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Review Article

Role of Probiotics in Health and Disease – A Review

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Abstract

Human intestinal microbiota has undergone a lot of research in recent years and we are beginning to expand our knowledge of the role of bacteria, fungi, viruses and helminths in our gut in health and disease.

Our gut contains myriad of over hundreds of millions of microbes that influence our body physiology, nutrition, metabolism, and immunity. A change in the type of these microbes has been shown to be associated with gastrointestinal diseases such as inflammatory bowel disease and systemic diseases like metabolic syndrome and cancer.

In this article, an attempt has been made to review some significant recent studies that have looked into the complex types of intestinal microbes and how they interact with the human body. This paper also serves to explain what probiotics are, and how they function as a separate "organ" within our body. It includes their method of action, the latest evidence - based research on their use in health and disease and some common sources of probiotic bacteria.

Keywords: *Gastrointestinal microbiome, Gut health, Probiotics, Evidence based medicine on probiotics.*

Introduction

The word probiotics derives from the Latin words pro ("for") and the Greek bios ("life"). The World Health Organization defines probiotics as "live microorganisms, when administered in recommended amounts, bestow a health benefit on the host" (Fijan, 2014).

Our body has millions of bacteria naturally living in and on various parts of our skin and mucous membranes. These used to be called "Commensals." Now, newer studies have revealed that many of these commensals actually produce positive beneficial effects on the body. They have therefore been renamed "probiotic" bacteria. Probiotics are the community of microbes living in our intestines and are considered a metabolic 'organ' due to their positive impact on human wellbeing, including our metabolism and immune function. Our gut microbiome has actually evolved as humans have undergone evolution and have shaped and interacted with our body over thousands of years, influencing our physiology (Ley *et al.*, 2006).

It is now becoming clear that disruption of the gut microbiota (called 'dysbiosis') can result in pathological conditions such as obesity and malnutrition, systematic diseases like diabetes inflammatory bowel disease (IBD) and infections. There is now increasing evidence that the food we eat is

influenced in part by the gut microbes, and that food in turn shapes the microbiota that colonise our gut (Kau *et al.*, 2011).

Objectives

Questions being addressed:

1. What are probiotics?
2. How do they act in our bodies to influence our health?
3. Evidence base on probiotic therapies.
4. Major sources of probiotics.

Study design

A search was performed using PubMed/Medscape/google scholar, and the terms ‘gastrointestinal microbiome,’ ‘gut health,’ ‘probiotics,’ ‘evidence based medicine on probiotics’ were used.

PROBIOTICS

History

The climate in India, the Middle East and Asia favoured the souring of milk products, which have been used to treat intestinal illness from times immemorial. In 1899, Henry Tissler, (Pasteur Institute in Paris, France) detected a Y-shaped bacteria in the intestines of breast-fed infants. He called the organisms “bifidobacteria.” Tissler found that babies with bifidobacteria suffered from fewer diarrheal episodes.

Nobel laureate Élie Metchnikoff, in the beginning of the 20th century (1908) reported for the first time, the positive role played by certain bacteria in health. Metchnikoff was looking for the ‘elixir of life’ and noted that fermented milk products had anti-aging health benefits. He named the organism found as “Lactobacillus bulgarius.” Metchnikoff is called the father of “probiotics.” Later, a German physician and scientist, Alfred Nissle, found that during an outbreak of shigella diarrhoea, a World War I soldier who carried shigella did not develop the diarrhoea. From his feces, Nissle isolated a new strain of Eschericia coli and used this strain to treat diarrhoea in other patients with great success.

The term "probiotics" was first used in 1953 by Werner Kollath (The History of Probiotics: The Candida Diet).

Human Microbiome

Microbiologists have known for some time that different diets create different gut flora. Human microbiota is composed of bacteria, yeasts, fungi and viruses (whose composition has not yet been completely described). New studies indicate that our microbiome can change incredibly fast in the human gut—within three or four days of a big shift in what we eat. Eating a mainly plant based diet supports health giving probiotics (Scarpellini, *et al.*, 2015). The beneficial microbiota has now been referred to as a "hidden organ," due to its critical role in our bodily functions (O’Hara, 2006).

