Role of Prebiotics and Probiotics in Improving Intestinal Microbiota for the Benefit of Human Health

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Abstract

An essential aspect of human health is nutrition. Eating a balanced diet that includes the foods necessary to maintain the intestinal microbiota in an optimal state is essential. This microbial community, made up mainly of bacteria, establishes a symbiotic relationship with the intestine. While the latter provides them with the environment and nutrients necessary for their development, the bacteria perform functions that the intestine is not capable of performing and that are essential for the correct functioning of the organism. The microbiota participates in a variety of functions, among which its important role in nutrition stands out, by contributing to the digestion of food, the absorption of nutrients, the production of amino acids and vitamins, and the recovery of energy. Likewise, it performs protective functions by preventing the invasion of pathogenic bacteria, also having an active participation in the degradation of toxins. Of the rest of its functions, its role in the stimulation of the immune system and the synthesis of neurotransmitters stands out. The imbalance of the intestinal microbiota (Dysbiosis) caused by chronic stress, poor eating habits associated with unhealthy diets, the use of antibiotics and lifestyles can have serious consequences for health.

Keywords: Microbiota, dysbiosis, eubiosis, nutrition, human health.

Cite this Article as: Palomino-Garibay MA, Durán-Lizarraga ME, Dios-Bravo MGD, Morales-Estrada AI and Hernández-Quiroz PM, 2025. Role of prebiotics and probiotics in improving intestinal microbiota for the benefit of human health. Holistic Health: xx-xx. https://doi.org/10.47278/book.HH/2025.xxx

Introduction

All processes carried out by the body depend on food intake, its processing and absorption of nutrients. That is why an essential aspect of human health is nutrition. A nutritious and balanced diet, which provides the body with the appropriate nutrients to be able to carry out daily activities, is essential for the correct functioning of the body, the fight against diseases and the maintenance of good health. In order for the body to be able to take advantage of the nutrients in food, the participation of the microbiota is essential, as it performs functions that the intestine does not have the capacity to perform. The microbiota has a fundamental role in nutrition, by promoting the production of amino acids and vitamins, as well as the absorption of nutrients during digestive processes. In addition, the microbiota performs protective functions, stimulation of the immune system and the synthesis of neurotransmitters, which together play a determining role in the state of health (Álvarez et al., 2021; Khanum et al., 2024).

Microbiota and its Functions in the Body

The gastrointestinal tract represents the main exchange surface between the internal environment of the organism and its environment. It participates in two fundamental processes: *Nutrition*, related to the intake, digestion and absorption of nutrients from the foods consumed in the diet (Mills et al., 2019). In addition, defense, actively participating in the metabolism of xenobiotics, as well as in the development of rejection mechanism of possible aggressions coming from the outside (substances, pathogenic microorganisms). In these processes, the intestinal microbiota assumes a leading role in health (Rajilić-Stojanović, 2013). In particular, for their contributions to the development of the immune system and homeostasis of the individual (Sommer & Bäckhed, 2013).

The microbiota corresponds to a community of microorganisms that occupy the digestive tract, mainly the colon, as their habitat. Made up of bacteria, viruses, fungi and archaea (Mafra et al., 2022; Ji et al., 2023). The largest proportion of the microbiota (more than 90%) corresponds to bacteria. The most diverse are Firmicutes (> 1,200 species), representing about 64% of all bacteria in the microbiota. Based on the number of species, the second ones belong to the Bacteroidetes (> 700), followed by the Proteobacteria, with a little more than 450 species (El-Mowafy et al., 2021; Palomino-Garibay et al., 2024). The most common genera of bacteria are *Lactobacillus, Bifidobacterium, Fusobacterium, Bacillus, Faecalibacterium, Bacteroides, Enterococcus, Roseburia, Eubacterium, Ruminococcus* and *Streptococcus*. Bacteriophages of the Microviridae family are the main representatives of viruses (Suárez, 2013; Scarpellini et al., 2015). In the case of fungi, they include species such as *Aspergilus* spp., *Clodosporium* spp., *Clavidospora* spp. *Cryptococcus* spp., *Cyberlindnera* spp., *Debaryomyces* spp. *Galactomyces* spp., *Malassezia restrica*, *M. globosa*, *Penicillium* spp., *Saccharomyces cerevisiae* and *Candida albicans* (Restrepo-Rivera & Cardona-Castro, 2022). Finally, methanogenic species predominate in Archaea, with a significant prevalence of *Methanobrevibacter smithii* (Mafra et al., 2022).

