

Health benefits of probiotics.

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Abstract

Probiotics are live cells refer to beneficial microorganisms that could have nutritional advantages because of having different beneficiary characteristics. They also provide health when regulated in sufficient sums. Probiotic strains exhibit powerful activity in human health improvement. The main probiotic groups are *Lactobacillus*, *Bifidobacterium*, *Pediococcus*, *Lactococcus*, *Bacillus* and yeasts strains which are used frequently. Probiotics recently have become a subject of great interest in the field of microbiology, especially their role in normal physiology and its impact on human health during infection. The utilization of probiotics has prompted promising outcomes in countless well-designed clinical studies. For example, as a therapeutic option for the treatment, forestall and control of various disorders and illnesses like, gastrointestinal diseases, allergy, urogenital infections, *Helicobacter pylori* infection, inflammatory bowel syndrome and diarrhea and colon cancer. Currently, it has become one of the fruit full and attractive research area as it can prevent and treat communicable and non-communicable human diseases. Different clinical study outcome supports this idea. The results of such extensively studied and explored could demonstrate the improvement of health and quality of life. Their prospective potential application is in functional foods for better health and nutrition of the society. This review presents all the information on probiotics use in human clinical traits and their functional application in health areas all information are presented. This article outlines the currently available data on the potential advantages of probiotics for health.

Keywords: Probiotics, Diseases, Mechanism, Safety, Gastro intestinal track, Lactic acid bacteria

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Introduction

Probiotics refer to harmless live normal flora /microorganisms that provide a health benefit on the host, when administered in adequate amounts and it also leads to have nutritional advantages. Regular utilization of food containing probiotic microorganisms is recommended to build a positive balance of the population of useful or beneficial microbes in the intestinal flora. Probiotic microorganisms such as *Bifidobacterium* and *Lactobacillus* strains are belongs here, it is found in GIT and food supplements, it is highly mind bogging and diverse, its composition and number differs. The gut microbiota plays a critical part in upkeep of human health [1-3].

Definitive objectives of microbiological interventions through probiotics might be to balance out or improve/ reestablish microbial community structure, composition and function in a body. In addition to these bring down pathogen invasion and colonization/development. Probiotic microorganisms have been reported to enhance GIT all over transit, produce vitamins and contribute vitamin availability to the human host. Probiotics have wider applications in food, feed, dairy and fermentation industry, as non-pharmacological approaches for health management [4]. Probiotic products can have specific target function in the human alimentary tract. Especially in reducing the risk and healing of human disease already known. Consumption of probiotic cells through food products is actually the most popular approach. The consumption of probiotics may also be

useful in reducing the risk of specific diseases, mitigating both objective and subjective symptoms. Probiotic microorganisms are usually available as culture concentrates in dried or deep-freeze form to be added to a food matrix. Probiotics are studied profoundly their function in enhancing all over immune system [5,6]. The normal flora in GIT contribute significant role in the maintenance of health. These are structure and histological function, metabolic functions and protective functions which is with the aid of microbes, enteric toxin reduction and cleansing takes place inside the body.

Probiotics are usually introduced to food, condiments and beverages as a component of fermentation process at appropriate stage. Due to their long time survival and multi-purpose capacity. There are different rout of administered mechanisms based on age class interval. It can be taken orally in the form of capsule or probiotic food. In order to crate and supply health effect, probiotic cells are constantly viable in the food carries and adapt extreme harsh environment of GIT. In another hand, it must be stable during Gastro intestinal transit and fulfill at least cell count become 10^6 CFU g^{-1} . Despite the fact that dairy-based items are proposed to be the principle bearers for the conveyance of probiotics, other nondairy based items [7]. The term probiotics includes countless bacteria and other different microorganisms, for example, yeast, and every probiotic strain acts particularly. In this manner, when a specific medical advantage has been built up for one strain, this does

not imply that all probiotics can present this medical advantage. Each strain must be tried for a specific impact independently.

The aim of this paper is to provide a better understanding about probiotics, push for more trials about the mentioned aspects of use and summarizes the up-to-date studies on probiotic effects on human health.

