

Review

Fermented Black Tea and Its Relationship with Gut Microbiota and Obesity: A Mini Review

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Abstract: Fermentation is one of the world's oldest techniques for food preservation, nutrient enhancement, and alcohol manufacturing. During fermentation, carbohydrates such as glucose and starch are converted into other molecules, such as alcohol and acid, anaerobically through enzymatic action while generating energy for the microorganism or cells involved. Black tea is among the most popular fermented beverages; it is made from the dried tea leaves of the evergreen shrub plant known as *Camellia sinensis*. The adequate consumption of black tea is beneficial to health as it contains high levels of flavanols, also known as catechins, which act as effective antioxidants and are responsible for protecting the body against the development of illnesses, such as inflammation, diabetes, hypertension, cancer, and obesity. The prevalence of obesity is a severe public health concern associated with the incidence of various serious diseases and is now increasing, including in Malaysia. Advances in 'omic' research have allowed researchers to identify the pivotal role of the gut microbiota in the development of obesity. This review explores fermented black tea and its correlation with the regulation of the gut microbiota and obesity.



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Keywords: fermentation; fermented black tea; gut microbiota; obesity

1. Introduction

The obesity epidemic has become a severe health problem in Malaysia and many other countries around the globe [1–5]. The prevalence of obesity is rising at an alarming rate worldwide, raising mortality and reducing quality of life [6,7]. Obesity is projected to affect around fifty percent of the world population by 2030, and Malaysia was reported to have the highest obese population (15%) among Asian countries in 2019 [8–10]. Research has focused on foods containing natural substances, as they cause fewer side effects; hence, they are increasingly utilized due to their health benefits [11]. Studies on fermented products have become the fastest-growing ventures, among other functional foods, due to increased consumer awareness of their multitude of beneficial effects on health [12–14]. The consumption of fermented-tea beverages is gaining popularity due to their probiotic nature and purported health benefits in many countries, including Malaysia [15–19]. Previous studies have reported several bioactivities of fermented black tea, including anti-oxidant, antimicrobial, anti-cancer, anti-diabetic, and anti-lipidemic properties [20–24]. The metabolites produced by microorganisms during fermentation are responsible for their sour taste and other bio-properties [25–28]. Recent progress in molecular biology, including the advent of platforms for next-generation sequencings, such as metagenomics or amplicon sequencing, has allowed the microbial consortium to be characterized, in turn allowing researchers to elucidate the connection between microbial population and obesity [29,30]. In his review, the relationship between fermented black tea and the regulation of the gut microbiota in obesity is discussed.

2. Fermentation

The fermentation process was found thousands of years ago and has been extensively practiced for its benefits in food preservation, nutrient enhancement, and alcohol manufacturing [31,32]. Traces of mixed fermentation in the form of an alcoholic beverages prepared from rice, fruits, and honey between 7000 and 6600 BC was found in pottery jars from the early Neolithic town of Jiahu, China, and was declared the earliest archaeological evidence of fermentation to have been discovered [33–35]. This makes fermented beverages, such as vinegar and wine, among the oldest fermented foods consumed by people [36,37]. Kimchi, for example, is a popular fermented food among Koreans and has become popular in other countries worldwide [38–40]. On the other hand, pickled cucumber is used not only when preparing burgers and sandwiches by Westerners, but also as a side dish in Asian countries [41,42]. Due to their distinct flavor and aroma, fermented foods and beverages become some of the first processed foods to be consumed by humans [31,43–45]. A brief timeline of fermentation's history, from the earliest archaeological evidence of beverage fermentation until the introduction of pasteurization, is illustrated in Figure 1.

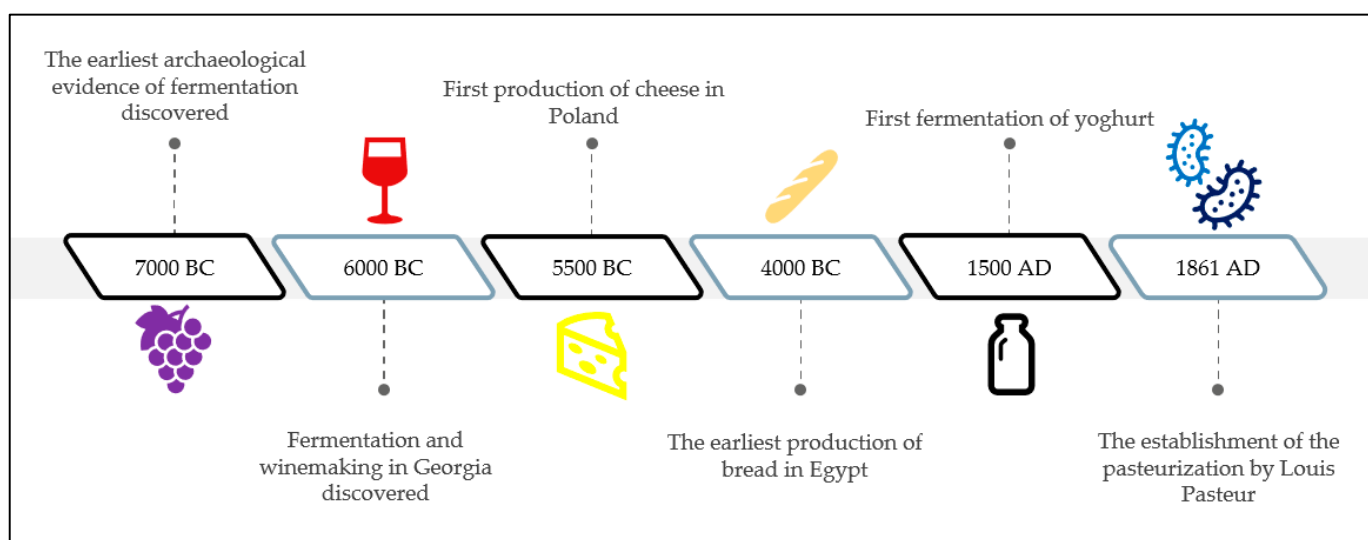


Figure 1. A brief timeline of fermentation history.

During fermentation, carbohydrates, such as glucose and starch, are converted into other molecules, such as alcohol and acid, anaerobically through enzymatic action, while generating energy for the microorganism or cells involved [15,46]. Evidence was found in ancient organics from the pottery jars used for fermentation and winemaking in Georgia in 6000 BC [34,47]. Due to the colonization of the Mediterranean by the Romans, winemaking spread throughout other regions, such as Asia. In the late nineteenth century, Louis Pasteur, a French microbiologist, discovered that living microbes were responsible for souring alcohol during the fermentation process, leading to the establishment of the pasteurization technique, which involves the heating and cooling of liquids to kill microbes and prevent spoiling [48,49]. Pasteur was among the pioneering researchers in food preservation, who believed that the bacteria formed from microscopic inoculums were not generated spontaneously. His theory was later supported by Eduard Buchner, who discovered zymase, a mixture of enzymes produced by yeast during fermentation [49]. This discovery led Eduard Buchner to receive a Nobel Prize in chemistry in 1907 [50]. Table 1 summarizes the changes in the nutritional values of fermented products over the last ten years across the world.

Table 1. Changes in nutritional values in fermented products.

Source	Fermented Product	Country of Origin	Changes in Nutritional Values during Fermentation	Reference
Bamboo shoot	Bamboo shoot biscuits	India	The cyanogen content in bamboo shoots decreased up to 86.59% after 24 h	[51]
	Khorisa	India	A significant decrease in fat, protein, carbohydrate, and vitamin C contents was observed in the fermented shoot	[52]
Cornelian cherry	Tarhana	Turkey	The total-dietary-fiber content was increased significantly after fermentation; however, total sugar, vitamin C, and anthocyanin contents decreased significantly after fermentation	[53]
Grain and milk	Kefir	North Caucasian	A significant increase in protein and saturated-fatty-acid contents and a significant decrease in monounsaturated-fatty-acid content were recorded after fermentation	[54]
Maize	Akamu	Nigeria	The concentrations of protein and total reducing sugar were increased by 5.7% and 12.3%, respectively, whereas starch concentration decreased by 30.7% after 72 h	[55]
	Doklu	Côte d'Ivoire	Most nutritional values (protein, fatty matters carbohydrate, and total sugars) of doklu decreased after fermentation; however, it increased in acidity, which is essential to ensure food safety	[56]
Mare milk	Koumiss	Mongolia	A significant increase in lactic-acid and amino-acid contents and a gradual decrease in lactose content were recorded along with fermentation time	[57]
Peanut	Black oncom	Indonesia	A significant decrease in carbohydrate, total fat, ash, crude protein, and energy were observed on a wet basis. Meanwhile, a substantial increase in total fat, crude protein, protein digestibility, water content, and crude fiber contents was observed on a dry basis.	[58]
Pearl millet	Pearl millet flour	Africa and India	The contents of carbohydrates, crude fiber, crude protein, and energy increased significantly after fermentation; however, ash, crude fat, and moisture contents decreased significantly after fermentation	[59]
Quinoa seed	Cereals	Peru and Bolivia	The contents of protein, carbohydrate, ash, free amino acid, vitamin B1, and vitamin B2 were increased by 20.62%, 4%, 7.72%, 1034.54%, 56.76%, and 50%, respectively, whereas fat and dietary-fiber concentrations decreased by 52.05% and 45.87%, respectively, after 24 h	[60]
Red pepper	Gochujang	Korea	An increase in acidity but a decrease in salt and reduced sugar contents after fermentation	[61]
Rice	Bhaati jaanr	India	A gradual increase in sodium, calcium, magnesium, manganese, and ferrous contents was recorded up to day 3 and day 4 of fermentation	[62]
	Dosa (Rice and black gram dal)	India	A decrease in starch, total soluble, reducing, and non-reducing sugars contents was recorded, whereas soluble proteins and total free-amino-acid contents were increased after fermentation	[63]

Table 1. Cont.

