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Impact of Probiotics on Human Health

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Abstract: - The purpose of this review is to investigate the health benefits of probiotics, which are live bacteria that favorably affect people when consumed in enough amounts. Probiotics such as yeast, bifidobacteria, and lactic acid bacteria are commonly utilized. As mentioned in this review, these beneficial bacteria may compete with pathogens that alter the gut microbiota and have anti-obesity, anti-diabetic, anti-cancer, and immunomodulatory properties. A number of medications, including antibiotics, can now be replaced with probiotics. A period of major changes is hinted at by the growth of fields devoted to the study of the microbiome and the role that probiotics play in enhancing it. An increasing number of potential probiotic species are being discovered that can target newly identified host targets and microbial niches based on data. In order to protect human health, probiotics, symbiotics, postbiotics, microbial consortia, live biotherapeutic products, and genetically modified organisms are among the new types of microbiome-modulating interventions under development. Polyphenols, fibers, and fermented foods are also receiving more attention. The effectiveness of probiotics is also influenced by the delivery system because the agents used in the delivery aid the bacteria in surviving in the hostile environment of the human gut.

Keywords: Probiotics, Gut microbes, Anti-diabetics, Antibiotics, Lactic acid bacteria.

1. Introduction:

In 1908, Nobel Prize winner Eli Metchnikoff proposed that the long lifespan of Bulgarian peasants was due to their use of fermented milk products, which is likely when the idea of probiotics first emerged [1]. The phrase "probiotic" was initially used in 1965 by Lilly and Stillwell to refer to compounds released by one organism that promote the growth of another [2]. According to Marteau *et al*. (2002), these are "microbial preparations or components of microbial cells that have a beneficial effect on health and well-being."[3]. There are countless microorganisms on the skin, in the mouth, and in the gastrointestinal system that coexist closely with humans. The GI tract, which has a surface area of over 400 m2, has the highest concentration of commensal microbes. The gut flora is vital to human homeostasis, is acquired quickly after birth, and is largely constant throughout life. Interactions between the intestinal microbiota and the host during development lead to the development of a unique intestinal immune system. In order to distinguish between infections and benign species, the host mucosal immune system must stimulate protective immunity without inducing an excessive inflammatory response that could compromise the integrity of the GI mucosa (4). Clinical studies on probiotics will yield information on their impact on human health, and recent and continuing research in microbiome science is opening up new research avenues for probiotics. Researchers will also be able to make discoveries about consumer-oriented probiotic products, their health-promoting mechanisms, their nutritional uses, and how to acquire novel probiotics thanks to these new lines of investigation.

Cunningham *et al*. (2021)5 assert that the growth of related fields of therapies targeting the microbiome and microbiota will usher in a new era of profound improvements in human health. In recent years, probiotic use has also started to be influenced by precision medicine and personalized nutrition (nutrigenetics and nutrigenomics), with an increasing interest in modifying the microbial fingerprints of health and illness. In nutrigenomics, we study how and what we eat, specifically how the bioactive nutrients we give our bodies through food can affect our gene behavior, i.e., increase, decrease, or block gene activity. Nutrigenetics deals with the identification of individual genetic variations that can contribute to the body's unfavorable responses when we consume certain types of food.

The definition of a microbiota is a community of microorganisms, such as bacteria, fungi, viruses, and yeasts, that are present in a specific environment and reside on or within human tissues (skin, lungs, oral mucosa, urogenital tract, gastrointestinal tract), according to https://internationalprobiotics.org (6). The

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microbiome, often known as a "living ecosystem," is defined as the microbiota (and its genes) that exist in a certain habitat. A key player in the two-way information flow between the gut and the brain, known as the microbiota–gut brain axis, is the gut microbiota (7).

As of now, the most widely recognized scientific definition of probiotics is "live microorganisms which, when administered in adequate amounts, confer a health benefit on the host," which was developed in 2002 by the World Health Organization and the Food and Agriculture Organization of the United Nations (8). When the Argentinean government requested a joint FAO/WHO Expert Consultation during a global trade dispute involving powdered milk that contained lactic acid bacteria, this definition was the result (9).

2. Mechanism of action:

In order to work, probiotics don't always colonize the digestive system. Some probiotics, such as *Bifidobacterium longum*, for instance, integrate into the human gut microbiota, whereas others, such as *Lactobacillus casei*, temporarily and indirectly influence or alter the preexisting microbial community (10). Data from the literature indicates that some of the primary mechanisms of action of probiotics include the development of the epithelial barrier, enhanced adhesion to the intestinal mucosa, the production of antibacterial substances, the competitive exclusion of pathogens, the simultaneous suppression of bacterial adhesion, and immune system modulation (Fig 1) (11,12,13,14,15). Because they compete with pathogens for resources and receptor-binding sites, probiotics make it harder for them to survive in the gut 16. Additionally, probiotics have antimicrobial properties through the production of compounds such as hydrogen peroxide, organic acids, short-chain fatty acids (SCFA) (17), and bacteriocins 18 thus decreasing pathogenic bacteria in the gut. Additionally, by promoting the synthesis of mucin proteins, probiotics enhance the function of the intestinal barrier (19) regulating the expression of tight junction proteins, including occluding and claudin 1, and controlling the immune response in the gut (20,21).

