

Probiotics as Agents of Health Improvement, Infection Control and Diseases Treatment: A Review

ABSTRACT

Aims: This review presents valuable information on the contribution of probiotics to the improvement of health and quality of life.

Background: Due to their roles in normal physiology and impacts on human health, probiotics have become a subject of great interests especially in the field of Microbiology. The results of several well-designed clinical studies have shown probiotics to be reliable therapeutic option for the prevention, treatment and control of various health conditions; gastrointestinal diseases, respiratory diseases, neurological disorders, depressive symptoms and autoimmune disorders. Probiotics enhance gastrointestinal tract (GIT) health via vitamins production and supply to the human host and have also been reported to improve immune function thus, inhibiting pathogen invasion and colonization/development. Some show direct/indirect immune modulating capabilities by enhancing mucosal barrier functions, modulating sensory motor functions and delivering antigens. Many probiotic foods possess antioxidant properties that enable them to withstand oxidative stress and strengthen hosts' anti oxidative defense mechanism.

Findings/Conclusion: The potential application of probiotics in functional foods and pharmaceuticals could demonstrate the improvement of health and quality of life.

Keywords: *Bifidobacteria, Gastrointestinal, Lactobacillus, Probiotic microbial strains, Prophylactic, Therapeutic*

1. INTRODUCTION

Over the past years, the enormous health benefits derived from probiotic strains and products have led to increased interests in placing "healthy" food on the market based on the 'quests' to live healthy. As a result, health benefits of products containing probiotic strains are being promoted and probiotic strains are been established in many different products with their numbers increasing steadily. The term "probiotic" is derived from the Latin

preposition “pro” meaning “for” and the Greek word “biotic” meaning “life”. Definition of probiotics has been modified with advancing insight in their mechanism of operation. In early nineties, Metchnikoff expressed probiotics scientifically as modification of floral/microbial diversity in human bodies, thus replacing the harmful microbes with beneficial ones [1]. However, the breakthrough came through Henry Tissier’ research, who observed that the microbial concentration of a particular type of bacteria in fecal samples of diarrhea infected children were significantly lower when compared to healthy children. His opinion of oral administration of live organisms (Bifidobacteria) to patients with diarrhea (infantile diarrhea) and its help to restore a healthy gut flora was a novel attempt [2]. The modern definition of probiotic as a viable mono or mixed culture of bacteria which when applied to animal or man, affects the host beneficially by improving the properties of the indigenous flora is generally accepted [3]. Probiotic microorganisms are usually available as culture concentrates in dried or deepfreeze form to be added to a food matrix as component of fermentation process [4]. The major sources of probiotics are fermented non-digestible carbohydrate compounds, food supplements, dairy based compounds, non-and non-dairy fermented foods.



Fig.1. Common forms of probiotic foods (Source: <https://www.nutriplanet.org/>)

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Probiotics have various mechanisms of action but three major mechanisms have been properly established. The first involves competition for nutrients and for ecological niche, thereby, limiting subsequent survival, adhesion and concentration of potentially pathogenic flora in the digestive tract, this is the major defense mechanism used to maintain internal health condition [5]. Lactobacilli and bifidobacteria have been shown to inhibit a broad range of pathogens by performing colonization of pathogenic bacteria and finally by exerting antagonistic activity against gastrointestinal pathogens [6, 7]. This principle in many cases is crucial for the prevention and treatment of infections and restoration of the microbial equilibrium in the gut. The second mechanism is the production of antimicrobial substances, bacteriocins, toxins, organic acids, short chain fatty acid production and lowering of gut pH [8]. These substances are responsible for inhibiting the growth of other harmful microbes such as foodborne pathogens and spoilage organisms in GIT environment; they create antagonistic condition that result in the inactivation of toxins and death of the pathogens [9, 10]. The third mechanism is the stimulation/modulation of specific and nonspecific immune response by T-cell activation, cytokine production/throughout immune-modulation by inducing phagocytosis and IgA secretion, modifying T-cell responses, enhancing Th1 responses, and attenuating Th2 responses, this mode of action is particularly important in the prevention and therapy of infectious diseases [11, 12]. Probiotic bacteria can exert an immune-modulatory effect as they possess the ability to interact with epithelial and dendritic cells (DCs) and with monocytes/macrophages and lymphocytes [13, 14]. The immunological advantages of probiotics can be because of activation of local macrophages and modulation of IgA production locally and systemically, to changes in pro/anti-inflammatory cytokine profiles, or to the modulation of response towards food antigens [15, 16].

To supply health effect, probiotic cells must be constantly viable in the food carries and adapt to extreme environment of the GIT such as; high temperature (37°C), exposure to gastric juice and enzymes, pH fluctuations when passing through the gastrointestinal tract,

oxygen tension and oxidative stresses, bile and pancreatic salts. In addition, it must be stable during gastro intestinal transit and fulfill, a cell count of at least, 10⁶ CFU/g and able to withstand the secondary products of the host and other gastrointestinal microflora [17]. This review evaluates the currently available data on probiotics and presents comprehensive findings on probiotic effects on human health.

2. PROBIOTIC MICROBIAL SPECIES

Common microbial species used as probiotics include bacteria and yeasts. However, bacterial species are the most predominantly used. *Lactobacillus* and *Bifidobacterium* are the main probiotic groups. However, probiotic potentials of *Enterococci*, *Propionibacteria*, *Bacillus*, and *Saccharomyces* yeasts have also been reported [18].

