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The microbiota of humans and animals and its relationship with the use of functional foods

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Abstract: In human and animal body, especially in the gastrointestinal tract, there are many microorganisms that coexist in a mutually beneficial relationship with the host. The main function of the intestinal microbiome is to ferment indigestible substrates and short-chain fatty acids, etc. to inhibit the proliferation of pathogens, among other functions. For example, by increasing beneficial microorganisms that produce important antimicrobial metabolites. The gut microbiota can prevent the colonization of pathogens through the mechanism of colonization resistance. Antibiotic exposure to the gut microbiome can trigger the response that affects colonization resistance. This review provides an overview of the gut microbiome and the effects of antibiotic therapy on pathogen and disease colonization, the relationship between diet and microbiota, and the use of functional foods.
Keywords: Functional food, microbiota, probiotic-prebiotic.

İnsan ve hayvanlarda mikrobiyota ve fonksiyonel gıdaların kullanımı ile ilişkisi

Özet: İnsan ve hayvan vücudunda, özellikle de mide-bağırsak sisteminde, konakçı ile karşılıklı olarak yararlı bir ilişki içinde birlikte gelişen birçok mikroorganizma bulunmaktadır. Bağırsak mikrobiyomunun ana rolü, sindirilemeyen substratların fermentasyonu ve diğer işlevlerin yanı sıra patojenlerin çoğalmasını engellemek için kısa zincirli yağ asitleri vb. gibi önemli antimikrobiyal metabolitler üreten faydalı mikroorganizmaların artmasıdır. Bağırsak mikrobiyotası, kolonizasyon direnci mekanizması yoluyla patojen kolonizasyonunu önleyebilir. Bağırsak mikrobiyomunu antibiyotik maruziyetine bırakmak, bağırsak kolonizasyon direncini etkileyen yanıtı tetikleyebilir. Bu derlemede, bağırsak mikrobiyomu ve antibiyotik tedavisinin patojen kolonizasyonu ve hastalıkları üzerindeki etkilerine, diyetin mikrobiyota ile ilişkisine ve fonksiyonel gıdaların kullanımına yönelik genel bir bakış sunulmaktadır.
Anahtar kelimeler: Fonksiyonel gıda, mikrobiyata, probiyotik-prebiyotik.

Introduction

Humans live in a biosphere where microorganisms have existed for 3.8 million years and have influenced the biosphere for 10 thousand years. Over the same period, we have also been influencing the microorganisms that make up our internal biosphere, i.e., our microbiota (Lederberg & McCray, 2001). Ecological communities formed by commensal, symbiotic, and pathogenic microorganisms found in various parts of the human body used to be referred to as normal body flora but are now called the "microbiota". The term microbiome refers to the sum of genomes of microorganisms living in an ecological niche (Köroğlu, 2017). The human microbiota is mainly composed of bacteria, viruses, fungi, and many eukaryotic microorganisms (Tuğ et al., 2002). It is reported that the bacterial genome in the human body is ~ 150 times larger than the human genome (Cénit et al., 2014; Walker & Lawley, 2013). This combination of human and microbial genomes is referred to as the "hologenome". In addition, it is reported that the number of microorganisms in the human body is ten times greater than the number of human cells, as they also have advantages in terms of their genome (Belkaid & Hand, 2014). Most of the human microbiota has occupied in the digestive system, skin, urogenital system, and respiratory system. The digestive system provides the most suitable environment for microorganisms to colonize due to its large surface area and abundance of nutrients. For this reason, the colon alone is reported to contain more than 70% of the microorganisms in our bodies (Whitman et al., 1998).

The relationship among microorganisms and between microorganisms and hosts is studied through microbiome studies. The Microbiome Project, launched in 2007 with 300 volunteers, aimed to determine all microorganisms in the human body and to investigate whether changes in the microbiome can be associated with the disease (Tuğ et al., 2002). The gastrointestinal microbiota more than 1500 species of microorganisms. The two dominant bacterial phyla Firmicutes and Bacteroides make about 90% of the gut microbiota of a healthy adult person, with lesser amounts of other phyla like Actinobacteria (mostly *Bifidobacterium*), Proteobacteria, Fusobacteria, and Verrucomicrobia (Kamada et al., 2013; Qin et al., 2010).