Source	Fermented Product	Country of Origin	Changes in Nutritional Values during Fermentation	Reference
Soybean	Soy yogurt	United States	The contents of moisture, lactose, and fat were decreased; however, protein content increased significantly after fermentation	[64]
		United States	The contents of protein, fat, ash, and carbohydrate increased slightly after fermentation, while moisture value decreased	[65]
	Soybean meal	China	An increase in crude protein, soluble protein, arginine, serine, threonine, aspartic acid, alanine, and glycine contents was observed, while a decrease in trypsin inhibitor and proline contents was observed after 72 h	[66]
	Tempeh	Indonesia	A considerable increase in crude protein, amino nitrogen, and vitamin B9 concentrations was observed, while a low content of vitamin B12 was detected only after fermentation	[67]
	Whole soybean flour	China	The contents of total protein, vitamin B1, vitamin B2, β -carotene, and total essential amino acids were increased by 14.45%, 26.5%, 192.3%, 92.37%, and 10.25%, respectively, after 72 h	[68]
Tea leaves	Cha-miang	Thailand	A significant increase in energy, sodium, potassium, iron, and zinc contents was recorded, while calcium and vitamins (B1, B2, B3, and C) decreased after fermentation	[69]
	Kombucha	China	The contents of total titrable acid and total flavonoid increased with fermentation time	[70]

3. Black Tea

Tea is an excellent alternative to energy drinks and coffee. Even though tea and coffee have multiple health benefits in common, such their caffeine and antioxidant contents [71,72], excessive coffee drinking (daily intake ≥ 400 mg for adults (4–5 cups of coffee) and ≥ 3 mg/kg for children [73]) may contribute to various adverse effects, such as headache [74], insomnia [75–82] and arrhythmia [75,82–85] due to caffeinism [76,82,86]. Compared to tea, coffee contains a higher concentration of caffeine, an energy-boosting psychostimulant. Studies showed that caffeine is widely used to promote alertness by increasing dopamine signaling in the brain [82], primarily via blocking adenosine [87–90], a known vasodilator and sleep-promoting receptor [91,92].

Tea is rich in natural bioactive compounds, such as flavonoids, methylxanthines, carbohydrates, and amino acids, which possess various health benefits [93–95]. Among these bioactive compounds, a high total content of flavonoids, a group of hydroxylated phenolic compounds found in different plants, including vegetables and fruits, was detected in tea [93]. In recent decades, flavonoids have become essential components in nutraceuticals [96–99]. They have been associated with human daily diet and health due to their therapeutic properties, such as antioxidants and anti-diabetic, anti-hypertensive, anti-cancer, and anti-inflammatory actions [72,73,79,80]. Flavonoids can be classified into subclasses based on their side-group position and substitutions, such as flavanols, flavonols, and flavanones [97,100–103]. Flavanols, also known as catechins, are the most abundant and vital constituents in black tea because the oxidation of catechins forms theaflavins and thearubigins, which are excellent antioxidative agents [103,104]. These antioxidants possess free-radical-scavenging properties; they can disrupt the oxidation reaction that causes oxidative stress in cells by donating an electron to the free radicals to form more stable phenoxyl radicals [72,73,86,87]. Oxidative stress is a hazardous process that occurs when free radicals are produced beyond the cell's ability to eliminate them [105,106].

According to various studies, including clinical evidence, excessive oxidative stress can damage DNA, proteins, lipid, and membranes, leading to various disorders, such as diabetes, cardiovascular disease, and neurodegenerative diseases, such as Alzheimer's and Parkinson's [105–108]. Antioxidants can scavenge and neutralize free radicals, thus reducing oxidative stress and assisting in the recovery process [89,90,92]. A previous study showed that theaflavins are the most effective antioxidants in black tea because they have a unique benzotropolone moiety that provides antioxidant protection to the favored oxidation site for electron donation [109–113], followed by catechins and thearubigins [114]. This finding was supported by He [115], who found that the free-radical scavenging activities in theaflavins are greater than in epigallocatechin gallate (EGCG), one of the most potent antiradical compounds found in foods. This circumstance is due to the presence of hydroxyl groups in theaflavins, which are essential for their radical-scavenging activities [116]. Theaflavins also showed anti-inflammatory properties by modulating the signal transducer and activating the NRF2 signaling pathway in vitro and in vivo, which is crucial for increasing the antioxidant defense [93,114,115,117–121]. Based on a systematic data-mining approach, Beresniak et al. [122] discovered that high black tea consumption was significantly associated with low diabetes prevalence; a single dose of black tea reduced peripheral vascular resistance, as well as the insulin response to the glucose load in both the upper and the lower extremities, in the 50 participating countries involved in the study. Hence, it can be concluded that flavonoids are the most vital compounds in black tea due to their crucial role in the bioactivities of black tea. Nevertheless, flavonoids' biological activities might vary depending on their type, mode of action, and bioavailability [123].

Fermentation of Black Tea

Tea is made from the processed dried tea leaves of the evergreen shrub plant known as *Camellia sinensis*, a member of the *Theaceae* family, and is the world's second most-consumed beverage after water [124–127]. *C. sinensis* is a native plant in Southeast Asia, specifically China, Myanmar, Laos, and Vietnam. According to Wang [128], tea was fortuitously discovered in 2737 BC by Shen Nung, an emperor of China, after he was poisoned. The efficacious use of tea to treat poisoning made tea a precious medicine during that era. However, the earliest physical evidence of tea consumption was found in tombs dating back to 207 BC [128,129]. Even with its extraordinary benefits, tea only gained in popularity and was recognized as a national beverage in China in 618 AD. Due to its benefits, tea spread and grew commercially worldwide [124–126,130]. Different types of tea are available commercially, such as black, green, and oolong tea. Although all kinds of tea are prepared from the same plant, different processing procedures and fermentation degrees produce various tea types [94,124]. Among these teas, only black tea is fully fermented and has the most significant production levels globally, accounting for 70% of total global tea production, followed by unfermented green tea, which accounts for 28%, and partially fermented oolong tea, which accounts for 2% [79,107,108,110].

The fermentation of sugared black tea by a tea fungus, a symbiotic relationship between *Acetobacteria* and osmophilic yeasts, produces a healthy beverage called kombucha, as illustrated in Figure 2 [131–133]. Kombucha originated in China and has been consumed since 220 BC. The name “Kombucha” is derived from a Korean physician named Kombu, who brought tea fungus to Japan in 414 AD to treat Emperor Inkyo, who was suffering from digestive problems [131–134]. Currently, kombucha is produced traditionally in many households worldwide, including Malaysia, and its consumption is widespread, principally in Korea, China, Europe, and the United States, because of its refreshing taste and beneficial effects on human health [131,133]. Tea and kombucha originated in China, as illustrated in Figure 3.

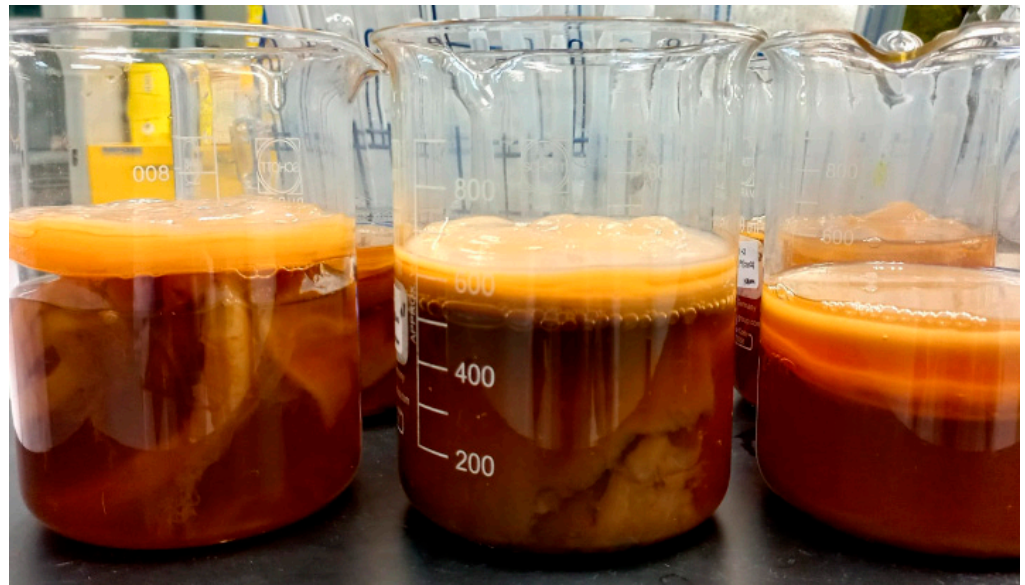


Figure 2. Laboratory-fermented black tea (kombucha).

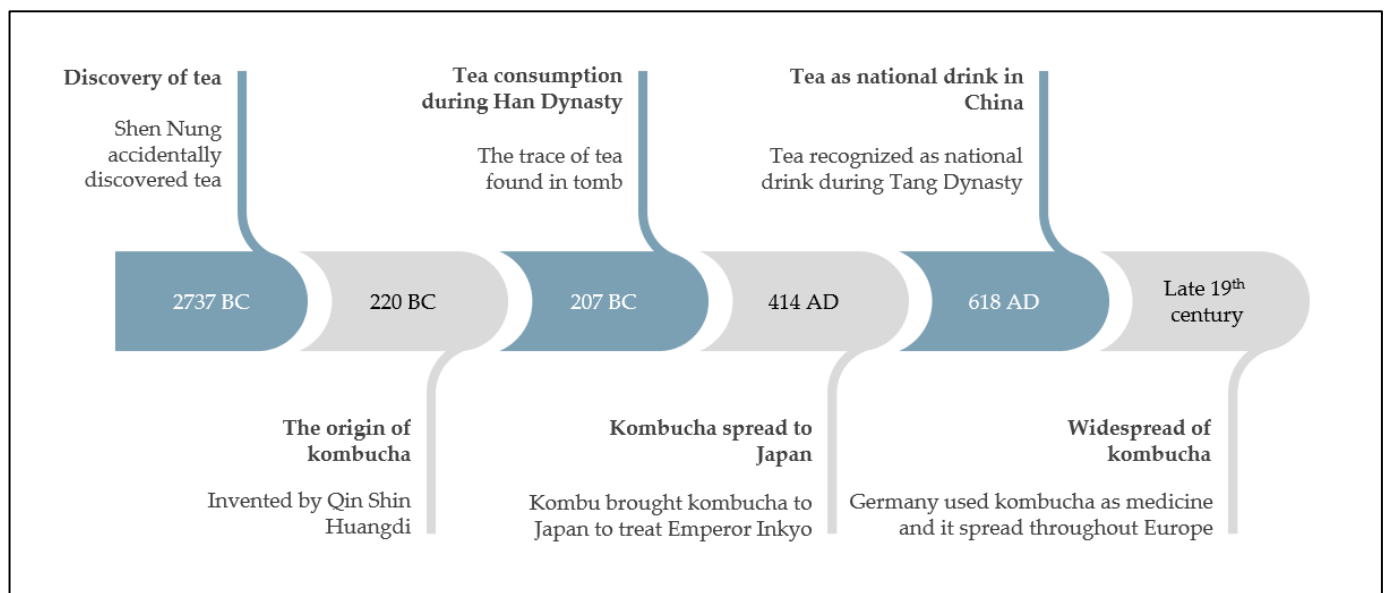


Figure 3. A brief timeline of tea and kombucha history.

