



# THE BENEFICIAL CONSTITUENTS AND PHENOMENAL EFFECTS OF PROBIOTICS ON HUMAN HEALTH

<sup>1\*</sup>Anjali Kumari, <sup>2</sup>Kumar Shubham, <sup>3</sup>Sadia Siddique, <sup>4</sup>Vinod Kumar Gupta <sup>4</sup>

<sup>1,2,3</sup> UG Students; <sup>4</sup>Scientist

<sup>1,2,3</sup> Department of Biotechnology, Anugrah Narayan College, Patna, India

<sup>4</sup>Rapture Biotech International Private Limited, Noida, India

**Abstract:** Probiotics are the living cell organisms. It is present in human and animal gut. The probiotic organisms can also be thought of as natural antibiotics in the human-animal gut. They also prove to be beneficial for health when regulated in sufficient sums. Probiotic group of bacteria includes *Lactobacillus*, *Bifidobacterium*, *Pediococcus*, *Lactococcus*, *Bacillus* and yeasts strains. *Lactobacillus* and *Bifidobacterium* are the main probiotic groups; however, there are reports on the probiotic potential of *Pediococcus*, *Lactococcus*, *Bacillus* and yeasts. Some of the identified probiotic strains exhibit powerful anti-inflammatory, anti-allergic and other important properties. Apart from that, the consumption of dairy and non-dairy products stimulates the immunity in different ways.

**Index Terms:** Probiotic, *Lactobacillus*, *Bifidobacterium*, anti-cancer, anti-inflammatory, anti-allergic, dairy products, non-dairy Products.

## I. INTRODUCTION

The word probiotic is made of two Greek words 'pro' and 'bios' which simply means 'for life' [1]. The most commonly quoted meaning was proposed by Fuller (1989) and he said that probiotics are live microbial feed supplement which beneficially affects the host animal by improving its intestinal balance. This correct definition is still commonly referred to, despite continual contention. Today, probiotics are often used in health-promoting "functional foods" for humans, as well as therapeutic, prophylactic growth supplements in animal production human health [2-4]. Other commonly studied probiotics include the spore-forming *Bacillus* spp. Yeasts. *Bacillus* spp. have been shown to possess adhesion abilities, produce bio activated molecules provide immuno-stimulation [5-7].

Usually introduced to food, condiments and beverages, probiotics act as a component of fermentation process at appropriate stage due to their long time survival and multi-purpose capacity. Their administration to a person is based on age class interval. It can be taken orally in the form of capsule or probiotic food. In order to create and supply health effect, probiotic cells are constantly viable in the food carries and adapt extreme harsh environment of Gastro Intestinal Tract (GIT). On the other hand, it must be stable during Gastro intestinal transit and fulfill the criterion that the cell count becomes at least  $10^6$  CFU  $g^{-1}$ . Despite the fact that dairy-based items are proposed to be the principle bearers for the conveyance of probiotics, other non dairy based items also contain large number of probiotic bacteria [8]. The term probiotics includes numerous bacteria and other different microorganisms, for example, yeast. It is important to note that every probiotic strain acts particularly. Hence, a specific medical advantage for one strain does not imply that all probiotics can present this medical advantage. Each strain must be tried for a specific impact independently. Probiotics also stimulate, modulate and regulate the host's immune response by initiating the activation of specific genes of localized host cells. Through bidirectional neuronal signalling, they even modulate the gastrointestinal hormone release and regulate brain behaviour, as part of the gut-brain axis [9].

## II. MECHANISMS OF ACTION OF PROBIOTICS

Probiotic bacteria can inhibit pathogens by the production of antagonistic compounds/by competitive exclusion (competition for nutrients attachment sites).