Throughout the digestive tract, there is a population density gradient, generally quantified by the number of bacteria present. In the esophagus, due to its position, colonization is absent; while in the small intestine the microbiota is usually scarce, both due to the acidity coming from the stomach and due to the action of bile and pancreatic fluids. In the stomach and duodenum, the microbiota has a density of 102/mL, while in the colon it is 1,012/mL (Suárez, 2013; Ain et al, 2024).

The intestinal microbiota fulfills different functions in the body:

- *Energy recovery:* Fermentative production from dietary fiber of short chain fatty acids (acetic, propionic, isobutyric, isovaleric, valeric, caproic and heptanoic acids). Important in intestinal health, due to their participation in the stimulation of blood flow in the colon, the absorption of fluids and electrolytes, as well as in the maintenance of the integrity of the intestinal tissue (Manrique & González, 2017).
- *Ion absorption:* They promote the absorption of Ca, Fe and Mg ions (Gomaa, 2020; Engevik & Engevik., 2021).
- *Amino acid extraction:* Participation in the extraction of amino acids from foods (Carding et al., 2015)
- *Vitamin synthesis:* Such as K, B_{12}, biotin, and folic and pantothenic acids (Hou et al., 2022).
- *Formation of a protective barrier:* The niches occupied by the microbiota in the intestine prevent the entry of foreign bacteria contained in the food, thanks to the secretion of bacteriocins with antimicrobial action (Mills et al., 2019; Hou et al., 2022).
- *Maturation of the epithelium:* Participates in the development and maturation of the intestinal epithelium, affecting the properties of the mucosa (Sommer & Bäckhed, 2013).
- *Cell proliferation:* They influence the maintenance of tight intracellular junctions and the proliferation of epithelial cells, which contributes to strengthening epithelial function as a physical barrier (Hou et al., 2022).
- *Regulation of the immune system:* Formation of metabolites from the anaerobic fermentation of food (exogenous) and compounds produced by microorganisms and the body (endogenous). It regulates the differentiation and activation of lymphocytes, the formation of antimicrobial peptide structures and immunoglobulin A (Sommer & Bäckhed, 2013; El-Mowafy et al., 2021).
- *Cytosine modulation:* Induction of interleukin production, maintaining intestinal homeostasis, preventing excessive inflammation. Likewise, they participate in the regulation of the immune response and intracellular communication (Jang et al., 2019; Christensen et al., 2022)
- *Enzyme contribution:* Enzymes not produced by the human body, used for the decomposition of polyphenols, polysaccharides and the synthesis of vitamins (Rowland et al., 2017).
- *Nutrient metabolism:* They metabolize non-assimilable nutrients, such as fiber (Hrncir, 2022).
- *Carbohydrate metabolism:* Processing of polysaccharides and oligosaccharides. The microbiota acts on chemical bonds on which the body's digestive enzymes could not act (Hou et al., 2022).
- *Protein metabolism:* Gastric acid suppresses the assimilation of some proteins (mainly of plant origin). The microbiota carries out their digestion when they reach the colon (Rajilić-Stojanović, 2013).
- *Xenobiotic metabolism:* Biotransformation (structural modification and activity) of xenobiotics. In Phase I, they transform external chemical substances that enter the body into polar metabolites. In Phase II they convert polar metabolites into conjugated metabolites to be excreted (Testa and Clement, 2015).
- *Action on insulin:* Modification of the body's resistance patterns to insulin and generate direct effects on its secretion (Kelly et al., 2015).
- *Synthesis of neurotransmitters*: Produces substances such as serotonin, dopamine, norepinephrine, acetylcholine and GABA (γ-aminobutyric acid), which influence mood and behavior. The production of serotonin, (responsible for peristaltic movement) produced by the microbiota at the intestinal level has its synthesis in the brain (Garza-Velazco et al., 2021).
- *Intervention in neurological functions:* Fundamental role in brain development, memory, learning and mobility (Zheng et al., 2019; Gomaa, 2020).

