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Honey: As Source of Prebiotics and Probiotics

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Abstract

Honey has been used for treating digestive ailments and with certain types of plants it possesses bio-active properties, including antibacterial and anti-inflammatory properties. Some honey contains indigestible carbs, which have been found to have prebiotic activity. Prebiotic promote changes in the gut microbiota,that is critical for human health. Health awareness has increased demand for non-dairy probiotic products due to concerns like allergies and lactose intolerance. Natural prebiotic oligosaccharides, which cannot be digested by pathogenic microorganisms, can enhance the functional attributes of these products. Honey, a natural food with rich nutritional and therapeutic values, is an excellent source of prebiotic oligosaccharides, which can enhance the growth and activity of probiotic microorganisms. This paper reviews the growing evidence supporting honey's prebiotic potential in promoting healthy gut function, regulating microbial communities, and reducing infection and inflammation.

Keywords: Honey; nutritional value; therapeutic value; probiotics; probiotics

1. Introduction

Honey, a naturally occurring substance produced by honeybees from the sweet, flavorful, and viscous liquid nectar of flowers, is a vital component of honey production. From the beginning of time, it has been utilized as a food and medicinal commodity [3]. Due to the presence of nutritious elements that are closely linked to its flower origin, it is widely recognized for its therapeutic and nutritional properties [56, 62]. Honey's formation and quality are influenced by various factors, such as the method of production, local climate, handling and storage conditions, and nectar source [114]. This naturally occurring substance is a concentrated aqueous solution of various carbohydrates such as oligo- and polysaccharides, fructose, glucose, maltose, and sucrose [29].

2. Honey

Honey is a rich source of simple carbohydrates, with 82.4% consisting of glucose and fructose, and the remaining 12.9% containing maltose, sucrose, and other sugars [60]. The remaining sugars include maltotriose, 1-kestose, panose,

isomaltosyl glucose, erlose, centose, isopanose, isomaltosyltetraose, isomaltosylpentaose, kojibiose, alpha beta-trehalose, gentiobiose, laminaribiose, andomaltose, nigerose, turanose, and maltulose. Some sugars are not found in nectar but develop during ripening or through other substances like acids and bee enzymes [51]. Honeybee species vary in protein content, which can be a significant factor in the production of honey. For instance, protein in Apis cerana ranges from 0.1% to 3.3%, but in Apis mellifera, it ranges from 0.2% to 1.6% [123]. Honey gets its acidity from organic acids, which make up 0.57% of the substance. Honey mostly contains citric and glutonic acids, which are useful markers for differentiating between floral and honey-derived products [53].

2.1 Formation of Honey

Honey composition varies based on floral source, processing circumstances, seasonality, and environmental factors, with floral sources being the most significant [3]. Honey's color and flavor are influenced by its mineral content, with higher mineral content resulting in a darker color and stronger flavor [37]. The shape of commercial honey might be fluid, viscous, partially or completely crystallized; however, consumers prefer a fluid, non-crystallized product, and raw honey, a liquid, can contain small or large crystals depending on factors like temperature, moisture, provenance, and sugar content [28]. The volatile chemicals that give honey its flavor might change depending on the time of year and the place of origin [103]. One of the other, and arguably most significant, characteristics of honey is its viscosity. This feature is crucial for beekeepers and honey processors as it affects shelf life and simplifies honey handling, packing, and processing [1].

Over the ages, cultures, and generations, honey has been extensively utilized in both food and medicine. Humans have applied honey topically to treat a wide range of illnesses, although it acquired prominence more recently due to its antibacterial and antimicrobial qualities. Numerous human disorders have been observed to benefit from the use of honey. According to clinical research, applying honey to seriously infected cutaneous wounds speeds up tissue recovery and quickly removes infection from the wound. Research revealed that honey possesses broad-spectrum antimicrobial (antiviral, antifungal, antibacterial, and anti-mycobacterial) qualities. The antimicrobial properties of this substance may be attributed to its low pH, high sugar concentration, antioxidants, polyphenols, phenolic acids, flavonoids, methylglyoxal, and bee peptides [48].

2.2 Nutritional Composition

Humans have been using honey as a health food and sweetener for a very long time. Honey was first recorded in texts from Egypt, India, and China as early as 5500 BC [48]. Foodstuffs like honey are consumed all over the world and are increasingly

being utilized in place of granulated sugar. Even though honey is the sweetest food, it has a low glycemic load [55]. Honey has been utilized as a food and medicinal component in traditional medicine since ancient times [6]. Honey is a natural source of antioxidants that have been shown in numerous studies to be beneficial in lowering the risk of various inflammatory processes, cancer, heart disease, cataracts, and immune system deterioration. Honey's antioxidative properties are due to its composition of ascorbic acid, phenolic acids, carotenoids, catalase, peroxidase, and Maillard reaction results [32]. The floral source of honey greatly influences its functional qualities for human health, which may be connected to its high osmolarity and antimicrobial qualities [30].