As the fermentation time increases, kombucha becomes mature, and the level of tartness of kombucha also changes throughout the process [32,135–137]. Kombucha's flavor transforms from a refreshingly sour, mildly bubbling flavor to a mild vinegar-like taste throughout its fermentation due to the bacterial production of organic acid during alcohol conversion [26,138–141]. Even though kombucha is usually fermented for 7 to 21 days, it is recommended to limit its incubation time to 14 days as extended incubation times will increase the tartness and sourness of kombucha [142–145]. Kombucha contains a broad spectrum of microbial populations, including yeast (*Zygosaccharomyces*, *Brettanomyces*, *Saccharomyces*, and *Pichia*), acetic-acid bacteria (*Komagataeibacter*, *Gluconobacter*, and *Acetobacter*), and lactic-acid bacteria (*Lactobacillus*, *Lactococcus*, and *Oenococcus*). Table 2 summarizes the microbial population of kombucha throughout the world.

Table 2. Microbial population in kombucha.

Country of Origin	Presence in Kombucha	Fermentation Period	Yeast	Bacteria	Reference
Canada	Solution	3 days	<i>Zygosaccharomyces</i>	<i>Komagataeibacter</i> <i>Lactobacillus</i> <i>Lactococcus</i>	[146]
		10 days	<i>Zygosaccharomyces</i>	<i>Komagataeibacter</i> <i>Lactobacillus</i>	
	Pellicle	10 days	<i>Zygosaccharomyces</i> <i>Pichia</i> <i>Leucosporidiella</i>	<i>Komagataeibacter</i> <i>Lactobacillus</i> <i>Lactococcus</i>	
France	Solution	14 days	<i>Brettanomyces bruxellensis</i> <i>Hanseniaspora valbyensis</i> <i>Saccharomyces cerevisiae</i> <i>Brettanomyces bruxellensis</i> <i>Hanseniaspora valbyensis</i> <i>Saccharomyces cerevisiae</i>	<i>Acetobacter indonesiensis</i> <i>Acetobacter papayae</i> <i>Komagataeibacter saccharivorans</i>	[141]
	Pellicle	14 days	<i>Hanseniaspora opuntiae</i> <i>Pichia fermentans</i> <i>Galactomyces geotrichum</i>	<i>Acetobacter indonesiensis</i> <i>Acetobacter papaya</i> <i>Komagataeibacter saccharivorans</i>	
Ireland	Solution	3 days	<i>Zygosaccharomyces</i>	<i>Komagataeibacter</i> <i>Lactobacillus</i> <i>Lactococcus</i>	[146]
		10 days	<i>Zygosaccharomyces</i>	<i>Komagataeibacter</i> <i>Lactobacillus</i> <i>Thermus</i>	
	Pellicle	10 days	<i>Zygosaccharomyces</i>	<i>Komagataeibacter</i> <i>Lactobacillus</i> <i>Lactococcus</i> <i>Acetobacter</i>	
Korea	Solution	21 days	-	<i>Komagataeibacter hansenii</i> <i>Gluconobacter oxydans</i> <i>Oenococcus oeni</i> <i>Lactobacillus</i>	[147]
North America	Pellicle	7 days	<i>Brettanomyces</i> <i>Zygosaccharomyces</i>	<i>Komagataeibacter</i> <i>Lactobacillus</i>	[148]
United Kingdom	Solution	3 days	-	<i>Komagataeibacter</i> <i>Lactobacillus</i>	[146]
		10 days	-	<i>Komagataeibacter</i> <i>Thermus</i> <i>Lactobacillus</i>	
	Pellicle	10 days	-	<i>Komagataeibacter</i> <i>Lactobacillus</i> <i>Lactococcus</i>	
United States	Solution	3 and 10 days	-	<i>Komagataeibacter</i> <i>Lactobacillus</i>	[149]
	Pellicle	10 days	-	<i>Komagataeibacter</i> <i>Bacillus coagulans</i>	
	Solution	-	<i>Brettanomyces</i> <i>Cyberlindnera jadinii</i> <i>Trigonopsis variabilis</i> <i>Issatchenkia orientalis</i>	<i>Komagataeibacter liquefaciens</i> <i>Lactobacillus nagelii</i> <i>Lactobacillus mali</i> <i>Gluconobacter</i>	
Unknown	Solution	0 day	-	<i>Kluyvera</i> <i>Komagataeibacter</i> <i>Enterobacter</i>	[150]
		2, 4, and 8 days	-	<i>Komagataeibacter</i> <i>Gluconobacter</i> <i>Enterobacter</i>	
	Pellicle	0 day 2, 4, and 8 days	- -	<i>Enterobacter</i> <i>Komagataeibacter</i> <i>Komagataeibacter</i>	

It has been proven that the consumption of black tea offers numerous benefits in terms of health; however, the excessive consumption of black tea may lead to indigestion due to the high concentration of tannins in black tea [151]. Tannins are excellent microbial inhibitors that could suppress lactic-acid bacteria and certain fungal activity; however, this effect may soon wear off with prolonged fermentation [152,153]. This issue, however, can be resolved by modifying its properties using the fermentation process, which can enhance its nutritional values at the same time [154]. A study by Chupeerach et al. [69] showed that fermentation considerably affects nutritional- and bioactive-component concentrations, which affects the properties of tea. On the other hand, Jolvis [94] showed that, during fermentation, tea leaves undergo an enzymatic oxidation process, in which the enzymes and chemical constituents of the leaves react with oxygen to form oxidized polyphenolic compounds. This process causes the total tannin content in the tea to gradually decrease with time during fermentation due to the action of the polyphenol oxidase enzyme, which oxidizes phenolics as they diffuse through cellular fluid [154,155].

In addition to tannin, black tea also contains abundant catechin, which acts as an effective antioxidant and is responsible for protecting the body against the development of illnesses [118]. Increases in these vitamins are favorable and beneficial for sustaining and maintaining good health [156–160]. In addition, fermentation is also shown to increase other nutrients, such as carbohydrates, fat, sodium, potassium, and minerals [69]. A similar finding was reported by Unban et al. [161], who showed increases in carbohydrate and fat contents in fermented tea compared to freshly made tea. According to Patel et al. [162], lipase activity by microorganisms breaks down lipid compounds, such as triglycerides, into fatty acids and glycerols through lipolysis, thus increasing the fat content in fermented tea. Due to high carbohydrate and fat contents, significantly higher energy was detected in fermented black tea than in fresh tea leaves [69].

On the other hand, the increase in sodium and potassium concentrations during fermentation may be related to the breakdown of covalent bonds in mineral–food-matrix complexes, which results in the improved bioavailability of the nutrients [69,163]. Furthermore, the fermentation of black tea was also shown to elevate mineral contents, such as iron and zinc, as a result of the metabolic activity of the microorganism [118,164]. However, their presence and nutritional value in different fermented black teas may vary, depending on the symbiotic culture employed, time and temperature of fermentation, sugar level, type of tea, and analysis methods used during the fermentation process [118].

4. Fermented Black Tea, Gut Microbiota, and Obesity

The prevalence of obesity, which is now an increasing trend, has become an epidemic globally, including in Malaysia [3,165–168]. Its association with the incidence of various serious diseases and health conditions, such as hypertension, heart disease, Type 2 diabetes, non-alcoholic fatty liver disease, and non-alcoholic steatohepatitis has been a significant issue for decades [20,169]. Obesity remains a serious public health concern that needs innovative nutritional and medicinal treatments, although various treatments for managing massive weight gain are currently practice. According to Ruiz Estrada et al. [167], obesity in Malaysia is rapidly increasing due to factors such as the high consumption of fast food and sugary soft drinks, long hours of sitting, poor national sports motivation, low water consumption, the high consumption of vitamins, and the dietary imbalance between the calories and carbohydrates consumed daily among Malaysians. Animal and human studies have shown compelling shreds of evidence on the significant role of the gut microbiota in the development of obesity [170]. This finding was supported by Aoun et al. [165] in a review involving animals and obese adult subjects, which found that a high-fat diet might trigger alterations in the gut microbiome's structures and functions in the host gut. It is well known that in addition to being responsible for absorbing, storing, and digesting nutrients, the gut microbiota also helps maintain metabolic homeostasis, increasing the host's immunity and gut barriers in humans [166,171]. Furthermore, John and Mullin [170] also suggested that preventing obesity and metabolic syndromes is possible with healthy

gut-microbiota composition. Ironically, an unhealthy diet can result in gut dysbiosis, which could encourage the proliferation of the pathogenic microorganisms associated with chronic inflammation, contributing significantly to the pathogenesis of chronic metabolic and intestinal disorders, including obesity [165,172].

As one of the well-known products of fermented black tea, kombucha consumption has been proven to elevate the defense mechanism against pathogens. This is because, in addition to polyphenol compounds, which can be naturally found in plant products, the probiotics in kombucha produce a variety of organic acids, such as acetic acid and lactic acid, which possess antimicrobial and antioxidant properties [32,118,131–133,173,174]. This finding was supported by Jung et al. [20], according to whom a significant drop in *Allobaculum* and *Turicibacter*, two pathogens associated with non-alcoholic fatty liver disease (NAFLD), was observed in kombucha treatment. Furthermore, the *Clostridium* genus is associated with obesity, NAFLD, and non-alcoholic steatohepatitis (NASH) due to its ability to increase sugar and fat absorption; the *Mucispirillum* genus, which is a pro-inflammatory bacterium, was also revealed to decline after kombucha consumption [20,175]. By contrast, the kombucha-treatment group recorded a significant increase in beneficial probiotic bacteria, such as *Lactobacillus*, which possess anti-inflammatory properties [176,177].