The relation of Probiotics to our health could be summarized in the following main points and facts:

1. Probiotics are helpful formed of friendly microorganisms.
2. Probiotics can fighters at any circumstance with harmful microorganisms and maintain/ colonize human digestive system.
3. Probiotics helps in breaking of food into much smaller complex by fermenting it and promoting our health by many different mechanisms.
4. Probiotic quantity and quality is minimized/declined due to many reasons such as: incorrect diet, alcohol, age and so on. This is why they should be taken through our regular diet.
5. Probiotics in some cases like after antibiotic treatments, where they are highly sensitive to be affected severely, so in order to overcome the challenge they must be taken in proper quantity through orally or with food.
6. Probiotics are actively encouraging health condition as it:
 - A. Pulverize the symptom of the pathogens or the hurtful microorganisms.
 - B. Nourishes the body with valuable byproducts.
 - C. Assists our digestive system by decrease its job.
 - D. Limit the impact of the primary assault of harmful compounds, rather than our cells, by their biofilm, which secures our digestive system.
 - E. Lessen the measure of food required by our bodies because of the right absorption and digestion of any amount of food.
 - F. In some cases probiotics could complement the deficiency in our hereditary material by helping us to borrow the products of their genes (such as in case of the lactose fermentation deficiency). Here we should feature that, Probiotics or anything in our lives ought not to surpass a specific farthest point and ought to be utilized shrewdly to give the best expected outcomes [8].

What are probiotics?

According to the currently adopted definition, by WHO/Food and Agriculture Organization (2010) probiotics are an oral supplement or a food product that contains a sufficient number of viable microorganisms to alter the micro flora of the host and has the potential for beneficial health effects on host, which when it is administered in adequate amounts [9,10].

Species used

Numerous microbial species have been used as probiotics. They can be yeast, bacteria or molds. But most commonly, bacterial species are predominant (Table 1) [2,11-16].

Characteristics of a good probiotics

In different research studies, probiotics have unique potential properties. To be considered for use and selection as probiotic its safety, technological, and functional characteristics must be sought. Moreover, the following criteria need to be fulfilled:

1. Probiotics should be able to create a beneficial effect on host animal by increasing resistance to diseases.
2. Probiotics must be from human origin.
3. Probiotics needed to have excessive cell viability.
4. Probiotics should be non-pathogenic and non-toxic.
5. It should be able enough to interact or send signals to immune modulator activity.
6. It must have ability to influence local metabolic activity.
7. It ought to be fit for surviving and processing in the gut condition like resistance to low pH and organic acids.
8. Probiotics must be stable, safe, effective and equipped for staying viable for periods under storage and field conditions.
9. It must have power of restore and replace the intestinal micro flora.
10. It should have anti-carcinogenic and anti-mutagenic activity, cholesterol lowering effects, can maintain mucosal integrity and can enhance bowel motility [13].
11. It should be able to speed up, facilitate and colonize/maintain the digestive tract.
12. They must have the ability to resist gastric juices and the exposure to bile acid which seems to be crucial for oral administration.
13. Adhesion to mucosal and epithelial surfaces, an important property for successful immune modulation, competitive exclusion of pathogens, as well as prevention of pathogen adhesion and colonization.
14. Antimicrobial activity against pathogenic bacteria.
15. Bile salt hydrolase activity [15-17].
16. Antibiotic resistance may help them to survive in the presence of administered drugs and other antimicrobial compounds [4,15,16,18].
17. Fast multiplication, with either permanent or temporary colonization of the gastrointestinal tract.
18. Stabilization of the intestinal micro flora and non-pathogenicity.
19. Survival on passing through gastrointestinal tract at low pH and in contact with bile [15,16,19,20].

The minimum requirements needed for probiotic status include:

1. Assessment of strain identity (genus, species and strain level).
2. *In vitro* tests to screen potential probiotics: such as resistance to gastric acidity, bile acid, and digestive enzymes as well as antimicrobial activity against potentially pathogenic bacteria.

Table 1. Species used as probiotics.

