fermentation

Review

Kombucha Healthy Drink—Recent Advances in Production, Chemical Composition and Health Benefits

Haruthairat Kitwetcharoen [1], Ly Tu Phung [1], Preekamol Klanrit [1,2], Sudarat Thanonkeo [3], Patcharaporn Tippayawat [4], Mamoru Yamada [5,6] and Pornthap Thanonkeo [1,2,*]

1 Department of Biotechnology, Faculty of Technology, Khon Kaen University, Khon Kaen 40002, Thailand
2 Fermentation Research Center for Value Added Agricultural Products (FerVAAPs), Khon Kaen University, Khon Kaen 40002, Thailand
3 Walai Rukhavej Botanical Research Institute, Mahasarakham University, Maha Sarakham 44150, Thailand
4 Faculty of Associated Medical Sciences, Khon Kaen University, Khon Kaen 40002, Thailand
5 Department of Biological Chemistry, Faculty of Agriculture, Yamaguchi University, Yamaguchi 753-8515, Japan
6 Research Center for Thermotolerant Microbial Resources, Yamaguchi University, Yamaguchi 753-8515, Japan
* Correspondence: portha@kku.ac.th; Tel.: +66-819-743-340

Abstract: Kombucha, one of the ordinary fermented beverages consumed worldwide, is produced by fermenting tea and sugar with a symbiotic culture of bacteria and yeasts or so-called SCOBY. Kombucha can be made from different types of tea, such as black, green, white, red, and oolong teas, yielding various health benefits and properties. Several species of bacteria and yeasts are involved in the fermentation process, which generates many beneficial compounds, such as polyphenols, organic acids, amino acids, vitamins, minerals, organic nitrogens, and hydrolytic enzymes, which have significant health effects and therapeutic properties, such as antioxidant, anti-inflammatory, anticancer, and antimicrobial properties. This review describes recent research on kombucha fermentation, the microbial community in SCOBY, the chemical composition of kombucha, and its health benefits. The adverse effects and prospects of kombucha production were also discussed.

Keywords: bacteria; fermented tea; health benefit; kombucha; scoby; yeast

check for updates

Citation: Kitwetcharoen, H.; Phung, L.T.; Klanrit, P.; Thanonkeo, S.; Tippayawat, P.; Yamada, M.; Thanonkeo, P. Kombucha Healthy Drink—Recent Advances in Production, Chemical Composition and Health Benefits. *Fermentation* **2023**, *9*, 48. https://doi.org/10.3390/fermentation9010048

Academic Editor: Zhao Jin

Received: 8 December 2022
Revised: 3 January 2023
Accepted: 4 January 2023
Published: 6 January 2023

1. Introduction

Kombucha is one of the valuable beverages fermented from the fusion of dried tea leaves (*Camellia sinensis*) and sugar (sugarcane or sugar beet) by a symbiotic culture of bacteria and yeasts, commonly called SCOBY, which is also known as "mushroom tea" or "tea fungus". Kombucha is traditionally prepared as homemade drinking without special brewing equipment. The word "Kombucha" is believed to originate from "Kombu", who introduced fermented tea to Japan, and "Cha", which refers to tea in Japanese [1]. Kombucha is known by different names, e.g., *kocha kinoko* in Japan, *shenxian cu* in China, *hongcha beoseo-tcha* in Korea, *grib* or *tea kvass* in Russia, and *Cha-mug* in Thailand. Kombucha is believed to be brewed initially in China in 220 BC [2]. Over thousands of years, kombucha has traveled throughout Asia and especially arrived in western countries around World War I. From the 1950s, kombucha became a popular beverage in Europe [3] because, after World War II, a German doctor utilized kombucha as a traditional medicine to cure various diseases, from diabetes to cancer. After the 1960s, much evidence has been reported that kombucha consumed regularly could support and resist harmful risks to human health. In the late 1990s, commercial production of kombucha beverages began at the large-scale industrial level using modern machines. Remarkably, the US retail brand GT's Living Foods first put kombucha on their store shelves in 1995, and GT's Living Foods recently became one of the leaders among top-selling kombucha companies [4,5]. More than 300 companies have recently produced kombucha beverages in the market, providing a wide range of brand and flavor options. In recent years, due to the high level of kombucha production and global consumption, kombucha is believed to be one of the most promising markets with various vital economic trends. Companies are discovering new products regarding healthy beverages with novel flavors to expand the number of customers. Commercial kombucha on the market is well known in two types: original flavor and flavor-added kombucha. Therefore, to promote the economic trend for kombucha products, companies are developing traditional kombucha tea by using alternative raw materials, adding natural flavor extracts from fruits or flowers, and innovating their packaging to attract consumers. The global kombucha market is expected to reach USD 5 billion by 2025 [6].

Kombucha contains numerous valuable components and biological activities attributed to its main ingredients. As a typical and beneficial drink, tea contains large amounts of polyphenols that potentially impact human health [7]. Moreover, numerous efficient bioactive properties produced in kombucha are due to the phenol content from the raw material and the collaboration between yeasts and bacteria during fermentation. The association of yeast and bacteria utilizes substrates in different metabolic pathways to generate several efficient metabolites, such as organic acids, vitamins, tea polyphenols, ethanol, amino acids, hydrolytic enzymes, and minerals [4]. Black tea is the traditional raw material used in kombucha production since it provides various nutrients for activating SCOBY. Research on kombucha and its beneficial health properties has been performed since the late 20th century, so kombucha has been proven to be an efficient source of antioxidant, antimicrobial, anti-inflammatory, and antiaging compounds, along with the capacity for improving the immune system and preventing some diseases, such as diabetes, hypertension, and cardiovascular diseases [8–11].

Kombucha has a slightly acidic flavor due to the generation of organic acids during fermentation. Furthermore, as a result of different biochemical reactions during fermentation, various compounds have also been formed. The most important compounds in kombucha are polyphenols as antioxidants supplemented from tea that play an essential role in reducing cardiovascular and neurodegenerative diseases [7]. Moreover, the bacteria in kombucha can utilize glucose and ethanol to create diverse organic acids, such as acetic acid, gluconic acid, glucuronic acid, lactic acid, and ascorbic acid, which are the primary components of various metabolic pathways in the human body [12,13]. Therefore, kombucha should be consumed as a daily diet, a valuable source providing health-promoting properties. Although kombucha provides excellent antioxidant properties and other beneficial substances from the numerous reactions presented during the fermentation process, the differences and concentration of substances in kombucha markedly originate and depend on the types of tea. Hence, the prospective research directions have been estimating kombucha's antioxidant, antibacterial, anti-inflammatory, and anticancer abilities using various tea types and a substrate as an alternative to sugar beet or sugarcane. Green tea, oolong tea, red tea, and white tea are also potential substrates for kombucha production instead of black tea in terms of increasing various supplements. Apart from tea types, fermentation time and temperature, and carbon source should be designed reasonably to enhance the yield of kombucha.

2. Kombucha Production

There are several procedures for producing kombucha; however, the typical method described by Jayabalan et al. [4], Kaewkod et al. [14], and Jakubczyk et al. [15] is illustrated in Figure 1. Briefly, to perfectly steep dried tea leaves, 5 g of tea leaves were added to 1 L of sterile water and boiled for 10–15 min. The utilization of sterilized distilled water can reduce microbial contamination in kombucha. Then, the boiled tea leaves were removed, and 50 g of sucrose was added to the hot tea and stirred until it completely dissolved. Alternatively, tea bags can also be used. The mixture was transferred into sterilized glass jars and left until the temperature cooled to room temperature. The pH of the mixture was adjusted to approximately 4.6 by adding a previously fermented kombucha beverage. This technique is not only for adjusting the pH of hot-sweetened tea but also for controlling undesirable contamination [15]. Then, 5–10% (*v/v*) SCOBY was inoculated into the sweetened tea, and the mouth of the glass jars was covered with a woven cotton cloth to protect the kombucha from contamination as well as allow the small amount of oxygen to pass through for the growth of SCOBY. The mixture was then incubated at around 20 to 30 °C or room temperature in the dark, dependent on the microbial community of SCOBY. The daughter SCOBY, a thin cellulose layer, is formed within a few days and covers the surface of the liquid within 10 to 14 days, depending on the source and composition of SCOBY and fermentation conditions. At this stage, the pH level of the liquid is reduced to as low as pH 2.0. The collaboration of microbes in SCOBY utilizes carbon sources from sugar to create a cellulose layer that enhances benefits during the kombucha process. The color of kombucha is changed depending on the substrate; e.g., kombucha produced from black tea exhibits a dark-brown color, while green tea and oolong tea show a light-brown color [14]. The fermentation duration may range from one week to two months, depending on the fermentation rate, the composition of SCOBY, and cultural practices [16]. However, the Food and Drug Administration (FDA) recommends a fermentation time of 10 days [17]. Long-term fermentation may cause excessive acidification of the kombucha product, which could reduce the health-promoting properties or have adverse effects on consumers [16]. At the final stage of fermentation, the mother SCOBY is carefully removed and kept in a small volume of fermented tea at low temperatures (4 to 10 °C) for future use. The remaining fermented tea is filtered, placed in sterile capped bottles to avoid cross-contamination, and stored at a low temperature (4 °C) until consumption.

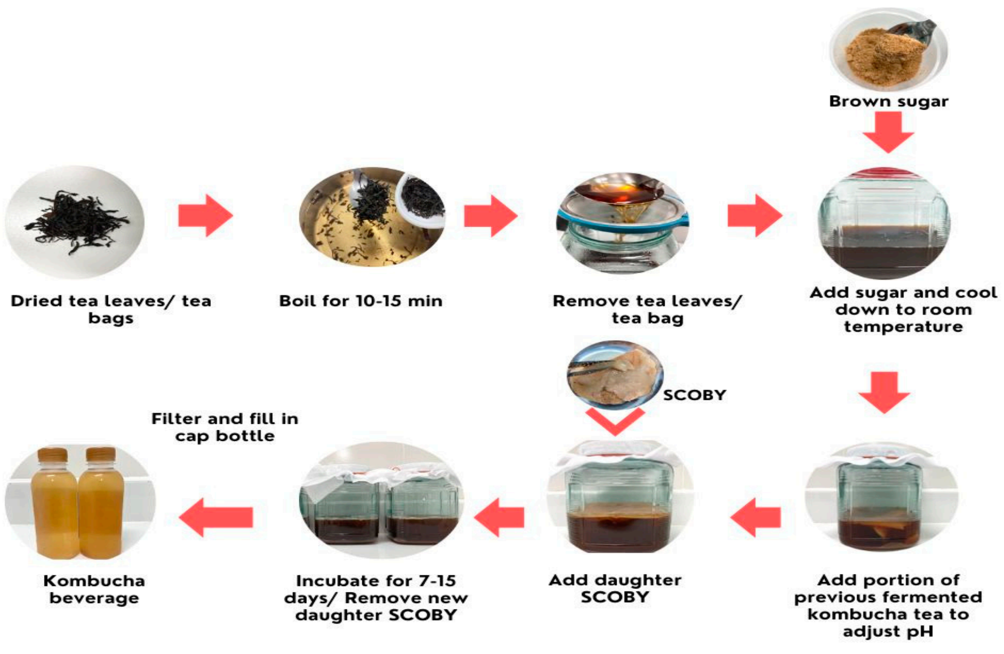

Figure 1. The production process of kombucha beverages (modified from Jayabalan et al. [4]; Kaewkod et al. [14]; Jakubczyk et al. [15].