Honeys with polyfloral flowers have stronger antioxidant activity than monofloral ones because they may contain larger concentrations of flavonoid and phenolic components. Consuming honey has the potential to improve health because of its antibacterial and antioxidant qualities [24]. Honey contains over 200 ingredients, with water, glucose, and fructose being the primary components [7]. Honey's composition and antioxidant activity are influenced by various factors such as flower source, time of year, environment, and processing [122].

2.3 Properties of Honey

Honey is a versatile fruit with numerous significant characteristics beyond its composition and flavor. Recently harvested honey is a thick liquid. Its viscosity fluctuates with its composition since it depends on a wide range of chemicals. Especially considering how much water it contains. Viscosity is a crucial technical factor in the production of honey because when processing, extracting, pumping, setting, filtering, combining, and bottling honey, it lowers the flow of honey.

Honey's hygroscopicity, which allows it to absorb and retain moisture, can be problematic during processing or storage due to excess water content, making preservation and storage challenging. Honey with a water content of 18.8% or less is considered normal honey. From air that has a relative humidity higher than 60%. Honey has a thermal conductivity ranging from 118 to 143x10 C13 = Cal/cm2 /sec/o. This method calculates the amount of heating, chilling, and mixing needed for a specific amount of honey before and after filtration or pasteurization. Since the crystals of glucose are white, honey becomes paler in color after crystallization. Honey's spectral color absorption was employed in more modern, albeit little used, color description techniques [89]. The process of honey crystallization is the consequence of monohydrate glucose crystals forming. The composition and storage conditions of honey significantly influence the quantity, shape, size, and quality of these crystals. The crystallization rate in honey increases with a decrease in water content and an increase in glucose content.

3. Probiotic

Probiotics, derived from the Greek word "for life," are live microorganisms that offer health benefits when provided at appropriate levels, according to an expert group commissioned by FAO and WHO [25]. Probiotic preparations typically consist of various bacteria such as Lactobacillus, Bifidobacterium, Escherichia, Enterococcus, Bacillus, and Streptococcus. The first probiotic, Lactobacillus rhamnosus GG (LGG), has gained significant clinical interest [39]. In 1985, Lactobacillus rhamnosus strain GG was identified as a desirable probiotic strain after the typical strain used in dairy fermentation failed to implant in the stomach [98]. Lactobacillus rhamnosus strain GG promotes gut immunity. The substance enhances the secretion of IgA and other immunoglobulins in the intestinal mucosa, promotes interferon release, and improves antigen transport to lymphoid cells, thereby increasing antigen uptake in Peyer's patches [87].

The recommended daily dose of $5x10^9$ colony forming units (CFU) for at least five days is advised for optimal health effects [41]. Probiotic microorganisms should be generally recognized as safe and resistant to bile, hydrochloric acid, and pancreatic juice. They possess anti-carcinogenic properties, stimulate the immune system, reduce intestinal permeability, produce lactic acid, and can withstand acidic and alkaline conditions in the stomach and duodenum [116].

TYPES OF PROBIOTICS	BENEFITS	FOOD SOURCE	REFERENCE
Lactobacillus	• Improves digestion and nutrient absorption. • Reduces lactose intolerance symptoms. • Enhances immune function. • Reduces diarrhea and irritable bowel syndrome (IBS) symptoms.	Yogurt, kefir, sauerkraut, kimchi, miso	H.B. Simon, 2002
Bifidobacterium	• Supports gut health and reduces gastrointestinal infections. • Enhances immune response. • Alleviates IBS and inflammatory bowel disease (IBD) symptoms. • May help lower cholesterol levels.	Yogurt, kefir, buttermilk, some cheeses	I.M. St George, 2001
Saccharomyces	• Prevents and treats diarrhea(especially antibiotic-associated diarrhea) • Supports gut health. • May help with inflammatory bowel conditions and acne.	Kefir, certain cheeses	J.K. Stoller, 2014
Streptococcus	• Improves lactose digestion and reduces symptoms of lactose. • Supports overall gut health.	Yogurt, cheese, buttermilk	C.H. Knight, 2016
Lactococcus	• Enhances digestion and nutrient absorption.	Cheese	L. Washington and K. Neylon, 2022
Enterococcus	• Supports gut health.	Cheese	P. Dear, 2012
Bacillus	• Supports gut health.	Fermented soy products	J. Sherwani *et.al.*, 2007

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Table 1. Different types of probiotics, their benefits and food source.