Eubiosis and Dysbiosis

Due to the functions it performs, there is a tendency to equate the microbiota as a true organ (Iebba et al., 2016; Merino et al., 2021). Since these functions are essential for the proper functioning of the body, the microbiota must be in optimal condition to be able to perform them. However, various factors (Figure 1) can alter the structure and composition of this community of microorganisms (Yan et al., 2022).

Eubiosis represents a condition of symbiotic balance between the microbiota in relation to the commensalism and mutualism of the organism, where the microbiota, in addition to high stability, shows resilience (Hou et al., 2022). A microbiota in this state presents a high abundance, predominantly including beneficial species that coexist with harmful microorganisms without causing alterations, and therefore, providing benefits to preserve health (Iebba et al., 2016; Álvarez et al., 2021; Suparan et al, 2022).

In contrast, *Dysbiosis* corresponds to an imbalance in this symbiotic relationship. There is a deviation from the eubiotic state, characterized by changes in both the proportions and diversity of microorganisms that make up the microbiota, as well as in the behavior of the species. Therefore, it integrates quantitative and qualitative alterations of the microbiota. Qualitatively, these originally benign pathobionts or pathogenic species have the capacity to cause certain pathologies when an alteration occurs in the conditions of the microbial ecosystem (Sebastián-Domingo & Sánchez-Sánchez, 2018; Tiffany & Bäumler, 2019).

Under these conditions, the functions performed by the microbiota in an optimal environment present alteration, giving way to the development of pathologies. The pathologies associated with dysbiosis include an important diversity of conditions, generally comprising four large groups (Figure 2) (Berg et al., 2020).

In inflammatory diseases, the continuous use of antibiotics and a poor diet are the main causes that trigger chronic inflammatory processes in the intestine. This occurs mainly due to the breakdown at specific sites of the intestinal barrier, promoting metabolites to diffuse into the circulation, which leads to the development of systemic inflammation processes (Elias-Oliveira et al., 2020). In systemic autoimmune diseases, alterations in the microbiota, such as changes in the composition of the microbiota (reduction of taxa) and population dynamics, produce imbalances between T cells (auxiliary and regulatory), which triggers different pathologies (Mousa et al., 2022). For their part, metabolic diseases due to dysbiosis occur due to the deficiency or excess of nutrients, associated with the diet. These variations generate alterations in energy homeostasis and nutrient metabolism, resulting in cellular stress. This stress, in turn, causes metabolic deregulation and tissue damage, as a preamble to these diseases (Chen et al., 2018). The pathologies associated with dysbiosis have effects on different target organs. Figure 3 shows some examples.

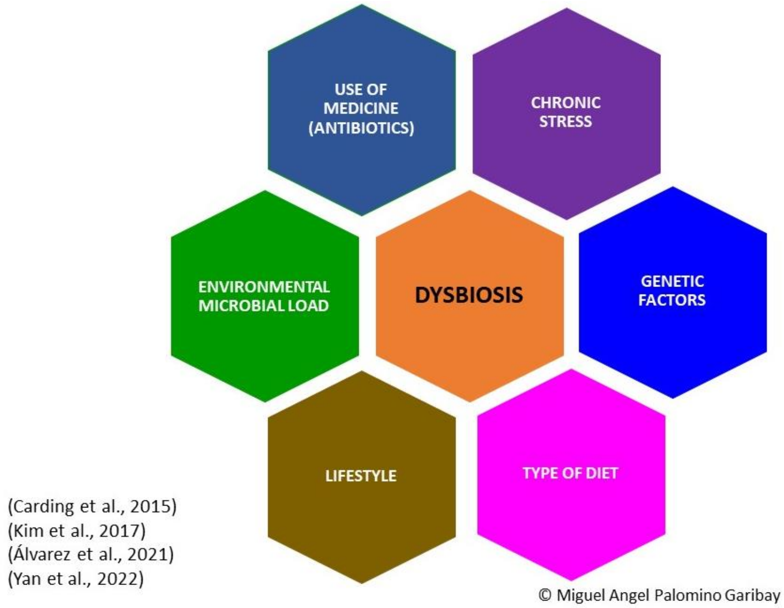

Fig. 1: Factors associated with dysbiosis. Own elaboration.