Different types of probiotics have different functions. Health benefits have mainly been demonstrated for specific probiotic strains.

a) Bacterial genera: Lactobacillus, Bifidobacterium, Lactococcus, Enterococcus, Streptococcus, Pediococcus, Bacillus, Escherichia coli.

b) Fungi: The genus Saccharomyces includes various yeasts such as: Saccharomyces cerevisiae (used for making wine, bread, beer), Saccharomyces bayanus (used for making wine) and Saccharomyces boulardii used in medicine as a probiotic.

c) Viruses: many plant-derived viruses reside in our gut, and it is suggested that our gut virome in turn, can change the resident bacterial flora.

Mechanism of Action

One of the largest interfaces of our body, after the skin, is the human intestinal mucosa. Host–microbe interactions occur mainly on this vast mucosal surface. The diverse bacterial, yeast and viral community is separated from our internal milieu by just a few layers of epithelial cells. Collectively, this resident microbiome has a metabolic

activity equal to a virtual organ within an organ.

At birth, a baby's intestines are sterile. During birth, the baby gets exposed to many microbes in the birth canal and maternal skin during delivery. By 3–4 days of age, the baby's gut microbiota composition resembles that of colostrum and breast milk. By about the age of three, the composition of intestinal microbiota becomes that of adult humans and become relatively stable, depending on the diet (Liu, 2016).

Developing research confirms that these pioneering bacteria can modulate gene expression in the baby to create a suitable environment for themselves and this can prevent growth of other bacteria introduced later into the child's ecosystem (Xu and Gordon, 2003).

The intestinal microbiota in the elderly has also been the subject of various studies. It has been seen that there are many physiological changes in the GI tract of older people that are due to a chronic low-grade inflammation in the gut which can lead to a microbial imbalance. It has been found that the composition of the gut microbiota of older people (>65 years) is different from that of younger adults. This difference is mainly related to the diet and environment of the elderly population. This and other studies indicate strongly that our gut microbiota is very important to the health and in the progression of disease and frailty in older people (Franceschi, 2008; Claesson *et al.*, 2012).

Proposed mechanisms of action of healthful benefits of probiotic micro-organisms include:

a) Blocking of adhesion of pathogenic bacteria to the intestinal epithelium by production of inhibitory agents
b) Suppression of the growth of pathogenic bacteria by directly binding to gram-negative bacteria
c) Maintenance of normal levels of short-chain fatty acids (SCFAs)
d) Suppression of intestinal pro-inflammatory cytokines
e) Repair of intestinal permeability by colonocyte multiplication
f) Up-regulation of intestinal electrolyte absorption
g) Enhancing the intestinal immune response
h) Regulation of lipid metabolism

(Vieira *et al.*, 2013; Kelly *et al.*, 2015).

Role of SCFAs in health

In the colon, SCFAs provide energy to the colonocytes. SCFAs are also absorbed and transported from the intestinal lumen into the blood and taken up by various organs where they act as substrates or signal molecules. SCFAs can regulate the balance between fatty acid synthesis, fatty acid oxidation and lipolysis in the liver, thus increasing insulin sensitivity. In-vitro and in-vivo experiments have shown that SCFAs increase leptin expression, thus regulating appetite. Oral administration of acetate and propionate reduced glycemia in diabetic hyperglycemic KK-A(y) mice and normal rats. This can influence glucose metabolism and type 2 diabetes (Hu *et al.*, 2010; Guinane and Cotter, 2013).

EVIDENCE FOR THE THERAPEUTIC USE OF PROBIOTICS

The effectiveness of Probiotic therapy can be species, dose and disease specific. There are unfortunately, very few clear guidelines on when to use probiotics and the most effective probiotic for different conditions (Dosage - Probiotic Advisor, 2019). This can lead to confusion for treating doctors as well as their patients. A Cochrane review has established that a dosage of 5 billion colony-forming units or greater per day was significantly more effective than a lower dosage (Fijan, 2014).