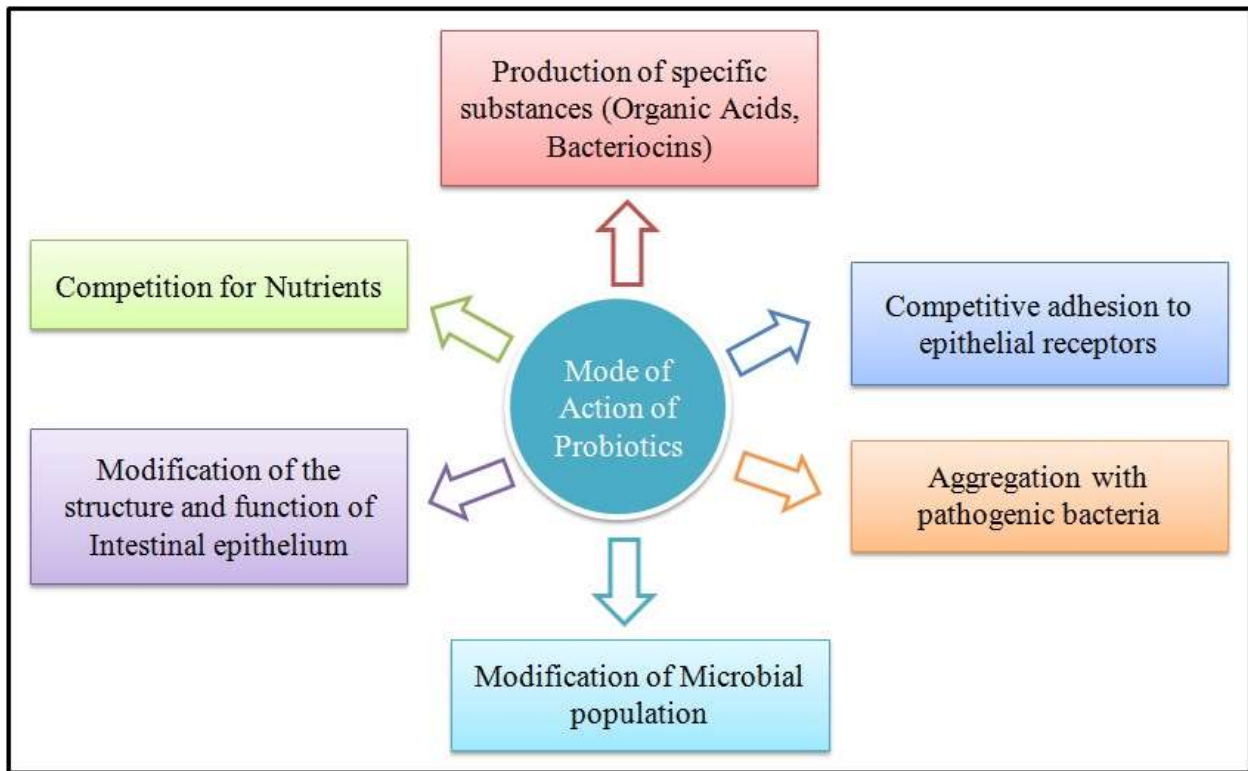


Fig 1. Mechanisms of action of probiotic

Probiotics are mainly considered as most suitable health-promoting bacteria and exert their benefits through following actions:

### 2.1 Interaction between bacteria and nutrients

For the maintenance of a healthy gut epithelium, vitamin production and bile acid metabolism; a metabolically active intestinal flora is very critical. These bacteria require energy-giving nutrients (food) to grow and reproduce. The interaction between bacteria and food in the colon causes carbohydrate fermentation. Numerous metabolites are produced, depending on the substrate available in the form of prebiotics and this leads to production of short-chain fatty acid (Acetic, Propionic and Butyric acid). These are responsible for physiological effect on host as they particularly affect colonic metabolism, hepatic regulation of lipids and sugars, as well as supply of energy to cells (e.g., Butyric acid is a sole substrate for colonocytes). Other beneficial effects include lipid hydrolysis, protein breakdown, vitamins and Calcium production. These bacteria multiply in the small intestine to a small extent because of short transit time and physiologic barriers [10].

The interaction between bacteria and food is critical for e.g. consumption of monosaccharides by a probiotic strain may reduce the growth of *Clostridium difficile*, which is dependent on monosaccharide for its growth [11]. Proteins and complex fats are broken down into components that are easily assimilated. These activities of lactobacilli in the gastrointestinal tract are of great value in infant, convalescent and geriatric nutrition.

The metabolic activities of probiotic bacteria which are responsible for their therapeutic benefits are as follows:

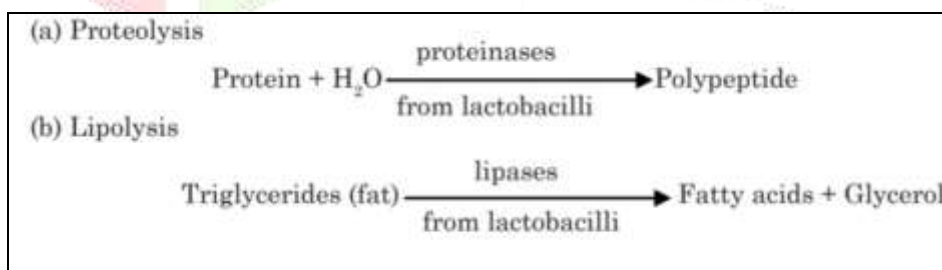


Fig 2: Process of Protein and Lipid breakdown by probiotics

### 2.2 Synthesis of vitamin B complex

An important function of the gut microflora is synthesis of vitamin B. Through experimental studies and research it has been revealed that only few Lactic Acid Bacteria (LAB) require Vitamin B for their metabolic activities, whereas, some LAB can even synthesize Vitamin B [12]. It should be therefore noted that the vitamin B content of fermented milk products is a function of presence of particular strain of LAB which are vitamin B producing.