Prebiotics, Probiotics and Microbiota

The clear implications that dysbiosis has on the stability and health of the organism underline the importance of maintaining the intestinal microbiota in an optimal state. For this purpose, a balanced and nutritious diet must integrate the consumption of prebiotics and probiotics in order to strengthen the development and functioning of the communities of microorganisms that make up the intestinal microbiota (Sánchez-Tapia et al., 2019; Garza-Velazco et al., 2021).

Prebiotics are fermentable components that make up many foods. They comprise a wide variety of compounds, such as fatty acids, amino acids, β-glucans (soluble and fermentable dietary fibers), resistant starch and unrefined grains (Pizarro et al., 2014). Likewise, it includes phytochemicals such as resveratrol, carotenoids, polyphenols, isoflavones, and flavonoids (Gasaly et al., 2020). The best-known prebiotics are galactoolisaccharides (GOS), fructooligosaccharides (FOS), lactulose, oligofructose and inulin (Merenstein & Salminen, 2017; Gomaa, 2020).

Prebiotics essentially made up of short-chain carbohydrates (oligosaccharides), or long-chain carbohydrates with a complex structure (polysaccharides). A fundamental characteristic is associated with the fact that during the digestive process carried out by the body, gastric juices, bile and enzymes are not able to differentiate them, therefore the body cannot absorb or assimilate them. However, they are of special relevance due to their contributions both in the nutrition of the intestinal microbiota and in the stimulation of the growth of beneficial bacteria, such as bifidobacteria (Lockyer & Stanner, 2019).

