Journal of Applied and Natural Science
15(2), 692 - 703 (2023)
ISSN : 0974-9411 (Print), 2231-5209 (Online)
journals.ansfoundation.org

Review Article

Gut microbiota and chronic diseases: Role of probiotics

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Article Info
https://doi.org/10.31018/jans.v15i2.4540
Received: March 3, 2023
Revised: May 22, 2023
Accepted: May 27, 2023

How to Cite
Bora, G. *et al.* (2023). Gut microbiota and chronic diseases: Role of probiotics. *Journal of Applied and Natural Science*, 15(2), 692 - 703. https://doi.org/10.31018/jans.v15i2.4540

Abstract
Probiotics are live organisms that generally give consumers health advantages by improving or restoring the gut flora. *Lactobacillus* and *Bifidobacterium* are the two most commonly known probiotics. They have vital role in the prevention and/or diagnosis of many diseases, such as obesity, cancer, asthma, diarrhoea, hay fever, diabetes, chronic fever, HIV, and atopic eczema. They also help to maintain the gut microflora of the intestine. Gut microbiota reside in the gastrointestinal tract of humans, which can be bacteria, fungi, viruses, or protozoa and bacteriophages, which are essential for maintaining healthy gut health. The most dominant gut microbial phyla consist of firmicutes, actinobacteria, proteobacteria, bacteroidetes, and fusobacteria. In 90% of the gut microbiata belongs to the two important phyla-firmicutes and bacteroidetes. Examples include *Lactobacillus acidophilus, Clostridium perfringens, Helicobacter pylori, Bacteroides fragilis, and Corynebacterium matruchotii.* This review paper focuses on the role of probiotic microorganisms in preventing certain chronic diseases. The role of gut microbiota in maintaining human health is very crucial. They are known to maintain the host's homeostasis by providing protection against pathogens, training the immune system, better processing dietary compounds, and assisting proper nutrient uptake.

Keywords: Actinobacteria, Bacteroides, Good health, Well-being, Gut microbiota

INTRODUCTION

Probiotics are organisms which are live when provided in sufficient amounts provide health benefits to host (Khan *et al*., 2021; Syiemlieh and Morya, 2022). The term “probiotic” is a Greek term which suggests “for life”. In 1954, Ferdin and Vergin formed the word “probiotic” in a review paper named “Anti-und Probiotika,” in which many organisms were studied to develop a record of helpful bacteria and to work out the damaging outcomes of antibacterial agents and antibiotics on the microbiota of the intestine. Some of the commonly used probiotic strains are those included in the group of Lactic acid bacteria (LAB) and bifidobacteria (Syiemlieh and Morya, 2022). LAB include *Streptococcus, Staphylococcus, Lactococcus, Pediococcus, Lactobacillus, Entercoccus, Leuconostoc* (Azad *et al.,* 2018). During metabolic processes, LAB produce lactic acid as a by-product. Due to the distinct nutritional properties of LAB it can easily thrive in various environmental conditions ranging from dairy-based products to the human gut. Daily consumption of probiotics and lactic acid fermented foods are great immune booster due to their therapeutic properties (Ayivi *et al.,* 2020)

The gut microbiome affects human health through the gut defensive system barrier, immunological response, food absorption, and perhaps through direct signalling with the gastric epithelium (Kumar and Morya, 2022). There are certain criteria's to be considered for a probiotic organism. It should provide advantageous effects to consumers, be regarded as safe and non-pathogenic, non-toxic, and non-carcinogenic, multiply and colonize in the gut; and have a minimum concentration of 10^6 CFU/ml should be there for more effective results (Morya *et al.,* 2017a). They play a major role in healthy intestinal microbiota, thus providing a beneficial environment for the intestine. Along with vitamins, minerals, and other food supplements, probiotics are also considered an alternative and complementary medicine (Salgaço *et al.,* 2019). Probiotics are found to be very beneficial when it comes to the prevalence of food allergies to alleviate food allergies, probiotics and their metabolites interact with immune cells and gut microbiota (Gu *et al*., 2023). According to International Scientific Association for Probiotics and Prebiotics (ISAPP) defines 'probiotic are living organisms when administered with efficient dose can be benefitted to consumer or host' (Sanders *et al.,* 2018). Probiotics are food preservatives that have multiple positive effects on the host's health, naturally present in vegetable foods or synthetically prepared by enzymatic conversion of sugars. Commonly used prebiotics consist of galactooligosaccarides (GOS) and derivatives of inulin. This favours the *Lactobacillus* and *Bifidobacterium* strains, which is beneficial due to the capacity to intimate its binding sites and prevent adhesion to epithelial cells (Ballini *et al.,* 2023).

Making a fermented product using probiotics helps to increase the nutritive value and health benefits to the consumer. Choosing the particular probiotic strain is important as it determines the unique end product texture and flavor (Morya *et al.,* 2017b). Recent animal studies have shown that probiotics have a positive result on Covid-19 and they act by preventing the infection of the epithelial cells. But, still, more studies and researches need to be done to know its effect on humans. Other than providing increased consumer immunity, probiotics also prevent cardiovascular disease (CVD) and have antimicrobial effects (Khan *et al.,* 2021).