The microbiome has some protective, metabolic, and structural effects. These protective effects are the removal of pathogenic microorganisms, competition with food, competition with receptors and the production of antimicrobial factors. Their structural effects are strengthening the mucosal barrier, induction of IgA, tightening the tight junctions, and developing the immune system. Its metabolic effects are control of epithelial cell differentiation and proliferation, metabolism of dietary carcinogens, synthesis of vitamins, epithelial-derived fermentation of indigestible food residues, and lowering pH (Hansen et al., 2015).

Relationship of microbiota with diseases: The bacteria in the microbiota contain a certain amount of beneficial and harmful bacteria. When the ratio between beneficial and harmful bacteria decreases, a pathological process called "microbial dysbiosis" begins. The healthy microbiota is called eubiosis (Whitman et al., 1998). The microbiota plays an important role in many bodily functions, including homeostasis, metabolism, the production of minerals and vitamins, the formation of some endocrine stimulation, the prevention of the colonization of some pathogenic microorganisms, the regulation of immune reactions, and the metabolism of xenobiotic substances (Barko et al., 2018; Nicholson et al., 2012). The microbiota also plays a critical role in the immune system's maturation, distinguishing between commensal and pathogenic bacteria and fostering tolerance and immunity to own and foreign antigens. The immunological balance of the mucosa has essential tasks, such as the correct differentiation between billions of harmless microorganisms and rare pathogenic invasive microorganisms. The immune system attempts to directly prevent pathogen colonization through local and generally systemic inflammatory responses (Barko et al., 2018).

Some microorganisms that live with us in the gastrointestinal tract are recognized by M cells and dendritic cells in the epithelium. These stimulate the maturation of T lymphocytes by turning into Regulatory T cells (Treg) cells that secrete cytokines that control the immune system and have an anti-inflammatory function. Lymphocytes, one of the most critical cells in our immune system, stimulate epithelial cells to secrete defensin-like substances with antimicrobial activity (Belkaid & Naik, 2013). In people with dysbiosis, the structure of the mucus layer deteriorates with the decrease in the diversity of the microbiota or the deterioration of the balance of the microbial composition in the intestinal contents and the composition of the microbiota and, consequently, the metabolism of the microbiome. This results in a deterioration of the functions of the mucus layer that are very beneficial to the host, such as maintaining the microbial composition in the gut and preventing colonization by pathogenic microorganisms (Haller, 2018). It has been reported to play a very influential role in gut microbial composition, digestive system peristalsis, and intestinal epithelial function (Björkstén et al., 2001; Vrieze et al., 2010). The bidirectional relationship between the gut microbiota and immune system development and function involves multiple interactions in homeostasis and disease states. At the same time, the immune system regulates the maintenance of the basic features of the relationship between the host and the symbiotic microbiota. In a genetically susceptible host, imbalances in the interactions between the microbiota and the immune system are thought to influence the pathogenesis of many immunological diseases (Shi et al., 2017).

Effects of antibiotics on microbiota: One of the most important factors affecting the microbiota is the use of antibiotics. Antibiotics not only have specific toxicity to the target pathogen, but they also affect the microbiota. The beta-lactam and fluoroquinolone group antibiotics are among the antibiotics that have the most effects on the microbiota due to their frequent use. On the other hand, combined effects on the microbiome often occur due to their frequent use for combined therapy applications (Panda et al., 2014). In one study, it was found that after a 7-day application of clindamycin, the Bacteroides phyla in the microbiota did not return to its normal composition even after two years (Jernberg et al., 2007).

According to the Canine Microbiota Dysbiosis Index data from the College of Texas, it has been reported that although the gut microbiota returns to its previous composition within a few weeks after antibiotic administration in many dogs, this process takes a long time in some animals (Suchodolski et al., 2016).

Microbiota interaction in animals and humans: The gastrointestinal tract is the most important habitat for the microbiota of humans and other animal species. The microbiota of the mammalian digestive tract is diverse and complex, consisting of many interdependent and noncompeting species. The composition of the microbiota varies throughout the gastrointestinal tract. It has been observed that anaerobic bacterial groups dominate in distal sections, whereas aerobic and anaerobic bacteria are more evenly distributed in proximal sections (Simpson et al., 2002; Suchodolski et al., 2008). Cats and dogs have a relatively simple gastrointestinal tract compared to humans and livestock (Eckburg et al., 2005; Ley et al., 2008). In a study using bacterial culture techniques from canine gastric biopsies, the number of bacteria in the stomach was 10^6 cfu/g and it was found that the most abundant indices belonged to the Proteobacteria phylum (99.6%). In addition, only a few (0.3%) indices belonging to the phylum Firmicutes were found (Benno et al., 1992; Garcia-Mazcorro et al., 2012).