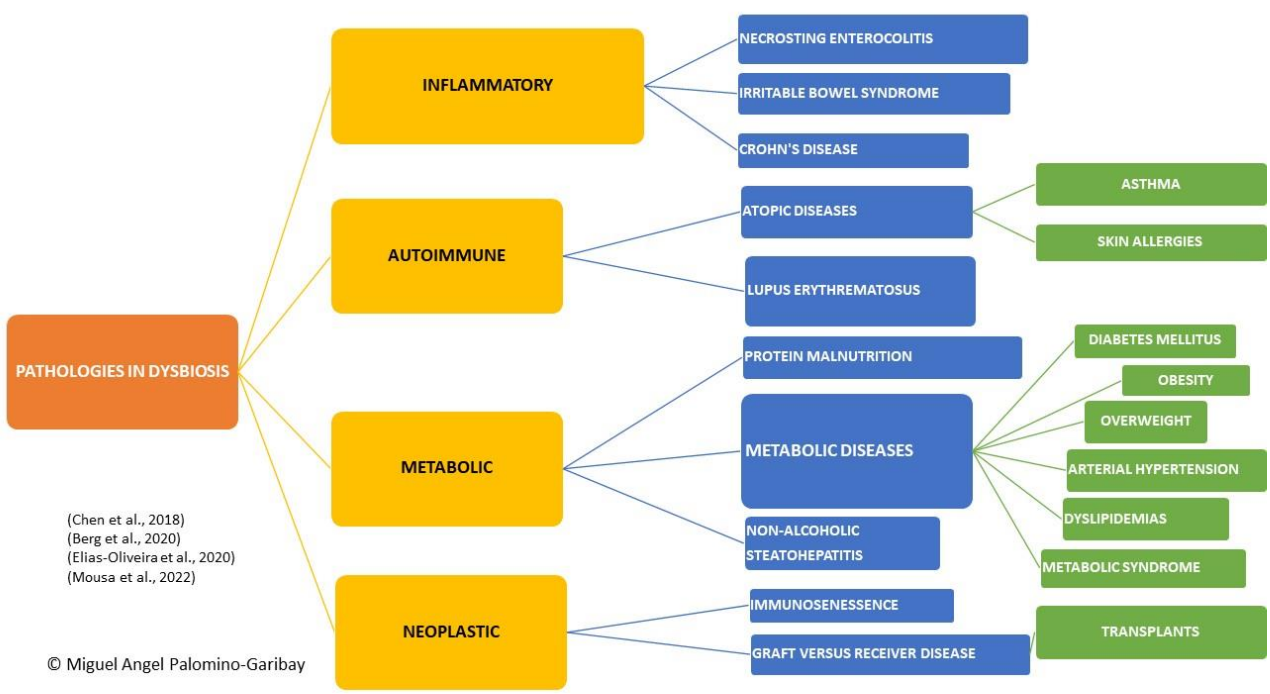

Fig. 2: Classification of conditions associated with Dysbiosis. Own elaboration

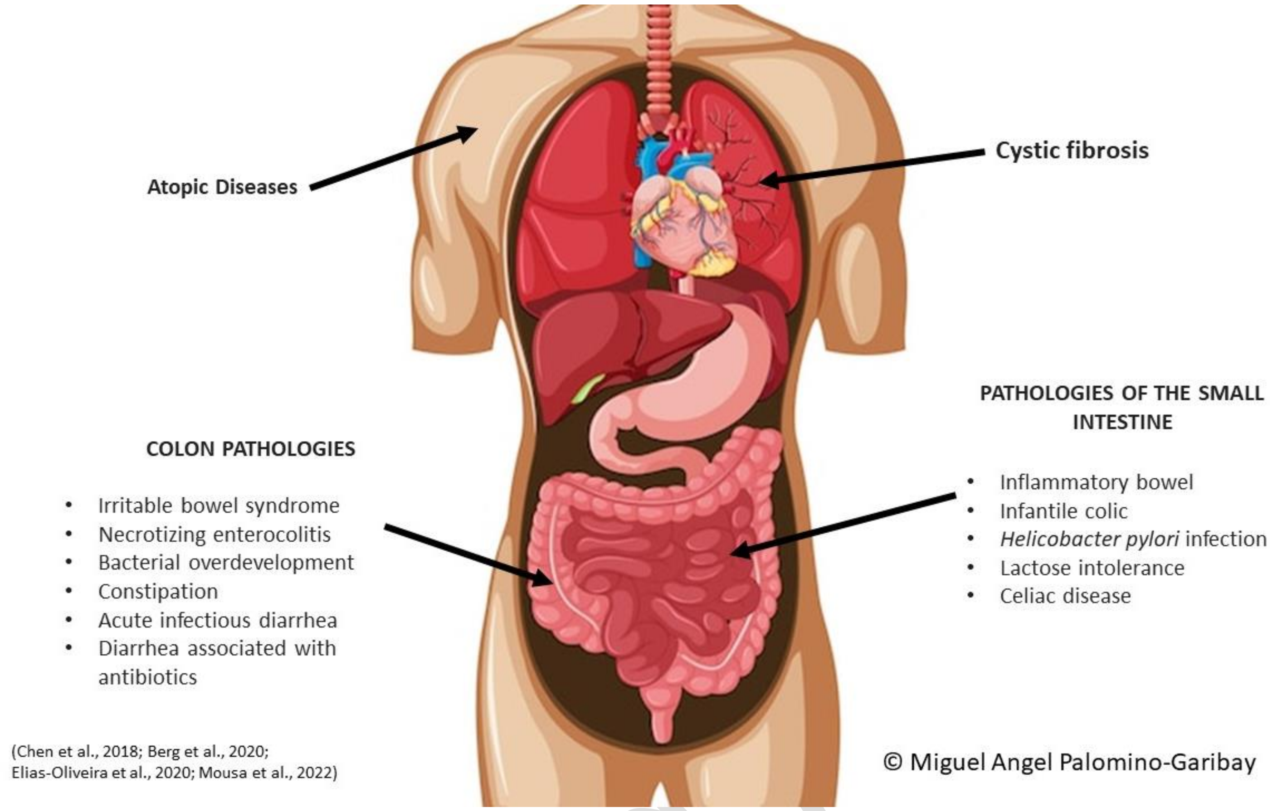

Fig. 3: Some pathologies associated with Dysbiosis. Own elaboration

During the digestive process of these components, the microbiota produces metabolites, micronutrients and energy. Subsequently, the body uses them to carry out its own metabolic processes. In this way, they carry out a process of optimization of food resources, because the food that cannot be digested and assimilated directly during human digestion serves as a food source for the microbiota and as a substrate for obtaining by products, which finally they are used by the organism (Slavin, 2013; Rastall et al., 2022). Prebiotics act selectively by stimulating the activity or growth of a certain type or quantity of microorganisms, modifying the composition of the microbiota, which results in improving the health of the organism (Markowiak & Śliżewska, 2017).

As a prebiotic, a food must meet three conditions: 1) Resistance to the action of fatty acids and hydrolysis by enzymes produced in the gastric tube. 2) Susceptibility to fermentation due to the action of the beneficial bacteria that make up the microbiota. 3) Have the ability to produce positive physiological effects on the health of the organism (Palomino-Garibay et al., 2024). Table 1 integrates some prebiotics, indicating the foods that contain them, as well as the main health benefits they provide.

Table 1: Prebiotics present in foods and their health benefits

Prebiotics	Foods	Health benefits	Reference
Amino acids	Milk, meat, fish, eggs, chickpeas, beans, whole wheat flour, corn flour, buckwheat, pistachios, lentils, tofu, legumes, nuts, soy derivatives, spinach, kale, walnuts and almonds.	• They help in the breakdown of food • Tissue repair • Reduced risk of chronic diseases • Active participation in the growth and maintenance of skin, hair and nails • Antioxidant properties associated with the role as chelating agents of some amino acids	(Matemu et al., 2021) (Lee et al., 2023)
Fatty acids	Whole grains, bananas, green leafy vegetables, onions, garlic, soybeans and artichokes.	• Acidification of colonic pH • Intestinal inflammation • Energy contribution to the body • Regulation of satiety • Control of glucose and cholesterol levels	(Vijay et al., 2020)
β-glucans (Soluble dietary fiber)	Barley, oats, algae and mushrooms.	• Effects on glycaemia • Decrease insulin levels in the blood (insulinemia) • Reduce cholesterol levels • Strengthen the immune system, preventing risks of infections • Modulation of metabolic deregulations associated with metabolic syndrome	(Pizarro et al., 2014)

