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A Review on Recent Prospects of Probiotics



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ABSTRACT

The probiotics are live microbial feed supplement which beneficially affects the host animal by improving its intestinal balance. The aim of the study is well stated to address in recent advance on probiotics in the past 50 years. Probiotics are living cell organisms. The probiotic organisms are natural antibiotics in the human-animal gut. Probiotics have been applied as various products with the food industry has been very active in studying and promoting them within this market. The probiotics have been incorporated in various products mainly acts fermented dairy foods. The present reviews focusing on the role of probiotics for their possible role in controlling and treating diseases such as urinary tract infection, diarrheal disease caused by bacteria, and cancer. This review also focuses on the mode of action and side effects. The review is an attempt to emphasize the possible benefaction of probiotics for improving human health, nutrition optimization, and regulation of common metabolic disorders or abnormalities. The purpose of this paper is to review the current documentation on the concept and the possible beneficial properties of probiotics bacteria in the literature, focusing on those available on food. In recent times there has been an increased interest in food and health applications of probiotics, the selection of new probiotic strains, and the development of the new application has gained much importance.

INTRODUCTION:

Probiotics mean simply life Originated from the Greek words “Pro and Bios”. The definition of probiotics has evolved simultaneously with the increase in the use of viable bacterial supplements and in relation to the progress made in understanding their mechanisms of action. Ferdinand virgin was invented the term probiotic in 1954 in this article entitled “Anti-und probiotic” comparing the harmful effects of antibiotics and other antibacterial agents on the intestinal microbiota with the beneficial effects. Probiotics were then redefined by Lilly and stillwell as “A product produced by one microorganism stimulating the growth of another microorganism”. Subsequently the term was further defined as “Non-pathogenic microorganisms which when ingested, exert a positive influence on host is health or physiology” by Fuller. The current definition, formulated in 2002 by FAO (Food and Agriculture Organisation of the United Nations) and WHO (World Health Organisation) working group experts, states that probiotics are live strains of strictly selected microorganisms which when administered in adequate amounts, confer a health benefit on the host. The definition was maintained by the International Scientific Association for Probiotics and Prebiotics (ISAPP) in 2013. The Consumption of probiotics in the form of powder, capsules, and drinks restore the beneficial microflora in the gut and in turn to help the human being by enhancing the immune system. Probiotics are live microbes that can be formulated into mainly different types of products including foods, drugs, and dietary supplements. The ability of probiotics to prevent disease and improve health at all ages is increasing the market potential at a high rate. Probiotics are commonly consumed as part of fermented foods with specially added active live cultures; Such as in Yogurt, Dahi, Yakult, or as dietary supplements. A probiotic may be made out of a single bacterial strain or it may be a consortium as well probiotics can be in powder form, liquid form, gel form, paste, granules or available in the form of capsules, sachets, etc. Probiotics promote immune health, digestive health, brain health, emotional wellness, and more. These goods bacteria produce enzymes that help balance your digestive system and support your body’s ability to absorb nutrients. Studies have found that certain strains of the *Lactobacillus* family can help you lose weight and belly fat. In one study, eating yogurt with *Lactobacillus fermentum* or *Lactobacillus amylovorus* reduced body fat by 3-4 % over a 6 week period. The concept of probiotics was first proposed by Metchnikoff, a noble Laureate of the year 1908.

Many of the microorganisms in probiotic products are the same as or similar to microorganisms that naturally live in our bodies. Probiotics bacteria should be safe for

consumption reach the intestines alive in large numbers and imparts specific health benefits to the host. These bacteria should maintain the balance of the intestinal flora by alerting favorably the gut environment in such a manner that the growths of friendly beneficial bacteria are promoted and harmful disease causing organisms are inhibited. Some of the commonly used probiotics bacteria include lactobacillus bifidobacterial and the yeast *Saccharomyces bouvardia* apart from their use as drugs. They are most commonly used in the form of probiotics dairy products and probiotics fortified foods, either singly or in combination. Today, there is emerging proof that probiotics offer innumerable benefits to the host by alleviating symptoms of lactose intolerance. They are also known to prevent acute diarrhea, travellers diarrhea, antibiotic-associated diarrhea (AAD), rotaviral diarrhea, etc. Research has also shown that probiotics help to prevent the recurrence of cancers, especially bladder and colorectal cancers. Probiotics do not work the same in everyone they may be more effective in older people than in younger ones since more mature bellies may have fewer good bacteria. The probiotics are live microbial feed supplement which beneficially affects the host animals by improving its intestinal balance. Today, probiotics are quite every day in health-promoting “functional foods” for humans as well as therapeutic prophylactic growth supplements in animal production human health. To describe food supplements that are non-digestible the host but can exert beneficial effects can exert beneficial effects by selective stimulation of growth or activity of microorganisms that are present in the intestine. Each individual has a unique signature of more than 100-1000 microbial species in organisation in gastro intestinal tract (GIT). Bacterial cells comprise half of the weight of colonic material and their numbers exceed 10-fold the number of tissue cells forming the human body. Bacterial colonization of the gut begins at birth when new-borns are first exposed to a non-sterile environment.

Manipulation of the gut microflora to increase the relative number of beneficial bacteria, which have a certain impact on immune function, digestion, metabolism and brain-gut communication. Any alterations in the diversity of intestinal microflora may result in several disorders and diseases for which conventional medicines provide very limited efficacy mainly due to the emergence of antibiotic resistance and tolerant pathogenic microbes. Generally, however, the composition of the core intestinal microflora is considered to be essentially stable throughout adulthood. Probiotics also stimulate, modulate, and regulate the hosts immune response by imitating the activation of specific genes by localized host cells. Notable age-specific composition shifts reported in gut microbiota composition include a

decrease in the *Bacteroidetes firmicutes* ratio and a marked decrease in bifidobacterial in people aged > 60 years around the time that the immune system starts to decline. The functional food market is expanding especially in Japan its birthplace with further growth prospects in Europe and the United States and in most countries the largest share of its products is held by probiotics. Probiotics products may contain either a single strain or a mixture of two or more strains. A Single strain may exhibit different benefits when used individually and in combination. The benefits of a probiotics formulation also differ with the patient group. Limited studies that have been performed have shown greater efficacy with multi-strain probiotics. Indian Probiotics Marketed is evaluated at 12 million in 2011, is expected to witness a CAGR of 11 percent by 2016.

