"Gut Allies: Unveiling the Power of Probiotics for Human Health"- A Comprehensive Review

**Abstract**: Probiotics are strains of selected microorganisms that provide a health benefit to the host. Probiotics must meet certain functional, technological, and safety requirements to be considered a probiotic. Through this study, we learned about the various probiotic microorganisms that are found in nature, as well as their traits, mode of action, and advantageous effects upon human health and the diseases as they are seen as major threats to food safety. The need for environmentally friendly agriculture and aquaculture is driving an increase in research on probiotics. Live microbial feed additives, or probiotics, have been shown to enhance the health of both people and other animals. This review's primary goals are to outline current developments in the field of gut microbiota research and demonstrate the crucial role those intestinal bacteria play in the emergence of many medical diseases. Lastly, probiotics hold enormous promise as a different and eco-friendly strategy and seem to be an effective way to manage microbial infections in various contexts. Studies on their actions and potential mechanisms of action against several pathogenic bacteria are highlighted in this review. As the probiotics industry develops further, this review study is a useful tool for scientists, medical professionals, and health enthusiasts looking for a more nuanced understanding of the potential and difficulties of using bacteria for human health and more.

**Keywords:** Probiotics, Gut microbiota, Human health, Digestive health, Immune modulation.

1. **Introduction:**

The term "probiotic" refers to bacteria that have positive impacts on human and animal health and is a modern term that means "for life." (Bagchi T, 2014)

The term "probiotic" originates from the Latin word "pro," which means "for," and the Greek adjective "biotic," or "bios," which means "life." Probiotics are defined as "living strains of strictly selected microorganisms which, when administered in adequate amounts, execute a health benefit on the host" in a 2002 definition created by experts from the working groups of the World Health Organization and the Food and Agriculture Organization of the United Nations” (Kerry et al., 2018). The International Scientific Association for Probiotics and Prebiotics (ISAPP) has revised the criteria, stating that "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host" are now considered qualifying (Hill et al., 2014)

Elie Metchnikoff, a Russian-born novelist, initially developed the idea of probiotics in 1907.

He saw that the long and healthy lives of the Bulgarian villagers who drink fermented milk. Metchnikoff found that the culture of Lactobacillus, which he isolated from fermented milk, produced a lot of lactic acid and was able to survive in the colon. (Sanders et al., 2012).

An essential mechanism by which the native (autochthonous) gut bacteria preserve their existence and provide niche protection against recently ingested microorganisms, including pathogens, is the advantageous use of intestinal microflora, also known as "colonization resistance" or the "barrier effect." (Lewis et al., 2015; Perez et al; 2015)

Probiotics plays a crucial role in initiating intestinal angio genesis by vascular endothelial growth factor receptor (VEGFR) signaling that, in turn, regulates acute and chronic inflammation in intestinal mucosal tissue produced by the advancement of inflammatory bowel disease (IBD) (Bakirtzi et al.,2016; Chen et al., 2013)

Probiotics also begins the activation of particular genes in localized host cells, which stimulates, modifies, and controls the host's immunological response. As part of the gut-brain axis, they even control the release of hormones from the gastrointestinal tract and govern brain activity through bidirectional neural communication. (Kristensen et al., 2016)

 **2. Selection criteria of probiotics:**

Numerous studies have demonstrated the possible unique capabilities of probiotics. In order to be selected and used as a probiotic, it must meet certain functional, technological, and safety requirements. Additionally, the following requirements must be met, as listed in table 1.

Table 1: Different selection criteria for Probiotics has been shown in table 1.