The following conditions have been shown to benefit from probiotic therapy till date:

Acute Infectious Diarrhoea: Probiotics are effective for acute infectious bacterial diarrhoea, but there are inconsistent results for their effectiveness in viral diarrhoeas. A Cochrane review of 63 randomized

controlled trials (RCTs) that included 8,014 infants, children, and adults with acute infectious diarrhoea found that probiotics significantly reduced the mean duration of diarrhoea (25 fewer hours), and led to approximately one fewer stool by the second day. Practice implications of this significant finding are that for patients with acute infectious diarrhoea, probiotics should be started at the onset of symptoms, and continued for one to two weeks after resolution of symptoms (Wilkins & Sequoia, 2017; Abou El-Soud *et al.*, 2015).

Traveller's diarrhoea: A 15% relative decrease in the risk of traveller's diarrhoea was seen with probiotic therapy in a meta-analysis of 12 RCTs with 5,171 participants. The practice implication is that for prevention of traveller's diarrhea, probiotics should be started two days before travel and continued throughout the trip (Wilkins & Sequoia, 2017).

Antibiotic-associated Diarrhea: Probiotics are effective in the prevention and treatment of antibiotic-associated diarrhea in children and adults. For C. difficile infection, the results are mixed, and depend on host immune factors. Patients should start probiotics on the first day of antibiotic treatment and continue for one to two weeks following completion of antibiotic therapy. To simplify the treatment regimen, patients may take probiotics at the same time as antibiotics. This has proven to be effective, and the antibiotic does not interfere with probiotic actions (Shan *et al.*, 2013; Song *et al.*, 2010).

Helicobacter pylori infection: Probiotics can be effective as adjuncts to antibiotic therapy to eradicate Helicobacter pylori in patients with peptic ulcers. A meta-analysis of nine RCTs involving 1,163 children and adults found that using Lactobacillus-containing probiotics as an adjunct to antibiotics increased the H. pylori eradication rate compared with control (NNT = 10) (Wilkins & Sequoia, 2017).

Hepatic Encephalopathy: Probiotics seem to be effective for the treatment of hepatic encephalopathy. A meta-analysis of six RCTs involving 496 adults with cirrhosis showed that probiotic therapy significantly reduced the development of overt hepatic encephalopathy (Saab *et al.*, 2015).

Ulcerative colitis: Probiotics are seen to be effective in increasing the remission rates in adults suffering from ulcerative colitis but not in the maintenance of its remission. Probiotics should be started at the onset of an exacerbation of ulcerative colitis, and continued for one to two weeks following resolution of symptoms. A meta-analysis of 23 RCTs with 1,763 adults found that probiotics significantly increased the remission rates in patients with active ulcerative colitis compared with placebo (Wilkins & Sequoia, 2017).

Irritable Bowel Syndrome and Functional Abdominal Pain: Probiotics were somewhat effective in children and adults with irritable bowel syndrome (IBS) and in children with functional abdominal pain, in clinical trials. Patients should start probiotics at the onset of symptoms and continue as needed for persistent symptoms. A meta-analysis of 23 trials involving 2,575 children and adults with IBS found that probiotics had significantly improved symptoms such as bloating, and flatulence compared with placebo (Wilkins & Sequoia, 2017).

Constipation: Probiotics are an effective treatment option for children and adults with constipation. Patients should start probiotics at the onset of symptoms and continue as long as symptoms persist. A meta-analysis of two trials including 165 adults with chronic idiopathic constipation reported a significant increase in the average number of stools per week in patients treated with probiotics as compared to the placebo group (Guinane & Cotter, 2013; Barichella *et al.*, 2016).

Necrotizing Enterocolitis: A Cochrane review found that probiotics compared with control or placebo significantly reduced the risk of severe necrotizing enterocolitis (20 studies with 5,529 infants) and mortality (17 studies with 5,112 infants). Therapy should be started in those at risk of the condition (e.g., sepsis, IUGR, formula feeds, maternal H2 blocker therapy, etc.) and continued as long as the increased risk persists. Strain-specific sub-meta-analyses of clinical trials showed Bifidobacteria to be most effective (Aceti *et al.*, 2015).