ROLE OF PROBIOTICS IN DISEASE CONTROL

Probiotics could enhance our well-being or manage disease-causing infections and facilitate real disease treatment and control. Probiotics and synbiotics have a major art in preventing many severe ailments because of their involvement in the modulation of the immune system and anti-inflammatory response (Plaza-Díaz *et al.,* 2017). These can be used to treat obesity, and it has been shown in a study that probiotics, when used alone or in synbiotic mixtures, through strain-specific or species-specific mechanisms like modulation of gut microbiota, lower insulin resistance, etc. can make use of their anti-obesity effects (Abenavoli *et al.,* 2019). These are useful in the prevention of AAD (Antibiotic-Associated Diarrhea) in all age groups, which can be reduced up to 51% with the help of probiotics. Due to various possible immunomodulatory mechanisms of the intestinal microbiota, probiotics have a huge role in preventing colorectal cancer (Kim *et al., 2019*). Table 1 highlights the different probiotic microbes and related preventive diseases.

MODE OF ACTION

Probiotics may enhance the gastrointestinal tract health by controlling the bacteria and provoking and developing the immunity, production, and increase in the availability of nutritive product. They may prevent the symptoms of hypolactasia and also prevent the complication of various diseases (Collado et al., 2009). Probiotics interact with the body's beneficial commensal microorganisms and encourage their growth while preventing the growth of pathogens ((Morya et al., 2022). In rare cases, they also speed up the host's antigenic response time, increasing the production of antimicrobial substances and possibly blocking the pathogen's potential binding site.

Moreover, probiotics cling to the human body and colonies it. Probiotics can prevent the dangerous germs continual growth. The production of glutamine by Bifidobacterium enhances the mucosal barrier's defences and maintains the integrity of the mucosa (Bodke and Jogdand, 2022). The major mode of actions of Probiotics include – The epithelial barrier enhancement, by increasing adhesion to intestinal mucosa, concomitant inhibition of adhesion of pathogens, producing various anti-microorganism substances and modulation of the immune system of humans. There are different known mechanisms of action of probiotics in diseases.

Host-probiotic interaction mechanism involved

Certain studies using laboratory models of animals and clinical interventions have shown the ability of probiotics on human well-being, especially in controlling and curing many diseases. The top four mechanisms of action of probiotic organisms are the involvement of probiotics with disease-causing organisms by competition with nutrients and adhesion sites: Modifying barrier activity of the epithelial cells, the modulation of the immune system (immunomodulation), through immune system and neurotransmitter production influencing the other body organs (Fig. 1.) (Sánchez *et al.,* 2017).

Probiotics' interactions with pathogens can be divided into three categories: their direct interactions with bac-

Table 1. Some of the important probiotic organisms, and their prevention of diseases

Organism	Characteristics	Disease	Reference
Genus Lactobacillus			
L. plantarum *L. johnsonii* *L. acidophilus* *L. sakei* *L. bulgaricus* *L. salivarius* *L. casei* *L. paracasei* *L. rhamnosus* *L. delbrueckii* subsp. *bulgaricus* *L. brevis* *L. fermentum*	Gram-positive, non-motile (some motile), non-spore forming, facultative and obligate anaerobes	Antibiotic-associated diarrhoea, traveller's dysentery, viral-associated pulmonary damage	Zheng *et al.*, 2020
Genus Bifidobacterium			
B. infantis *B. adolescentis* *B. animalis subsp. animalis* *B. animalis subsp. Lactis* *B. bifidum* *B. longum* *B. breve*	Gram-positive, non-motile, spore-forming, anaerobes	Dyschezia, traveller's dysentery, antibiotic-associated diarrhoea, IBD, colitis gravis	Alessandri *et al.*, 2021
Genus Saccharomyces			
S. cerevisiae *S. bayanus* *S. boulardii*	Round, oval, or cylindrical, pseudohyphae, diploid, anaerobic or semi-anaerobic fermentation	Diarrhoea	Fijan, 2014
Genus Lactococcus			
L. lactis subsp. *Lactis*	Gram-positive, non-motile, non-sporing, facultative anaerobes	Mastitis	Rodrigues *et al.,* 2016
Genus Streptococcus			
S. pyogenes *S. pneumoniae* *S. thermophiles*	Gram-positive, non-motile, non-sporing, facultative and obligate anaerobes	Antibiotic-associated diarrhoea	Tagg *et al.,* 2011
Genus Enterococcus			
E. faecium *E. durans*	Gram-positive, non-motile, non-sporing, facultative anaerobes	Antibiotic-associated diarrhoea	Bin-Asif and Ali, 2019
Genus Bacillus			
B. subtilis *B. coagulans* *B. cereus*	Gram-positive, motile (except *B. anthracis*), spore-forming, aerobes	Antibiotic-associated diarrhoea, H. pylori eradication in humans	Zeigler and Perkins, 2015
Genus Escherichia			
E. coli Nissle 1917	Gram negative, motile, non-sporing, facultative anaerobes	Dyschezia, atopic dermatitis, IBD, gastroenteritis, enterocolitis, chron's enteritis, colorectal cancer	Welch., 2006

teria, their interactions with the immune system, and their indirect interactions with other bacteria. Probiotics may interact with infections in many ways, either directly or indirectly, but their ingestion may have positive health effects (Khaneghah *et al*., 2020). Figure 1 highlights the mechanism of action of probiotic organisms.