3.1 Uses

Probiotics most significant and well-researched positive benefits include reducing the risk of diarrhea and slow bowel movement, altering the conjugation of bile salts, enhancing their antibacterial action, and reducing inflammation. Probiotics enhance nutrient production and bioavailability, with some showing anti-oxidative properties in intact cells or lysates [44]. Probiotics have been found to naturally reduce symptoms of allergies, cancer, AIDS, respiratory, and urinary tract infections. Additionally probiotics can treat and prevent a variety of diarrheal illnesses with varying etiologies. Many dietary probiotics microorganisms have been successfully studied for their potential to prevent and treat diarrhea [81]. In addition to the probiotic yeast the potential medical benefits of Sacchromyces boulardii have been studied, both as single strain and mixed culture probiotics [20].The following list of mechanisms is believed to be connected to the advantageous benefits of probiotics:

1. Manufacturing of compounds that inhibit, such as bacteriocins, organic acids, H2O2, etc.
2. Obstruction of harmful bacteria's attachment sites.
3. Competing for resources with the harmful microbe.
4. Poisons' breakdown and the blockage of their receptors,
5. Immunogenic response modification

Role in infections of the urogenital tract:

A female is more likely to experience symptoms of a vaginal or bladder infection if her vaginal microbiota is aberrant. Two strains seem to be useful for colonization and safeguarding the urogenital tract: Lactobacillus GG and Lactobacillus rhamnosus GR [38]. The several lactobacillus metabolic byproducts that are hostile to vaginal and urinary pathogens include coaggregation molecules that stop the spread of the pathogens, bio-surfactants and acids, bacteriocins, and hydrogen peroxide are substances that inhibit growth and adherence, respectively [85]. Oral self-medication of Lactobacillus rhamnosus GR-1 and L. fermentum RC-14 is crucial for preventing and treating uro-genital infections, thereby maintaining and restoring urogenital health [86]. Probiotics may also assist lower infant mortality and premature labor in pregnant women by lowering the risk of bacterial vaginosis.

Probiotics have shown potential in treating serious gastrointestinal tract disorders, such as acute pancreatitis, and their role is growing. Probiotics have been found to decrease the prevalence of encephalopathy in individuals with cirrhotic conditions. Probiotic use has also been shown to reduce Stevens-Johnson syndrome colonic involvement [79].

3.2 Application

These probiotics are added, either separately or in combination, to foods, especially fermented dairy products. Probiotic strains and genera are always evolving as a result of more sophisticated and targeted research initiatives. Probiotic goods contain one or multiple bacteria strains, such as VSL3, which is a blend of eight distinct strains. Probiotics' effects are strain-specific and not universally applicable, with potential benefits from using a single strain individually or in combination. A probiotic formulation's advantages vary depending on the patient population. Fewer research have demonstrated that multi-strain probiotics are more effective [13]. Probiotic preparations should be safe, resistant to bile, hydrochloric acid, and pancreatic juice, and possess anti-carcinogenic activity and immune system stimulation; they should have reduced intestinal permeability, produce lactic acid, and be capable of enduring acidic environments in the duodenum and stomach [116].

Additional hypothesized pathways for the impact on gut bacteria include reducing intestinal pH, releasing compounds that protect the gut, controlling intestinal motility, and producing mucus. The main barrier separating the immune system from the outside world is the gut mucosa. Antigen transfer increases whenever intestinal microflora decreases, suggesting that the healthy gut microbiota keeps the gut defenses in place [64]. Non-pathogenic probiotic bacteria initiate immunological signals by interacting with immune cells and gut epithelial cells. Bacteria require interaction with gut epithelial cells, immune cells, and M cells in the Peyers patches. It has been demonstrated that probiotic bacteria affect the synthesis of immunoglobulins. Secretory IgA is a crucial component in mucosal immunity, acting as a barrier against pathogenic bacteria and viruses. The study found that probiotic bacteria and fermented milk yogurt significantly increased the number of IgA-producing cells [47,110]. Stimulation with TNF-α, IFN-γ, and IL-10 has been linked to an increase in the profiles of these cytokines [4]. In order to maintain intestinal homeostasis and control immunological responses, cytokines are released under certain conditions. The interaction between probiotic microorganisms and gut-associated lymphoid tissue, their immune system modulation, and their anti-inflammatory properties remain unclear.

