

Health Benefits Of Probiotic Bacteria As Nutraceuticals

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ABSTRACT-

Nowadays, variety of food available in the market, which have serious health, environmental and social impact. Their consumption is not good for health. Due to all these things, people are fighting with many diseases like diabetes, obesity, cancer, osteoporosis and other allergic health related issues. So, probiotics play an important role in controlling many diseases and ameliorate nutritional, immunological and physiological functions. Basically, it aids proper digestion and improve intestinal health. Probiotics have both nutritive and medicinal values. As it refines physical health, increase longevity and reduces symptoms of many diseases. Also, Nutraceuticals gained popularity among people. They are available in the market in the form of supplements and various food products. By consuming the probiotic as a supplement and food products, people are living active lifestyle. This review summarizes the effect of probiotic on intestinal health and potential of probiotic as nutraceuticals.

1. PROBIOTICS-

Probiotics are live microorganisms that offer a health benefits to human. Basically it aids proper digestion. These are often called as good bacteria that maintains gut microflora. It helps to enhance or restore health to our gut microbiome [1]. Many microorganisms that naturally live in our body are similar to microorganisms in probiotic food, Drinks and dietary supplements [2]. Probiotics when taken in requisite amount improves the intestinal microbial balance. Probiotics have both nutritional and medicinal value.

Probiotic bacteria are found in fermented dairy products like yoghurt, sauerkraut etc. It is not mandatory that all fermented foods are probiotic [3]. Properties that are considered to be as a Probiotic includes sufficient living bacteria that survive food processing and bacteria that survive have to benefit human health as based on research studies. Probiotics generally include below mentioned bacteria-

1. Lactobacilli (Phylum- Firmicutes)- *L. acidophilus*, *L. bulgaricus*, *L. casei*
2. Bifidobacterium (Phyla- Actinobacterium)- *L. bifidum*, *B. thermophilum*
3. Gram positive Cocci- *Lactococcus lactis*, *Streptococcus thermophilus*, *Streptococcus salivarins*

Some examples of probiotics in food are Baby milk which nowadays is added with *L. acidophilus* and *Bifidus* bacteria, Yoghurt rich with bacterial culture such as *L. bulgaricus* and *S. thermophilus*, friendly bacteria that is added in cheese is *Lactobacillus* and buttermilk is added with *L. bulgaricus* etc.

NUTRACEUTICALS-

Nutraceutical is the term coined by Dr. Stephen De Felice in 1989 which is the combination of two words i.e. Nutrition and Pharmaceutical. Nutraceuticals are biologically active substance that may be contemplated as food or part of a food which provides health benefits and useful in the treatment of diseases [4]. Most of the diseases occur due to incorrect diet and life style such as obesity, diabetes, cardiovascular problems etc. Nutraceutical play an important role in disease prevention as well as it promotes good health.

Various constituents of plants like catechins, carotenoids, lycopene, polyphenols etc. are used in Nutraceutical which have been very effective in the prevention of some diseases like cancer, arthritis etc. It strengthens the body defense mechanism and refines the body immunity towards diseases.

Nutraceutical can be taken in the form of capsule, tablet or liquid form. They are labelled as 'Dietary Supplements'. It can be categorized as dietary fibre, prebiotics, probiotics, antioxidants, poly unsaturated fatty acids and other natural foods.

Categorization of Nutraceuticals: - Depending upon various characteristics, nutraceuticals are categorized into-

-On the basis of foods available in the market

-On the basis of their mechanism of action

-On the basis of their Chemical nature

- On the basis of foods available in the market [5,6]

1. Traditional Nutraceuticals

2. Non- Traditional Nutraceuticals

1. Traditional Nutraceuticals- These are simple, directly extracted from natural resources without any changes to the food. Food contains few nutritional values, such as lycopene in tomatoes.

Further, they are grouped into-

a) Chemical constituents-

- i. Nutrients- These are those substances which have nutritional function in them. For example; vitamins, amino acids, minerals and fatty acids.