TYPES OF CHRONIC DISEASES AND THEIR RELATIONSHIP WITH PROBIOTICS

Diabetes and obesity

Diabetes is a severe disorder caused by the low production of insulin or the inability of the pancreas to produce insulin. Diabetes or diabetes mellitus and can be acquired or inherited. It causes about 420 million people worldwide and may increase in the future. Mainly three forms of diabetes, namely: type I, type II, and gestational diabetes, are seen (Salgaço *et al.,* 2019). Probiotics provide certain advantageous results to insulin resistance patients via related and unrelated inflammation by modulating the microbiota of the intestine (Homayouni-Rad *et al.,* 2017). *Bifidobacterium* and *Lactobacillus* provide a major health benefit in maintaining a healthy intestine and immune system. Certain studies have shown the part of probiotics and gut microbiota in Type II Diabetes Mellitus (T2DM) therapy. A

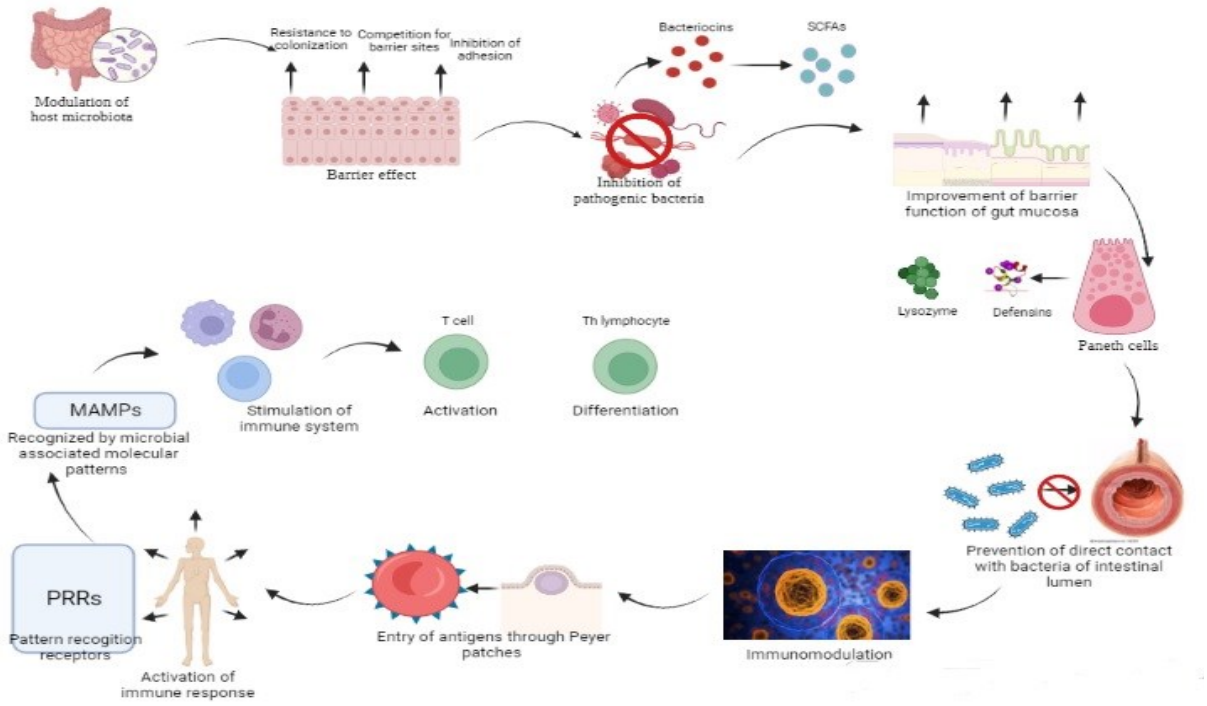

Fig. 1. *Mechanism of action of probiotic organisms*

decrease in lipopolysaccharide levels, reduction in endoplasmic reticulum stress, and increased intestinal integrity area result from probiotic intake (Salgaço *et al.,* 2019). Incase of type 2 diabetes, gut microbes are different as compared to healthy population, here the number of *Bacteroides* and *Proteobacteria* is higher and the amount of *Firmicutes* Bacteria is lower in the gastrointestinal tract of a person undergoing type-2 diabetes (Kocsis *et al.,* 2020).Certain studies have shown that Probiotic have aglucose–lowering effect in Type-II diabetic patients and this effect appears more in those individuals who poorly controls diabetes and those who do not undergo insulin therapy (Rittiphairoj *et al.,* 2021).

