Impact of Fermentation Processes on the Bioactive Profile and Health-Promoting Properties of Bee Bread, Mead and Honey Vinegar

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Keywords: health benefits, lactic acid bacteria, Fermentation, mead, honey vinegar, volatile compounds, bee bread

Abstract:

Recently, an increasing interest is paid to bee products obtained as a result of the fermentation process. Some of them can be consumed directly (bee-collected pollen, honey, bee bread etc.), while others are the result of lactic and/or acid fermentation (honey vinegar and honey wine). Bee bread is the result of pollens' lactic fermentation, whereas mead is obtained by honeys' lactic fermentation. Moreover, as a result of honey acetic acid fermentation, honey vinegar is obtained. Sensory characteristics and aroma composition have been scarcely studied, which may depend on the starter culture and fermentation process. Along with the medicinal properties they are a vital resource for future researches as they are of particular importance in the food market. In this review, we discuss the aroma-active compounds, taste, and sensorial characteristics of fermented bee products along with the approaches that can be developed for the flavor improvement based on existing technologies. Furthermore, the beneficial effects on human health are also described, with special attention that should be attributed to finding the use of probiotics in these fermented products as health-promoting effects.

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Review

Impact of Fermentation Processes on the Bioactive Profile and Health-Promoting Properties of Bee Bread, Mead and Honey Vinegar

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Abstract: Recently, an increasing interest is paid to bee products obtained as a result of the fermentation process. Some of them can be consumed directly (bee-collected pollen, honey, bee bread etc.), while others are the result of lactic and/or acid fermentation (honey vinegar and honey wine). Bee bread is the result of pollens' lactic fermentation, whereas mead is obtained by honeys' lactic fermentation. Moreover, as a result of honey acetic acid fermentation, honey vinegar is obtained. Sensory characteristics and aroma composition have been scarcely studied, which may depend on the starter culture and fermentation process. Along with the medicinal properties they are a vital resource for future researches as they are of particular importance in the food market. In this review, we discuss the aroma-active compounds, taste, and sensorial characteristics of fermented bee products along with the approaches that can be developed for the flavor improvement based on existing technologies. Furthermore, the beneficial effects on human health are also described, with special attention that should be attributed to finding the use of probiotics in these fermented products as health-promoting effects.

Keywords: bee bread; mead; honey vinegar; volatile compounds; lactic acid bacteria; fermentation; health benefits

1. Introduction

Fermented foods and beverages are the basic component of the nutritional culture of every society in the world and carry the cultural history of ethnic communities [1]. From ancient times, fermented and alcoholic beverages, culturally and socially consumed products for food, traditional, and religious practices have been accepted [2,3].

Fermentation is one of the methods used in economic food production and conservation. There is a wide variety of fermented dairy products used as human food (yogurt, kefir, koumiss, and cheese), fermented meat products (sausages and ham), fermented fruits and vegetables (pickles), yeast-leavened bread, fermented cereals, tarhana, and other fermented foods which are widely consumed [4–6]. Worldwide, the interest in the consumption of fermented foods and beverages has increased by each year due to the fact that fermented products contain biological functions such as the preservation of perishable foods, enrichment of nutritional value, production of antioxidants, and therapeutic and immunological effects [1]. Honey bee collected pollen (BCP), bee bread (BB), and royal jelly, which are bee products, are recognized as functional foodsat this time [7]. As bee-gut has high

microbiological activity, the growth of pathogens is efficiently suppressed by probiotic microbiota. Lactic acid bacteria (LAB) are a bacterial group with high significance in the food industry, especially in dairy products. The microbiota from the honey bee (*Apis mellifera* L.) is mostly composed of yeasts, such as Gram-positive bacteria (*Bacillus* spp., *Lactobacillus* spp., *Clostridium* spp., and *Streptococcus* spp.), and Gram-negative bacteria (*Pseudomonas* spp., *Achromobacter* spp., *Citrobacter* spp., *Enterobacter* spp., *Escherichia coli*, *Flavobacterium* spp., and *Klebsiella* spp.) [8]. They play a key role in honey [9] and BB production [10,11], as well as in long-term stored food for larvae and adult honeybees. LABs found in animals and humans have a significant role in host protection by producing antimicrobial metabolites which activate immune responses. LAB microbiota produces antimicrobial agents, such as proteins, enzymes, peptides, organic acids, and bacteriocin [12]. Other LAB strains are also considered safe food-grade microorganisms (i.e., probiotics) being used in health and nutrition-related systems [13].

This article aims to present research advances on the production of bee bread, honey vinegar, and wine from fermented bee products, focusing on aroma-active compounds, as well as the use of LAB strains as new health-oriented products.

2. Bee Bread Production and Volatile Compounds

2.1. Bee Bread Fermentation Process, Yeasts Used, and Production

The pollen brought into the hive by bees results in a valuable product (bee bread) created by adding honey, digestive enzymes, and fermenting lactic acid during storage in the honeybee combs cells. In beekeeping, this valuable product can be offered for consumption as a food and/or nutraceutical supplement.

The lactic fermentation process of pollen is caused by some microorganisms which spontaneously occur in the honeycombs, under anaerobic conditions [10]. The fermentation process protects it against the loss of properties and increases its content in new compounds as a result of enzymatic transformations.

As a result of biochemical changes and microbial metabolism, BCP is converted to BB, mainly by lactic acid fermentation caused by bacteria (*Pseudomonas* spp. and *Lactobacillus* spp.) and yeasts (*Saccharmomyces* spp.). The conversion process lasts approximately seven days post the growth of LAB, yeasts, indole-producing bacteria (*Escherichia* spp.), and aerobic bacteria. The conversion to BB comprises several stages; the first phase lasts 12 h during which the growth of a heterogeneous group of microorganisms occurs to include yeasts. In the second phase, anaerobic LABs (*Streptococcus* spp.) are using nutrients produced by bacteria and yeasts, followed by lowering the pollen pH. In the third phase there is a loss of *Streptococcus* bacteria and the growth of *Lactobacillus* bacteria. The fourth phase starts at the end of the seventh day in which the death of LAB and certain yeast occurs due to the generated lactic acid. The pollen reaches a pH of 4, becoming microbially sterile [14].

It is known that the lactic acid concentration in BB is six-fold higher than in BCP [15]. BB obtained from *Betula* spp. (birch) pollen contains six-fold more lactic acid compared to the pollen grains derived from the same plant. The conversion process of BCP to BB is followed by biochemical reactions, as the result of microorganisms' activity, particularly LAB [16]. The presence of LAB preserves the BB, which may affect the ability of longer storage of the resulting product.

Fuenmayor et al. [17] evaluated the parameters which produce a better fermentation by means of using Colombian BCP with *Lactobacillus acidophilus*, *Lactobacillus paracasei*, and two commercial strains, several BCP mixtures by adding different concentrations of water and honey, enzymes, different inoculum amounts, and heat treatments. The best results were obtained at a previous heat treatment (121 °C/15 min), incubation at 25 °C, with an inoculum amount of 1×10^8 CFU of *L. acidophilus* strain in a 2:1 BCP and water mixture. In 2010, Vamanu et al. [18] used multiple different bacteria strains from BCP: lactobacilli strains (*Lactococcus fermentum*, *Lactococcus plantarum*, and *Lactococcus paracasei*) and *Bifidobacterium* strains (*Bifidobacterium bifidum* 1 and 2) which were added to prebiotic substrates, such as inulin, raffinose, and lactulose, in order to evaluate the effect on cell viability, lactic acid production and

antioxidant capacity. Their results showed that the prebiotics inulin and lactulose had better results compared to the other prebiotics used.

According to DeGrandi-Hoffman et al. [19], the bactericidal compounds, lactic acid and carbohydrates found in BCP and BB are useful in reducing the growth of spoilage bacteria and mold. Therefore, it was demonstrated that *Bifidobacterium* and *Lactobacillus* have inhibitory effects against the growth of *Clostridium difficile*, *Listeria monocytogenes*, *Staphylococcus aureus*, Gram-negative bacteria strains *Escherichia coli*, *Campylobacter jejuni*, rods of *Salmonella, Shigella, Vibrio, Klebsiella*, and *Candida* yeasts. The lowering of pH during the conversion of BCP to BB is due to LAB activity which is introduced into BB from the bees' gastrointestinal tract. Biotechnological alternatives to BB have been proposed, as harvesting from the honeycombs proves to be difficult, which results in a scarce production quantity. Recently, artificial pollen fermentation processes were developed in an effort to create products similar to BB [20].

The fermentation of yogurt infused with BB resulted in slightly higher values of pH compared to control group. Sensory analysis revealed that the color, taste, smell, and texture of BB infusedyogurt had a major effect on the acceptability of the final product ($p < 0.05$). Further research has been reported which explores the future benefits of BB in the manufacture of yogurt [21].

In a different study, commercial BCP was added to grape must in six different doses (control, 0.1, 0.25, 1, 5, 10, and 20 g/L) followed by a fermentation process under controlled conditions in order to evaluate the effect of the addition of BCP on the volatile compounds, odor values, as well as the sensory profiles of the resulted white wines. It has been found that BCP increases the volatile compounds, depending on the variety of grapes and dose, as well as an increase in the synthesis of high and reducing alcohols, methanol, esters, acetaldehyde, terpenes, and fatty acids. Furthermore, wines with low doses of BCP (0.1–0.25 g/L) increased the odor activity values in their aromatic profile [22].

2.2. Volatile Organic Compounds Found in Bee Bread

Regardless of the recognized health benefits of lactic acid fermented beverages, they are poorly accepted by consumers due to their taste in about 60% of cases, while nutritional characteristics are regarded as important in mostly 36% of the cases [23]. Furthermore, flavor improvement of lactic fermentation is another important characteristic demanded by consumers. Due to flavonoids, a group of minor compounds, which gives BB its color and flavor characterized as astringent, sour, fruity, and sweet.

According to Kaškonienė et al. [24] the volatile components in BB revealed large quantities of unsaturated aliphatic acids, carbohydrates, amino acids, alcohols, aldehydes, terpene derivatives, ketones, nitriles, and furfural (Table 1). The volatile components of BB and honey samples are characterized by means of solid-phase micro-extraction (SPME) and analysed by GC/MS along with the melissopalynological method. The palynological analysis of the sample showed a mixture of honey and BB, with predominant *Brassica napus* L. (spring rape)—35.9%, followed by *Trifolium repens* L. (white clover)—15.8%, *Centaurea cyanus* L. (bluebottle)—12.2%, *Salix alba* L. (willow)—10.1%, *Tilia* spp. (linden)—7.9%, *Sinapis arvesis* L. (charlock)—7.9%; *Carum carvi* L. (caraway)—5.8%; alder (*Frangula* L.)—2.9% and *Trifolium* spp. (clover)—1.4%. In the following table we present the volatile compounds present in the BB samples.

