

Probiotics in treating diseases – short review

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ABSTRACT

In the last 20 years, probiotics have attracted specialists attention being conducted over 50 studies investigating the probiotics use in human diseases treatment. These studies revealed that the probiotics potential is ranging from constipation to hepatic encephalopathy. Probiotics are able to normalize the intestinal microbial ecosystem, to improve the gut barrier function, to inhibit potential pathogens and to modulate the immune and anti-inflammatory activities. Further studies need to clarify the optimal effective dosage for specific diseases, the most effective probiotic for distinctive diseases, to emphasize the interactions with food, and to determine if single-species probiotics would provide health benefits.

Keywords: probiotics, lactobacilli species, bifidobacteria species, microbiome

INTRODUCTION

During the `70s-`80s years, researchers from Yale laboratories demonstrated that there is a relationship between the intestinal bacteria and substances (foods, liquids, medicines) that entered the digestive tract. Afterwards, the specialists realized the importance of the microbiota and thus, the Human Microbiome Project was developed [1]. This project gathers data about human microbiota and the nutrients that feed these organisms. The microbiome is very dynamic and it can be changed by different amounts of prebiotics or dietary fiber. Depending on this, the ingestion of different nutrients (prebiotics, dietary fiber etc.) stimulates the growth of some beneficial bacteria. The human microbiome consists principally of diverse bacteria, but also there are present fungi, viruses, archaea and protozoans. All these species

together are known as commensal microbiota. In the human colon it can be found about 1000-1500 distinct species, specialists estimate that each person has almost 160 species [2]. Several studies established that probiotics administered in daily doses of 10⁸-10¹⁰ colony-forming units (CFU) improve the general health of humans [3].

Probiotics includes *Lactobacillus* species (*L. rhamnosus* GG, *L. reuteri*, *L. casei*, *L. paracasei*), *Bacillus* species (*B. coagulans*, *B. clausii*), *Bifidobacterium* species (*B. infantis*, *B. longum*, *B. bifidum*), *Saccharomyces* species (*S. boulardii*, *S. cerevisiae*), *Streptococcus thermophiles* and *Escherichia coli* Nissle 1917. Usually, probiotics are mixtures of several species [3].

The probiotic market has exceeded US 37.7 billion dollars in 2016, claiming over 100 distinct benefits [3,4]. On the opposite side the Food and Drug

Administration (FDA) stated: “To date, the U.S. FDA has not approved health claims for any probiotic”, proving that FDA, but also European Medicines Agency, are essentially focused and interested in probiotics safety, quality and efficacy. [5].

BENEFITS OF PROBIOTICS

Probiotics (beneficial bacteria, good bacteria) are live microorganisms involved in maintaining human health, ranging from improving nutrient absorption to preventing cancer and cardiovascular-related diseases. Thereby, probiotics are widely studied through basic and clinical research, taking into account the increasing use of nutritional supplements and pharmaceutical products.

Intestinal dysfunctions are due to disruption of the colonic flora (due to the antibiotic use, diseases, pathogens etc.), dietary antigens, ingestion of the harmful substances etc. Probiotics prevent enteropathogenic infections by several mechanisms: decreasing the luminal pH; blocking the supply of the pathogens with nutrients; producing compounds with inhibitory action [6].

Studies showed that some probiotics, like lactobacilli and bifidobacteria species, can inhibit

some enteropathogenic species based on an inhibitory mechanism [6]. Other studies revealed that probiotics act by altering the microbiome function and modulate the immune response [7]. Today it is well known that some probiotics have shown promise in prevention and treatment of diseases in which aberrant microbiota have been reported, such as: infectious diarrhoea, allergy, cancer, inflammatory bowel disease, irritable bowel syndrome [8].

The efficacy of probiotics reported by studies and meta-analysis are shown in Table 1 [3].

PROBIOTICS RISKS

Even though the health benefits of probiotics are well known, the risks are too little acquainted. One of them is that antibiotic-resistant determinants carried by probiotics can be transferred to opportunistic pathogens thus increasing resistance [9,10]. Previous *in vitro* and *in vivo* studies highlighted the transfer between probiotics or between probiotics and pathogens of genes involved in antibiotic resistance [11,12]. Also, it is certain that some probiotics (mainly *Lactobacillus*) are not stable (are degraded) in the presence of acids and bile salts [10]. In order to increase their stability, while transiting the gastrointestinal tract,

in commercial probiotic supplements with strains of *Lactobacillus* are added buffers (saccharides, proteins) which will keep the pH within a range. Moreover, for the industrial obtaining it is used encapsulation as technology in order to promote stability and survivability for this species [13-15]. Some of the probiotics side effects include gas, abdominal bloating, metabolic disorder, abnormal immune response, D-lactate encephalopathy and mental processes disorder [16-19].

