BENEFICIAL MICROBIOTA OF GASTROINTESTINAL TRACT

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ABSTRACT
Probiotic and prebiotic foods enhance the growth of healthy microorganisms in body.Probiotics are the healthy microflora that live in digestive tract and prebiotics are the nutrients that they use to thrive. Synbiotic products combine probiotics and prebiotics to enhance their beneficial effects. The human gastrointestinal tract is colonized by a complex ecosystem of microorganisms. Many microbial species live commensally on mucosal tissues of the nose, mouth, and GI tract. Probiotics and prebiotics may help normalize a gut microbiota disturbed by antibiotics or other stressors and improve health of people.Beneficial intestinal bacteria have numerous and important functions, e.g., they produce various nutrients for their host, prevent infections caused by intestinal pathogens, and modulate a normal immunological response. The introduction of probiotics and prebiotics into human diet is favorable for the intestinal microbiota. Abiotic components are dead cell components (such as enzymes), metabolic by-products (bioactive peptides), and others.Probiotics, probiotics and synbiotics have systemic effects on the host's health metabolism and immune system. They may be consumed in the form of raw vegetables and fruit, fermented pickles, or dairy products. Most commonly used probiotic strains are present in *Bifidobacterium, Lactobacillus*and *Saccharomyces boulardii.* Some of the prebiotics are inulin, oligosaccharides, disaccharides, monosaccharides, and short-chain fatty acids. Prebiotics are the most commonly used fibers which when used together with probiotics are termed synbiotics and are able to improve the viability of the probiotics. Synbiotics aid digestion and absorption of nutrients, synthesize certain vitamins and amino acids, and improve immune function. They also keep the pathogens in check by crowding them out or secreting substances that reduce their numbers. Dietary fiber is not digested in the small intestines, when it makes its way to the large intestines, the healthy bacteria break it down releasing short chain fatty acids.Utilization of prebiotics by probiotics should be a pre-requisite in order to maintain a good synergy and maximize the beneficial effects.Nonviable probiotics exert beneficial effects on the health of people.

Keywords: Probiotics, Prebiotics, Synbiotic, Microbiota

1.1. Introduction
A normal healthy gastrointestinal (GI) microbiota in humans provides resistance against intestinal pathogens. Beneficialbacteria can affect intestinal flora and influence the incidence and severity of enteric infections. Hundreds of microbial species live commensally on mucosal tissues of the nose, mouth,and GItract. ThehumanGI tractisa nutrient-richenvironmentinhabited by up to 100 trillion (10^{14}) microorganisms and can change markedly with diet, age, and lifestyle. When microorganisms are consumed together with foods, most of them lose their viability in the stomach due to high acidic environment and are removed by peristaltic movement of the GI tract (Erkmen and Bozoglu, 2016a). The GI microbiota is responsible with the decomposition of nutrients, inhibition of pathogenic microorganisms, hydrolyses of bile salt, immunomodulation of the mucosal immunity system, and other benefits. Microbiota number and type in the GI system depend on many factors: the composition of the normal microflora, diet, age, and the genetic or physiological conditions.

Severe disturbances in the GI tract (such as antibiotic therapy, enteric infections, or dietary stress) can disrupt normal microflora of intestines. These populations recover quickly as the host returns to normality (Erkmen and Bozoglu, 2016a; Markowiak andSlizewska, 2017;Erkmen, 2018).

There are thousands of species of gut microbes that live in the gut; some healthy (symbionts) and some unhealthy (pathogens). Symbionts aid digestion and absorption of nutrients, synthesize certain vitamins and amino acids, and improve immune function. They also keep the pathogens in check by crowding them out or secreting substances that reduce their numbers (Requena et al., 2013).Since dietary fiber is not digested in the small intestines, when it makes its way to the large intestines, the healthy bacteria break it down releasing short chain fatty acids (SCFA). These SCFA improve the strength of the mucosal lining of the intestine that eases essential mineral absorption, improves fat metabolism for weight control, and reduces type 2 diabetes risk (Conlon and Bird, 2015). SCFA reduce inflammation, a common cause for many chronic diseases (Vinolo et al., 2011)

Most people are severely deficient in probiotics. These friendly microorganisms are killed off by antibiotics in medications, meat and poultry raised on factory farms, and hand sanitizers, as well as by pesticides in food and beverages, fluoride and chlorine in drinking water, and other toxins. For this reason, people need to eat probiotic-richfoods.Probiotics are live microorganisms when taken in sufficient numbers and they provide health benefits (Erkmen and Bozoglu, 2016b).The aim of the review was to discuss the probiotics, prebiotics, and synbiotics, as well as the current insight into their effect on human health.