Table 1. Odor and flavor descriptors of some volatile compounds found in BB (adapted from [24]).

Volatile Compound	Odor Descriptor	Taste Descriptor	Odor Threshold (μg/L)	References
Ethanol (0.6%) (alcohol)	smoky, strong alcoholic	pungent, burning	-	[25]
Dimethyl sulphide (20%)	garlic, sulphurous	sulfurous, vegetative with a dairy creaminess and a slight minty after-note	8100	[25,26]
Acetic acid (13.4%)	sharp vinegar	pungent, sour, overripe fruit	200,000	[25]
Pentanonitrile (0.6%)	odorless	N/A	-	[27]
Dimethyl disulphide (3.0%)	garlic, sulphurous vegetable	sulfurous cabbage, malt, cream	1200	[28]
1-Phenylpropan-2-ol (0.4%)	weak rose	sweet, pineapple	-	[29]
2,4-Dimethylheptane (3.9%)	N/A	N/A	-	[24]
Dimethyl trisulphide (0.5%)	garlic, sulphurous, savory, meaty and vegetative with a fresh, green top-note	sulfurous, alliaceous, with a fresh, vegetative nuance	10	[25,28]
2-octene (0.5%)	N/A	N/A	-	[24]
Furfural (9.8%)	sweet, woody, bready, caramellic, with a slight phenolic nuance	brown, sweet, wood, nut, caramel with a burnt astringent nuance	710,000	[25,26]
3-Furaldehyde (0.7%)	almond, caramel, burnt sugar	N/A	-	[24]
2-Hepten-1-ol (2.0%)	green	N/A	-	[24]
2-Heptanone (0.4%)	cheese, fruity, green, creamy nuance	cheese, fruity, pear, coconut, waxy	71,000	[25,30]
Nonane (10.4%)	gasoline	N/A	21,000	[24]
Benzaldehyde (0.9%)	almond, fruity, powdery, nutty	sweet, almond, cherry, nutty and woody	200	[31,32]
Hexanoic acid (3.2%)	mild, fatty, cheese	sharp, acidic, cheesy, fruity notes	300	[25]
Decane (0.8%)	gasoline-like	N/A	-	[24]
Octanal (0.9%)	aldehydic, waxy, citrus orange with a green peely nuance	aldehyde, green with a citrus or orange note	700	[31,32]
Benzyl alcohol (0.5%)	sweet, floral, fruity with chemical nuances	sharp burning taste, fruity with balsamic nuances	100,000	[25,33]
Heptanoic acid (0.4%)	cheese, fermented, pineapple and fruity	cheese, fruity and fatty	300,000	[25]
p-Cymenene (0.3%)	spicy, coffee and nutty nuances	spicy, balsamic, musty with a nutty nuance	-	[25]
Undecane (1.1%)	gasoline-like to odorless	N/A	-	[24]
Ho-trienol (0.2%) (alcohol)	Sweet, tropical, fennel, ginger	floral, fresh, woody	-	[34]
Nonanal (1.2%)	waxy, citrus, with a fresh slightly green lemon peel like nuance	effervescent, citrus, cucumber, and melon rind, with raw potato and coconut like nuances	100	[33]
Benzyl nitrile (1.0%)	aromatic	N/A	-	[25]
Benzoic acid (1.3%)	odorless or with a slight benzaldehyde odor	slightly bitter	-	[33,35]
Dodecane (4.4%)	alkane	N/A	3	[24]

Table 1. *Cont.*

Volatile Compound	Odor Descriptor	Taste Descriptor	Odor Threshold (µg/L)	References
Decanal (0.7%)	sweet, orange, waxy and citrus coat	fatty, citrus, and orange peel with a slight melon nuance	200	[32]
4-Ethyl-4-methyl-1-hexene (0.5%)	spice	N/A	-	[24]
5-Hydroxymethylfurfural (2.5%)	fatty, butter, caramel	herbal, hay, tobacco	770	[25]
Tridecane (0.7%)	hydrocarbon	N/A	-	[24]
1-Heptadecene (13.9%)	alkane	N/A	-	[24]

Note: N/A, not available.

As it can be foreseen high percentages of acetic acid and 1-heptadecen are observed as the volatile profiles of BB samples were collected from monofloral (rape, caraway, and white clover) and polyfloral (a mixture of the monofloral products) sources.

The chromatographic profile showed that the largest peaks were attributed to dimethyl sulfide (20.0%), 1-heptadecene (13.9%), acetic acid (13.4%), nonane (10.4%), and furfural (9.8%). The volatile profiles of BB samples collected from monofloral (rape, caraway, and white clover) and polyfloral sources showed highest percentages in 1-heptadecena and acetic acid, while benzaldehyde was found in relatively low amounts (0.9%), while in 10 honey samples the content exceeded 5%. Furthermore, BB differed from honey samples also in the content of acetic acid, 1-phenylpropan-2-ol, 3-furaldehyde, 2-heptanone, 4-ethyl-4-methyl-1-hexene, 5-hydroxymethyl furfural, tridecane, and 1-heptadecene, respectively.

Kaškonienė et al. [36] determined the total amounts of phenolics and flavonoids, radical scavenging activities and volatile profiles of 14 BCP samples from the Baltic region. The volatiles were determined by solid-phase micro-extraction (SPME) fiber coated with 100-µm polydimethylsiloxane layer, separated, finally identifying more than forty volatile compounds by GC-mass spectrometry (MS). Dodecane (1.2–34.6%), tridecane (1.4–24.7%), and nonanal (1.5–20.1%) were identified in all tested samples. The identified chemical compounds were acids (2-methylpropanoic, pentanoic, hexanoic etc.), alcohols (1-pentanol, 2,3-butanediol, 3-hexen-1-ol, benzyl alcohol, etc.), ketones (6-methyl-5-hepten-2-one and 3,5-octadien-2-one), aldehydes (hexanal, heptanal, 6-nonenal etc.), esters (acetic acid, octyl ester, benzoic acid ethyl ester, etc.), terpenes (α-pinene, β-myrcene, eucalyptol, and limonene), and unsaturated and saturated hydrocarbons (decane, undecane, 2,5-dimethyl-2-undecene, etc.). Hexanal was identified in almost all tested samples, while 6-methyl-5-hepten-2-one was detected in 12 samples. 2-methylbutanoic acid, limonene, and pentadecane were indentified in 10 samples, followed by 3,5-octadien-2-one and butyrolactone detected in 9 samples.

Future studies are needed in order to evaluate the changes that may occur in the volatile compounds based on geographical and botanical origin of BB.

3. Honey Wine (Mead) Production and Volatile Compounds

3.1. Honey Wine Fermentation Process, Yeasts Used, and Production

Honey (especially fructose and glucose monosaccharides) is a sweet product obtained by bees from the nectar of flowers. Its high sugar content is a good source to produce alcohol, carbon dioxide and for the yeast fermentation. Honey wine (i.e., mead) is used in different grades of alcohol, with different fermentation techniques (temperature, duration, yeasts, etc.) [2,37–39].

Alcoholic fermentation (i.e., ethanol fermentation) is a biological process in which yeasts obtain energy via the conversion of various sugars into ethanol and carbon dioxide. The main yeast species responsible for fermentation is *Saccharomyces cerevisiae*, which for thousands of years was used in the production of both alcoholic beverages and baked products [40–42].

Since ancient times, humans introduced in their daily diets beverages obtained from fermented honey, such as mead and vinegar. Generally, mead has positive effects on metabolism and particularly on digestion, possesses physiological benefits and reduces the risk of chronic diseases beyond basic nutritional functions [43–45]. Multiple studies focused on characterizing honey samples by specific chemical marker compounds, mostly analyzing the volatile and semi-volatile compounds used for floral and geographical characterization [46,47]. Furthermore, several environmental contaminants, including pesticides such as naphthalene, 1,2-dibromoethane, and 1,4-dichlorobenzene can be identified in the honey volatile fraction [48].

That being said, there are multiple circumstances that could influence the precise correlation between the honeys' floral origin and volatile profile. Firstly, geographical origin, climatic conditions and extraction technique might influence the composition of honeys' volatile compounds. Secondly, considering that monofloral honeys are not always monofloral, it is likely that the nectar of various flowers can contribute to the volatile composition of honeys [49]. Nevertheless, there are no data regarding a possible link between the honey samples pollen profile (major and minor components) and their volatile composition.

Prior to alcoholic fermentation honey is diluted and the resulted mead contains up to 17% (*v/v*) ethanol [50]. This alcoholic beverage is well known around the world by different names, such as metheglin, hydromel, aguamiel, medovukha, and ogol, and is also used to produce vinegar [51].

Wort fermentation and mead maturing relatively needs a long period of time from several months to years depending on the final concentration needed [52]. Furthermore, difficulties in the fermentation process can occur due to high acidity, as well as a lack of substances necessary for yeast development. For these reasons, researches are conducted to optimize the production process of these beverages.

The production of traditional mead can be influenced by multiple factors, such as the type of honey, its composition, available essential nutrients, and yeast strains used [45,53–55]. A major problem in mead production is a slow fermentation. This difficulty reflects the low levels of minerals and nitrogenous substances from honey, which are required for yeast growth, and the acidic pH of the fermentative broth, which influences the speed of the process [54]. Another factor which influences the sensory quality of the final product is the amount of nitrogen, which might result in unpleasant aroma-active compounds [56]. Few studies evaluated the sensory characteristics of mead, focusing on the addition of honey or pollen for aroma enhancing [37,56,57]. Although it is made from honey, water, and yeast, mead can be flavored with various additives [37,39], such as spices, aromatic mixtures of plants or fruits (apple juice, grape juice, mulberry, etc.) [58,59]. In traditional mead, small quantities of fruits, spices, and herbs are added, with careful attention to not mask the honeys' original flavor and aroma [60]. According to theproduction method, mead can be classified as follows: pyments, cysers, melomels, and metheglin, which include the addition of fruits (grapes, apples, etc.) and spices, respectively. Spiced pyment can also be classified as a hippocras [60]. These components were used to add flavor to mead, while in medicines specific herbs were added.

Another important factor for mead quality is the yeast strains used. The yeast from *S. cerevisiae* strain, used in wine and beer production, is also used as a starter in mead production. *S. cerevisiae* metabolizes fructose and glucose during the Embden–Meyerhof pathway forming 2 mol of pyruvate/1 mole of hexose. The pyruvate is decarboxylated to acetaldehyde, then reduced to ethanol along with the NADH co-enzyme oxidation (glyceraldehyde 3-phosphate to 1,3-diphosphoglyceric acid). The effective ethanol yield depends on the strain and fermentative environment (temperature and must composition). In addition to ethanol, *S. cerevisiae* produces small amounts of glycerol, higher alcohols, diacetyl, acetoin, 2,3-butanediol, succinic acid, and traces of acetic acid, lactic acid, and acetaldehyde, which have an impact on aroma composition and final taste [61,62].

