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Review

Fermented Beverages Revisited: From Terroir to Customized Functional Products

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Abstract: Fermented beverages have been a constant companion of humans throughout their history. A wide range of products have been developed with time, depending on the availability of raw materials and ambient conditions. Their differentiation was based on the specific characteristics of each product, resulting from the cultivation of different varieties and the variability of environmental conditions and agricultural practices, collectively described by the term 'terroir' that was developed in winemaking. The health benefits that have been associated with their consumption, which include the control of blood pressure and glycemic control, along with immunomodulatory, hypocholesterolemic, hepatoprotective, and antiproliferative activities, directed their re-discovery that occurred over the last few decades. Thus, the dynamics of the microbial communities of fermented beverages during fermentation and storage have been thoroughly assessed. The functional potential of fermented beverages has been attributed to the chemical composition of the raw materials and the bioconversions that take place during fermentation and storage, due to the metabolic capacity of the driving microbiota. Thus, the proper combination of raw materials with certain microorganisms may allow for the modulation of the organoleptic properties, as well as enrichment with specific functional ingredients, enabling targeted nutritional interventions. This plasticity of fermented beverages is their great advantage that offers limitless capabilities. The present article aims to critically summarize and present the current knowledge on the microbiota and functional potential of fermented beverages and highlight the great potential of these products.

Keywords: wine; kefir; kombucha; functional ingredients

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1. Introduction

Fermented beverages are produced since antiquity, with wine being the most characteristic example. They can be classified according to the nature of the raw materials, or the type of fermentation employed. According to the first, two classes of fermented beverages are distinguished: plant-based and dairy. The plant-based ones can be further subdivided into cereal-based products, such as boza, cheka, pozol, kvass, the various types of beer, etc. [1–6]; fruit-based products, such as the various types of wine, cider, gilaburu, etc. [7–11]; and herbal-based products, such as kombucha [12,13]. As far as fermented dairy beverages are concerned, several types have been described, such as kefir, kumis, viili, acidophilus milk, etc. [14], each with a unique history, production procedure and microecosystem composition. If the predominant type of fermentation is taken as a criterion, fermented beverages can be classified into acidic, alcoholic, and mixed fermented products; kefir and kombucha can serve as examples of acidic beverages, wine of alcoholic, and boza of mixed fermented beverages.

The term 'terroir' has been developed and is currently in use in wine technology. It indicates a specific geographical area along with the associated grape cultivars and oenological practices, which altogether define the specific features of the produced wines. Nowadays, the health benefits that accompany food consumption have also been at the epicenter of consumer interest. This trend has led to the intensive study of fermented beverages throughout the world, their functional ingredients as well as the molecular mechanisms that are implicated. Apart from grape wine, two fermented beverages have also been distinguished for their functional potential, namely kefir and kombucha.

Thus, moderate wine consumption has been correlated with reduced risk of cardiovascular events [15,16], neurodegenerative diseases [17,18], and type 2 diabetes [19,20], as well as systolic blood pressure decrease [21–23], improvement of the gastrointestinal tract function [24–26] and the main symptoms of fibromyalgia [27]. These have all been principally attributed to the phenolic compounds that it contains. Kombucha consumption has been correlated with a series of effects, such as antidiabetic, antihypertensive, antimicrobial, antiproliferative, hepatoprotective, hypocholesterolemic and immunomodulatory [28–37]. As in the case of grape wine, these activities have been attributed to kombucha phenolic content. Finally, kefir consumption has been correlated with a series of effects, including antiproliferative and immunomodulatory capacity, effective glycemic control, prevention and treatment of atherosclerosis and liver damage, as well as control of blood pressure [38–44]. These activities have been attributed to the amino acid and peptide content of kefir.

The present study aimed to comprehensively and critically present the microbiota of fermented beverages, the functional properties that have been associated with the consumption of the most prominent ones, along with the underlying molecular mechanisms, as well as the strategies that have been employed towards their customization, in order to summarize the current knowledge and facilitate the identification of research gaps.

2. The Microbiota of Traditional Fermented Beverages

In Table 1, the microbiota of traditional fermented beverages around the world is presented. Three aspects are immediately noticed: (1) the diversity of the raw materials employed, (2) the diversity of the microorganisms implicated in each type of fermentation, and (3) some products have attracted scientific attention and are therefore heavily studied, while the microecosystem of others has been less intensively assessed.

The availability of raw materials combined with suitable environmental conditions has led to the development of a wide range of fermented beverages, some of which are considered as characteristic of certain geographical areas. Indeed, products such as kombucha and bhaati jaanr, which are based on tea and rice, respectively, have Asian origins; products based on maize, such as pozol, chicha, and atole agrio originate from America, whereas milk and cereal-based fermented beverages are abundant in Africa and Europe. Despite the current globalization of production, traditional knowledge may still be derived from the cradle in which each product was originally developed.

In the majority of the cases, the microbial consortium that drives fermentation of the products reported in Table 1 consists of yeasts and bacteria, and more specifically, lactic and acetic acid bacteria. This can be attributed to the composition of the raw materials and the conditions used for fermented product manufacture but is biased by the number of samples analyzed and the identification methodology employed. In general, the higher the number of samples analyzed, the more likely is to enrich the biodiversity already reported in the literature. A wide range of techniques are currently available, the correct application of which may lead to reliable identification at species or subspecies level. The specific nutritional and growth requirements of each microorganism, at strain level, define the nature of the relationships that will be developed within the microecosystem. Despite the large number of studies, at least in the case of kombucha and kefir, the trophic relationships between the microorganisms are still far from being understood. The only exception seems to be wine must fermentation. In that case, the requirements and the capacity of the implicated yeast species have been extensively studied, and this knowledge

is already considered as established. On the other hand, research is currently focused on understanding the physiological attributes of the lactic acid bacteria that carry out malolactic fermentation [45].

Table 1. The microbiota of representative traditional fermented beverages around the world.