The gut microbiota is a diverse community of microorganisms composed of various anaerobic bacteria, eukarya, and archaea, which inhabit the gastrointestinal tract through diet [178,179]. Over millennia, the gut microbiota and the host have co-evolved, resulting in a sophisticated and mutually beneficial interaction between them [20,180]. Previous studies revealed that the gut microbiota from *Bacteroidetes*, *Firmicutes*, and *Actinobacteria* phyla are crucial for sustaining immunological and metabolic homeostasis and defense pathogens [181,182]. These findings were supported by Bäumler and Sperandio [183] and Gensollen et al. [184], who showed how the gut microbiota protects the gastrointestinal tract by providing resistance to pathogenic bacteria and fungi and regulating host immunity. Nevertheless, there is also a report on the pathogenesis of the gut microbiota. For example, a study showed that the occurrence of dysbiosis, in which the balance of the gut microbiota is disrupted and the number of pathobionts increases, resulting in infection and various inflammatory diseases, such as obesity, diabetes type 2, and fatty-liver disease [20,148,153]. A recent study by Costa et al. [185] postulated that gut dysbiosis could be treated or reduced by consuming fermented black tea. They also found that kombucha consumption aids in controlling and treating obesity and its associated complications and modulating the gut microbiota in vivo. The probiotic bacteria in kombucha, such as *Lactobacillus* and *Bifidobacterium*, help promote the proliferation of good microbes in the gastrointestinal tract to compete with the pathogenic microbes for nutrients and binding sites of the host cell [186]. Probiotic bacteria, which possess antimicrobial properties and contain high short-chain fatty acids (SCFAs) and other metabolites, strengthen the immune system and aid in balancing the human microbiota [186].

5. Conclusions

This mini review examined the benefits of adequate kombucha consumption in preventing and treating obesity. We highlighted the crucial role of the metabolites produced by microorganisms during the fermentation process in promoting beneficial microbes' growth and inhibiting pathogenic-gut-microbes' growth in the digestive system. Indeed, the bioactive compounds present in kombucha, such as catechins, can protect the body against various illnesses. Based on the evidence, it can be concluded that the consumption of kombucha can promote a healthy human gut due to its antimicrobial properties against enteric pathogens. However, pre-clinical and clinical research supporting fermented black tea's effect on obesity and the gut is still lacking.

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References

1. Cesare, M.D.; Sorić, M.; Bovet, P.; Miranda, J.J.; Bhutta, Z.; Stevens, G.A.; Laxmaiah, A.; Kengne, A.-P.; Bentham, J. The epidemiological burden of obesity in childhood: A worldwide epidemic requiring urgent action. *BMC Med.* **2019**, *17*, 212. [CrossRef] [PubMed]
2. Sala, L.L.; Pontiroli, A.E. Prevention of diabetes and cardiovascular disease in obesity. *Int. J. Mol. Sci.* **2020**, *21*, 8178. [CrossRef] [PubMed]
3. Mohd-Sidik, S.; Lekhraj, R.; Foo, C.N. Prevalence, associated factors and psychological determinants of obesity among adults in Selangor, Malaysia. *Int. J. Environ. Res. Public Health* **2021**, *18*, 868. [CrossRef] [PubMed]
4. Reilly, J.J.; El-Hamdouchi, A.; Diouf, A.; Monyeki, A.; Somda, S.A. Determining the worldwide prevalence of obesity. *Lancet* **2018**, *391*, 1773–1774. [CrossRef]
5. Zhao, C.; Hu, W.; Xu, Y.; Wang, D.; Wang, Y.; Lv, W.; Xiong, M.; Yi, Y.; Wang, H.; Zhang, Q.; et al. Current landscape: The mechanism and therapeutic impact of obesity for breast cancer. *Front. Oncol.* **2021**, *11*, 704893. [CrossRef]
6. Loos, R.J.F.; Yeo, G.S.H. The genetics of obesity: From discovery to biology. *Nat. Rev. Genet.* **2022**, *23*, 120–133. [CrossRef]
7. Rubio-Almanza, M.; Cámara-Gómez, R.; Merino-Torres, J.F. Endocrinología, diabetes y nutrición obesity and type 2 diabetes: Also linked in therapeutic. *Endocrinol. Diabetes Nutr.* **2018**, *66*, 140–149. [CrossRef]
8. Abdullah, Z.; Putri, K.Y.S.; Raza, S.H.; Istiyanto, S.B. Contrariwise obesity through organic food consumption in Malaysia: A signaling theory perspective. *BMC Public Health* **2022**, *22*, 99. [CrossRef]
9. The Academy of Medical Sciences Addressing the Global Health Challenge of Obesity in Malaysia Workshop Report. 2017.
10. Yale Global Online. Available online: <https://archive-yaleglobal.yale.edu/content/world-population-2020-overview> (accessed on 29 August 2022).
11. Wan, M.L.Y.; Ling, K.H.; El-Nezami, H.; Wang, M.F. Influence of functional food components on gut health. *Crit. Rev. Food Sci. Nutr.* **2019**, *59*, 1927–1936. [CrossRef]
12. Plasek, B.; Temesi, Á. The credibility of the effects of functional food products and consumers' willingness to purchase/willingness to pay—Review. *Appetite* **2019**, *143*, 104398. [CrossRef]
13. Sarkar, S. Potentiality of probiotic yoghurt as a functional food—A review. *Nutr. Food Sci.* **2019**, *49*, 182–202. [CrossRef]
14. Wong, C.B.; Odumaki, T.; Xiao, J.Z. Beneficial effects of bifidobacterium Longum Subsp. Longum BB536 on human health: Modulation of gut microbiome as the principal action. *J. Funct. Foods* **2019**, *54*, 506–519. [CrossRef]
15. Dimidi, E.; Cox, S.R.; Rossi, M.; Whelan, K. Fermented foods: Definitions and characteristics, impact on the gut microbiota and effects on gastrointestinal health and disease. *Nutrients* **2019**, *11*, 1806. [CrossRef] [PubMed]
16. Kasron, N.; Manan, M.A.; Hafiz, M.N.; Azmin, M.; Saari, N.A.; Latip, M.A. Consumer acceptance of fermented drinks in Malaysia. *Malaysian J. Soc. Sci. Humanit.* **2021**, *6*, 306–314. [CrossRef]
17. Mousavi, S.M.; Hashemi, S.A.; Zarei, M.; Gholami, A.; Lai, C.W.; Chiang, W.H.; Omidifar, N.; Bahrani, S.; Mazraedoost, S. Recent progress in chemical composition, production, and pharmaceutical effects of kombucha beverage: A complementary and alternative medicine. *Evid.-Based Complement. Altern. Med.* **2020**, *2020*, 4397543. [CrossRef]
18. Nyhan, L.M.; Lynch, K.M.; Sahin, A.W.; Arendt, E.K. Advances in kombucha tea fermentation: A review. *Appl. Microbiol.* **2022**, *2*, 73–103. [CrossRef]
19. 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. *Malaysian J. Fundam. Appl. Sci. Spec. Issue Int. Conf. Agric.* **2018**, *15*, 298–302. [CrossRef]
20. 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 non-alcoholic fatty liver disease. *Food Sci. Biotechnol.* **2019**, *28*, 261–267. [CrossRef]
21. 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]
22. 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 nonalcoholic fatty liver disease/nonalcoholic steatohepatitis. *Int. J. Mol. Sci.* **2019**, *20*, 2369. [CrossRef]
23. Zou, C.; Li, R.Y.; Chen, J.X.; Wang, F.; Gao, Y.; Fu, Y.Q.; Xu, Y.Q.; Yin, J.F. Zijuan tea-based kombucha: Physicochemical, sensorial, and antioxidant profile. *Food Chem.* **2021**, *363*, 130322. [CrossRef] [PubMed]
24. Zubaidah, E.; Afgani, C.A.; Kalsum, U.; Srianta, I.; Blanc, P.J. Comparison of in vivo antidiabetes activity of snake fruit kombucha, black tea kombucha and metformin. *Biocatal. Agric. Biotechnol.* **2019**, *17*, 465–469. [CrossRef]