The quality, chemical composition, and total beneficial health effects of kombucha depend on several fermentation parameters, such as the microbial community of kombucha cultures, fermentation time and temperature, and raw materials [18]. Although yeasts and bacteria, particularly acetic acid bacteria (AAB), are the most predominant microbes in kombucha SCOBY, the variation in microbial cell counts also affects the fermentation kinetics, chemical composition, and health-promoting properties of kombucha. The experiment carried out by Villarreal-Soto [19] demonstrated the relationship between the distribution of kombucha microbiota and fermentation kinetics, as well as secondary metabolite production. Furthermore, differences in microbiota also correlated with the difference in the biological profiles of kombucha products.

Although kombucha is generally fermented in the range of 10 to 14 days, fermentation time dramatically affects kombucha's composition and total beneficial properties. For instance, Ivanišová et al. [20] reported a high level of polyphenols (412.25 mg GAE/L) and antioxidant activity (1318.56 mg TEAC/L) of kombucha beverage after 7 days of fermentation at 22 °C. Jakubczyk et al. [15] demonstrated that polyphenols of green tea kombucha increased from 299.6 mg GAE/L on day 7 to 320.1 mg GAE/mL on day 14, while those values of black tea kombucha were not different between day 7 and 14 of fermentation at 28 °C. Diverse values of polyphenols and antioxidant activities of kombucha product versus fermentation time were also described in some works, e.g., Gaggia et al. [21] pointed out that polyphenols of green tea kombucha increase up to 100.33 mg/g dry weight (DW) on day 7 and decrease to 67.40 mg/g DW on day 14 of fermentation at 27 °C. Similarly, an increase in polyphenols and antioxidant activity of black tea kombucha on day 8 and a decrease after 12 days of fermentation was noted by Ahmed et al. [22]. Therefore, optimizing the fermentation time has an important impact on the chemical properties of kombucha beverages.

Several studies demonstrated that the fermentation temperature influences the metabolic activity of a microbial community of SCOBY, resulting in different bioactive substances formation with various health benefits. Generally, the optimum growth temperature for yeasts is between 25 and 30 °C [23], while that for AAB and LAB ranged from 25 to 30 °C [24] and 20 to 40 °C [25], respectively. Thavasi et al. [26] stated that the incubation temperature significantly impacts the activity of β-glucosidase involved in releasing free aglycones from phenolic glycosides, which are considered high antioxidant activity. De Filippis et al. [27] demonstrated that the diversity of bacteria and organic acids, such as gluconic and glucuronic acid, increased when the fermentation temperature of black tea kombucha rose from 20 to 30 °C, while the total phenolic compounds decreased at a temperature of 30 °C after 15 days of fermentation.

pH is another fermentation parameter that affects kombucha fermentation. It influences not only microbial growth and enzyme activity but also the structural changes in the bioactive substances, which may affect the biological properties of kombucha products [28]. Although the generation of organic acids during kombucha fermentation results in a lowering of pH, the lowest acceptable pH value of the finished products should not be below 3.0, based on the recommendation of the FDA. The total acidity of kombucha should be in the range of 4.0 to 5.0 g/L, a value that provides a sour taste to the products [29]. Thus, the fermentation period to obtain the acceptable pH and total acidity values should be optimized, even though it may differ depending on other factors, such as the microbial community in kombucha SCOBY, fermentation conditions, and raw materials used [8].

Even though black tea is traditionally used as a major raw material for kombucha production, other kinds of tea, such as green tea, oolong tea, lemon balm tea, mulberry tea, jasmine tea, and peppermint tea, are also available [4]. Several homemade kombucha microbreweries have recently developed large-scale production and produced a range of differently flavored kombucha drinks. Several ingredients have been investigated and used as supplements or blends with kombucha tea, such as cherry [30], grape [31], thyme, lemon verbena, rosemary, fennel [32], wheatgrass [33], coconut water [34], banana peel, nettles [35], garlic [36], oak leaf [37], guava leaf [38], olive leaf, and honey [39]. These ingredients provide not only a flavor or aroma but also significant beneficial health effects, such as anti-inflammatory, hypoglycemic, antibacterial, antidiarrheal, and antioxidant properties.

3. Microorganisms Involved in Kombucha Fermentation

Kombucha prepared by mixing black tea and sucrose through biological fermentation using SCOBY is considered the most popular kombucha beverage. Generally, the microbiological composition of SCOBY varies with the source, geographical regions, cultivation medium, and fermentation conditions [4,16]. In general, SCOBY consists mainly of AAB, osmophilic yeasts, and a small number of LAB. The most prominent bacteria and yeasts in SCOBY are summarized in Table 1. These microorganisms play a vital role in creating various beneficial metabolites to enhance the quality of kombucha tea. For instance, yeasts simultaneously release invertase (β-fructofuranosidase) to hydrolyze complex sugars and sucrose into glucose and fructose and convert these sugars into ethanol via the glycolysis pathway. Some yeast species, such as *Brettanomyces bruxellensis*, can produce high contents of ethanol and acetic acid under aerobic conditions [40], or *Schizosaccharomyces pombe* can convert malic acid to ethanol [41]. Under high osmotic pressure, yeasts can produce sugar alcohol, i.e., glycerol, which AAB can further metabolize to dihydroxyacetone (DHA) [42]. AAB additionally utilizes ethanol and the remaining glucose and fructose to create various organic acids, such as acetic acid, gluconic acid, glucuronic acid, ascorbic acid, succinic acid, and other valuable substances, thereby reducing the ethanol and sugar content in the kombucha. In general, *Acetobacter* and *Komagataeibacter* prefer to oxidize ethanol rather than glucose, whereas *Gluconobacter* prefers glucose and glycerol [42]. The production of cellulose biofilm and D-saccharide acid-1,4 lactone (DSL) in kombucha is also associated with the presence of the AAB, particularly *Komagataeibacter* [8,43]. Furthermore, a group of homofermentative LAB can convert glucose into lactic acid via the Embden–Meyerhof–Parnas pathway, and heterofermentative LAB can utilize glucose via the pentose phosphate pathway and produce lactic acid, ethanol, and carbon dioxide as the primary metabolites [42]. Some LAB species also produce glucuronic acid and a promising detoxifying and antioxidant agent, DSL [43]. It has been reported that ethanol and acetic acid in kombucha can prevent the growth of pathogenic bacteria, thus protecting the contamination of kombucha from undesired pathogens [44].

Table 1. Microbial species mainly found in SCOBY for kombucha fermentation.

Microorganisms	Name	References
Acetic acid bacteria	*Acetobacter xylinum*	[45]
	Acetobacter aceti	[46]
	Acetobacter pausterianus, Acetobacter intermedius	[19,47,48]
	Acetobacter peroxydans	[17]
	Acetobacter pomorum, Acetobacter malorum	[19]
	Acetobacter tropicalis, Acetobacter senegalensis	[19,49]
	Acetobacter nitrogenifigens	[50,51]
	Gluconobacter oxydans	[17,49]
	Gluconacetobacter entanii	[21]
	Komagataeibacter europaeus	[17,46,49]
	Komagataeibacter kombuchae	[51]
	Komagataeibacter medellinensis	[49]
	Komagataeibacter nataicola	[49]
	Komagataeibacter rhaeticus	[19,49]
	Komagataeibacter saccharivorans	[46,49]
	Komagataeibacter xylinus	[49]
Lactic acid bacteria	*Bifidobacterium* sp., *Lactococcus* sp., *Leuconostoc* sp.,	[52]
	Lactobacillus kefiranofaciens	[53]
	Lactobacillus mali	[54]
	Lactiplantibacillus plantarum	
	Liquorilactobacillus nagelii	[49,52]
	Liquorilactobacillus satsumensis	[52]
	Limosilactobacillus fermentum	[46]
	Oenococcus oeni	[17]

Table 1. *Cont.*

Microorganisms	Name	References
Yeasts	*Arxula adeninivorans*	[46]
	Saccharomyces cerevisiae	[46,49,55]
	Saccharomyces bisporus	[56]
	Saccharomycodes ludwigii	[49,57]
	Schizosaccharomyces pombe	[19,49,58]
	Starmerella davenpoortii, Zygosaccharomyces bisporus	[49]
	Zygosaccharomyces rouxii	[59]
	Zygosaccharomyces bailii	[17,19,47,60]
	Zygosaccharomyces parabailii	[21]
	Zygosaccharomyces kombuchaensis	[60,61]
	Brettanomyces intermedius	[59]
	Brettanomyces bruxellensis	[17,19,49,58]
	Brettanomyces anomalus	[17,49]
	Brettanomyces claussenii	[62]
	Brettanomyces/Dekkera sp.	[63]
	Candida arabinofermentans	[19]
	Candida guilliermondii, Candida colleculosa, Candida kefyr, Candida krusei, Candida stellata	[57,58]
	Hanseniaspora valbyensis, Hanseniaspora vineae	[17,60]
	Kloeckera apiculata, Kluyeromyces africanus	[55]
	Pichia membranefaciens	[59]
	Torulaspora delbrueckii	[58,60]

The microbial community of kombucha is classically determined using culture-based methods, which involve morphological, physiological, and biochemical assays. For instance, the traditional classification of AAB includes cellular morphological analysis and biochemical tests, such as catalase, oxidation of ethanol or lactate, and hydrolysis of D-glucose analyses. Morphological tests using the wet-mount technique or carbon and nitrogen fermentation and assimilation tests using commercial yeast identification kits are needed for yeast identification [1]. However, these conventional techniques are time-consuming, labor-intensive, difficult to discriminate at species levels for closely related species, and unable to identify unculturable microbial species in kombucha samples [1,64].

The genotypic identification based on molecular techniques, which are generally more reliable and rapid, such as polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP), random amplified polymorphic DNA (RAPD), denaturing gradient gel electrophoresis (DGGE), and real-time PCR (qPCR), has been successfully used to detect and quantify the microbial community of kombucha cultures [1,65]. In addition, the current development of sequence-based analysis and high-throughput sequencing technologies known as next-generation sequencing (NGS) has provided an opportunity to examine the phylogenetic diversity, community composition and function, dynamic structural changes in SCOBY microbiota, and the relationships between microbial species in the communities with environmental factors, such as temperature, pH, osmotic pressure, ethanol or acetic acid stress [17,27,52,64,66–68]. Furthermore, NGS also offers some advantages, such as eliminating polymerase chain reaction (PCR) bias and recovering microbial genomes [69].