Product	Main Ingredient	Microbiota	References
Kombucha	Sweetened black or green tea	**LAB**: *O. oeni*, *Lq. nagelii* **AAB**: *A. aceti*, *A. musti*, *A. okinawensis*, *A. pasteurianus*, *A. peroxydans*, *A. senegalensis*, *A. tropicalis*, *A. xylinoides*, *A. xylinum*, *Ga. europaeus*, *Ga. hansenii*, *Ga. intermedius*, *Ga. xylinus*, *Gb. oxydans*, *Kb. europaeus*, *Kb. hansenii*, *Kb. intermedius*, *Kb. rhaeticus*, *Kb. saccharivorans*, *Kb. xylinus* **Yeasts**: *Br. anomalus*, *Br. bruxellensis*, *Br. lambicus*, *Ca. albicans*, *Ca. boidinii*, *Ca. colleculosa*, *Ca. guilliermondii*, *Ca. kefyr*, *Ca. krusei*, *Ca. sake*, *Ca. stellata*, *De. anomala*, *De. bruxellensis*, *H. valbyensis*, *K. marxianus*, *Kz. unispora*, *Lh. fermentati*, *Pi. fermentans*, *Pi. membranifaciens*, *R. mucilaginosa*, *S. cerevisiae*, *S. uvarum*, *Sd. ludwigii*, *Sz. pombe*, *T. delbrueckii*, *Z. bailii*, *Z. lentus*, *Z. parabaillii*, *Zt. fiorentina*	[12,13,46–54]
Kefir	Milk	**LAB**: *E. durans*, *E. faecalis*, *La. casei*, *La. paracasei*, *Lp. plantarum*, *Lb. acidophilus*, *Lb. amylovorus*, *Lb. delbrueckii*, *Lb. crispatus*, *Lb. helveticus*, *Lb. kefiranofaciens*, *Lc. lactis*, *Lt. buchneri*, *Lt. kefiri*, *Lt. parabuchneri*, *Lt. parakefiri*, *Le. parakefiri*, *Ln. mesenteroides*, *Ln. paramesenteroides*, *Ln. pseudomesenteroides*, *Lq. uvarum*, *Lq. satsumensis*, *Lv. brevis*, *Str. durans*, *Str. thermophilus* **AAB**: *A. aceti*, *A. fabarum*, *A. lovaniensis*, *A. okinawensis*, *A. orientalis*, *A. rancens*, *A. syzygii*, *Gb. frateurii*, *Gb. japonicus* **Yeasts**: *Br. anomalus*, *Ca. colliculosa*, *Ca. inconspicua*, *Ca. kefyr*, *Ca. krusei*, *Ca. lambica*, *Ca. maris*, *De. anomala*, *K. lactis*, *K. marxianus*, *Kz. aerobia*, *Kz. exigua*, *Kz. kefir*, *Kz. unispora*, *Lh. meyersii*, *M. guilliermondii*, *Pi. kudriavzevii*, *Pi. guilliermondii*, *S. cerevisiae*, *S. fragilis*, *S. turicensis*, *T. delbrueckii*	[55–81]
Wine	Fruits	**Yeasts**: *Au. pullulans*, *Ca. fermentati*, *Ca. intermedia*, *Ca. parapsilopsis*, *Ca. pulcherrima*, *Ca. quercitrusa*, *Ca. zemplinina*, *H. uvarum*, *H. guillermondii*, *H. uvarum*, *H. valbyensis*, *I. occidentalis*, *I. orientalis*, *I. terricola*, *Kc. apiculata*, *Lh. thermotolerans*, *Pi. fermentans*, *R. graminis*, *R. mucilaginosa*, *S. bayanus*, *S. cerevisiae*, *S. italicus*, *S. pastorianus*, *S. uvarum*, *Sd. ludwigii*, *Sz. pombe*, *T. delbrueckii*, *T. globispora*, *Y. lipolytica*, *Z. bailii*, *Z. fermentati*	[9,10,82–86]
Apple cider	Apples	**Yeasts**: *H. osmophila*, *H. uvarum*, *H. valbyensis*, *M. pulcherrima*, *Pi. guillermondii*, *S. bayanus*, *S. cerevisiae*	[8]
Amabere amaruranu	Milk	**LAB**: *Ln. mesenteroides*, *Lp. plantarum*, *Str. thermophilus* **Yeasts**: *Ca. albicans*, *Ca. famata*, *S. cerevisiae*, *Tr. mucoides*	[87]
Andean chicha	Cereals	**Yeasts**: *H. guiermondii*, *H. opuntiae*, *H. uvarum*, *Ko. ohmeri*, *R. slooffiae*, *Mz. guillermondii*, *Pi. kluyveri*, *Pi. kudriavzevii*, *R. mucilaginosa*, *Wi. anomalus*, *S. cerevisiae*, *Y. lipolytica*	[88]
Atole agrio	Maize	**LAB**: *Ag. composti*, *E. hirae*, *La. casei*, *La. paracasei*, *La. rhamnosus*, *Lc. lactis*, *Lc. piscium*, *Li. aviarius*, *Ln. garlicum*, *Ln. mesenteroides*, *Ln. pseudomesenteroides*, *Lo. coryniformis*, *Lp. fabifermentans*, *Lp. paraplantarum*, *Lp. pentosus*, *Lp. plantarum*, *Lt. curvatus*, *Lv. brevis*, *P. pentosaceus*, *P. stilesii*, *W. cibaria*, *W. confusa*, *W. hellenica*, *W. paramesenteroides*, *Str. equinus* **AAB**: *A. estunensis*, *A. indonesiensis*, *A. pasteurianus*, *A. tropicalis*, *Gb. frateurii*	[89]
Bacaba chicha	*Oenocarpus bacaba*	**LAB**: *E. durans*, *E. hirae*, *Ln. lactis* **Yeasts**: *Pi. caribbica*, *Pi. guillermondii*	[90]
Bhaati jaanr	Rice	**LAB**: *Lo. bifermentans*, *P. pentosaceus* **Yeasts**: *Ca. glabrata*, *Pi. anomala*, *S. cerevisiae*, *Sp. fibuligera*	[91]
Bili bili	Sorghum	**Yeasts**: *Ca. melibiosica*, *Cr. albidius*, *D. hansenii*, *De. bruxelensis*, *K. marxianus*, *R. mucilaginosa*, *S. cerevisiae*, *T. delbrueckii*	[92]
Borde	Cereals	**LAB**: *Lv. brevis*, *P. pentosaceus*, *W. confusa*, *W. viridescens*	[93]