25. Sahu, L.; Panda, S.K. Kefir, kombucha, and sour beers. *Probiotic Beverages* **2021**, 287–307. [\[CrossRef\]](#)
26. Laureys, D.; Britton, S.J.; De Clippeleer, J. Kombucha tea fermentation: A review. *J. Am. Soc. Brew. Chem.* **2020**, *78*, 165–174. [\[CrossRef\]](#)
27. Tran, T.; Billet, K.; Torres-Cobos, B.; Vichi, S.; Verdier, F.; Martin, A.; Alexandre, H.; Grandvalet, C.; Tourdot-Maréchal, R. Use of a minimal microbial consortium to determine the origin of kombucha flavor. *Front. Microbiol.* **2022**, *13*, 836617. [\[CrossRef\]](#)
28. Abaci, N.; Senol Deniz, F.S.; Orhan, I.E. Kombucha—An ancient fermented beverage with desired bioactivities: A narrowed review. *Food Chem.* **2022**, *14*, 100302. [\[CrossRef\]](#)
29. Osman, M.A.; Neoh, H.M.; Mutalib, N.S.A.; Chin, S.F.; Jamal, R. 16S rRNA gene sequencing for deciphering the colorectal cancer gut microbiome: Current protocols and workflows. *Front. Microbiol.* **2018**, *9*, 767. [\[CrossRef\]](#)
30. Mataragas, M.; Alessandria, V.; Ferrocino, I.; Rantsiou, K.; Cocolin, L. A bioinformatics pipeline integrating predictive metagenomics profiling for the analysis of 16S rDNA/rRNA sequencing data originated from foods. *Food Microbiol.* **2018**, *76*, 279–286. [\[CrossRef\]](#)
31. Anal, A. Quality ingredients and safety concerns for traditional fermented foods and beverages from Asia: A review. *Fermentation* **2019**, *5*, 8. [\[CrossRef\]](#)
32. Coelho, R.M.D.; de Almeida, A.L.; do Amaral, R.Q.G.; da Mota, R.N.; Sousa, P.H.M.D. Kombucha: Review. *Int. J. Gastron. Food Sci.* **2020**, *22*, 100272. [\[CrossRef\]](#)
33. Anagnostopoulos, D.A.; Tsaltas, D. Fermented foods and beverages. *Innov. Tradit. Foods* **2019**, 257–291. [\[CrossRef\]](#)
34. McGovern, P.E.; Zhang, J.; Tang, J.; Zhang, Z.; Hall, G.R.; Moreau, R.A.; Nuñez, A.; Butrym, E.D.; Richards, M.P.; Wang, C.S.; et al. Fermented beverages of pre- and proto-historic China. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 17593–17598. [\[CrossRef\]](#) [\[PubMed\]](#)
35. Pretorius, I.S.; Hoj, P.B. Grape and wine biotechnology: Challenges, opportunities and potential benefits. *Aust. J. Grape Wine Res.* **2005**, *11*, 83–108. [\[CrossRef\]](#)
36. Lynch, K.M.; Zannini, E.; Wilkinson, S.; Daenen, L.; Arendt, E.K. Physiology of acetic acid bacteria and their role in vinegar and fermented beverages. *Compr. Rev. Food Sci. Food Saf.* **2019**, *18*, 587–625. [\[CrossRef\]](#)
37. Tamang, J.P.; Cotter, P.D.; Endo, A.; Han, N.S.; Kort, R.; Liu, S.Q.; Mayo, B.; Westerik, N.; Hutkins, R. Fermented foods in a global age: East meets west. *Compr. Rev. Food Sci. Food Saf.* **2020**, *19*, 184–217. [\[CrossRef\]](#)
38. Chilton, S.N.; Burton, J.P.; Reid, G. Inclusion of fermented foods in food guides around the world. *Nutrition* **2015**, *7*, 390–404. [\[CrossRef\]](#)
39. Park, K.Y.; Jeong, J.K.; Lee, Y.E.; Daily, J.W. Health benefits of kimchi (Korean fermented vegetables) as a probiotic food. *J. Med. Food* **2014**, *17*, 6–20. [\[CrossRef\]](#)
40. Song, H.J.; Lee, H.-J. Consumption of kimchi, a salt fermented vegetable, is not associated with hypertension prevalence. *J. Ethn. Foods* **2014**, *1*, 8–12. [\[CrossRef\]](#)
41. Ashaolu, T.J.; Reale, A. A holistic review on euro-asian lactic acid bacteria fermented cereals and vegetables. *Microorganisms* **2020**, *8*, 1176. [\[CrossRef\]](#)
42. Swain, M.R.; Anandharaj, M.; Ray, R.C.; Rani, R.P. Fermented fruits and vegetables of Asia: A potential source of probiotics. *Biotechnol. Res. Int.* **2014**, *2014*, 250424. [\[CrossRef\]](#)
43. Narzary, Y.; Brahma, J.; Brahma, C.; Das, S. A study on indigenous fermented foods and beverages of Kokrajhar, Assam, India. *J. Ethn. Foods* **2016**, *3*, 284–291. [\[CrossRef\]](#)
44. Sharma, R.; Garg, P.; Kumar, P.; Bhatia, S.K.; Kulshrestha, S. Microbial fermentation and its role in quality improvement of fermented foods. *Fermentation* **2020**, *6*, 106. [\[CrossRef\]](#)
45. Copetti, M.V. Yeasts and molds in fermented food production: An ancient bioprocess. *Curr. Opin. Food Sci.* **2019**, *25*, 57–61. [\[CrossRef\]](#)
46. Marco, M.L.; Heeney, D.; Binda, S.; Cifelli, C.J.; Cotter, P.D.; Foligné, B.; Gänzle, M.; Kort, R.; Pasin, G.; Pihlanto, A.; et al. Health benefits of fermented foods: Microbiota and beyond. *Curr. Opin. Biotechnol.* **2017**, *44*, 94–102. [\[CrossRef\]](#) [\[PubMed\]](#)
47. McGovern, P.; Jalabadze, M.; Batiuk, S.; Callahan, M.P.; Smith, K.E.; Hall, G.R.; Kvavadze, E.; Maghradze, D.; Rusishvili, N.; Bouby, L.; et al. Early neolithic wine of georgia in the south caucasus. *Proc. Natl. Acad. Sci. USA* **2017**, *114*, E10309–E10318. [\[CrossRef\]](#) [\[PubMed\]](#)
48. Gasbarrini, G.; Bonvicini, F.; Gramenzi, A. Probiotics history. *J. Clin. Gastroenterol.* **2016**, *50*, S116–S119. [\[CrossRef\]](#)
49. Mani, A. Food preservation by fermentation and fermented food products. *Int. J. Acad. Res. Dev.* **2018**, *1*, 51–57.
50. Jaenicke, L. Centenary of the award of a nobel prize to eduard buchner, the father of biochemistry in a test tube and thus of experimental molecular bioscience. *Angew. Chemie Int. Ed.* **2007**, *46*, 6776–6782. [\[CrossRef\]](#)
51. Santosh, O.; Kaur Bajwa, H.; Singh Bisht, M.; Nirmala, C. Quality evaluation of biscuits fortified with bamboo shoot for their sensory properties. *J. Pharmacogn. Phytochem.* **2021**, *10*, 330–337.
52. Badwaik, L.S.; Borah, P.K.; Borah, K.; Das, A.J.; Deka, S.C.; Sharma, H.K. Influence of fermentation on nutritional compositions, antioxidant activity, total phenolic and microbial load of bamboo shoot. *Food Sci. Technol. Res.* **2014**, *20*, 255–262. [\[CrossRef\]](#)
53. Karademir, E.; Yalçın, E. Effect of fermentation on some quality properties of cornelian cherry tarhana produced from different cereal/pseudocereal flours. *Qual. Assur. Saf. Crop. Foods* **2019**, *11*, 127–135. [\[CrossRef\]](#)
54. Vieira, C.P.; Álvares, T.S.; Gomes, L.S.; Torres, A.G.; Paschoalin, V.M.F.; Conte, C.A. Kefir grains change fatty acid profile of milk during fermentation and storage. *PLoS ONE* **2015**, *10*, e0139910. [\[CrossRef\]](#) [\[PubMed\]](#)
55. Nwokoro, O.; Chukwu, B.C. Studies on akamu, a traditional fermented maize food. *Rev. Chil. Nutr.* **2012**, *39*, 180–184.

56. Assohoun, M.C.N.; Djeni, T.N.; Koussémon-Camara, M.; Brou, K. Effect of fermentation process on nutritional composition and aflatoxins concentration of doklu, a fermented maize based food. *Food Nutr. Sci.* **2013**, *4*, 1120–1127. [\[CrossRef\]](#)
57. Liu, W.; Wang, J.; Zhang, J.; Mi, Z.; Gesudu, Q.; Sun, T. Dynamic evaluation of the nutritional composition of homemade koumiss from inner mongolia during the fermentation process. *J. Food Process. Preserv.* **2019**, *43*, e14022. [\[CrossRef\]](#)
58. Rohimah, A.; Setiawan, B.; Roosita, K.; Palupi, E. The effects of soaking treatments and fermentation process on nutritional and aflatoxin contents of fermented peanut cake (black oncom). *Pol. J. Nat. Sci.* **2021**, *36*, 59–78.
59. Adebisi, J.A.; Obadina, A.O.; Adebo, O.A.; Kayitesi, E. Comparison of nutritional quality and sensory acceptability of biscuits obtained from native, fermented, and malted pearl millet (*Pennisetum glaucum*) flour. *Food Chem.* **2017**, *232*, 210–217. [\[CrossRef\]](#)
60. Li, S.; Chen, C.; Ji, Y.; Lin, J.; Chen, X.; Qi, B. Improvement of nutritional value, bioactivity and volatile constituents of quinoa seeds by fermentation with lactobacillus casei. *J. Cereal Sci.* **2018**, *84*, 83–89. [\[CrossRef\]](#)
61. Ryu, J.A.; Kim, E.; Kim, M.J.; Lee, S.; Yoon, S.R.; Ryu, J.G.; Kim, H.Y. Physicochemical characteristics and microbial communities in gochujang, a traditional Korean fermented hot pepper paste. *Front. Microbiol.* **2021**, *11*, 3543. [\[CrossRef\]](#)
62. Giri, S.S.; Sen, S.S.; Saha, S.; Sukumaran, V.; Park, S.C. Use of a potential probiotic, lactobacillus plantarum l7, for the preparation of a rice-based fermented beverage. *Front. Microbiol.* **2018**, *9*, 473. [\[CrossRef\]](#)
63. Devi, P.B.; Rajendran, S. Impact of starter culture on nutraceutical and functional properties of underutilized millet-legume co-fermented Indian traditional product. *LWT* **2021**, *149*, 111818. [\[CrossRef\]](#)
64. Rahmawati, I.S.; Suntornsuk, W. Effects of fermentation and storage on bioactive activities in milks and yoghurts. *Procedia Chem.* **2016**, *18*, 53–62. [\[CrossRef\]](#)
65. Júnior, S.S.; Tavano, O.; Demonte, A.; Rossi, E.; Pinto, R. Nutritional evaluation of soy yoghurt in comparison to soymilk and commercial milk yoghurt. Effect of fermentation on soy protein. *Acta Aliment.* **2012**, *41*, 443–450. [\[CrossRef\]](#)
66. Teng, D.; Gao, M.; Yang, Y.; Liu, B.; Tian, Z.; Wang, J. Bio-modification of soybean meal with bacillus subtilis or aspergillus oryzae. *Biocatal. Agric. Biotechnol.* **2012**, *1*, 32–38. [\[CrossRef\]](#)
67. Mo, H.; Kariluoto, S.; Piironen, V.; Zhu, Y.; Sanders, M.G.; Vincken, J.-P.; Wolters-Rooijackers, J.; Nout, M.J.R. Effect of soybean processing on content and bioaccessibility of folate, vitamin B12 and isoflavones in tofu and tempe. *Food Chem.* **2013**, *141*, 2418–2425. [\[CrossRef\]](#) [\[PubMed\]](#)
68. Li, S.; Jin, Z.; Hu, D.; Yang, W.; Yan, Y.; Nie, X.; Lin, J.; Zhang, Q.; Gai, D.; Ji, Y.; et al. Effect of solid-state fermentation with lactobacillus casei on the nutritional value, isoflavones, phenolic acids and antioxidant activity of whole soybean flour. *LWT* **2020**, *125*, 109264. [\[CrossRef\]](#)
69. Chupeerach, C.; Aursalung, A.; Watcharachaisoponsiri, T.; Whanmek, K.; Thiyajai, P.; Yosphan, K.; Sritalahareuthai, V.; Sahasakul, Y.; Santivarangkna, C.; Suttisansanee, U. The effect of steaming and fermentation on nutritive values, antioxidant activities, and inhibitory properties of tea leaves. *Foods* **2021**, *10*, 117. [\[CrossRef\]](#)
70. Franeck, A.; Wünsch, R.; Dwiputri, M.C.; Feroniasanti, Y.L. Effect of fermentation to total titrable acids, flavonoid and antioxidant activity of butterfly pea kombucha. *J. Phys. Conf. Ser.* **2019**, *1241*, 012014. [\[CrossRef\]](#)
71. Castillo, M.D.d.; Iriondo-DeHond, A.; Fernandez-Gomez, B.; Martinez-Saez, N.; Rebollo-Hernanz, M.; Martín-Cabrejas, M.A.; Farah, A. Coffee Antioxidants in Chronic Diseases. In *Coffee: Consumption and Health Implications*; Farah, A., Ed.; Royal Society of Chemistry: London, UK, 2019; pp. 20–56. ISBN 978-1-78801-497-7.
72. Gan, R.Y.; Zhang, D.; Wang, M.; Corke, H. Health benefits of bioactive compounds from the genus ilex, a source of traditional caffeinated beverages. *Nutrients* **2018**, *10*, 1682. [\[CrossRef\]](#)
73. Agostoni, C.; Canani, R.B.; Fairweather-Tait, S.; Heinonen, M.; Korhonen, H.; Vieille, S.L.; Marchelli, R.; Martin, A.; Naska, A.; Neuhauser-Berthold, M.; et al. Scientific Opinion on the Safety of Caffeine. *EFSA J.* **2015**, *13*, 4102. [\[CrossRef\]](#)
74. Nowaczewska, M.; Wiciński, M.; Kaźmierczak, W. The ambiguous role of caffeine in migraine headache: From trigger to treatment. *Nutrients* **2020**, *12*, 2259. [\[CrossRef\]](#) [\[PubMed\]](#)
75. Kharaba, Z.; Sammani, N.; Ashour, S.; Ghemrawi, R.; Al Meslamani, A.Z.; Al-Azayzih, A.; Buabeid, M.A.; Alfoteih, Y. Caffeine consumption among various university students in the UAE, exploring the frequencies, different sources and reporting adverse effects and withdrawal symptoms. *J. Nutr. Metab.* **2022**, *2022*, 5762299. [\[CrossRef\]](#) [\[PubMed\]](#)
76. Richards, G.; Smith, A. Caffeine consumption and self-assessed stress, anxiety, and depression in secondary school children. *J. Psychopharmacol.* **2015**, *29*, 1236–1247. [\[CrossRef\]](#) [\[PubMed\]](#)
77. Choi, J. Motivations influencing caffeine consumption behaviors among college students in Korea: Associations with sleep quality. *Nutrients* **2020**, *12*, 953. [\[CrossRef\]](#) [\[PubMed\]](#)
78. Samaha, A.; Al Tassi, A.; Yahfoufi, N.; Gebbawi, M.; Rached, M.; Fawaz, M.A. Data on the relationship between caffeine addiction and stress among lebanese medical students in lebanon. *Data Br.* **2020**, *28*, 104845. [\[CrossRef\]](#) [\[PubMed\]](#)
79. Watson, E.J.; Coates, A.M.; Kohler, M.; Banks, S. Caffeine consumption and sleep quality in Australian adults. *Nutrients* **2016**, *8*, 479. [\[CrossRef\]](#)
80. Park, S.; Lee, Y.; Lee, J.H. Association between energy drink intake, sleep, stress, and suicidality in Korean adolescents: Energy drink use in isolation or in combination with junk food consumption. *Nutr. J.* **2016**, *15*, 87. [\[CrossRef\]](#)
81. Lieberman, H.R. Why are certain caffeine-containing products associated with serious adverse effects? *Mayo Clin. Proc.* **2020**, *95*, 1562–1564. [\[CrossRef\]](#)
82. Jee, H.J.; Lee, S.G.; Bormate, K.J.; Jung, Y.S. Effect of caffeine consumption on the risk for neurological and psychiatric disorders: Sex differences in human. *Nutrients* **2020**, *12*, 3080. [\[CrossRef\]](#)