Probiotic microorganisms from the honeybee’s stomach during the honey-making process have also been reported to be accommodated in honey. Additionally, reports of Bacillus sp. being found in honey have been made. In 2012, Esawy and his team isolated Bacillus spp. from spores found in honey from three Gulf nations (Libya, Saudi Arabia, and Egypt). They showed negative hemolytic test findings and good tolerance to pH 3 and pH 9 for up to 6 hours with variable degrees of viability. The isolates also exhibited antibacterial and antioxidant qualities, indicating that they might thrive in the gastrointestinal tract and serve as possible sources of

antibiotics [27]. Recently, 106 yeast strains were discovered in three samples of honey bees, in addition to bacteria [126].

4. Prebiotic

Honey's prebiotics come from its unbreakable carbohydrates, which are not absorbed in the upper gastrointestinal tract and cannot be digested by human enzymes. Encouraging the growth and metabolic activity of colon occupants can significantly improve overall health, particularly in the intestinal system [68]. Prebiotics are indigestible food elements that selectively promote the growth of the host, resulting in positive effects on the host and the presence or activity of beneficial bacteria in the colon can significantly improve host health [33]. Pathogenic bacteria cannot consume prebiotics [113, 31]. They facilitate or support the growth of probiotic bacteria (bifidobacteria and lactobacilli) and enable them to proliferate primarily [10]. Poly- or oligosaccharides are the most common types of prebiotic. Bananas, garlic, wheat, tomatoes, onions, and legumes are among the fruits and vegetables that naturally contain prebiotics [16]. Prebiotics, including lactulose, FOS, GOS, soya-oligosaccharides, xylo-oligosaccharides, pyrodextrins, and isomalto-oligosaccharides, are widely recognized as beneficial microorganisms. Prebiotics are primarily carbohydrate-based substances like lactulose, GOS, and both short and long-chain β-fructans. Dietary prebiotics are defined as "a selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health" [35]. The classification of a substance as a prebiotic is determined by applying specific standards. The substance should be acidic, fermentable by intestinal microbiota, hydrolyzed by mammalian enzymes, and selectively stimulate intestinal bacteria, thereby improving host health.

TYPES OF PREBIOTICS	BENEFITS	FOOD SOURCE	REFERENCES
Inulin	• Promotes growth of beneficial bacteria, • Improves digestion • Enhances calcium absorption	Chicory root, onions, garlic, leeks	J. Slavin, 2013
Fructo oligosaccharides (FOS)	• Promotes growth of beneficial bacteria • Reduces levels of harmful bacteria • Improves gut health	Onions, garlic, leeks, asparagus, bananas	J. Slavin, 2013
Galacto oligosaccharides (GOS)	• Enhances growth of beneficial gut bacteria • Improves bowel function • Boosts immune response	Beans, lentils, dairy products (yogurt, milk)	Y. Bouhnik *et.al.*, 2004
Beta-glucans	• Enhances immune function • Lowers cholesterol • Improves blood sugar control	Oats, barley, mushrooms	M. Jayachandran *et.al.*, 2018
Lactulose	• Improves gut health, • Acts as a mild laxative • Supports liver function	Synthesized from lactose; found in small amounts in dairy products	J.Slavin, 2013
Xylo oligosaccharides (XOS)	• Promotes growth of beneficial bacteria • Supports immune function • Improves digestion	Bamboo shoots, fruits (plums, bananas), vegetables (broccoli, cabbage), honey	G.R. Gibson and M.B. Roberfroid, 1995.
Pectin	• Supports gut health • Lowers cholesterol • Improves blood sugar control	Apples, citrus fruits (oranges, grapefruits), carrots	G.R. Gibson and M.B. Roberfroid, 1995.

Table 2. Different types of prebiotic, their benefits and food source.

4.1 Uses

Honey has been extensively researched as a prebiotic source of probiotics in dairy and non-dairy meals. Foods containing either mono-floral or poly-floral honey can be excellent sources of prebiotics. Yogurt is made from dairy products such as; fresh milk of buffaloes, goats camels, and cows. The most widely employed starting cultures of probiotics in yogurt production are L. delbrueckii ssp. bulgaricus and S. thermophilus. The results of multiple studies showed that foods containing honey had a much higher concentration of probiotics. Eucalyptus and greenbrier honey, along with polyfloral honey, were found to be effective prebiotic sources for growing Bifidobacteria strains of various subspecies [105, 88]. By giving probiotic microbes enough nutrition, honey's prebiotic properties can promote their growth. More probiotics may improve the digestive system's health and strengthen its defenses against pathogen infections by reducing the overall surface area available for nutrient absorption [77].