It is reported that the part with the greatest similarity in the microbiota of humans and animals living together is the skin and hair regions. Microbiologically, studies have shown that the skin microbiota of adults is more similar to the microbiota of their dog or dogs than to that of other dogs. People with dogs share more common bacterial phylotypes than people without dogs (Song et al., 2013). The taxa that share the most significant similarity between dogs and their owners are the Betaproteobacteria (Methylophilaceae), the Actinobacteria, and the Acidobacteria pylotype (Lauber et al., 2009).

It has been observed that the microbiota of the digestive system benefits the host through many mechanisms. Commensal bacteria in the digestive tract form a temporary defense barrier against pathogens. They aid in the digestion of nutrients, provide important metabolites for the host, and have important functions in modulating the host's immune system (Suchodolski, 2011).

The idea that pets are beneficial to human health was first introduced in 1989 by David Strachan, who attributed the risk of allergic disease to a highly hygienic environment (Strachan, 1989). With further evidence that dysbiosis of the gut microbiome in infancy is associated with the development of allergic disease, this view has been revised as the microbiota hypothesis

(Ezell et al., 2013; Hesselmar et al., 1999; Litonjua et al., 2002; Lodge et al., 2012; Nermes et al., 2013; Ownby et al., 2002; Wold, 1998). In a pilot study including 24 newborns, it was discovered that 3-month-old infants who were around dogs had increased gut microbial richness and variety, as well as more *Bifidobacterium pseudolongum,* an important marker of the transition from animal to human (Azad et al., 2013; Lodge et al., 2012; Nermes et al., 2013). Additionally, *Alistipies*, *Pseudomonas*, *Slackia*, *Subdoligranulum*, the bacterial group *Eubacterium coprostanoligenes*, and *Barnesiella* were not discovered in the gut microbiota of dogs in a study comparing the gut microbiota of wild wolves and domestic dogs to evaluate the domestication of dogs and their coexistence with humans. This indicates that, unlike their wild ancestors, the microbiota of style of living and human influence. In parallel, the same study found that the *Dorea*, *Parabacteroides*, *Streptococcus* family and, Bacteriodales, and Clostridiales pylum, which are not found in wild wolves, are found in humans and domestic dogs (Alessandri et al., 2019).

According to the researches, most of the studies on respiratory microbiota have been conducted on humans. Information on the composition of the respiratory microbiota in domestic animals sharing the same environment as humans seems to be rather limited. A recently developed PCR-based algorithm called the "dysbiosis index" is a tool that veterinarians can use to measure gut dysbiosis and can be used to monitor disease progression and response to treatment (AlShawaqfeh et al., 2017).

In recent studies, Protobacteria, Tenericutes, and Actinobacteria phylum have been identified in the respiratory tract microbiota of dogs, and these data in healthy dogs have been determined to be important for understanding the role of microbial communities in infectious and non-infectious inflammatory respiratory diseases (Ericsson et al., 2016). No study has yet documented the composition of a healthy respiratory microbiota composition in cats yet (Vientós-Plotts et al., 2017). In microbiota studies in dogs, it was determined that the bacterial and fungal communities in the microbiota of animals with atopic dermatitis have been found to be less diverse than in healthy animals. Similar to humans, the different skin areas in each dog are surrounded by a diverse and unique microbiota, with significant individual differences in different dogs and different regions and higher microbial diversity in hairy areas than on mucosal surfaces (i.e. lips, nose, ear, and conjunctiva). The nostril and conjunctiva contained the lowest microbial density, whereas the axillary region and dorsal part of the nose had the highest microbial diversity. The dominant phyla on all these surfaces were Proteobacteria, Firmicutes, Actinobacteria, and Bacteroidetes (Rodrigues-Hoffmann et al., 2020).