PROPERTIES

Some currently determined properties by *in vitro* tests are –

- Acid and bile tolerance seems to be crucial for oral administration.
- Adhesion to mucosal and epithelial surfaces an important property for successful immune modulation, competitive exclusion of pathogen adhesion and colonization.
- Antimicrobial activity against pathogenic bacteria.
- Bile salt hydrolase activity.

CHARACTERISTICS

- i) Optimum growth temperature for most probiotics is 37°C but some strains such as *L. Casei* prefer 30°C.
- ii) Bifidobacterium are anaerobic but some species are aero-tolerant.
- iii) Probiotics should have the ability to interact with the host microflora and compete with microbial pathogens bacterial, viral, and fungal.
- iv) Some probiotics strain can reduce intestinal transit time, improve the quality of migrating motor complexes and temporary increase the role of mitosis in enterocytes.
- v) In general most probiotics are gram-positive, usually catalyse negative rods, with rounded ends, and occur in pairs, short or long chains. They are non-flagellated, non-motile and non-spore-forming.

MECHANISM OF ACTION

Probiotics bacteria can inhibit pathogens by the production of antagonistic compounds/by competitive exclusion. Probiotic bacteria directly take up or decompose the organic matter and improve the water quality of an aquatic ecosystem. Beneficial microbial cultures produce a variety of exoenzymes such as amylase, protease, and lipase which help to degrade the unconsumed feed faces in the pond, in addition to the nutrition of the animals by improving feed digestibility and feed utilization. The modes of action of probiotics include the inhibition of a pathogen through the production of bacteriocin- like compounds, competition for attachment sites, Ex-Probiotics such as *Lactobacillus rhamnoses* strain GG and *Lactobacillus plantarum* 299 showed the ability to inhibit attachment of enteropathogenic *E. coli* in the gastrointestinal tract.

Competition for nutrients (particularly iron in marine microbes) alteration of the enzymatic activity of pathogens, immunostimulatory functions and nutritional benefits. Probiotics do maintain the intestinal barrier integrity by anchoring and adhering to the intestinal mucosa. Several lactobacillus proteins have been shown to promote mucosa adhesions by integrate with complex glycoprotein mixture (i.e. mucin) secreted by the intestinal epithelial cell to provide competitive exclusion of pathogens from the mucus. Another proposed mechanism of probiotic is the modification of the microbial flora through the synthesis of low molecular weight compounds such as organic acid as well as large molecule weight antimicrobial compounds termed as bacterial.

Bacteriocins are compounds produced by probiotics bacteria that have a biologically active protein moiety and antibacterial activity these compounds were proven to be effective against food-borne pathogen and its common mechanism includes destruction of target cells by pore formation and/or inhibition of cell wall synthesis. The organic acids like acetic acid and lactic acid give its actions by lowering the intracellular pH or accumulating the ionized form of organic acid which will disrupt the pH balance of the growth of the pathogen. It is well known that probiotic bacteria can stimulate the immune response by modulating the adequate and innate response of the host. However, most preventive and therapeutic mechanisms of probiotics are generally species and disease-specific. Probiotics such as *B. infantis* Y, *L. acidophils* MB 443, *L. Plantarum* MB 452, *L. paracasei* MB 451, *L. bylgaricus* MB453 inhibit pathogens from binding to gut cell wall and also produce short-chain fatty acids (SCFA) which decrease the pH of the gut to selectively favor the growth of desirable

microbes. The positive influence of probiotic bacillus strains on the growth and composition of commensal and beneficial species on gut could be mediated by the production of extracellular enzymes, vitamins, and peptides. The mechanism behind the establishment of gut homeostasis involves the promotion of growth of other beneficial microbes and suppression of pathogen and pathogen induced inflammatory response of intestinal mucosa. Daily intake of spores forming bacillus probiotics is resulted in increased their colonization in the gut resulting in an increased number of beneficial microbial population and decreased a number of pathogenic strains. Moreover, SFBP could proliferate anti-inflammatory cytokines to maintain immune homeostasis. Regulation of intestinal microbial homeostasis = healthy gut has the optimum balance of beneficial bacteria. Altered equilibrium of microbial community may change luminal immune and inflammatory response as well as the metabolism of epithelial cells.

Immuno-modulation=probiotics interact with epithelial cells and dendritic cells and exert an immuno-modulatory effect. The effects are strain-dependent, induce by profiles of cytokines secreted by lymphocytes or dendritic cells. Interaction of probiotics with these cell's surface receptors activates some intracellular signalling pathways and induce the immune system.