Table 1. *Cont.*

Product	Main Ingredient	Microbiota	References
Boza	Cereals	**LAB**: *Fr. sanfransiscensis*, *La. casei*, *La. paracasei*, *Lb. acidophilus*, *Lc. lactis*, *Li. salivarius*, *Lm. fermentum*, *Ln. amelibiosum*, *Ln. mesenteroides*, *Ln. paramesenteroides*, *Ln. pseudomesenteroides*, *Lo. coryniformis*, *Lp. plantarum*, *Lt. buchneri*, *Lt. parabuchneri*, *Lt. sakei*, *P. parvulus*, *W. confusa* **Yeasts**: *Ca. glabrata*, *Ca. tropicalis*, *Pi. fermentans*, *Pi. guillermondii*, *Pi. norvegensis*, *S. cerevisiae*, *S. uvarum*	[94–96]
Burukutu	Sorghum	**LAB**: *Lb. acidopilus*, *Lc. lactis*, *Lm. fermentum*, *Lp. plantarum*, *Lv. brevis* **Yeasts**: *S. cerevisiae*	[97]
Chicha	Maize	**LAB**: *Lm. fermentum*, *Lp. plantarum*, *W. cibaria*, *Str. alactolyticus*, *Str. luteciae* **AAB**: *A. okinawensis*	[98]
Ikigage	Sorghum	**Yeasts**: *Ca. humilis*, *Ca. inconspicua*, *Ca. magnolia*, *S. cerevisae*, *I. orientalis* **LAB**: *Le. buchneri*, *Lm. fermentum*	[99]
Gilaburu	European cranberry	**LAB**: *La. casei*, *La. pantheris*, *Le. buchneri*, *Le. parabuchneri*, *Ln. pseudomesenteroides*, *Lp. plantarum*, *Lv. brevis*, *Sc. harbinensis*	[11]
Mahewu	Cereals	**LAB**: *E. hermanniensis*, *E. lactis*, *Fu. rossiae*, *Lc. lactis*, *Lm. fermentum*, *Ln. holzapfelii*, *Ln. pseudomesenteroides*, *Lp. plantarum*, *P. pentosaceus*, *W. cibaria*, *W. confusa* **Yeasts**: *Ca. glabrata*, *S. cerevisiae*	[100]
Fermented masau	*Ziziphus mauritiana*	**LAB**: *Cb. divergens*, *Le. hilgardii*, *Li. agilis*, *Lo. bifermentans*, *Lm. fermentum*, *Lp. plantarum*, *W. minor* **Yeasts**: *Ca. glabrata*, *H. opuntiae*, *I. orientalis*, *Pi. fabianii*, *S. cerevisiae*, *Sp. fibuligera*	[7]
Pito	Cereals	**Yeasts**: *Ca. tropicalis*, *Ha. anomala*, *K. africanus*, *Kc. apiculata*, *S. cerevisiae*, *Sz. pombe*, *T. delbrueckii*	[1]
Pozol	Maize	**LAB**: *C. alimentarius*, *E. saccharolyticus*, *La. casei*, *Lb. delbrueckii*, *Lc. lactis*, *Lm. fermentum*, *Lp. plantarum*, *Str. bovis*, *Str. suis* **Yeasts**: *Ca. guilliermondii*, *Cs. cladosporioides*, *D. hansenii*, *Ge. candidum*, *K. lactis*, *Pe. fellutanum*, *Ph. fimeti*, *Ph. glomerata*, *R. minuta*, *R. mucilaginosa*	[2,101,102]
Pulque	*Agave* spp.	**LAB**: *Fr. sanfranciscensis*, *Lb. acetotolerans*, *Lb. acidophilus*, *Lb. delbrueckii*, *Lc. lactis*, *Le. hilgardii*, *Le. kefiri*, *Ln. citreum*, *Ln. gasocomitatum*, *Ln. kimchi*, *Ln. mesenteroides*, *Ln. pseudomesenteroides*, *Lp. plantarum*, *P. urinaeequi*, *Se. paracollinoides*, *Str. deviesei* **AAB**: *A. aceti*, *A. malorum*, *A. orientalis*, *A. pomorum*, *Gb. oxydans* **Yeasts**: *Ca. parapsilosis*, *Ca. valida*, *Cl. lusitaniae*, *D. carsonii*, *H. uvarum*, *Ge. candidum*, *K. lactis*, *K. marxianus*, *Pi. guilliermondii*, *Pi. membranifaciens*, *R. mucilaginosa*, *S. bayanus*, *S. cerevisiae*, *S. pastorianus*, *T. delbrueckii*	[103–106]

AAB: *Acetic acid bacteria*; LAB: *lactic acid bacteria*. *A.*: *Acetobacter*; *Ag.*: *Agrilactobacillus*; *Au.*: *Aureobasidium*; *Br.*: *Brettanomyces*; *C.*: *Companilactobacillus*; *Ca.*: *Candida*; *Cb.*: *Carnobacterium*; *Cl.*: *Clavispora*; *Cr.*: *Cryptococcus*; *Cs.*: *Cladosporium*; *D.*: *Debaryomyces*; *De.*: *Dekkera*; *E.*: *Enterococcus*; *Fr.*: *Fructilactobacillus*; *Fu.*: *Furfurilactobacillus*; *Ga*: *Gluconacetobacter*; *Gb.*, *Gluconobacter*; *Ge.*: *Geotrichum*; *I.*: *Issatschenkia*; *Kb.*: *Komagataeibacter*; *H.*: *Hanseniaspora*; *Ha.*: *Hansenula*; *K.*: *Kluyveromyces*; *Kc.*: *Kloeckera*; *Ko.*: *Kodamaea*; *Kz.*: *Kazachstania*; *La.*: *Lacticaseibacillus*; *Lb.*: *Lactobacillus*; *Lc.*: *Lactococcus*; *Le.*: *Lentilactobacillus*; *Lh.*, *Lachancea*; *Li.*: *Ligilactobacillus*; *Lm.*: *Limosilactobacillus*; *Ln.*: *Leuconostoc*; *Lo.*: *Loigolactobacillus*; *Lp.*: *Lactiplantibacillus*; *Lq. Liquorilactobacillus*; *Lt.*: *Latilactobacillus*; *Lv.*: *Levilactobacillus*; *M.*: *Metschnikowia*; *Mz.*: *Meyerozyma*; *O.*: *Oenococcus*; *P.*: *Pediococcus*; *Pe.*: *Penicillium*; *Ph.*: *Phoma*; *Pi.*: *Pichia*; *R.*: *Rhodotorula*; *S.*: *Saccharomyces*; *Sc.*: *Schleiferilactobacillus*; *Sd.*: *Saccharomycodes*; *Se.*: *Secundilactobacillus*; *Sp.*: *Saccharomycopsis*; *Str.*: *Streptococcus*; *Sz.*: *Schizosaccharomyces*; *T.*: *Torulospora*; *Tr.*: *Trichosporon*; *W.*: *Weissella*; *Wi.*: *Wickeramomyces*; *Y.*: *Yarrowia*; *Z.*: *Zygosaccharomyces*; *Za.*: *Zygoascus*; *Zt.*: *Zygotorulaspora*.