2.1 Lactobacillus species: *Lactobacillus* refers to lactic acid and short chain fatty acid producing bacteria of the phylum Firmicutes. Naturally, they are associated with mucosal surfaces in the gastrointestinal tracts, vaginal and oral cavities of both humans and animals. They are Gram positive, rod-shaped, non-spore forming facultative anaerobic, fermentative bacteria often used as starter cultures in fermentation processes for foods such as; milk, meat, wine, fruits, cereal grains and vegetables [19]. *Lactobacilli* are very common starters or complementary cultures of dairy products like yoghurt and cheese, also useful in the preservation of foods like cured meat, sauerkrauts, pickled vegetables, salami, olives, etc [20]. They are currently, one of the most important probiotic bacteria widely used in food supplements and beverages. *Lactobacillus bulgaris* and *L. delbreuckii* are useful probiotics in yoghurt production. Kefir, another fermented dairy product is obtained by the fermentation activities of *L. helveticus*, *L. lactis*, *L. brevis*, *L. fermentum*, *L. acidophilus*, *L. bulgaricus* and *L. casei subsp. lactis* [21, 22]. Kimchi, a fermented spicy Korean side dish commonly made from cabbages contains the lactic acid bacteria, *Lactobacillus kimchii*. The probiotic activities of *Lactobacilli* particularly *L. plantarum* and *L. fermentum* in Nigeria fermented foods; garri, iru, ogi, emu, ugha, okpehe, lafun, and kokoro have been reported [23, 24].

2.2 Bifidobacteria: *Bifidobacteria* are Gram positive, non-motile, anaerobic non-spore forming organisms. In the last decade, interests in the use of *Bifidobacterium* as probiotic have increased, especially in dairy products. However, compared to the traditional starter cultures used in fermented dairy products, *Bifidobacteria* have inferior characteristics because; they have weaker growth and acid production rates, require low redox potentials and anaerobic conditions for their growth as well as longer fermentation times. Hence, in selecting preferred strains for incorporation into dairies, it is paramount to consider strains with desirable attributes such as; fast growing strains, growth in combination with other starter cultures and strains that produce compounds, flavours or textures that do not reduce, rather, enhance the quality of the products [25]. The *bifidobacteria*; *B. bifidum* and *B. longum* play important roles in the ripening of Canestrato Pugliese, a hard cheese. Cheddar cheese is manufactured with the *bifidobacterium*, *B. infantis* [26]. *B. bifidum* strains have been also used in the fermentation process for bifidhurt and bio-yoghurt.

2.3 Propionibacteria: *Propionibacteria* satisfy the criteria for classification as probiotics as they are able to endure digestive stress conditions to persist within the gut and are also able to adhere strongly to epithelial cells [27]. Dairy *propionibacteria* are generally regarded as safe (GRAS) and also make up the qualified presumption of safety (QPS) list. They produce nutraceuticals and metabolites such as; surface proteins, short chain fatty acids, 1,4-dihydroxy-2-naphthoic acid that possess beneficial probiotic attributes [28]. Dairy

probiotic bacteria; *P. freudenreichii* and *P. acidipropionici* serve as useful additives and starter cultures in cheese ripening and as bio-preservatives.

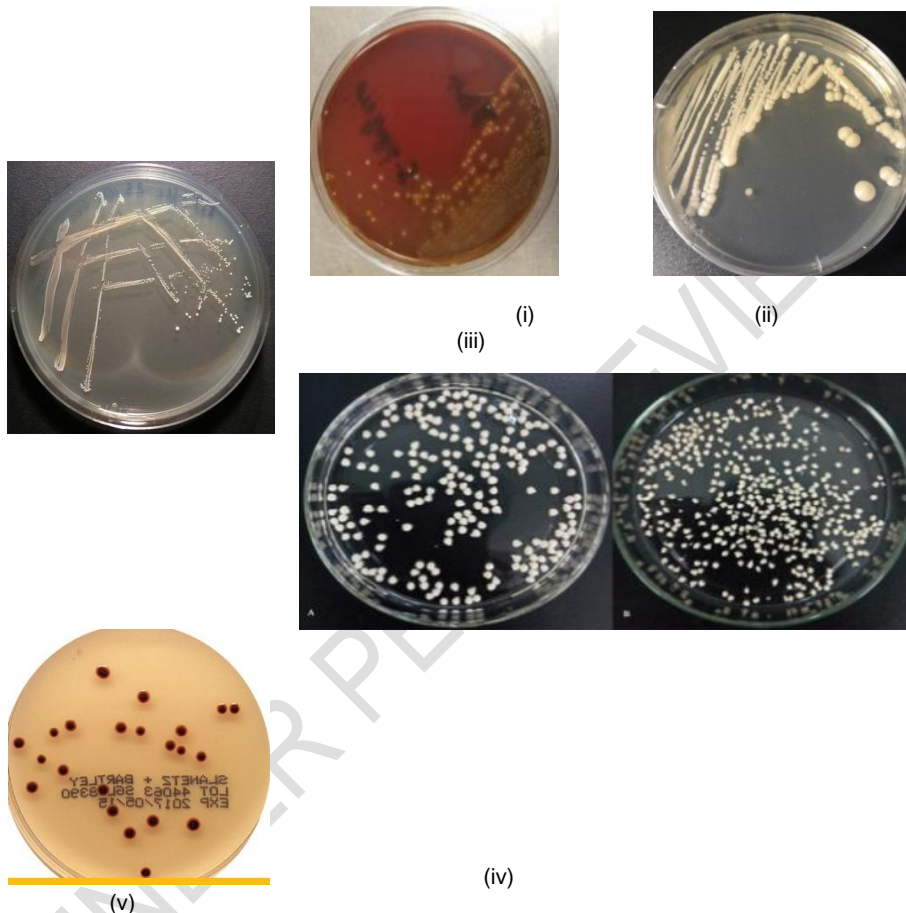


Fig.2. Morphology of (i) *Lactobacillus* sp (ii) *Priopionibacterium* sp (iii) *Saccharomyces* spp (iv) *Bifidobacterium* spp and (v) *Enterococcus* sp on culture media [29, 30].