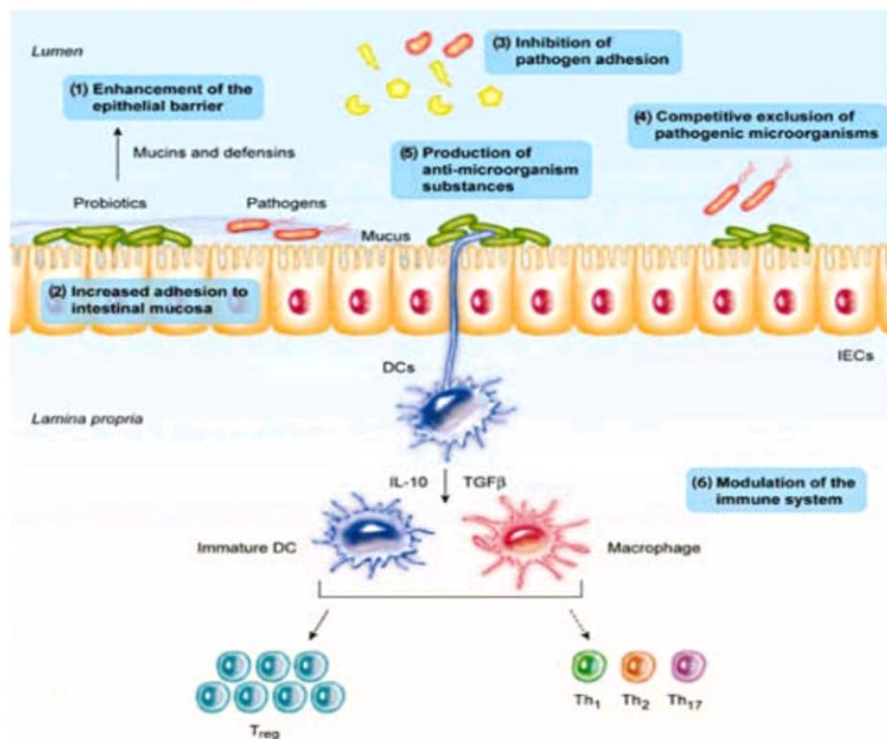


Figure No. 1 Mechanism of action of profiotics

PREBIOTICS, SYNBIOTICS AND POSTBIOTICS

They can be best explained as a microbe or a group of microbes that inhabits within the gut and nourishes the host body internally. They are commonly consumed as preparations with active live cultures and contain bacteria such as lactobacilli, lactococcal or bifidobacterial that has been isolated from natural environments. During the last years the concept of functional food has also been developed in order to describe foods containing ingredients with positive effects on host health beyond their nutritive value.

Table No. 1: Probiotics, Synbiotics, and Postbiotics

Sr. No.	Probiotics Bacterial genera	Species involved
01	Propionobacterium	<i>P. jensenii</i> , <i>P. freudenreichii</i>
02	Peptostreptococcus	<i>P. products.</i>
03	Bacillus	<i>B. coagulans</i> , <i>B. subtilis</i> , <i>B. laterosporus.</i>
04	Enterococcus	<i>E. faecium</i>
05	Pediococcus	<i>P. acidilactici</i> , <i>P. pentosaceus</i>
06	Akkermansia	<i>A. muciniphila.</i>

PREBIOTICS

Prebiotics are not the same as probiotics. The term “Prebiotics” refers to dietary substances that favor the growth of beneficial over harmful ones. Prebiotics are usually in the form of oligosaccharides, which may occur naturally but can also be added as dietary supplements to foods, beverages, and infant formula. Chicory root is considered the richest natural source. Prebiotic provide health benefits beyond basic nutrition they are also available in supplement form, pre occur naturally in several common foods with high fibre content. These are certain nutrients that modify the gut microbial flora although not easily digested by humans but have a selective role in the stimulation of growth or activity of beneficial bacterial species in the gut. Prebiotics like bifidobacterial cause the fermentation of carbohydrates which represent a major source of energy for epithelial cells in the colon. Prebiotics not only serve as an energy source but prebiotics like insulin and pectin exhibit several health benefits such as reducing the prevalence and duration of diarrhea, providing relief from inflammation and other

symptoms associated with intestinal bowel disorders, and exerting protection. Prebiotic is also implicated in enhancing the bioavailability and uptake of minerals lowering of some risk factors for cardiovascular disease and promoting satiety and weight loss.

SOURCES

Prebiotic foods are like fuel for good bacteria. They help to build a healthy microbe, which is our defense system against toxins. Fruits, vegetables, milk, yogurts, grains, soybeans, insulin sources, raw oats, honey, and tubers rich in prebiotics. Oligosaccharides sugar, which contains certain fibrous carbohydrates that nourish the good bacteria to help it to growth.

An ideal prebiotics should be – resistance to the actions of acids in the stomach, bile salts and other hydrolysing enzymes in the intestine, should not be absorbed in the upper gastrointestinal tract, be easily fermentable by the beneficial intestinal microflora.

SYNBIOTICS

Synbiotics is a fusion of probiotics and prebiotics products and helps in enhancing the survival and the implantation of live microbial dietary supplements in the gut. The synergistic benefits are more efficiently promoted when both the probiotic and prebiotic work together in the living system. Symbiosis was developed to overcome possible survival difficulties for probiotics. Several factors like P_H , H_2O_2 , Organic acids, oxygen, moisture stress, etc. have been claimed to affect the viability of probiotics especially in dairy products like yogurts. The health benefits claimed by synbiotics consumption by humans include Increased levels of Lactobacilli and bifidobacterial and balanced gut microbiota, improvement of liver function in cirrhotic patients, improvement of immunomodulating ability, prevention of bacterial translocation and reduced infections in surgical patients, etc.

POSTBIOTICS

Postbiotics can be defined as non-viable bacterial products or metabolic by-products from probiotics microorganisms that have biological activity in the host. General postbiotics include bacterial metabolic by-products such as bacteriocins, organic acids, ethanol diacetyl, acetaldehydes organic acids, ethanol diacetyl, acetaldehydes, and hydrogen peroxide, but it is also found that certain heat-killed probiotics can also retain important bacterial structures that may exert biological activity in the host. Research shows that these metabolic products have a broad inhibitory property towards pathogen microbes and therefore can be used as an

alternative to antibiotics. Postbiotics are non-toxic, non-pathogenic, and resistant to hydrolysis by mammalian enzymes, as these are non-viable bacterial products. In some instances, postbiotics can also enhance barrier function against species like *Saccharomyces bouvardia* and improve angiogenesis *in vitro* and *in vivo* in epithelial cells by activating $\alpha 2\beta 1$ integrin/collage receptors.