Additionally, via influencing dendritic cells (DC), macrophages B, and T lymphocytes, probiotics control both the innate and adaptive immune responses. Along with interacting with intestinal epithelial cells and drawing in macrophages and mononuclear cells, probiotics also boost the production of anti-inflammatory cytokines (22).

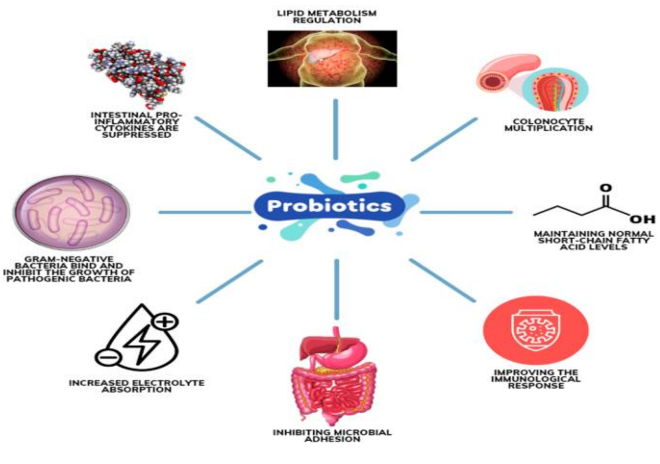

Fig 1: Action of Mechanism of Probiotics

Additionally, via means of the gut-brain axis, probiotics can generate neurotransmitters in the gut. Certain strains of probiotics have the ability to alter dopamine, gamma-aminobutyric acid (GABA), and serotonin levels, which can impact mood, behavior, gut motility, and stress-related pathways (23, 24, 25).

3. Probiotics and Human Health:

Probiotics are said to have positive impacts on intestinal health, immunological response, serum cholesterol, and cancer prevention, and there is growing evidence to support these claims. These health characteristics vary with strain and are influenced by the methods listed above. Other health advantages need further research to be demonstrated, while some are well-known. There is strong evidence that probiotics can improve lactose metabolism, reduce antibiotic-associated diarrhoea, and treat acute diarrhoeal illnesses. In some therapeutic disorders, however, there is not enough evidence to support their use. As per Grom *et al*. (2020), probiotics have been linked to the prevention and reduction of numerous illnesses, including inflammatory bowel disease, lactose intolerance, cancer, allergic diseases, diarrhoea, and irritable bowel syndrome (26).

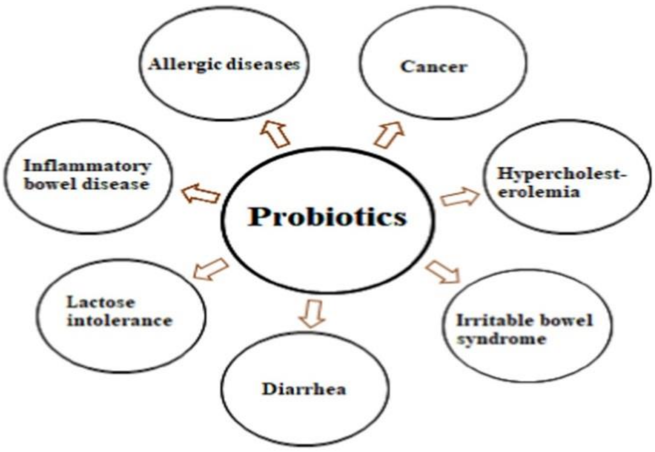

Fig 2: Health attributes of probiotics

3.1 Antiallergic effect of probiotics:

Type I hypersensitivity, the term for allergy, is an immune system hypersensitivity illness that is described as a "disease following a response by the immune system to an antigen." In North America and Europe, allergies impact about half of the population, and their prevalence is rising. Antigens or common environmental chemicals are the cause of these allergic responses (27). According to Lopez-Santamarina *et al*. (2021), the most frequent allergic reactions are hay fever, rhinitis, atopic eczema, dermatitis, urticaria, angioedema, asthma, and hypersensitivity to foods, medications, and insects (28). According to Harata *et al*. (2016) (29), gut microbiota is a promising therapeutic target for the treatment of allergic illnesses because it influences the development of sensitization and allergy by modifying the inflammatory and immunological response (30).