Recently, Pereira et al. evaluated the capacity of *S. cerevisiae* strains, isolated from Portuguese honeys to produce mead [45]. The authors showed that mead production outcome depends on the honey composition and additional supplements. Furthermore, Sroka and Tuszynski [52] study showed that during honey fermentation the formation of succinic and acetic acid reduces the pH and leads to an increase in fatty acid content. This results in a large amount of medium chain fatty acids and a slow or arrested fermentation.

Generally, 5 L of honey wine can be obtained from about 1 kg of honey [63]. It is formed by adding ammonium sulfate and ammonium phosphate to the honey juice syrup. Subsequently, *S. cerevisiae* (4 g/L) is inoculated and ethanol production is carried out for 84 h at room temperature. In the study conducted by Ilha et al. (2000) it was reported that the obtained mead contained 17.11% total sugars (*w/v*) and 8% alcohol (*v/v*). The efficiency of alcoholic fermentation was determined to be 81.34%. Roldan et al. [56] showed that different grape juice fermentation activators were used as a means to improve the honey fermentation, such as thiamine chlorhydrate, yeast extracts, BCP, and royal jelly. Their results showed that pollen was the best activator which also improved the fermentation kinetics. Pereira et al. [45] also showed that the most common difficulty in mead production is the attempt to ferment honey with lower pollen content.

An important parameter for mead quality is the temperature of fermentation. Chemical reaction speeds, particularly of *S. cerevisiae* enzymes, are known to increase along with temperature. Studies have shown that heat treatment increases the fermentation process and retains the product properties. Conversely, fermenting at higher temperatures and improper storage conditions can have a negative impact on the production of desirable aroma compounds and final product quality [64–66]. The best fermentation performances have been reported as a result of the better use of fructose by microorganisms. The disadvantage of the heating process leads to the formation of 5-hydroxymethylfurfural (HMF), which can affect the products' value [67]. Recently, Kahoun et al. [66] firstly introduced the effects of heat treatment and storage conditions on potential changes in the phenolic compounds and antioxidant activity by means of several extraction techniques. Their results showed that the compounds content slightly decreased prior to heat treatments. Conversely, storage at room temperature (20–25 °C, daylight) increased the phenolic acids content compared to cold storage, especially in gallic, protocatechuic, and vanillic acid. Furthermore, significant differences were observed in HMF content which increased by heat treatment and storage at room temperature. No significant changes were observed in the antioxidant activity by either heat treatment or storage conditions.

3.2. *Volatile Organic Compounds Found in Honey Wine (Mead)*

The aroma profile is one of the most important traits for both meads' sensorial quality and authenticity. The aroma derives from the type of honey, inoculated yeast, and technological processes [55,58,68–70]. As in the case of other fermented products (BB and honey vinegar) the quality and aroma depend on the botanical and geographical origin of the product. As honey aroma involves multiple volatile compounds the impact of a certain compound depends on the extent to which the concentration exceeds its odor threshold (Table 2). It is significant to confirm that synergistic and/or antagonistic interactions may occur among compounds (major and minor compounds), which can contribute to honey aroma [49,71].

In the following table major volatile organic compounds identified in the meads resulted from fermentation processes carried out by multiple yeast strains can be observed.

Table 2. Floral markers used to determine the botanical origin of mono and multifloral honey.

Mead Source	Strain/Fermentation Process	Major Compounds	Extraction Method	Origin	Reference
Castanea spp. and *Erica* spp.	*S. cerevisiae* Lalvin QA23; *S. cerevisiae* Lalvin ICV D47	3-methyl-1-butanol, 1-propanol, 2-phenylethanol, ethyl acetate; 4-vinylguaiacol; 4-vinylphenol; octanoic acid; decanoic acid; hexanoic acid	GC-FID and GC-MS	Portugal	[72]
Dark multifloral *Castanea* spp. and *Erica* spp	*S. cerevisiae* QA23, *S. cerevisiae* ICV D47	3-methyl-1-butanol, 4-vinylphenol, 4-vinylguaiacol, octanoic acid, hexanoic acid	GC-FID and GC–MS	Portugal	[69]
Dark honey (*Fagopyrum* spp. and/or *Erica* spp.)	*S.cerevisiae* Lalvin ICV D47	2-phenylethanol, acetaldehyde, acetoin, furfural, 5-hydroxymethylfurfural, ethyl lactate; ethyl acetate, octanoic acid, *trans*-Furan linalool oxide	GC-FID and GC-MS	Portugal	[73]
Erica spp.	*S. cerevisiae* UCD522	Ethyl acetate; octanoic acid; hexanoic acid; decanoic acid; isoamyl alcohol	GC-MS	Portugal	[55]
Multifloral honey	*S. cerevisiae*, ENSIS-LE5	2-methyl butanol, 3-methyl butanol, isovaleric acid, hexanoic acid, octanoic acid	GC-FID and GC-MS	Spain	[56]
Buckweat (*Fagopyrum esculentum*) mead; Soy (*Glygine max*) mead	*S. cerevisiae*	Ethyl-butyrate, isomayl acetate, ethyl decanoate, isoamyl alcohol, 2-phenylethanol	HSPME-GC-MS	USA	[74]
Blossom honey (sunflower, thistle nectar)	*S. cerevisiae* var. *bayanus* MT-R1B, MM-R2, and FM-R-Fix1	Isobutyl alcohol, Isopentyl alcohol, Ethyl acetate	SPMCE-GC	Slovakia	[75]
Multifloral honey	*S. cerevisiae* var. *bayanus* strains (QA23, Spark, and AWRI-R2)	2-Phenylethanol, 2,3-Butanodiol, 3-Methyl-1-butanol, Octanoic acid	SPME with DVB/CAR/PDMS 50/30 µm fiber	Brazil	[76]
Acacia and *Prunus* honey	*S. cerevisiae*	Ethyl acetate, propanol	SPMCE-GC	Slovakia	[77]
wild natural plants of Eastern Cape *(Metalasia muricata, Acacia, Eucalyptus)*	Roots of succulents of the *Trichodiadema* genera	Ethyl acetate, propanol, i-butanol, isoamyl alcohol	SPMCE-GC	Eastern Cape in South Africa	[77]
Dimocarpus longan honey	*S. cerevisiae* 1 (IOC B 2000)	3-Methyl-1-butanol, Isoamyl acetate, Ethyl acetate	GC	Taichung, Taiwan	[68]
Vitex, *Acacia*, *Tilia*, and *Ziziphus* honey	*S. cerevisiae* strain Lalvin EC1118, *Torulaspora delbrueckii* of ZYMAFLORE AlphaT, *Kluyveromyces thermotolerans*	Isopentanol, a-Phenylethyl alcohol, Ethyl Acetate, Ethyl octanoate	HSPME-GC-MS	China (Linyi and Tonghua)	[78]
Mandarin orange (*Citrus reticulata*) honey	*S. cerevisiae* W4, *S. cerevisiae* ET99, *S. cerevisiae* K7	2-Methylpropanol, 3-Methylbutanol, Propan-1-ol, Ethyl acetate	GC	Japan	[79]

Note: DVB/CAR/PDMS, divinylbenzene/carboxenon polydimethylsiloxane; GC-FID, Gas Chromatography with Flame-Ionization Detection; GC-MS, Gas Chromatography Mass Spectrometry; HSPME-GC-MS, headspace-solid phase micro-extraction/gas chromatography-mass spectrometry; and SPMCE-GC, solid-phase micro-column extraction gas chromatography.

Sensory evaluation (aroma and flavour), is one of the most significant tools in honey classification [80,81]. The aroma traits proposed comprise acidic, floral, fruity, candy, caramel, citric, spicy, waxy, resin, wood, balsamic, fermented, herbaceous, chocolate, and coffee. Out of these, for flavor description the attributes sweet, astringent, ripened fruit, acid, caramel, and spicy have been selected. The sensory profiles of honeys differ based on the botanic and geographical origins (Table 3). For instance, the major variables among honey samples from India were flowery, fruity, waxy, chemical, and caramel notes [82]. Castro-Vazquez et al. [80] identified the volatile compounds and odor descriptors of different monofloral honeys (i.e., citrus, eucalyptus, heather, lavender, rosemary, and thyme). Their results showed that eucalyptus honeys had *p*-cymene and hydroxyketones compounds which correspond to the aromas of hay and cheese, while citrus honeys were characterized by high amounts of linalool equivalent to citric and fresh fruits aromas. The lavender honeys were characterized by high contents of hotrienol, hexanol, coumarin, and nerolidol oxide and the sensorial attributes aromatic herbs, citric and floral aromas, while heather honeys had significant amounts of propyl anisol with ripe fruit and spicy aromas.

The volatile composition and sensory profile of chestnut honeys from Spain was shown to be strongly influenced by the geographical origin. The authors showed that the honey samples had high amounts of volatile phenols, alcohols, aldehydes, and lactones which are related to spicy, wood, and herbal notes. Honey samples from the north-west area exhibited higher concentrations of esters, terpens, and benzene derivatives, associated with honey, fruity and floral aromas [81]. An overview of the compounds found repeatedly during liquid honey-based fermentations using LAB starter cultures are listed in the following table.

Table 3. Odor threshold and odor descriptor of volatile compounds found in different mead types.