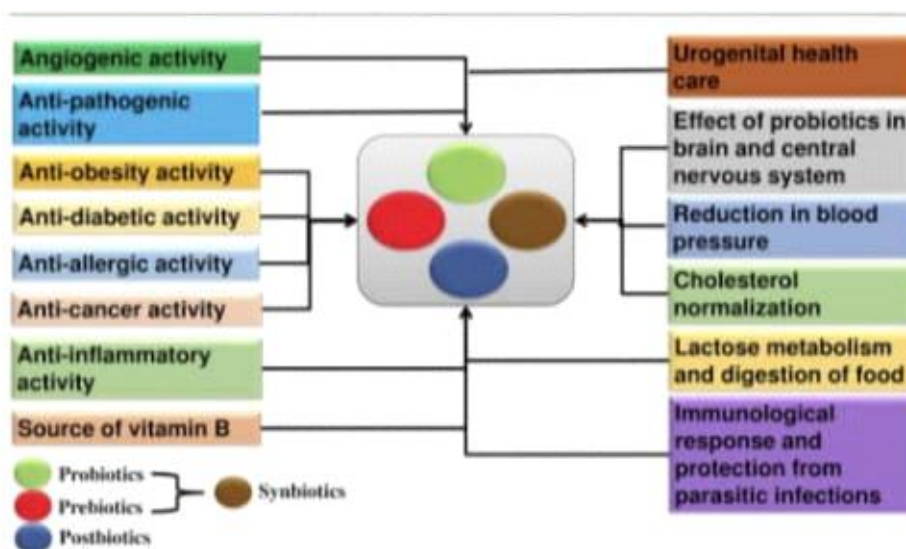
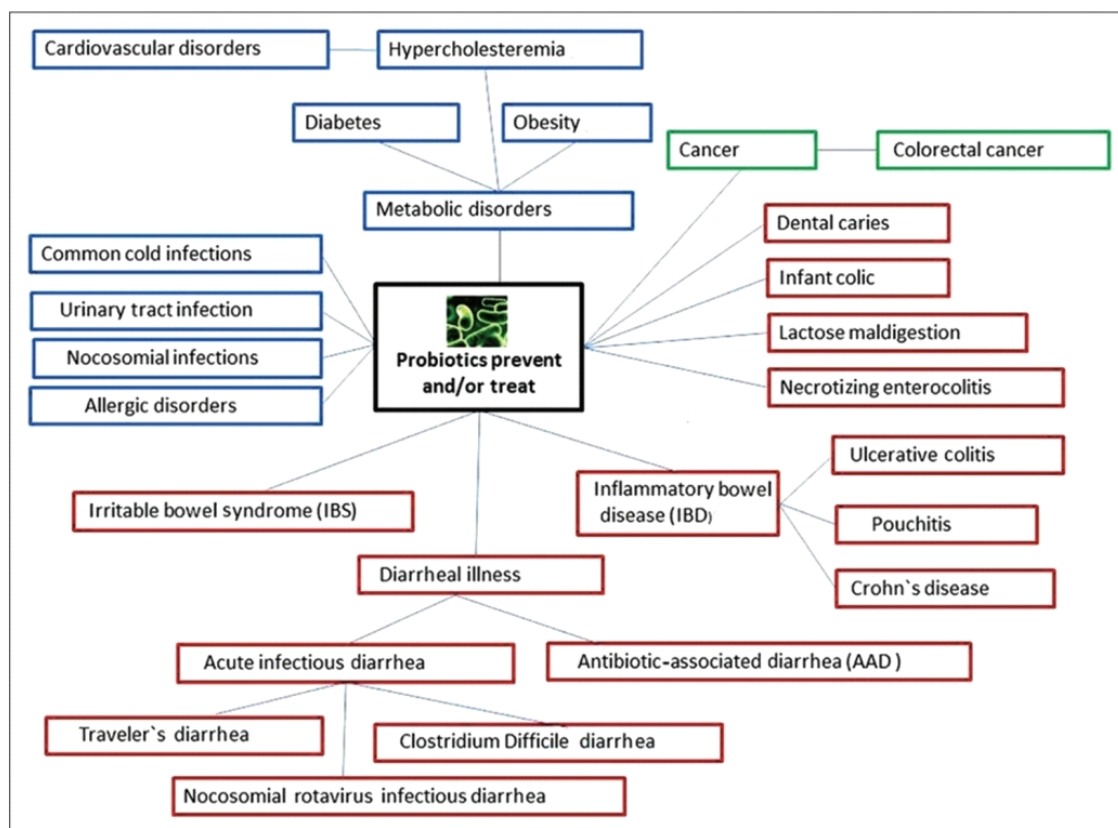


Figure No. 2: Health Benefits of Probiotics

HEALTH BENEFITS OF PROBIOTICS

Probiotics have shown to provide a diversity of health benefits to humans. However, the viability of the microorganisms throughout the processing and storage plays an important role in transferring the claimed health effects. Therefore, the health benefits must be documented with the specific strain and specific dosage. The use of probiotics for clinical health benefits is a fascinating area of research that the present era has yet to explore some important properties of probiotics, such as anti-pathogenicity, anti-diabetic, anti-obesity, anti-inflammatory, anti-cancer, anti-allergic, and angiogenic activities and their effect on the brain and central nervous system are discussed below.



Anti-Pathogenic Activity of Probiotic

Anti-pathogenic activity is regarded as one of the most beneficial effects of probiotics because unlike classic antibiotics disturbance or alteration in the composition of the complex population of the gut microbiota is inhibited. Tejera shrined investigated the influence of probiotics on the survival of *Salmonella enterica*, *Serovar typhimurium*, and *Clostridium difficile* in an *in vitro* model and postulated that probiotics inhibit pathogens by the production of short-chain fatty acids (SCFAS), such as acetic propionic, butyric, and lactic acids. SCFAS help to maintain an appropriate pH in the colonic lumen, which is imperative in the expression of numerous bacterial enzymes and in the metabolism of foreign compounds and carcinogens in the gut. Islam also suggested that a wide variety of anti-pathogenic compounds like bacteriocins, ethanol, organic acids like bacteriocins, ethanol, organic acids, diacetyl acetaldehydes hydrogen peroxide (H₂O₂) and peptides are produced by many probiotics. In addition probiotics also stimulate host antipathogenic defence pathways, such as stimulating or activating the pathways involved in the production of defence that are cationic antimicrobial peptides produced in several cell types including paneth cells in the crypts of the small intestine and intestinal epithelial cells. Also by competing for pathogen

binding and receptors sites, as well as for available nutrients and growth, probiotics exert anti-pathogens actions.