3.2 Probiotics and Gastrointestinal Diseases:

The literature provides strong evidence of probiotics' positive benefits on diarrhea, particularly in treating children's acute diarrhea and preventing traveler's diarrhea (31, 32, 33). The two probiotic strains that are most commonly utilized and linked to positive outcomes in diarrhoeal illnesses are *Saccharomyces boulardii* and *Lactobacillus rhamnosus* GG. But according to a Cochrane review of 82 research including both adults and children, probiotics still have a limited, if not unproven, capacity to shorten the duration of acute diarrhea (34).

There is also evidence that *S. boulardii* and *L. rhamnosus* GG lower the risk of antibiotic-associated diarrhoea (AAD). *Clostridium difficile* diarrhoea and/or AAD can be avoided with both probiotic strains (35,36,37,38).

Higher doses work best in these conditions, according to the researchers' findings. Probiotics are not very helpful in treating the symptoms of irritable bowel syndrome (IBS), which include constipation. *Bifidobacteria* and *Lactobacilli* were utilized in the majority of reported investigations. Nonetheless, probiotic use significantly decreased gastrointestinal transit, enhanced stool consistency, and increased stool frequency in a meta-analysis of 15 randomized controlled trials (RCTs) (40).

3.3 Probiotics on the urogenital infection:

The reproductive system and the urinary expansion are combined to form the urogenital system. Due to their exposure to the external environment, both systems are susceptible to diseases. While urogenital tract microbiota imbalances cause certain infections, others are acquired externally. Urinary infections are typically caused by bacteria found in the colon and its lower part, the rectum. After being inserted, they multiply in the urethra and proceed to the bladder. Eighty to eighty-five percent of all isolates are *E. coli*, and five to ten percent are *Staphylococcus saprophyticus*, the most prevalent bacteria that cause UTIs. According to Perrotta *et al*. (2008), UTIs can be caused by a variety of bacteria, including *Klebsiella*, *Proteus*, *Pseudomonas, Enterococcus*, and Enterobacter spp (41). UTIs are a result of anatomical problems in women that lead to rapid bacterial access to the bladder as a result of sexual activity, poor cleanliness, and the use of reproductive tablets. Urogenital infections have a substantial impact on bladder infection consequences, such as cystitis, urethritis, and pyelonephritis among others. According to Hanson *et al.* (2016), recent studies have examined the importance of a *Lactobacilli*-dominated, healthy microbiome in preserving women's quality of life and limiting the spread of sexually transmitted diseases and premature labor (42).

The existence, development, colonization, and persistence of non-endogenous microorganisms in the vaginal canal are all regulated by *Lactobacillus* species, an important microbial component. Recently, the development of biofilms covering urogenital cells has been associated with *lactobacilli*. Clinical research has demonstrated that *Lactobacilli* play a role in the management of bacterial vaginosis. *Lactobacilli* helped to maintain urogenital health by strengthening the immune system and adhering to the vaginal tract cells, urine, and vaginal epithelium to compete with other microbes for resources. Additionally, they produced an acidic environment by producing organic acid and several antibacterial compounds (such as hydrogen peroxide and bacteriocins), which eliminated the vaginal pathogens (43).

3.4 Probiotics on liver disease:

The intestinal lumen's gut microbiota compromises hepatocyte function. According to Javadi *et al*. (2017), changes in the gut microbiota in the gastrointestinal (GI) tract may have detrimental and severe impacts on liver dysfunction, including cirrhosis, alcoholic liver disease, non-alcoholic fatty liver disease, and hepatic encephalopathy (44). According to Javadi *et al.* (2017), a novel treatment for liver disease involves the use of probiotics to regulate, regenerate, and alter the gut microbiota (44). Probiotics also lowered the pH of feces and reduced ammonia adsorption. Through the strengthening of the intestinal barrier, probiotics help treat chronic liver disorders. There was a correlation between a lower incidence of liver illness and having a healthy, balanced gut (45). The term "gut liver axis" is used by Loguercio *et al*. to imply that the microbiota may have an impact on the liver and contribute to the development of chronic liver disease. This could occur through ethanol's modulation of chronic damage or by causing consequences like encephalopathy (which is caused by the formation of ethanol, acetaldehyde, phenols, endotoxins, benzodiazepines, and ammonia) (46).