- ii. Herbals- These are those products which are derived from natural sources it may be either herb or botanical products used as concentrated extracts. For example; Parsley contains flavonoids which are useful in diuretic and antipyretic.

- iii. Phytochemicals- These are the biologically active compounds present in plants. Well known phytochemicals are flavonoids. Flavonoid is a secondary metabolite helps in prevention of various diseases like cancer, heart and kidney related problems through it anti- oxidant properties [7].

b) Probiotic Microorganisms- This means live microorganisms which when consumed in adequate amounts, confers the health of an individual. They are a friendly bacterium that enhances healthy digestion and absorption of food or some specific nutrients. Probiotic products are easily available in the market as food supplement.

Some sources are- Milk (*L. lactis*), Yoghurt (*S. thermophilus*), and gastrointestinal tract (*L. johnsonii*).

c) Nutraceutical Enzymes- Enzymes are the key essential part of the body and life. Enzymes are produced by the cell inside body which regulate various metabolic pathways and act as a biocatalyst. These enzymes are proteinous in structure. Those people who are suffering from Blood sugar, Hypoglycemia, obesity etc. get rid of symptoms by adding enzyme to their daily diet. These enzymes are derived from microbes, plant and animal sources.

For example, Microbial enzymes are Invertase (sucrase) and Lactase. Plant enzymes are Pectinase (obtained from cell wall).

2. Non- Traditional Nutraceuticals- These are the artificially prepared or created foods. Food samples contain bioactive compounds.

These are arranged into-

- a) Fortified Nutraceuticals- These constitute fortified food from agricultural breeding or added nutrients. For example- Orange juice is fortified with calcium, cereals with added vitamins and minerals, and for vitamin D deficiency, milk is fortified with cholecalciferol [8].
- b) Recombinant Nutraceuticals- Energy providing foods such as bread, alcohol, yoghurt and many more products are produced with the help of Biotechnology.

Characteristics features of Probiotics-

There are various bacterial strains used as probiotics and the most common microbial strain used as probiotic are lactic acid bacteria, E. coli and Bifidobacterium [9].

Some features of bacterial strain which provide health benefit and their properties are considered as probiotics include-

1. Impervious to gastric activity
2. Resistant to Bile acid
3. Adhesive to Mucus or cell lines of human
4. Antimicrobial property in opposition to pathogens
5. Thermo- tolerant
6. Capability to lessen pathogen adherence

It is advised that bacteria used as probiotic at least have pH 3.0 to tolerate acidic environment. Thermo-tolerates are those who can thrive in high temperature. Thus, increased temperature results in strong viability of strain. Lysosomes play an important role in antimicrobial effect. Cell walls are affected by lysosomal enzyme treatment. Also, adhesions to mucus or cell lines are important in production of various enzymes, Vitamins and antimicrobial compounds to lessen pathogen adherence [10].

POTENTIAL OF PROBIOTICS AS NUTRACEUTICALS-

A lactic acid bacterium (LAB) is gram positive and non-toxic bacteria. It is used as a main product of carbohydrate fermentation. It is used as a preservative and flavoring agent in various kinds of food products. LAB is considered as most common microorganisms generally used in fermentation [11]. LAB shows two types of fermentation patterns i.e. they are classified as Homofermentative (seen in Lactococcus and Streptococcus) and heterofermentative (seen in Leuconostoc and Weissella), produces 2 moles of lactate per mole via EMP pathway and utilizes pentose phosphate pathway (PPP) to give equal moles of lactate, carbon dioxide, ethanol and glucose respectively [12].

Now days, there is a rising demand for using probiotics as nutraceuticals such as used in capsules, tablets and other fermented probiotic products. Hence, it is used as dietary supplements. LAB is used in nutraceutical products which are available in market nowadays are Yakult [13], Nestle LC1 and culturelle. These nutraceutical produced by LAB have various health benefits. They are used as food additives and low calorie sweetener. They are indulged in Biosynthesis of Nucleotide; act as antioxidant, anticancer and anti- plaque agent. Hence, it confers various health benefits like help in preventing obesity, colon cancer, arthritis and various other diseases as shown in figure1 [14].