Comment [JLSdS2]: indicate the respective culture media used to demonstrate the morphology of bacterial colonies.

2.4 Enterococci: this is a large genus of Gram positive, cocci, lactic acid bacteria of the phylum Firmicutes. They are typically present in the gut and bowel as part of the intestinal flora of human and animals. Due to their inherent biotechnological traits in enterocin production, citrate breakdown, lipolytic, esterolytic and proteolytic activities, enterococci have been used as starters in food fermentation or protective cultures in bio-preservation [31, 32, 33]. *E. faecalis*, *E. casseliflavus*, *E. lactis*, *E. italicus* and *E. faecium* are examples of enterococci species isolated from milk, fermented vegetables and meat [34]. Also, they play beneficial roles in cheese fermentation, ripening and development of desirable flavour, taste and texture. However the use of enterococci as probiotics have raised serious concerns as

they are well known multidrug resistant and opportunistic pathogens of human and animal disease.

2.5 Saccharomyces: The use of yeasts as probiotics is highly advantageous since they play important roles as part of the gut microbiota and are not affected by anti-bacterial compounds. Probiotic yeasts contain numerous immune-stimulants such as; proteases, β -glucans and manna oligosaccharides that function in detoxification of the immune system. *S. cerevisiae* exerts probiotic effects by promoting metabolic processes of digestion and nutrient utilization. It also maintains the gastrointestinal tract's flora by excluding pathogens and increasing the population of useful microbes. *Sacchramomyes boulardii* stimulates immune response by secreting proteolytic enzymes that degrade bacterial toxins and inhibit their adherence to gastrointestinal epithelial cells [35].

3. HEALTH BENEFITS OF PROBIOTICS

Probiotic organisms confer health benefits in diverse ways. However, probiotic impacts have been shown to be strain specific as the particular impacts depicted for one strain can't be specifically applied to others, this necessitates unambiguous identification to species and strain level. As earlier mentioned, owing to the numerous health benefits they offer, probiotics are widely used in fermented food and feed to boost host's health. In pharmaceutical industries, the antimicrobial activities of probiotic strains are extracted and incorporated into drops or tablets as remedies for gastrointestinal diseases [36]. This is in part, due to their abilities to exert anti-pathogenic effects by producing bacteriocins and increasing the acidity of the GIT, such that, subsequent invasion by enteric pathogens such as *Escherichia coli*, *Shigella spp* or *Salmonella spp* is warded off [6, 37]. Some function by inhibiting metabolic activities via reduction of cholesterol levels and increasing lactose tolerance or by modulating the metabolic and nutritional activities of commensal bacteria in the gut to modify the populations of the gut microbiota [38]. One of the essential effects exerted by probiotics is stimulation of intestinal short-chain fatty acid (SCFA) production. An increase in Lactobacilli population stimulate lactic acid production, the resulting lactate is not accumulated but metabolized to SCFA; acetate or butyrate by lactate-utilizing bacteria. Acetate increases blood flow in the colon and enhances motility of the ileum. Butyrate on the other hand, play important role in the prevention of colitis and other colonic disorders [39, 40]. Lactic acid bacteria also function in the prevention of colon cancer through modification of the metabolic activities of intestinal micro flora, alteration of physicochemical conditions in the colon as well as binding site, production of anti-tumorigenic or mutagenic compounds due to their ability to decrease or inhibit the activity of enzyme called β glucuronidase and the pro-cancerous enzymatic activity of colonic microorganisms [41].

Furthermore, Lactobacilli and Bifidobacteria species help in the destruction of the adverse effects of *Helicobacter pylori* through the release of bacteriocins, production of organic acids, and competitive colonization in epithelial or mucosal cells which limits its growth, adhesion and bacterial load [42].

Bifidobacterium animalis subsp. lactis and *Lactobacillus lactis subsp. lactis* act at the brain-gut axis to improve mental health by contributing to the early development of normal social and cognitive behaviors and modulating the functionality of the central nervous system through metabolic, neuro-endocrine and immune pathways [43].

Gut flora are important determinants of susceptibility to obesity and type 2 diabetes mellitus (T2DM) due to their abilities to promote body weight gain, insulin resistance and chronic inflammatory conditions via dysbiosis. Hence, a potential target against obesity and diabetic conditions is to modulate the gut flora. Probiotics have been reported to play important roles

in the prevention of and treatment for diabetes and obesity by acting as gut flora modulators and impeding the progression and complications of diabetes through enhanced antioxidant system. Recent studies have found that; probiotic strains of Bifidobacteria and Lactobacilli show beneficial effects on obesity and type-2 diabetes by decreasing insulin resistance and inflammatory markers in human subjects [44, 45, 46].

More beneficial health effects include; vitamins synthesis and protein pre-digestion, immune system strengthening, reduction of depressive disorders, reduction in ulcers and intestinal tract infections, reduction of metabolic disorder, stimulation of repair cells' repair mechanism, improvement of feed digestibility protection against vaginal or urinary tract infections, increased nutritional value and maintenance of mucosal integrity, reduction in catabolic products eliminated by kidney and liver, break down and rebuilding of hormones, decalcification of bones in the aged, relieving anxiety and formation, maintenance, or reconstruction of a well-balanced indigenous microbial communities of the intestinal and/or respiratory system(s) [32].