Anti-Cancer: By modulating intestinal microbiota and immune response, some strains of probiotics can be used as an adjuvant for cancer prevention or/and treatment. Some human trials tested this effect and found that probiotics can exert anti-carcinogenic effects (Yu and Li, 2016).

Cardiovascular risk factors: Some studies have demonstrated that strains of Lactobacilli are able to lower serum cholesterol levels. The mechanism remains unknown, but it is hypothesized that enzymatic deconjugation of bile acids by bile-salt hydrolase of probiotics, assimilation of cholesterol by probiotics, co-precipitation of cholesterol with deconjugated bile, and production of short-chain fatty acids upon fermentation of prebiotics are likely mechanisms (Ooi & Liong, 2010). Probiotic yogurt was seen to improve total cholesterol and LDL-C concentrations in patients of type 2 diabetes and could contribute to the improvement in cardiovascular disease risk factors (Ejtahed *et al.*, 2011).

Lactobacillus sp, and Bifidobacterium were incorporated into soymilk supplemented with fructo-oligosaccharides (FOS). Supplementation probiotic-fermented soymilk was found to enhance the in-vitro effect of anti-hypertensives. Therefore, fermented soymilk could potentially be used to reduce the risk of hypertension (Yeo & Liong, 2010).

Mineral Absorption: Synbiotics, a combination of probiotics and prebiotics, have shown positive effects on mineral absorption, metabolism and composition and architecture of bones in some studies (Scholz-Ahrens *et al.*, 2007). The underlying mechanisms are due to increased solubility of minerals by short-chain fatty acids; an enlargement of the absorption surface by proliferation of enterocytes; degradation of phytic acid which can form complexes with mineral, preventing absorption; and release of phytoestrogens from foods; phytoestrogens can modulate bone formation and architecture (Parvaneh *et al.*, 2014).

Atopic Dermatitis: Supplementation with probiotic L. fermentum is seen to be beneficial in improving the extent and severity of allergic dermatitis in atopic children (Weston, 2005).

Rheumatoid Arthritis: Lactobacillus casei 01 supplementation reduced disease activity and inflammation and lowered pro-inflammatory cytokines IL-6 in patients with RA. However, the reason for these clinical effects is still unclear. Further studies are needed to confirm these results and deduce its mechanism of action (Vaghef-Mehrabany *et al.*, 2014).

Probiotics and Weight Loss: Disturbances in the composition of the intestinal microbiota can cause disruption in its function of enhancing the gut barrier, resulting in low-grade chronic inflammation. This has considerable effects for host adiposity and insulin resistance. The central role of the intestinal microbiomes in the regulation of appetite and the resultant effects of obesity are now becoming clear (Patterson *et al.*, 2016).

Metabolic syndrome: Numerous clinical studies have demonstrated the beneficial effects of high fibre diet on the metabolic syndrome. The principal beneficial effects of a fibre-rich diet in these patients are the prevention of obesity, improved glucose levels, and control of serum lipids. Dietary fibre may also favour the control of arterial blood pressure. The mechanism occurs though the activation of AMP by activated protein kinase (AMPK), which functions as and a master regulator of metabolic homeostasis. Several evidences suggest that AMPK can be activated by short-chain fatty acids (SCFA) either directly or indirectly. It is hypothesized that the mechanism by which a high fibre diet benefits in patients of metabolic syndrome is the increased SCFA production in the colon from fermentation of the fibre by probiotic bacteria. This results in a higher concentration of SCFAs in the portal vein, which in turn, activates AMPK in the liver (Hu *et al.*, 2010).

Critical illness: During any critical illness, there is a characteristic loss of beneficial flora in the gut, and an overgrowth of pathogenic bacteria. This change leads to a higher susceptibility to nosocomial infections. Probiotics are effective in reducing infections, including VAP

(ventilator associated pneumonias) in critical illness. Further high quality clinical trials are needed to conclusively prove these benefits (Manzanares, 2016).