3. Functional Properties of Fermented Beverages

The consumption of fermented beverages has been associated with a series of functional properties. These have been attributed to the chemical composition of the raw materials employed and the bioconversions that take place during the fermentation process. Thus, the same functional properties may be assigned to the same or different bioactive compounds, the formation of which depends upon the metabolic capacity of the microorganisms that constitute the driving micro-community. In the next paragraphs, the functional properties of wine, kombucha and kefir, the most studied fermented beverages, are summarized.

3.1. Functional Properties of Wine

A series of functional properties have been associated with wine and are mainly attributed to the phenolic compounds that it contains. The type and amount of phenolic compounds depend upon factors such as grape variety, environmental conditions, agricultural practices and winemaking technology [107]. In general, the major phenolic compounds of wine are distinguished into flavonoids and non-flavonoids. Flavonols (quercetin, kaempferol and myricetin), anthocyanins (cyanin, petunin, peonin and malvin), and flavan-3-ols (catechin, epicatechin, gallocatechin, procyanidins and condensed tannins) belong to the first category, while phenolic acids (hydroxybenzoic and hydroxycinnamic acids), volatile phenols (ethyl phenol, vinyl phenol, guaiacol, etc.), and stilbenes (resveratrol and its polymers) belong to the second one [108,109]. The total amount of flavonoids in white and red wines has been reported to range between 25–30 and 700–1000 mg of gallic acid equivalent (GAE/L), respectively. Catechins and soluble tannins are quantitatively the most abundant classes of compounds in white and red wines, respectively. On the other hand, the total amount of non-flavonoids has been reported to range between 160–260 and 230–500 mg GAE/L in white and red wines, respectively, with cinnamates being, in both cases, the most abundant class of compounds, with approximately 150 mg of GAE/L [108]. The bioavailability of the aforementioned compounds is a key issue as it affects their biological function. In general, wine phenolic compounds are only partially bioavailable, not only because of their chemical structure but also due to the biotransformations that take place during digestion [110]; it has been reported to range between 2–25% [111–113].

Excessive alcohol consumption has been correlated with an increased incidence of disease [114]. On the contrary, moderate alcohol consumption, particularly wine, seems to have a protective role on human health [115]. The concept of moderate or low-risk wine consumption has been exhaustively debated [115,116]. From a quantitative point of view, the consumption of up to 25–40 g alcohol per day for males and 13–25 g for females is generally accepted as moderate [117]. A range of health benefits have been associated with moderate wine consumption, such as lowering the risk of cardiovascular disease and neurodegenerative disease development, protection against type 2 diabetes, and generally life span prolongation. The capacity of wine to confer these health benefits has been assessed through in vitro, in vivo and clinical studies. The next paragraphs focus on the underlying mechanisms that validate the latter.

An association between moderate wine consumption and reduced risk of cardiovascular events, even among persons with established heart diseases, has been reported [15,118]. This has been attributed to the modulation of circulating cholesterol and anti-platelet activity of alcohol and to the antioxidant, anti-inflammatory and anti-platelet activities of the phenolic compounds [119,120]. The antioxidant activity is expressed through free radical scavenging and through the upregulation of Nrf2, which in turn induces antioxidant gene expression [121]. Regarding their anti-inflammatory activities, a series of mechanisms have been proposed, such as switching off the NF-κB pathway [122], blocking oxysterol-related NOX1 induction [123], suppression of NLRP3 inflammasome activation [124], suppression of the JAK/STAT inflammatory pathway and modulation of Nrf2 activity [125], as well as decrease in IL-1β, IL-6 and IL-8 secretion [126,127]. Finally, the capacity of red wine to inhibit thrombin, ADP- and PAF-induced platelet aggregation has been reported [128–133] and attributed to ethanol and polyphenols, particularly quercetin, tyrosol and trans-resveratrol [132,133]. In addition, the inhibition of PAF biosynthesis by tyrosol and resveratrol has also been reported in U-937 cells under inflammatory conditions [134].

An association between moderate wine consumption and reduction in the risk of neurodegenerative diseases has also been developed [17]. The mode through which wine consumption may affect the onset of Alzheimer's and Parkinson's diseases has been extensively studied. In the first case, protection may take place through the antioxidant and anti-inflammatory activities of wine, as well as through more specific functions such as the modulation of secretase enzymes, the enhancement of amyloid clearance, the inhibition of amyloid aggregation and the prevention of tau protein hyperphosphorylation [135–137]. In-

deed, the activation of α-secretase activity by 6% Cabernet Sauvignon, myricetin, quercetin, resveratrol, and caffeic acid [138–143], along with the inhibition of BACE1 activity by resveratrol and some of its oligomers, epicatechin, myricetin, quercetin, kaempherol and caffeic acid [142–154] and inhibition of γ-secretase by resveratrol, oxy-resveratrol, and piceatannol [155,156], have been reported. In addition, amyloid accumulation and aggregation seem to be prevented by a variety of mechanisms. Amyloid clearance or the induction of degradation mechanisms, activities that have been reported for resveratrol [157–159] and quercetin [160], have been reported to prevent amyloid accumulation. On the other hand, resveratrol, quercetin, and grape seed pro-anthocyanidin consisting of catechin, epicatechin, and epicatechin gallate, have presented an anti-aggregation capacity [161–165]. Finally, the inhibition of tau protein hyperphosphorylation has been reported for resveratrol, quercetin and caffeic acid [166–169]. Regarding Parkinson's disease, protection may take place through the antioxidant activity and neuroprotective effects of resveratrol, which seem to be related to its SIRT-activating potential [170–174], and quercetin, which seems to be related to the induction of the PKD1/CREB/BDNF axis [175,176]. In addition, other constituents such as caffeic acid, gallic acid and catechins have also been reported to contribute to the aforementioned activities [177–179].

The association between wine consumption and a reduced risk of type 2 diabetes has been repeatedly reported [19,20]. This association was further improved by Ma et al. [180], which highlighted that this protective action takes place when moderate alcohol drinking, especially wine, takes place with meals. The mode of action includes the inhibition of α-amylase and α-glucosidase activities, the inhibition of sodium-dependent glucose transporter 1 (SGLT1) and the activation of 5-adenosine monophosphate-activated protein kinase (AMPK) [181–184]. Regarding diabetic patients, wine consumption has been reported to attenuate insulin resistance, with no effect on vascular reactivity and nitric oxide production [185], to reduce the diastolic blood pressure and total cholesterol but not glucose parameters and other cardiovascular risk factors [186], and to reduce the risks of cardiovascular events and all-cause mortality [187]. In addition, the initiation of red wine consumption has been associated with increased high-density lipoprotein cholesterol (HDL-C) and apolipoprotein(a)1 level and decreased the ratio of total cholesterol to HDL-C [188]. In addition, wine consumption improved glycemic control, in terms of fasting plasma glucose, homeostatic model assessment of insulin resistance and hemoglobin A1c, but only in patients carrying the alcohol dehydrogenase alleles [ADH1B*1], i.e., the slow ethanol metabolizers.