Microbiota-diet relationship: It is well known that nutrient composition or dietary content significantly affects gastrointestinal function, microbiota composition, and bacterial metabolites in the gut (Grześkowiak et al., 2015). Some carbohydrate ingredients are not enzymatically digested in the small intestine or not be absorbed in the upper gastrointestinal tract, but are fermented by the gut microbiota and represent the main source of energy and carbon for the gut microbiota. These indigestible carbohydrates (mostly fibers) are called prebiotics and increase the activity of beneficial microorganisms in the gut microbiota. Prebiotics; consist of soybeans, inulin, unrefined wheat, raw oats, fructans, polydextrose, fructooligosaccharides, galactooligosaccharides, xylooligosaccharides, and arabinooligosaccharides (Pandey et al., 2015). Regardless of the specific bacteria, prebiotics have been reported to increase lactic acid bacteria and beneficial bacteria, and whole grain products have beneficial effects on the gut microbiota due to their high fiber content (Halmos et al., 2015).

Fava et al. (2013) studied the effects of dietary fat content on the gut microbiota and found that a low-fat diet increased bifidobacteria density, resulting in a decrease in fasting glucose and total cholesterol. On the other hand, it was found that feeding monounsaturated fatty acids had no effect on bacterial gene richness but decreased total bacterial load and LDL cholesterol.

Probiotics used as functional food: Functional foods; these are foods and food ingredients that provide additional benefits to human physiology and metabolic functions beyond meeting basic nutrient needs, thus protecting against disease and enabling healthier living. In addition, these foods are defined as foods that can be consumed in the form of food in the daily diet, do not contain synthetic compounds, and have health- and wellness-promoting properties (Erbaş, 2006). For a food to be functional, it must contain factors such as bioactive compounds, probiotic microorganisms, and prebiotic substances, and these factors must reach the right part of the body in sufficient quantities (Dayısoylu et al., 2014). Probiotics are also defined as "live microorganisms that, when ingested in sufficient quantities, improve the properties of the body's microflora and positively affect the health of the host”. For a product define as a probiotic, it must be resistant to gastric acid and bile acids, survive in the digestive tract, adhere to the intestinal epithelium, adapt to the microbiota, colonize in the digestive tract, secrete antimicrobial substances (such as bacteriocin), be nonpathogenic and toxic, and have a positive effect on host health. It must have beneficial effects and be stable and viable during production and storage (FAO/WHO, 2002).

Although many microorganisms are used as probiotics, the most commonly used group of microorganisms are the bacteria belonging to the genera *Lactobacillus* and *Bifidobacterium*.

In addition, some other bacterial species, yeast and mold species are also used for probiotic production (Uymaz, 2010; Yılmaz, 2004). The most commonly produced probiotic products are yogurt and fermented milk drinks. In recent years, probiotic cultures are added to the composition of fermented milk products in addition to the classic yogurt starters, which give the product additional physiological effects and higher nutritional value (Canbulat & Ozcan, 2015). Nowadays, different methods are used for probiotic cultures to settle in the host digestive system and become resistant to harmful factors that could prevent them from maintaining their viability. Among these methods, the selection of acid-resistant and bile-resistant strains, the use of oxygen-tight packaging, two-stage fermentation, stress adaptation, the addition of peptide- and amino acid-containing micronutrients, and microencapsulation are commonly preferred (Martín et al., 2015; Pradeep Prasanna & Charalampopoulos, 2018).

Conclusion

Studies have shown that proper manipulation of the microbiota contributes to the treatment of some diseases, and it seems that the potential therapeutic efficacy of prebiotics and probiotics (a symbiotic combination) is being elucidated day by day. The mechanisms underlying the prevention of colonization of the gut by pathogens by the gut microbiota are controversial due to the lack of detailed mechanisms and direct evidence. A better understanding of how the commensal microbiota interacts with the host is essential to determine the pathogenic and pathophysiological aspects of disease and developing more effective therapeutic agents. On the other hand, the complex structure of the microbiota, its functions, and its effects on the organism have only recently been explored and considered in veterinary medicine. Existing studies on microbiota indicate that microbiota research in veterinary medicine has an important counterpart in the fields of health and economics. Future research projects in microbiome-based disease diagnosis, prognosis monitoring, prophylaxis, and treatment have the potential to revolutionize current disease prevention and treatment measures.

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Ethical Statement

This study does not present any ethical concerns.

Conflict of Interest

The authors declared that there is no conflict of interest.

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