### 2.3 Production of Antimicrobial Substances

One of the proposed mechanisms involved in the health benefits afforded by probiotics includes the formation of Low Molecular Weight (LMW) compounds (11,000 Dalton), such as organic acids; and the production of antibacterial substances termed Bacteriocins (11,000 Dalton).

Organic acids, in particular Acetic acid and Lactic acid, have a strong inhibitory effect against Gram-negative bacteria, and they have also been considered to be the main antimicrobial compounds responsible for the inhibitory activity of probiotics against pathogens [13–15]. The undissociated form of the organic acid enters the bacterial cell and dissociates inside its cytoplasm. The eventual lowering of the intracellular pH or the intracellular accumulation of the ionized form of the organic acid can eventually lead to the death of the pathogen [16,17].

Probiotic bacteria are also known to inhibit the growth of harmful putrefactive microorganisms through other metabolic products such as Hydrogen Peroxide (H<sub>2</sub>O<sub>2</sub>), Carbon Dioxide and diacetyl (Table 1). *Lactobacillus GG* produces compounds that inhibit the growth of several gram-positive and Gram negative bacteria by producing antimicrobial substances such as Lactic acid, Hydrogen peroxide and pyroglutamate.[18,19].

**Table 1: Antagonistic activities caused by Lactic Acid Bacteria (LAB)**

Metabolic Product of LAB	Mode of Antagonistic Action
<b>Bacteriocins</b>	Affect on membranes, DNA synthesis and protein synthesis
<b>Carbon Dioxide</b>	Reduction of membrane permeability; inhibition of decarboxylation
<b>Diacetyl</b>	Interaction with Arginine-binding proteins
<b>Hydrogen peroxide/ Lactoperoxidase</b>	Oxidization of basic proteins
<b>Lactic acid</b>	Undissociated Lactic acid causes penetration of the membranes, lowering the intracellular pH; It also interferes with metabolic processes such as oxidative phosphorylation

### 2.4 ENHANCEMENT OF THE EPITHELIAL BARRIER

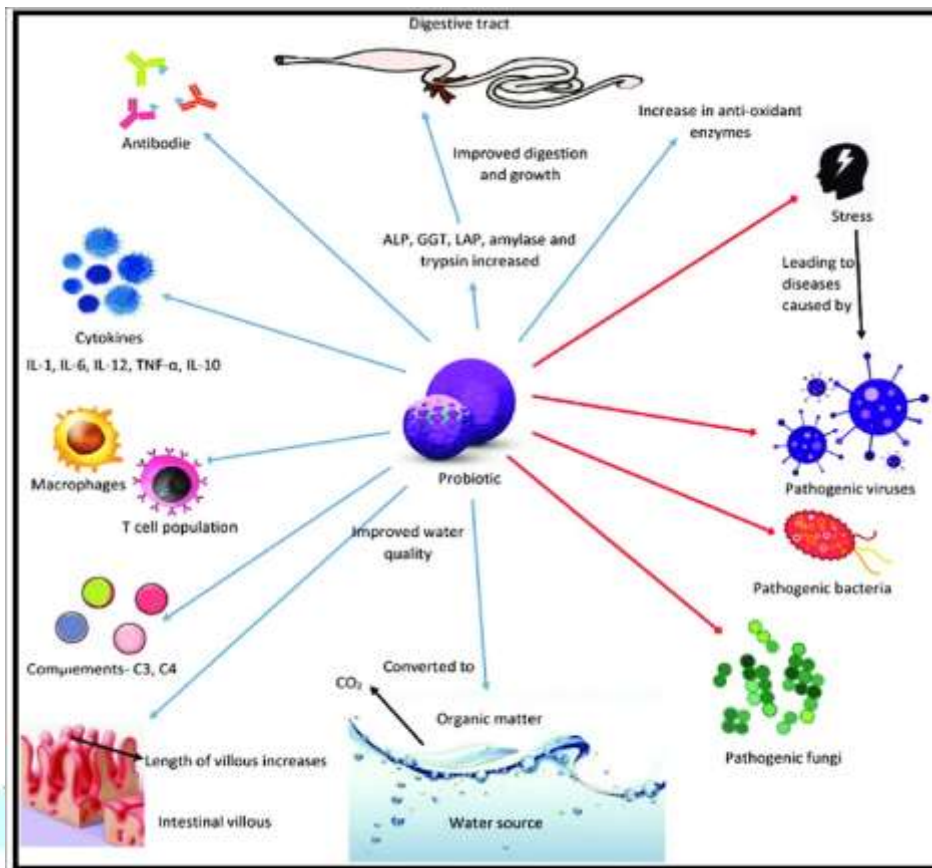
The intestinal epithelium is in permanent contact with luminal contents and the variable, dynamic enteric flora. The intestinal barrier acts as a major defence mechanism which is used to maintain epithelial integrity and protects the organism from the environment. Defences of the intestinal barrier consist of the mucous layer, antimicrobial peptides, secretory Immunoglobulin A (IgA) and the epithelial junction adhesion complex [20]. Once this barrier function is disrupted, bacterial and food antigens can reach the sub mucosa and can induce inflammatory responses, which may result in intestinal disorders, such as Inflammatory Bowel Disease (IBD) [21- 23]. Consuming non-pathogenic bacteria can contribute to intestinal barrier function, and there have been extensive studies and research on probiotic bacteria for their involvement in the maintenance of this barrier. However, the mechanisms by which augmentation in intestinal barrier function occurs by probiotics, is not yet fully understood.