Several other health benefits have been correlated with moderate wine consumption, such as the decrease in systolic blood pressure [21–23], the improvement of gastrointestinal tract function [24–26] and the improvement of the main symptoms of fibromyalgia [27]. However, further research is still necessary in order to identify the responsible molecular mechanisms.

3.2. Functional Properties of Kombucha

Kombucha is commercially available as a non-alcoholic beverage; therefore, the ethanol content should not exceed 0.5% alcohol by volume (ABV). However, in many cases, this limit is not respected [189–191] and the production of kombucha with ethanol content as high as 5.83 mg/mL has been reported [49]. A series of functional properties, such as antioxidant, antiproliferative, immunomodulatory, antihypertensive, antidiabetic, hypocholesterolemic, hepatoprotective and antimicrobial, have been attributed to kombucha. In all cases, the functional properties have been attributed, at least partially, to specific compounds that are either present in the raw materials or are formed during fermentation. Therefore, every factor that affects the production of the raw materials or the fermentation procedure is expected to affect the functional properties of the final product, to a greater or lesser degree [32,192–196]. Below, a short description of studies assessing these properties is offered.

The antioxidant capacity of kombucha has been principally attributed to the presence of phenolic compounds. The phenolic concentration and diversity in black-tea kombucha have been reported to be greater than those of green-tea kombucha [35]. This has been attributed to the processing steps that are necessary for black tea production. During these steps, the concentration of theaflavins and thearubigins increases, and they become the main polyphenols in black tea [197]. During fermentation, these compounds are subjected to enzymatic or chemical biotransformation, resulting in the formation of a wealth of lower-molecular-weight phenolic compounds. Indeed, Cardoso et al. [35] identified 126 phenolic compounds in the samples of green and black-tea kombucha that they analyzed, of which, 50 compounds were common, 75 were unique to black-tea kombucha, and only one, namely verbascoside, was unique to green-tea kombucha. Interestingly, the occurrence of five phenolic compounds in green-tea kombucha and 30 phenolic compounds in black-tea kombucha was solely assigned to the fermentation process.

The antioxidant activity of kombucha is usually assessed in vitro through free-radical scavenging assays such as DPPH, FRAP, ABTS, MCA, Curpac, etc. [35,198,199]. In vivo studies are generally lacking; only a few are currently available, the main findings of which are described in the following lines. Dipti et al. [200] used a lead acetate solution to induce oxidative stress on male albino (Sprague Dawley) rats and studied the antioxidant effect of black-tea kombucha. The results of kombucha oral administration included the reduction of DNA damage and lipid peroxidation, as well as the increase of glutathione level and GPx activity. Yang et al. [201] used mice from the Institute of Cancer Research and fed them with a hypocholesterolemic diet (HCD) combined with 66 mL Kg^{-1} DW of traditional kombucha tea (TKT) or modified kombucha tea (MKT) (sweetened black tea fermented with *Gluconoacetobacter* sp. strain A4) or 60 mg Kg^{-1} DW of D-saccharic acid-1,4-lactone (DSL) for 12 weeks. The antioxidant activity, measured as total antioxidant capacity (TAOC), superoxide dismutase (SOD) and malonaldehyde (MDA) was assessed in the serum after the end of the 12 weeks of the treatment. The hypocholesterolemic diet resulted in a statistically significant decrease in TAOC and SOD and an increase in MDA values. These values were restored when the HCD was supplemented with TKT, MKT, or DSL. Vazquez-Cabral et al. [202] measured the antioxidant activities of kombucha and a kombucha analog (KAO) made of *Quercus resinosa* leaves against the oxidative damage caused by H_2O_2 in activated THP-1 human monocyte cells and reported the capacity of KAO to decrease oxidative stress. Finally, Gaggia et al. [49] studied the capacity of kombucha made from *Aspalathus linearis* leaves, fermented for 7 and 14 days, to decrease oxidative stress in L929 mouse fibroblasts caused by H_2O_2. When the treatment with the kombucha preceded the H_2O_2 application, the cell viability was partially restored by both products. When the treatment with the kombucha followed the application of H_2O_2, only the kombucha fermented for 14 days was able to restore the viability of the cells.

The antioxidant capacity of kombucha has also been reported to result in hypocholesterolemic and antidiabetic effects. Indeed, kombucha administration has been reported to decrease total and LDL cholesterol in rabbits and mice fed a high-cholesterol diet, as well as attenuate histological effects, such as lesions in the intima [30,34,201–203]. As far as the antidiabetic effect is concerned, this is attributed not only to the antioxidant capacity of kombucha, which addresses the oxidative stress caused by diabetes, but also to the reduction in blood glucose and the increase in plasma insulin, which have been reported as the effects of kombucha administration in experimental rats with induced diabetic consequences [31,33,204,205].

The antiproliferative capacity of kombucha has been demonstrated in vitro using human cancer cell lines. More precisely, the cytotoxicity against lung carcinoma (A549), osteosarcoma (U2OS), renal carcinoma (786-O), ileocecal colorectal adenocarcinoma (HCT8), colorectal adenocarcinoma (CACO-2), rhabdomyosarcoma (RD), cervix carcinoma (Hep2c), prostate cancer (PC-3), colon cancer (HCT-116), breast cancer (MCF-7) and a murine fibroblast (L2OB) has been exhibited [32,35,206,207]. Jayabalan et al. [206] proposed that Dimethyl 2-(2-hydroxy-2-methoxypropylidene) malonate and vitexin may contribute to

these cytotoxic effects. Cardoso et al. [35] attributed the higher antiproliferative capacity of green-tea kombucha, compared to that of black-tea kombucha, to the presence of higher concentrations of catechins and verbascoside, the antitumor activity of which has already been reported [208,209]. However, not all cell lines were affected by black-tea kombucha [210]. In addition, Srihari et al. [211] reported that the survival of the prostate cancer cell line (PC-3) decreased after treatment with lyophilized kombucha extract, most likely due to the downregulation of the angiogenesis-associated genes HIF-1α, VEGF, IL-8, COX-2, MMP-2, and MMP-9. Despite these promising results, clinical studies are still lacking.