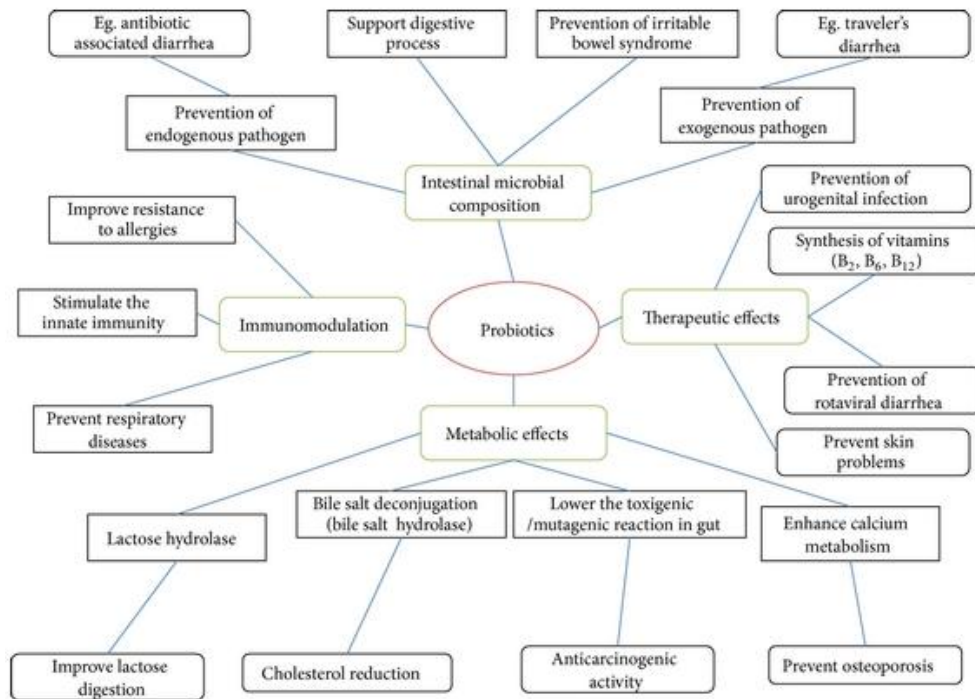
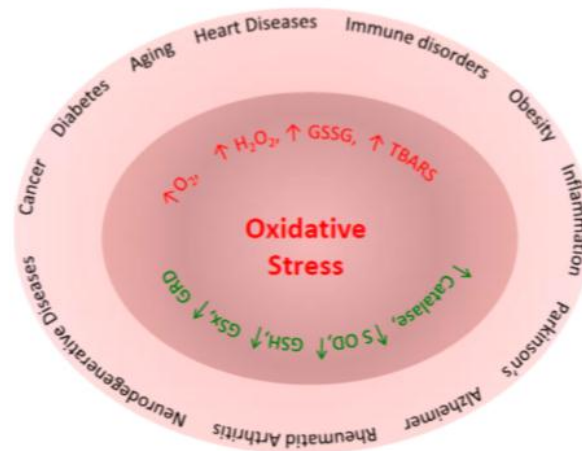


Figure 1- Health benefits of probiotics in various diseases.

1. Probiotics as Anticancer agents- Some of the studies have shown that probiotics can act as an anticancer agent [15]. Probiotics may reduce the risk of colon cancer by suppressing the growth or proliferation of pro- carcinogenic bacteria and enhances intestinal immunity. This suppression is done by probiotic bacteria by inactivation of harmful compounds and lowering the absorption of mutagenic compounds from intestinal cell walls, achieved by apoptosis which helps in producing short chain fatty acids and inhibits the tyrosine- kinase signaling pathway [15]. Probiotic metabolites like lipopolysaccharide (LPS) and exopolysaccharide (EPS) helps in prevention and treatment of cancer. LPS is a compound found in outer membrane of gram negative bacteria. It activates immune T- cell mediated response against cancerous cells [16]. EPS is produced by LAB species has an anticancer effect on colon tumor cells by inducing mechanism of apoptosis. They have direct cytotoxic effect on cancer cells [17].