### 2.5 COMPETITIVE EXCLUSION OF PATHOGENIC MICROORGANISMS

In a report addressing the total exclusion of *Salmonella typhimurium* from maggots of blowflies published in 1969, Greenberg [24] first used the 'competitive exclusion' term for the scenario in which one species of bacteria more vigorously competes for receptor sites in the intestinal tract than another species. The mechanisms used by one species of bacteria to exclude or reduce the growth of another species are varied, including the following mechanisms: creation of a hostile micro ecology, elimination of available bacterial receptor sites, production and secretion of antimicrobial substances and selective metabolites, and competitive depletion of essential nutrients [25]. Specific adhesiveness properties due to the interaction between surface proteins and mucins may inhibit the colonization of pathogenic bacteria and are a result of antagonistic activity by some strains of probiotics against adhesion of gastrointestinal pathogens [26]. The production of antimicrobial substances, such as Lactic and Acetic acid, is one example of this type of environmental modification [27]. Some *Lactobacilli* and *Bifidobacterium* share carbohydrate-binding specificities with some Enteropathogens [28, 29], which makes it feasible for the strains to compete with specific pathogens for the receptor sites on host cells [30].

### 2.6 PROBIOTIC ACTION IN FISH GUT BACTERIA

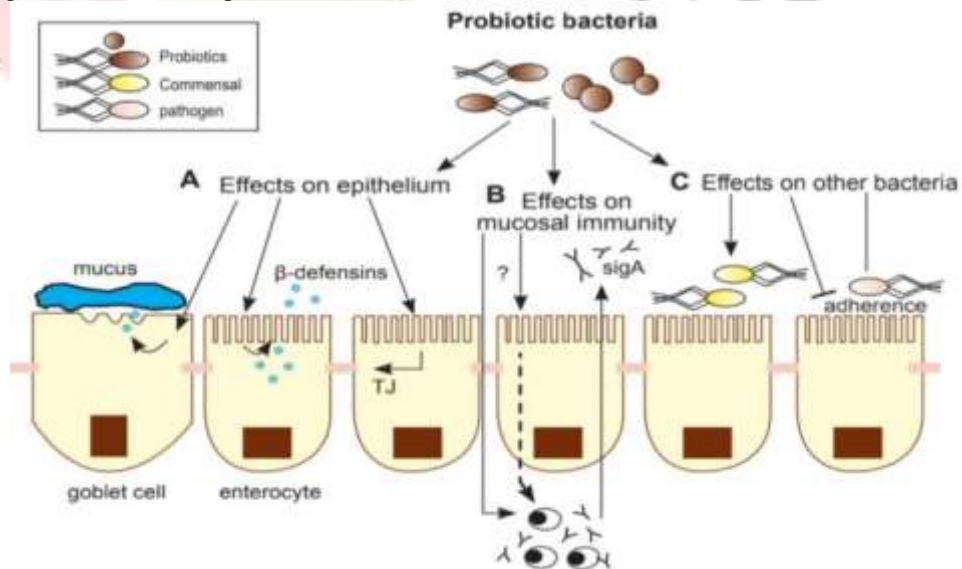
The use of probiotic for aquatic animals is increasing with the for environment-friendly sustainable aquaculture [31]. The gut microbiota of aquatic animals is probably constituted by indigenous microbiota jointly with artificially high levels of microorganisms so maintained by their constant ingestion from the surrounding water [32]. Probiotic strain increased the survival of larvae of the crab and Gazami Crab (*Portunus trituberculatus*) which is one of the most fished species of crab in the world, also reduced the amount of *Vibrio* sp. in the water used to rear the larvae.[33,34-36] Thereafter, it has been reported that bacterial strains associated with intestinal skin mucus of adult marine turbot (*Scophthalmus maximus*) dab (*Limandalimanda*), suppressed the growth of the fish pathogen *Vibrio anguillarum* [33,37].