4.2 Applications

Prebiotic foods, like non-digestible carbohydrates, are not absorbed in the upper gut but reach the colon, where they are used selectively by gut microbiota. This leads to the selective stimulation of beneficial microbial populations and functions in the gut [34]. Prebiotics found in food have been linked to numerous health benefits, including enhanced immunity, Improved digestion and absorption, improved vitamin synthesis, lower cholesterol, and decreased gas distension, control over the growth of opportunistic and invading pathogens, better absorption of minerals , fermentation products can modify lipid metabolism, providing anti-inflammatory properties and reducing the risk of heart disease and cancer [22]. It is commonly known that bacteria play a significant role in the colon's metabolism of carbohydrates. Peptides, oligosaccharides, polysaccharides, and indigestible complex carbohydrates are crucial elements that influence the composition and activity of gut microbes [74].

Honey's diverse composition and therapeutic properties complicate mechanistic studies of its bioactivity, but offer a focused approach for various health goals due to its antibacterial, antiinflammatory, and prebiotic properties. These bioactivities can be associated with the developing field of customized medicine, which aims to provide individuals with more individualized therapeutic treatment and preventative choices [65]. The numbers show that cardiovascular diseases accounted for 30% of all deaths in the US in 2013. People's changing food and lifestyle habits are the primary cause of this developing trend [69]. The natural gut microflora hydrolyzes prebiotics since human digestive enzymes lack β-glycosidases. Among the well-known prebiotics are lactulose, xylooligosaccharide, fructose-oligosaccharides (FOS), inulin, and pyrodextrins [118]. Inulobiose, kestose, and nystose are examples

of fructo-oligosaccharides that have been detected in samples of Malaysian honey [12]. In honey from New Zealand, the oligosaccharides isomaltose and melezitose have been identified [120]. Italian honey has been found to contain raffinose. Honey is recognized as a prebiotic material because it contains a large number of oligosaccharides and low molecular weight polysaccharides that withstand breakdown by host enzymes and continue to serve as a nutrition source for the intestinal microflora [78]. Prebiotics promote the growth and activity of beneficial bacteria in the colon, which are then transported to the lower part of the gastrointestinal tract. Bifidobacteria and Lactobacilli bacteria protect hosts by influencing the immune system and competing with bacterial and fungal pathogens for nutrients and space. Honey is primarily composed of monosaccharides, which are easily absorbed in the small intestine, with minor amounts of di-, tri-, and oligosaccharides [9,96]. Honey contains low-weight polysaccharides and oligosaccharides that may withstand breakdown by host enzymes and enter the lower intestine to have prebiotic effects [97]. Honey's prebiotic potential has been demonstrated in in-vitro studies and in probiotic food products like honey-supplemented milk or yogurt [82, 63].

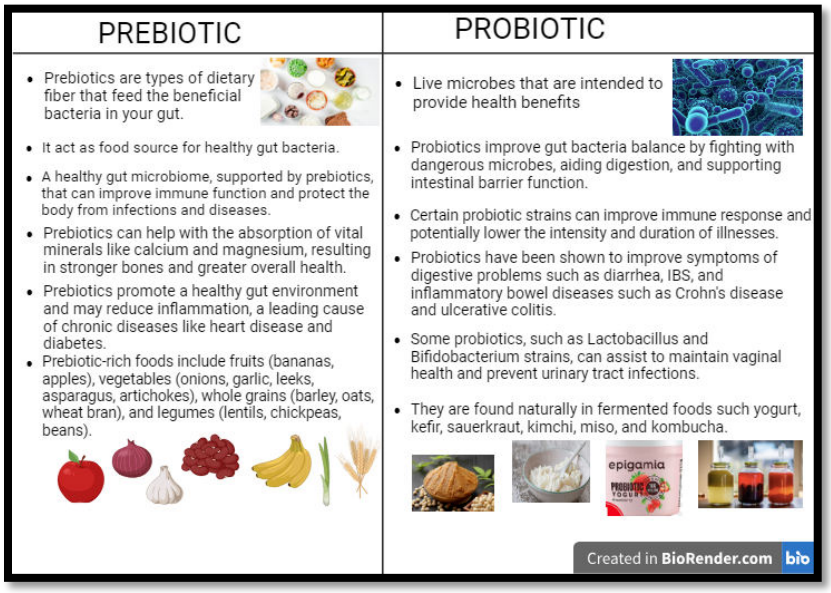

Figure 1. Prebiotics and probiotics [C. Cremon et al., 2018, M. Cunningham et al., 2021]