List of probiotic species	Group of Microbes	Reference
<i>Lactobacillus acidophilus</i> , <i>Lactobacillus bulgaricus</i> , <i>Lactobacillus casei</i> , <i>Lactobacillus fermentum</i> , <i>Lactobacillus lactis</i> , <i>Lactobacillus acidophilus</i> , <i>Lactobacillus paracasei</i> , <i>L. rhamnosus</i> , <i>L. delbrueckii subsp. bulgaricus</i> , <i>L. brevis</i> , <i>L. johnsonii</i> , <i>Lactobacillus plantarum</i> , <i>Lactobacillus salivarius</i> , <i>Lactobacillus fermentum</i> , <i>Lactobacillus kefir</i>	Lactic acid producing bacteria	[2,11-16]
<i>Enterococcus faecalis</i> , <i>Enterococcus faecium</i> , <i>Escherichia coli</i> Nissle, <i>Streptococcus thermophiles</i> , <i>Propionibacterium</i>	Non lactic acid producing bacteria	
<i>Bifidobacterium adolescentis</i> , <i>Bifidobacterium bifidum</i> , <i>Bifidobacterium breve</i> , <i>Bifidobacterium lactis</i> , <i>Bifidobacterium longum</i> , <i>Bifidobacterium infantis</i> , <i>B. animalis subsp animalis</i> , <i>B. animalis subsp lactis</i> , <i>B. bifidum</i>	Bifidobacterium species	
<i>Sacchromyces boulardii</i>	Nonpathogenic yeast	
<i>Coccobacillus</i> , <i>Lactobacillus</i> , <i>Streptococcus</i> , <i>Leuconostoc</i> , <i>Lactococcus lactis subsp. Lactis</i> , <i>Pediococcus</i> , <i>Propionibacterium</i> , <i>Enterococcus</i> , <i>Enterococcus durans</i> , <i>Bifidobacterium</i> , <i>Bacillus</i> , <i>Bacillus coagulans</i> , <i>Bacillus subtilis</i> , <i>Saccharomyces cerevisiae</i> , <i>Candida pintolopesii</i> , <i>Aspergillus niger</i> , <i>A. oryzae</i> , <i>Bacillus licheniformis</i> , <i>B. cereus var. toyoi</i> , <i>B. clausii</i> , <i>B. coagulans</i> , <i>B. laterosporus</i> , <i>B. pumilus</i> , <i>B. racemilacticus</i> , <i>Streptococcus thermophiles</i>	Non spore forming	

3. Safety assessment: requirements for proof that a probiotic strain is safe and without contamination in its delivery form.

4. *In vivo* studies for substantiation of the health effects in the target host.

Mechanism of action

Probiotics have various mechanisms of action currently, three major ways of action of probiotics have been revealed. The first one is a competition for nutrients and for ecological niche at this time the indigenous anaerobic flora limits the concentration of potentially pathogenic flora in the digestive tract. Probiotics can have a direct effect on other microorganisms through inhibition of pathogen adhesion this kind of major defense mechanism is used to maintain internal health condition. *Lactobacilli* and *bifidobacteria* have been shown to inhibit a broad range of pathogens by performing colonization of pathogenic bacteria and finally by doing antagonistic activity against gastrointestinal pathogens. 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 involved in the production of anti-microorganism substances, bacteriocins, toxins, organic acids, short chain fatty acid production, lowering of gut pH. These substances are responsible for inhibit the growth of other harmful microbes such as foodborne pathogens and spoilage organisms in GIT environment then lead to the death of the pathogen by creating antagonistic condition, and such action may result in the inactivation of toxins. Probiotic mode of effects are carried out based on microbial products which is determine a specific probiotic action and its effective application for the prevention or treatment of a certain disease by destruction of target cell. The third mechanism is the stimulation/modulation of specific and nonspecific immune response by T-cell activation, to cytokine production/throughout immunomodulation by inducing phagocytosis and IgA secretion, modifying T-cell responses, enhancing Th1 responses, and attenuating Th2 responses. This mode of action is most likely important in the prevention and therapy of infectious diseases [17,21-24]. Probiotic bacteria can exert an immunomodulatory effect. These bacteria have the ability to interact with epithelial and dendritic cells (DCs) and with monocytes/macrophages and lymphocytes. In various strategies they are interact and modulate the immune system in a good manner [2]. 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 [25,26].

The probiotics have a three step action mechanism

(i) It stimulates and modulates immune response.

(ii) It normalize intestinal microflora by ensures colonization resistance and controls irritable bowel syndrome and other inflammatory bowel diseases.

(iii)The final mechanism is also have the metabolic effects like-bile salt deconjugation and secretion, lactose hydrolysis, reduction in toxigenic and mutagenic reactions in gut, Supply of nutrients to colon epithelium [27].

Origin of Probiotics

The major origin of probiotics are fermented non-digestible carbohydrate compounds, food supplements, dairy based compounds, non-dairy fermented food and non-intestinal sources. Probiotic microorganisms can isolated, screened, identified and characterized from numerous natural substrates. The sources of the power full strain in recent years, wide and up to now still growing. This idea also supported by team of researcher listed below. In addition to this, peoples are explored live cell containing food because it is enhance nutritive quality, bioavailability of the micro nutrients and possess anti oxidative property. Anti-oxidative property helps to fight oxidative stress, strengthens host anti oxidative defense mechanism and delays aging. Bioavailability of the micro nutrients, possess anti oxidative property also. Anti-oxidative property helps to fight oxidative stress, strengthens host anti oxidative defense mechanism and delays aging. Therefore, many probiotic foods can effective in full fill the interest of the people at all age [15,18,28-34].