**Figure 3:** Beneficial effects of probiotics in aquaculture. Blue arrow indicates effects. Red lines indicate inhibitory effect [38]

Depending on the strain of bacteria or yeast and the model used, probiotics target the epithelial barrier in the following areas:

- a) **Effects on the epithelium:** Probiotics can increase mucin expression and secretion by goblet cells, thus limiting bacterial movement across the mucous layer. Augmentation of defensin expression and secretion into the mucus by epithelial cells also helps in preventing the proliferation of commensals and pathogens, thus also contributing to barrier integrity.
- b) **Effects on mucosal immunity:** Probiotics can increase levels of IgA-producing cells in the lamina propria and promote secretory IgA (sIgA) secretion into the luminal mucous layer. These antibodies limit epithelial colonization by binding bacteria and their antigens, thus contributing to gut homeostasis.
- c) **Effects on other surrounding or infecting bacteria:** Probiotics can alter the microbiota composition and/or gene expression, leading to indirect enhancement of the barrier through the commensal bacteria. Furthermore, some probiotics can directly kill or inhibit growth of pathogenic bacteria via expression of antimicrobial factors such as bacteriocins.



**Figure 4:** Probiotics and barrier function

### III. PROBIOTIC MICROORGANISMS

The probiotic potential of different bacterial strains differs even intraspecifically. Different strains of the same species are always unique, hence they may have differing areas of adherence (site-specific) and specific immunological effects. Hence, actions on a healthy mucosal layer as compared to an inflamed mucosal milieu may be distinct from each other. Ongoing probiotic researches aim at the characterization of the normal, healthy gut microbiota in each individual, assessing the species composition as well as the concentrations of different bacteria in each part of the intestine. The target is also to understand host–microbe interactions within the gut, microbe–microbe interactions within the microbiota and the combined health effects of these interactions. The ultimate goal is to define and characterize the microbiota both as a tool for nutritional management of specific gut-related diseases and as a source of new microbes for future probiotic bacterio-therapy applications. This may eventually include organisms specifically isolated to provide site-specific actions in disorders such as the irritable bowel syndrome (39).

**Table 2. Commercial probiotic microorganisms**

Microorganism	Strain	Company (product)	Bacteria used to cure Disease/ Disorder	Ref.
<i>Bifidobacterium adolescentis</i>	ATCC 15703		Liver damage	40-43, 44
<i>Bifidobacterium animalis</i>	Bb-12	Chr. Hansen		40-43
<i>Bifidobacterium essencis</i>		Danone® (Activia)		40-43
<i>Bifidobacterium lactis</i>	Bb-02, Lafti™ B94	DSM	Constipation	40-43, 45
<i>Bifidobacterium</i>	CRL 431		Constipation	40-43, 45
<i>Bifidobacterium longum</i>	PBS078		Kidney/Urinary stones	46
<i>Bifidobacterium breve</i>	PBS077		Kidney/Urinary stones	46
<i>Bifidobacterium animalis</i>	Bb-12	Chr. Hansen		40-43
<i>Bifidobacterium animalis</i>	DN -173010	Activa yogurt		
<i>Lactobacillus bulgaricus</i>	Lb12		Constipation	40-43, 45
<i>Lactobacillus casei</i>	Shirota	Yakult (Yakult®)	Diarrhoea	40-43
<i>Lactobacillus fermentum</i>	RC-14	Urex biotech		40-43
<i>Lactobacillus fermentum</i>	FTDC 812		Hypercholesterolemia	47
<i>Lactobacillus plantarum</i>	299v Lp01	Probi AB	Irritable bowel syndrom (IBS)	40-43
<i>Lactobacillus helveticus</i>	B02		Salmonella infection	40-43
<i>Lactobacillus paracasei</i>	CRL 431	Chr. Hansen		40-43
<i>Lactobacillus rhamnosus</i>	GG GR-1 LB21 271	Valio Urex Biotech Essum AB Probi AB	Atopic Diseases	40-43
<i>Lactobacillus reuteri</i>	SD2112/ MM2	Biogaia	Colic	40-43
<i>Lactobacillus casei</i>	BL23		CRC (Colorectal Cancer/ Carcinoma)	48
<i>Bacillus lactis</i>	DR10	Danisco (Howaru™)		40-43
<i>Lactobacillus delbrueckii ssp. bulgaricus</i>			Colic	40-43

### IV. SAFETY AND SIDE EFFECTS

Theoretically, probiotics may be responsible for four types of side effects in susceptible individuals: systemic infections, deleterious metabolic activities, excessive immune stimulation, and gene transfer. Practically, however, *Lactobacilli* and *Bifidobacterium* (and probiotics based on these organisms) are extremely rare causes of infections in humans. This lack of pathogenicity extends across all age groups and also to immuno-compromised individuals [49].