5. Honey as a Source of Probiotics

It has also been observed that probiotics belonging to the genus Bacillus reside in the digestive tract of honey bees and are absent from Japanese honey bees. At the end of the fifth day, one isolate inhibited M. plutonius, indicating a significantly lower death rate compared to the untreated group of A. mellifera larvae [125]. Two recently obtained B. subtilis strains (MENO2 and HMNig-2) have been isolated from

the microbiome of bees and honey, the study demonstrated probiotic properties and produced various beneficial components, including levan [43]. Levan is utilized in the food industry as a flavor carrier, food coating material, thickening, stabilizing, emulsifying, and encapsulating agent. In the field of biomedicine has shown potential as an antiviral, anti-inflammatory, hyperglycemic inhibitor, and antihyperlipidemic drug [70]. A. mellifera species' guts also contained a number of other Bacillus species and yeasts, including B. licheniformis, P. polymyxa , W. anomalus, L. thermotolerans, and Z. mellis. The bacteria showed resistance to low pH up to 1.5 and survived in high bile salt concentrations, indicating their strong potential as probiotics after three hours of incubation. Probiotic bacteria from the honeybee's stomach are also known to be accommodated in honey throughout the beehive's honey-making process. A. dorsata honeycomb-isolated LAB contains Lactobacillus kunkeei and additional Lactobacillus species. This is the first study of its kind to be published on lactobacilli in the honeycomb of a massive A. dorsata wild bee in Malaysia, demonstrating the potential for honeycombs to serve as natural food preservatives and sources of novel probiotic microbes [111]. A. monocytogenes and E. coli were the two pathogens that other LAB types derived from A. mellifera honey were sensitive to, with the sensitivity to E. coli being higher. The bacterial cell wall's outer layer is broken down, causing the pH in the surrounding environment to decrease the LAB's antibacterial action stops infections from spreading or living longer [80].

During the evaluation period, all strains demonstrated resistance to 1% bile salt. When compared to Lactobacillus sp., B. subtilis and B. megaterium were discovered to be important probiotic candidates because they did not include any virulence genes [84]. B. subtilis and another species, B. endophyticus, were also isolated from other honey varieties, including persimmon and mountain honey [117]. It has been discovered that a single Bacillus species isolated from honey inhibits the pathogenic fungus Candida albicans as well as the bacteria S. aureus and E. coli. Bacillus sp. attaches pathogens, causing their form to change and destruction, leading to disruption and leakage on their cell wall. It may aid in regulating the host's microbiota as an efficient probiotic [52]. In addition to bacteria, strains of yeast were also found in honey. Six yeast strains were recently discovered in three honey bee samples over half of the isolates' strains showed a commendable survival rate in restored gastrointestinal conditions; the temperature was 37^0C, the bile salt content was 0.3% (w/v), and the ranged from 2.0–2.5. Certain strains that were separated seemed to exhibit increased auto-aggregation, ranging from 80 to 100%. This could potentially result in the utilization of various sugars, such as galactose and xylose. Yeast isolates have the potential to produce probiotics for the functional food and feed sector and metabolite producers for lignocellulosic biorefinery [126]. Honey bees' digestive processes provide a special source of bacteria. They are divided

into three major phylums: Firmicutes, Actinobacteria, and Proteobacteria, some of which have LAB classifications [71]. Honey bees' digestive tract contains several LAB strains that can serve as beneficial probiotics for health [115]. Antimicrobial peptide is one of the bioactive components in the LAB, isolated from the intestines of honey bees. Antimicrobial peptide is a crucial component of the immune system and a potential replacement for the existing antibiotic treatment or microbial infection prevention [46, 17].

The different antimicrobial peptide included in honey allow honeybee LAB to function as probiotics, inhibiting harmful bacteria. Numerous studies have demonstrated LAB's inhibitory effect on bacterial infections [73, 5, 93]. Three LAB varieties from honey bees, L. kunkeei Fhon, L. kunkeei Lahm, and L. kunkeei Yubipro, were found to produce bioactive chemicals with antibiotic-like activity. Broad spectrum antibiotic chemicals produced by lactic acid bacteria can combat variety of pathogenic microorganisms, including S. marcescens, P. aeruginosa, K. aerogenes, E. coli, S. aureus, and MRSA [95]. According to all of these investigations, LAB may be a good source of antibacterial compounds that can fight both pathogenic Gram-positive and Gram-negative bacteria. Lactobacillus has the strongest antioxidant effect in addition to its antibacterial capability, as demonstrated by the identification of Lactobacillus plantarum H28 and H24 from honey bee digestive tracts [58]. Probiotic qualities include their great survivability in the artificially changed digestive tract system, their lack of hemolytic activity, and their safety in relation to antibiotic susceptibility. According to the current research, these strains may be able to survive in the gastrointestinal tracts of both people and animals after being exposed to severe environmental circumstances [26].