TABLE 1. Probiotic reported efficacy

Crt. no.	Condition	Probiotic
1	Abdominal pain in children	Various
2	Antibiotic-associated diarrhea	Bifidobacterium
3	Blood glucose in type II diabetes mellitus	Various
4	Constipation	Lactobacillus, Bifidobacillus
5	Halitosis	Lactobacillus
6	Helicobacter pylori eradication	Various
7	Hepatic encephalopathy	Various
8	Infant colic	Lactobacillus reuteri
9	Infection risk in the critically ill	Various
10	Irritable bowel syndrome	Saccharomyces cerevisiae, Bifidobacterium infantis
11	Late-onset sepsis in preterm infants	Various
12	Prevention of C. difficile infections in hospitalized patients	Various
13	Prevention of necrotizing enterocolitis	Various
14	Prevention of radiation-associated diarrhea	Lactobacillus, Bifidobacterium bifidum
15	Small intestinal bacterial overgrowth	Various
16	Surgical site infections	Synbiotic
17	Total cholesterol and LDL-cholesterol lowering	Lactobacillus reuteri, Lactobacillus plantarum
18	Ulcerative colitis	Various

PROBIOTICS IN DISEASES

Infectious diarrhoea

Enteric and diarrhoeal disease usually has viral origin, and occurs when there is no access to safe water, to sanitary facilities and also personal hygiene is poorly. It leads to acute/chronic undernutrition, deficits in growth and cognition. Also, it causes morbidity and mortality among children.

Several studies evaluated their efficacy concluding that treatments with probiotics reduce diarrhoea duration by about one day. There were investigated strains of *Saccharomyces boulardi* and *Lactobacillus rhamnosus GG*, reported data showing that the frequency of diarrhoea episodes is reduced by 50%. Also, investigation of *Bifidobacterium infantis* and *Streptococcus thermophiles*, which were added in infant formula, proved to reduce the frequency of acute infectious diarrhoea [20]. Despite all these data, for critically ill patients there is no probiotics recommendation.

Inflammatory bowel disease

Regardless of the great expectations, no effects were recorded for probiotic treating Crohn's disease. Instead, for ulcerative colitis with mild to moderate symptoms a combination of *Lactobacillus*, *Bifidobacterium*, *Streptococcus*, *Escherichia coli* strain Nissle 1917 probiotics benefits were described. Also, studies revealed that dietary strategies are alternative treatments to enhance the human microbiome function or decrease the pathogens activities in order to provide a better healthy state in inflammatory bowel disease [21, 22].

Irritable bowel syndrome

Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder with a diversity of symptoms like abdominal pain, bloating, distension, bowel movements, diarrhoea, constipation, also anxiety, depression and other symptoms unrelated to the intestine. There are studies suggesting that patients with IBS present enteric microbiota alterations that affect normal brain functions and signaling leading to neurological disorders, the gut-brain axis being a new concept. Several meta-analyses concluded that probiotics, like lactic acid bacteria, *Bifidobacterium bifidum*, have benefits in treating IBS [23, 24, 25].

Cancer therapy

In the top three cancers is colorectal cancer one of the most common cancers globally. Age, smoking, diet, genetic mutations and other risk factors lead to colorectal cancer. The newest scientific breakthrough suggested that specific alteration in human microbial metabolism is related to colorectal cancer, but the oncogenic mechanism is not yet known. However, many scientists state that on precancerous lesions probiotics proved to have beneficial effects, potential mechanisms described in literature include enteric pH modification, colonic inflammation decrease etc. [26,27]. A Japanese study suggests that after 4 years of *Lactobacillus casei* administration the development of the colorectal tumors was prevented [28]. Other studies point out that probiotics daily intake has shown an improvement in the health status of patients with colorectal tumors treated with chemotherapy or radiation [29,30].

Allergy

It is well known that bacterial dysbiosis are closely related with allergic disorders. Even if several studies have been reported clinical improvements in atopic dermatitis when probiotics were used [31,32], nevertheless the probiotics efficacy has not been yet proved in such allergic disorders [33]. Also, no benefits were recorded on asthma and allergic rhinitis therefore recommendation of probiotics remains empirical and not based on scientific evidence.

CONCLUSIONS

Probiotics are promising supplements in order to prevent several important diseases, but further validation studies are needed. It is important to underline their clinical properties for a better acceptance by the patients.

Probiotics were found to be beneficial in infantile colic, acute infectious diarrhoea, inflammatory bowel syndrome and in reducing infections, with no severe adverse events recorded, being safer than most pharmaceuticals.

Potential risks are associated with probiotics therefore human intake of probiotics must be supervised by health professionals.

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Conflict of interest: none declared
Financial support: none declared