83. Ellermann, C.; Hakenes, T.; Wolfes, J.; Wegner, F.K.; Willy, K.; Leitz, P.; Rath, B.; Eckardt, L.; Frommeyer, G. Cardiovascular risk of energy drinks: Caffeine and taurine facilitate ventricular arrhythmias in a sensitive whole-heart model. *J. Cardiovasc. Electrophysiol.* **2022**, *33*, 1290–1297. [\[CrossRef\]](#)
84. Tang, W.H.W.; Kitai, T.; Hazen, S.L. Gut microbiota in cardiovascular health and disease. *Circ. Res.* **2017**, *120*, 1183–1196. [\[CrossRef\]](#) [\[PubMed\]](#)
85. Depaula, J.; Farah, A. Caffeine consumption through coffee: Content in the beverage, metabolism, health benefits and risks. *Beverages* **2019**, *5*, 37. [\[CrossRef\]](#)
86. Willson, C. The clinical toxicology of caffeine: A review and case study. *Toxicol. Rep.* **2018**, *5*, 1140. [\[CrossRef\]](#) [\[PubMed\]](#)
87. Fredholm, B.B.; Svenningsson, P. Adenosine—Dopamine interactions. *Neurology* **2003**, *61*, S5–S9. [\[CrossRef\]](#) [\[PubMed\]](#)
88. Manalo, R.V.M.; Medina, P.M.B. Caffeine protects dopaminergic neurons from dopamine-induced neurodegeneration via synergistic adenosine-dopamine D2-like receptor interactions in transgenic caenorhabditis elegans. *Front. Neurosci.* **2018**, *12*, 137. [\[CrossRef\]](#) [\[PubMed\]](#)
89. Volkow, N.D.; Wang, G.J.; Logan, J.; Alexoff, D.; Fowler, J.S.; Thanos, P.K.; Wong, C.; Casado, V.; Ferre, S.; Tomasi, D. Caffeine increases striatal dopamine D2/D3 receptor availability in the human brain. *Transl. Psychiatry* **2015**, *5*, e549. [\[CrossRef\]](#) [\[PubMed\]](#)
90. Alstadhaug, K.B.; Andreou, A.P. Caffeine and primary (migraine) headaches—Friend or foe? *Front. Neurol.* **2019**, *10*, 1275. [\[CrossRef\]](#)
91. Fried, N.T.; Elliott, M.B.; Oshinsky, M.L. The role of adenosine signaling in headache: A review. *Brain Sci.* **2017**, *7*, 30. [\[CrossRef\]](#)
92. Lazarus, M.; Oishi, Y.; Bjorness, T.E.; Greene, R.W. Gating and the need for sleep: Dissociable effects of adenosine A₁ and A_{2A} receptors. *Front. Neurosci.* **2019**, *13*, 740. [\[CrossRef\]](#)
93. Gargi, S.; Nilanjan, S.; Moutusi, N.; Subhasis, M. Bioactive components of tea. *Arch. Food Nutr. Sci.* **2020**, *4*, 1–9. [\[CrossRef\]](#)
94. Pou, K.R.J. Fermentation: The key step in the processing of black tea. *J. Biosyst. Eng.* **2016**, *41*, 85–92. [\[CrossRef\]](#)
95. Rasheed, Z. Molecular evidences of health benefits of drinking black tea. *Int. J. Health Sci.* **2019**, *13*, 1.
96. Kaleem, M.; Ahmad, A. Flavonoids as Nutraceuticals. In *Therapeutic, Probiotic, and Unconventional Foods*; Grumezescu, A.M., Holban, A.M., Eds.; Academic Press: Cambridge, MA, USA, 2018; pp. 137–155. ISBN 978-0-12-814625-5.
97. Panche, A.N.; Diwan, A.D.; Chandra, S.R. Flavonoids: An overview. *J. Nutr. Sci.* **2016**, *5*, e47. [\[CrossRef\]](#) [\[PubMed\]](#)
98. Prior, R.L. Polyphenols and Flavonoids. In *Modern Nutrition in Health and Disease: Eleventh Edition*; Ross, A.C., Caballero, B.H., Cousins, R.J., Tucker, K.L., Ziegler, T.R., Eds.; Wolters Kluwer Health Adis (ESP), 2012; pp. 494–505 ISBN 9781605474618. Taylor, L.P.; Grotewold, E. Flavonoids as developmental regulators. *Curr. Opin. Plant Biol.* **2005**, *8*, 317–323. [\[CrossRef\]](#)
99. Singla, R.K.; Dubey, A.K.; Garg, A.; Sharma, R.K.; Fiorino, M.; Ameen, S.M.; Haddad, M.A.; Al-Hiary, M. Natural polyphenols: Chemical classification, definition of classes, subcategories, and structures. *J. AOAC Int.* **2019**, *102*, 1397–1400. [\[CrossRef\]](#)
100. Shen, N.; Wang, T.; Gan, Q.; Liu, S.; Wang, L.; Jin, B. Plant flavonoids: Classification, distribution, biosynthesis, and antioxidant activity. *Food Chem.* **2022**, *383*, 132531. [\[CrossRef\]](#)
101. Wang, T.Y.; Li, Q.; Bi, K.S. Bioactive flavonoids in medicinal plants: Structure, activity and biological fate. *Asian J. Pharm. Sci.* **2018**, *13*, 12–23. [\[CrossRef\]](#)
102. Koech, K.R.; Wachira, F.N.; Ngure, R.M.; Wanyoko, J.K.; Bii, C.C.; Karori, S.M.; Kerio, L.C. Antimicrobial, Synergistic and Antioxidant Activities of Tea Polyphenols. 2013. [\[CrossRef\]](#)
103. Liu, Z.; Bruins, M.E.; Ni, L.; Vincken, J.P. Green and black tea phenolics: Bioavailability, transformation by colonic microbiota, and modulation of colonic microbiota. *J. Agric. Food Chem.* **2018**, *66*, 8469–8477. [\[CrossRef\]](#)
104. Jakubczyk, K.; Dec, K.; Kałduńska, J.; Kawczuga, D.; Kochman, J.; Janda, K. Reactive oxygen species—Sources, functions, oxidative damage. *Pol. Merkuri Lekarski* **2020**, *48*, 124–127.
105. Engwa, G.A. Free radicals and the role of plant phytochemicals as antioxidants against oxidative stress-related diseases. *Phytochem.-Source Antioxid. Role Dis. Prev.* **2018**, *7*, 49–74. [\[CrossRef\]](#)
106. Federico, A.; Morgillo, F.; Tuccillo, C.; Ciardiello, F.; Loguercio, C. Chronic inflammation and oxidative stress in human carcinogenesis. *Int. J. Cancer* **2007**, *121*, 2381–2386. [\[CrossRef\]](#) [\[PubMed\]](#)
107. Guo, J.D.; Zhao, X.; Li, Y.; Li, G.R.; Liu, X.L. Damage to dopaminergic neurons by oxidative stress in parkinson's disease (review). *Int. J. Mol. Med.* **2018**, *41*, 1817–1825. [\[CrossRef\]](#) [\[PubMed\]](#)
108. Jhoo, J.W.; Lo, C.Y.; Li, S.; Sang, S.; Ang, C.Y.W.; Heinze, T.M.; Ho, C.T. Stability of black tea polyphenol, theaflavin, and identification of theanaphthoquinone as its major radical reaction product. *J. Agric. Food Chem.* **2005**, *53*, 6146–6150. [\[CrossRef\]](#) [\[PubMed\]](#)
109. Khan, N.; Mukhtar, H. Tea polyphenols for health promotion. *Life Sci.* **2007**, *81*, 519. [\[CrossRef\]](#) [\[PubMed\]](#)
110. Zhang, L.; Ho, C.T.; Zhou, J.; Santos, J.S.; Armstrong, L.; Granato, D. Chemistry and biological activities of processed *Camellia sinensis* teas: A comprehensive review. *Compr. Rev. Food Sci. Food Saf.* **2019**, *18*, 1474–1495. [\[CrossRef\]](#)
111. Zhang, L.; Wang, Y.; Wan, X. Introductory of Basic Chemistry and Health Effects of Tea. In *Tea as a Food Ingredient*; Yin, J., Fu, Z., Xu, Y., Eds.; CRC Press: Boca Raton, FL, USA, 2022; pp. 1–14. ISBN 9781003152828.
112. Sharma, N.; Phan, H.T.; Chikae, M.; Takamura, Y.; Azo-Oussou, A.F.; Vestergaard, M.C. Black tea polyphenol theaflavin as promising antioxidant and potential copper chelator. *J. Sci. Food Agric.* **2020**, *100*, 3126–3135. [\[CrossRef\]](#)
113. Koch, W. Theaflavins, Thearubigins, and Theasinensins. In *Handbook of Dietary Phytochemicals*; Xiao, J., Sarker, S.D., Asakawa, Y., Eds.; Springer: Singapore, 2020; pp. 975–1003. ISBN 978-981-15-4147-6.