Obesity is a disease which is caused due to excess intake of food, which leads to the deposition of fat, thereby affecting health. About 2-7% of people are affected by obesity in developed countries (Kopelman, 2000). Obesity has come up as an epidemic that constitutes an unrivalled public health challenge. It is linked with damaged body function and is mainly caused by certain environmental factors (Upadhyay *et al.,* 2018). By three main mechanisms of action (antimicrobial activity, barrier function, and immunomodulation) probiotics take part in obesity treatment, thereby modulating the gut microbiota and metabolism of the host. Some studies have shown that administering *Lactobacillus rhamnosus* to a pregnant lady one month before delivery and continuing the treatment six months after delivery helped reduce weight gain (Abenavoli *et al.,* 2019). The gut flora influences the absorption, storage, and use of energy from dietary intake. Recent animal research has also demonstrated that gut microbiome regulates food intake by influencing metabolic function hormones. This so-called “gut microbiota-brain axis” is a bidirectional signaling axis that balances hunger, energy storage, and energy expenditure to control body weight (Cerdó *et al.,* 2019).

Heart disease

Congenital heart disease (CHD) is an important reason for mortality, disease condition, and the risk factor in infants for necrotizing enterocolitis. In a specific study, the administration of probiotic strains showed an improvement in the fecal microbiota of neonates, maintained the intestinal microbiota, and reduced abnormalities caused by *Enterobacteriaceae* (Tarhani and Nezami, 2019). Cardiovascular disease (CVD) is another heart disease which is a common health issue worldwide. It is the major cause of mortality. Gut microbiota is an important factor for controlling disease and regulating the number of disease-causing organisms. Supplementation with probiotics leads to the lowering of the risk of CVD. It causes a change in the gut microbiota (Antony and de-Leon, 2018).

A major source of reactive oxygen species (ROS) is the NADPH oxidase (NOX) complex. This NOX helps to provide defense for the host and also helps to regulate gene expression. A study have shown that the intake of probiotic strains like *Lactobacillus fermentum* CECT5716, *Lactobacillus coryniformis* CECT5711, and *Lactobacillus gasseri* CECT5714 reduced the NOX complex and mRNA expression in hypertensive rats (Oniszczuk *et al.,*2021). Supplementation of *Lactobacil-*

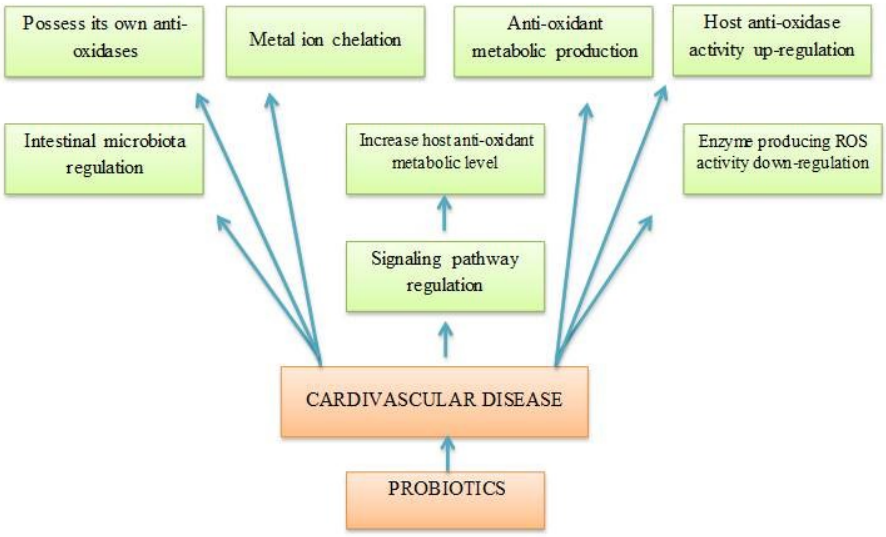

Fig. 2. *Role of probiotics in the modulation of anti-oxidation*

lus casei reduced the systolic pressure, *Lactobacillus reuteri* reduced LDL, total and non-HDL cholesterol, *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, and *Bifidobacterium bifidum* showed a gradual decrease in blood glucose level by 38% (Antony and de-Leon, 2018). Figure 2 shows the role of probiotics in the modulation of anti-oxidation.

Cancer

Nowadays, one of the most important causes of mortality is the increased risk of cancer. It is mainly dependent on immunity and genetic factors. Currently, probiotics is gaining more importance because it modulates the proliferation and apoptosis of cancer cells (Górska *et al.,* 2019). Probiotics work to improve intestinal microbiota structure, intestinal microbiota metabolic activity, short-chain fatty acid and conjugated linoleic acid synthesis, cancer cell apoptosis induction, influence of mutagenic and carcinogenic factors, carcinogenic compound degradation and binding, immunomodulation, and intestinal barrier function (Śliżewska *et al.,* 2020).

Certain studies showed that giving live *Lactobacillus casei* ATCC393 provided growth-inhibitory, anti-proliferative, and pro-apoptotic effects. Anti-proliferative effects were shown by eight different strains of *Lactobacillus* in leukemia patients. Also, when strains of *Bifidobacterium,* when provided alone or with immunotherapy shown to have effects in controlling melanoma (So *et al.,* 2017).