|  |  |  |
| --- | --- | --- |
| Criteria | Required Properties | References |
| Safety | 1. Originating from either human or animal sources.
2. Isolated from healthy persons' gastrointestinal tracts.
3. Demonstrated history of safe use, showing non-pathogenicity and non-toxicity.
4. Accurate diagnostic identification using phenotype and genotype traits.
5. No evidence linking them to infectious diseases.
6. Lack of ability to break down bile acid salts.
7. No adverse effects reported.
 | (Bandhopadhay et al., 2014) (O’Bryan et al., 2013) (Hill et al., 2014) (Abetenh et al., 2018) (Howarth, G. S & Wang H, 2013) (Miriam at al., 2012) (Taverniti et al., 2013)(Revata et al., 2016)(Divya, P. 2016)(Bayane et al., 2010) |
| Functionality | 1. Has the ability to compete with the existing gut microbiota.
2. Ability to survive, metabolize, and grow in the target site, including functions like cholesterol assimilation and vitamin production.
3. Resistance to bile salts, digestive enzymes, and low stomach pH.
4. Ability to compete with other gut bacteria, including closely similar species.
5. Antagonism towards pathogens such as-*Salmonella* spp., *Listeria* spp., and *Helicobacter pylori*, monocytogenes.
6. Resistance to acids and bacteriocins generated by the gut microbiota.
7. Ability to adhere and colonize in particular areas of the host, with a reasonable rate of survival in the gastrointestinal tract.
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| Technological Usability | 1. Ability to produce high biomass and cultures efficiently.
2. Maintaining viability and stability of desired properties during processing (e.g., freezing, drying), preparation, and distribution of probiotic products.
3. High survival rate in both aerobic and micro-aerophilic settings for completed products.
4. Ensuring that final products have the necessary sensory qualities, particularly in the food sector.
5. Genetic stability.
6. Ability to withstand bacteriophages.
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Various types of Species of microorganisms used as probiotics are given in table no 2.

|  |  |  |
| --- | --- | --- |
| Group of Microbes | List of Probiotic Species | Reference |
| Lactic Acid Producing Bacteria | *Lactobacillus acidophilus, Lactobacillus bulgaricus, Lactobacillus casei,*  | (Miriam at al., 2012) (Taverniti et al., 2013)(Revata et al., 2016)(Divya, P. 2016)(Bayane et al., 2010)(Adel, M.M. & Sari, A.M, 2017) (Mohammed et al., 2017)  |
| Non-Lactic Acid Producing Bacteria | *Bifidobacterium adolescentis, Bifidobacterium bifidum, Bifidobacterium infantis, Streptococcus thermophiles, Propinobacterium* |
| Non-Pathogenic Yeast | *Saccharomyces boulardii* |
| Non-Spore Forming Bacteria | *Coccobacillus, Lactobacillus, Streptococcus, Leuconostoc, Lactococcus lactis subsp. Bacillus coagulans, Bacillus subtilis, Saccharomyces cerevisiae, Candida pintolopesii, Aspergillus niger, A. oryzae, Bacillus lichenformis, Streptococcus thermophiles* |

Table 2: Species Types utilized as Probiotics

1. **Mode of action of Probiotics in regard to Human Health:**

Probiotics can act in many different ways- they can modulate the host's good microflora, which involves improving the good microbial balance through the interaction of oral viable microbes with the microflora in the gastro-intestinal tract lumen; they can alter the host's metabolic activities, such as by stabilizing the pattern of digesting enzymes; and they can alter the host's immune system, which involves activating and regulating responses related to the mucosa and the systemic immune system. Additionally, these forms of action rely on strain (Hill et al., 2014)

**3.1 Competition for nutrients:**

It can be observed in gut health that both harmful and good bacteria use the same kind of nutrients. As resulted, there is widespread competition among the bacteria for these nutrients in order for them to proliferate and grow. (Vanderpool et al., 2008)

**3.2 Barrier Function:**

Modifications in intestinal permeability, mucin composition, and the balance between the rate of damaged enterocyte death and the generation of new enterocytes all impact the integrity of the intestinal barrier. An upset stomach barrier can result from illnesses including colon cancer and inflammatory bowel disease. Some probiotics have the capability to alter the properties of the gut (Abatenh et al., 2018)

*Lactobacillus* species have been observed to enhance the expression of mucin in vitro in human intestinal epithelial cells, thereby blocking the adhesion and invasion of pathogenic *Escherichia coli.* It has been shown that *Lactobacillus rhamnosus* GG possesses mitogenic qualities, stimulates mucosal regeneration, and prevents intestinal epithelial cells from inflaming and dying on their own (Gogineni et al., 2013)