Strong indications of the immunomodulatory capacity of kombucha have been reported. More precisely, black-tea kombucha administration in male Swiss albino mice with indomethacin-induced stomach ulceration resulted in effective healing, which was attributed to the antioxidant activity and the reduction of gastric acid secretion [28]. The delay in the onset and severity of experimental autoimmune encephalomyelitis induced in female C57BL/6 mice through black-tea kombucha administration was reported by Marzban et al. [212]. In addition, the suppression of TNF-α and IL-6 levels in lipopolysaccharide-stimulated macrophages, as well as the in vitro inhibition of 5-LOX enzyme activity by black-tea kombucha extract, has also been reported [32,201].

As far as the antihypertensive activity is concerned, this is indicated by the detection of ACE inhibitory capacity. Certain flavonoids [213] with certain structural features [214] have an excellent antihypertensive capacity. The ACE inhibitory activity of green- and black-tea kombucha, as well as a series of analogues, has been reported [37,215].

The hepatoprotective activity of kombucha has been repeatedly exhibited in animal models. Indeed, the protective effect of black-tea kombucha against tertiary butyl hydroperoxide-induced cytotoxicity in murine hepatocytes of male albino Swiss mice, by reducing ROS generation, as well as through the inhibition of glutathione depletion and the attenuation of malonaldehyde levels, was reported by Bhattacharya et al. [216]. Abshenas et al. [29] induced hepatotoxicity in male Balb/c mice through acetaminophen treatment. Kombucha consumption for 7 days before acetaminophen treatment reduced its toxicity through the reduction of the serum aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, and alkaline phosphatase levels. In addition, the decrease of histopathological changes, such as hepatocellular glycogen storage degeneration and necrosis, mononuclear cell infiltration in the portal area, dilation of central veins and capillarization, was also reported. Acetaminophen was also used by Wang et al. [160] to induce hepatotoxicity in male ICR mice. The administration of traditional black-tea kombucha as well as kombucha fermented only by *Gluconoacetobacter* sp. strain A4 effectively inhibited the increase of alanine aminotransferase, alkaline phosphatase, triglyceride and malondialdehyde, which were induced by acetaminophen treatment. These positive effects were largely attributed to the D-saccharic acid-1,4-lactone produced by the bacterial strain. Kabiri et al. [217] induced hepatotoxicity in male Wistar rats with thioacetamide and studied the effect of black-tea kombucha. Administration of kombucha for 3 weeks before TAA or after TAA treatment had all biochemical parameters assessed (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, lactate dehydrogenase, total, LDL and HDL cholesterol, triglycerides, and bilirubin) at comparable levels to the control group, accompanied by normal histology. Hyun et al. [218] induced hepatic steatosis in male C57BLKS and C57BLKS db/db mice through a methionine/choline-deficient diet. Black-tea kombucha administration was reported to reduce the liver weight/body weight ratio to control-group levels through the reduction of fatty acids uptake and triglyceride synthesis, which were also indicated through the application of reverse-transcription quantitative PCR.

The antimicrobial activity of kombucha, as well as a series of analogues, has been extensively assessed. The methods of choice are diffusion and microdilution. The inhibition of the growth of a series of microorganisms, including molds such as *Aspergillus flavus* and *As. niger*; yeasts such as *Candida albicans*, *Ca. glabrata*, *Ca. krusei*, and *Ca. tropicalis*; Gram-positive bacteria such as *Alicyclobacillus acidoterrestris*, *Bacillus cereus*, *Listeria monocytogenes*, *Micrococcus luteus*, *Staphylococcus aureus*, and *St. epidermidis*; and Gram-negative bacteria

such as *Aeromonas hydrophila*, *Agrobacterium tumefaciens*, *Campylobacter jejuni*, *Enterobacter cloacae*, *Escherichia coli*, *Esch. coli* O157:H7, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pr. vulgaris*, *Pseudomonas aeruginosa*, *Salmonella* Enteritidis, *Sa.* Typhi, *Sa.* Typhimurium, *Shigella dysenteriae*, *Sh. sonnei*, *Vibrio cholerae,* and *Yersinia enterocolitica* has been reported [35,36,207,219–224].

The ingredients to which this antimicrobial activity has been primarily attributed are organic acids, mainly acetic acid, as well as a series of compounds with antimicrobial capacity, such as catechins, unsaturated lactones, hydroxylactones and verbascoside [225–227]. Qualitative and quantitative differences between different types of kombucha have also been attributed to differences in their chemical composition [35,220,224].

In summary, kombucha seems to possess a wealth of functional properties, which have been assessed either in vitro or using animal models. Further study is still necessary, including clinical trials [228].

3.3. Functional Properties of Kefir

Kefir is another thoroughly studied non-alcoholic beverage. As in the case of kombucha, the limit of 0.5% ABV is not always respected [229], and the production of kefir with as much as 10% ethanol has been reported [230]. Many functional properties have been described for kefir and attributed to its amino acid and peptide content. The type of milk, the proteolytic capacity of the micro-consortium that drives fermentation, and the storage time [231] greatly affect these properties. The most important kefir activities that play an essential role in its functional properties are the antioxidant and anti-inflammatory ones. The first is attributed to a series of enzymatic and non-enzymatic systems. Catalase, superoxide dismutase, and glutathione peroxidase account for the enzymatic ones, while vitamin E and β-carotene—along with peptides resulting from the proteolytic breakdown of casein and amino acids, especially methionine, lysine and tryptophan, which seem to possess higher antioxidant activity than threonine, serine, alanine, valine, isoleucine and phenylalanine—account for the non-enzymatic ones [232–235]. The anti-inflammatory activity of kefir is evidenced through the reduction of the levels of proinflammatory mediators, such as TNF-a and IL-6β, and the increase of the levels of anti-inflammatory cytokines such as IL-10 [236–242]. The bacteria themselves [238], their extracellular vesicles (as in the case of *Lactobacillus kefiranofaciens* subsp. *kefirgranum* PRCC-1301 [243]), their micro integral membrane protein (such as the one of *Lactiplantibacillus plantarum* [244]) as well as kefir peptides [44,245] seem to contribute to this activity.