Compound	M1 [72]	M2 [73]	M3 [55]	M4 [74]	M5[1] [75]	M5[2] [75]	M5[3] [75]	M6 [54]	M7 [69]	M8 [76]	Odor Threshold (μg·L^{-1}) [83]	Odor Descriptor [83]	Flavor Descriptor
Alcohols													
Methanol	+	-	-	-	-	-	-	+	-	-	500	sweet, alcohol	N/A
1-propanol	+	+	-	-	+	+	+	+	+	+	830,000	fruity, alcohol	N/A
2-methyl-1-propanol	+	+	-	-	-	-	-	+	+	+	75	ether, wine	N/A
1-octanol	-	-	-	-	+	+	+	-	-	-	120	jasmine, lemon, wax, green, citrus, coconut	wax, green, citrus, orange
2,3-butanediol	-	-	-	-	-	-	-	-	-	+	150,000	fruity	N/A
Benzyl alcohol	-	-	-	-	-	-	-	-	-	+	200,000	sweet, fruity	N/A
2-ethyl hexanol	-	-	-	-	-	-	-	-	-	+	800	floral	N/A
Isobutyl alcohol	-	-	-	-	+	+	-	-	-	-	40,000	balsam, sweet, whiskey	fusel, banana
2-methyl-1-butanol	+	+	-	-	+	+	+	+	+	-	40,000	roasted, wine, onion, fruity	fusel, whiskey
3-methyl-1-butanol	+	+	-	+	+	+	+	+	+	+	30,000	cheese; nail polish, herbaceous, slightly fruity, nut-like, bitter at high levels	fermented, fruity, banana, cognac
1-hexanol	-	+	-	-	-	-	-	-	-	+	8000	herbaceous, grass	N/A
1-heptanol	-	-	-	-	-	-	-	-	-	+	300	lemon, orange, copper	N/A
1-nonanol	-	-	-	-	-	-	-	-	-	+	600	fruity	N/A
1-dodecanol	-	-	-	-	-	-	-	-	-	+	1000	flowery	N/A
3-ethoxy-1-propanol	+	+	-	-	-	-	-	+	+	+	100	fruity	N/A
3-(methylthio)-1-propanol	+	-	-	-	-	-	-	+	+	+	120	sulfureous, onion	N/A
2-phenyl ethanol	+	+	+	+	+	+	+	+	+	+	10,000–14,000	rose; flowery, pollen, perfume	floral, sweet, rose
Tyrosol	-	+		-	-	-	-	-	-	-			N/A
Esters													
ethyl acetate	+	+	+	-	+	+	+	+	+	+	7500–12,300	nail polish, fruity	sweet, cherry nuance
ethyl butyrate	+	+	+	+	+	+	+	-	+	+	20	fruity, butter, sweet	fresh, fruity, sweet
Ethyl 2-methylbutyrate	-	-	-	+	-	-	-	-	-	-	1	fruity, tropical notes	mango and cherry notes

Table 3. *Cont.*

Compound	M1 [72]	M2 [73]	M3 [55]	M4 [74]	M5[1] [75]	M5[2] [75]	M5[3] [75]	M6 [54]	M7 [69]	M8 [76]	Odor Threshold (μg·L^{-1}) [83]	Odor Descriptor [83]	Flavor Descriptor
Ethyl 3-methylbutyrate	-	-	-	+	-	-	-	-	-	-	3	sweet, fruity	blueberry, sweet, green
isoamyl acetate	+	+	+	+	-	-	-	+	+	-	30	banana, fruity	sweet, banana, green nuance
ethyl hexanoate	+	+	+	+	+	+	+	+	+	+	5–14	fruity, aniseed	fruit, fat
ethyl lactate	+	-	-	-	-	-	-	+	+	-		fruity, butter	N/A
ethyl octanoate	+	+	+	+	-	-	-	+	+	+	2–5	fruity, apple, beer	N/A
ethyl decanoate	-	-	+	+	-	-	-	+	+	+	200	soap, nut-like	N/A
ethyl phenylacetate	+	-	-	-	-	-	-	+	+	+	650	floral honey, dark chocolate and cocoa notes	strong sweet, rose, honey and balsamic cocoa-like
2-phenylethyl acetate	+	+	+	-	-	-	+	+	+	+	250	roses, honey	sweet, honey, flower
ethyl dodecanoate	+	-	-	-	-	-	-	+	-	+	150	sweet, wax, rummy with a creamy, floral nuance	wax, floral with a creamy and fruity nuance
ethyl propionate	-	-	+	-	-	-	-	-	-	-		sweet, fruity, rum, grape, pineapple	ether, fruit, sweet, wine, bubble gum, apple and grape notes
Ethyl isobutyrate	-	-	+	-	-	-	-	-	-	-		sweet, fruity, rum	pungent, fruity with rum notes
Ethyl butyrate	-	-	+	-	-	-	-	+	-	-	20	fruity, cognac, pineapple	fruity, sweet, apple
Volatile phenols													
4-vinylguaiacol	+	-	-	-	-	-	-	+	+	+	130	clove	N/A
4-vinylphenol	+	-	-	-	-	-	-	+	+	-	180	almond shell	N/A
4-methylphenol	-	-	-	+	-	-	-	-	-	-	1000	phenol, narcissus	phenol
Volatile fatty acids													
2-Methylpropanoic acid	-	+	-	-	-	-	-	-	-	-		rancid, soy	N/A
isobutyric acid	+	-	-	-	-	-	-	+	+	-		cheese, butter	acidic, sour, cheese

Table 3. *Cont.*

Compound	M1 [72]	M2 [73]	M3 [55]	M4 [74]	M5[1] [75]	M5[2] [75]	M5[3] [75]	M6 [54]	M7 [69]	M8 [76]	Odor Threshold (μg·L^{-1}) [83]	Odor Descriptor [83]	Flavor Descriptor
butanoic acid	+	+	-	-	-	-	-	+	+	-		cheese, butter, fruity notes	dairy, cream, fruity
hexanoic acid	+	+	+	-	-	-	-	+	+	+	420	cheese, geranium, vegetable	N/A
octanoic acid	+	+	+	-	+	+	+	+	+	-	500	fat, rancid, cheese	rancid, soap, brandy
Heptanoic acid	-	-	-	-	-	-	-	-	-	+	3000	sweet, cheese	N/A
decanoic acid	+	+	+	-	-	-	-	+	+	+	10,000	fat, soap	N/A
Nonanic acid	-	-	-	-	-	-	-	-	-	+	3000	fat	N/A
dodecanoic acid	+	-	-	-	-	-	-	+	+	+	1000	fat, coconut oil	fat, wax
Phenylacetic acid	-	+	-	-	-	-	-	-	-	-		honey, flower	N/A
acetaldehyde	+	+	-	-	+	+	+	+	+	+	500–10,000	fresh, fruity, must	fresh, green
Acetoin	-	+	-	-	-	-	-	-	-	-	110	butter, cream	N/A
Furfural	-	+	-	-	-	-	-	-	-		770	bread, almond, sweet	N/A
Benzaldehyde	-	+	-	-	-	-	-	-	-	+	200	almond	N/A
5-Hydroxymethylfurfural	-	+	-	-	-	-	-	-	-	-	770	almond, caramel, burnt sugar	N/A
Diethyl malate	-	+	-	-	-	-	-	-	-	-		brown sugar, sweet	N/A
Monoethyl succinate	-	+	-	-	-	-	-	-	-	-		N/A	N/A
Lactones and terpenes													
Pantolactone	-	+	-	-	-	-	-	-	-	-		cotton candy	N/A
trans-Furan linalool oxide	-	+	-	-	-	-	-	-	-	-		flower	N/A
cis-Furan linalool oxide	-	+	-	-	-	-	-	-	-	-		flower, wood	N/A
Ho-trienol	-	+	-	-	-	-	-	-	-	+	110	linden	N/A
α-Terpineol	-	+	-	-	-	-	-	-	-	+	40	flower, sweet	N/A
Linalool	-	-	-	-	-	-	-	-	-	+	50	citrus, floral	N/A
Nerol	-	-	-	-	-	-	-	-	-	+	400	rose, lime	N/A
Citronellol	-	-	-	-	-	-	-	-	-	+	400	citrus	N/A
Nerolidol	-	-	-	-	-	-	-	-	-	+	700	rose, green, citrus	N/A

Note: +, present; -, not present; N/A, not available; M1—Multifloral honey (*Castanea* spp. and *Erica* spp. honey) + *Saccharomyces cerevisiae* Lalvin QA23 and Lalvin ICV D47; M2—Dark honey + *S. cerevisiae* Lalvin ICV D47; M3—Honey (*Erica* spp) + *S. cerevisiae* UCD522; M4—Buckweat (*Fagopyrum esculentum*) and soy (*Glycine max*) honey + *S. cerevisiae*; M5[1]—Blossom honey + *S. cerevisiae* var. *bayanus* MT-R1B; M5[2]—Blossom honey + *S. cerevisiae* var. *bayanus* MM-R2; M5[3]—Blossom honey + *S. cerevisiae* var. *bayanus* FM-R-Fix1; M6—Dark honey (*Castanea* spp. and *Erica* spp.) + *S. cerevisiae* QA23 and ICV D47; M7—Dark honey (*Castanea* spp. and *Erica* spp.) + *S. cerevisiae* QA23 and ICV D47; and M8—Multifloral honey+ *S. cerevisiae* var *bayanus* (QA23, Spark, and AWRI-R2).

As it can be foreseen, quantitatively the largest group of volatile compounds is occupied by alcohols, whereas the major compound found in all meads is 3-methyl-1-butanol.

In decreasing order the compounds that showed the highest concentrations are as follows: acetaldehyde, 3-methyl-1-butanol, ethyl acetate, 2-phenylethanol, 1-propanol, 2-methyl-1-propanol, 2-methyl-1-butanol, ethyl lactate, octanoic acid, 5-hydroxymethylfurfural, and hexanoic acid. These findings are in accordance with those reported in wine [84,85]. It is important to highlight that even if the other volatile compounds exhibited higher concentrations than 1 mg/L (trace) they can also contribute to the beverages' aroma. Furthermore, the yeast strains used can have a significant effect on the production of volatile compounds. For example, Pererira et al. [72] noticed that meads fermented with multiple *S. cerevisiae* strains under different conditions influenced the alcohol compounds production, such as methanol, 2-methyl-1-butanol, 3-methyl-1-butanol, 2-methyl-1-propanol, and 3-(methylthio)-1-propanol. They also evaluated the sensorial characteristics of meads fermented with free or immobilized cells of the *S. cerevisiae* strains QA23 and ICV D47 and their correlation with the volatile compounds. Their results showed that in the volatile composition of mead, the effect of yeast condition was more important than the strain, while in the sensorial analysis, the meads obtained with free yeast cells gave the most pleasant aromas.

The yeasts used in the production of mead are usually strains of *S. cerevisiae*, *Zygosaccharomyces* spp., *Torulopsis* spp., and *Hansenula anomala*, related to those used in the production of beer, wine, champagne, etc. The yeasts metabolize sugars (glucose and fructose), which results in the formation of carbon dioxide and ethanol [86].

Strains of *S. cerevisiae* used include C11-3, BRL-7 [87], and UCD522 [55] from culture collections, as well as commercial strains, such as Premier cru [45] and ENSIS-LE5 [56], but honey and wine musts differ in sugar content and nitrogen concentrations. Therefore, wine yeast strains are not always suitable for mead production. This can be avoided by studying the correlation between the yeasts isolated from honey and the fermentation process [45]. In order to gain knowledge on this subject, Pereira (2008) [88] and Pereira et al. (2009) [45] isolated yeasts from several honey samples and studied their stress resistance. This type of analysis can be used as a standard for selecting yeasts for honey and pollen-derived fermented products, since there is a relation between the yeast fermentation performance and stress resistance [89]. Seven *S. cerevisiae* strains were characterized for their resistance to sulphur dioxide, ethanol [90], and osmotic stress. Pereira, 2008 and Pereira et al. (2009) [45,88] showed that there are no significant differences between the strains used. *S. cerevisiae* strains isolated from honey were related to reference and commercial strains, which makes them suitable for mead production. Other studies have investigated microorganisms inducing alcoholic fermentation of beverages in tropical and subtropical areas. For example, *S. cerevisiae* strains (ET99, W4, and K7), isolated from ogol, an indigenous Ethiopian honey wine had different results in the levels of aromatic compounds. High amounts of 2-methylpropanol, ethyl acetate, and isoamyl acetate were observed in honey wine made with W4 yeast, propan-1-ol, and acetaldehyde in wine made with ET99 yeast and 3-methylbutanol with K7 yeast [79].