* 1. **Production of antimicrobial substances:**

Probiotics hinder infections and stop epithelial invasion by either releasing peptides directly or by stimulating host cells to create them. The intestinal epithelial cells express antimicrobial peptides called defensins (hBD protein) and cathelicidins, which demonstrate antibacterial efficacy against a variety of fungus, bacteria, and viruses. Probiotics have been observed to inhibit the growth of pathogens by releasing a range of antimicrobial agents, including nitric oxide, hydrogen peroxide, defensins, and short chain fatty acids (SCFA), which lower the pH of the lumen. Gram-negative pathogens' outer membranes can be damaged by SCFA, which inhibits the pathogen's ability to proliferate (Gogineni et al., 2013, Rastall, R.A. & Gibson 2014)

* 1. **Immune modulation:**

In a manner unique to each strain, probiotic bacteria bind to epithelial cells and the mucous membrane that surrounds them to combat invasive infections. The reduced bacterial adherence has been shown to be caused by a heat-labile component secreted by *S. boulardii.* (Parvez et al., 2006)

3.5 **Immunoglobulin Responses:**

Major antibody immunoglobulin A (IgA) is released across intestinal mucosal linings and is essential for mucosal immunity. consumption of probiotics on increased host immunity through IgA synthesis (Howarth, G.S & Wang. H., 2013)

* 1. **Interference with quorum sensing signalling:**

According to research by Medellin-Pena et al., Lactobacillus acidophilus secretes a chemical that either directly interacts with the E. coli O157 gene transcription, which is involved in colonization, or suppresses quorum sensing signalling, hence preventing bacterial toxicity ((Gogineni et al., 2013; Rastall, R.A. & Gibson 2014; Parvez et al., 2006; Howarth, G.S & Wang. H., 2013; Medellin et al., 2007). Here in the table different mode of action of probiotics are shown here.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Mode | Process | Mechanism of action | Example | References |
| Barrier Function | Reduced cell apoptosis | Decreased production of TNF-α | *Lactobacillus rhamnosus GG* | (Vanderpool et al., 2008) (Abetenh et al., 2018) (Howarth, G. S & Wang H, 2013) (Miriam at al., 2012),(Revata et al., 2016)(Divya, P. 2016)(Bayane et al., 2010)(Adel, M.M. & Sari, A.M, 2017) (Mohammed et al., 2017)(Gogineni et al., 2013) (Rastall, R.A. & Gibson 2014) (Parvez et al., 2006) (Howarth, G.S & Wang. H., 2013) (Medellin et al., 2007) (McFarland, L.V 2006) |
| Increased mucin production | Enhanced expression of MUC 2 | *Lactobacillus species* |
| Antimicrobial Peptides in Host Cells | Defensins (hBD protein) | Increased production of defensin | *E. coli strain* DSM 17252S2 |
| Cathelicidins | Induced by butyrate production |
| Antimicrobial Factors of Probiotic | Decreases luminal pH | Secretion of SCFA’s | Maximumprobiotic bacteria |
| Production of Bacteriocin | Generated by probiotics that are Gram-positive |
| Microcin production | Produced by Gram-negative probiotics |
| Epithelial Adherence | Competition with pathogens | Blocking adherence directly or by producing proteins | *-* |
| Immune Modulation | Inhibiting pro-inflammatory molecules | Attenuating IL-8 secretion or blocking IκB degradation | *Salmonella typhimurium* VSL#3 *probiotics* |
| Enhancing mucosal immunity | Increasing IgA production | *L. casei* |
| Interference with Signals from Quorum Sensing | Disrupting pathogenic bacteria communication | Producing molecules that block quorum sensing signalling | *L. acidophilus* |