Traditional dairy strains of Lactic acid bacteria (LAB) have a long history of safe use. LAB, including different species of *Lactobacillus* and *Enterococcus*, have been used in daily consumption since humans started to use fermented milk as food. Probiotic species such as *Lactobacillus acidophilus* have been safely used for almost more than 70 years.

The safety of probiotics has been considered in reviews and clinical reports which have drawn attention to isolate cases of human bacteraemia [50-52]. Surveillance studies support the safety of commercial LAB [53]. Available data indicate that no harmful effects have been observed in controlled clinical studies with lactobacilli and bifidobacterium [54].

## V. CLINICAL SIGNIFICANCE OF PROBIOTICS AND ITS POTENTIAL APPLICATIONS

The use of probiotics for clinical health benefits is an interesting area of research that is yet to be explored in the current era. Some of the elite properties of probiotics, such as anti-pathogenicity, anti-diabetic, anti-obesity, anti-inflammatory, anti-cancer, anti-allergic and angiogenic activities along with their effect on the brain and central nervous system (CNS) have been briefly discussed below and also depicted in Fig.5.

### 5.1. ANTI-PATHOGENIC ACTIVITY OF PROBIOTICS

Anti-pathogenic activity is regarded as one of the most beneficial effects of probiotics because unlike classic antibiotics, there is no disturbance or alteration in the composition of the complex population of the gut microbiota. There has been considerable research on the anti-pathogenic activity of probiotics or a probiotic mixture. Tejero-Sarinena et al. [55] investigated the influence of probiotics on the survival of *Salmonella enteric* subsp. *serovar typhimurium* and *Clostridium difficile* in an in vitro model and postulated that inhibition of these pathogens by probiotics is done by the production of short-chain fatty acids (SCFAs), such as Acetic, Propionic, Butyric and Lactic acids. SCFAs also help to maintain an appropriate pH in the colonic lumen, which is imperative in the expression of numerous bacterial enzymes and in metabolism of foreign compounds and carcinogens in the gut [56].

### 5.2. UROGENITAL HEALTH CARE

According to the Centre for Disease Control and Prevention (CDCP), more than one billion women around the world suffer from non-sexually transmitted urogenital infections, such as bacterial vaginosis (BV), urinary tract infection (UTI) and several other yeast infections [57].

The major issue currently is that microbes, among others, are simultaneously becoming resistant to the present medicines. Therefore, instead of developing new medicines, we should focus presently on developing new live supplements, like non-pathogenic microbes that act against the pathogens. The major advantage of having sophisticated medicines to treat various medical conditions, these pathogenic like non-pathogenic microbes that act against the pathogens.

It is well-known that there is an association between abnormal vaginal microbial flora and an increased incidence of urinary tract infection (UTI). There are about 50 different species inhabiting the vagina, like *Lactobacillus brevis*, *Lactobacillus casei*, *Lactobacillus vaginalis*, *Lactobacillus delbrueckii*, *Lactobacillus salivarius*, *Lactobacillus reuteri*, and *Lactobacillus rhamnosus*. These are regarded as the main regulators of the vaginal micro-environment. Imbalance in the microbial composition greatly influences the health of the vaginal microenvironment, potentially leading to compromised state of bacterial vaginosis (BV) and UTI. These compromised states can be reassured by balancing the number of *Lactobacillus* sp. via the supplementation of Probiotics [57].

### 5.3. ANTI-DIABETIC ACTIVITIES OF PROBIOTICS

According to the International Diabetes Federation (IDF) of Southeast Asia, 425 million people suffer from diabetes worldwide including 78 million people in the Southeast Asian region [58]. Moreover, this number is expected to rise to 629 million by 2045 if nothing is done. A similar pattern has been implicated in the development of auto-immune diseases, such as type-1 diabetes [59-61]. Another convincing strategy is management of type-2 diabetes by modulating gut hormones, such as gastric inhibitory polypeptide and glucagon-like peptide-1, via probiotic and prebiotic interventions. In this context, hormones play an implicated role in glucose homeostasis, which results in neutralizing the disorder caused by peripheral insulin resistance or failure of b-cells to produce insulin [62]. Current research is focused on generating new prebiotics, such as asarabinoxylan and arabinosaccharides, which show promising results in counteracting related metabolic disorders, because both carbohydrates have been linked to adiposity reduction.