Terminology (Tramaroli and Backhed, 2012; Erkmen and Bozoglu, 2016b)

- Microbiota refers to a group of bacteria living in a specific environment such as the gut, skin, or another part of the body.
- Prebiotics are non-digestible carbohydrates that stimulate the growth and activity of healthy bacteria species in the large intestines.
- Probiotics are live microorganisms present in fermented food or supplements and offer health benefits to the human host.
- Abiotics are released components after microbial cell lyses.

2.1. Probiotics and Prebiotics

2.1.1. Abiotics

Nonviableprobiotics exert beneficial effects on the health of people. Abiotic components are dead cell components (such as enzymes), metabolic by-products (bioactive peptides), and others. They play an important role in the beneficial effectsofprobiotics.Theexamples arerelease oflactase bydeadcells andimmune system modulation by cellular components (Erkmen and Bozoglu, 2016b).

2.1.2. Prebiotics

A prebiotic is a non-digestible food ingredient that beneficially affects the human health by selectively stimulating the growth and/or activity of probioticmicroorganisms in the intestine. Prebiotics pass to the small intestine without being digested. Food ingredients as prebiotics generally exhibit the following characteristics (Erkmen and Bozoglu, 2016b):

- limited hydrolysis and absorption in the GI tract,
- selectively stimulate the growth of beneficial bacteria in the intestinal tract,
- potential to inhibit pathogens and limit their virulence characteristics,
- decrease intestinal pH,
- stimulate mucosal immunity,
- reduce colon (large intestine) cancer,

- reduce serum triglycerides and
- enhance mineral absorption (such as calcium, magnesium, iron, and zinc).

Some of the prebiotics are inulin, oligosaccharides, disaccharides, monosaccharides, and short-chain fatty acids. Oligosaccharides are derived from foods. The inulin is recovered by water extraction from the chicory root. Inulin is composed of glucose-fructose polymers. Some of the traditional dietary sources of prebiotic fibers are given in Table 1. Some of the oligosaccharides that naturally occur in breast milk play an important role in the development of a healthy immune system in infants. Prebiotic oligosaccharides are increasingly added to foods, such as fructooligosaccharides, xylooligosaccharides, polydextrose, monosaccharides, and galactooligosaccharides. Moreover, disaccharides (such as lactulose) or some monosaccharides (such as tagatose) are used as prebiotics. Growth factors stimulating the growth of Bifidobacterium are called bifidogenic factors. Bifidogenic factors are typically complex carbohydrates (such as galactosyllactose in breast milk) that are not metabolized by the microflora in the intestines. Characteristics considered in the development of prebiotics are noncarcinogenic, good preservative, easily drying, low caloric value, and controllable viscosity (Sanders, 1999; Erkmen and Bozoglu, 2016b; Markowiak andSlizewska, 2017).
Some of foods are best sources of prebiotics. Most prebiotics are present in the grains (such as oats and corn) andwhole grain products (such as brown rice, breads, wheat pasta, barley, oatmeal, flax, and chia). All of these things should be a regular part of a healthy diet. They contain soluble fiber. The same is true of fruits and vegetables. Asparagus, leeks, artichokes, garlic, carrots, peas, beans, onions, chicory, jicama, broccoli, tomatoes, cauliflower, spinach, kale, and chard all contain prebiotics. Cooking these vegetables doesn't negatively affect the prebiotic fiber content. As for fruits, fresh or frozen bananas, cherries, apples, pears, oranges, strawberries, cranberries, kiwi, and berries are good sources of probiotics. Nuts are also a prebiotic source (Anonymous, 2011;Erkmen and Bozoglu, 2016b).