Table 3: Mode of action of different Probiotics

* **Mechanism of probiotics at a glance:**

**PROBIOTIC**

Increase of turnover of enterocytes

Effect on reduction of cholesterol

Reduction of Food Allergy

Immunomodulatory activity

Trigger of cytokine synthesis from enterocytes

Maintenance of normal intestinal flora

Competitive exclusion of enteric pathogen by adhesion

Pathogen growth inhibition by lactic acid and bacteriocin

 **Figure 1: Proposed mode of action of probiotics**

1. **Health benefits and therapeutic effects of using probiotics:**

Probiotics repair damaged digestive systems, reduce inflammation, boost immunity, and fortify the lining of your stomach to cure allergies. Probiotics alter antigen structures, decreasing intestinal permeability, immunogenicity, and the production of pro-inflammatory cytokines that are prominent in individuals with a wide range of allergy problems. In addition to reducing the symptoms of food allergies, Lactobacillus GG and L. rhamnosus GG also significantly lower the chance of acquiring allergic illness (Abatenh et al., 2018)

**4.1 Anti- pathogenic activity of Probiotics:**

Probiotics are thought to have anti-pathogenic activity because, in contrast to traditional antibiotics, they prevent disruption or change in the complex population of the gut microbiota. (Kerry et al., 2018). Probiotics include yeast and a variety of bacterial species, such as *Lactobacillus fermentum, Lactobacillus acidophilus, and Lactobacillus rhamnosusGG. Saccharomyces boulardii* are useful in lowering the frequency of diarrhea brought on by antibiotics. (McFarland, L.V 2006). *Lactobacillus* *GG* demonstrated efficacy against viral and idiopathic diarrhea, but *Saccharomyces boulardii* was found to be more efficient against bacterial diarrhea. To avoid traveler's diarrhea, prophylactic usage of lactobacilli, bifidobacteria, enterococci, and streptococci has been implemented (McFarland, L.V 2007). By producing bacteriocins (nisin A, pediocin PO2, leucosin K, and reuterin (3-hydroxy propionaldehyde) and short-chain fatty acids (formic, acetic, propionic, butyric, and lactic), probiotics can suppress *H. pylori*. Several probiotics have been researched in recent years to see if they can eradicate *H. pylori*. (Rijkers et al., 2011). Tejero-Sarinena et al. (2013) claimed that probiotics work by preventing the synthesis of short-chain fatty acids (SCFAs), which include lactic, propionic, butyric, and acetic acids, which inhibit infections. SCFAs support the colonic lumen's proper pH, which is necessary for the production of several bacterial enzymes as well as the gut's digestion of foreign substances and carcinogens.

**4.2 Anti-cancer activity of probiotics:**

Some LAB (*Lactobacillus delbrueckii subsp. bulgaricus*) stains can bind with heterocyclic amines, which are carcinogenic and can help prevent colon cancer, these stains have demonstrated anti-mutagenic benefits (Iqbal et al., 2014). Probiotic strains Lactobacillus fermentum NCIMB-5221 and -8829 have been shown in vitro to be extremely effective at inhibiting colonrectal cancer cells and promoting the proliferation of normal epithelial colon cells by producing SCFAs (ferulic acid). Additionally, this capability was contrasted with those of other probiotics, specifically *L. acidophilus* ATCC 314 and *L. rhamnosus* ATCC 51303, both of which have been shown to exhibit tumorigenic activity. (Kahaouli et al., 2015). Yet again, it has been discovered that two distinct probiotic strains, *Lactobacillus acidophilus* LA102 and *Lactobacillus casei* LC232, exhibit strong cytotoxic properties, as well as in vitro anti-proliferative activity against two colorectal cancer cell lines (Caco-2 and HRT-18) (Awaisheh et al., 2016)

**4.3 Anti-diabetic activities of probiotics:**

The gut microenvironment is dominated by two distinct bacterial phyla: Gram-negative bacteroidetes and Gram-positive fungi. Obesity is linked to a gradual rise in bacteroidetes and a decrease in firmicutes, according to recent studies. (Barz et al., 2015; Kobiliak et al., 2016). More precisely, the bacteroidetes/firmicutes ratio has increased in patients with type-2 diabetes due to a considerable decrease in firmicutes species, which has a positive correlation with plasma glucose concentration. (Barret et al., 2012). Modulating gut hormones, such as glucagon-like peptide-1 and gastric inhibitory polypeptide, using probiotic and prebiotic therapies is another compelling method for managing type-2 diabetes. In this scenario, hormones are involved in glucose homeostasis, which counteracts the condition brought on by peripheral insulin resistance or b-cell inability to make insulin. (Grover et al., 2012)