2. Probiotics as Antioxidant agents- Antioxidant supplements or probiotic isolated from LAB family have the ability to produce natural antioxidants [18]. A Probiotic bacterium produces bioactive peptides such as glutathione, GPX, CAT [19]. They possess antioxidative activities and provide protection in opposition to peroxidation of fatty acids [20]. Oxidative stress plays the main role in the development of diseases [21]. So, these antioxidants help in lowering down the oxidative damage, forage rate and activity of antioxidative enzymes (Figure 2) [22].



3. Probiotics as Antiplaque agents- The growth of good bacteria in oral cavity help in preventing tooth decay and can also provide good mucosal immunity as they are the primary part of the gastrointestinal tract [23]. Streptococcus mutans mainly causes dental caries. L. rhamnosus, probiotic bacteria inhibit the growth of S. mutans and lessen the risk of caries or tooth decay especially in children [24]. Also, daily intake of probiotic Lactobacilli or Bifidobacteria help in reducing S. mutans in saliva or plaque [25]

Action mechanism of probiotics-

It includes following modes of action-

1. Improvement of epithelial barrier function- probiotics improves health of the host, its functions is maintained by intestinal cell lines or barrier which includes secretion of mucous, water secretion and binding with epithelial cells [26]. Probiotic bacteria and yeast affect the epithelium barrier in various ways-
 - a) Effect on epithelium- Mucus is the first defensive layer and act as a barrier [27]. Firstly, pathogenic bacteria have to cross the mucosal layer to reach epithelial cells. Goblet cells are present all around the intestinal tract as well as on the mucosal surface. These goblet cells are secreted to form mucous layer in the lumen [28]. This gel layer provides protection from pathogens by providing safety to the epithelium. Goblet cell expresses mucin. These mucins bind to the epithelial cell surface and bind tightly with mucosa [29]. Probiotic increases the mucosal activity and act on goblet cells. It decreases bacterial movement against the membrane. β - Defensin is secreted into mucus by the epithelial cells which further prevent the division of bacteria and maintain barrier function. Then, it finally improves the tight junction stability and limits the movement of bacteria and its toxic products. Also, some probiotic limit chloride and water secretion [30]. For example, L. acidophilus and S. thermophilus kills S. aureus, s. typhimurium, Klebisella pneumoniae but not Lactobacillus or Bifidobacterium and prevent from s. typhimurium illness [31].
 - b) Effect on mucosal immunity- IgA producing cell level is increased by probiotics which then promote IgA secretion in mucosal layer. They contribute in gut homeostasis by limiting epithelial colonization by binding bacteria and their antigens [32].

- c) Effect on other bacteria or pathogens- probiotic bacteria act in two different ways. It directly kills pathogenic bacteria or inhibits their growth by producing bacteriocins. Also, some probiotic compete with pathogenic bacteria for binding sites present on epithelial cells, thus prevent their colonization or growth on mucins and contribute to barrier functions [33].