Phytochemicals			
β-carotene (Carotenoid)	Papaya, carrot, spinach, broccoli, pumpkins, mango.	• Antioxidant action • Anti-cancer • Skin protector	(Castañeda, 2018)
Lycopene (Carotenoid)	Tomato, guava, red grape, melon, orange	• Anti-cancer • Antioxidant • Antifungal • Counteracts or prevents atherosclerosis (antiatherogenic effect) • Antitoxic	(Martel et al., 2020)
Daidzein (Isoflavone)	Soybeans and their derivatives such as tofu, tempech and miso.	• Reduced risk of developing osteoporosis • Therapeutic strategy for estrogen-dependent conditions (breast and prostate cancer, diabetes, cardiovascular diseases) • Reduction of oxidative damage • Regulation of the immune reaction • Induction of apoptosis in carcinogenic processes • Antihemolytic • Anti-inflammatory • Antioxidant • Anti-cancer • Antiteratogenic	(Ludueña et al., 2007) (Alshehri et al., 2021)
Genistein (Isofalvone)	Tofu, soymilk, tempeh, edamame, soybeans, green beans, red lentils and parsley leaves.	• Antioxidant • Antiangiogenic activity • Inhibition of the proliferation of cancer cells. • Induction of cellular differentiation and apoptosis of cancer cells. • Reduction of glucose uptake in cancer cell lines • Reduces menopause symptoms • Cardioprotective function	(Jaiswal et al., 2019)
Quercetin (Flavonoid type polyphenol)	Apple, tea, onion, nuts, berries, cauliflower, cabbage.	• Cardioprotective • Anti-cancer • Reduces symptoms of diabetes • Anti-inflammatory effects • Antitoxic • Prevents diseases related to obesity (type 2 diabetes mellitus, high blood pressure, hypercholesterolemia, metabolic syndrome, fatty liver, cardiovascular diseases and strokes, bone and joint problems, osteoarthritis, among others)	(Martel et al., 2020)
Routine (Flavonoid type polyphenol)	Buckwheat, citrus, black tea, nonis, apple peel, coriander, garlic, turmeric, onion, sunflower and pumpkin seeds.	• Antioxidant • Counteracts or prevents atherosclerosis (antiatherogenic effect) • Strengthens capillaries • Metal ion chelator • Reduction of venous edema • Anti-inflammatory effects	(Dingeo et al., 2020)
Coumarin	Licorice, strawberries, apricots, cherries	• Antifungicide • Anti-cancer • Thins the blood • Antithrombotic	(Castañeda, 2018)
Resveratrol (Polyphenol, stilbene type)	Grapes (mainly in the skin), blackberries and peanuts.	• Antioxidant • Anti-cancer • Beneficial for controlling diabetes • Cardioprotective • Antitoxic	(Dingeo et al., 2020)