4. ROLES IN DISEASES PREVENTION AND CONTROL

4.1 Probiotics and Allergy: Allergies are hypersensitivity reaction in response to a particular foreign substance called allergens. This is often initiated by an immunological mechanisms directed solemnly towards the alien agent. However, it is often over-reactive in action, thereby, causing harm to the body system. Research has shown that probiotics can help alleviate the effect of allergic reaction by decreasing the inflammation which ensue as a result of such reaction, stabilizing the body immune system, strengthening the gut lining and finally providing healing mechanism to the damaged digestive system. The probiotic does this by altering the appearance of the foreign agent (antigen), thereby making it available for unbinding, hence phagocytosed by mobile cells. It can also reduce their capacity to produce immune response, intestinal permeability or promote inflammatory cytokines that are characteristics of individuals with diverse allergies reaction [47]. Examples of such probiotics include *Lactobacillus* GG and *L. rhamnosus* GG which reduce food allergies and risk to develop allergic diseases in general [48]. Other well established methods to quench this disorder is by blocking the translocation of antigen to blood barrier, enhancing the mucosal barrier functioning and keeping in check, over-reactive immunological response.

4.2 Probiotics and Blood Pressure: Probiotics have also been found to reduce blood pressure. It does this by regulating all mechanism associated with body's blood pressure and water content – improving the level of total cholesterol and low-density lipoprotein, reducing the blood glucose level and insulin resistance and maintaining the renin-angiotensin system [49]. Commonly used Probiotics include *Lactobacillus rhamnosus* GG, *Lactobacillus casei*, *Lactobacillus rhamnosus*, *Lactobacillus bulgaricus*, *Bifidobacterium longum*, *Saccharomyces cerevisiae*, *Streptococcus thermophiles*, *Bifidobacterium breve*, *Lactobacillus delbrueckii subsp. bulgaricus*, *Lactobacillus helveticus* and *Lactobacillus kefir* [50].

4.3 Probiotics and Inflammatory Bowel Disease: Inflammatory bowel disease commonly associated with the inflammation of the colon results to diarrhea, cramping, loss of appetite and weight, which can be relieved by probiotics. Crohn's disease, Ulcerative colitis can be treated by stabilizing the immunologic barrier in the gut mucosa thereby preventing the provocation of inflammatory cells. In addition, probiotics help inhibits the growth of pathogenic microorganisms, produce useful products such as antimicrobial

substances and improve the barrier function of epithelial cells and immune regulation. It is noteworthy to add here that probiotics are strain- and dose-dependent [51].

4.4 Probiotics and Urogenital infections (Bacterial vaginitis): Vaginitis, which is an abnormal condition that results in the proliferation of pathogenic organisms in the vaginal, is characterized by heavy unpleasant discharges. Urinary tract infection on the other hand is an infection which involves the kidney, ureter, bladder or urethra. As a result of changes in the vaginal environmental condition which decreases the number of beneficial microbes Lactobacilli, the urogenital infection sets in. *Lactobacillus* spp are the most abundant microflora of the vaginal ducts that dominate over the persistence of opportunistic microorganisms present in vagina. They, in aggregate produce biofilm that covers the urogenital area, and therefore proffer security. As they diminish in number, the protection they rendered against the bad microbes hitherto diminishes, hence giving room for colonization. Irrefutable clinical trials abound that support the positivity of Lactobacilli. Examples of probiotic used as capsule that has shown to be very effective to prevent recurrent bacterial vaginitis include *Lactobacillus vaginalis*, *Lactobacillus rhamnosus*, *Lactobacillus acidophilus*, *Streptococcus thermophilus*, *Lactobacillus crispatus* and *Lactobacillus reuteri* [52].

These organisms achieve this by:

- Provoking an immune response;
- Competing for space, nutrients and other essential product with pathogenic organisms thereby dominating over them and hence reducing their number to quantum;
- *Lactobacillus* spp. for example lowers the pH condition of the vaginal environment corollary turning it acidic which is mostly unsuitable for the proliferation of other organisms [53];
- Others produce antimicrobial substances, for examples bacteriocins, hydrogen peroxide which serve as inhibitive substances to pathogenic organisms and increase the abundance of probiotics.

4.5 Probiotics and Liver Diseases: Research has shown that liver diseases can be curbed by probiotics. Numerous normal flora which resides in the intestinal mucosa plays a significant role in the hepatocytes function. Changes in these organisms or their numbers predispose the liver to dysfunctions such as cirrhosis, hepatic encephalopathy, nonalcoholic fatty liver disease and alcoholic liver disease. Probiotics as a novel treatment strategy against liver disease is used to regulate, restore and alter the gut microflora and improve the immune functions [54]. They may help in the treatment of chronic liver diseases since they block the entry of microorganisms to blood flow and therefore to liver, thereby, increasing their barrier [55].