The association between kefir consumption and effective glycemic control through reduction of IL-1β and increase of IL-10 expression, as well as a reduction of fasting glucose and insulin levels and reduction of insulin resistance, has been reported [39,40,239,246,247]. Although the exact mode of action is still to be elucidated, it includes the release of bioactive peptides from caseins, most likely through the proteolytic activity of the kefir microbiota [247]. These bioactive peptides may also include ACE-inhibitory ones [38,248], which contribute to the effective control of blood pressure. Indeed, a series of studies have highlighted the antihypertensive capacity of kefir and indicated that ACE-inhibitory activity is among the most important mechanisms [249–251]. Kefir has also been reported to have an immunomodulatory capacity [43] and act towards the prevention and treatment of atherosclerosis [44] and liver damage [41], mostly due to its antioxidant and anti-inflammatory activities. In addition, it may also act as a psychobiotic due to the occurrence of LAB capable of producing gamma-aminobutyric acid, a major inhibitory neurotransmitter of the mammalian central nervous system [252], combined with anti-inflammatory activities [253,254].

The anti-carcinogenic capacity of kefir has been assessed in a variety of human cancer cell lines, such as the gastric AGS and SGC7901, mammary MCF-7, myeloid leukemia HL60/AR, colorectal Caco-2 and HT-29, etc. [255–259]. In the majority of cases, inhibition of proliferation and apoptosis induction were reported, mediated by molecular mechanisms that included downregulation of TGF-α and Bcl-2, decreased polarization of mitochondrial

membrane potential, as well as the upregulation of TGF-β1, Bax, caspase 3, caspase 8, caspase 9, etc. [42,256–258,260–262].

4. Customization of Fermented Beverages

In the previous paragraphs, the importance of raw materials in terms of their chemical composition, as well as the importance of the microbiota involved in fermentation in terms of metabolic capacity, have been highlighted. The functional properties of fermented beverages are achieved through the combination of these two parameters.

Product customization is as old as fermentation itself. The use of starter cultures is a form of customization, which, before the dawn of microbiology, took place through back-slopping. Nowadays, customization is facilitated by a wealth of information regarding the molecular mechanisms of disease and the mode of action of bioactive compounds. The customization of fermented beverages aims at achieving reproducibility, and therefore, the standardization of the product, and enhancing its functional properties. The first is principally achieved through the use of starter cultures. Indeed, the use of defined monocultures or micro-consortia allows the acceleration of the fermentation procedure, as well as the predictability of the outcome [263]. On the other hand, the enhancement of functional properties has been achieved mostly through the use of alternative and/or supplementary raw materials. In Table 2, representative studies on the customization of fermented beverages are exhibited.

Table 2. Representative studies on customization of fermented beverages.

Product	Customization Strategy-Outcome	References
Fruit-based fermented beverage	Improvement in the antioxidant activity of kiwifruit pulp through fermentation with a *Lp. plantarum* strain. The increase in DPPH and ABTS scavenging activities were correlated with the increase in total phenolic and flavonoid content.	[264]
Fruit-based fermented beverage	Pomegranate juice was fermented with *Lp. paraplantarum* CRL2051 and *Lp. plantarum* CRL2030 and administered to C57BL/6 mice fed a high-fat diet. The fermented juice offered protection against weight gain, liver damage, and dyslipidemia.	[265]
Fermented mango juice	Different mango cultivars were subjected to lactic acid fermentation with two LAB strains, namely *Lp. plantarum* 75 and *Ln. pseudomesenteroides* 56. The latter strain improved the retention of carotenoids, while the former enhanced the phenolic content and the antioxidant activity of all mango cultivars.	[266]
Whey-based fermented beverage	Commercially available probiotic LAB cultures, capable of producing conjugated linoleic acid (CLA), were used to ferment whey that was enriched with walnut oil lipolyzed by endogenous lipases as a source of free linoleic acid. After the optimization of the fermentation conditions, the whey-based beverage, apart from the CLA content, which could reach 36 mg/g fat, also presented a remarkable antioxidant capacity, most likely due to the presence of phenolic compounds and tocopherol in the walnut oil.	[267]
Kombucha analog	A kombucha analog with the use of coffee (*Coffea arabica*) by-product infusion, instead of *Camellia sinensis* infusion, was developed. The antioxidant activity (as estimated through the reduction in intracellular ROS and uric acid concentration in HK-2 model cells) and the anti-inflammatory activity (as estimated through a reduction in NO formation in LPS-induced macrophages of the kombucha analog and black-tea kombucha) were comparable.	[268]
Kombucha analog	Hops (*Humulus lupulus* L.), madimak (*Polygonum cognatum*), and hawthorn (*Crataegus monogyna*) were used to supplement black-tea kombucha, using the same SCOBY. After fermentation, the antioxidant activity of traditional kombucha was higher than that of the ones supplemented with herbs. All kombuchas exhibited comparative antiproliferative capacity against two cancer cell lines, namely HCT116 and Mahlavu.	[269]

Table 2. *Cont.*

Product	Customization Strategy-Outcome	References
Kombucha analog	*Hibiscus sabdarifa* L. leaves and stems were used to develop kombucha analogs. The products exhibited similar antioxidant capacity and no cytotoxicity against noncancer cells.	[270]
Kombucha analog	Infusions of blackcurrant (*Ribes nigrum*), black chokeberry (*Aronia melanocarpa*), and blueberry (*Vaccinium myrtillus*) were fermented using the same SCOBY, resulting in products with a significant content of polyphenolic compounds. The kombucha analogs exhibited significant antioxidant activity, assessed both in vitro and with the use of human keratinocytes (HaCaT) and fibroblasts (BJ).	[271]
Enhanced kombucha	Incorporation of *Echium amoenum* in kombucha resulted in a significant increase in the total phenol, anthocyanin, and flavonoid content, as well as the antioxidant activity. The kombucha prepared solely via *E. amoenum* infusion exhibited enhanced cytotoxicity against the human prostate cancer cell line (PC3) compared to the products containing both black tea and *E. amoenum* infusions.	[272]
Fermented soy beverage	Commercially available probiotic strains *La. rhamnosus* GG and *B. longum* BB536, along with isolates with probiotic potential, namely *B. breve* INIA P734, *B. longum* INIA P132, *La. paracasei* INIA P272 and *La. rhamnosus* INIA P344, were used to ferment a commercially available soy beverage. The product obtained with *La. rhamnosus* GG and *La. rhamnosus* INIA P344 contained high levels of bioactive isoflavone aglycones. The viability of the strains, along with the bioactive compounds, was maintained during refrigerated storage for 28 d.	[273]

B.: *Bifidobacterium*; *La.*: *Lacticaseibacillus*; *Ln.*: *Leuconostoc*; *Lp.*: *Lactiplantibacillus*.