Urogenital Health Care

According to the centers for disease control and prevention (CDCP) more than one billion women around world suffer from non-sexually transmitted Urogenital infections such as bacterial vaginosis (BV), urinary tract infection (UTI) and several other yeast infections. The species typically associated with BV include *Gardnerella vaginalis*, *Ureaplasma urealyticum*, and *Mycoplasma hominis*. But many medical conditions becoming resistant to the present medicines, therefore instead of developing new live supplements, like non-pathogenic microbes that act against the pathogens. It is well-known that there is an association between abnormal vaginal microorganism flora and an increased incidence of urinary tract infection like (UTI). There are about 50 different species inhabiting the vagina like lactobacillus Species that the main regulation of the vaginal microorganisms. Imbalances in the microbial composition greatly influence the health of the vaginal micro-environment which can be cured by balancing the number of Lactobacillus sp. via supplementation of probiotics. Lactobacillus has been shown to produce biosurfactants and collagen-binding proteins that inhibit pathogens adhesion to cells. This may account for why the vaginal mucosa is dominated by lactobacilli making it less receptive to pathogens.

Anti-inflammatory Activity of Probiotics

Crohn's disease (CD) and ulcerative colitis (UC) are among the most chronic inflammatory disease of the GIT and are collectively called IBD. Research has shown that an imbalance in the gut microbiota plays an important pathophysiological role in the positive regulation of IBD. It is also understood that the disorder could be altered by supplementation with probiotics, prebiotics and synbiotics. IBD is being associated with impaired production of SCFAS, particularly, acetate, butyrate and propionate. They possess anti-inflammatory effects and improve the propulsive colonic function. Lactobacillus, Bifidobacterium, Enterobacteria are the most widely used probiotics in foods. Apart from these organisms new or genetically modified should be developed to counteract IBD.

Anti-cancer activity of probiotics

Concurrently many new drugs using nanotechnology and biotechnology (nanocapsule) with fascinating properties of luminescent have been discovered but still tolerance to their burden

and side effect has been a major limitation to it. Natural sources that confer carcinogenic effects such as probiotics have been receiving prime focus in recent years. *In vitro* studies have demonstrated that probiotics strains, *Lactobacillus fermentum* NCIMB-5221 and 8829 have highly potent in suppressing colorectal cancer cells and promoting normal epithelial colon cell growth through the production of SCFAS (ferulic acid). This ability was also compared with other probiotics namely *L. Rhamnosus* ATCC 51303 both of which were previously characterized with tumorigenic activity. Again two different probiotics strain *L. acidophilus* L A 102 and *L. casei* L.C 232 have also been found to show pronounced cytotoxic activities with *in vitro* antiproliferative activity against two colorectal cancer cell lines (CaCo-2 and HRT -18). Though probiotics could play a significant role in neutralizing cancer, research is limited only to *in vitro* tests. Goldin and Gorbach (1980) reported that the introduction of acidophilus into the diet lowers the incidences of chemically induced colon tumors in rats. In 1984, they also suggested that diet and antibiotics can lower the generation of carcinogens in the colon and reduce chemically induced tumors. *L. acidophilus* is known to prolong the induction of colon tumors. It was demonstrated that feeding milk *L. acidophilus* resulted in 16-41% reduction in tumor proliferation. *L. bulgaricus* has also been reported to induce antitumor activity against sarcoma-180 and solid Ehrlich ascites tumors. The proposed mechanisms by which probiotics exerts anti-tumor activity include me} Altering the immune function associated with immune response. ii} Anti-proliferative effects vi regulation of apoptosis and cell differentiation iii} Supporting the production of enzymes like β - Glucuronidase, urease, choloylglycine hydrolase, azedoreductase and nitro-reductase by bad bacteria especially enteropathogens such as *E. coli* and *Clostridium perfringens*.

PROBIOTICS USES IN CANCER THERAPEUTIC APPLICATIONS

- i) A few studies have shown that probiotics bacteria prevent pytative preneoplastic lesions or tumors induced by carcinogens such as 1,2-dimethylhydrazine or azoxymethane.
- ii) Also, there is direct evidence for antitumor activities of LAB obtained in studies using preimplanted tumor cells in animal models.
- iii) The probiotics are suppressed the harmful bacteria, by controlling pH of the large intestine through the production of lactic acetic acids. Microbial based therapy of cancer is one of the emerging cancer treatment modalities.

iv) Important advancements have been made to study develop live bacteria or bacterial products such as proteins, enzymes, immunotoxins secondary metabolites of bacteria fungi which specifically target cancer cells cause tumor regression through growth.

Anti-allergic activity of probiotics

In recent times, the beneficial role of probiotics in the protection and management of allergic diseases had advanced the understanding of their cause and prevention. *In vitro* studies of certain probiotics, such as *Lactobacillus plantarum* L 67, have shown the potential to prevent allergy-associated disorders with the production of interleukin-12 and interferon- γ in their host. In another study, *L. plantarum* 06CC2 significantly alleviated allergic symptoms and reduced the levels of total immunoglobulin E, ovalbumin- specific immunoglobulin E, and histamine in the sera of ovalbumin-sensitized mice. In spleen cells of the mice, *L. plantarum* 06CC2 is known to significantly enhance the secretions of interferon γ and interleukin- α , which are responsible for alleviating allergic symptoms. In a recent study of breastfed infants suffering from atopic eczema *B. lactic* and *L. rhamnosus* GG were found to be effective in decreasing the eczema severity, further more *L. rhamnosus* GG has been found successful in preventing the occurrence of atopic eczema in high risk infants, when supplied prenatally to selected mothers who had at least one first degree relative with atopic eczema, allergic rhinitis, or asthma. An allergy occurs when a person's immune system reacts with a substance in the environment known as allergen. Allergic reactions include anaphylaxis, asthma and contact dermatitis.