Based on the NGS-based amplicon (16S rRNA gene and Internal Transcribed Spacer [ITS]) sequencing using different sets of primers, such as 926f (5′-AAACTCAAKGAATTGACGG-3′) and 1062r (5′-CTCACRRCACGAGCTGAC-3′) for bacterial identification [70] or ITS1F (5′-CTTGGTCATTTAGAGGAAGTAA-3′) and ITS2R (5′-GCTGCGTTCTTCATCGATGC-3′) for fungal identification [71,72], and the development of new bioinformatics tools, the microbial community assembly, and function of microbial species, both culturable and unculturable, on kombucha fermentation can be identified and predicted. Several NGS-based microbiomes have been recently used to determine the microbial communities of kombucha SCOBY, dynamic changes, and their function during kombucha fermentation. For instance, Reva et al. [64] reported the application of DNA metabarcoding based on NGS to determine the composition of kombucha microbial cultures grown in different growth conditions. The authors stated that *Komagataeibacter* and *Gluconobacter* were the most predominant bacteria, and *Brettanomyces* and *Pichia* were the most dominant yeasts. Other bacteria that have never been described in kombucha microbial cultures, such as *Herbaspirillum* spp. and *Holomonas* spp., were also found to be minor but permanent community members. Zhao et al. [46] evaluated the microbial community of fermentation broth during kombucha fermentation using amplicon (16S rDNA and ITS) sequencing, and they mentioned that *Komagataeibacter*, *Acetobacter*, and *Lactobacillus* were the main bacterial genera, while *Saccharomyces* and *Arxula* were the most predominant fungal genera. Arikan et al. [68] determined the microbial composition of homemade kombucha fermentation from day 3 to day 15 using a combination of whole metagenome sequencing (WMS) and amplicon (16S rRNA gene and ITS1) sequencing. The authors stated that *Komagataeibacter* and *Zygosaccharomyces* were the dominant bacterial and fungal genera found in all kombucha samples at all time points. Furthermore, based on the gene prediction and functional annotation of the reconstructed genomes and plasmid metagenomes of these dominant species, various potential functional properties, such as vitamin production, copper binding, acidic tolerance, and antimicrobial production, were proposed. Harrison and Curtin [49] used DNA metabarcoding based on the high-throughput sequencing approaches to evaluate spatial homogeneity within a single commercial SCOBY, and taxonomic diversity across a large number of SCOBY starter cultures used by commercial kombucha brewers in North America, and they demonstrated that *Brettanomyces* and *Komagataeibacter* were the most prevalent and abundant yeast and bacteria, respectively. In addition, *Zygosaccharomyces*, *Lachancea*, and *Starmerella* were the major fungal genera of all kombucha SCOBY. Further information regarding microbial communities involved in kombucha fermentation and their identification and classification can be found in Wang et al. [1].

4. Chemical Compositions of Kombucha

There are significant changes in the chemical properties of kombucha during fermentation, particularly the component and concentration of the substances in kombucha undergoing a positive impact by some potential factors, such as tea types, the initial content of sugar and tea leaves, fermentation period, incubation temperature, concentration, and composition of SCOBY [4]. Chemical compositions in the kombucha products include not only polyphenols released from tea leaves but also a range of beneficial metabolites generated from the microbial collaboration activities of bacteria and yeasts in SCOBY during the fermentation process, such as organic acids, vitamins, organic nitrogens, enzymes, minerals, and other substances. The primary chemical substances in kombucha are summarized in Table 2 and Figure 2.

Table 2. Chemical compositions in kombucha beverages.

Component	Chemical	References
Organic acids	acetic acid, lactic acid, citric acid, gluconic acid, glucuronic acid, malic acid, tartaric acid, succinic acid, pyruvic acid, oxalic acid, butyric acid	[31,43,73,74]
Polyphenols	catechins [α-epicatechin, α-epicatechin-3-gallate (ECG), α-epigallocatechin (EGC), α-epigallocatechin-3-gallate (EGCG), α-gallocatechin, β-catechin], caffeine, theaflavin, thearubigins, gallotannins	[73,75,76]

Table 2. *Cont.*

Component	Chemical	References
Vitamins	vitamin B_1, B_2, B_6, B_9, B_{12}, C	[74,77,78]
Amino acids	isoleucine, leucine, lysine, methionine, phenylalanine, threonine, valine, tryptophan, alanine, arginine, aspartic acid, cysteine, glutamic acid, glycine, histidine, proline, serine, tyrosine	[79]
Proteins/organic nitrogen/hydrolytic enzymes	peptides, biogenic amines (ethylamine, choline, adenine, histamine tyramine, putrescine, cadaverine, β-phenylethylamine, tryptamine, spermidine, spermine), proteinase, peptidase, catalase	[80–82]
Minerals/anions	manganese, iron, nickel, copper, zinc, cobalt, nitrate, phosphate, sulfate, bromide, chloride, iodide, fluoride	[77,83,84]
Alcohol	Ethanol	[85]
Other substances	Flavonoids (quercetin, kaempferol, myricetin, rutin), alkaloids, purines, lipids, D-saccharic acid-1,4-lactone (DSL), carbon dioxide	[4,7]

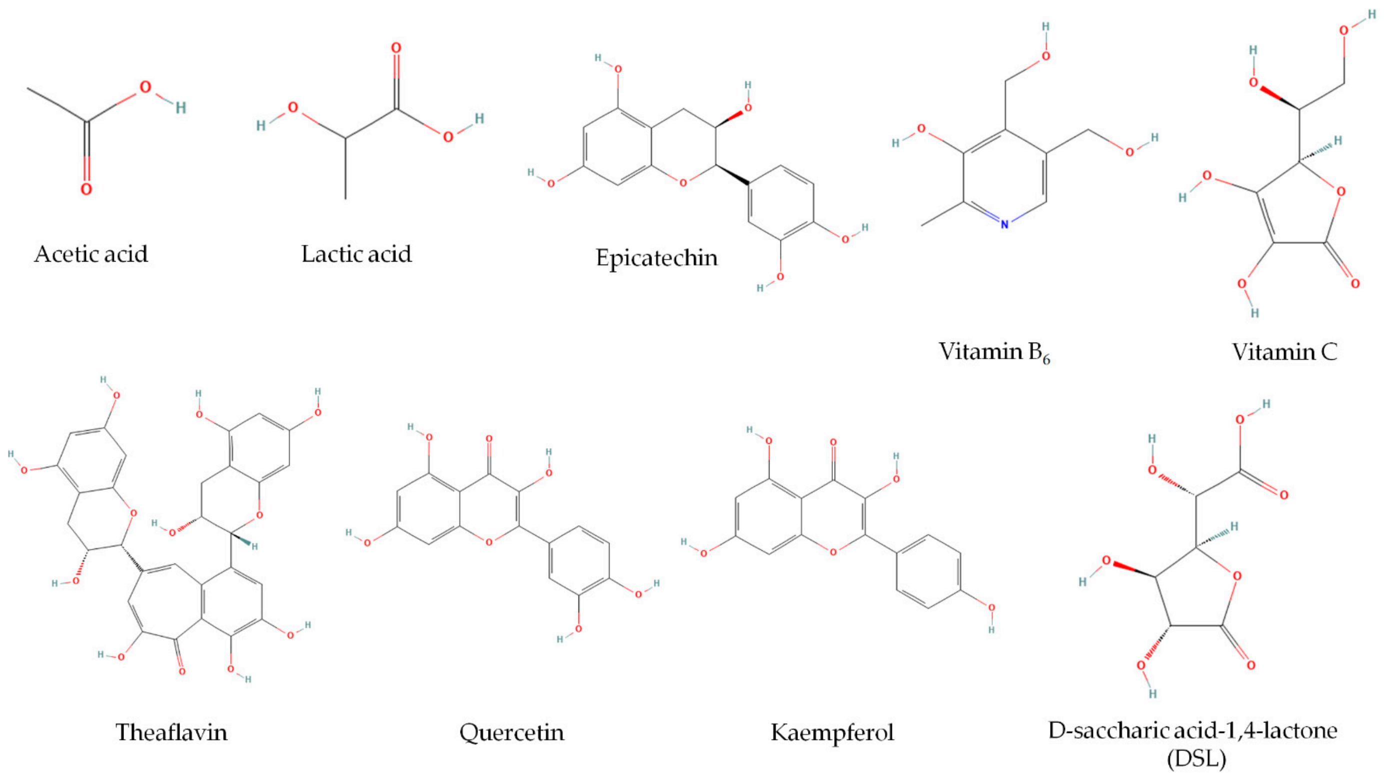

Figure 2. Chemical structures of some bioactive substances present in kombucha [86,87].

Black tea is a well-known nutritional beverage alternative to coffee or energy drinking due to its health properties, and it is commonly used as raw material for kombucha production. Black tea creates various bioactive properties, including theaflavins, thearubigins, volatile compounds, and alkaloids, through the fermentation period, as well as maintaining high levels of polyphenols from fresh tea leaves, such as catechins and flavonoids. In addition to promoting the health benefits and biological activity of kombucha, other teas, particularly green tea and oolong tea, are also potential choices for kombucha production because they have antioxidant, anticancer, antiaging, and anti-inflammatory activity as well as the ability to reduce neurodegenerative and cardiovascular diseases and support the immune system [7,14]. The health-promoting influences of green tea come mainly from phenolic and flavonoid compounds, such as α-epicatechin (EC), α-epicatechin-3-gallate (ECG), α-epigallocatechin (EGC), α-epigallocatechin-3-gallate (EGCG), α-gallocatechin, and catechin gallate. In particular, EGCG is the primary polyphenol in green tea, with antioxidant activity approximately 25–100 times higher than the antioxidant activity of vitamins C and E. Similarly, rooibos tea (*Asplathus linearis*), which has been consumed as a traditional medicine in southern Africa, seems to be an excellent option for kombucha fermentation. Rooibos tea consists of two major types: red tea as a conventional fermented form and white tea-unfermented form, which are widely used as a prolonged medicine to reduce allergies, asthma, and skin disorders in southern Africa. Rooibos tea is well known for its potent antioxidant ability, anti-inflammation, and biological activities due to its abundant phenolic and flavonoid components and high levels of dihydrochalcones aspalathin and nothofagin. In addition, oolong tea, a semifermented tea leaf, is also considered a promising raw material for kombucha production since it perfectly combines green tea's freshness and black tea's fragrance. Therefore, other tea types seem to be potential choices for kombucha production in terms of increasing the composition and content of health properties.