Prevents Radiotherapy side-effects: Research performed at the Washington University School of Medicine in St. Louis, USA, have revealed that cancer patients undergoing radiotherapy who take probiotics before the procedure have a reduced incidence of radiation induced diarrhoea. For their study, researchers compared the effects of radiotherapy on mice, some of which were given probiotics prior to and after radiation exposure. They found that those who had received a probiotics (*Lactobacillus rhamnosus*) before exposure were protected against radioactive damage to their intestines (Ciorba *et al.*, 2011).

Acute upper respiratory tract infections: A meta-analysis that included 13 RCTs compared probiotics with placebo or no treatment in the prevention of acute URTIs. In people at risk for acute URTIs, it was found that the probiotics fed group experienced reduced episodes of acute URTI by about 47% and a reduction in duration of an episode by about 1.89 days, as compared to the placebo group. Probiotics also slightly reduced antibiotic use and cold-related school absences. The overall quality of the evidence was low because of a small sample size (Hao *et al.*, 1996).

Psychobiotics: A psychobiotic is defined as a live organism that, when ingested in adequate amounts, produces health benefits in patients suffering from psychiatric illness. These bacteria produce and deliver neuroactive substances such as gamma-aminobutyric acid and serotonin to the brain, which act on the brain-gut axis, leading to improvement in psychiatric morbidity (Dinan, Stanton & Cryan, 2013). Investigators at Queen's University, Kingston, Canada, found that after just 4 weeks of probiotic therapy, symptoms of mood, anhedonia and sleep disturbance were significantly reduced, with results maintained up to 8 weeks. For this study, the researchers used *Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175, strains known to act on the gut-brain axis (Wallace & Milev, 2017).

Infant Gut Microbiome and Cognitive Development: In one interesting study, 3 groups of 2 year-old children were defined by their faecal bacterial composition. A cluster analysis of Mullen scores (Gross Motor, Visual Reception, Fine Motor, Expressive Language, and Receptive Language) was performed at 2 years of age. It showed significant differences between clusters. Cluster 2, which had toddlers with a higher abundance of Bacteroides showed the best scores. The take-home message from the authors of this study is that diversity in gut microbes due to breastfeeding and vaginal delivery can have positive benefits on cognitive development at 2 years of age (Carlson *et al.*, 2018).

Vaccinations: In an animal study, it was demonstrated that certain probiotic strains can enhance the immune response to a vaccine as well as reduce the risk of subsequent infection. Human studies are much fewer, but an increasing number of well-controlled trials are indicating that the response to vaccines against influenza, cholera and other childhood diseases are enhanced by selected probiotics. The effects are strain-specific to the probiotic. In one study, there was evidence that subsequent risk of infection by the influenza virus was reduced (Prebiotics/Probiotics pdf).

Trichuris suis therapy in Crohn's disease: When the researchers fed some mice worm eggs, the population of the good bacteria Clostridiales, increased significantly. The mice also had reduced inflammation in the gut. This led to a reduced incidence of inflammatory bowel disorders (Summers, 2005).

In another landmark study in Malaysia it was seen that Orang Asli experience virtually no inflammatory bowel diseases, and a high percentage of them have chronic parasitic worm infections. Before the worms were removed, the cohorts being studied had higher levels of helpful bacteria and lower levels of harmful bacteria. After

taking a deworming drug, that healthy ratio was changed (Ramanan *et al.*, 2016).

Conditions for which Probiotics Are Ineffective:

Asthma: On a pragmatic community-based study in people with asthma, there was no evidence that advising use of winter probiotics reduces antibiotic prescribing (Smith *et al.*, 2016).

Crohn disease: Lactobacillus GG was given for 1 year in patients with Crohn's disease. It was seen that the supplementation neither prevented endoscopic recurrence at one year nor did it reduce the severity of recurrent lesions (Prantera *et al.*, 2002).