**4.4 Anti-inflammatory activity of probiotics:**

Ulcerative Colitis is a chronic inflammatory illness of the rectum's mucous membrane or the rectum and colon that can cause perforation, ulceration, and necrosis in certain cases. (Sarowska et al., 2013) Utilizing several probiotic species such as Bifidobacterium bifidum, Lactobacillus casei, and S. boulardii has demonstrated encouraging outcomes (Pandey et al., 2015)

IBDs such as Crohn's disease, which can occur anywhere from the mouth to the end of the rectum, typically affect the intestines. It results in inflammation and ulceration, which impairs the body's capacity to properly digest food, absorb nutrients, and get rid of waste. It has shown to be more successful in keeping Crohn's disease patients from relapsing. There has been some evidence that *S. boulardii* can effectively relieve the symptoms of active Crohn's disease, such with decreased frequency of stools and disease activity (Khan, M.A. & Moshed, M.N, 2015)

**4.5 Anti-obesity activity of probiotics:**

Probiotics have physiological properties that help maintain the host environment's health by controlling microorganisms. Most of the time, thermogenic and lipolytic reactions that activate the sympathetic nervous system aid in weight loss. (Karimi et al., 2015) Lactobacillus gasseri BNR17, a probiotic strain, has demonstrated the ability to reduce leptin release by preventing the growth of adipocyte tissue, which is the primary source of leptin and adiponectin. (Kang et al., 2013)

**4.6 Effect of probiotics on brain and CNS:**

Both gastrointestinal and GIT disorders are closely linked to the microbial colonization in the GIT. Furthermore, a lot of research has been done recently to clarify how the gut microbiota affects the central nervous system. The GIT and CNS exchange regulatory signals to create the "microbiota-gut-brain axis," an interactive, two-way communication system. (Mayer et al., 2015) Probiotics' impact on the central nervous system has mostly been investigated in clinical studies, where it has been shown that gut bacteria affect how the human brain develops and functions. (Tillisch K., 2014). Rao et al. demonstrated that giving L. casei strain Shirota to patients with chronic fatigue syndrome reduced their anxiety symptoms.(Rao et al., 2009). According to Szajewska, administering L. rhamnosus to the mother four weeks prior to the anticipated delivery could prevent attention-deficit/hyperactivity problems and autism spectrum disorders in children (Szajewska H., 2016). Numerous gut bacteria have been shown to produce neuroactive substances that are comparable to those made in the host brain. G-aminobutyric acid, a brain neurotransmitter that aids in the suppression of anxiety and sadness in humans, has been found to be produced in significant quantities by human intestinally derived strains of *Bifidobacterium dentium* and *L. brevis* DPC6108. (Barret et al., 2012), It has been demonstrated that taking L. acidophilus orally helps people control their emotions toward rewards and addictive behavior. (Nogueiras et al., 2012)

Table 4: List of probiotic strains used for enhancing human health, preventing infections, treating illnesses, and management