114. He, H.F. Research progress on theaflavins: Efficacy, formation, and preparation. *SNF Swedish Nutr. Found.* **2017**, *61*, 1344521. [[CrossRef](#)]
115. Nimse, S.B.; Pal, D. Free radicals, natural antioxidants, and their reaction mechanisms. *RSC Adv.* **2015**, *5*, 27986–28006. [[CrossRef](#)]
116. Ahmed, S.M.U.; Luo, L.; Namani, A.; Wang, X.J.; Tang, X. Nrf2 signaling pathway: Pivotal roles in inflammation. *Biochim. Biophys. Acta-Mol. Basis Dis.* **2017**, *1863*, 585–597. [[CrossRef](#)]
117. 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](#)]
118. Zhang, Y.; Yang, X.; Cattani, C.; Rao, R.V.; Wang, S.; Phillips, P. Tea category identification using a novel fractional fourier entropy and jaya algorithm. *Entropy* **2016**, *18*, 77. [[CrossRef](#)]
119. Li, Z.; Zhu, J.; Wan, Z.; Li, G.; Chen, L.; Guo, Y. Theaflavin ameliorates renal ischemia/reperfusion injury by activating the Nrf2 signalling pathway in vivo and in vitro. *Biomed. Pharmacother.* **2021**, *134*, 111097. [[CrossRef](#)] [[PubMed](#)]
120. Shan, Z.; Nisar, M.F.; Li, M.; Zhang, C.; Wan, C. Theaflavin chemistry and its health benefits. *Oxid. Med. Cell. Longev.* **2021**, *2021*, 6256618. [[CrossRef](#)] [[PubMed](#)]
121. Beresniak, A.; Duru, G.; Berger, G.; Bremond-Gignac, D. Relationships between black tea consumption and key health indicators in the world: An ecological study. *BMJ Open* **2012**, *2*, e000648. [[CrossRef](#)] [[PubMed](#)]
122. Ullah, A.; Munir, S.; Badshah, S.L.; Khan, N.; Ghani, L.; Poulson, B.G.; Emwas, A.H.; Jaremko, M. Important flavonoids and their role as a therapeutic agent. *Molecules* **2020**, *25*, 5243. [[CrossRef](#)]
123. Sharma, V.; Jagan, L.; Rao, M.; Jagan, L. A thought on the biological activities of black tea. *Crit. Rev. Food Sci. Nutr.* **2009**, *49*, 379–404. [[CrossRef](#)]
124. Shivashankara, A.R.; Kumar, A.; Ravi, R.; Simon, P.; Rai, P.; Francis, A.; Baliga, M.S. Hepatoprotective effects of green tea and its polyphenols: Preclinical observations. *Polyphenols Hum. Health Dis.* **2014**, *1*, 715–721. [[CrossRef](#)]
125. Shivashankara, A.R.; Rao, S.; George, T.; Abraham, S.; Colin, M.D.; Palatty, P.L.; Baliga, M.S. Tea (*Camellia sinensis* L. Kuntze) as hepatoprotective agent: A revisit. *Diet. Interv. Liver Dis. Foods, Nutr. Diet. Suppl.* **2019**, 183–192. [[CrossRef](#)]
126. Stodt, U.W.; Blauth, N.; Niemann, S.; Stark, J.; Pawar, V.; Jayaraman, S.; Koek, J.; Engelhardt, U.H. Investigation of processes in black tea manufacture through model fermentation (oxidation) experiments. *J. Agric. Food Chem.* **2014**, *62*, 7854–7861. [[CrossRef](#)]
127. Wang, N. A comparison of Chinese and British tea culture. *Asian Cult. Hist.* **2011**, *3*, 13. [[CrossRef](#)]
128. Lu, H.; Zhang, J.; Yang, Y.; Yang, X.; Xu, B.; Yang, W.; Tong, T.; Jin, S.; Shen, C.; Rao, H.; et al. Earliest tea as evidence for one branch of the silk road across the tibetan plateau. *Sci. Rep.* **2016**, *6*, 18955. [[CrossRef](#)] [[PubMed](#)]
129. Li, Y.; Xu, Q.; Huang, Z.; Lv, L.; Liu, X.; Yin, C.; Yan, H.; Yuan, J. Effect of bacillus subtilis CGMCC 1.1086 on the growth performance and intestinal microbiota of broilers. *J. Appl. Microbiol.* **2016**, *120*, 195–204. [[CrossRef](#)]
130. Bhat, R. Fermentation of black tea broth (kombucha): I. effects of sucrose concentration and fermentation time on the yield of microbial cellulose. *Int. Food Res. J.* **2012**, *19*, 109–117.
131. Dufresne, C.; Farnworth, E. Tea, kombucha, and health: A review. *Food Res. Int.* **2000**, *33*, 409–491. [[CrossRef](#)]
132. Jayabalan, R.; Malbaša, R.V.; Lončar, 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. Food Saf.* **2014**, *13*, 538–550. [[CrossRef](#)] [[PubMed](#)]
133. Teoh, A.L.; Heard, G.; Cox, J. Yeast ecology of kombucha fermentation. *Int. J. Food Microbiol.* **2004**, *95*, 119–126. [[CrossRef](#)]
134. de Miranda, J.F.; Ruiz, L.F.; Silva, C.B.; Uekane, T.M.; Silva, K.A.; Gonzalez, A.G.M.; Fernandes, F.F.; Lima, A.R. Kombucha: A Review of substrates, regulations, composition, and biological properties. *J. Food Sci.* **2022**, *87*, 503–527. [[CrossRef](#)]
135. de Noronha, M.C.; Cardoso, R.R.; dos Santos D’Almeida, C.T.; Vieira do Carmo, M.A.; Azevedo, L.; Maltarollo, V.G.; Júnior, J.I.R.; Eller, M.R.; Cameron, L.C.; Ferreira, M.S.L.; et al. Black tea kombucha: Physicochemical, microbiological and comprehensive phenolic profile changes during fermentation, and antimalarial activity. *Food Chem.* **2022**, *384*, 132515. [[CrossRef](#)]
136. Kumar, V.; Joshi, V.K. Kombucha: Technology, microbiology, production, composition and therapeutic value. *Int. J. Food Ferment. Technol.* **2016**, *6*, 13. [[CrossRef](#)]
137. 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](#)]
138. Jayabalan, R.; Malbaša, R.V.; Sathishkumar, M. Kombucha tea: Metabolites. In *Fungal Metabolites*; Springer: Cham, Switzerland, 2017; pp. 965–978. [[CrossRef](#)]
139. Neffe-Skocińska, K.; Sionek, B.; Ścibisz, I.; Kołożyn-Krajewska, D. Acid contents and the effect of fermentation condition of kombucha tea beverages on physicochemical, microbiological and sensory properties. *CYTA J. Food* **2017**, *15*, 601–607. [[CrossRef](#)]
140. Tran, T.; Grandvalet, C.; Verdier, F.; Martin, A.; Alexandre, H.; Tourdot-Maréchal, R. Microbial dynamics between yeasts and acetic acid bacteria in kombucha: Impacts on the chemical composition of the beverage. *Foods* **2020**, *9*, 963. [[CrossRef](#)] [[PubMed](#)]
141. 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](#)]
142. Phetxumphou, K.; Vick, R.; Blanc, L.; Lahne, J. Processing condition effects on sensory profiles of kombucha through sensory descriptive analysis. *J. Am. Soc. Brew. Chem.* **2022**, 1–10. [[CrossRef](#)]
143. Sinir, G.Ö.; Tamer, C.E.; Suna, S. Kombucha tea: A promising fermented functional beverage. *Fermented Beverages Sci. Beverages* **2019**, *5*, 401–432. [[CrossRef](#)]
144. 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](#)] [[PubMed](#)]