The employment of alternative raw materials, as partial or complete replacements of traditional ones, has been extensively exercised in the case of kefir and kombucha beverages. In fact, this strategy has been so extensively employed that it has led to a whole new class of products, namely kefir analogs and kombucha analogs. In both cases, the aim was to meet the consumer needs of nutritionally dense and organoleptically appealing products. Especially the latter seems quite a challenge, taking into consideration the varying taste preferences [274]. Therefore, a variety of raw materials have been employed, resulting in variable nutritional and sensorial outcomes. In the case of kefir analogs, the utilization of fruits, vegetables, and sugar solutions is most commonly reported [275–282], while for the production of kombucha analogs, the employment of herbal infusions and fruits is most frequently encountered [283–297]. Apart from using kefir or kombucha cultures to ferment their analogs, the development of fruit- and vegetable-based beverages through the fermentation of substrates not traditionally considered for that purpose, using cultures that could effectively carry out fermentation and enhance their functional potential, has been extensively assessed. Indeed, a series of fruit or vegetable juices and pulps have been subjected to fermentation, principally lactic acid fermentation [298–308]. Apart from the organoleptically interesting products, in the majority of cases, the results exhibited an increase in the concentration of bioactive compounds, such as the total phenolic content, vitamin C, shikimic acid, etc., along with an increase in the antioxidant capacity, which, in some cases, was further verified through in vitro experimentation.

The enhancement of functional properties has also been achieved through the direct addition of compounds or their precursor molecules. An example of the first strategy is the study by Frolova et al. [309], in which pre-dissolved inulin and a vitamin premix consisting of thiamine, riboflavin, pyridoxine, folic acid and niacin were added to the already fermented black-tea kombucha at concentrations corresponding to 100% of the recommended daily intake (RDI) of inulin and 29–44% of the RDI of the vitamins. In addition, an infusion of frozen strawberries and lime leaves was created and added after the primary fermentation, and a secondary one was allowed, at 23 °C, for 24 h. The final product exhibited a 82% DPPH inhibitory activity and it was highly accepted by the sensory evaluation panel. Another example of the direct addition of functional compounds is the

study by Shahbazi et al. [292]. In that study, medicinal plants, namely cinnamon, cardamom, and shirazi thyme, were added to the green-tea concoction and allowed to ferment using the same SCOBY. The cinnamon-flavored kombucha exhibited higher antioxidant and antimicrobial activity, as well as better sensorial scores, than the green-tea kombucha that served as the control and the cardamom- and shirazi thyme-flavored ones. Based on these results, cinnamon was used to partially or completely replace green tea. Increasing the cinnamon concentration resulted in an increased total phenolic content and radical scavenging activity and had a variable effect on the minimum inhibitory concentration against the Gram-positive and Gram-negative pathogenic bacteria that were examined; the authors noted that the Gram-negative ones seemed to be more susceptible. Similarly, Ozturk et al. [269] combined black tea leaves with hops (*Humulus lupulus* L.), madimak (*Polygonum cognatum*), or hawthorn (*Crataegus monogyna*) dry leaves and created a concoction that was left to ferment into kombucha. The herbs employed had no additive effect on the antioxidant capacity of the black-tea kombucha that served as the control and all products had a comparable antiproliferative activity against the human colorectal carcinoma cell line HCT116 and the human hepatocellular carcinoma cell line Mahlavu. Both studies, along with many similar ones, can be considered as a non-targeted attempt to improve the functionality of the final product. The term 'non-targeted' is used to highlight that the aim of the studies was to enhance the total phenolic content, and therefore, the antioxidant capacity, and not the concentration of a specific compound. In the case of kombucha, an example of such a compound would be epigallocatechin gallate (ECGC), the most studied bioactive compound of green tea. There is a strong indication that ECGC exhibits significant antiproliferative and antihypertensive activity through a variety of mechanisms [310,311]. Therefore, targeting the increase in this compound would create a product with specific capacities. However, research is still necessary in order to verify these actions and elucidate the underlying molecular mechanisms. This targeted approach was employed by Moslemi et al. [267], aiming to enhance the conjugated linoleic acid (CLA) concentration of a whey-based beverage. CLA is a group of linoleic acid isomers, the consumption of which has been correlated with a series of health benefits [312,313]. In that study, walnut oil that was already lipolyzed by endogenous lipases was added to a whey-based formulation, homogenized, and allowed to ferment with commercially available starter and probiotic cultures. The lipolysis of the walnut oil was necessary in order to liberate the esterified linoleic acid and thus enable the microorganisms to use it as a precursor for conjugated linoleic acid synthesis. Although the maximum produced amount of 36 mg/g of fat does not meet the recommended daily intake, this study proved that supplementation with substrates used by microorganisms for the production of bioactive compounds is an effective strategy and definitely worth further assessment.

Finally, the valorization of market surplus food, especially bread, into fermented beverages with functional potential has also been considered. Indeed, Massa et al. [314] reported the development of a non-alcoholic beverage using *Saccharomyces bayanus* 995, a SCOBY, or water kefir grains. The authors proposed a saccharification pre-treatment with *Aspergillus oryzae* and the supplementation of the thermally treated infusion with 1% *w*/*v* multiflora honey. The final product was sensorially evaluated, and the beverage prepared with *S. bayanus* was more preferred. On the other hand, Nguyen et al. [315] inoculated a sterilized slurry made after the homogenization of finely cut bread and water with *La. rhamnosus* GG and/or *S. cerevisiae* CNCM I-3856. Before sterilization, the addition of commercially available zero-calorie sweetener mix and a stabilizer took place. After fermentation at 37 °C for 72 h, the beverage fermented with a consortium of both strains contained the highest amount of amino acids, such as leucine, valine, glycine and GABA, throughout storage at 5 and 30 °C for 6 w. More recently, Siguenza-Andres et al. [316] applied desalting and treatment with a-amylase and glucoamylase to dried and milled surplus bread before inoculation with *La. rhamnosus* GG or a microconsortium consisting of *Bifidobacterium* sp., *Lb. delbrueckii* subsp. *bulgaricus,* and *Streptococcus thermophilus*. Fermentation took place at 38 °C for 24 h. The authors reported that the enzyme treatment

allowed faster acidification to occur, whereas desalting restricted the maximum rates of growth, pH reduction and acidification.

5. Conclusions

Fermented beverages have a long tradition and a very promising future due to their great capabilities, spanning from their capacity to fit into the mentality of subsequent generations, including the current 'on the go' generation, to their customization potential. Especially regarding the latter, the wide range of raw materials that can be used, combined with the metabolic potential of food-grade microorganisms, can give birth to customized products that meet the extensive range of organoleptic preferences and enable targeted nutritional interventions. Although a lot of research is still necessary, this exciting future seems to be within reach.

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