The initial concentration of bioactive substances in the raw material (tea leaves) can change due to the metabolic activity of the microbial community in SCOBY during kombucha fermentation. For instance, the contents of polyphenols and flavonoids in black tea kombucha fermented at 28 °C for 21 days increased compared to unfermented or sweetened black tea, which resulted from the degradation of the complex compounds into smaller substances by kombucha SCOBY [88]. Jafari et al. [89] reported an increase in black tea kombucha's phenolic content and antioxidant activity due to the rise of invertase activity during fermentation at room temperature for 14 days. Changes in the composition of phenolic compounds in black and green tea kombucha fermented at 25 °C for 10 days were also reported by Cardoso et al. [90], in which black tea kombucha exhibited more potent antioxidant activity than green tea kombucha, which resulted from a greater diversity of phenolic compounds in black tea during fermentation.

Several organic acids are found in kombucha beverages; however, the most predominant acids are acetic acid, lactic acid, gluconic acid, glucuronic acid, and ascorbic acid, which are generated during fermentation by the metabolic activity of kombucha SCOBY [9]. The composition and concentration of organic acids in kombucha vary depending on several parameters, such as the microbial community of kombucha starter cultures, the concentration of sugar and tea, and the temperature and time of fermentation [34,73,85,91]. A study by Kaewkod et al. [14] and Jakubczyk et al. [15] demonstrated that most of the organic acids start to be generated on day 7 of fermentation and reach a maximum level after 14 days. Furthermore, black tea kombucha possessed higher organic acids, such as acetic acid, gluconic acid, glucuronic acid, ascorbic acid, and D-saccharic acid-1,4-lactone (DSL), than oolong and green tea kombucha.

Many amino acids being identified in kombucha naturally come from tea leaves and are also generated during fermentation by the metabolic activity of microbial in kombucha SCOBY. A significantly large amount of amino acids in kombucha SCOBY are lysine, leucine, and isoleucine, while other amino acids, such as alanine, aspartic acid, glutamic acid, methionine, phenylalanine, proline, threonine, tryptophan, and valine are present at low levels [9]. A derivative of glutamine, theanine, which originates mainly from tea leaves accounting for 50% of the total amino acids, is also found in kombucha products [7]. Microbial decarboxylation during fermentation can transform amino acids into different types and concentrations of biogenic amines, depending on starting materials, microbial compositions, production process, and storage conditions [92]. Although many are essential for cellular metabolic activity, consumption at high levels of some biogenic amines, such as histamine tyramine, putrescine, cadaverine, b-phenylethylamine, tryptamine, spermidine, and spermine, may harm the human body [82].

Several techniques or platforms have been applied to determine bioactive substances in kombucha products. Some of the most widely used techniques or platforms are summarized in Table 3.

Table 3. Techniques or platforms widely used to determine bioactive compounds in kombucha products.

Component	Techniques or Platforms	References
Organic acids	High-performance liquid chromatography (HPLC) equipped with an Agilent ZORBAX® SB-C18 column and a UV detector	[93]
	HPLC equipped with a C18 column and a UV detector	[14]
Polyphenols (catechins), caffeine	HPLC equipped with a Waters Symmetry C18 column and a UV detector	[94]
	HPLC coupled with a photodiode array detector (HPLC-PDAD) and an Agilent Zorbax Eclipse XDB-C18 column	[95]
Sugars (sucrose, glucose, fructose)	HPLC equipped with a Waters XBridge™ Amdie column and an evaporative light-scattering detector	[96]
Pigments (anthocyanins)	HPLC equipped with an Agilent ZORBAX® SB-C18 column and a UV detector	[97]
Alcohol	Ebuliometer	[14]
	Alcoholometer	[15]
	Ultra-performance liquid chromatography (UPLC)	[12]
Volatile compounds	Gas chromatography–mass spectrometry (GC-MS)	[19,46]

5. Health Benefits of Kombucha

Kombucha has many beneficial effects on human health, such as detoxifying the blood and reducing cholesterol levels, blood pressure, kidney calcification, inflammatory problems, arthritis, rheumatism, gout symptoms, obesity, menstrual disorders, menopausal hot flashes, insomnia, stress, and nervous disturbances. Kombucha is also known to stimulate liver functions, glandular systems, the immune system, and interferon production; improve hair, skin, and nail health; improve eyesight; normalize intestinal activity and balance intestinal flora; and prevent the formation of bladder infections [4,44]. The beneficial effects of kombucha are known to be attributed to the metabolites released during the fermentation process. A few such health benefits are summarized in this review (Figure 3) based on available reports.

5.1. Antioxidant Activity

An antioxidant is defined as the ability of any substance to protect the cells against oxidation, a chemical reaction that generates free radicals, either in the form of scavenging properties of molecules, binding of pro-oxidant metals, or inhibition of pro-oxidant enzymes [98]. These antioxidant properties have been reported to be associated with health benefits, such as reducing cardiovascular disease and cancer cells, stimulating the immune system, and alleviating inflammation and arthritis [4]. Research studies on the health-promoting benefits of kombucha beverages proved that kombucha contains a high level of many compounds with antioxidant properties that are more elevated than those levels of nonfermented tea, such as polyphenols, catechins, ascorbic acid, and DSL. Polyphenols are reducing agents that have been considered potent antioxidants in protecting cells against oxidative stress by neutralizing free radicals and reactive oxygen species (ROS) [2]. The polyphenol content in kombucha varies depending on tea types, fermentation periods, and metabolic reactions during kombucha fermentation. Kaewkod et al. [14] demonstrated that kombucha produced using green, oolong, and black tea yielded the maximum level of polyphenols after 3 days of fermentation, while red and white tea exhibited the highest phenolic content after 14 days of fermentation. Green tea kombucha displayed greater total phenolic content than kombucha fermented using black tea [15]. Degirmencioglu et al. [39] demonstrated that the longer the fermentation, the higher the amounts of polyphenols generated. Supplementing other ingredients during fermentation also enhanced Kombucha's phenolic content and bioaccessibility, the quantity of a compound digested in the gastrointestinal tract to be obtainable for absorption. For instance, adding olive leaves and honey increased the bioaccessibility of phenolic and antioxidant activity of kombucha [39].

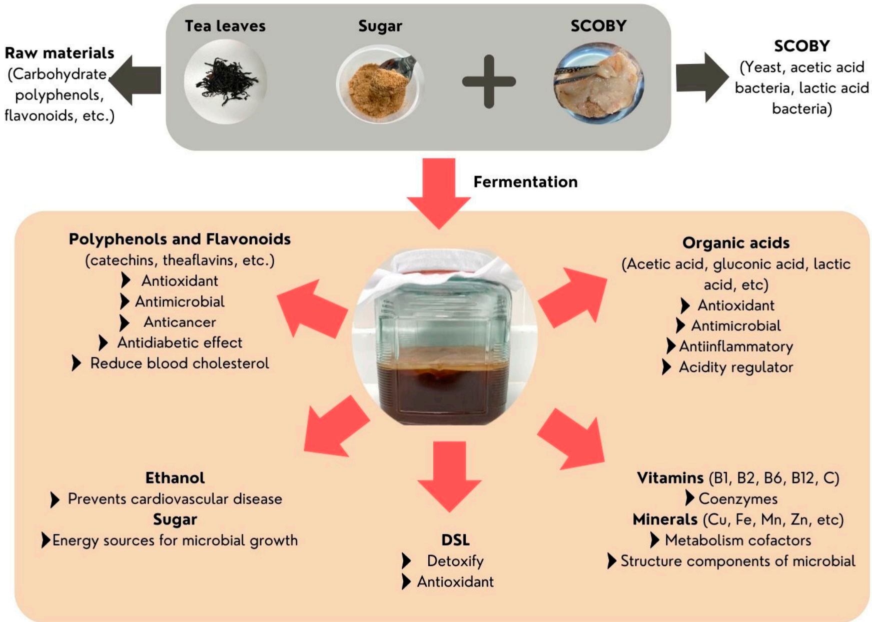

Figure 3. Kombucha beneficial compounds (modified from Leal et al. [9].

The complex mixture of phenolic compounds can be degraded into smaller and simpler molecules under an acidic environment due to the lowering pH value during kombucha fermentation or by the action of corresponding enzymes released from microbes in SCOBY, leading to an increase in phenolic content and promoting the antioxidant capacity of kombucha [2]. In addition, various organic acids formed during fermentation also have antioxidant, acidifying, anti-inflammatory, and antibacterial properties. Jakubczyk et al. [15] and Vohra et al. [99] demonstrated that the acetic acid content in the kombucha increased as fermentation time increased, which led to high antioxidant activity. Furthermore, black tea kombucha has been shown to have more significant organic acids than green and oolong tea kombucha [14].

It has also been reported that kombucha exhibited pro-oxidant potential, which can trigger a cascade of oxidative reactions leading to cellular damage [100]. An excess of antioxidants or the association of antioxidants and a particular molecule or ion can exhibit a pro-oxidant effect. For example, catechins, tocopherol, and some organic acids can cause a synergistic pro-oxidant effect [101]. In addition, the presence of Cu^{2+}, Fe^{3+}, or hydrogen peroxide (H_2O_2) with phenolic compounds and vitamin C also demonstrated a pro-oxidant potential [102].

5.2. Antimicrobial Activity

Kombucha has been reported to exhibit potent antimicrobial activity against a broad range of Gram-positive and Gram-negative microorganisms. The antimicrobial property of kombucha is correlated with various components found in kombucha tea, including polyphenols, organic acids, and other compounds released from raw material and microbial activity. Black tea kombucha has been shown to have not only high antibacterial activity to inhibit a wide range of foodborne pathogens but also high antifungal activity [103]. Other kombucha products made from green or oolong tea also displayed their antibacterial activity against pathogenic enteric bacteria, such as *Escherichia coli*, *E. coli* O157:H7, *Shigella dysenteriae*, *Salmonella typhi*, and *Vibrio cholera* [14]. Kaewkod et al. [14] also pointed out that the antibacterial components in kombucha are thermostable at 100 °C for 20 min. Cetojević-Simin et al. [104] demonstrated that kombucha tea supplemented with lemon balm (*Melissa officinalis* L.) exhibited a powerful antimicrobial ability to prevent the growth of various pathogenic microbes, such as Gram-negative bacteria (*Pseudomonas aeruginosa* (American Type Culture Collection (ATCC) 27853), *Proteus mirabilis* (ATCC 35659), *E. coli* (ATCC 25922), *S. enteritidis* (ATCC 13076), *Erwinia carotovora* (NCPPB 595), Gram-positive bacteria (*Staphylococcus aureus* ATCC 25923, *Bacillus cereus* ATCC 10876, *Sarcina lutea* ATCC 9341), yeasts (*Saccharomyces cerevisiae*, *Candida pseudotropicalis*, *Rhodotorula* sp.), and molds (*Aspergillus niger* ATCC 16404, *Penicillium aurantiogriseum*, and *A. flavus*). Most of the research studies proved that the antimicrobial activity is attributed primarily to the presence of various organic acids (particularly acetic acid) and the high level of phenolic compounds created during fermentation. In addition, kombucha has been reported to possibly contain antibiotic substances that have antimicrobial properties [105].