3.5 Probiotics on Oral Health:

Probiotics have several benefits for the oral cavity, one of which is the reduction of inflammation. In order to protect teeth and gums from harmful oral microbes, probiotics can prevent these infections. Probiotics are a natural medication that should not cause any side effects. According to Lesan *et al*. (2017), *B. lactis* and *L. acidophilus* were recognized for their antifungal properties (47). According to recent studies, probiotic use may improve oral health by reducing the risk of halitosis, dental caries, periodontal infections, and oral diseases (48). By preventing the production of biofilms, the probiotic *L. fermentum* KU200060 shows anti-cavity potentiality (49).

4. Sources of Probiotics:

Probiotics are live yeasts and bacteria that may be beneficial to one's health. They are present in the human digestive tract and in certain foods and supplements. It is advantageous to have probiotic bacteria around. Though most people primarily think of the stomach and intestines when they think of them, they are present throughout the body. Probiotics can be found in fermented foods like kimchi and yogurt. A range of live microbial cultures grow and undergo metabolic activity to produce fermented meals. Numerous of these meals are abundant in live, potentially helpful microorganisms. Sourdough bread and the majority of commercial pickles are examples of fermented foods that are treated after fermentation and do not include live cultures in the form that is consumed. *Streptococcus thermophilus* and *Lactobacillus bulgaricus* are two examples of the probiotic microbes found in many commercial yogurts, another kind of fermented food.

Yogurt and many other fermented foods are made with live microorganisms that usually survive well in the product for the duration of its shelf life. However, they typically do not make it past the stomach and may not be able to withstand being broken down by bile salts and hydrolytic enzymes in the small intestine. As a result, they may not make it to the distal gut (50,51). On the other hand, healthy probiotic bacteria found in foods like yogurt do make it through intestinal transit. Miso (a fermented soybean-based paste), pickles, kimchi (a Korean fermented cabbage dish), kombucha (a fermented tea), sauerkraut (fermented cabbage), various types of cheese, and raw unfiltered apple cider vinegar made from fermented apple sugars are examples of fermented foods that contain live cultures but do not usually contain proven probiotic microorganisms (51).

5. Side Effects and Risks of Probiotics:

Fermented foods containing live microbes have been used for generations without endangering human health. As nutritional supplements, probiotics are governed as foods rather than medications (52). Most people are safe to take probiotic supplements daily, which contain a range of microorganisms in powder, tablet, or liquid form. Even though probiotics offer many advantages, some people have reported moderate adverse effects, many of which will go away when the body's microbiome settles (53). Bloating, gas, diarrhea, constipation, nausea (54,55), thirst, headaches and migraines, and skin responses are typical side effects of probiotic use (53). In most cases, mild gastrointestinal symptoms like gas and bloating go away in a few weeks (55). As their systems become used to the new balance of gut flora, some people who start taking yeast probiotics report feeling thirstier, especially during the first week. Most people experience symptoms that go away on their own (53). Histamine, tyramine, tryptamine, and phenylethylamine are among the biogenic amines found in high concentrations in some probiotic foods, particularly fermented foods like kimchi and sauerkraut. These substances can cause headaches and migraines in certain individuals. Additionally, certain yogurts included biogenic amines, albeit to a considerably lesser extent (53). Rarely, rashes or itchy skin might be brought on by probiotics. The reason for this could be an adverse reaction to one of the supplement's ingredients. Usually, it will go away quickly once the person stops using the additive (53). Because probiotics are live organisms, they carry the danger of causing infections that require antibiotic treatment in addition to negative effects, particularly in individuals with underlying medical disorders. Many of the probiotic strains are genetically altered in the lab to reap their health benefits. In order to prevent them from building up in the environment, having antibiotic selection markers, or passing on any damaging genetic information to other bacteria, the safety of each strain must be ensured and closely monitored (52).

6. Conclusion:

There is currently substantial data supporting the significance of the microbiome and microbiota in both acute and chronic human health, with the caveat that the impact of our microbes extends beyond the gut to include the brain, metabolism, and immune system. The microbiome's variety and composition are influenced by aging and genetics, but other controllable factors—like nutrition, exercise, exposure to exogenous bacteria, and antibiotic use—may be more crucial for reaching microbiota eubiosis. This presents an opportunity for individuals to embrace customized lifestyles, but it also presents a number of obstacles, such as obtaining sufficient data to determine which microbiota interventions are suitable for which demographics, comprehending the mechanisms underlying these processes, and creating novel, efficacious probiotic products. According to a review of the research, probiotics or fermented foods or supplements that contain probiotics in their matrix present a tantalizing chance to discover ways to coexist peacefully with our microbiome, which could have significant health benefits. The components that offer an efficient method for preventing or treating a variety of illnesses are probiotics. However, information about the best matrix and the ideal dosage for each strain should be gathered for future studies. Future research should also ascertain whether probiotic strains—whether they are ancient or modern—colonize our intestines or if they are merely fleeting microbes with positive effects.

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