Health Benefits of Probiotics

Dairy strains of lactic acid bacteria (LAB) have a long history of utilization. LAB, including diverse types of *Lactobacillus* and *Enterococcus* species, that has been consumed daily since humans started to use fermented milk as food. Probiotic impacts are strain particular the impacts depicted for one strain can't be specifically applied to others and every individual Probiotic bacterial strain has its own health benefits. The major beneficial effects are correlated against various disease conditions. Probiotics have a colossal criticalness and application in controlling different kinds of microbial infections.

Table 2. Role of probiotics in health improvement, infection control and disease treatment.

Probiotic Strains	Types of diseases or disorder	Probiotic outcomes/results	References
<i>Oxalobacter formigenes</i> , <i>Lactobacillus</i> and <i>Bifidobacterium</i> species, (<i>Lactobacillus plantarum</i> PBS067, <i>Lactobacillus acidophilus</i> LA-14, <i>Bifidobacterium breve</i> PBS077, <i>Bifidobacterium longum</i> PBS078)	Kidney/Urinary stones	(i)Modify or utilize several types of urinary stone. (ii) Act as a key tool to manipulate, metabolize and degrade a toxic compound.	[35-37]
<i>Lactobacillus</i> GG, <i>L. rhamnosus</i> Lactis, <i>Lactobacillus fermentum</i> , <i>Bifidobacterium bifidum</i> , <i>Bifidobacterium lactis</i> , <i>L. acidophilus</i> , <i>L. casei</i> , <i>L. salivarius</i> and <i>Lactococcus lactis</i>	Atopic Diseases	(i) Atopic eczema reduction is observed, and skin condition also improved. (ii) Atopic dermatitis symptoms are removed from infants who found in moderate-to severe condition. It is mainly depends on the selection of specific probiotic strains, time of administration (on set time), duration of exposure, and dosage.	[38,39]
<i>L. casei</i> , <i>L. rhamnosus</i> , <i>S. thermophilus</i> , <i>B. breve</i> , <i>L. acidophilus</i> , <i>B. infantis</i> , <i>L. delbrueckii</i> subsp. <i>Bulgaricus</i> , <i>L. reuteri</i> DSM 17938	Colic	Very effective in reducing colic in breastfed infants and children.	[40-42]
<i>Lactobacillus</i> , <i>Bifidobacterium</i> and <i>L. johnsonii</i>	<i>Helicobacter pylori</i> infection	Destruction the adverse effects of <i>H. pylori</i> through the release of bacteriocins, production of organic acids, and competitive colonization in epithelial or mucosal cells. At that time can hinder its growth, adhesion and bacterial load.	[7,43-45]
<i>Lactobacillus rhamnosus</i> , <i>L. rhamnosus</i> GG, <i>B. animalis</i> subsp. <i>lactis</i> alone or in combination with <i>S. thermophilus</i> , and <i>L. reuteri</i> , <i>L. rhamnosus</i> (not GG), and <i>L. acidophilus</i> , <i>Saccharomyces boulardii</i> , <i>Lactobacillus casei</i>	Acute and antibiotic-associated diarrhea	(i)Competitive blockage of receptor site signals regulating secretory and motility defenses. (ii) Enhancement of the immune response, and production of substances that directly inactivate the viral particles. (iii)Inhibit the growth by preventing adhesion and invasion of pathogens.	[46,47]
<i>Lactobacillus rhamnosus</i> , <i>Lactobacillus reuteri</i> , <i>Propionibacterium freudenreichii</i>	<i>Candida</i> infection	Used as a therapeutic option to combat fungal pathogen.	[48,49]
<i>Bifidobacterium</i> species, <i>Bifidobacterium lactis</i> , <i>Bifidobacterium longum</i> , <i>Bifidobacterium breve</i> , <i>Bifidobacterium infantis</i> , <i>Lactobacillus casei</i> , <i>Lactobacillus rhamnosus</i> , <i>Streptococcus thermophilus</i> , <i>Lactobacillus acidophilus</i> , <i>Lactobacillus bulgaricus</i>	Constipation	(i)Altering microflora and restoring disturbed community in side GIT, (ii) Participating and solving undesired gastro intestinal problems. (iii)Improving/ managing whole gut transit time, stool frequency and consistency.	[50-52]
<i>L. acidophilus</i> , <i>L. plantarum</i> , <i>L. casei</i> , <i>B. lactis</i> , <i>S. cerevisiae</i>	Irritable bowel syndrom	(i) Reduction of irritable bowel syndrome symptoms. (ii) Effective in alleviating and managing symptoms of this unpleasant condition.	[53-55]
<i>L. GG</i> , <i>L. casei</i> Shirota, <i>L. acidophilus</i> , <i>B. bifidum</i> , <i>L. rhamnosus</i> , <i>L. plantarum</i> and <i>L. paracase</i> , <i>Streptococcus salivarius</i> , <i>Bifidobacterium animalis</i> subsp. <i>lactis</i>	Acute viral upper respiratory infections	(i)Colonizing epithelial cells and keep away from adherence of pathogens. (ii) Create adhesion, binding sites, nutrients and space competition lastly able to avoid risk of upper respiratory track completely.	[56-59]
<i>B. animalis</i> subsp. <i>Lactis</i> , <i>L. lactis</i> subsp. <i>lactis</i>	Modulation of gut –brain axis	(i) Modulation of brain activity and Provide mental health.(ii) Maintaining the functionality of the central nervous system through metabolic, neuroendocrine and immune pathways.(iii) Contribute to the early development of normal social and cognitive behaviors. (iv) Useful strains having positive direct effect on central nervous system and also solve disorders.	[60,61]
<i>Lactic acid bacteria</i>	Colon Cancer	(i) Comprise modification of the metabolic activities of intestinal micro flora and alteration of physicochemical conditions in the colon as well as binding site. (ii) Biodegradation of potential carcinogens. (iii) Production of anti-tumorigenic or mutagenic compounds due to ability to decrease the activity of enzyme called β glucuronidase. (iv) Increasing the host immune response, by alteration in pro-cancerous enzymatic activity of colonic microorganisms.	[62,63]
<i>Lactobacillus acidophilus</i> NCFM, <i>Lactobacillus gasseri</i> SBT2055, <i>L. rhamnosus</i> CGMCC1.3724	Diabetes and Obesity	(i) Decrease the risk of type two diabetes mellitus and insulin resistance. (ii) By improving and maintaining the metabolic equilibrium of the host then actual weight loss is observed significantly.	[64-67]