Probiotics and their benefits

Probiotic	Benefits	References
Lactobacillus rhamnosus	Promotes Gut immunity, boosts IgA and immunoglobulins secreting cells, promotes interferons release, enhances antigen transport to lymphoid cells.	[87]
Lactobacillus GG	Stops the spread of pathogens, biosurfactants, acids, bacteriocins in urinary tract.	[85]
L.fermantum RC-14	This involves maintaining	[86]

	and restoring urogenital health.	
L. rhamnosus GR-1	It maintains and restores urogenital health	[86]
Lactobacillus acidophilus	This supplement enhances digestion, supports immune function, and alleviates symptoms of IBS.	[94]
Bifidobacterium bifidum	This supplement not only alleviates constipation but also enhances the immune response and improves gut health.	[75]
Saccharomyces boulardii	Prevents diarrhea, supports gut health, and reduces inflammation.	[66]
Bifidobacterium lactis	Enhances immune response, improves digestion, and reduces infection risk.	[36]
Lactobacillus rhamnosus	The supplement reduces the likelihood of respiratory infections, promotes gut health, and alleviates diarrhea.	[67]

5.1 Honeys as a Source of Probiotic for Human Being

Probiotics were initially utilized to enhance the health of both animals and humans by enhancing intestinal health and enhancing the immune response, the reduction of serum cholesterol and cancer prevention are key objectives [57]. These microbial communities are capable of surviving in harsh bodily conditions, such as low pH, salivary enzymes and pancreatic juice are used to colonize intestinal epithelial cells, improving host health by controlling microorganisms and performing biological

tasks [127]. The study investigated the effectiveness of thirteen Lactobacillus strains from A. mellifera in treating severe wounds resistant to methicillin. Pseudomonas aeruginosa, vancomycin-resistant Enterococcus, and Methicillin-resistant staphylococcus aureus (MRSA) exhibit strong and coordinated antibacterial activity against these pathogens [73]. Probiotics are frequently touted as having the ability to prevent infectious disorders of the gastrointestinal tract (GIT). New strategies, including the use of live bio-therapeutic agents like bacterial isolates, are being explored for their potential in treating various diseases, have been tried to treat these disorders in place of antibiotics [76]. Some pathogens were inhibited and antibiotic resistance was not present in the majority of the Bacillus and Lactobacillus species that were isolated from Iranian honey. These qualities are thought to be advantageous for microorganisms employed in the production of dietary probiotics, B. megaterium demonstrated exceptional resistance to relatively low pH for 4 hours, alongside strong resistance to acidic pH and concentrated bile salts, the time transition of food in the stomach is typically between 2 and 3 hours.

6. Honey as a Source of Prebiotic

Prebiotics are essential components that enhance health. Scientists have demonstrated that prebiotics provide numerous health benefits, including promoting the growth of gut bacteria, this substance enhances mineral absorption, reduces cholesterol, boosts immunity, and may even serve as an anticancer agent. Prebiotics, naturally occurring in food, are primarily oligosaccharides, specifically fructo-oligosaccharides (FOS) and galacto-oligosaccharides (GOS). Honey is a significant source of prebiotic oligosaccharides [109]. Panose, kestose, maltotriose, raffinose, and isomaltose are the most common forms of isolated oligosaccharides found in honey [90]. Food has a big impact on how the gut microbiota functions and is composed. Dietary influences the gut microbiome as early as infancy, when breastfed and formula-fed infants had substantially different microbiota compositions and diversities [100]. Studies suggest that food and gut microbiota may co-evolve. Acinetobacteria, Bacteroidetes, and a particular abundance of Xylanibacter and Prevotella were found to be present in the African microbiome, which was found to have a depletion of Firmicutes. The study suggests that this could potentially improve children's capacity to absorb calories from the indigestible plant polysaccharides they consume. The study analyzed the diet and gut microbiota of children from Europe and a rural African village [19]. The gut microbial community composition and population-wide patterns, such as the abundance of Bacteroides and Prevotella, play a crucial role in gut health, long-term dietary patterns, particularly those focusing on protein and animal fat over carbohydrates and fiber, are linked to various health issues [124]. Short-term dietary changes can alter the

composition and function of the gut microbiota, despite the generally stable adult microbial community associated with long-term diets [18, 112].