Human immuno deficiency virus (HIV)

HIV is a type of virus which results in Acquired Immuno Deficiency Syndrome (AIDS). It is a condition that results in low immunity leading to other chronic infectious diseases. Usually, HIV is caused by unprotected sex, through used syringes, blood, mother to baby etc. (Kapila *et al.,* 2016). Proper nutrition management and related nutrition problems in newborns and children with higher nutritional needs a significant challenge. The intricate relationship between HIV infection, diet, and the immune system is supported by a number of research. In recent studies, probiotics are being used as a novel strategy to treat microbiome imbalance and gut mucosal damage in HIV infection. By lowering immune activation, this innovative approach may be able to manage dysbiosis and gut-mucosal dysfunction in children with HIV, potentially preventing negative health effects (Fabusoro and Mejia, 2021). The anti-inflammatory process in HIV inflammation is shown in fig 3.

In healthy and HIV infected patients, the administration of probiotics is known to be safe. A study conducted by Dizzell et al. (2019) showed *Lactobacillus rhamnosus* (GR-1) and *Lactobacillus 0reuteri* (RC-14) when given to HIV patients promoted the barrier function of epithelial cells of genital area. Also a pre-treatment with estrogen prevented the leakage of TNF-α production and when combined with *Lactobacilli*, it prevented HIV-mediated epithelial barrier disruption (Dizzell *et al.,* 2019).

Chronic liver diseases

The liver is the main centre for several physiological processes like the assimilation of macronutrients, controlling blood volume, aiding the immune system, endocrine regulation of growth signalling pathways, lipid and cholesterol homeostasis, and disintegration of xenobiotic compounds. The liver comprises hepatocytes, stellate cells, Kupffer cells, cholangiocytes, and liver sinusoidal endothelial cells (Trefts *et al.,* 2017).

1) Nonalcoholic fatty liver disease (NAFLD)

NAFLD encloses a wide spectrum of chronic hepatic states varying from simple steatosis to NASH, which

can lead to hepatic cirrhosis and liver cancer. NAFLD is widely seen in Western countries, affecting about 20-40% of the population, mainly due to type 2 diabetes and obesity (Meroni *et al.,* 2019).

The mode of action of probiotics on NAFLD is as follows a) modulation of gut microbiota structure so as to approach in healthy directions; b) gut microbiota metabolite modulation; c) lipid assimilation modulation; d) modulation of unrelated gene expression related to lipogenesis; e) improvement of intestinal tight junction, and; f) reduces the inflammatory action that associates with NAFLD (Elshaghabee, 2017).

Supplementation of probiotics reduces the risk of NAFLD. Certain *in vivo* studies showed that when *Lactobacillus plantarum* NCU116 was given to rats with NAFLD, it reduced the accumulation of fat and liver function was improved when given for 5 weeks. Another study showed that supplementation of a combination of *Lactobacillus rhamnosus* GG (LGG) and *Lactobacillus plantarum* in rats helped lower total cholesterol, fat accumulation in liver, free fatty acids, and serum levels of TG (Yao *et al.,* 2021). A study conducted by Kulvinder and team showed that there was an improvement in the sensitivity of insulin, amount of total fatty acids, and amount of ALT (serum alanine aminotransferase) when a mixture of *S. thermophilus*, and species of *Bifidobacterium* and *Lactobacillus* was given to $Lep^{0b/ob}$ mice for 4 weeks (Kaur *et al.,* 2020). Probiotics' therapeutic effects in NAFLD patients have been the subject of numerous clinical trials. BMI and alanine transaminase (ALT), TNF-, and antipeptidoglycan-polysaccharide antibodies were significantly reduced when LGG was given to obese children with NAFLD for eight weeks. In a concentrate in which L. acidophilus was directed multiple times daily to grown-up NAFLD patients for multi-month, aminotransferase (AST) and ALT were essentially diminished. This demonstrated that the patient's liver's inflammatory condition was helped by lactobacillus. Body mass index (BMI), waist circumference, and liver inflammation were reduced and improved in a three-month study involving NASH patients treated with L. reuteri and inulin. According to the findings, Lactobacillus could be a promising treatment option for NAFLD (Jeong *et al.,* 2022).

2) Hepatocellular carcinoma (HCC)

HCC, also known as liver cancer, is one of the leading causes of cancer worldwide and contributes to over