Probiotics are applicable in human health improvement, infection control, diseases treatment and management (Table 2) [7,35-67].

Probiotics and Allergy

Allergies are misguided reactions of the immune system in response to (what should be harmless) particles. Probiotics treat allergies by healing your damaged digestive system, which decreases inflammation, stabilizes your immune system, and strengthens your gut lining. An allergy is a hypersensitivity reaction initiated by immunological mechanisms. Probiotics modify the structure of antigens, reduce their immunogenicity, intestinal permeability and the generation of pro-inflammatory cytokines that are eminent in patients with a diversity of allergic disorders [68]. *Lactobacillus GG* and *L. rhamnosus GG* is alleviating the symptoms of food allergies at the same time have

significant role in reduction of risk for developing allergic disease [19,69]. Already known strategies to solve allergic disorder by prevention of antigen translocation into blood stream, improve mucosal barrier function and prevent excessive immunologic responses to increased amount of antigen stimulation of the gut.

Probiotics and Blood Pressure

It has also been demonstrated that probiotics and their products can improve Blood pressure through mechanisms including improving total cholesterol and low-density lipoprotein cholesterol levels [70,71]. Reducing blood glucose level and insulin resistance, regulating the renin–angiotensin system and significant reduction takes place in blood or serum cholesterol when cholesterol is elevated. Interestingly, probiotic supplementation might positively help in reducing Blood pressure in the hypertensive conditions. *Lactobacillus helveticus*,

Saccharomyces cerevisiae, *Lactobacillus rhamnosus* GG, *Lactobacillus casei*, *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus bulgaricus*, *Bifidobacterium breve*, *Bifidobacterium longum* *Streptococcus thermophiles*, *Lactobacillus delbrueckii ssp. Bulgaricus*, *Lactobacillus kefir* are the common one used for anti-hypertension [72,73].

Probiotics and Inflammatory Bowel Disease

Incorporation of probiotic bacteria has an ability to become stable the immunological barrier in the gut mucosa by declining the generation of local pro-inflammatory cytokines. Probiotics is used for treatment of the inflammatory bowel disease, such as ulcerative colitis, Crohn's disease and Pouchitis. Potential mechanisms include suppression of growth or epithelial binding and invasion by pathogenic bacteria, production of antimicrobial substances, improved epithelial barrier function, and immunoregulation. The effects of probiotic are probably both strain-dependent and dose dependent [74].