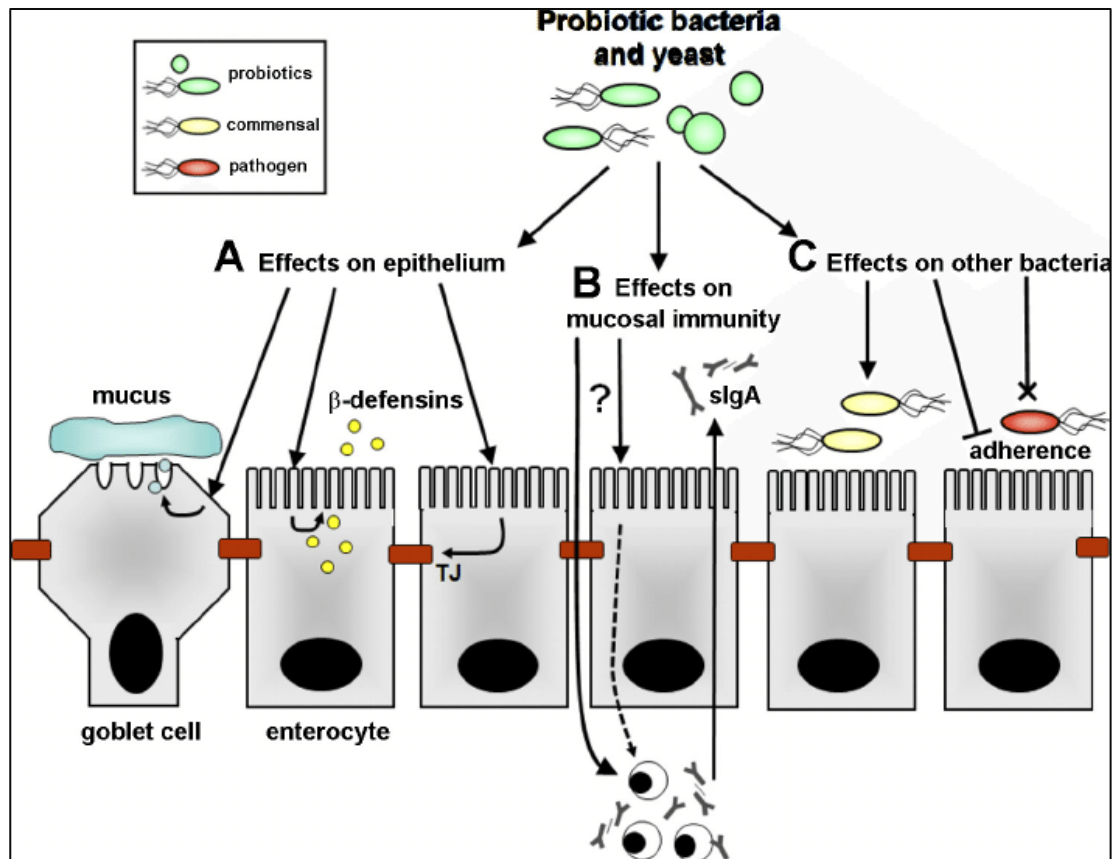


Figure 3- Action mechanism of probiotics in improvement of epithelial barrier function [34].

2. Intestinal epithelial cells adhesion- Probiotic bacteria improves host health by adhering to the lining of gut and adhere very strongly with epithelial cells. After adhesion to the epithelial cells, it also releases chemokine's and cytokines in its primary stage and stimulate mucosal layer in its secondary stage [35]. Human intestinal epithelial cell lines of mucosal membrane CoCO-2 and HT- 29, lactobacilli thus increases MUC 2 and adheres to colonic cells in human [36].
3. Removal of pathogenic microbes by competition- Probiotic bacteria creates a microenvironment by lowering its pH and produces acids which removes or reduces the functioning of harmful pathogens. Probiotic bacterial also competes with pathogens for nutrition and energy by blocking their sites [37]. Hence, in this way pathogenic microbes are invaded by probiotic bacteria.
4. Antimicrobial production- LAB produces antimicrobial peptides, secrete antimicrobial substances and metabolites like arginine, glutamine etc. Reutrin is an antimicrobial peptide secreted by *L. reutri* strain which act on fungi, protozoa, parasites and various viruses [38].

5. Articulation of Immune system- Probiotic bacteria produces Immuno-modulatory properties like, enunciation of cytokine production, Ig A production stimulation, Increase phagocytic activity of macrophages [39] and also enhance the activity of natural killer cells [40].