Effect of probiotic on brain and CNS

Moreover, in recent years many studies have been devoted to, elucidating the influence of gut microbiota on the CNS. The effect of probiotics on the CNS has been mainly studied in clinical trials, where it has been evident that gut microbiota influence human brain development function. In children with autism spectrum disorder a daily dose of *L. plantarum* WCFS, (4.5×10^{10} FU/day) led to an improvement in their school records and attitude towards food. In clinical trials Rao showed decreased anxiety symptoms by administration of *L. casei* strain shirota to patients suffering from chronic fatigue syndrome. Szdjewska reported that autism spectrum and attention-deficit/hyperactivity disorder in children could be prevented by *L. rhamnosus* administration to the mother at 4 weeks from expected delivery. Human intestinally derived strains of *L. brevis* DPC6108 and *Bifidobacterium dentium* were reported to produce large amounts of γ – amino butyric acid, a brain neurotransmitter that

helps humans to suppress anxiety and depression. Oral intake of *L. acidophilus* has been shown to assist people to regulate their mood towards rewards and addictive behavior. The finding suggests that probiotics could one day support the treatment of mental health issues, such as anxiety and depression.

Diarrhea

In the last 2 decades several investigations on probiotics micro-organisms by *in vitro* studies, animal experiments, and appropriate well-designed clinical studies have validated the positive effects of probiotics consumption in arresting diarrhea of different types.

Acute infantile diarrhea- Aid caused by rotavirus is the most studied gastrointestinal condition and rapid oral rehydration is the primary treatment. Probiotics are useful as an adjunct to rehydration therapy, the minimal effective dose in the children is 10 billion CFU within the first 48 hours. It is also found to stimulate specific intestinal antitoxin A immunoglobulin to combat the causative factor for diarrhea. The benefits of probiotics such as *L. reuteri*, *L. rhamnosus*, *G. G L. casei*, and *S. boulardii* in reducing the duration of acute diarrhea in children has been demonstrated.

Antibiotics associated diarrhoea- Disturbance of the indigenous microflora caused by antibiotics treatments often leads to diarrhea. The main mechanism by which antibiotics cause diarrhea is through impaired resistance to pathogens as a result of disruption of the gut microbial flora and subsequent alterations in the metabolism of carbohydrates, short-chain fatty acids, and bile acids. Probiotics including various bacterial species like *L. acidophilus*, *L. rhamnosus* G.G, *L. delbrückii*, and the yeast *S. boulardii* are effective in reducing the incidence of antibiotics induced diarrhea. The name of the condition is derived from the plaque – like adhesion of fibrinopurulent material to the damaged mucosal layer and it is characterized by diarrhoea, abdominal distension, vomiting, fever, and leukocytosis and if complications such as toxic megacolon and perforation. A recent meta-analysis evaluating the available evidence on probiotics for the prevention and treatment of antibiotics associated diarrhoea concluded that probiotic administration (namely, *L. rhamnosus*, *L. casei*, and the yeast *S. boulardii*) is associated with a reduced risk of the condition.

Travellers diarrhea- 20-60% of travellers around the world are affected by traveller's diarrhea. Lactobacilli, Bifidobacteria, Enterococci, and streptococci have been used prophylactically to prevent traveller's diarrhea.

Irritable Bowel Syndrome (IBS)

Irritable Bowel Syndrome is one of the most common functional gastrointestinal disorders. Probiotics *Escherichia coli* Nissle 1917 has also been proved effective in IBS treatment, especially in patients with altered enteric microflora. Soluble, non viscous fibers as prebiotics may also be potentially useful in alleviating symptoms of inflammatory conditions. VSL#3, a mixture of 8 probiotics strains and *Lactobacillus plantarum* decreased flatulence and relieved abdominal bloating. A 2019 review conclude that a multistrain probiotics might improve IBS symptoms.

Inflammatory bowel disorder

Inflammatory bowel disorder is a chronic relapsing multifactorial disorder causing inflammation of the GIT that causes severe watery and bloody diarrhea. A recent study has shown promising potential for the use of *Faecalibacterium prausnitzii* as a probiotic with anti-inflammatory properties in the treatment of CD.

Ulcerative Colitis- Ulcerative Colitis like IBD mainly affects the 4 linings of the large intestine and rectum. Long standing UC is a risk factor for colon cancer. Use of various probiotics species like *S. boulardii*, *Lactobacillus casei* and *Bifidobacteria bifidium* have shown promising result. A pilot study suggested that ferment milk containing *B. breve*, *B. bifidum* and *L. acidophilus* was beneficial induce mild degree remission in patients.

Crohn's Disease- Crohn's disease is a form of IBD which usually affects the intestine. But may occur anywhere from the mouth to the end of rectum. Reports are suggesting the effectiveness of probiotics in countering the problem of CD (ex. *E. coli* Nissel 1917, *S. boulardii*, VSL 3, L.GG) in humans. The therapeutic effects of probiotics consumption on CD are reported to be due to competitive action with common pathogenic flora and an influence on the immune response system. Probiotics also prevent IBD by restoring the integrity of the "Protective intestinal mucosa" (Pena 2007).

Pauchitis- Pouchitis is another type of IBD where the ideal pouch gets inflamed especially after colectomy and ideal pouch canal anastomosis. A significant reduction in the number of Bacteroidetes in feces was reported in patients with chronic pouchitis treated with 24g per day of inulin. VSL # 3 probiotic mixture was found to be highly effective for maintaining remission of chronic pauchitis. Probiotics also have been reported to play a beneficial role in controlling the IBD.