4.6 Probiotics and Cholesterol Assimilation: Increase cholesterol level in the blood is considered a major health risk factor for the development of coronary heart disease. Therefore, reducing this risk is of utmost health importance. The Lactic acid bacteria strains (LAB) are used as probiotic to bring down the mechanism of cholesterol. Cholesterol, which is normally synthesized in the liver, can be brought down by direct or indirect means. Direct means can be achieved by inhibition of the first line of synthesis or decrease their intestinal dietary absorption. This decrease is amplified by three methods namely – assimilation, in which the probiont takes them up for their digestion; or binding, in which the probionts attach to the cholesterol molecules, making them unavailable to be synthesized in the level, and

lastly by degradation, here the probiotics break them down into small molecules (catabolic products). The other way as mentioned involve indirect way. Here, the cholesterol level is decreased by splitting the cholesterol by bile acids, thereby lessening their build up [56]. Some of the LAB essential in this includes *Lactobacillus plantarum*, *L. pentosus* LP05, *L. reuteri* and *L. brevis* LB32 [57].

4.7 Probiotics and Dental Caries: Dental caries, a progressive decay in area of the tooth which usually results to death of the tooth can be mitigated by probiotics. This corrosive demineralization following changes in the stability of the oral environment that prompts propagation of biofilm, notoriously compose of *Streptococci mutans* group. To be potential inhibiting organism, probiotics must be overly able to spread and stick to the dental surfaces thereby competing for space, nutrients and metabolic advantage with the dental biofilm. It must coordinate and antagonize the oral pathogenic organisms, thereby, hindering their proliferation. The incorporation of probiotics in dairy products is in their ability to neutralize their acidity. Hence, probiotics should, characteristically, result in minimal acid production. For instance, organisms in cheese prevent this demineralization and advance the re-mineralization of the enamel [58].

4.8 Probiotics and Orthodontic Treatment: Orthodontic treatment which usually left white lesion spots is caused by *Streptococcus mutans* and be curbed by probiotics. These friendly microbes address this by fine-tuning lopsidedness in the oral cavity, thereby reducing the numbers of pathogenic organism therein and adjusting the pH to favorable condition, not conducive for the pathogens [59]. In addition, just like medical instrument, appliances use in the orthodontic treatment can house or promote the proliferation of microbes and subsequently increase biofilms formation. *Lactobacilli brevis*, *Bifidobacterium animalis subsp. lactis* BB-12 and *Bifidobacterium lactis*, all have been shown to reduce *S. mutans* levels in dental plaque [60].

4.9 Probiotics and Oral Health: Probiotics has shown to destroy the presence of harmful microbes and maintaining a healthy gum and teeth. As probiotics is a natural product, it is expected not to associate with any side effects [61, 62]. Halitosis or offensive breath results from the anaerobic proliferation of organism in the mouth which leads to unpleasant odor. Other causes are typical to specific foods, metabolic disorders, respiratory tract infections and some irregularities in the normal flora of the oral cavity. As stated earlier, it begins from the action of anaerobes that implicate saliva, then break down the proteins to form amino acids, then to sulphur compounds, including methane thiol and hydrogen. Of importance is *Streptococcus salivarius* that act as a commensal probiotic of the oral cavity [63]. *S. salivarius* produces bacteriocin, an essential natural product that potentially diminishes the quantity of sulphur-producing organisms in the oral milieu. [64] claims that, gum or capsules containing *S. salivarius* K12 reduces the levels of volatile sulphur compounds among patients diagnosed with halitosis. There is copious evidence that taking a probiotic supplement regularly such as *Lactobacillus casei*, *L. reuteri*, *L. salivarius*, *Weissella cibaria* and *Streptococcus salivarius* could regulate the growth of harmful bacteria [65].

4.10 Probiotics and Periodontal Diseases: Periodontal diseases are diseases of the gum and its environments. Studies have reviewed that the persistence of Lactobacilli,

most especially *Lactobacillus gasseri* and *L. fermentum*, in the oral cavity were found to be more common among health participants than patients with chronic periodontitis. Other Lactobacilli have been reported to offer protection by repressing the development of periodontal pathogens, including *Porphyromonas gingivalis*, *Prevotella intermedia* and *Aggregatibacter actinomycetemcomitans*. It was recommended that Lactobacilli living in the dental cavum could play a key role in the ecological reconstitution of the area (Gupta, 2011). These and other organisms such as *Lactobacillus casei*, *L. reuteri*, *L. brevis*, *L. salivarius*, and *Bacillus subtilis*, aid in anti-inflammatory activity by decreasing the pathogens implicated with periodontal tissues [66].

Comment [JLSdS3]: Bring together topics 2.7, 2.8, 2.9 and 2.10 in a single section, as they talk about common issues.

4.11 Immunologic Enhancement/ Immunity Stimulation: Generally, as a natural product, probiotic, as seen in some of their mechanisms of action can enhance or provoke the stimulation of immune response. It does this by activating the modulation of IgA and local macrophages or food antigens, to modification in the pro- and anti-inflammatory cytokins [67]. The immuno-stimulatory effects of Lactobacilli make them an excellent candidate for probiotic application. They help in defense against tumors and infections, adjunct the impact of antigen-antibody response, regulate Th₁ and Th₂ cells, produce anti-inflammatory proteins, improve granulocytes engulfment and enhance the release of immunoglobulin in blood so as to scale up antibody production [68].

4.12 Probiotics and Human Immunodeficiency Virus (HIV): As probiotics stimulate innate immunity that provide the frontline defense, improve gut barrier function, and proffer supports for a strong maintenance of epithelia layer, they can therefore help minimize the jumping of bacterial pathogens and viral particles. When an immune system is well established, it prevents the fervent replication of HIV virus and slows down the progressive development of AIDS in host. It therefore observed that daily intake of probiotics for a prolonged period improves the counts of CD4 in the target cells of HIV virus. Research also has revealed that screening of volunteers' saliva taking Lactobacillus strains produced some kinds of proteins that fit for binding mannose found on HIV envelope which makes them unbind-able to host CD4 cells. Moreover, it is believed that Lactobacilli trigger the cluster of immobilize cells that housed HIV, hence prevent them from infecting other nearby cells [69].