Several factors can be taken into considerations before incorporating into food products. Probiotics are added carefully into supplements that it must retain the viability of culture and activate the gastrointestinal activity. Successful metabolic engineering strategies should be employed in LAB because it produces several products like vitamin (B2, B12 or B9), sorbitol, mannitol etc. [41].

Therapeutic uses-

There are various scientific proofs that support the vital role of probiotics in maintaining the health of digestive system, and shows remarkable effect in reducing symptoms of specific disease [42].

1. Inflammatory Bowel Disease (IBD) - Deregulation in the immune system leads to the inflammation of gastrointestinal tract (GIT). IBD includes pouchitis, ulcerative colitis and crohn's disease. In Crohn's, small intestine is affected. Inflammation occurs and can affect the permeability and decreases nutrient absorption. Some of the probiotics are used in a mixture like Lactobacillus strain (acidophilus and johnsonii), Bifidobacterium strain (bifidum, animalis), Saccharomyces boulardii and ECN have been studied for their effectiveness in the therapy of IBD [43]. Multiple strains of VSL3 have shown efficacy in prevention of pouchitis [44]. S. boulardii has shown the effectiveness in treatment of Crohn's disease and reduce relapse [45].
2. Irritable Bowel Syndrome (IBS) - It is a chronic disease which is almost non- curative. Treatment is aimed at alleviating the symptoms [46]. The mixture of B. longum, L. acidophilus, L. lactis and S. thermophilus have shown the satisfactory results in relieving the IBS symptoms [47]. Also, the use of bacterial lysate of Enterococcus faecalis and E.coli has shown the efficacy in reducing IBS symptoms [48].
3. Lactose Intolerance- Deficiency of Betagalactosidase or lactase causes lactose intolerance. This is genetically determined deficiency in which lactose is not hydrolyzed into monosaccharide glucose and galactose. After the consumption of milk or any milk product, symptoms like diarrhea and abdominal discomfort can be seen in an individual. The mixture of S. thermophilus and L. delbrueckii has shown the effective results in the treatment of lactose intolerant patients, because of using these strains, which have higher Betagalactosidase activity help in treating lactose intolerant patients [49].
4. Rotavirus and Traveller's Diarrhea- Rotavirus is the most common source of acute infantile diarrhea. Traveller's diarrhea is caused when an individual travels to warmer climate and symptoms can be seen [50]. S. boulardii and mixture of mixture of L. acidophilus and B. bifidum can shorten the mean duration as compared to the conventional one. This probiotic mixture had shown the effective therapy for traveller's disease [51]. Also, clinical studies shown that mixture of L. rhamnosus, B. animalis, L. reutri can shorten the duration of rotavirus diarrhea [52].
5. Urinary Tract Infections (UTI) – This is the common amongst women and have tendency to recur. E. coli, Klebisella, staphylococcus are the causative agent of urinary tract

infections [53]. The decrease in the vaginal lactobacilli is related with UTI. The effectiveness of lactobacillus is shown in preventing UTI. But the authors stated that randomized clinical trials are required [54].

2. CONCLUSION-

There are many scientific studies or evidences that support the consumption of probiotic in maintaining health. Probiotic have been used as a traditional medicine with the aim of enhancing health of gut microflora. It increases epithelial barrier function and inhibit the growth of pathogenic bacteria. They are found in numerous fermented foods such as yakult. LAB is considered most common microbe used in various kinds of fermented food products and nutraceutical products. Nutraceuticals are the bioactive substance that provides beneficial results in the treatment of diseases like diabetes, obesity, arthritis and colon cancer. They act as antioxidants, anti- cancer and anti- plaque agents. There are numerous scientific proofs that support the probiotic effect in reducing symptoms of many diseases. By using specific microorganisms strain mixture, it has shown the effective results in treatment of antibiotic-associated diarrhea, IBS, IBD and urinary tract infections. Also, a large number of evidences are still emerging to achieve their potential.

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