|  |  |  |  |
| --- | --- | --- | --- |
| Disease Name | Probiotic Strains | Treatment Outcome | References |
| Constipation | *Bifidobacterium species, B. lactis, B. longum, B. breve, B. infantis, L. casei, L. rhamnosus, Streptococcus thermophiles, L. bulgaricus* | * Alters the microflora and restores the disturbed community in the gastrointestinal tract.
* Helps solve undesired gastrointestinal problems.
* Enhances and regulates frequency, uniformity, and whole-gut transit time.
 | (Howarth, G. S & Wang H, 2013) (Miriam at al., 2012), (Revata et al., 2016)(Divya, P. 2016)(Bayane et al., 2010)(Adel, M.M. & Sari, A.M, 2017) (Mohammed et al., 2017)(Gogineni et al., 2013) (McFarland, L.V 2006)(McFarland, L.V 2007)(Sarowska et al., 2013)(Pandey et al., 2015)(Khan, M.A. & Moshed, M.N, 2015)(Tuohy et al., 2003)(Rijkers et al., 2011)(Iqbal et al., 2014)(Abatenh et al., 2018) |
| Irritable Bowel Syndrome | *L. acidophilus, L. plantarum, L. casei, B. lactis, S. cerevisiae* | * Reduces the symptoms of irritable bowel syndrome (IBS)
* Effectively alleviates and manages symptoms of this condition.
 |
| Colon Cancer | Lactic acid bacteria | * Modifies the physicochemical conditions in the colon and binding sites, as well as the metabolic activities of the intestinal microbiota.
* Biodegrades potential carcinogens. - Produces anti-tumourous or mutagenic compounds by decreasing the activity of the enzyme β-glucuronidase.
* Increases the host immune response.
 |
| Diabetes and Obesity | *Lactobacillus acidophilus NCFM, Lactobacillus gasseri SBT2055, L. rhamnosus CGMCC1.3724* | * Decreases the risk of insulin resistance with type 2 diabetes mellitus.
* Improves and maintains the metabolic equilibrium of the host, leading to significant weight loss.
 |
| Acute Viral Upper Respiratory Infections | *B. animalis subsp. lactis, L. lactis subsp. Lactis* | * Improvises brain activity and provides mental health.
* Perpetuate the central nervous system's capacity via immunological, neuroendocrine, and metabolic processes.
* Aids the early development of typical social and cognitive behaviours.
* Beneficial strains alleviate diseases and have a direct favourable impact on the CNS.
 |
| Helicobacter pylori Infection | *Lactobacillus, Bifidobacterium, L. johnsonii* | * Decreases the adverse effects of *H. pylori* through the release of bacteriocins, production of organic acids, and competitive colonization in epithelial or mucosal cells, hindering its growth, adhesion, and bacterial load.
 |
| Atopic Disease | *Lactobacillus GG, L. rhamnosus Lactis, L. fermentum, Bifidobacterium bifidum, B. lactis, L. acidophilus, L. casei, L. salivarius, Lactococcus lactis* | * Reduces atopic eczema and improves skin condition.
* Removes the symptoms of atopic dermatitis in infants with moderate to severe conditions.
 |
| Colic | *L. casei, S. thermophilus, B. breve, L. acidophilus, B. infantis* | * Highly effective in reducing colic in breastfed infants and children.
 |

1. **Conclusion:**

This study not only tells us the importance of probiotics in human health but also in several sectors like aquaculture and agriculture. Through this study, we learned about the various probiotic microorganisms that are found in nature, as well as their traits, mode of action, and advantageous effects. Probiotics have significant functional qualities that could meet the majority of our fundamental needs for clinical supplements and nutrition. These microorganisms have demonstrated beneficial responses to clinical treatment for a number of illnesses and conditions, including rotavirus-related diarrhea, IBS, and food allergies. Furthermore, a fascinating and quickly developing field of study is the role that probiotics play in the prevention and treatment of diseases linked to pathogenic microbes, diabetes, obesity, and cancer. Dairy products are typically used in dietary probiotic supplementation, but probiotics can also be added to fermented food products that aren't dairy, offering a more beneficial and alternate source when testing out novel probiotic strains.
Additionally, recent nutritional and clinical analyses have been successful in highlighting some of the unique roles played by specific probiotic strains. Particularly, the control of energy in different catabolic and anabolic processes, tolerance to bile and acid, adhesion to gut epithelial cells, ability to fight off infections, and a few other qualities like their safety-enhancing qualities, suitability as food, and advantageous supplements for human health. Consequently, the current emphasis is on assessing novel probiotic strains and their suitability for biomedical and clinical research, opening up new avenues for probiotic exploration and exploitation targeted at enhancing human. Furthermore, some noteworthy roles of specific probiotic strains have been successfully revealed by recent clinical and nutritional assessments. In particular, energy regulation in different catabolic and anabolic processes, tolerance to acid and bile, adhesion to gut epithelial cells, ability to fight off infections, and a few other qualities like their safety-enhancing qualities, suitability as food, and health-promoting supplements. Thus, the current emphasis is on assessing novel probiotic strains and their suitability for biomedical and clinical research, opening up new avenues for probiotic exploration and exploitation with the goal of enhancing human health.

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