Probiotics and Urogenital infections (Bacterial vaginitis)

Bacterial vaginosis is an abnormal vaginal condition that is characterized by vaginal discharges and results from an overgrowth of atypical bacteria in the vagina. A urinary tract infection is an infection involving the kidneys, ureters, bladder, or urethra. These are the structures that urine passes through before being eliminated from the body. Urogenital infection is occurs due to change in vaginal environmental in which *lactobacilli* decrease in concentrations or absent. *Lactobacillus spp.*, are the prominent microbial factors that governs the presence, growth, colonization and persistence of non-endogenous microorganisms in vagina. As the *Lactobacillus spp.* count decreases, the protection provided by them against uropathogens also decreases. It is also proposed that *lactobacilli* produce biofilms, which cover the urogenital cells. *Lactobacilli* use in bacterial vaginosis is supported by positive results obtained in clinical trials. Probiotic capsules for example *Lactobacillus rhamnosus*, *Lactobacillus crispatus*, *Lactobacillus gasseri*, *Lactobacillus vaginalis*, *Lactobacillus acidophilus*, *Lactobacillus reuteri* and *Streptococcus thermophilus* are effectiveness for recurrent bacterial vaginosis prevention [75-77]. The principal mechanisms by which *lactobacilli* exert their protective functions in urogenital health care are:

1. Stimulation of the immune system.
2. Competition with other microorganisms for nutrients and for adherence to the vaginal epithelium, urinary and vaginal tract cells.
3. Reduction of the vaginal pH by the production of organic acids, especially lactic acid.
4. Production of antimicrobial substances and competitive exclusion Inhibitor production, such as bacteriocins, and hydrogen peroxide.

Probiotics and Liver Diseases

Micro flora resident in intestinal lumen plays a significant role in hepatocytes function. Alterations to the type and amount of microorganisms that live in the intestinal tract can result

in serious and harmful liver dysfunctions such as cirrhosis, nonalcoholic fatty liver disease, alcoholic liver disease, and hepatic encephalopathy. Probiotic is used as a novel treatment strategy against liver disease in a mechanism of regulation, restoration and alteration of gut micro flora and immune function [78,79]. Probiotics are useful in the treatment of chronic liver diseases as they block entry of microorganisms to blood flow and ultimately to liver by increasing the strength of intestinal barrier [80].

Probiotics and Cholesterol Assimilation

Probiotic strains, particularly lactic acid microscopic organisms (bacteria) have a noteworthy part to play in the cholesterol by bringing down the mechanism. The cholesterol levels can be cut down direct or indirect by using probiotics. Direct mechanism involves inhibition of denovo synthesis or decrease in the intestinal absorption of dietary cholesterol. The decrease in dietary cholesterol retention can be diminished by three ways -assimilation, binding or by degradation. Probiotic strains absorb the cholesterol for their own particular digestion. Probiotic strains can attach to the cholesterol particle, and they are capable for debasing cholesterol to its catabolic products. The cholesterol level can be decreased in an indirect way by deconjugating the cholesterol to bile acids, in this way lessening the aggregate body pool. Reduction of total cholesterol to be done in *B. animalis subsp. lactis MB 202/DSMZ 23733*, *B. bifidum*, *B. breve* [81]. Hypercholesterolemia (elevated blood cholesterol level) is considered a major risk factor for the development of coronary heart disease. Therefore, lowering the serum cholesterol level is important to prevent the disease. The cholesterol removing ability of LAB isolates was assessed *in vitro* and *in vivo* mechanisms. *Lactobacillus pentosus LP05*, *L. brevis LB32*, *L. reuteri* and *L. plantarum* are powerful [82-84].

Probiotics and Dental Caries

Dental caries is a multifactorial disease of bacterial origin that is described by corrosive demineralization of the tooth enamel. It seems following changes in the homeostasis of the oral environment prompting multiplication of the bacterial biofilm, composed notably of streptococci from the mutans group. To have a helpful impact in restricting or averting dental caries, a probiotic must have the ability to stick to dental surfaces and coordinate into the bacterial groups making up the dental biofilm. It must also compete with and antagonize the cariogenic bacteria and thus prevent their proliferation. Finally, metabolism of food-grade sugars by the probiotic should result in low acid production. The advantage of incorporating probiotics into dairy products lies in their capacity to neutralize acidic conditions. For instance, it has just been accounted for that cheese prevents demineralization of the enamel and advances its remineralisation [48,85].

Probiotics and Orthodontic Treatment

White spot lesions are caused by streptococcus mutans and they are the basic scars found amid and after orthodontic treatment. The wellbeing advancing microbes can address the lopsidedness in the oral biofilm by intensely hindering the pathogens and moving the oral mileau to a higher pH thereby, turning around the demineralization. Fixed orthodontic appliances are

considered to endanger dental wellbeing because of gathering of microorganisms that may cause enamel demineralization, clinically visible as white spot lesions. Besides, the intricate plan of orthodontic bands and brackets may make a biological environment that encourages the foundation and development of cariogenic mutans streptococci strains. White spot lesion formation can be viewed as imbalance between mineral loss and mineral gain and the latest orderly audits have examined methods to prevent this side effect of orthodontic treatment. Studies are required to clear up if utilization of probiotics can be powerful as an alternative method for the prevention of demineralization and white spots [86]. *Lactobacilli brevis*, *Bifidobacterium animalis subsp. Lactis BB-12* and *Bifidobacterium lactis* derived probiotic through a lozenge tablet could reduce the levels of *S. mutans* in plaque around orthodontic brackets [87,88].