Unprocessed carbohydrates and other prebiotic meals do not enter the upper digestive tract and arrive in the colon undigested, where the gut microbiota can use them as a selective substrate. This causes the numbers and activities of advantageous microbes in the gut to be selectively stimulated [35]. Prebiotics found in food have been related to a number of health benefits, such as increased immunity, better digestion and absorption, vitamin synthesis, lower cholesterol, less gas in the stomach, control over the growth of opportunistic and invading pathogens, better absorption of minerals (particularly calcium), fermentation products can modify lipid metabolism, promote anti-inflammatory activity, and reduce the risk of heart disease and cancer [23, 35]. Peptides, oligosaccharides, polysaccharides, and indigestible complex carbohydrates are important factors that influence the makeup and activity of gut microbes. Finding sources of these carbohydrates to employ as prebiotics is therefore of tremendous importance [74].

6.1 Honey as a Source of Prebiotic for Human Being

Honey has been a significant component of human diets throughout history. Honey and bee larvae from wild honey may have provided prehistoric humans with protein, fat, and energy [15]. Regular honey consumption is believed to have influenced the shift from a low-calorie to a high-energy, high-calorie diet that supported increased brain activity during the evolution of larger hominin brains, this is an effective and nutritious food source that complements meat and plant foods [91]. The Oldowan tools, which were around 50,000-10,000 BCE, were known for their practice of honey gathering and rock art supports the idea that food consumption requires less mechanical breakdown due to the reduction in molar size. Honey is a widely recognized treatment for digestive issues. In around 25 AD, Roman physicians recommended various types of honey to treat constipation and diarrhea. Similarly, Islamic holy manuscripts from the eighth century depict Prophet Muhammad promoting the use of honey for treating diarrhea [14,8]. There are frequent reports of using honey to cure and prevent gastritis, gastroenteritis, and peptic ulcers.

Honey eating reduces the duration of bacterial diarrhea in youngsters and very ill tube-fed patients, who have also been proven to be less likely to have organ failure when getting honey treatment, according to numerous contemporary studies on the benefits of honey for digestive health [42,101]. Additionally, honey helped individuals with viral gastroenteritis recover more quickly. Honey may protect the stomach, according to several studies. Consuming large amounts of honey (50-100 g) may have a mild laxative effect due to inadequate absorption of fructose [92, 2].

6.2 Health Benefits of Prebiotics

Acute gastroenteritis is a common health issue caused by consuming food or water contaminated with pathogenic microorganisms or their toxins. Common bacteria causing infections include Shigellae, Salmonellae, Yersinia enterocolitica, Campylobacter jejuni, Escherichia coli, Vibrio cholera, and Clostridium perfringens. Pathogens can colonize and thrive in the gastrointestinal system before invading host tissue, They may emit poisons that contaminate food before it is consumed. This type of toxin disrupts the function of the intestinal mucosa, leading to symptoms such as nausea, vomiting, and diarrhea. Larger quantities of beneficial bacteria in the large intestine, combined with factors like immunological state, may offer better protection. This may be more effective than probiotics due to survival difficulties.

Research is underway to combine prebiotic and anti-adhesive characteristics. This would significantly improve the method of changing gut pathogens. Many intestinal pathogens utilize monosaccharide or short oligosaccharide sequences as receptors. The comprehension of these receptor sites is crucial for the creation of prebiotics that offer biological advantages. According to [54]. Viruses bind to receptors as the initial stage in colonization. Clinical testing is currently underway on several pharmacological formulations based on oligosaccharides. These medicines are multivalent sugar derivatives that act as blocking factors, causing the adhering pathogen to dislodge [50]. Prebiotics with receptor monosaccharide or oligosaccharide sequences have high potential for development. These molecules should be anti-adhesive enough to prevent infections from binding at low doses. Prebiotics have been found to potentially decrease the virulence of certain food-borne diseases.

Conclusion and Future perspectives

Honey is complex nature may hinder the growth of most microorganisms, but its prebiotic content has been found to stimulate the growth and activity of probiotic microorganisms. Also honey is a stable natural food with health benefits and prebiotic oligosaccharides, can be used as an exceptional food matrix for honey production. Further research is needed to develop safe, high-resistance probiotics for human consumption or disease treatment, and to develop alternative therapeutics for antibiotic-resistant pathogens. Honey, despite its complex nature, has been found to stimulate the growth and activity of probiotic microorganisms due to its prebiotic content at room temperature.

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