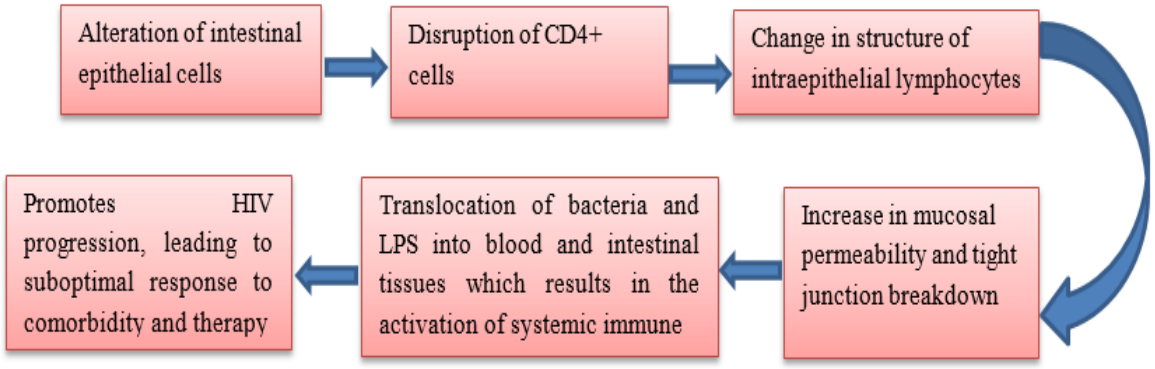

Fig. 3. *Anti-inflammatory process in HIV*

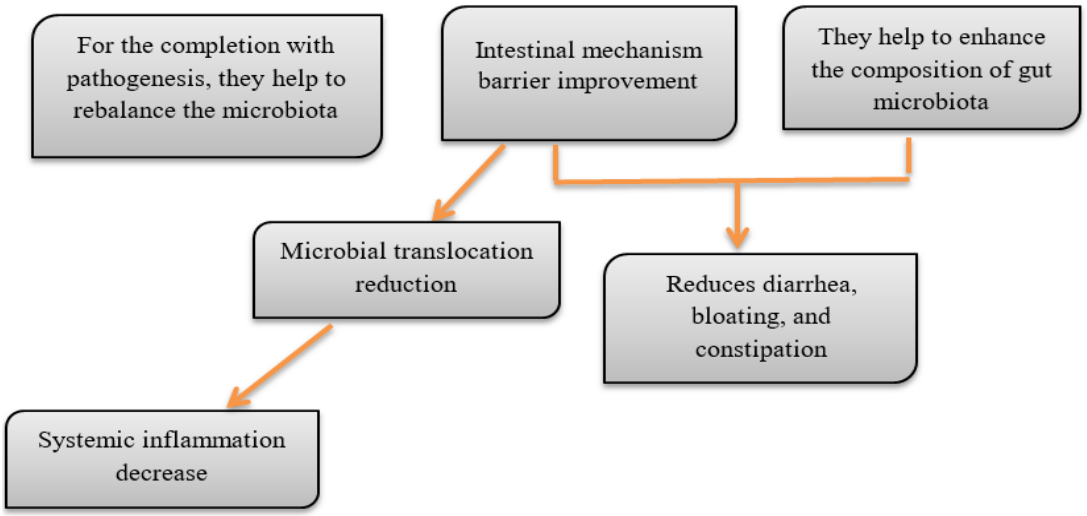

Fig. 4. *Beneficial effects of probiotics on HIV*

70,000 deaths yearly. HCC occurs due to severe regeneration and inflammatory processes (Wan and El-Nezami, 2018).

In vivo and *in vitro* mechanisms can attenuate HCC pathogenesis by probiotic organisms. Gut microbiota releases anti-inflammatory metabolites with tumour-repressing action, which is favoured by probiotics. Probiotics also help in the growth of gut microbiota. Diabetes-induced DNA damage can be prevented by administering *L. paraplanatarum* in albino Wistar rats. It also reduces liver inflammation and fibrogenesis (Thilakarathna *et al.,* 2021).

Allergic diseases

Over the past few years, allergic diseases like respiratory, cutaneous, and food allergy have increased greatly. Some studies pointed out that gut microbiota is the reason for this, which is caused by several environmental and dietary factors. Changes in the structure and functioning of the gut microbiome are related to immune dysfunction in asthma and atopy. In case of skin, the microbiota of the skin depends on body site samples. Lung was considered to be sterile, but some evidence has shown that the lung has been harbouring certain organisms like Acinetobacter, Bacteroidetes, Firmicutes, and Proteobacteria. Allergic sanitization and inflammation were protected by *Acinetobacter* species (Pascal *et al.,* 2018).

1) Asthma

Asthma is a Th-2-type of inflammatory state (Niu et al., 2021). It is shown by severe airway inflammation within and associated with eosinophils, mast cells,and activated The lymphocytes (Hamid and Tulic, 2009). Asthma can be allergic, non-allergic, nocturnal occupational, and asthma during pregnancy (Gupta *et al.,* 2017).

In consonance with our recent perception of immune mechanism, the immune system needs systematized environmental pressure to advance accordingly. Probiotics release two important substances: T-cell lineages that balance the dominance of the pro-allergic Th2-directed immune response and Th-1 cells and the Th3/ T regulatory-1 cells (Ruszczyński and Feleszko, 2016).

A study showed *L. reuteri* could improve Interlukin-10 and lower inflammation, resulting in low symptoms. It also reduced inflammation of the bronchi. On the other hand, *L.acidophilus* CUL60, CUL21, *B. bifidum* CUL20, *B. animalis* CUL34 did not have any effect (Eslami *et al.,* 2020).