5. CONCLUSION

Probiotics have been widely studied and explored commercially in many different products in the world and have been reported to offer potential benefits such as; improved nutrition, improved growth, prevention of various gastrointestinal disorders and their profoundly function in enhancing the immune system. In some countries, probiotics are taken as prophylactic agents like in the prevention of infantile diarrhea, while in some, they are popular therapeutic agent. Definitive microbiological interventions through probiotic research aims to minimize pathogen invasion and colonization of the body by -----the specific target function of probiotics/ probiotic products in the human alimentary canal particularly in the prophylaxis and therapy of already known human diseases. Probiotics have wider applications in food industries, as non-pharmacological approaches for health management and have been reported to enhance GIT all over transit because they produce vitamins and contribute to vitamin availability in the human host. The consumption of probiotics is also useful in reducing the risks, objective and subjective symptoms of specific human diseases.

5.1 Future perspective

Probiotics are generally unstable and most of the time, lose their function and useful property/viability to low stomach pH and high bile salt conditions in the intestine. Recently, research are being focused on solving the problem of probiotic stability and viability and several technological innovations are being developed, one of these is encapsulation. Encapsulation works by trapping the potentially sensitive probiotic strains to shield it from external influence via a mechanical or physicochemical process. This allows storage of viable bacteria at room temperature and subsequent incorporation into a wide range of food and pharmaceutical products. More studies should be focused on discovering microbial encapsulators that not only serve as a delivery channel, but also directly or indirectly improve the overall characteristics of the probiotic strain. brief acknowledgement section may be given after the conclusion section just before the references. The acknowledgments of people who provided assistance in manuscript preparation, funding for research, etc. should be listed in this section. All sources of funding should be declared as an acknowledgement. Authors should declare the role of funding agency, if any, in the study design, collection, analysis and interpretation of data; in the writing of the manuscript. If the study sponsors had no such involvement, the authors should so state.

REFERENCES

1. Morgan XC, Segata N, Huttenhower C. Biodiversity and functional genomics in the human microbiome. *Trends Genet.* 2013; 29(1), 51–58.
2. McKenzie YA, Thompson J, Gulia P, Lomer MCE. British Dietetic Association systematic review of systematic reviews and evidence-based practice guidelines for the use of probiotics in the management of irritable bowel syndrome in adults (2016 update). *J Hum Nutr Diet.* 2016; 29(5), 576–592.
3. Singh U, Sanadi RM. Probiotics and Prebiotics. *Int Educ Res J.* 2018; 4(9): 16-18.
4. Carlos RS, Luciana Porto de Souza V, Michele RS. The potential of probiotics. *Food Tech Biotech.* 2010; 48(4):413–434.
5. Vijayaram S and Kannan S. Probiotics: The marvelous factor and health benefits. *Biomed Biotechnol Res J.* 2018; 2:1-8.
6. Almada CN., Martinez RC, Sant'Ana AS.. Characterization of the intestinal microbiota and its interaction with probiotics and health impacts. *Appl Microbiol Biotechnol.* 2015; 99: 4175–4199.
7. Babak H, Minoo H, Yousef N. Probiotic assessment of *Lactobacillus plantarum* 15HN and *Enterococcus mundtii* 50H isolated from traditional dairies microbiota. *Adv Pharm Bull.* 2016; 6(1):37-47.
8. Ciorba MA. A gastroenterologist's guide to probiotics. *Clin Gastroenterol Hepatol.* 2012; 10(9): 960-968.
9. Ahmed Z, Haque M, Sayeed N, Uddin ME, Akter T. Review on probiotics: It's uses and applications. *World J Pharm Res.* 2016; 5(5): 24-34.
10. Adel MM, Sari AM. Probiotic characterization of lactic acid bacteria isolated from local fermented vegetables (makdoos). *Int J Curr Microbiol Appl Sci.* 2017; 6(2):1673-86.
11. Maria K, Dimitrios B, Stavroula K. Health Benefits of probiotics: A review. *ISRN Nutr.* 2013; 1-7.
12. Stefania P, Marco R. 2017. Description of a novel probiotic concept: Implications for the modulation of the immune system. *Am J Immunol.* 2017; 13(2):107-13.