5.3. Anti-inflammatory and Anticancer Activities

Inflammation is a crucial process for protecting the human body from infections. Inflammation is also associated with many diseases that involve the maintenance of severe disorders, such as arthritis, asthma, and cardiovascular diseases. In particular, chronic inflammation has been described as related to the precancerous status, which leads to cancer, the most high-risk disease resulting in annual deaths worldwide. Therefore, anti-inflammatory properties have become a target for cancer prevention and therapy. In recent years, kombucha has been demonstrated to have anti-inflammatory and anticancer activities attributed to many polyphenols and other essential metabolites produced from a chain of metabolic reactions during fermentation. A study carried out by Četojević-Simin et al. [104] demonstrated that supplementation of kombucha with dried lemon balm leaves exhibited significant antigenotoxicity to human tumor cell lines with high antiproliferative activity on HeLa (human cervix cancer cell line), MCF7 (human breast cancer cell line), and HT-29 (human colon cancer cell line) compared to ordinary kombucha without supplementation. Some potential components, such as vitamin C, glucuronic acid, polyphenols, and lactic acid, are also attributed to the decrease in stomach cancer proliferation [106]. Jayabalan et al. [107] reported that black tea kombucha possessed the potential anticancer ability for various cancerous cells, such as A549 (human lung carcinoma), U2OS (human osteosarcoma), and 786-O (human renal carcinoma). They demonstrated that kombucha caused a toxicity effect on 786-O and U2OS cells and decreased matrix metalloproteinase (MMP-2 and MMP-9) activities in 786-O cells and MMP-2 activity in A549 cells as well as significantly inhibiting cell invasion and motility in all tested cancer cells. Based on this information, kombucha could be used as a promising treatment for various cancer cell types.

5.4. Other Benefits

Kombucha has been found to have a cytotoxic ability to destroy cancer cells, which is attributed to the efficient components presented in tea leaves and the metabolites released from SCOBY activity. Kaewkod et al. [14] demonstrated that black tea kombucha effectively displayed cytotoxicity on Caco-2 colorectal cancer cells greater than normal cells. The boiled black tea kombucha still revealed remarkable cytotoxicity against Caco-2 cancer cells. Additionally, the presence of various organic acids and the low pH value of kombucha products beneficially increase anticancer ability, particularly the toxicity of Caco-2 colorectal cancer cells. The cytotoxic effects of kombucha on human renal carcinoma, human osteosarcoma cells, and human lung carcinoma have also been reported [107]. In a mouse model, kombucha tea decreased the cytotoxicity induced by phenol [108]. The positive hepatoprotective capacity of kombucha to reduce liver damage through hepatotoxicity by toxic chemical substances has also been reported.

The presence of organic acids in the kombucha products also enhanced health benefits, such as body detoxification, maintaining hormonal balance, and improved bioavailability of phenolic compounds. Glucuronic acid, for example, is considered the most potent detoxifying metabolite, which can bind toxin substances in the liver, allowing their effective excretion [109]. Glucuronic acid is a precursor for vitamin C biosynthesis. It also takes part in glucuronization, which plays a crucial role in hormonal balances and helps increase the bioavailability of phenolic compounds, which in turn causes the neutralization of free radicals, preventing oxidative damage [110]. Lactic acid has been shown to positively impact human health by improving blood circulation and preventing the formation of blood clots. In addition, the lower pH of kombucha by lactic acid is also attributed to antimicrobial activity [44].

Based on clinical investigations in animal models, kombucha has a hepatoprotective effect on various liver contaminants [79,111]. Jung et al. [112] reported that black tea kombucha had positive effects in promoting intestinal microbes in mice that helped to reduce nonalcoholic fatty liver disease, the most common liver disorder. Microbial communities in SCOBY have been considered probiotics, which can balance digestion and absorption processes in the gut and improve the immune system. The micro cellulose present in kombucha also promotes the development of beneficial microorganisms in the intestine [113]. In addition, kombucha has also been reported to increase vitality, reduce skin inflammation, wrinkles, and acne, improve constipation, increase weight loss, and relieve arthritis [86,114].

6. Adverse Effects of Kombucha

Kombucha is generally considered a safe fermented beverage from a food safety point of view if it is well prepared, stored, and consumed. However, in some cases, mainly homemade kombucha, food safety issues should be a concern since some risks are associated with kombucha preparation and consumption. According to the International Association for Food Protection, the potential risks of kombucha include biological, chemical, and allergy hazards. Foodborne pathogens, for example, can occur throughout the kombucha preparation; thus, sterilizing the containers and utensils, utilizing boiled water to make the tea, and applying good quality SCOBY are recommended. Because of the low pH level of kombucha products, the corrosiveness of the vessels used to ferment and store them can also cause a potential chemical hazard that severely affects human health. Excessive consumption of the final product can cause lactic acidosis, an acid accumulation in the blood, to which people with compromised immune systems are more susceptible, heavy alcohol drinkers, and pregnant women [115,116]. Furthermore, kombucha has also been implicated in hyponatremia [117], toxic hepatitis [118], antiJo1 myositis [119], and cholestatic hepatitis [120].

7. Clinical Trials of Kombucha Health Benefits

The numerous health benefits of kombucha are mainly determined using in vitro and in vivo studies. Several human cell lines, such as Caco-2 colorectal cancer cells, human renal carcinoma, human osteosarcoma, and human lung carcinoma cells, have been tested for cytotoxicity of kombucha [14,107]. Based on the literature review described by Kapp et al. [116], the biological properties of kombucha have been evaluated using several animals, such as rats, mice, rabbits, chickens, ducks, dogs, pigs, and cattle. A recent study by Mallmann et al. [121] demonstrated that kombucha could increase high-density lipoprotein (HDL) levels in diabetic rats. To date, there is no report on empirical evidence of the health benefits of kombucha in human subjects [116]. Thus, clinical trials examining kombucha's potential human health benefits need to be addressed.

8. Conclusions and Prospects

Due to its various health-promoting properties, kombucha has recently become popular among healthy drinks. The raw material, mainly tea, and the microbial community in SCOBY play an essential role in forming several beneficial health substances, such as polyphenols, organic acids, amino acids, vitamins, minerals, and hydrolytic enzymes. Several health benefits of kombucha based on in vitro and in vivo studies have been documented, such as antioxidant, antimicrobial, anti-inflammatory, and anticancer activities, as well as other therapeutic properties in improving the human immune system and preventing some chronic diseases.

Most commercial kombucha products are naturally fermented using the indigenous microbial community highly present in SCOBY, which varies between each batch and is challenging to control. Thus, direct fermentation using high-potential selected strains of yeasts and bacteria may be needed for product quality control in large-scale production. In order to meet the needs of consumers, several ingredients have recently been used to supplement or blend with kombucha, which not only improves the flavor or aroma but also increases the health benefits of the finished products. In this sense, the health-beneficial properties of the blend or infusion products also need to be addressed. Since most of the health benefits of kombucha are claimed based on in vitro and in vivo studies, human clinical trials to provide the inside human health benefit of kombucha are also required, particularly the relationship between the biological functions and the active compounds of kombucha [1,116]. Although kombucha is generally considered a safe fermented beverage, improper preparation, storage and consumption may cause adverse effects on human health. Further studies on food safety issues, standardized process flow for brewing, consumer population, and consumption dosage are also recommended.

Author Contributions: Conceptualization, P.K., S.T., P.T. (Patcharaporn Tippayawat), M.Y. and P.T. (Pornthap Thanonkeo); resources, H.K., L.T.P. and P.T. (Pornthap Thanonkeo); writing—original draft preparation, H.K., L.T.P. and S.T.; writing—review and editing, P.K. and P.T. (Pornthap Thanonkeo); visualization, H.K. and S.T.; supervision, P.K., P.T. (Patcharaporn Tippayawat) and M.Y.; funding acquisition, P.T. (Pornthap Thanonkeo). All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Program Management Unit for Human Resources and Institutional Development, Research and Innovation (PMU-B), and the Research and Graduate Studies, Khon Kaen University, through the Research Program of the Fermentation Research Center for Value Added Agricultural Products (FerVAAPs). The authors thank the Research University Network (RUN) for the financial fund (Grant no.: RUN 2563-14).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: The authors thank the Faculty of Technology and Khon Kaen University for a scholarship to L.T.P. and the Program Management Unit for Human Resources and Institutional Development, Research and Innovation (PMU-B) for the postdoctoral training program supporting H.K. (KKU-PMU-C). We also thank the Research and Graduate Studies, Khon Kaen University, through the Research Program of the Fermentation Research Center for Value Added Agricultural Products (FerVAAPs), and the Research University Network (RUN) for the financial fund (Grant no.: RUN 2563-14).