Phenolic compounds	Coffee, pear, apple, citrus, raspberry, cherry, artichoke, strawberry, seeds, nuts and whole grains.	• Antioxidants • Anticancer • Antimutagenic • Chemoprotective effect • Antivirals • Antibacterial • Antifungals • Anti-inflammatories • Antimicrobials • Reduce the risk of atherosclerosis • Lower incidence of chronic non-communicable diseases (type 2 diabetes mellitus, cardiovascular diseases, high blood pressure, fatty liver, among others). • Reduction of oxidative stress.	(Cereceres-Aragón et al., 2019) (Liu et al., 2022)
Polyphenols	Blueberries, strawberries, plums, pomegranates, apples, grapefruits, lychees, blackberries, parsley, cilantro, spinach, broccoli, peppers, cauliflower, beets, eggplant, lentils, beans, peas, soybeans, beans, celery seeds, green tea, tea black, oregano, sage, rosemary, thyme, cocoa.	• Stimulation of key bacterial species for intestinal health (*Akkermansia muciniphila, Bacteroides thetaiotaomicrom, Faecalibacterium prausnitzii,* Bifidobacteria and Lactobacilli • Improve intestinal health • Anti-inflammatory effects • Reduce the risk of developing metabolic and inflammatory diseases • Antioxidant properties • They improve the lipid profile • Reduce the oxidation of low-density lipoproteins (LDL cholesterol) • Improve glucose homeostasis • Counteract insulin resistance • Counteract adiposity	(Tomás-Barberán et al., 2016) (Rodríguez-Daza et al., 2021) (Plamada & Vodnar, 2021)
Flavonoids	Citrus fruits, berries, apples, soy, cocoa, tea, nuts and whole grains.	• Antioxidant properties by blocking free radicals. • They reduce the risk of developing chronic diseases (cardiovascular diseases, diabetes, arthritis, obesity, chronic obstructive pulmonary disease, multiple sclerosis and cancer). • Antibacterial effects • Anti-inflammatories, improving the function of blood vessels. • Anti-allergy • Combat viral infections. • Stress modulation, reducing the probability of developing disorders such as depression. • Increased elasticity and combats sagging skin. • Reduction in the risk of developing heart disease. • Reduction of oxidative stress related to pathologies that develop in older adulthood such as Parkinson and Alzheimer.	(Estrada-Reyes et al., 2012) (Neri-Numa et al., 2020)
Phytoestrogens	Soybeans, flax seeds, wheat bran, oats, barley, rye and vegetables.	• Lower risk of suffering from symptoms associated with menopause (hot flashes and osteoporosis) • Decrease in total cholesterol. • Improvements in cardiac function. • Prevention of cardiovascular diseases. • Lower risks of suffering from metabolic diseases (obesity, metabolic syndrome and type 2 diabetes, mainly). • Reduction of developing brain disorders and cancer (breast, prostate, stomach, liver, pancreas and others). • Regulation of blood sugar levels. • Improvements in cognitive function	(Rietjens et al., 2017)
Tocopherols	Vegetable oils, nuts, green leafy vegetables and whole grains.	• Most important fat-soluble antioxidants. • Prevention of different types of cancer. • Prevention of heart diseases. • Prevention of chronic and chronic-degenerative diseases.	(Shahidi & de Camargo, 2016)