13. Bermudez-Brito M, Plaza-Díaz J, Muñoz-Quezada S, Gómez-Llrente, C, Gil A. Probiotic mechanisms of action. *Annals of Nutrition and Metabolism*. 2012; 61:160-74.
14. Miriam BB, Julio PD, Sergio MQ. Probiotic mechanisms of action. *Ann Nutr Metab*. 2012; 61:160–174.
15. Ghadimi D, Folster Holst R, de Vrese M. Effects of probiotic bacteria and their genomic DNA on TH1/TH2cytokineproduction by peripheral blood mononuclear cells (PBMCs) of healthy and allergic subjects. *Immunobiology*. 2008; 213:677-692.
16. Lehtoranta L, Latvala S, Lehtinen MJ. Role of Probiotics in Stimulating the Immune System in Viral Respiratory Tract Infections: A Narrative Review. *Nutrients*. 2020; 12:3163.
17. Ravinder N, Ashwani K, Manoj K. Probiotics, their health benefits and applications for developing healthier foods: a review. *FEMS Microbiol Lett*. 2012; 334:1–15.
18. Taverniti V, Scabiosi C, Arioli S. Short-term daily intake of 6 billion live probiotic cells can be insufficient in healthy adults to modulate the intestinal *Bifidobacteria* and *Lactobacilli*. *J Funct Foods*. 2013; 6:482–491.
19. Bintsis T. Lactic acid bacteria: their application in foods. *J Bacteriol Mycol*. 2018. <https://doi.org/10.15406/jbmoa.2018.06.00182>.
20. Linares DM, Gómez C, Renes E, Fresno JM, Tornadijo ME, Ross RP. et al. Lactic acid bacteria and bifidobacteria with potential to design natural biofunctional health-promoting dairy foods. *Front Microbiol*. 2017; 8:846.
21. Boostani A, MahmoodianFard HR, Ashayerizadeh A, Aminafshar M. Growth performance, carcass yield and intestinal microflora populations of broilers fed diets containing Thepax and yoghurt. *Braz J Poult Sci*. 2013; 15: 1-6.
22. Toghyani M, Mosavi SK, Modaresi M, Landy N. Evaluation of kefir as a potential probiotic on growth performance, blood biochemistry and immune responses in broiler chicks. *Anim Nutr*. 2015; 1:305-309.
23. Oranusi S, Dahunsi SO. Preliminary study on hazards and critical control points of kokoro, a Nigerian indigenous fermented maize snack. *SpringerPlus*. 2015; 4:253.
24. Adesulu-Dahunsi AT, Dahunsi SO, Olayanju A. Synergistic microbial interactions between lactic acid bacteria and yeasts during production of Nigerian Indigenous fermented foods and beverages. *Food Control*. 2019. <https://doi.org/10.1016/j.foodcont.2019.106963>.
25. Prasannaa PHP, Grandison AS, Charalampopoulou D. Bifidobacteria in milk products: An overview of physiological and biochemical properties, exopolysaccharide production, selection criteria of milk products and health benefits. *Food Res Int*. 2014; 55:247-262.
26. Corbo MR, Albenzio M, De Angelis M, Sevi A, Gobbetti, M. Microbiological and biochemical properties of Canestrato Pugliese hard cheese supplemented with bifidobacteria. *J Dairy Sci*. 2001; 84:551-561.
27. Altieri C.. Dairy propionibacteria as probiotics: Recent evidences. *World J Microbiol Biotechnol*. 2016; 32: 172.
28. Houem R, Fillipe LR, Gwenael J. 2017. Dairy Propionibacteria: Versatile Probiotics. *Microorganisms*. 2017; 5(2): 24.
29. Hossain S, Al-Bari A, Wahed I. Biochemical characterization of probiotics available in Bangladesh. *J Sci Res*. 2016; 8(1): 101.
30. Mulero-Cerezo J, Briz-Redón A, Serrano-Aroca Á. *Saccharomyces cerevisiae* var.bourladii: Valuable probiotic starter for craft beer production. *J Appl Sci*. 2019; 9(16): 3250.
31. Yunita D, Dodd CE. Microbial community dynamics of a blue-veined raw milk cheese from the United Kingdom. *J Dairy Sci*. 2018; 101(6): 4923–4935.
32. Braiek OB, Smaoui S. Enterococci: Between Emerging Pathogens and Potential Probiotics. *Biomed Res Int*. 2019. <https://doi.org/10.1155/2019/5938210>.

33. Vandera E, Kakouri A, Koukkou A, Samelis J. Major ecological shifts within the dominant nonstarter lactic acid bacteria in mature Greek Graviera cheese as affected by the starter culture type. *Int J Food Microbiol.* 2019; 290:15–26.
34. Gaaloul N, Ben Braiek O, Hani K, Volski A, Chikindas ML, Ghrairi T. Isolation and characterization of large spectrum and multiple bacteriocin-producing *Enterococcus faecium* strain from raw bovine milk. *J Appl Microbiol.* 2015; 118(2): 343–355.
35. Fernandez-Pacheco P, Arevalo-Villena M, Bevilacqua A, Corbo MR, Perez AB. Probiotic characteristics in *Saccharomyces cerevisiae* strains: Properties for application in food industries. *LWT-Food Sci Technol.* 2018; 97:332-340.
36. Herbel SR, Vahjen W, Wieler LH, Guenther S. Timely approaches to identify probiotic species of the genus *Lactobacillus*. *Gut pathog.* 2013; 5:27.
37. Suárez JE. Microbiota autóctona, probióticos y prebióticos. *Nutr Hosp.* 2015; 31: 3–9. Spanish.
38. Ilavenil S, Vijayakumar M, Kim DH, Arasu M, Park HS, Ravikumar S. et al. Assessment of probiotic, antifungal and cholesterol lowering properties of *Pediococcus pentosaceus* KCC-23 isolated from Italian Ryegrass. *J Sci Food Agric.* 2016; 96: 593–601.
39. Giardina S, Scilironi C, Michelotti A. In vitro anti-inflammatory activity of selected oxalate-degrading probiotic bacteria: potential applications in the prevention and treatment of hyperoxaluria. *J Food Sci.* 2014; 79 (3):384-390.
40. Kumar K, Sastry N, Polaki H, Mishra V. Colon cancer prevention through probiotics: An overview. *J Cancer Sci Ther.* 2015; 7:81-92.
41. Kahouli I, Tomaro-Duchesneau C, Prakash S. Probiotics in colorectal cancer (CRC) with emphasis on mechanisms of action and current perspectives. *J Med Microbiol.* 2013; 62:1107–1123.
42. Yvan V, Geert H, Georges D. 2015. Probiotics: An update. *J Pediatr (Rio J).* 91(1):6-21.
43. Tillisch K, Labus J, Kilpatrick L. Consumption of fermented milk product with probiotic modulates brain activity. *Gastroenterol.* 2013; 144:1394–1401.
44. Tilg H, Moschen AR. Microbiota and diabetes: An evolving relationship. *Gut.* 2014; 63(9): 1513-1521.
45. Zhang YJ, Li S, Gan R, Zhou T, Xu D, Li H. Impacts of gut bacteria on human health and diseases. *Int J Mol Sci.* 2015; 16(4): 7493-7159.
46. Shah NJ, Swami OC. Role of probiotics in diabetes: A review of their rationale and efficacy. *EMJ Diabet.* 2017; 5(1): 104-110.
47. Shyamala R, Gowri P, Meenambigai P. Probiotics and its effects on human health-A Review. *Int J Curr Microbiol Appl Sci.* 2016; 5(4):384-392.
48. Licciardi PV, Ismail IH, Balloch A. Maternal supplementation with LGG reduces vaccine-specific immune responses in infants at high-risk of developing allergic disease. *Front Microbiol.* 2013; 4:381.
49. Golnaz E, Mitra Z, Sharma A. Effects of symbiotic and vitamin e supplementation on blood pressure, nitric oxide and inflammatory factors in non-alcoholic fatty liver disease. *EXCLI J.* 2017; 16:278-290.
50. Rerksupphol S, Rerksupphol L. A Randomized doubleblind controlled trial of *Lactobacillus acidophilus* Plus *Bifidobacterium bifidum* versus placebo in patients with hypercholesterolemia. *J Clin Diagn Res.* 2015; 9(3):1-4.
51. Momir MM, Maja PS, Gordana MB. Probiotics as a promising treatment for inflammatory bowel disease. *Hospital Pharmacology - International Multidisciplinary Journal.* 2014; 1(1):52-60.
52. Lorenzo S, Francesca P, Diana IS. Determination of antibacterial and technological properties of vaginal *Lactobacilli* for their potential application in dairy products. *Front Microbiol.* 2017; 8(166):1-12.