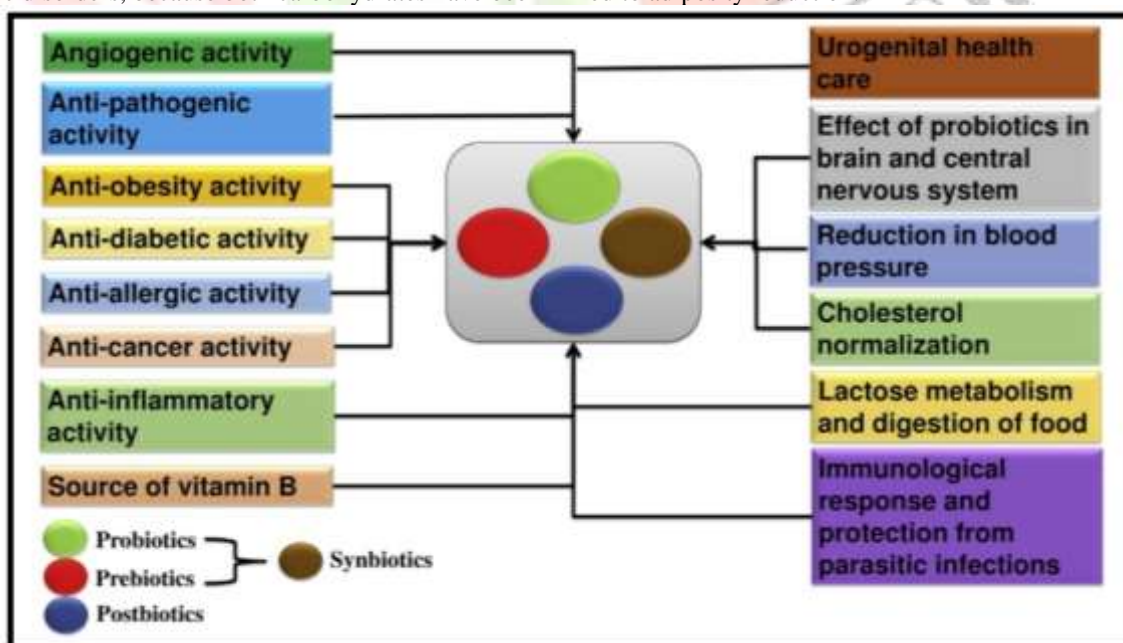


Fig. 5 - Applications of probiotics and their mode of action.

#### 5.4 ANTI-OBESITY ACTIVITY OF PROBIOTICS

Abnormal or excessive fat (obesity) accumulation directly impairs health condition which is linked to an increase in energy availability, sedentariness and a greater control of ambient temperature, leading to an imbalance in energy intake and expenditure [63].

Probiotics possess physiological functions that contribute to the health of host environment regulating microbes. In most instances, weight loss is facilitated by thermogenic and lipolytic responses through stimulating the sympathetic nervous system [64]. Probiotic strains, *Lactobacillus gasseri* BNR17 have shown properties of inhibiting the increase in adipocyte tissue that are the main source of leptin and adiponectin and thereby, limiting leptin secretion [65]. Hypocholesterolaemic effects have also been reported by other probiotic microbes such as *L. casei*, *Lactobacillus acidophilus* and *Bifidobacterium longum* [66].

#### 5.5 ANTI-INFLAMMATORY ACTIVITY OF PROBIOTICS

Crohn's disease (CD) and ulcerative colitis (UC) are among the most chronic inflammatory diseases of the GIT and are collectively called Inflammatory Bowel Disease (IBD) [67]. CD can affect any part of the GIT like the mucosa, sub-mucosa, and serosa, and the inflammation can even spread to the whole GIT.

On the other hand, Ulcerative colitis characteristically involves the larger part of the bowel; specifically the mucosa and sub-mucosa of the colon [68]. Therefore, it is reasonable to consider that supplementation with indigestible carbohydrates and fiber (prebiotic) alone, or in combination with probiotics to increase the production of Short Chain Fatty Acids could be useful therapeutic approaches. Presently, progress in the field is mostly concerned with developing genetically engineered probiotic bacterial strains that are able to produce and discharge immuno modulators, such as interleukin 10, trefoil factors (compact proteins co-expressed with mucins in the GIT), or lipoteichoic acid (a major constituent of the cell wall of Gram-positive bacteria) that can impact the host immune system, resulting in the restoration of the level of protective commensal bacterial species [69]. The most widely used probiotics in foods are *Lactobacillus*, *Bifidobacterium*, *Enterobacter* and *E. coli*. Apart from these organisms, new or genetically modified should be developed to counteract IBD [70].