Steatohepatitis: There was no definitive evidence of probiotics effectiveness for non-alcoholic fatty liver disease and non-alcoholic steatohepatitis (NAFLD and NASH) in clinical trials. At present, probiotic use as an adjunct in the treatment of NAFLD needs validation by further clinical trials with a larger sample size and longer term follow up (Kelishadi *et al.*, 2013).

SOURCES OF PROBIOTICS

Fermented foods are made by using live microbes, but these microbes may not survive in the final food product due to processing steps used in their manufacture. However, some fermented foods made at home like yogurts and cultured milk are sources of probiotics and have been studied in controlled clinical trials that have documented health benefits (Sanders *et al.*, 2018).

Probiotics are available in two main forms: food and dietary supplements. Dietary supplements are regulated by the Food and Drug Administration (FDA).

Probiotics in our Diet: Dietary sources are yoghurt and prebiotics like fibre and resistant starches. As noted earlier, fermentation of foods is a simple and natural method used by many ancient cultures to promote good digestion, preserve food, and improve health. The bacteria in fermented foods increase its levels of vitamins B, C, and K, deactivate harmful nutrients such as the protein inhibitors and phytic acid, and release nutrients from food that would otherwise have passed through the intestines undigested.

Yoghurt is a dairy product produced by bacterial fermentation of milk.
Worldwide, cow's milk is most commonly used to make yogurt, but milk from water buffalo, goats, sheep, horses, camels and yaks is also used in various parts of the world. Dairy yogurt is produced using a culture of *Lactobacillus bulgaricus* and Streptococcus salivarius subsp. Thermophiles bacteria. In addition, other lactobacilli and bifidobacteria are also sometimes added during processing.

Live cheeses also contain probiotics, such as LiveActive natural cheese snacks, and yogurt Cheese (prepared with the probiotic live cultures Lactobacillus acidophilus and bifidobacterium). Other good sources of probiotics include blue cheese and other aged cheeses. Probiotic-rich cheeses often feature words such as "live culture," "active culture" or "probiotics" on the packaging.

Buttermilk is the liquid left behind after churning butter out of cream. Today, commercial cultured buttermilk is produced from cow's milk using either Streptococcus lactis or Lactobacillus bulgaricus. Buttermilk made with the latter is called Bulgarian buttermilk (Probiotics Promote Good Health – articles. mercola).

Kefir originated in the Caucasus of Russia and Turkey. It is a fermented milk drink containing bacteria like Lactobacillus acidophilus, brevis, casei, delbrueckii subsp. Bulgaricus; and yeasts like *Candida humilis, Kazachstania unispora, Kluyveromyces lactis*.

Kombucha is a Chinese tangy/sweet "mushroom tea." In the past, during the Chinese Qin Dynasty, it was referred to as the "immortal health elixir." The mushroom culture is a round pancake-like firm jelly structure made of yeasts and bacteria that covers the top of the liquid drink. The yeast component of kombucha may contain *Saccharomyces cerevisiae, Brettanomyces bruxellensis*, or *Candida stellata*. The bacterial component is made up of *Gluconacetobacter xylinu*. The drink

supports the intestinal tract and is also known to supply B vitamins.

Sauerkraut is the ancient art of culturing, fermenting and pickling vegetables that dates back thousands of years. The word “sauerkraut” comes from German, meaning “sour plants." The Korean version is known as *"kimchee."* The vegetable fermentations contain four species of lactic acid bacteria, *Leuconostoc mesenteroides, Lactobacillus plantarum, Pediococcus pentosaceus*, and *Lactobacillus brevis*. Kimchi also contains *Lactobacillus kimchii*.

Tempeh is a fermented whole-bean cake. Tempeh originated over 2,000 years ago in Indonesia and the island of Java. The white mycelium of the spore, *Rhizopus oligosporus*, forms a solid bean cake, which can be sliced, fried or steamed as an alternative to meat. For those wanting to reduce meat consumption, it is a good alternative with the added advantage of being cholesterol free.