Probiotics and Oral Health

A standout amongst the most imperative advantages of probiotics in the oral cavity is lessening of inflammation. Probiotics can help to destroy the harmful microbes in the oral cavity by fighting against them and helps in maintaining healthy gums and teeth. Since probiotics is an all-natural treatment it should not have any side effects [89,90]. Both *lactobacillus acidophilus* and *bifidobacterium lactis* have well known antifungal property [91].

Probiotics and Voice Prosthesis

Probiotics emphatically diminish the occurrence of pathogenic bacteria in voice prosthetic biofilms. Effectively disposes of biofilm development on indwelling voice prostheses, possibly related to the presence of *Streptococcus thermophiles* and *Lactobacillus bulgaricus* [13].

Probiotics and Halitosis

Halitosis or Bad Breath is the condition when the breath has unpleasant odor. It has many causes, for example, utilization of specific foods, metabolic disorders, respiratory tract infections and related with an irregularity of the commensal microflora of the oral cavity. Essentially, it is started from the activity of anaerobic bacteria that corrupt salivary and food proteins to create amino acids, which are thusly changed into volatile sulphur compounds, including hydrogen sulfide and methane thiol. *Streptococcus salivarius* act as a commensal probiotic of the oral cavity this strain screened and recognized typically from people groups without halitosis [92,93]. *S. salivarius* is known to create bacteriocins, which could add to lessening the quantity of microscopic organisms that produce volatile sulphur compounds. The utilization of gum or capsules containing *S. salivarius K12* (BLIS Technologies Ltd., Dunedin, New Zealand) diminished levels of volatile sulphur compounds among patients diagnosed to have halitosis [93]. Take a probiotic supplement regularly. There is good evidence it helps to regulate the growth of harmful bacteria. *S. salivariu*, *L. salivarius*, *L. reuteri*, *L.casei* and *W. Cibaria* was supplied for management option [94].

Probiotics and Periodontal Diseases

Studies have demonstrated that the pervasiveness of *lactobacilli*, especially *Lactobacillus gasseri* and *L. fermentum*, in the oral

cavity was more prominent among healthy participants than among patients with chronic periodontitis. Different studies have detailed the limit of lactobacilli to repress the development of periodonto pathogens, including *P. gingivalis*, *Prevotella intermedia* and *A. actinomycetemcomitans*. Together, these perceptions recommend that *lactobacilli* living in the oral cavity could play a role in the oral ecological balance [95]. *L. brevis*, *L. casei*, *L. salivarius*, *reuteri* strains, *Bacillus subtilis*, *L. reuteri* and *L. brevis* the involvement cared out in anti-inflammatory activity decreasing the number of pathogens in periodontal tissues [96].

Immunologic Enhancement/ Immunity Stimulation

Probiotics have biological effect in Immunological functionality. The immunological benefits of probiotics can be due to 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 [26]. The intrinsic properties of lactobacilli to modulate the immune system make them appealing for wellbeing applications. The Proposed systems engaged with reinforcing of nonspecific and antigen-specific defense against infection and tumors, adjuvant impact in antigen-particular immune responses, Regulating/affecting Th1/Th2 cells, production of anti-inflammatory cytokines, improving phagocytic action of granulocytes, cytokine discharge in lymphocytes, and increases immunoglobulin-emitting cells in blood in order to scale up antibody production. This is ordinary reactions of probiotics, which are all demonstrative of changes in the immune system. An inflammatory immune response delivered cytokine-actuated monocytes and macrophages, causing the arrival of cytotoxic particles fit for lysing tumor cells and pathogens in the body.

Probiotics and HIV

Probiotics appear to support maintenance of a strong gut epithelia layer, improve gut barrier function and stimulation of innate immunity which act as the first layer of defense against translocation of viral particles and bacterial pathogens. When immune system is well developed, able to prevent HIV replication and slow down the progression of AIDS in host. Daily consumption of probiotics over a prolonged period of time can improve CD4 count in people living with HIV. A screening of saliva taken from several volunteers demonstrated that some *Lactobacillus* strains created proteins that are fit for binding a specific type of sugar, called mannose, found on HIV envelope. The binding of the sugar empowers the microscopic organisms (bacteria) to adhere to the mucosal coating of the mouth and gastric tract and colonize them. One of the strain indicated copious mannose-binding protein particles into its surroundings which binded to the sugar coating henceforth neutralizing HIV. It is also observed that the trapped immune cell by *lactobacilli* leads to formation of clumps leading immobilization of any immune cells harboring HIV and preventing them to infect other cells [27].

