E.R.; El-Newehy, M.H. Biologically Active Polymers. IV. Synthesis and Antimicrobial Activity of Tartaric Acid Polyamides. *J. Appl. Polym. Sci.* **2006**, *102*, 4780–4790. [CrossRef]
127. Bondock, S.; Fadaly, W.; Metwally, M.A. Synthesis and antimicrobial activity of some new thiazole, thiophene and pyrazole derivatives containing benzothiazole moiety. *Eur. J. Med. Chem.* **2010**, *45*, 3692–3701. [CrossRef]
128. Saeed, S.; Rashid, N.; Jones, P.G.; Ali, M.; Hussain, R. Synthesis, characterization and biological evaluation of some thiourea derivatives bearing benzothiazole moiety as potential antimicrobial and anticancer agents. *Eur. J. Med. Chem.* **2010**, *45*, 1323–1331. [CrossRef]
129. Guarda, A.; Rubilar, J.F.; Miltz, J.; Galotto, M.J. The antimicrobial activity of microencapsulated thymol and carvacrol. *Int. J. Food Microbiol.* **2011**, *146*, 144–150. [CrossRef]
130. Bayrak, H.; Demirbas, A.; Karaoglu, S.A.; Demirbas, N. Synthesis of some new 1,2,4-triazoles, their Mannich and Schiff bases and evaluation of their antimicrobial activities. *Eur. J. Med. Chem.* **2009**, *44*, 1057–1066. [CrossRef]
131. Dolezalova, M.; Janis, R.; Svobodova, H.; Kasparkova, V.; Humpolicek, P.; Krejci, J. Antimicrobial properties of 1-monoacylglycerols prepared from undecanoic (C11:0) and undecanoic (C11:1) acid. *Eur. J. Lipid Sci. Technol.* **2010**, *112*, 1106–1114. [CrossRef]
132. Grether-Beck, S.; Felsner, I.; Brenden, H.; Kohne, Z.; Majora, M.; Marini, A.; Jaenicke, T.; Rodriguez-Martin, M.; Trullas, C.; Hupe, M.; et al. Urea Uptake Enhances Barrier Function and Antimicrobial Defense in Humans by Regulating Epidermal Gene Expression. *J. Investig. Dermatol.* **2012**, *132*, 1561–1572. [CrossRef] [PubMed]
133. Kawsar, S.M.A.; Islam, M.; Jesmin, S.; Manchur, M.A.; Hasan, I.; Rajia, S. Evaluation of the antimicrobial activity and cytotoxic effect of some uridine derivatives. *Int. J. Biosci.* **2018**, *12*, 211–219.
134. Wheatley, R.E. The consequences of volatile organic compound mediated bacterial and fungal interactions. *Antonie Van Leeuwenhoek* **2002**, *81*, 357–364. [CrossRef] [PubMed]
135. Audrain, B.; Farag, M.A.; Ryu, C.M.; Ghigo, J.M. Role of bacterial volatile compounds in bacterial biology. *FEMS Microbiol. Rev.* **2015**, *39*, 222–233. [CrossRef] [PubMed]
136. Caulier, S.; Nannan, C.; Gillis, A.; Licciardi, F.; Bragard, C.; Mahilon, J. Overview of the Antimicrobial Compounds Produced by Members of the *Bacillus subtilis* Group. *Front. Microbiol.* **2019**, *10*, 302. [CrossRef]
137. Stein, T. *Bacillus subtilis* antibiotics: Structures, syntheses and specific functions. *Mol. Microbiol.* **2005**, *56*, 845–857. [CrossRef]
138. Reis, J.A.; Paula, A.T.; Casarotti, S.N.; Penna, A.L.B. Lactic acid bacteria Antimicrobial Compounds: Characteristics and Applications. *Food Eng. Rev.* **2012**, *4*, 124–140. [CrossRef]
139. Niku-Paavola, M.L.; Laitila, A.; Mattila-Sandholm, T.; Haikara, A. New types of antimicrobial compounds produced by *Lactobacillus plantarum*. *J. Appl. Microbiol.* **1999**, *86*, 29–35. [CrossRef]
140. Siedler, S.; Balti, R.; Neves, A.R. Bioprotective mechanisms of lactic acid bacteria against fungal spoilage of food. *Curr. Opin. Biotechnol.* **2019**, *56*, 138–146. [CrossRef]