Miso is a traditional Japanese food, whose origins date back to China in the 3rd century BC. Koji is the culture substrate, and contains *Aspergillus oryzae* spore. It is used to ferment the beans and grains. Bacteria found in miso include *Tetragenococcus halophilus* and *Lactobaccilus acidophilus*.

Soy sauce (also called soya sauce) is a condiment produced by fermenting soybeans with *Aspergillus oryzae* or *Aspergillus sojae* molds, along with water and salt. Soy sauce is also rich in lactic acid bacteria.

Natto is a traditional Japanese food of fermented soybeans. Natto soybeans are steam-cooked and then fermented with *Bacillus subtilis*. Natto is especially rich in vitamin K (Melissa Conrad Stoppler, 2017).

Supplements: Probiotic supplements come in tablet, powder, capsule, and liquid forms. They do not provide the nutrition like probiotic foods, but they are an option to promote healthy gut bacteria. Many supplements are readily available in the market. It is very important to note that some brands require refrigeration and some need to be stored in a dark, cool place.

Probiotics supplements are not necessary for normal, healthy individuals. For healthy adults, daily consumption of probiotics-rich foods, like yoghurt and cultured milk drinks, and fibre rich diets (prebiotics) should adequately supply the amount of probiotics required to maintain a healthy digestive system and overall wellbeing (Wilkins & Sequoia, 2017).

SIDE-EFFECTS AND RISKS

Live microorganisms from fermented foods have been used for centuries without causing illness in people. Probiotic products taken as a dietary supplement are regulated as foods, not drugs. However, probiotics' safety had not been previously studied scientifically. More studies are needed on their safety, especially regarding young children, the elderly, and people with compromised immunity.

Most Probiotics' side effects tend to be mild such as gas or bloating.

There is a risk that probiotics, being live organisms, might cause infections that need to be treated with antibiotics, especially in people with underlying health conditions. Many probiotic strains are genetically modified in the laboratory for their health benefits. The safety of each strain needs to be guaranteed and strictly monitored so that they do not accumulate in the environment, possess antibiotic selection markers, or transfer any harmful genetic information to other bacteria.

In an important study on the use of probiotics in patients suffering severe acute pancreatitis, a significantly higher mortality was observed for the probiotics group than for the placebo (Besselink *et al.,* 2008).

In another study, term and preterm infants were supplemented with probiotics to prevent adverse effects of antibiotic administration and necrotizing enterocolitis. However, the supplementation with Lactobacillus rhamnosus GG was associated with the development of sepsis in 4 preterm infants. There was also a reported case of L. acidophilus bacteremia in a patient who had HIV infection and Hodgkin disease and a case of

Lactobacillus infection after a bone marrow transplant (Coviello *et al.*, 2015).

Therefore, probiotic supplementation should be used with caution in populations at risk. These include:

a) Those on anti-rejection medication after stem cell or solid organ transplant, immunosuppressive drugs for autoimmune disease; or corticosteroids and cancer chemotherapy.

b) Structural heart disease with valve abnormality or valve replacement or history of infective endocarditis.

c) Presence of an active intestinal perforation and leak, acute abdomen, active intestinal disease including colitis; presence of neutropenia or anticipation of neutropenia after chemotherapy and radiation therapy.

(Doron & Snydman, 2015).

Conclusion & Recommendations

Current research results have contributed greatly to the understanding of the role of intestinal commensal organisms in their symbiotic health-giving relationship with humans. Probiotics can impact the host directly or indirectly through “cross-talk” or communication between the gut microbiome and the host, giving the host a slew of health benefits. However, one critically important factor to consider is that probiotics used for disease should be strain-specific unless otherwise stated in guidelines.

A diet high in resistant starches and fibre provides prebiotics, which can also help to keep a healthy population of probiotics in our intestines. Supplements should be prescribed only when indicated by evidenced based medical guidelines.

This review attempts to summarise the available evidence based guidelines for the use probiotics today. It is important to note that a balanced diet can incorporate many probiotics and there is a growing body of evidence showing their health benefits.

Conflict of Interest: *None*

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