Table 1. Foods containing prebiotic fibers

Food	Content by weight
Gum Arabic	85.6%
Raw chicory root	64.6%
Raw Jerusalem artichoke	31.5%
Raw dandelion greens	24.3%
Raw garlic	17.5%
Raw leek	11.7%
Raw onion	8.6%
Cooked onion	5%
Raw asparagus	5%
Raw wheat bran	5%
Whole wheat flour cooked	4.8%
Raw oats	4.0%
Raw banana	1%
Beans	1%

2.1.3. Probiotics

Probiotics (meaning "for life") are the living microorganisms introduced in adequate numbers into the GI system of humans to improve health and intestinal balance or metabolic activity of beneficial microorganisms. They are resistant to gastric,bile,andpancreaticsecretions,attachtoepithelialcells,andcolonizeinthe human intestines. Probiotic bacteria must arrive at the site of action in high enough numbers to exert their effect, and this might most easily be achieved by using resistant microorganisms or by providing

large numbers of live microorganisms to compensateforlossesduringpassagethroughtheGItract.Probioticsshouldsurvivein the low-pH conditions of the stomach (the pH will be 1.5) and show resistance to the bile salt in the duodenum. For health benefits, the probiotic food with a sufficient number of live bacteria (10^7-10^{11} cells per day) must be consumed regularly. Probiotics must be able to retain viability in foods, and to survive and grow in the human intestine. Probiotics exhibit poor growth rates in synthetic media.Probioticsaregenerallyofintestinalorigin;manyprobioticsaresensitiveto high temperatures (such as pasteurization), acid, and oxygen during food processing. The bifidobacteria are strictly anaerobic microorganisms with complex nutritional requirements. Fermented dairy foods, including milk and yogurt, are among the most accepted food carriers for viable probiotic cultures to the human GI tract (Erkmen,2000; Erkmen and Bozoglu, 2016b).

As live microbes, probiotics can influence the microbes that colonize human body.

- Although few in number compared to gut microbiota, probiotics can grow, metabolize and interact with resident microorganisms. Rarely do probiotics permanently colonize.
- Probiotics may exert effects on the microbiota as they travel through the less densely colonized regions of our GI tract (stomach and small intestine).
- Probiotics may use similar mechanisms as our colonizing microbes to improve health. For example, the ability of probiotics to influence immune system can impact colonizing microbiota and health.

Microorganisms from many different genera are being used as probiotics, including *Lactobacillus*, *Bifidobacterium*, *Propionibacterium*, *Enterococcus* and *Saccharomyces*. However, nonpathogenic *Bacillus* and yeast members are also used as probiotics (Table 2). *Lactobacillus* spp. are the most commonly used probiotics in food, whereas *Bifidobacterium* spp. are used less, as they are sensitive to oxygen and have stricter growth requirements, making them technologically more unsuitable for use. Ideally, a probiotic microorganism should have a number of desirable properties (Table 3). The probiotics should be safe, have GRAS (generally recognized as safe) status, and have a long history of safe use in foods. All probiotic strains should be nonpathogenic, should successfully adhere to and colonize in the intestinalcells,andshouldshowtolerancetoantimicrobial substances,butshould notbeabletotransmitsuchresistancetootherbacteria.Adhesion to the intestinal mucosa is considered important for immune modulation, preservation of pathogens, and removal of pathogens from the GI tract. Probiotic microorganisms should be technologically suitable for incorporation into food products, such that they retain viability in food product both prior to and following consumption. Probiotics should be resistant to digestive enzymes and peristalsis of the stomach. Foods, such as yogurt and milk, provide protection to probiotic microorganisms throughout the GI tract. Probiotics can produce antimicrobial substances including lactic acid, hydrogen peroxide, and bacteriocins (such as nisin and plantaricin). Hydrogen peroxide production by probiotics is desirable in urogenital infections (Sanders, 1999; Erkmen,2000; Pandey et al., 2015, Erkmen and Bozoglu, 2016b; Markowiak and Slizewska, 2017).

Table 2. Some of the probiotic microorganisms

Bifidobacterium animalis	*Lactobacillus gasseri*
Bifidobacterium bifidum	*Lactobacillus reuteri*
Bifidobacterium breve	*Lactobacillus rhamnosus*
Bifidobacterium lactis	*Lactobacillus salivarius*
Bifidobacterium longum	*Bacillus clausii*

Lactobacillus acidophilus	*Bacillus subtilis*
Lactobacillus casei	*Enterococcus faecalis*
Lactobacillus johnsonii	*Enterococcus faecium*
Lactobacillus fermentum	*Prop. freudenreichii*subsp.*shermanii*
Lactobacillus paracasei	*Saccharomyces boulardii*
Lactobacillus plantarum	*Sac. cerevisiae* subsp.*boulardii*