Safety aspects and harmful side effects of probiotics

Probiotics may be responsible for four types of side effects in susceptible individuals: systemic infections, deleterious

metabolic activities, excessive immune stimulation, and gene transfer. When the dose of intake is very high extends to causes of infections in humans not only in all age groups but also in immunocompromised individuals. Three approaches can be used to assess the safety of a probiotic strain: studies on the intrinsic properties of the strain, studies on the pharmacokinetics of the strain (survival, action in the digestive tract, dose–reaction connections, fecal and mucosal recuperation) and studies hunting down for interaction between the strain and the host [97]. Symptoms of side effects are accepted to come about because of bacteria-host interactions in which the probiotic supplement might be contrary with the present living space of the user's microbiota, eventually setting off a response. Cases of normal reactions from probiotics include: abnormal bowel movements, bloating, flatulence, gurgling, and stomach aches. It is happened in rare case. May be producing an active infection, although this risk is quite low but, allow to stimulate the situation in immunosuppressed patients. Administration during pregnancy and early infancy is considered safe. Available data indicate that not those much harmful effects have been observed in controlled clinical studies with *lactobacilli* and *bifidobacteria* [98]. So I would recommend scientists to conduct research in the area about its negative impact in human all over status profoundly.

The capacities of probiotics to survive and be metabolically active in the GIT and to associate with the gastrointestinal mucosa and gastrointestinal microflora have prompted four zones of worry about safety:

1. Potential for bacteria to translocate/transmigrate, crossing the gastrointestinal tract boundary and bringing about intrusive infection. Translocation by intestinal bacteria is encouraged by various elements including intestinal mucosal damage, immunodeficiency, gut prematurity and abnormal bacterial flora and adherence of the bacteria to the mucosal surface.
2. The likelihood for some probiotic life forms is to harbor protection from anti-infection agents (antibiotics), prompting a potential for antibiotic resistance that is to be exchanged from probiotic bacteria to other possibly pathogenic bacteria. With the goal that such organisms may harbor genes that may add to opportunistic infections on the grounds that the antibiotic resistance gene can be exchanged by conjugation, transduction or transformation way.
3. Metabolic activity and immunologic effects of probiotics leading to possible deleterious metabolic effects and excessive immune stimulation.
4. last but not the least all the concerns that we have is all about product quality, since products that does not contain the probiotic on the label, or that contain contaminants may likewise put the consumer in danger.

Due to potential impact of the use of probiotics on gastrointestinal physiology, Gastrointestinal toxicity studies should be studied as one part of safety concern, as there may be production of metabolites that are undesirable, chance that there can be generation of metabolites that are unfortunate, chance that the probiotic bacteria might lead to crate, encourage or increment

the danger of various physiological and anatomical issues [97,99].

Future Perspectives of Probiotics

Now a day, technological innovations contribute a mechanism to solve the problem of probiotic stability and viability. Pure and active viability of cells is very necessary in food processing and gastro intestinal transit to reach the intended site of action in sufficient numbers. Most of the time probiotics are loss their function and useful property/viability. Due to passage through the low pH environment of the stomach and high bile salt conditions in the intestine. The only way of to overcome the challenge is introducing to sublethal stress, applying encapsulation and using in food matrix/ carriers. Encapsulation is a mechanical or physicochemical process that traps a potentially sensitive material and provides a protective barrier between it and the external conditions. The new microencapsulation technologies/methods have been developed to protect the bacteria from damage caused by external environment through a protective outer coating. Microencapsulation of probiotics enables storage of viable bacteria at room temperature and may allow incorporation of probiotics into a wide range of food products. The spray-drying, emulsion and extrusion techniques are well known encapsulation methods for the production of microcapsules containing probiotics [100]. The future attitude regarding to improve overall characteristics of the strain and to get power full desired trait is apply genetic engineering on the area.

Conclusion

The consumption of probiotics helps to lead a healthy life. Currently, this is globally a well-accepted concept and guarantee for the next generation. Probiotics are widely used in order to solve and simplify particular diseases. In the future highly emphasize further *in vitro* and *in vivo* experiments should be designed and conducted to identify true probiotics and to select the most suitable ones for the prevention/ treatment of diseases. Lastly recommend further practical studies need confirmation about its effect in human health with in high quality research and well-designed clinical trials.

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Conflicts of Interest

The author has no conflicts of interest to declare.

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