Benefits of Prebiotics for the Microbiota

Prebiotics provide multiple benefits to the microbiota, by stimulating its activity within the body (Rastall et al., 2022). They include changes in the ecology of bacteria, favoring the increase in syntrophic relationships, due to their effects on the functional modulation and structural composition of the microbiota (Rodríguez-Daza et al., 2021). These changes at a functional and structural level cause the relative abundances of beneficial bacteria to increase, while those of harmful bacteria decrease (Gasaly et al., 2020).

Likewise, prebiotics promote the absorption of minerals such as Calcium (Ca), Magnesium (Mg), Iron (Fe) and Zinc (Zn) (Lockyer & Stanner, 2019), stimulate the production of short-chain fatty acids (Slavin, 2013) and improve the barrier function and resistance of the microbiota (Li et al., 2021).

Because prebiotics produce a state of saccharolytic fermentation (biodegradability) on the bacterial populations of Bifidum and Lactobacillus, they promote the ecological niches occupied by harmful bacterial communities to decrease (Castañeda, 2018). In the control of harmful bacteria, the decrease in intestinal pH acts as a regulatory mechanism (Corzo et al., 2015).

In addition to prebiotics, both the intestinal microbiota and health can benefit from the consumption of *Probiotics*. They correspond to food supplements made with strains of living organisms that, when consumed in adequate quantities, generate benefits for the body. It is essential that these products include sufficient proportions of viable bacteria to fulfill their purpose (Al-Habsi et al., 2024). The classification of products contemplates the conditions of the organisms. True Probiotics (TP) include live, active cells. Pseudoprobiotics (PP) formulated with live but inactive cells, corresponding to spores or vegetative bodies. Ghost probiotics (GP) incorporate lysed, dead and non-viable cells (Zendeboodi et al., 2020).

Its main source comes from yeasts and bacteria (highlighting the genera *Bifidobacterium* and *Lactobacillus*) present in fermented foods, such as yogurt, brem, kimchi, gundruk among many others (Soemarie et al., 2021). They act by modulating the microbiota, keeping the proportion of harmful microorganisms under control, preventing their colonization. With this, they strengthen the immune system and the body's defense mechanisms. Its benefits aimed at intestinal health are useful for the treatment of diarrheal diseases and inflammatory processes in the intestine, especially irritable bowel syndrome. They provide protection to the digestive tract against harmful microorganisms, thanks to their active role in strengthening the intestinal barrier. The role of bifidobacteria stands out in improving digestion and intestinal function (Abatenh et al., 2018).

Conclusions

The quality of the diet is one of the main factors that contribute to diversifying the intestinal microbiota. A healthy and balanced diet rich in fruits, whole grains, lean proteins and foods rich in fiber is essential for health, due to the benefits they provide to the intestinal microbiota. The consumption of foods rich in prebiotics and probiotics is of special importance due to the important contributions they make to this community of microorganisms. Meanwhile, prebiotics stimulate the production of fatty acids that help enhance the population density of beneficial bacteria. Probiotics are adjuvants in regulating intestinal homeostasis, strengthening the immune system, counteracting the action of harmful microorganisms, as well as neuroendocrine functioning. This is why taking care of your diet goes beyond weight monitoring and control, as it directly influences the structure and composition of the intestinal microbiota. Thus, diet plays a crucial role in modulating these microorganisms. Any alteration produced to the microbiota associated with lifestyles, environmental factors and poor diet has direct effects on the homeostasis of the organism. This leads us to keep in mind that the consumption of nutrients is essential for both human health and that of the intestinal microbiota.

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