53. Lunia MK, Sharma BC, Sharma P. Probiotics prevent hepatic encephalopathy in patients with cirrhosis: A randomized controlled trial. *Clin Gastroenterol Hepatol*. 2014; 12:1003–1008.
54. Leila J, Mostafa G, Manouchehr K. The effect of probiotic and/or prebiotic on liver function tests in patients with nonalcoholic fatty liver disease: A double blind randomized clinical trial. *Iran Red Crescent Med J*. 2017; 1-9.
55. Cesaroa C, Tisoa A, Pretea AD. Gut microbiota and probiotics in chronic liver diseases. *Digest Liver Dis*. 2011; 43:431-438.
56. Bordoni A, Amaretti A, Leonardi A. Cholesterol lowering probiotics: In vitro selection and in vivo testing of bifidobacteria. *Appl Microbiol Biotechnol*. 2013; 9:8273–8281.
57. Narwal A. Probiotics in dentistry – A review. *J Nutr Food Sci*. 2011; 1(5):1-4.
58. Tandon V, Arora V, Yadav V. Concept of probiotics in dentistry. *International Journal of Dental and Medical Research*. 2015; 1(6):206-209.
59. Armelia SW, Shirley TY, Tjokro P. Consumption of yogurt containing probiotic *Bifidobacterium lactis* reduces *Streptococcus mutans* in orthodontic patients. *Sci Dent J*. 2018; 1:19-25.
60. Chitra N. Bacteremia associated with probiotic use in medicine and dentistry. *Int J Innov Res Sci Eng Technol*. 2013; 2(12):7322-7325.
61. Dhawan R, Dhawan, S. Role of probiotics on oral health: A randomized, double-blind, placebo-controlled study. *J Interdiscip Dent*. 2016; 3:71-8.
62. Lesan S, Hajifattahi F, Rahbar M. The effect of probiotic yoghurt on the frequency of salivary candida. *J Res Dentomaxillofacial Sci*. 2017; 2(2):1-7.
63. Bonafait L, Chandad F, Grenier D. Probiotics for oral health: Myth or Reality. *J Can Dent Assoc*. 2009; 75(8):585-590.
64. Gupta G. Probiotics and periodontal health. *J Med Life*. 2011; 4(4):387-394.
65. Zohreh K, Sayyed HG, Mahboobeh MN. Probiotic bacteria against halitosis producing bacteria, in the presence of the hep 2 cells. *Acta Medica Mediterr*. 2017; 33:301-4.
66. Monica, V., Antonio, S. and Deborah, V. Clinical changes in periodontal subjects with the probiotic *Lactobacillus reuteriprodentis*: A preliminary randomized clinical trial. *Acta Odontol Scand*. 2013; 71:813–819.
67. Kabeerdoss J, Devi RS, Mary RR. Effect of yoghurt containing *Bifidobacterium lactis Bb12* on fecal excretion of secretory immunoglobulin A and human beta-defensin 2 in healthy adult volunteers. *Nutr J*. 2011; 10:138.
68. Maldonado GC, Cazorla SI, Lemme Dumit JM, Vélez E, Perdigon G. Beneficial effects of probiotic consumption on the immune system. *Ann Nut Metab*. 2019; 74: 115-124.
69. Pranay J, Priyanka S. 2012. Probiotics and their efficacy in improving oral health: A review. *J Appl Pharmacol Sci*. 2012; 2(11):151-163.