4. Honey Vinegar Production and Volatile Compounds

4.1. Honey Vinegar Fermentation Process, Yeasts Used, and Production

Vinegar is a special agent used as a preservative and flavoring in different foods. Worldwide, vinegars are produced using different raw materials and production processes. There are two methods used: (1) the slow process, where acetic acid bacteria (AAB) grows on the liquid surface which contains the raw material, and (2) the quick process where oxygenation is secured by agitation in closed recipients. Usually, the quick process is used for honey vinegar production [91,92]. In the past years, an increasing interest was given to vinegar as a food product, its nutritional and chemical properties being determined by production method and raw materials used for fermentation [63].

Honey vinegar microflora contains mainly AAB (*Acetobacter* spp. and *Gluconacetobacter* spp.) and yeasts (*S. cerevisiae, Torulopsis* spp., and *Zygosaccharomyces* spp.), but some types of mould and LAB (*Lactobacillus, Streptococcus, Leuconostoc*, and *Pediococcus* spp.) have key-roles in the production of various special vinegars [63,93,94]. Vinegar has antimicrobial effects against different microorganisms due to its high acidity, phenolic substances, organic acids, and microbial metabolites in its composition [95].

Honey is very rich in sugars (70–80% *w/w*), mostly sucrose, fructose, and glucose, the proportions being influenced by the nectars' botanical origin. With its multiple health benefits, honey is an ideal raw material for the development of vinegar products [63]. Honey used in vinegar production has been similarly characterized to traditional wine vinegars, indicating that it could be easily accepted by consumers. Furthermore, during sensory evaluation, all attributes of the honey vinegar (appearance, color, odor, and flavor) were highly appreciated.

From a technologically point of view, as a result of the acetic fermentation, the resulted vinegar contains approximately about 9% acetic acid (*w/v*) and 1% alcohol (*v/v*), whereas the acetic fermentation is 91–97% [63]. Under control conditions, the alcoholic fermentation occurs when yeasts change natural sugars to alcohol at room temperature for 84 h resulting in wine 8% *v/v* ethanol content. The acetic fermentation with mixed AAB (*Acetobacter* or *Gluconacetobacter* spp.) culture results in vinegar containing up to 9% *w/v* acetic acid and 1% *v/v* residual alcohol. Honey vinegar contains multiple vitamins, phenolic compounds, riboflavin, thiamine, and mineral salts derived from honey which gives vinegar its distinct flavor [63].

Linden tree (*Tilia cordata* L.) honey along with *Saccharomycodes ludwigii*, *Acetobacter aceti* and *Lactobacillus acidophilus* were used to study the effects of honey vinegar drink using L_9 (3^4) orthogonal array study and symbiotic fermentation for seven days. The results showed that the optimum conditions are the symbiotic fermentation temperature of 32 °C, inoculation at 4% and inoculation proportion of 1:3:1 (*S. ludwigii*:*Acetobacter aceti*:*Lactob. acidophilus*). In this fermented condition, the sugar concentration of honey vinegar drink was 65 g/L and the total acetic acid content 51 g/L, respectively [96].

4.2. Volatile Organic Compounds Found in Honey Vinegar

The unique aroma and flavor of vinegars are mainly attributed to the acetic acid fermentation process. However, apart from acetic acid, other fermentation products in vinegars, such as esters, aldehydes, ketones, and organic acids also act as vinegar odor descriptors (Table 4) [97]. These compounds are produced during the fermentation and ageing process, in which acetic acid acts as the precursor in the development of these products [98]. The final quality and volatile compounds can be influenced by both the raw material and the process used [99]. Based on the raw material used as substrate in the fermentation process, different types of vinegar result, such as wine, malt, cider vinegar, etc. In a study, aroma compounds of *Sapium discolour* (milktree) honey vinegar were extracted by solid phase micro-extraction (SPME), separated, and analyzed by GC-MS. About 50 different compounds were identified, including acids, esters, alcohols, aldehydes, ketones, phenols, and hydrocarbons. Component percentages were quantified by peak area normalization method. All 50 compounds accounted for 98.93% of the total volatile composition, with 30.38% esters, 27.4% acids, 18.79% alcohols, 15.22% aldehydes, 3.09% ketones, 2.51% phenols, and 1.07% hydrocarbons, which formed the basis of the particular flavor of *S. discolour* honey vinegar [100].

Table 4. Volatile organic compounds found in honey vinegar.

Volatile Compound	Odor Descriptor [28,101]	Taste Descriptor [28,101]	Odor Threshold (μg/L) [102]	References
		Esters		
2-phenylethyl ester	honey, sweet, rose, slight yeasty note and cocoa nuance	sweet, honey, rosy, slight green nectar note	250	[28,92,101,103]
1-Phenylethyl acetate	green, must, berry nuances	fruity, berry, green, slightly nutty	250	[28,37,92,103]
2,3-Diethyl-5-methylpyrazine	must, vegetable, roasted hazelnut, green	musty, toast, nut	-	[28,92,103]
2-heptanone	cheese, fruity, green banana, creamy nuance	cheese, fruity, coconut, wax, green	1,400,000	[28,92,103]
n-butyl acetate	sharp, ether, fruity banana	sweet, ripe banana, tropical, candy, green note	66,000	[28,92,103]
ethyl pentanoate	sweet, fruity, acidic, green, berry	sweet, strawberry, tropical fruit	10	[18,101]
isoamyl acetate (0.6%)	sweet, banana, fruity	fruity, banana, green ripe nuance	30	[92,101]
ethyl hexanoate	sweet, fruity, pineapple, wax, green banana note	sweet, pineapple, fruity, wax, banana with a green nuance	14	[101,103]
3-hydroxy-2-butanone (105.5 mg/L)	sweet butter, creamy, dairy, fat	cream, sweet, butter	30,000	[28,101]
ethyl decanoate (traces)	sweet, wax, apple	wax, fruity	200	[28,92,101,103]
benzyl acetate (traces)	sweet, fruity, floral	fruity, sweet, jasmine floral notes	200,000	[28,92,101,103]
ethyl phenylacetate (traces)	floral honey, rosy with dark chocolate and cocoa notes, anise and liquorice notes	strong sweet, rosy honey cocoa-like and yeasty nuances	650,000	[28,92,101,103]
2-phenylethyl acetate (0.203%)	floral rosy, slight yeasty honey note, cocoa and balsamic nuances	honey, floral, rosy with a slight green nectar note	250	[28,94,103,104]
α-ionone (traces)	sweet, woody, floral violet iris (iris root), tropical	floral, powdery berry	-	[28,92,101,103]
4-ethylguaiacol (0.087%)	spicy, clove-like with medicinal, vanilla notes	wood, spicy, vanilla	9.5	[28,92,101,103]
4-ethylphenol (0.067%)	smoke, creosote	smoke, bacon, and ham	605	[28,92,101,103]
		Alcohols		
2-phenylethanol (9.3%)	floral, dried rose	sweet, rose, and bready	10,000	[28,92,101,103]
benzyl alcohol (traces)	sweet, rose, balsamic	Fruity, cherry, almond, bitter	200,000	[28,92,101,103]
2-methyl-1-butanol (2.86%)	wine, onion, whiskey	whiskey	40,000	[28,101]
3-methyl-1-butanol (2.82%)	alcoholic, pungent, cognac, fruity, banana and molasses	fermented, fruity, banana, cognac	40,000	[28,101]
2-methyl-1-propanol (1.78%)	nail polish, wine	whiskey	40,000	[28,76,101]
2,3-butanediol (19.7 mg/L)	fruity, cream, butter	-	-	[28,101]
Tyrosol	mild sweet, floral, fruity	N/A	-	[28,101]

Table 4. *Cont.*

Volatile Compound	Odor Descriptor [28,101]	Taste Descriptor [28,101]	Odor Threshold (μg/L) [102]	References
Volatile Phenols				
Hydroxymethyl furfural	fatty buttery musty waxy caramellic	herbal hay tobacco	770	[28,69]
2-furaldehyde	sweet, almond, caramel	sweet, woody, baked bread, nut, caramel	-	[28,101]
p-hydroxybenzoic acid	Phenolic, nutty	N/A	-	[28,101]
p-hydroxybenzaldehyde	nut, almond, vanilla and honey notes	creamy, must, vanilla and honey nuances	-	[69]
Medium chain fatty acids				
decanoic acid (0.061%)	sour, fat, citrus	soap, wax, fruity	1000	[71,101]
octanoic acid (0.625%)	wax, vegetable, cheese	soap, cheese, brandy	500	[71,101]
isopentanoic acid (17.3%)	cheese, dairy, sour, fruity	cream, fermented, sweet, wax, berry notes	-	[28,101]
Aldehydes				
Phenyl acetaldehyde	honey, rose, powdery, fermented, chocolate	honey, chocolate, spicy notes	400	[28,76,101]
benzaldehyde	almond, fruity, powder	sweet, cherry, nut, wood	200	[28,76]
Other compounds				
diethyl succinate (0.34%)	fruity, cooked apple, ylang-ylang	tropical, floral, passion fruit	100,000	[28,76]

Note: N/A, not available.

The major volatile compounds quantified were 3-hydroxy-2-butanone (105.5 mg/L) followed by 2,3-butanediol (19.7%) and isopentanoic acid (17.3%), which gives the vinegar fruity and sweet buttery aroma.

Alak et al. (2015) [93] reported that the color values of honey vinegar samples were 0.58–33.00 L* (lightness), 0.17–15.76 a* (redness and greenness), and 2.91–28.35 b* (yellowness and blueness). The ash contents were 0.11–2.72 g/L, dry matter 1.23–5.92 g/L; the total acidity values ranged between 7.80–46.20 g/L acetic acid, pH values 2.19–3.35, density 1.00–1.15 g/cm^3. The antioxidant activity was 233.01–1431.01 mg TROLOX/kg dw (dry weight) (DPPH), total phenol content 105.18–890.27 mg GAE/kg dw; content of organic acid tartaric acid, malic acid, citric acid, succinic acid, and acetic acid, respectively were 183.796–603.55, 106.32–534.81, 305.25–1852.02, 1248.91–48,624.69, and 11,010.34–39,199.39 mg/kg.