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

References

1. Wang, B.; Rutherfurd-Markwick, K.; Zhang, X.X.; Mutukumira, A.N. Kombucha: Production and microbiological research. *Foods* **2022**, *11*, 3456. [CrossRef]
2. Srihari, T.; Satyanarayana, U. Changes in free radical scavenging activity of kombucha during fermentation. *J. Pharm. Sci. Res.* **2012**, *4*, 1978–1981.
3. Sreeramulu, G.; Zhu, Y.; Knol, W. Kombucha fermentation and its antimicrobial activity. *J. Agric. Food Chem.* **2000**, *48*, 2589–2594. [CrossRef]
4. Jayabalan, R.; Malbaša, R.V.; Loncar, E.S.; Vitas, J.S.; Sathishkumar, M. A review on kombucha tea–microbiology, composition, fermentation, beneficial effects, toxicity, and tea fungus. *Compr. Rev. Food Sci.* **2014**, *13*, 538–550. [CrossRef] [PubMed]
5. Dutta, H.; Paul, S.K. Kombucha drink: Production, quality, and safety aspects. In *Production and Management of Beverages*; Grumezescu, A.M., Holban, A.M., Eds.; Woodhead Publishing: Sawston, UK, 2019; pp. 259–288.
6. Kim, J.; Adhikari, K. Current trends in kombucha: Marketing perspectives and the need for improved sensory research. *Beverages* **2020**, *6*, 15. [CrossRef]
7. Sen, G.; Sarkar, N.; Nath, M.; Maity, S. Bioactive components of tea. *Arch. Food Nutr. Sci.* **2020**, *4*, 001–009.
8. Villarreal-Soto, S.A.; Beaufort, S.; Bouajila, J.; Souchard, J.P.; Taillandier, P. Understanding kombucha tea fermentation: A review. *J. Food Sci.* **2018**, *83*, 580–588. [CrossRef]
9. Leal, J.M.; Suárez, L.V.; Jayabalan, R.; Oros, J.H.; Escalante-Aburto, A. A review on health benefits of kombucha nutritional compounds and metabolites. *CYTA—J. Food* **2018**, *16*, 390–399. [CrossRef]
10. Applegate, K.B.; Cheek, P.R.; Inlow, J.K. Analysis of kombucha to teach biochemical concepts and techniques to undergraduate students. *Biochem. Mol. Biol. Educ.* **2019**, *47*, 459–467. [CrossRef]
11. Chakravorty, S.; Bhattacharya, S.; Bhattacharya, D.; Sarkar, S.; Gachhui, R. Kombucha: A promising functional beverage prepared from tea. In *Nonalcoholic Beverages*; Grumezescu, A.M., Holban, A.M., Eds.; Woodhead Publishing: Sawston, UK, 2019; pp. 285–327.
12. Villarreal-Soto, S.A.; Beaufort, S.; Bouajila, J.; Souch, J.P.; Renard, T.; Rollan, S.; Taillandier, P. Impact of fermentation conditions on the production of bioactive compounds with anticancer, anti-inflammatory and antioxidant properties in kombucha tea extracts. *Process Biochem.* **2019**, *83*, 44–54. [CrossRef]
13. Leal, J.M.; Garcia, N.P.; Escalante-Aburto, A. Recent evidence of the beneficial effects associated with glucuronic acid contained in kombucha beverages. *Curr. Nutr. Rep.* **2020**, *9*, 163–170. [CrossRef] [PubMed]
14. Kaewkod, T.; Bovonsombut, S.; Tragoolpua, Y. Efficacy of kombucha obtained from green, oolong, and black teas on inhibition of pathogenic bacteria, antioxidation, and toxicity on colorectal cancer cell line. *Microorganisms* **2019**, *7*, 700. [CrossRef] [PubMed]
15. Jakubczyk, K.; Kalduñska, J.; Kochman, J.; Janda, K. Chemical profile and antioxidant activity of the kombucha beverage derived from white, green, black and red tea. *Antioxidants* **2020**, *9*, 447. [CrossRef]
16. Watawana, M.I.; Jayawardena, N.; Gunawardhana, C.B.; Waisundara, V.Y. Health, wellness, and safety aspects of the consumption of kombucha. *J. Chem.* **2015**, *2015*, 591869. [CrossRef]
17. Coton, M.; Pawtowski, A.; Taminiau, B.; Burgaud, G.; Deniel, F.; Coulloumme-Labarthe, L.; Fall, A.; Daube, G.; Coton, E. Unraveling microbial ecology of industrial-scale kombucha fermentations by metabarcoding and culture-based methods. *FEMS Microbiol. Ecol.* **2017**, *1*, 93. [CrossRef]
18. de Oliveira, I.A.C.L.; Rolim, V.A.O.; Gaspar, R.P.L.; Rossini, D.Q.; de Souza, R.; Bogsan, C.S.B. The technological perspectives of kombucha and its implications for production. *Fermentation* **2022**, *8*, 185. [CrossRef]
19. Villarreal-Soto, S.A.; Bouajila, J.; Pace, M.; Leech, J.; Cotter, P.D.; Souchard, J.P.; Taillandier, P.; Beaufort, S. Metabolome-microbiome signatures in the fermented beverage, kombucha. *Int. J. Food Microbiol.* **2020**, *333*, 108778. [CrossRef]
20. Ivanišová, E.; Menhartová, K.; Terentjeva, M.; Harangozo, L.; Kántor, A.; Kacaniová, M. The evaluation of chemical, antioxidant, antimicrobial and sensory properties of kombucha tea beverage. *J. Food Sci. Technol.* **2020**, *57*, 1840–1846. [CrossRef]
21. Gaggia, F.; Baffoni, L.; Galiano, M.; Nielsen, D.S.; Jakobsen, R.R.; Castro-Mejia, J.L.; Bosi, S.; Truzzi, F.; Musumeci, F.; Dinelli, G.; et al. Kombucha beverage from green, black and rooibos teas: A comparative study looking at microbiology, chemistry and antioxidant activity. *Nutrients* **2018**, *11*, 1. [CrossRef]
22. Ahmed, R.F.; Hikal, M.S.; Abou-Taleb, K.A. Biological, chemical and antioxidant activities of different types kombucha. *Ann. Agric. Sci.* **2020**, *65*, 35–41. [CrossRef]
23. Salvadó, Z.; Arroyo-López, F.N.; Guillamón, J.M.; Salazar, G.; Querol, A.; Barrio, E. Temperature adaptation markedly determines evolution within the genus Saccharomyces. *Appl. Environ. Microbiol.* **2011**, *77*, 2292–2302. [CrossRef] [PubMed]
24. Mamlouk, D.; Gullo, M. Acetic acid bacteria: Physiology and carbon sources oxidation. *Indian J. Microbiol.* **2013**, *53*, 377–384. [CrossRef] [PubMed]
25. Matejceková, Z.; Liptáková, D.; Spodniaková, S.; Valik, L. Characterization of the growth of *Lactobacillus plantarum* in milk in dependence on temperature. *Acta Chim. Slovaca* **2016**, *9*, 104–108. [CrossRef]
26. Thavasi, V.; Bettens, R.P.A.; Leong, L.P. Temperature and solvent effects on radical scavenging ability of phenols. *J. Phys. Chem. A* **2009**, *113*, 3068–3077. [CrossRef]
27. De Filippis, F.; Troise, A.D.; Vitaglione, P.; Ercolini, D. Different temperatures select distinctive acetic acid bacteria species and promotes organic acids production during kombucha tea fermentation. *Food Microbiol.* **2018**, *73*, 11–16. [CrossRef]
28. Hur, S.J.; Lee, S.Y.; Kim, Y.C.; Choi, I.; Kim, G.B. Effect of fermentation on the antioxidant activity in plant-based foods. *Food Chem.* **2014**, *160*, 346–356. [CrossRef]

29. Šaponjac, V.T.T.; Vulic, J.J. Antioxidant and antibacterial activity of the beverage obtained by fermentation of sweetened lemon balm (Melissa officinalis L.) tea with symbiotic consortium of bacteria and yeasts. *Food Technol. Biotechnol.* **2014**, *52*, 420–429.
30. Yavari, N.; Assadi, M.M.; Larijani, K.; Moghadam, M.B. Response surface methodology for optimization of glucuronic acid production using kombucha layer on sour cherry juice. *Aust. J. Basic Appl. Sci.* **2010**, *4*, 3250–3256.
31. Yavari, N.; Assadi, M.M.; Moghadam, M.B.; Larijani, K. Optimizing glucuronic acid production using tea fungus on grape juice by response surface methodology. *Aust. J. Basic Appl. Sci.* **2011**, *5*, 1788–1794.
32. Battikh, H.; Bakhrouf, A.; Ammar, E. Antimicrobial effect of kombucha analogues. *LWT—Food Sci. Technol.* **2012**, *47*, 71–77. [CrossRef]
33. Sun, T.Y.; Li, J.S.; Chen, C. Effects of blending wheatgrass juice on enhancing phenolic compounds and antioxidant activities of traditional kombucha beverage. *J. Food Drug Anal.* **2015**, *23*, 709–718. [CrossRef] [PubMed]
34. Watawana, M.I.; Jayawardena, N.; Gunawardhana, C.B.; Waisundara, V.Y. Enhancement of the antioxidant and starch hydrolase inhibitory activities of king coconut water (*Cocos nucifera* var. Aurantiaca) by fermentation with kombucha "tea fungus". *Int. J. Food Sci. Technol.* **2016**, *51*, 490–498. [CrossRef]
35. Pure, A.E.; Pure, M.E. Antioxidant and antibacterial activity of kombucha beverages prepared using banana peel, common nettles and black tea infusions. *Appl. Food Biotechnol.* **2016**, *3*, 125–130.
36. Pure, A.E.; Pure, M.E. Antioxidant, antibacterial and color analysis of garlic fermented in kombucha and red grape vinegar. *Appl. Food Biotechnol.* **2016**, *3*, 246–252.
37. Vazquez-Cabral, B.D.; Larrosa-Pérez, M.; Gallegos-Infante, J.A.; Moreno-Jiménez, M.R.; González-Laredo, R.F.; Rutiaga-Quiñones, J.G.; Gamboa-Gómez, C.I.; Rocha-Guzmán, N.E. Oak kombucha protects against oxidative stress and inflammatory processes. *Chem. Biol. Interact.* **2017**, *272*, 1–9. [CrossRef] [PubMed]
38. Moreno-Jiménez, M.R.; Rocha-Guzmán, N.E.; Rutiaga-Quiñones, G.J.; Medrano-Núñez, D.; Rojas-Contreras, J.A.; González-Laredo, R.F.; Gallegos-Infante, J.A. Polyphenolic profile, sugar consumption and organic acids generation along fermentation of infusions from guava (Pisidium guajava) by the kombucha consortium. *Recent Res. Sci. Technol.* **2018**, *10*, 16–22.
39. Degirmencioglu, N.; Yildiz, E.; Guldas, M.; Gurbuz, O. Health benefits of kombucha tea enriched with olive leaf and honey. *J. Obes. Chronic Dis.* **2020**, *4*, 1–5. [CrossRef]
40. Agnolucci, M.; Tirelli, A.; Cocolin, L.; Toffanin, A. Brettanomyces bruxellensis yeasts: Impact on wine and winemaking. *World J. Microbiol. Biotechnol.* **2017**, *33*, 180. [CrossRef]
41. Loira, I.; Morata, A.; Palomero, F.; González, C.; Suárez-Lepe, J.A. Schizosaccharomyces pombe: A promising biotechnology for modulating wine composition. *Fermentation* **2018**, *4*, 70. [CrossRef]
42. Laureys, D.; Britton, S.J.; De Clippeleer, J. Kombucha tea fermentation: A review. *J. Am. Soc. Brew. Chem.* **2020**, *78*, 165–174. [CrossRef]
43. Yang, Z.; Zhou, F.; Ji, B.; Li, B.; Luo, Y.; Yang, L.; Li, T. Symbiosis between microorganisms from kombucha and kefir: Potential significance to the enhancement of kombucha function. *Appl. Biochem. Biotechnol.* **2010**, *160*, 446–455. [CrossRef] [PubMed]
44. Dufresne, C.; Farnworth, E. Tea, kombucha, and health: A review. *Food Res. Int.* **2000**, *33*, 409–421. [CrossRef]
45. Sievers, M.; Lanini, C.; Weber, A.; Schuler-Schmid, U.; Teuber, M. Microbiology and fermentation balance in kombucha beverage obtained from a tea fungus fermentation. *Syst. Appl. Microbiol.* **1995**, *18*, 590–594. [CrossRef]
46. Zhao, Z.J.; Sui, Y.C.; Wu, H.W.; Zhou, C.B.; Hu, X.C.; Zhang, J. Flavour chemical dynamics during fermentation of kombucha tea. *Emir. J. Food Agric.* **2018**, *30*, 732–741.
47. Goh, W.N.A.; Rosma, A.; Kaur, B.; Fazilah, B.; Karim, A.A.; Bhat, R. Fermentation of black tea broth (kombucha): I. Effects of sucrose concentration and fermentation time on yield of microbial cellulose. *Int. Food Res. J.* **2012**, *19*, 109–117.
48. Boesch, T.; Trcek, J.; Sievers, M.; Teuber, M. *Acetobacter intermedius*, sp. *nov. Syst. Appl. Microbiol.* **1998**, *21*, 220. [CrossRef]
49. Harrison, K.; Curtin, C. Microbial composition of SCOBY starter cultures used by commercial kombucha brewers in North America. *Microorganisms* **2021**, *9*, 1060. [CrossRef]
50. Dutta, D.; Gachhui, R. Novel nitrogen-fixing Acetobacter nitrogenifigens sp. nov., isolated from kombucha tea. *Int. J. Syst. Evol. Microbiol.* **2006**, *56*, 1899–1903. [CrossRef]
51. Dutta, D.; Gachhui, R. Nitrogen-fixing and cellulose-producing Gluconacetobacter kombuchae sp. nov., isolated from kombucha tea. *Int. J. Syst. Evol. Microbiol.* **2007**, *57*, 353–357. [CrossRef]
52. Marsh, A.J.; O'Sullivan, O.; Hill, C.; Ross, R.P.; Cotter, P.D. Sequence-based analysis of the bacterial and fungal compositions of multiple kombucha (tea fungus) samples. *Food Microbiol.* **2014**, *38*, 171–178. [CrossRef]
53. Yang, J.; Lagishetty, V.; Kurnia, P.; Henning, S.M.; Ahdoot, A.I.; Jacobs, J.P. Microbial and chemical profiles of commercial kombucha products. *Nutrients* **2022**, *14*, 670. [CrossRef] [PubMed]
54. Pei, J.; Jin, W.; Abd El-Aty, A.; Baranenko, D.A.; Gou, X.; Zhang, H.; Geng, J.; Jiang, L.; Chen, D.; Yue, T. Isolation, purification, and structural identification of a new bacteriocin made by Lactobacillus plantarum found in conventional kombucha. *Food Control* **2020**, *110*, 106923. [CrossRef]
55. Safak, S.; Mercan, N.; Aslim, B.; Beyatli, Y. A study on the production of poly-beta-hydroxybutyrate by some eukaryotic microorganisms. *Turk. Electron. J. Biotechnol.* **2002**, 11–17.
56. Markov, S.L.; Malbaša, R.V.; Hauk, M.J.; Cvetkovic, D.D. Investigation of tea fungus microbe associations. I. The yeast. *Acta Period. Technol.* **2001**, *32*, 133–138.