Nonpathogenic bacteria called probiotics have been extensively employed in premedical research to treat asthma. Different probiotic strains can change the production of cytokines in the stomach and associated lymphoid organs. Lactic acid bacteria improve T helper 1 (Th1) immune response, suppress T helper 2 (Th2) immune response, and lessen allergic response in mice that have ovalbumin (OVA)-induced allergic symptoms. (Yang *et al.,*2022)

2) Allergic Rhinitis (Hay Fever)

It is a disease linked to pink eye (conjunctivitis) and asthma. It is the nasal mucosa inflammation. Hay Fever is the most typical form of severe rhinitis, causing 10%-20% of the population (Small et al., 2018). Manifestations like nasal cavity congestion, sneezing, itching, etc., can occur (Schuler IV and Montejo, 2021). Manifestations will negatively impact the patients' quality of life, typically hinder sleep, and lead to poor performance at work and school (Hoyte and Nelson, 2018). Some of the causative agents of allergic rhinitis are airborne pollen, dust, mites, animals, etc.

A study revealed that administering *L. casei* to children suffering from allergic rhinitis reduced its episodes when it was tested in 64 pre-school children (Tang *et al.,* 2015). A reduction in the symptoms of allergic rhinitis was seen in 212 children of age less than 5 from Pakistan. There was given a combination of *L. paracasei* for 6 weeks and Cetirizine tablet once daily (Meirlaen *et al.,* 2021).

Probiotics may slow the inflammatory cascade by encouraging the creation of anti-inflammatory mediators, such as short-chain fatty acids (mostly 3) that lower cellular infiltration. The function of allergen-specific Tregs may also be restored by probiotics, which would enhance the production of regulatory cytokines including IL-10 and TGF-. There is proof that probiotics may help allergic people by resetting their immune systems and boosting their mucosal defences against infections. However, more methodologically sound research is required to confirm these probiotics' potential impacts (Ciprandi and Tosca, 2022).

Atopic dermatitis (Atopic eczema)

It is a frequent, severe, and worsening inflammatory disorder of the skin with a rising prevalence throughout the past few years, particularly in developed countries. It has become a worldwide health problem because it affects high health-care prices globally and is related to significant morbidity and quality of life and damage, disease burden similar to other severe diseases like seizure disorders, diabetes, and, fibrocystic disease of pancreas (Torres *et al.,* 2019).

A study showed that those at high risk of getting atopic dermatitis (pregnant women, infants, breastfeeding mothers) can be reduced in the early stage by giving probiotic strains of *Lactobacillus* GG (Sestito *et al.,* 2020). An early study showed that the symptoms of eczema in children and infants could be reduced by supplementing *B. lactis* Bb12, *L. rhamnosus* GG, or B. breve M-16V strain (Eslami *et al.,* 2020).

Food allergy

Food allergy is an immune reaction activated by the protein antigens in food. It is a pathological and deadly disease. They are a type of hypersensitivity reaction and can be classified as IgE, non-IgE mediated and mixed food allergies (Yu *et al.,* 2016). Foods like cow milk, egg, peanut, soy, and wheat cause allergic reactions in children. For adults, it may be tree nuts, peanuts, shellfish, and includes fish. Some patients may show signs after ingesting culprit food followed within a few hours by exertion or exercise. It leads to food-dependent, exercise-induced anaphylaxis (Iweala *et al.,* 2018). A study showed that administering *Lactobacillus* and *Bifidobacterium* may help modulate allergic sensitisation to foods when given to pregnant women and infants daily. But it cannot be said that it can fully prevent food allergies (Sestito *et al.,* 2020).

GUT MICROBIOTA AND PROBIOTICS

Gut microbiota (GM)

"Microbiome" refers to a group of microorganisms that inhabit on or inside other organisms. They can be beneficial or pathogenic depending on their interaction with each other and the host. The majority includes bacteria, fungi, viruses, and protozoans that inhabit and colonize the gastrointestinal tract (Alesa *et al.,* 2019). The gut microbiota helps in the contribution of the build-up of the barrier function of intestinal epithelia, maturation of gut-associated lymphoid tissues (GALT), and support of immune and intestine epithelial cells towards commensal organisms and dietary antigens (Serra *et al.,* 2019). The human colon has a variety of organisms like *E. coli, C. jejuni, S. enterica, V. cholera,* and *B. fragilis,* which is seen in very low levels. Certain factors like genetics, diet, mode of delivery at birth, geographic location, and exposure to medical treatments can influence the structure and functioning of GM (Safari and Gérard, 2019). Intestinal microbiota plays a vital role in progressing and preventing metabolic dysfunction. Some recent studies suggest that some species of bacteria react with host metabolism through metabolite-mediated stimulation of enteric hormones and other systems outside GI tract. When the availability of these species decline there is a disruption of symbiosis, resulting in the worsening of host metabolic health (Patterson *et al., 2*016). The gut microbiota supports many body processes, including as recovering energy from food digestion, guarding against pathogens, controlling immunological response, and bolstering the biochemical barriers of the stomach and intestine. Modifications in microbial makeup may impact these processes. While the gut contains some helpful bacteria, some dangerous bacteria can enter the GI tract and lead to infection. These infections include gastroenteritis (GI) illnesses that cause diarrhoea, vomiting, and food poisoning (Yoo et al., 2020).