Other countries produce flower-based vinegars with floral and fruity odors. Zhao et al. (2020) [105] identified the volatile aroma compounds of traditional Chinese rose vinegar by headspace solid-phase micro extraction gas chromatography–mass spectrometry (HS–SPME–GC–MS) and GC–MS–olfactometry (GC–MS–O), while the metabolites were identified by silylation–GC–MS. A total of 48 and 76 flavors and metabolites were detected, with aldehydes and acids present in relatively high amounts. Furthermore, their study suggests that the presence of aldehydes contribute to vinegar aroma, particularly nonanal (rose), 3–methyl–butanal (apple), decanal (orange peel), heptanal (fruity), and dodecanal (violet scents). Moreover, 14 kinds of hydroxy acids, such as lactic acid, citric acid, 3–phenyllactic acid (PLA), and d–gluconic acid were detected in rose vinegar.

5. The Effects of LAB from Bee Products on Human Health

5.1. Health Benefits of Bee Bread

It has been reported that BB contains approximately 20% protein, 24–35% carbohydrates, 3% lipids, and 3% vitamins and minerals. It consists of fully balanced proteins that contain all the essential aminoacids, vitamins (B1, B2, C, E, H, P, nicotinic, and folic acid), pantothenic acid, pigments, and other active compounds. It also contains enzymes such as sucrose, amylase, phosphatases, flavanoids, carotenoids, and hormones. Furthermore, BB contains more than twenty-five different macro and micro elements, such as Ca, Fe, P, K, Co, Zn, Se, and Mg [15,104–109]. Flavonoids are an important group of compounds found in BB. In the study conducted by Hudz et al. (2017) [110], the total flavonoid content from ethanol extracts ranged from 10 to 166 mg/L and flavanols were mainly in the form of glycosides and flavones from BB. While the acidity in the titration increases during the conversion of BCP into BB, sitosterol and vitamin content (ascorbic acid and pyridoxine) decreases. In BB, significant amounts of proteins, vitamins, natural antioxidants, and phenolic compounds are detected [111]. BB composition varies significantly depending on the floras' botanical origin and the region of the colony. Furthermore, BB offers a more advantageous possibility of preservation against the risk of nutritional loss of dry and frozen pollen [107,108,112,113]. Recently, Urcan et al. [114] evaluated the phenolic profiles by high-performance liquid chromatography with a diode array detector (HPLC/DAD) of several BB samples collected from India and Romania, which helps in filling the gap of available studies on the phenolic profile of BB. Their results showed that the concentration of phenolic acids and flavonoids was almost identical in all analysed samples, as well as with previous studies from other countries (Brazil, Oman, Portugal, and Slovakia) and all gave an identical profile of phenolic and polyphenolic compounds.

Based on environmental conditions, LABs are found as commensals within humans, animals, insects, as well as foods and plants [115]. They are a significantly important group of bacteria for the food industry and dairy fermented products. Genera within LAB are functionally related by phenotypic characteristics [116] and considered as beneficial organisms commonly found as both exogenous and endogenous microbes in healthy individuals. They protect their hosts via antimicrobial metabolites and modulation of immune response [117,118]. One of the most important genera within

LAB is *Lactobacillus*, continuously being under taxonomic discussion and includes almost 250 species. Compositional surveys using 16S rRNA genes revealed a variation in the abundance of honeybee core taxa. Usually, a cluster of *Lactobacillus* strains known as Firm-5 phylotype is the most abundant, followed by *Lactob.* Firm-4, *Bifidobacterium* spp., *Gilliamella apicola*, and *Snodgrassella alvi*. Ocassionally, *Apibacter adventoris, Bartonella apis, Frischella perrara*, and *Parasaccharibacter apium* are present at variable levels [119].

The LAB microbiota of the *A. mellifera* L. honey crop is added by bees to their brood food and corbicular pollen which is significant in honey and BB production (Figure 1) [9,10]. For centuries, *Lactobacillus* and *Bifidobacterium* species have been used in food preservation in order to prevent microbial spoilage [120]. Previously, it was demonstrated that aside from *Bifidobacterium* and *Lactobacillus*, a new bacterium was found belonging to the Pasteurelaceae family [10], which needs to be further characterized in order to assess its importance in BB production.

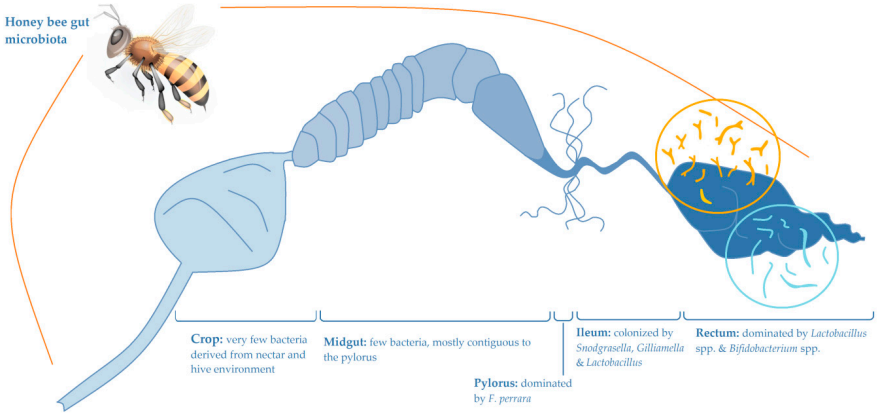

Figure 1. Schematic distributions of honey bee gut microbiota.

5.1.1. Potential Probiotic Use of LAB from BB

Nowadays, there is an increasing interest in the selection of LAB that may be of probiotic significance. Commercial probiotic products intended for human consumption with viable LAB contain approximately the same amount (10^8) of most single LAB g^{-1} products [121,122]. Theoretically, strains of *Bifidobacterium* and *Lactobacillus* from honey can similarly function as LABs in food preservation or as a defense system against microorganisms invading humans.

The microbiota analysis of honey bee products, demonstrated that *Lactobacillus kunkeei* is the dominant specie in BPC, BB, and honey [123,124]. Multiple LABs have been isolated from honey bee products, such as *L. kunkeei* and *Bifidobacterium* spp. from BCP and BB [10,123].

As previously stated, the most significant LAB representatives are *Bifidobacterium* and *Lactobacillus* which are widely used as probiotics for humans and animals. Asama et al. (2015) [125] isolated *Lactobacillus* and *Bifidobacterium* bacteria from the digestive tract of honey bee *A. mellifera*, BCP, and BB. In their study it was demonstrated that *Lactobacillus* was the dominant microflora present in royal jelly (93.3%), honey (90.9% of all bacteria), followed by BB (83.9%), and BCP (74.6%). Furthermore, the conducted phylogenetic analyzes showed that LAB flora consists of twelve different phenotypes [126]. As previously stated, the dominant bacteria isolated from honey, BCP, and BB was *L. kunkeei* [11,127], which showed antibacterial activity against *Melissococcus plutonius*, a pathogen responsible for European foulbrood.

Vamanu et al. [128] used *L. acidophilus*, *L. plantarum*, and a mixture of these strains in substrates with multiple BCP concentrations to obtain a probiotic characterized product, which was daily administered to Wistar rats divided into three groups (G1-2 mg/kg; G2-20 mg/kg; and G3-200 mg/kg) for four weeks. Their results showed that due to the fermentation process the products' taste changed to sweet and sour. Furthermore, a decrease in the cholesterol levels was noticed in the probiotic-groups. This aspect

was further investigated by Huang et al. [129] which demonstrated that *L. plantarum* addition to food products reduces the levels of cholesterol in blood serum.

In addition to the well-described characteristic of LAB to produce exopolysaccharides, other mechanisms in biofilm formation and adhesion include the production of proteins, carbohydrates, enzymes, nucleic acids, lipids, or membrane bound receptors. Exopolysaccharides are the main component in extracellular polymeric substances (EPS) which provide protection to bacteria when secreted into the environment. Several studies have suggested that exopolysaccharides formed by LAB may have health benefits in humans [130–132] and honeybees [11]. There are also studies which state that the rods of the genera *Lactobacillus* and *Bifidobacterium* decreases hydrogen production intake and improves symptoms in lactose-intolerant patients [133,134].

5.1.2. Anti-Cancer Effects

Park et al. [135] investigated the effects of *L. acidophilus* on the development of inflammatory bowel disease (IBD), by orally administered in mice with dextran sodium sulfate (DSS)-induced colitis. Their results showed that treatment with *L. acidophilus* alleviated the symptoms of DSS-induced colitis in mice. It suppressed the pro-inflammatory cytokines, like interleukin (IL)-6, tumor necrosis factor-α, IL-1β, and IL-17 in the colon tissues, as well as decreasing the levels of α-smooth muscle actin, a marker of activated myofibroblasts, and type I collagen compared to control mice. Furthermore, the in vitro treatment directly induced T regulatory (Treg) cells and the production of IL-10, while splenocytes suppressed the production of IL-17 [135].

In a recent study, Uțoiu et al. [136] enhanced the health-related benefits of BCP by fermentation with a Kombucha/SCOBY (symbiotic culture of bacteria and yeasts) conglomerate. Their results showed that the BCP addition increased LAB proportion in the total number of SCOBY microbial strains, as well as the content of bioactive compounds (polyphenols, soluble silicon species, and short chain fatty acids), which is higher in the fermented pollen. Furthemore, the product showed a moderate anti-tumoral effect on human colon adenocarcinoma cells (Caco-2) cells and laryngeal epidermoid carcinoma cells (Hep-2). In a different study, BB improved testicular germ cell proliferation by attenuating apoptosis in obese male rats induced by a high fat diet [137].

5.1.3. Anti-Allergic Activity

On the basis of their study, O'Sullivan et al. [138] demonstrated that LABs have a significant anti-allergic activity. The ability to synthesize several metabolites (organic acids, diacetyl, acetoin, acetaldehyde, and bacteriocins) and their number largely depend on species, strain, and external factors, such as medium's chemical composition, environmental pH, temperature, and time of incubation. It has been demonstrated that along their anti-allergic effects, LABs can also normalize the gut microbiota [139,140]. They also influence the mucosal immune system in the intestines, promotes the production of immunoglobulin A (IgA) in Peyer's patch cells, mice, and later in humans [125,141]. LAB-mediated immunomodulation tends to be stronger with heat-killed than live bacteria [142]. Salivary SIgA secretion rate, which was significantly increased by intake of heat-killed YB38, represents the actual amount of SIgA available on the mucosal surfaces for protection against pathogens [143]. The SIgA secretion rate from saliva is also the most useful clinical biomarker of upper respiratory tract infections (URTIs) [144]. Therefore, heat-killed *L. kunkeei* YB38 may reduce the risk for URTI.

5.1.4. Gastrointestinal Tract Effects and Gut Microbiota Modulation

Through fermentation, polysaccharides from BCP of Chinese wolfberry (WBPPS) influenced the intestinal tract ecosystem by promoting the production of SCFAs (short-chain fatty acids), especially acetic and propionic acids. Additionally, WBPPS shapes the gut microbiota, by increasing the genera of *Alloprevotella*, *Dialister*, *Prevotella*, *Faecalibacterium*, and decreasing the genera of *Bacteroides*, *Clostridium*, *Escherichia*, *Parabacteroides*, and *Fusobacterium*. Their results suggest that WBPPS has the potential to be

developed as functional ingredients to improving human health and prevent diseases by promoting gut health [145].