Lactose intolerance

Lactose intolerance is the most common type of carbohydrate intolerance and attributed to lack of digestion of Lactose due to low level of β galactosidase enzyme activity. 2 possible pharmacological interventions for lactose intolerance are treatment with commercially available lactose tablets OR II with probiotics such as *Lactobacillus bulgaricus* and *Streptococcus thermophiles*. It is also observed that the consumption of milk containing *Bifidobacterium longum* and *L. acidophilus* causes significantly less hydrogen production and flatulence. Milk containing *L. acidophilus* gave breath hydrogen values which were significantly lower than those from subjects ingesting supplemented milk (Gilliland and Kim 1982). Lactose intolerant individuals develop diarrhea, abdominal discomfort and flatulence after consumption of milk and milk products. The combination of *Lactobacillus casei* *Shirota* and *Bifidobacterium breve* Yakult has shown better effects and improved the symptoms of Lactose intolerance significantly. **Cardiovascular Disease and Lipid Metabolism.**

Mann and Spoerry were the first to suggest the possible effect of probiotics consumption on lipid metabolism. They reported reduction in serum cholesterol levels in the maasai people on the consumption of fermented milk. The hypocholesterolemic effect by probiotics could be due to a decrease in hydroxy-Methyl glutaryl coenzymes-A reductase in liver, a significant conversion of cholesterol into bile acids, cholesterol may be removed by probiotics by incorporation into the cellular membranes during growth, one study in hamsters using insulin demonstrated a 29 and 63% increase in total cholesterol and triglycerides respectively. A chronic treatment of chicory insulin (20 g / day) for 3 weeks reduces serum triglycerides in men with hypercholesterolemia. A 2017 review concluded that consuming foods containing probiotics lactobacillus bacteria could reduce levels of low-density lipoprotein, or “bad” cholesterol. A significant decrease in serum cholesterol level in rats fed milk fermented with *L. acidophilus* has been reported. Mann (1977) showed that a large dietary intake of yogurt lowered the cholesterolemia in humans. Probiotics lower cholesterol levels by hypothesis like deconjugation of bile via bile salt hydrolase, binding of cholesterol to probiotics cellular surface and incorporation of cholesterol molecules into the probiotics cellular membrane, production of short-chain fatty acids from oligosaccharides, co-precipitation of cholesterol molecules into the probiotics cellular membrane, production of short-chain fatty acids from oligosaccharides, co-precipitation of cholesterol with deconjugated, co-precipitation of cholesterol oligosaccharides, co-precipitation cholesterol with deconjugated bile, and

cholesterol conversion to coprostanolin. Among all the hypothesis, the bile salt hydroxylase theory is most popular. The other popular application of probiotics in maintaining human health is by reducing serum cholesterol level in blood. High content of low-density lipoprotein cholesterol (LDL-C) is a major precursor to hypertension, hyperlipidaemia, and coronary heart disease as well as causing the build-up of atherosclerotic plaque in the arteries. By reducing cholesterol levels in the blood, the risk of developing coronary heart disease, hypertension, atherosclerosis, heart attack, and stroke is reduced by nearly. Therefore, probiotics supplementation could be a potential adjuvant for coronary heart disease, hypertension, atherosclerosis, heart attack, and stroke treatment.

Food Applications of Probiotics-Today an increase in Knowledge of functional foods has led to developing foods with health benefits beyond, adequate nutrition. The last 20 years have shown an increased interest among consumers in functional food including those containing probiotics. This has led to industries focusing on different applications of probiotics in food products and creating a new generation of 'Probiotic health benefits'. The main products existing in the market are dairy-based ones including fermented kinds of milk, cheese, ice cream, buttermilk, milk powder and yogurts. Non-dairy food applications include soy-based products nutrition bars, cereals and a variety of juices as appropriate means of probiotics delivery to the consumers. Microencapsulation technologies have been developed to protect the bacteria from damage caused by the external environment.

Applications of probiotics in food products are given below-

Diary and non-diary based probiotics foods - Milk and its products are good vehicles of probiotics strains. Dairy products play important role in delivering probiotics bacteria to human as these products provide a suitable environment for probiotics bacteria that support their growth and viability.

Drinkable fresh milk and fermented kinds of milk- Dairy drinks were the first commercialized products that are still consumed in larger quantities than other probiotics beverages. Among the probiotics bacteria used in the manufacture of dairy beverages, *L. rhamnosus* GG is the most widely used. Functional dairy beverages can be grouped in two categories-1) Fortified dairy beverages 2) Whey-based beverages. Acidity, pH, dissolved oxygen content, redox potential, hydrogen peroxide, the potential presence of flavoring compounds, and various additives (including preservatives) affect the viability of probiotics

bacteria. Acidophilus and sweet acidophilus milk, bifidus milk, acidophilus buttermilk, yakult, procult drink, actimel proviva are the probiotics containing dairy beverages.

Yogurt- Yogurt is one of the natural sources of probiotics. It is known for its nutritional value and health benefits. Yogurt is produced using a culture of *L. delbrueckii* subsp. *bulgaricus* and *Streptococcus salivarius* subsp. *thermophilus* bacteria. Lactobacilli and bifidobacteria are also added sometimes. The factors like strains of probiotics bacteria, pH, presence of hydrogen peroxide and dissolved oxygen, concentration of metabolites such as lactic acid and acetic acids, buffering capacity of media and storage temperature affects the survival of Lactobacillus and Bifidobacterium spp. In yogurt lactic acid bacteria (LAB) which have been used for food fermentation since the ancient time, can serve a dual function by acting as food fermenting agent potentially health benefits provider. Survival and viability of probiotic in yogurt was found to be strain dependant. The addition of fruit in yogurt may have negative effect on the viability of probiotics since fruit and berries might have antimicrobial activities. The presence of probiotics was found to affect some characteristics of yogurt like acidity, texture, flavour and appearance. These traditional lactic acid bacteria pose good positive impact on the body by forming metabolites which inhibit the putrefactive and pathogenic flora or of the progress of the use of lactose.

Cheese- Cheese have a number of advantages over yogurt and fermented milks because they have high pH, and buffering capacity highly nutritious, high energy more solid consistency relatively higher fat content, and longer shelf. Several studies have demonstrated a high survival rate of probiotics in cheese at the end of shelf life and high viable cells. Cheese was introduced to probiotics industry in 2006 when Danisco decided to test the growth and survival of probiotic strains in cheese. A commercial probiotics cheese was first developed by the Mills DA, Oslo, Norway.