145. 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. [\[CrossRef\]](#)
146. Lee, K.R.; Jo, K.; Ra, K.S.; Suh, H.J.; Hong, K.-B. Kombucha fermentation using commercial kombucha pellicle and culture broth as starter. *Food Sci. Technol.* **2021**, *42*. [\[CrossRef\]](#)
147. Harrison, K.; Curtin, C. Microbial composition of SCOBY starter cultures used by commercial kombucha brewers in North America. *Microorganisms* **2021**, *9*, 1060. [\[CrossRef\]](#)
148. 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. [\[CrossRef\]](#)
149. Tran, T.; Grandvalet, C.; Verdier, F.; Martin, A.; Alexandre, H.; Tourdot-Maréchal, R. Microbiological and technological parameters impacting the chemical composition and sensory quality of kombucha. *Compr. Rev. Food Sci. Food Saf.* **2020**, *19*, 2050–2070. [\[CrossRef\]](#) [\[PubMed\]](#)
150. Besky, S. Empire and indigestion: Materializing tannins in the indian tea industry. *Soc. Stud. Sci.* **2020**, *50*, 398–417. [\[CrossRef\]](#) [\[PubMed\]](#)
151. Bule, M.; Khan, F.; Nisar, M.F.; Niaz, K. Tannins (Hydrolysable tannins, condensed tannins, phlorotannins, flavono-ellagitannins). In *Recent Advances in Natural Products Analysis*; Elsevier: Amsterdam, The Netherlands, 2020; pp. 132–146.
152. Giuberti, G.; Rocchetti, G.; Lucini, L. Interactions between phenolic compounds, amylolytic enzymes and starch: An updated overview. *Curr. Opin. Food Sci.* **2020**, *31*, 102–113. [\[CrossRef\]](#)
153. Pasha, C.; Reddy, G. Nutritional and medicinal improvement of black tea by yeast fermentation. *Food Chem.* **2005**, *89*, 449–453. [\[CrossRef\]](#)
154. Haile, M.; Kang, W.H. Antioxidant activity, total polyphenol, flavonoid and tannin contents of fermented green coffee beans with selected yeasts. *Fermentation* **2019**, *5*, 29. [\[CrossRef\]](#)
155. Calderón-Ospina, C.A.; Nava-Mesa, M.O. B vitamins in the nervous system: Current knowledge of the biochemical modes of action and synergies of thiamine, pyridoxine, and cobalamin. *CNS Neurosci. Ther.* **2020**, *26*, 5–13. [\[CrossRef\]](#)
156. Maruvada, P.; Stover, P.J.; Mason, J.B.; Bailey, R.L.; Davis, C.D.; Field, M.S.; Finnell, R.H.; Garza, C.; Green, R.; Gueant, J.L.; et al. Knowledge gaps in understanding the metabolic and clinical effects of excess folates/folic acid: A summary, and perspectives, from an NIH workshop. *Am. J. Clin. Nutr.* **2020**, *112*, 1390–1403. [\[CrossRef\]](#)
157. McNulty, H.; Ward, M.; Hoey, L.; Hughes, C.F.; Pentieva, K. Addressing optimal folate and related B-vitamin status through the lifecycle: Health impacts and challenges. *Proc. Nutr. Soc.* **2019**, *78*, 449–462. [\[CrossRef\]](#)
158. Park, J.; Hosomi, K.; Kawashima, H.; Chen, Y.-A.; Mohsen, A.; Ohno, H.; Konishi, K.; Tanisawa, K.; Kifushi, M.; Kogawa, M.; et al. Dietary vitamin B1 intake influences gut microbial community and the consequent production of short-chain fatty acids. *Nutrients* **2022**, *14*, 2078. [\[CrossRef\]](#)
159. Suwannasom, N.; Kao, I.; Pruß, A.; Georgieva, R.; Bäumler, H. Riboflavin: The health benefits of a forgotten natural vitamin. *Int. J. Mol. Sci.* **2020**, *21*, 950. [\[CrossRef\]](#)
160. Unban, K.; Khatthongngam, N.; Shetty, K.; Khanongnuch, C. Nutritional biotransformation in traditional fermented tea (miang) from North Thailand and its impact on antioxidant and antimicrobial activities. *J. Food Sci. Technol.* **2019**, *56*, 2687. [\[CrossRef\]](#) [\[PubMed\]](#)
161. Patel, N.; Rai, D.; Shivam; Shahane, S.; Mishra, U. Lipases: Sources, production, purification, and applications. *Recent Pat. Biotechnol.* **2018**, *13*, 45–56. [\[CrossRef\]](#) [\[PubMed\]](#)
162. Pranoto, Y.; Anggrahini, S.; Efendi, Z. Effect of natural and lactobacillus plantarum fermentation on in-vitro protein and starch digestibilities of sorghum flour. *Food Biosci.* **2013**, *2*, 46–52. [\[CrossRef\]](#)
163. 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. [\[CrossRef\]](#)
164. Aoun, A.; Darwish, F.; Hamod, N. The influence of the gut microbiome on obesity in adults and the role of probiotics prebiotics and synbiotics for weight loss. *Prev. Nutr. Food Sci.* **2020**, *25*, 113–123. [\[CrossRef\]](#)
165. Gentile, C.L.; Weir, T.L. The gut microbiota at the intersection of diet and human health. *Science* **2018**, *362*, 776–780. [\[CrossRef\]](#)
166. Estrada, M.A.R.; Kheng, K.S.; Ating, R. The evaluation of obesity in Malaysia. *SSRN Electron. J.* **2019**. [\[CrossRef\]](#)
167. Wilkins, L.J.; Monga, M.; Miller, A.W. Defining dysbiosis for a cluster of chronic diseases. *Sci. Rep.* **2019**, *9*, 12918. [\[CrossRef\]](#)
168. Kyrou, I.; Randeva, H.S.; Tsigos, C.; Kaltsas, G.; Weickert, M.O. Clinical Problems Caused by Obesity. In *Endotext*; Feingold, K.R., Anawalt, B., Boyce, A., Eds.; MDText.com, Inc.: South Dartmouth, MA, USA, 2018.
169. John, G.K.; Mullin, G.E. The gut microbiome and obesity. *Curr. Oncol. Reports* **2016**, *18*, 45. [\[CrossRef\]](#)
170. Okubo, H.; Nakatsu, Y.; Kushiya, A.; Yamamotoya, T.; Matsunaga, Y.; Inoue, M.; Fujishiro, M.; Sakoda, H.; Ohno, H.; Yoneda, M.; et al. Gut microbiota as a therapeutic target for metabolic disorders. *Curr. Med. Chem.* **2018**, *25*, 984–1001. [\[CrossRef\]](#)
171. Turrone, F.; Ventura, M.; Buttó, L.F.; Duranti, S.; O'Toole, P.W.; Motherway, M.O.C.; Van Sinderen, D. Molecular dialogue between the human gut microbiota and the host: A lactobacillus and bifidobacterium perspective. *Cell. Mol. Life Sci.* **2014**, *71*, 183–203. [\[CrossRef\]](#) [\[PubMed\]](#)
172. Al-Mohammadi, A.R.; Ismaiel, A.A.; Ibrahim, R.A.; Moustafa, A.H.; Zeid, A.A.; Enan, G. Chemical constitution and antimicrobial activity of kombucha fermented beverage. *Molecules* **2021**, *26*, 5026. [\[CrossRef\]](#) [\[PubMed\]](#)

173. 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](#)]
174. Woting, A.; Pfeiffer, N.; Loh, G.; Klaus, S.; Blaut, M. *Clostridium ramosum* promotes high-fat diet-induced obesity in gnotobiotic mouse models. *MBio* **2014**, *5*, e01530-14. [[CrossRef](#)] [[PubMed](#)]
175. Devi, S.M.; Kurrey, N.K.; Halami, P.M. In vitro anti-inflammatory activity among probiotic lactobacillus species isolated from fermented foods. *J. Funct. Foods* **2018**, *47*, 19–27. [[CrossRef](#)]
176. Li, C.; Nie, S.P.; Zhu, K.X.; Ding, Q.; Li, C.; Xiong, T.; Xie, M.Y. *Lactobacillus plantarum* NCU116 improves liver function, oxidative stress and lipid metabolism in rats with high fat diet induced non-alcoholic fatty liver disease. *Food Funct.* **2014**, *5*, 3216–3223. [[CrossRef](#)]
177. Gomma, E.Z. Human gut microbiota/microbiome in health and diseases: A review. *Antonie Van Leeuwenhoek* **2020**, *113*, 2019–2040. [[CrossRef](#)]
178. Matijašić, M.; Meštrović, T.; Paljetak, H.Č.; Perić, M.; Barešić, A.; Verbanac, D. Gut microbiota beyond bacteria—Mycobiome, virome, archaeome, and eukaryotic parasites in IBD. *Int. J. Mol. Sci.* **2020**, *21*, 2668. [[CrossRef](#)]
179. Thursby, E.; Juge, N. Introduction to the human gut microbiota. *Biochem. J.* **2017**, *474*, 1823. [[CrossRef](#)]
180. Binda, C.; Lopetuso, L.R.; Rizzatti, G.; Gibiino, G.; Cennamo, V.; Gasbarrini, A. Actinobacteria: A relevant minority for the maintenance of gut homeostasis. *Dig. Liver Dis.* **2018**, *50*, 421–428. [[CrossRef](#)]
181. Stojanov, S.; Berlec, A.; Štrukelj, B. The influence of probiotics on the firmicutes/bacteroidetes ratio in the treatment of obesity and inflammatory bowel disease. *Microorganisms* **2020**, *8*, 1715. [[CrossRef](#)] [[PubMed](#)]
182. Bäuml, A.J.; Sperandio, V. Interactions between the microbiota and pathogenic bacteria in the gut. *Nature* **2016**, *535*, 85–93. [[CrossRef](#)]
183. Gensollen, T.; Iyer, S.S.; Kasper, D.L.; Blumberg, R.S. How colonization by microbiota in early life shapes the immune system. *Science* **2016**, *352*, 539–544. [[CrossRef](#)] [[PubMed](#)]
184. Costa, M.A.d.C.; Vilela, D.L.d.S.; Fraiz, G.M.; Lopes, I.L.; Coelho, A.I.M.; Castro, L.C.V.; Martin, J.G.P. Effect of kombucha intake on the gut microbiota and obesity-related comorbidities: A systematic review. *Crit. Rev. Food Sci. Nutr.* **2021**, *1–16*. [[CrossRef](#)] [[PubMed](#)]
185. Lukic, J.; Chen, V.; Strahinic, I.; Begovic, J.; Lev-Tov, H.; Davis, S.C.; Tomic-Canic, M.; Pastar, I. Probiotics or pro-healers: The role of beneficial bacteria in tissue repair. *Wound Repair Regen.* **2017**, *25*, 912–922. [[CrossRef](#)] [[PubMed](#)]
186. Galdeano, C.M.; Cazorla, S.I.; Dumit, J.M.L.; Vélez, E.; Perdígón, G. Beneficial effects of probiotic consumption on the immune system. *Ann. Nutr. Metab.* **2019**, *74*, 115–124. [[CrossRef](#)]