5.1.5. Antibacterial and Antifungal Activity

For centuries, LABs were used in the fermentation process of dough bread, plant silage, cheese curd and matured cheese, fermented milk, meat, fish, legumes production, etc. The starter cultures of selected LAB strains have been used in dairy, as well as fruit and vegetable industries. A significant importance is paid to the possibility of using these microorganisms in the production of BB in laboratory conditions (bioreactor). Misiewicz et al. [146] presented the in vitro BB preparation method using wort and BCP combined with the strains of *Lactobacillus delbrueckii*. The BB preparation process lasted 14 days under anaerobic conditions, with a 3% lactic acid content in the resulted BB.

Audisio et al. [147] discovered that a thermoresistant bacteriocin produced by *Enterococcus avium* isolated from *A. mellifera* BB has a strain-dependent inhibitory effect on *Listeria monocytogenes* Scott A. Recent studies suggest that the artificial solid-state fermentation of BCP shows a positive effect on antioxidant properties and antimicrobial activity. The growth inhibitory effect of non-fermented and fermented BCP inoculated with *Lactobacillus rhamnosus* GG (ATCC 53103) and *Lactococcus lactis* 23R were evaluated on *Staphylococcus aureus* ATCC 6538, *Micrococcus luteus* ATCC 4698, and *Escherichia coli* ATCC 8739, as well as the antifungal activity against *Penicilium roqueforti* PA. The results showed that total flavonoid content and radical scavenging activity increased almost two-fold in fermented BCP [20]. Fermentation also increased the antibacterial and antifungal activity, results consistent with a previous study [148].

5.1.6. Hepato-Protective Effects

In another study, BP and BB have a positive effect against bacteria comparatively to antibiotics, ampicillin, and amoxicillin. The protective effects on *Staphylococcus aureus*-induced toxicity in the liver of mice was observed by a decrease in the LPO levels and antioxidant enzymes [149].

Furthermore, parameters of better wound healing, such as tensile strength of the wound, non-vascularization, and fibroblast number in the incisive wound of rabbits supplemented with BB were observed, but with no significant difference in epithelialization and hydroxyproline content compared to control. This experiment revealed the possibility of using BB to improve the operation in undernourished patients [150]. Kaur et al. [151] evaluated the effect of BCP and BB, administered as a feed additive to mice. Mice were divided into three groups and were orally administered BCP (250 mg/kg bw) and BB (250 mg/kg bw) for 21 days. It was established that the level of lipid peroxidation (LPO) decreased in the group in which BCP and BB was administered compared to the control. The activity of glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), glutathione-S-transferase (GST), glutathione reductase (GR), and glutathione peroxidise (GP) in the liver increased in the groups treated with BCP and BB compared to the control. Furthermore, BB-treated groups have been shown to have higher antioxidant potential.

In summary, several studies have demonstrated the biological activities of LABs from BB, highlighting its antimicrobial, anti-inflammatory, anti-allergic, hepato-protective effect, as well as its potential probiotic use and gut microbiota modulation. Nevertheless, further in vivo and in vitro studies of long-term effects on animal and human patients are still needed to demonstrate its efficacy.

5.2. Health Benefits of Honey Wine (Mead)

Since ancient times, honey has been used as an effective treatment due to its therapeutic properties including antioxidant, antimicrobial, anti-inflammatory, and immuno-modulatory effects. Its antimicrobial activity has been attributed to four main factors namely, high osmotic pressure, acidity (pH), hydrogen peroxide content, and non-peroxide factors (phytochemicals). Additional aspects comprise low protein content and redox potential, viscosity, bee defensin-1, and induction of increased phagocytic and lymphocyte activity [71].

Probiotic food products are formulations containing sufficient numbers of selected live microorganisms (10^6–10^7 CFU/mL) that can beneficially modify the intestinal microbiota of the host [152]. Fiorda et al. [153] evaluated the use of several substrates (soybean hydrolyzed extract, colostrum, and honey) to create novel probiotic beverages using kefir grains as starter culture. Their results showed that honey-based kefir beverage had a high antioxidant activity. Furthermore, the final product contained high levels of LAB and yeast populations (over 10^6 CFU/mL) composed of potential probiotic strains, mainly *Bacillus megaterium*, *Lachancea fermentati*, *Lactobacillus statsumensis*, *Leuconostoc mesenteroides*, and *Saccharomyces cerevisiae*. Bellow, we present data regarding the beneficial effects of mead consumption on human health. Special attention is given to the yeast selection used in mead fermentation process, which has been scarcely evaluated in health-related studies.

5.2.1. Anti-Viral Activity

Asama et al. [154] evaluated the effect of orally administered heat-killed YB38 treatment to prevent the infection with influenza virus (IFV) in female BALB/c mice for 21 days. The YB38-treated group received a daily dose of 100 mg/kg and showed an increased survival rate after IFV infection compared to the control. In the YB38-treated group (100 mg/kg) the IgA secretion in the respiratory epithelium was significantly increased after six days of infection, while interleukin-6 (IL-6) production in the same respiratory site and the number of cells infiltrating into alveoli decreased significantly. Furthermore, a reduction of lung tissue damage that appeared after IFV infection was observed. Furthermore, the terpenes isolated from honey are active against a wide range of microorganisms, including Gram-positive and -negative bacteria, viruses, and fungi [71].

5.2.2. Gastrointestinal Tract Effects

The beneficial effect of *Lact. kunkeei* YB38 on human intestinal microbiota has been evaluated. *Bacteroides fragilis* is part of the normal microbiota of the human colon, but its increase is a risk factor for inflammatory bowel disease and colon cancer. Heat-killed *Lact. kunkeei* YB38 administered to patients (10 mg day^{-1}) decreased the high levels of *Bact. fragilis*. Therefore, the intake of *L. kunkeei* may be effective in modulating the intestinal microbiota and improving the intestinal resistance, finally protecting the host against infections. It has been also demonstrated that *L. kunkeei* YB38 increased bowel movement in healthy women with a tendency for constipation. This can be explained by the fact that *L. kunkeei* raises the level of acetic acid, which stimulates the motility of the large bowel [155].

5.2.3. Wound Healing

The effects of LAB in relation to animal health have been poorly studied, and most of the research has focused on the use of LAB mixture with honey to heal animal wounds. Olofsson et al. [156] showed that *Calluna vulgaris* (L) Hull (common heather) honey mixture made with viable LAB isolated from honeybee stomach promoted horse wound healing, showing a reduction in the wound size and healing effects. In a different study, the same mixture of *Lactobacillus* and *Bifidobacterium* from honey has been shown to inhibit mastitis pathogens [157]. Therefore, the bee honey gut microbiota could be a future promising alternative for treating and bovine mastitis.

5.2.4. Antimicrobial Activity

Elzeini et al. (2020) [8] isolated from the gut of *A. mellifera* L the following LAB: *Lactobacillus brevis* MH191230, *Lactobacillus casei* KT273339, and *Enterococcus faecalis* MG890204, KX073783, and EU594564, and evaluated their antibacterial activity against different types of bacteria with positive effects. The mechanisms of action by all LABs are elucidated by the production of several active compounds such as organic acids (acetic, lactic, oxalic, and glutaric acids). Moreover, for many years *E. faecalis* strains were used as pharmaceutical probiotics preparations without any reported problems regarding the number of ingestions [158]. However, major variation in the overall antibacterial activity between

honey types is based on the level of hydrogen peroxide (HPO) and, sometimes on the level of non-peroxide factors. HPO can be destroyed by light, heat, or honey constituents. Despite this, there are honeys which possess non-peroxide antibacterial factors (phytochemicals), such as manuka (*Leptospermum scoparium*) and tantoon (*Leptospermum polygalifolium*) [71]. Furthermore, blueberry and honey vinegar obtained using a bench-scale bioreactor, exhibited antimicrobial ability against *Bacillus subtilis* ATCC 19659 and *Salmonella enterica* Typhimurium ATCC 0028 [159].

5.2.5. Anti-Cancer Effects

Multiple in vitro and in vivo studies on various types of cancer have been conducted in order to investigate the inhibitory effect of honey [160]. The mechanism of action of polyohenols (flavonoids and phenolic acids) has been studied based on their present bioactive compounds [161,162]. Particularly, among the flavonoid groups, only the flavonols (galangin, isorhamnetin, kaempferol, 8-methoxy kaempferol, 7-dimethyl ether, myricetin, pinobanksin, rutin, quercetin, and quercetin-3-methyl ether), flavones (apigenin, chrysin, genkwanin, luteolin, and tricetin), and flavanones (pinocembrin and pinostrobin) subclasses are present in honey. Among the phenolic acid group, the hydroxybenzoic acids (benzoic acid, ellagic acid, gallic acid, methyl syringate, protocatechuic acid, syringic acid, and 4-hydroxybenzoic acid), hydroxycinnamic acids (caffeic, chlorogenic, ferulic, vanillic, and *p*-coumaric acids), and hydroxy-phenylacetic acids (homogentisic and phenylacetic acids) subclasses were detected in multiple honey samples. Several in vivo studies strongly suggest that long term consumption of diets rich in these types of polyphenols significantly ameliorates the adverse effects of several brain, heart, liver, kidney, and pancreas-associated diseases as well as those of genetic disorders such as cancer and tumors. With all these, data regarding the possible role, especially if the combinations of these compounds are responsible for honeys' anticancer activities are scarce.

Using a DNA microarray Taranu et al. [163] studied the differences in genome-wide gene expression induced by a mix of three *Lactobacillus* strains (*L. paracasei, L. rhamnosus*, and *L. plantarum*) in unchallenged intestinal porcine epithelial cells (IPEC-1) cultivated under normal functional conditions. Their results showed that an enhanced expression for *AXIN2* (axis inhibition protein 2-*AXIN2*) gene, a negative regulator of β-catenin with a key role in human cancer. Furthermore, an increase in the NF1 gene encoding the neurofibromin protein, a tumor suppressor which prevents cells from uncontrolled proliferation was observed. Their study showed the significant protective role of *Lactobacillus* in epithelial barrier function against inflammation and in activating immune responses. Fauzi et al. investigated the effect of *Koompassia excels* (Becc.) Taub. (tualang) honey in breast (MCF-7 and MDA-MB-231) and cervical (HeLa) cancer cell lines, which had a cytotoxic effect due to a reduction of mitochondrial membrane potential and the activation of pro-apoptotic proteins (caspase 3 and 9) [164]. Another in vivo study investigated the effect of Tualang and Manuka honey on breast cancer. A reduction of tumor growth, estrogenic activity, and hematological parameters was demonstrated. Additionally, an increase in the expression of pro-apoptotic proteins (caspase 9 and p53) and in the proteins of the inflammation pathway (TNF-α and COX-2) were observed [165]. In a different in vivo study, the anticancer effect on colon cancer in Sprague Dawely rats injected with methylnitrosourea (MNU) was demonstrated. The results showed that diet supplementation with honey and *Nigella sativa* L. (black caraway) has a protective effect against MNU-induced oxidative stress, inflammatory response, and carcinogenesis [166].