Functions of gut microbiota

In early life, before birth, human gut microbiota establishment starts. They play a vital role in the functioning of the host. Upon interaction with the host, a positive or negative effect is seen on human health, caused by several metabolic products produced by the gut microbiota. Replication of the gut microbiota occurs on the intestine's surface, thereby preventing harmful microorganisms' entry, and creating a stable system (Gomaa, 2020).

Role in nutrition and health

The gut microbiota affects the metabolism of energy, appetite, innate immunity, etc. Human health can benefit by targeting GM with dietary fibre or probiotics, probably reducing obesity. Gut microbiota can be affected greatly by food, antibiotics, drugs, and pesticides (Valdes e*t al.,* 2018). From birth to death, there is always an interaction between the GM and host and is settled during childhood. The GM regulates many metabolic pathways through complex interactive and symbiotic host-microbiome signalling systems. Moreover, the GM synthesizes molecules that will affect the epigenetic modification in apoptosis, inflammation, etc. (Espín, 2017). The host can receive various health benefits from probiotics either directly or indirectly through "cross-talk" or communication between the gut microbiome and the host. However, unless otherwise specified in guidelines, strain-specific probiotics should be taken for disease. This is a crucially important issue to take into account. Prebiotics are produced by a diet strong in fibre and resistant starches, which can also aid in maintaining a balanced probiotic population in our intestines (Sen, 2019).

Modulation of gut microbiota and probiotics

The GM consists of bacteria, fungi, virus, protozoa, and archaea, which influences the health and physiology of the host by interaction with each other and host. When the gut ecosystem experiences some irregular changes, the modulation of GM is harmful. GM modulation eases many health problems; feeding with probiotics resulted in a high-fat diet which caused and change of the GM structure, leading to the lowering of gram-positive phyla Firmicutes and Actinobacteria in mice. It is obvious that probiotics take part in a vital role in sustaining the gut ecosystem in animals and humans (Azad *et al.,* 2018). Dietary micro and macronutrients play a great role in modulating gut microbiota. Some of the essential micronutrients involved are – polyphenols such as phenolic acid, ligans, flavonoids etc from fruits, vegetables, various cereals, tea, coffee and wine. Vita-

mins such as vitamin A, B-group (B6, B12), vitamin C and D. Vitamin D intake significantly participates in the process of calcium balancing and neurotransmitter synthesis that eventually helps reduce the risk of depression. Macronutrients involved in this process are carbohydrates, fats, and protein (Yang *et al*., 2020).

Future prospects

At present, GM has been known as a significant factor which leads to NAFLD and GM-related mechanisms. Furthermore, the procedures for gut microbiota-targeted therapy on NAFLD is greatly valued in the context of the advantages of modulation of gut microbiota by using probiotics, antibiotics, prebiotics, and synbiotics (Ma *et al.,* 2017). In the case of obesity, many links have been found between obesity and gut microbiota (Khan *et al.,* 2021), but the mechanism is not yet clear about how and when the obese state is affected by the microbiome. New therapeutic possibilities have been seen through probiotics, prebiotics, and antibiotics for treating obesity. By knowing the metabolic interaction between modulated bacteria and the host, there is a possibility of treating obesity through gut microbiota modulation in the future (Gomes *et al.,* 2018). The in vivo and in vitro studies reveal the effect of probiotics (belonging to genera *Lactobacillus* and *Bifidobacterium*) on the execution of the anti-carcinogenic effect. But only some researchers strongly correlate biotherapeutics with cancer therapy (Rai *et al.,* 2021). The next important class of therapeutics for cancer are the probiotic-derivated anticancer pharmaceuticals. Future studies of anticancer probiotics mainly depend on investigating the relationship between humans and probiotics at the molecular level and their interaction with cancer cells (Kumar and Dhanda, 2017). In order to enhance the host's health, several studies need to be done to identify new probiotics and isolation from the microbiome and mixture of probiotic species. The dose and strain to be used need to be known for a better understanding of the therapeutic effects of probiotics. Several other studies are also in progress to know the mechanism of action of probiotics on various diseases. Certain chronic diseases like HIV, cancer, heart disease, diabetes, etc., can be reduced by enhancement of the immune system by probiotics.

Conclusion

Technology is entering a period where one can enhance health through food and other technologies. Probiotics and gut microbiota have a definable properties for preventing or treating many chronic diseases like Cancer, HIV, heart diseases, diabetes, obesity, high blood pressure, eczema etc. The diseases can be prevented by using probiotics which increase the beneficial microbial population, barrier function of the gut epithelium, and the synthesis of cytokines. Probiotics have been considered a health booster in recent years because they can help combat patients with various health issues and are available cheaply and reasonably priced in the market without prescription. If there is variation in gut microbes, it may cause the development of many diseases. Probiotics work by replacing, altering and restoring the complex range of organisms already living within the human gut. Therefore, probiotics play an important role in achieving sustainable development goal 3, i.e. Good health and well-being. The present review has shown the role of intestinal microbiota and host in a symbiotic relationship. Since there is a close relationship between gut microbiota and human health, there is a need to maintain the gut flora in adequate amounts.

ACKNOWLEDGEMENTS

The authors would like to thank the scientists, researchers and academicians whose work has been cited in this manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

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