57. Ramadani, A.S.; Abulreesh, H.H. Isolation and identification of yeast flora in local kombucha sample: Al Nabtah. *Umm Al-Qura Univ. J. App. Sci.* **2010**, *2*, 42–51.
58. Teoh, A.L.; Heard, G.; Cox, J. Yeast ecology of kombucha fermentation. *Int. J. Food Microbiol.* **2004**, *95*, 119–126. [CrossRef]
59. Herrera, T.; Calderon-Villagomez, A. Species of yeasts isolated in Mexico from the tea fungus. *Rev. Mex. Micol.* **1989**, *5*, 205–210.
60. Bellut, K.; Michel, M.; Zarnkow, M.; Hutzler, M.; Jacob, F.; De Schutter, D.P.; Daenen, L.; Lynch, K.M.; Zannini, E.; Arendt, E.K. Application of non-Saccharomyces yeasts isolated from kombucha in the production of alcohol-free beer. *Fermentation* **2018**, *4*, 66. [CrossRef]
61. Kurtzman, C.P.; Robnett, C.J.; Basehoar-Powers, E. Zygosaccharomyces kombuchaensis, a new ascosporogenous yeast from "Kombucha tea". *FEMS Yeast Res.* **2001**, *1*, 133–138. [CrossRef]
62. Jayabalan, R.; Subathradevi, P.; Marimuthu, S.; Sathishkumar, M.; Swaminathan, K. Changes in free-radical scavenging ability of kombucha tea during fermentation. *Food Chem.* **2008**, *109*, 227–234. [CrossRef]
63. Tu, C.; Tang, S.; Azi, F.; Hu, W.; Dong, M. Use of kombucha consortium to transform soy whey into a novel functional beverage. *J. Funct. Foods.* **2019**, *52*, 81–89. [CrossRef]
64. Reva, O.N.; Zaets, I.E.; Ovcharenko, L.P.; Kukharenko, O.E.; Shpylova, S.P.; Podolich, O.V.; de Vera, J.P.; Kozyrovska, N.O. Metabarcoding of the kombucha microbial community grown in different microenvironments. *AMB Express* **2015**, *5*, 124. [CrossRef] [PubMed]
65. Andrés-Barrao, C.; Barja, F.; Pérez, R.O.; Chappuis, M.L.; Braito, S. Identification techniques of acetic acid bacteria: Comparison between MALDI-TOF MS and molecular biology technique. In *Acetic Acid Bacteria*; CRC Press: Boca Raton, FL, USA, 2017; pp. 162–192.
66. Shade, A.; Caporaso, G.; Handelsman, J.; Knight, R.; Fierer, N. A meta-analysis of changes in bacterial and archaeal communities with time. *ISME J.* **2013**, *7*, 1493–1506. [CrossRef]
67. Chakravorty, S.; Bhattacharya, S.; Chatzinotas, A.; Chakraborty, W.; Bhattacharya, D.; Gachhui, R. Kombucha tea fermentation: Microbial and biochemical dynamics. *Int. J. Food Microbiol.* **2016**, *220*, 63–72. [CrossRef] [PubMed]
68. Arikan, M.; Mitchell, A.; Finn, R.D.; Gürel, F. Microbial composition of kombucha determined using amplicon sequencing and shotgun metagenomics. *J. Food Sci.* **2020**, *85*, 455–464. [CrossRef]
69. De Filippis, F.; Parente, E.; Ercolini, D. Metagenomics insights into food fermentations. *Microb. Biotechnol.* **2017**, *10*, 91–102. [CrossRef] [PubMed]
70. Unban, K.; Khatthongngam, N.; Pattananandecha, T.; Saenjum, C.; Shetty, K.; Khanongnuch, C. Microbial community dynamics during the non-filamentous fungi growth-based fermentation process of miang, a traditional fermented tea of north Thailand and their product characterizations. *Front. Microbiol.* **2020**, *11*, 1515. [CrossRef] [PubMed]
71. Gardes, M.; Bruns, T.D. ITS primers with enhanced specificity for basidiomycetes-application to the identification of mycorrhizae and rusts. *Mol. Ecol.* **1993**, *2*, 113–118. [CrossRef]
72. White, T.J.; Bruns, T.; Lee, S.; Taylor, J. Amplification and direct sequencing of fungal ribosomal RNA genes for phylogenetics. In *PCR Protocols: A Guide to Methods and Applications*; Elsevier: New York, NY, USA, 1990; pp. 315–322.
73. Jayabalan, R.; Marimuthu, S.; Swaminathan, K. Changes in content of organic acids and tea polyphenols during kombucha tea fermentation. *Food Chem.* **2007**, *102*, 392–398. [CrossRef]
74. Malbasa, R.V.; Loncar, E.S.; Vitas, J.S.; Canadanovic-Brunet, J.M. Influence of starter cultures on the antioxidant activity of kombucha beverage. *Food Chem.* **2011**, *127*, 1727–1731. [CrossRef]
75. Morshedi, A.; Dashti-Rahmatabadi, M.H. Chronic consumption of kombucha and black tea prevents weight loss in diabetic rats. Iran. J. *Diabetes Obes.* **2010**, *2*, 23–26.
76. Sharma, V.K.; Bhattacharya, A.; Kumar, A.; Sharma, H.K. Health benefits of tea consumption. *Trop. J. Pharm. Res.* **2007**, *6*, 785–792. [CrossRef]
77. Bauer-Petrovska, B.; Petrushevska-Tozi, L. Mineral and water soluble vitamin content in the kombucha drink. *Int. J. Food Sci. Technol.* **2000**, *35*, 201–205. [CrossRef]
78. Vitas, J.S.; Malbasa, R.V.; Grahovac, J.A.; Loncar, E.S. The antioxidant activity of kombucha fermented milk products with stinging nettle and winter savory. *Chem. Ind. Chem. Eng. Q.* **2013**, *19*, 129–139. [CrossRef]
79. Jayabalan, R.; Baskaran, S.; Marimuthu, S.; Swaminathan, K.; Yun, S.E. Effect of kombucha tea on aflatoxin B1 induced acute hepatotoxicity in albino rats-prophylatic and curative studies. J. *Korean Soc. Appl. Biol. Chem.* **2010**, *53*, 407–416. [CrossRef]
80. Gonzalez-Gonzalez, C.R.; Tuohy, K.M.; Jauregi, P. Production of angiotensin-I-converting enzyme (ACE) inhibitory activity in milk fermented with probiotic strains: Effects of calcium, pH and peptides on the ACE-inhibitory activity. *Int. Dairy J.* **2011**, *21*, 615–622. [CrossRef]
81. Elkhtab, E.; El-Alfy, M.; Shenana, M.; Mohamed, A.; Yousef, A.E. New potentially antihypertensive peptides liberated in milk during fermentation with selected lactic acid bacteria and kombucha cultures. *J. Dairy Sci.* **2017**, *100*, 9508–9520. [CrossRef]
82. Vinci, G.; Maddaloni, L. Biogenic amines in alcohol-free beverages. *Beverages* **2020**, *6*, 17. [CrossRef]
83. Chu, S.C.; Chen, C. Effects of origins and fermentation time on the antioxidant activities of kombucha. *Food Chem.* **2006**, *98*, 502–507. [CrossRef]
84. Kumar, S.D.; Narayan, G.; Hassarajani, S. Determination of anionic minerals in black and kombucha tea using ion chromatography. *Food Chem.* **2008**, *111*, 784–788. [CrossRef]