5.2.6. Antioxidant and Anti-Inflammatory Effects

S. cerevisiae, the main yeast responsible for alcoholic fermentation, produces compounds which promote health has been scarcely investigated. In a recent publication, Guerrini et al. [167] evaluated the capacity of several commercial and local *S. cerevisiae* strains to produce bioactive compounds (glutathione, hydroxytyrosol, melatonin, tryptophol, and tyrosol) during alcoholic fermentation. Their results showed that the bioactive compounds are produced depending on the used strain. From the used strains, BM45 produced the highest amounts of all the bioactive compounds. Furthermore,

immunonolgical assays established that different *S. cerevisiae* strains used in the production of experimental synthetic wines and treated for the removal of the ethanol content showed significant antioxidant and anti-inflammatory activities. In the case of *S. cerevisiae* strains, BM45, EC1118, and R6 strain, the antioxidant activity proved to be similar to that of ascorbic acid (control).

Socha et al. [168] evaluated the antioxidant activity and phenolic profile of multiple meads with different concentrations, produced with the addition of herbs, root spices, and fruit juices. The total phenolic content in meads was between 15–70 mg/dm^3 and the meads originated form dark honey exhibited higher antioxidant activity. Their results showed that hydroxybenzoic acids, particularly gallic and protocatechuic acid were the predominant phenolic compounds from honey-originated meads. On the other hand, among the hydroxycinnamic acids, chlorogenic acid was the major phenolic compound, derived mainly from meads produced with plant additives. In the following table, the phenolic content and radical scavenging activity from different types of mead are summarized (Table 5). Their differences are mainly caused by the botanical origin of nectar and BCP.

Table 5. Antioxidant activity of different types of mead.

Type of Mead	Total Phenolic Content (mg/mL Gallic Acid Eq.)	DPPH Radical Scavenging Activity (mM Trolox Eq.)	Reference
Commercial mead	3102.9	16.0	[58]
Home-brewed mead from soy honey	163.6	7.1	
Buckweat mead	300.6	3.8	
Soy mead	167.7	3.4	
Chinese milk vetch honey mead	100	0.3	[169]
Chinese milk vetch honey and polished rice mead	100	0.09	
Chinese milk vetch honey and black rice mead	200	0.3	
Buckwheat honey and black rice mead	400	0.4	
Buckwheat honey and polished rice mead	300	0.4	
Buckwheat honey mead	300	0.39	
Chinese milk vetch honey mead	194	0.20	[170]
Clover honey mead	198	0.24	
mixture of clover and acacia honey mead	198	0.24	
lemon honey mead	210	0.28	
acacia honey mead	208	0.22	
Dry mead	2.67	1.54	[38]
Sweet mead	2.47	1.41	
MBW	419.27	1.01	[67]
MBM	416.97	1.02	
MBF	446.10	0.98	
MPW	250.43	0.63	
MPM	259.87	0.75	
MPF	213.57	0.74	
HBW	254.80	0.62	
HBM	269.57	0.86	
HBF	266.40	0.87	
HPW	215.67	0.59	
HPM	248.80	0.73	
HPF	177.30	0.83	

Note: DPPH—2,2-diphenyl-1-picrylhydrazyl; HBF-honeydew gently boiled mead fermented with Safspirit Fruit yeast strain; HBM—honeydew gently boiled mead fermented with Safspirit Malt yeast strain; HBW—honeydew gently boiled honey wort; HPF—honeydew pasteurized mead fermented with Safspirit Fruit yeast strain; HPM—honeydew pasteurized mead fermented with Safspirit Malt yeast strain; HPW—honeydew pasteurized honey wort; MBF—multiflorus gently boiled mead fermented with Safspirit Fruit yeast strain; MBM—multiflorus gently boiled mead fermented with Safspirit Malt yeast strain; MBW—multiflorus gently boiled honey wort); MPF—multiflorus pasteurized mead fermented with Safspirit Fruit yeast strain); MPM—multiflorus pasteurized mead fermented with Safspirit Malt yeast strain; and MPW—multiflorus pasteurized honey wort.

Recent studies demonstrated that compared to white wines, meads exhibit higher phenolic content and antioxidant [74], emphasizing their significant role for future studies as health-oriented products for human consumption.

These findings suggest that honey is potentially a source of novel bacteria with probiotic activities in honey or as a natural preservative in the food industry. Furthermore, the use of specific *S. cerevisiae* strains represents a key-tool in enhancing the content of several health-promoting compounds.

5.3. Health Benefits of Honey Vinegar

Vinegar has been used for sweetening and as a food preservative, wound healing, fighting infections, and managing diabetes. The father of medicine, Hippocrates (460–377 BC) recommended the use of vinegar preparations to fight infections, sores treatment, as well as cleaning ulcerations. A popular ancient medicine, known as oxymel was used in the treatment of severe coughs [171]. The formulation of oxymel was detailed in the *German Pharmacopoeia* (1872), *British Pharmacopoeia* (1898) and the *French Codex* (1898), which states that the medicine was a mixture of honey and white wine vinegar (4:1) [172].

5.3.1. Anti-Cancer Effect

Vojvodic et al. [173] found that first and second larval instars mainly contained Acetobacteraceae, while later instars were dominated by one or two very different *Lactobacillus* spp. Acetobacteraceae includes AAB, which are well adapted to sugary and alcoholised fluid such as vinegar, fruit juice, sap water, alcoholic beverages, and flowers. AAB of the genera *Acetobacter*, *Gluconacetobacter*, *Gluconobacter*, and *Saccharibacter* were reported as bee symbionts that may regulate the innate immune system homeostasis in insects [174]. Furthermore, AAB have been reported to contain almost as much lipopolysaccharides (LPS) as the Gram-negative bacteria known to be immunostimulatory and to induce macrophage activation [175,176]. In this aspect, Hashimoto et al. (2016) [176] isolated LPS produced by *Acetobacter pasteurianus* NBRC 3283 bacterial cells and characterized the structure of its lipid A component. Their results revealed that both LPS and lipid A moiety induced tumour necrosis factor-α (TNF-α) production in murine cells via Toll-like receptor 4. Moreover, it has been demonstrated that oral intake of LPS contained in food has an immunopotentiating effect [177].

5.3.2. Cardio-Protective Effect

Recent studies demonstrated that vinegar intake may reduce the glucose response to carbohydrate load in healthy adults and in individuals with diabetes. These findings are supported by evidences that vinegar intake contributes to the improvement of fatigue recovery in exhausted rats [178,179].

5.3.3. Anti-Atherogenic Effect

Naseem et al. [180] demonstrated that the ingestion of a herbal mixture (40 mL each of apple cider vinegar, lemon, ginger, and garlic juice, and 120 mL of honey) has cardio protective and anti-atherogenic effects when orally administered to New Zealand white rabbits for four weeks. The rabbits were randomly divided into three groups (G1-Control; G2-1 g butter fat/ 100 g of daily diet; and G3-1 g butter fat and 1 g of herbal extract/100 g of daily diet). In G3, plasma triglyceride (TG), plasma total cholesterol (TC), and plasma lipoptotein density levels (VLDL) decreased. Additionally, an increase in plasma high density lipoprotein (HDL), plasma low density lipoprotein (LDL) and plasma GSH levels was noticed. It is known that elevated plasma TG levels can greatly increase the risk of atherosclerosis. The beneficial hypolipidemic effects of natural honey, a rich source of antioxidants and nutritional elements have been scarcely studied. Therefore, Ishak et al. [181] investigated the effect of a mixture consisting of apple cider vinegar, garlic, ginger, lemon, and honey in lowering glucose levels in non-diabetic individuals who performed or not exercises. The individuals were also subjected to a high-carbohydrate meal. Their findings revealed that the mixture intake in combination with exercises lowered the glucose levels in all individuals. Yaghoobi et al. [182] observed that consumption of

70 g of natural honey dissolved in 250 mL of tap water significantly decreased plasma TG and other lipoproteins in hyperlipidemic individuals.

5.3.4. Anti-Inflammatory Effect

In a recent study by Lucia et al. [183], honey vinegar (10 mL/kg bw) was orally administered to hypercholesterolemic rats (*Rattus norvegicus*) for 14 days. The experiment consisted in three groups. From which the first group was given demineralised water. The second group (positive control) was given fried oil (4 mL/kg bw) and pork oil (5 mL/kg bw), and the third (test group) received fried oil (4 mL/kg bw), pork oil (5 mL/kg bw), and honey vinegar (10 mL/kg bw). Their results showed that the test group had a significantly lower lipid profile compared to the positive control (test group: mean total cholesterol level 68.9 ± 12.7 mg/dL, mean HDL-C 41.6 ± 1.3 mg/dL, mean LDL-C 19.0 ± 4.3 mg/dL, and mean triglyceride 64.9 ± 19.6 mg/dL). These are in accordance with the findings of Derakshandeh-Rishehri et al. [184], which found that honey vinegar decreased total cholesterol and HDL-cholesterol levels, but with no significant effect on LDL and triglyceride levels. The mechanism underlying the decrease in lipid profiles due to honey vinegar remains unclear. As honey mainly consists of fructose and glucose, it is known that fructose can reduce the activity of lecithin cholesterol acyl transferase (LCAT) and lipoprotein lipase (LPL). Furthemore, LCAT plays an important role in the synthesis pathway of HDL-C.

6. Conclusions and Future Perspectives

The products obtained as a result of bee activities (honey, BCP, BB, and royal jelly) and products obtained by fermentation of honey (honey vinegar and honey wine) are rapidly gaining interest due to their multiple positive effects on human health. Adequate intake of nutrient-rich products is required for the immune system to function efficiently. Increasing the consumption of bee products is significant in order to protect the body against multiple diseases. Nowadays, food industries focus on the production of antibiotic-free foods, while scientific studies recommend the usage of LAB as a significant tool in future production systems. Furthermore, mass-production of fermented bee products is imperative in order to assure a health-oriented lifestyle and also indulge in the aroma-active compounds.

Further works on the characterization of aroma compounds, flavor impact by aroma-organic acids interaction, selection of LAB starter culture, fermentation process, and consumer needs investigations will provide significant advances towards flavor improvement of bee fermented products for a promising market. Furthermore, the search for value-added products, with health benefits, vitamins, valuable bio-elements, macro- and micro-nutrients is of great interest, which gain special attention over time. Therefore, the consumption of these valuable bee products by all people is an expected demand for the beekeeping industry.

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