Nondairy based probiotics products- Nondairy probiotics products have shown a big interest among vegetarians and lactose intolerance customers.

Vegetable- Based probiotics products fermented vegetables can offer suitable media to deliver probiotics. Probiotics of *L. rhamnosus*, *L. casei* and *L. plantarum* are better adapted to the vegetable during fermentation. The suitability of carrot juice as a raw material for the production of probiotics food with Bifidobacterium strains was investigated. Yoon and others studied the suitability of tomato juice for the production of a probiotics product by *L. acidophilus*, *L. plantarum*, *L. casei* and *L. delbrueckii* also they tested the suitability of

cabbage to produce probiotic cabbage juice support the viability of probiotics and serve as a healthy beverage. Soybean has received attention from the researchers due to its high protein and quality. Soymilk is suitable for the growth of LAB and Bifidobacterial. Soymilk is now known for their health benefits such as prevention of chronic disease such as menopausal disorder cancer, atherosclerosis and Osteoporosis.

Fruits based probiotics products- The fruits juices contain beneficial nutrients that can be an ideal medium for probiotics. The fruits are rich in several nutrients such as minerals, vitamins, dietary fibers, antioxidants. The suitability of noni juice as a raw material for the production of probiotics was studied by wang and others and found that *B. longum* and *L. plantarum* can be optional probiotics for fermented noni juice. Pomegranate juice was proved to be a suitable probiotics drink as results have shown desirable microbial growth and viability for *L. plantarum* and *L. delbruekii*, *L. casei* has suitable survival ability in cashew apple juice during 42 days of refrigerated storage. It was observed that *L. casei* grew during the refrigerated storage and cashew apple juice showed to be a suitable probiotic product.

Cereal based probiotics products- The developments of new functional foods which combine the beneficial effects of cereals and health-promoting bacteria is a challenging issue. Cereals are good substrates for the growth of probiotics strains and due to the presence of non digestible components of the cereal matrix may also serve as prebiotics. Angelov and others have used a whole grain oat substrate to obtain a drink with probiotics and oat prebiotics beta-glucan. Charalampopoulos and others reported that many cereals supported the growth of probiotics with some difference. Malt medium supported the growth of all examined strains (*L. plantarum*, *L. fermentum*, *L. acidophilus*, and *L. reuteri*) better than barley and wheat media due to its chemical composition. Yosa is a snack food made from oat bran pudding cooked in water and fermented with LAB and Bifidobacteria. It is therefore considered a healthy food due to its content of oat fiber and probiotics LAB, Which combine the effect of beta-glucan for cholesterol reduction and the effect of LAB benefits to maintain and improve the intestinal microbiota balance of the consumer.

Meat-based probiotics foods- Probiotics applications are restricted to fermented meats, such as dry sausages. Meat starter culture was defined as preparations which contain living or resting microorganisms that develop the desired metabolic activity in the meat. LAB are the most common used started culture in meat which produce Lactic acid from glucose or Lactose. Dry sausages are non heated meat products, which may be a suitable carrier for

probiotics into the human gastrointestinal tract. Lactic acid bacteria and staphylococci were used as starter cultures to ferment the sausage. It could be concluded that dry sausage is suitable carrier for probiotics.

Probiotics in Aquarium - LAB are also known to be present in the intestine of healthy fish. The use of probiotics for growth promoter in aquatic animals is increasing with the demand for environment-friendly sustainable aquaculture. The use of antibiotics to cure bacterial infection prevent fish mortality in aquaculture is becoming limited as pathogens develop resistance to drugs. The role of probiotics in the nutrition health of certain aquaculture species has also been investigated by fuller. Several bacteria have been reported as pathogenic to fish, like *Aeromonas*, *citrobacter*, have been reported for their pathogenicity. Probiotics strain increased the survival of larvae of the crab and *Portunus trituberculatus* also reduced the amount of vibrio sp. in the water used to rear the larvae. However, to effectively apply prebiotics or probiotics in aquaculture, the microbial community of finfishes has to be better characterized understood.

Side Effects of Probiotics and Prebiotics- Occurrences of probiotics causing harm are rare, but the most commonly encountered side effect is gastrointestinal distress like bloating *S. boulardii* and *Lactobacillus GG* has been reported to accelerate the complications in specific patient groups especially the immune compromised subjects. Pregnant women, newborn and elderly people are at higher risk of potential probiotics infection because they are immune-compromised. Fermentation of FOS in the colon leads to the production of H and CO₂ can cause discomfort to people. Excessive intake of prebiotics especially Oligosaccharides like FOS, GOS, etc causes abdominal discomfort like bloating and distension as well as significant levels of Flatulence. The people who are most at risk of serve side effects include critically ill patients, those who have had surgery, very sick infant, and people with weakened immunity.

CONCLUSION

The uses of probiotics and their applications have shown tremendous increases in the last two decades. The probiotics are most commonly used in many ways such as foods and drugs scientific research etc. Probiotics possess important functional attributes that could fulfill most of our basic nutritional and clinical supplementation requirements. The best-documented effects of probiotics include treating diarrhea, irritable bowel disease, cardiac diseases, Lactose intolerance, asymptomatic bacterial vaginosis, hypercholesterolemia.

Dietary probiotics supplementation generally involves dairy products but probiotics can also be incorporated into non-dairy fermented food products, presenting an alternative and more advantageous source in the process of evaluating new probiotics strains. Particularly yogurt, continue to be the most important vehicles for delivery of probiotics bacteria to the consumer with the non-dairy sector continuously evolving as well, as a result of food technology advances and the growing demand. Overall in this review probiotics, prebiotics and synbiotics have been discussed concerning the systemic effects they exert on the host's health, metabolism and immune system. Probiotics are also used in the development of aquaculture therapeutic applications.

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