85. Chen, C.; Liu, B.Y. Changes in major components of tea fungus metabolites during prolonged fermentation. *J. Appl. Microbiol.* **2000**, *89*, 834–839. [CrossRef] [PubMed]
86. Bishop, P.; Pitts, E.R.; Budner, D.; Thompson-Witrick, K.A. Chemical composition of kombucha. *Beverages* **2022**, *8*, 45. [CrossRef]
87. Kim, S.; Chen, J.; Cheng, T.; Gindulyte, A.; He, J.; He, S.; Li, Q.; Shoemaker, B.A.; Thiessen, P.A.; Yu, B.; et al. PubChem in 2021: New data content and improved web interfaces. *Nucleic Acids Res.* **2021**, *49*, D1388–D1395. [CrossRef]
88. Bhattacharya, D.; Bhattacharya, S.; Patra, M.M.; Chakravorty, S.; Sarkar, S.; Chakraborty, W.; Koley, H.; Gachhui, R. Antibacterial activity of polyphenolic fraction of kombucha against enteric bacterial pathogens. *Curr. Microbiol.* **2016**, *73*, 885–896. [CrossRef] [PubMed]
89. Jafari, R.; Naghavi, N.S.; Khosravi-Darani, K.; Doudi, M.; Shahanipour, K. Kombucha microbial starter with enhanced production of antioxidant compounds and invertase. *Biocatal. Agric. Biotechnol.* **2020**, *29*, 101789. [CrossRef]
90. Cardoso, R.R.; Neto, R.O.; dos Santos D'Almeida, C.T.; do Nascimento, T.P.; Pressete, C.G.; Azevedo, L.; Martino, H.S.D.; Cameron, L.C.; Ferreira, M.S.L.; Barros, F.A.R. Kombuchas from green and black teas have different phenolic profile, with impacts their antioxidant capacities, antibacterial and antiproliferative activities. *Food Res. Int.* **2020**, *128*, 108782. [CrossRef]
91. Nguyen, N.K.; Nguyen, P.B.; Nguyen, H.T.; Le, P.H. Screening the optimal ratio of symbiosis between isolated yeast and acetic acid bacteria strain from traditional kombucha for high-level production of glucuronic acid. *LWT Food Sci. Technol.* **2015**, *64*, 1149–1155. [CrossRef]
92. Ruiz-Capillas, C.; Herrero, A. Impact of biogenic amines on food quality and safety. *Foods* **2019**, *8*, 62. [CrossRef]
93. Utoiu, E.; Matei, F.; Toma, A.; Diguta, C.; Stefan, L.; Manoiu, S.; Vrajmasu, V.V.; Moraru, I.; Oancea, A.; Israel-Roming, F.; et al. Bee collected pollen with enhanced health benefits, produced by fermentation with a kombucha consortium. *Nutrients* **2018**, *10*, 1365. [CrossRef]
94. Cao, Q.Q.; Zou, C.; Zhang, Y.H.; Du, Q.Z.; Yin, J.F.; Shi, J.; Xue, S.; Xu, Y.Q. Improving the taste of autumn green tea with tannase. *Food Chem.* **2019**, *277*, 432–437. [CrossRef]
95. Zhou, D.D.; Saimaiti, A.; Luo, M.; Huang, S.Y.; Xiong, R.G.; Shang, A.; Gan, R.Y. Fermentation with tea residues enhances antioxidant activities and polyphenol contents in kombucha beverages. *Antioxidants* **2022**, *11*, 155. [CrossRef] [PubMed]
96. Al-Suod, H.; Gadzaia-Kopeiuch, R.; Buszewski, B. Simultaneous HPLC-ELSD determination of sugars and cyclitols in different parts of Phacelia tanacelifolia Benth. *Biochem. Syst. Ecol.* **2018**, *80*, 32–38. [CrossRef]
97. Jiang, L.; Shen, X.; Shoji, T.; Kanda, T.; Zhou, J.; Zhao, L. Characterization and activity of anthocyanins in Zijuan tea (Camellia sinensis var. Kitamura). *J. Agri. Food Chem.* **2013**, *61*, 3306–3310. [CrossRef] [PubMed]
98. Shebis, Y.; Iluz, D.; Kinel-Tahan, Y.; Dubinsky, Z.; Yehoshua, Y. Natural antioxidants: Function and sources. *Food Nutr. Sci.* **2013**, *4*, 643–649. [CrossRef]
99. Vohra, B.M.; Fazry, S.; Sairi, F.; Babul-Airianah, O. Effects of medium variation and fermentation time on the antioxidant and antimicrobial properties of kombucha. *Malays. J. Fund. Appl. Sci.* **2019**, *15*, 298–302. [CrossRef]
100. Oliveira, J.T.; da Costa, F.M.; da Silva, T.G.; Simoes, G.D.; Pereira, E.S.; da Costa, P.Q.; Andreazza, R.; Schenkel, P.C.; Pieniz, S. Green tea and kombucha characterization: Phenolic composition, antioxidant capacity and enzymatic inhibition potential. *Food Chem.* **2023**, *408*, 135206. [CrossRef]
101. Antony, J.I.X.; Shankaranaryana, M.L. Polyphenols of green tea. *Int. Food Ingred.* **1997**, *5*, 47–50.
102. Yen, G.C.; Chen, H.Y.; Peng, H.H. Antioxidant and prooxidant effects of various tea extracts. *J. Agri. Food Chem.* **1997**, *45*, 30–34. [CrossRef]
103. Battikh, H.; Chaieb, K.; Bakhrouf, A.; Ammar, E. Antibacterial and antifungal activities of black and green kombucha teas. *J. Food Biochem.* **2013**, *37*, 231–236. [CrossRef]
104. Cetojevic-Simin, D.D.; Velicanski, A.S.; Cvetkovic, D.D.; Markov, S.L.; Mrdanovic, J.Z.; Bogdanovic, V.V.; Solajic, S.V. Bioactivity of lemon balm kombucha. *Food Bioprocess Technol.* **2012**, *5*, 1756–1765. [CrossRef]
105. Deghrigue, M.; Chriaa, J.; Battikh, H.; Abid, K.; Bakhrouf, A. Antiproliferative and antimicrobial activities of kombucha tea. *Afr. J. Microbiol. Res.* **2013**, *7*, 3466–3470.
106. Xia, X.; Dai, Y.; Wu, H.; Liu, X.; Wang, Y.; Yin, L.; Wang, Z.; Li, X.; Zhou, J. Kombucha fermentation enhances the health-promoting properties of soymilk beverage. *J. Func. Food.* **2019**, *62*, 103549. [CrossRef]
107. Jayabalan, R.; Chen, P.N.; Hsieh, Y.S.; Prabhakaran, K.; Pitchai, P.; Marimuthu, S.; Thangaraj, P.; Swaminathan, K.; Yun, S.E. Effect of solvent fractions of kombucha tea on viability and invasiveness of cancer cells—Characterization of dimethyl 2-(2-hydroxy-2-methoxypropylidine) malonate and vitexin. *Indian J. Biotechnol.* **2011**, *10*, 75–82.
108. Yapar, K.; Cavusoglu, K.; Oruc, E.; Yalcin, E. Protective effect of kombucha mushroom (KM) tea on phenol-induced cytotoxicity in albino mice. *J. Environ. Biol.* **2010**, *31*, 615–621.
109. Coelho, R.M.D.; de Almeida, A.L.; do Amaral, R.Q.G.; da Mota, R.N.; de Sousa, P.H.M. Kombucha: Review. *Int. J. Gastron. Food Sci.* **2020**, *22*, 100272. [CrossRef]
110. Antolak, H.; Piechota, D.; Kucharska, A. Kombucha tea-a double power of bioactive compounds from tea and symbiotic culture of bacteria and yeasts (SCOBY). *Antioxidants* **2012**, *10*, 1541. [CrossRef]
111. Lee, C.; Kim, J.; Wang, S.; Sung, S.; Kim, N.; Lee, H.H.; Seo, Y.S.; Jung, Y. Hepatoprotective effect of kombucha tea in rodent model of nanalcoholic fatty liver disease/nonalcoholic steatohepatitis. *Int. J. Mol. Sci.* **2019**, *20*, 2369. [CrossRef]
112. Jung, Y.; Kim, I.; Mannaa, M.; Kim, J.; Wang, S.; Park, I.; Kim, J.; Seo, Y.S. Effect of kombucha on gut-microbiota in mouse having nonalcoholic fatty liver disease. *Food Sci. Biotechnol.* **2019**, *28*, 261–267. [CrossRef]

113. Kozyrovska, N.O.; Reva, O.M.; Goginyan, V.B.; Devera, J.P. Kombucha microbiome as a probiotic: A view from the perspective of post-genomics and synthetic ecology. *Biopolym. Cell* **2012**, *28*, 103–113. [CrossRef]
114. Greenwalt, C.J.; Steinkraus, K.H.; Ledford, R.A. Kombucha, the fermented tea: Microbiology, composition, and claimed health effects. *J. Food Prot.* **2000**, *63*, 976–981. [CrossRef]
115. Murphy, T.E.; Walia, K.; Farber, J.M. Safety aspects and guidance for consumers on the safe preparation, handling and storage of kombucha—A fermented tea beverage. *Food Prot. Trends* **2018**, *38*, 329–337.
116. Kapp, J.M.; Summer, W. Kombucha: A systematic review of the empirical evidence of human health benefit. *Ann. Epidemiol.* **2019**, *30*, 66–70. [CrossRef] [PubMed]
117. Bailowitz, Z.; Grams, R.; Teeple, D.; Hew-Butler, T. Exercise-associated hyponatremia in a lactating female. *Clin. J. Sport Med.* **2017**, *27*, e55–e57. [CrossRef] [PubMed]
118. Kovacevic, Z.; Davidovic, G.; Vuckovic-Filipovic, J.; Janicijevic-Petrovic, M.A.; Janicijevic, K.; Popovic, A. A toxic hepatitis caused the kombucha tea—Case report. *Maced. J. Med. Sci.* **2014**, *2*, 128–131. [CrossRef]
119. Derk, C.T.; Sandorfi, N.; Curtis, M.T. A case of anti-Jo1 myositis with pleural effusions and pericardial tamponade developing after exposure to a fermented kombucha beverage. *Clin. Rheumatol.* **2004**, *23*, 355–357. [CrossRef]
120. Gedela, M.; Potu, K.C.; Gali, V.L.; Alyamany, K.; Jha, L.K. A case of hepatotoxicity related to kombucha tea consumption. *SD Med.* **2016**, *69*, 26–28.
121. Mallmann, M.M.; Valderramas, S.; Garcia, A.C.; Petterle, R.R.; Duarte, M.L.; Junior, O.R. Kombucha: A systemtic review and meta-analysis of experimental evidence of its effects on blood glucose, dyslipidemia and body weight in diabetes mellitus. *Res. Soc. Dev.* **2022**, *11*, e49011629278. [CrossRef]