Table 3. Desirable properties of probiotic microorganisms

1. GRAS status.
2. provide health benefits on humans.
3. Antimutagenic and anticarcinogenic properties.
4. Nonpathogenic.
5. Tolerance to antimicrobial substances.
6. Able to grow and colonize in intestines.
7. Adherence to intestinal mucosa.
8. Ability to reduce pathogen adhesion on the intestinal mucosa.
9. Antagonistic and antimicrobial activity against pathogenic bacteria.
10. Immunostimulation without proinflammatory effect.
11. Acid tolerance and able to survive the acidic conditions in stomach.
12. Human gastric juice tolerance.
13. Bile salt tolerance.
14. Desired metabolic activity.
15. Good sensory properties.
16. Retain viability during food processing, storage and following consumption.

3.1Synbiotics

The combination of probiotic and prebiotic therapies is referred to as synbiotics. The strategy of combining a probiotic with its preferred nutrient may allow for probiotics to stay in body for longer (Markowiak and Slizewska, 2017). Synbiotics are used not only for the improved survival of beneficial microorganisms added to food or feed, but also for the stimulation of specific native bacterial strains present in the gastrointestinal tract (Gourbeyre et al., 2011). The effect of synbiotics on metabolic health remains unclear. It should be mentioned that the health effect of synbiotics is probably associated with the individual combination of a probiotic and prebiotic (De Vrese et al., 2008). Considering a huge number of possible combinations, the application of synbiotics for the modulation of intestinal microbiota in humans seems promising (Scavuzzi et al., 2014; Erkmen, 2018).

The first aspect to be taken into account when composing a synbiotic formula should be a selection of an appropriate probiotic and prebiotic, exerting a positive effect on the host's health as compared with the use separately. The determination of specific properties to be possessed by a prebiotic to have a favorable effect on the probiotic seems to be the most appropriate approach. A prebiotic should selectively stimulate the growth of microorganisms, having a beneficial effect on health, with simultaneous absent (or limited) stimulation of other microorganisms (Markowiak and Slizewska, 2017).

A combination of *Bifidobacterium* or *Lactobacillus*spp. with fructooligosaccharides in synbiotic products seems to be the most popular. Table 4 presents the most commonly used combinations of probiotics and prebiotics.Considering the fact that a probiotic is essentially active in the small and large intestine, and the effect of a prebiotic is observed mainly in the

large intestine, the combination of the two may have a synergistic effect (Hamasalim, 2016). Prebiotics are used mostly as a selective medium for the growth of a probiotic strain, fermentation, and intestinal passage. When prebiotics are used together with probiotics, probiotic microorganisms acquire higher tolerance to environmental conditions, including: oxygenation, pH and temperature in the intestine of a particular organism (Sekhon and Jairath, 2010). However, the mechanism of action of an extra energy source that provides higher tolerance to these factors is not sufficiently explained. That combination of components leads to the creation of viable microbiological dietary supplements, and ensuring an appropriate environment allows a positive impact on the host's health (Markowiak and Slizewska, 2017).

Probiotic organisms are crucial for the maintenance of balance of human intestinal microbiota. They have positive effect in the host's health (Erkmen, 2018). It seems also that probiotics may be helpful in the treatment of irritable bowel syndrome, enteritis, bacterial infections, and various gastrointestinal disorders and diarrheas. Probiotic microorganisms are also effective in the alleviation of lactose intolerance and the treatment of atopic dermatitis. Prebiotics may be used as an additional support for them. It turns out that the development of bio-therapeutic formulas containing both appropriate microbial strains and synergistic prebiotics may lead to the enhancement of the probiotic effect in the small intestine and the colon. Those "enhanced" probiotic products may be even more effective. Probiotics, probiotics and synbiotics have systemic effects on the host's health metabolism and immune system. Utilization of prebiotics by probiotics should be a pre-requisite for symbiotic selection, in order to maintain a good synergy between the two and maximize the beneficial effects. The ability to regulate the composition of the microbiota by prebiotic dietary substances and probiotic microorganisms is an interesting approach in the control and treatment of some major diseases. The ability to target specific microorganisms in the large intestine for defined, health-promoting purposes would be of great value. There are considerable differences in bacterial carbohydrate utilization patterns among the different strains as well as species, which is to be kept in mind for developing new synbiotics.

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