#### 5.6. ANTI-CANCER ACTIVITY OF PROBIOTICS

As per WHO cancer fact sheet [71], cancer has been a dreadful disease affecting people of all ages across the globe and approximately 14 million new cases and 8.2 million cancer-related deaths occurred till 2012. More than 70% of the global cancer deaths are from Asian, African, and American continents. In vitro studies have demonstrated that probiotic strains such as, *Lactobacillus fermentum* NCIMB-5221 and -8829, have high potential to suppress 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. acidophilus* ATCC 314 and *L. rhamnosus* ATCC 51303 both of which were previously characterized with tumorigenic activity [72]. Again two different probiotic strains *L. Acidophilus* LA102 and *L. casei* LC232 have also been found to show pronounced cytotoxic activities, with in vitro anti-proliferative activity against two colorectal cancer cell lines (Caco-2 and HRT-18) [73]. Though probiotics could play a significant role in neutralizing cancer, research is limited only to in vitro tests i.e. under lab condition. Hence, the anti-cancer potential of probiotics are yet to be proven in-vivo models and proceed further towards animal and clinical trials.

#### 5.7. ANTI-ALLERGIC ACTIVITY OF PROBIOTICS

The increasing prevalence of allergic diseases caused by immune disorders is a worrisome factor and also a serious economic and social burden worldwide. Comprehending the fundamental molecular mechanism that contributes to the etiology of allergic diseases, as well as new treatment approaches is vital for the follow-up and prevention of these diseases [74].

In recent times, the beneficial role of probiotics in 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* L67, have shown the potential to prevent allergy-associated disorders with the production of Interleukin-12 and interferon-g in their host [75]. In another study, *L. plantarum* 06CC2 gave significant relief from allergic symptoms and reduced the levels of total Immunoglobulin E (IgE), ovalbumin-specific immunoglobulin E, and histamine in the sera of ovalbumin-sensitized mice. In spleen cells of the mice, *L. plantarum* 06CC2 was seen to significantly enhance the secretions of interferon-g and interleukin-4, which are responsible for alleviating allergic symptoms [76].

#### 5.8. ANGIOGENIC ACTIVITY OF PROBIOTICS

Angiogenesis is an important phenomenon and is necessary for wound healing process through delineated cellular responses to regenerate damaged tissues [77].

Non-pathogenic probiotic yeast, *Saccharomyces boulardii*, has been reported to protect against intestinal injury and inflammation. However, there is little knowledge about the molecular mechanisms by which probiotics mediate these beneficial effects. The potential mechanisms of probiotics in angiogenesis process may include alteration of inflammatory cytokine profiles, down-regulation of pro-inflammatory cascades or induction of regulatory mechanisms in a strain-specific manner, epithelial barrier function enhancement, visceral hypersensitivity reduction, spinal afferent traffic, and stress response.

#### 5.9. EFFECT OF PROBIOTICS ON BRAIN AND CNS

The colonization of microbiota in the GIT is well-associated with both GIT and gastrointestinal diseases. Moreover, in recent years, many studies have been devoted towards elucidating the influence of gut microbiota on the CNS. The "microbiota-gut-brain axis" is an interactive, bidirectional communication established by the exchange of regulatory signals between the Gastro-Intestinal tract (GIT) and Central Nervous system (CNS) [78]. 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 [79].

In another clinical trial, Rao et al. [80] showed a decrease in anxiety symptoms by administration of *L. casei* strain Shirota to patients suffering from chronic fatigue syndrome. However, despite an increase in the *Lactobacillus* and *Bifidobacteria* levels, the bowel functions were not studied. Hence, it is feasible that the reduced anxiety was due to improved bowel function. Dosage of multispecies probiotic containing *L. brevis* W, *B. lactis* W, *L. acidophilus* W37, *Bifidobacterium bifidum* W2, *L. salivarius* W2, *L. casei* W5, and *Lactococcus lactis* (W19 and W58) to healthy humans showed a significant overall reduction in the cognitive reactivity to sad mood [81]. However, probiotic trials involving patients suffering from anxiety and clinical depression are lacking and therefore require more time

and work is required to validate this effect. Oral intake of *L. acidophilus* has been shown to assist people to regulate their mood towards rewards and addictive behaviour [82].

## VI. CONCLUSION

The use of probiotics in the day-to-day medicine in the treatment of gastrointestinal disorders is increasing with the discovery of the beneficial effects of these agents. This study reviewed the mechanisms of action of probiotics. Several important mechanisms underlying the antagonistic effects of probiotics on various microorganisms include the following: modification of the gut microbiota, competitive adherence to the mucosa and epithelium, strengthening of the gut epithelial barrier and modulation of the immune system to convey an advantage to the host. Therefore, current focus is on evaluating new strains of probiotics and their application in biomedical/clinical research, paving a new direction for exploration and exploitation of probiotics aimed at improving human health.

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