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THE ROLE OF PROBIOTICS IN IMMUNITY, PATHOGENESIS AND GENERAL HEALTH PROMOTION / A REVIEW ARTICLE

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Abstract:
Probiotics are a group of beneficial microorganisms that can improve the health of humans and animals. They have a variety of biological activities, including antimicrobial, immunomodulatory, and anti-inflammatory effects. In addition, probiotics have been shown to benefit a wide range of diseases, including diabetes mellitus, rheumatoid arthritis, and obstructive pulmonary disease. In this review, we discuss the direct and indirect aspects of probiotic techniques aimed at improving the production of dairy cows and enhancing soil agrochemical properties, including total and nitrate nitrogen, humic acid, total and accessible phosphorus, organic carbon and humus content.

Keywords: Probiotic, Immunity, Pathogenesis, General health

1-INTRODUCTION:

The term probiotics comes from the Greek words "pro" and "bios," meaning "life" and it means giving host organisms the ability to modify their intestinal microbiota (1). Early detection of probiotics as natural and useful intestinal microbes at the close of the 1800s: Probiotics can enhance or restore the physiological digestive system when ingested. Researchers found that these microorganisms colonize the gastrointestinal tracts of healthy individuals. These bacteria can interact with pathogenic germs and colonize the intestine and development of microflora (2). Probiotics are microorganisms that, when given in sufficient quantities, have a beneficial and healthy effect on the host through different mechanisms. louis in the early 1900s first detected the microorganism and found it was responsible food fermentation, Elie Metchnikoff detected the longevity Bulgarian people in rural regions was related to daily consumption of daily products such as yogurt, and the history fermented food was long the first reported of fermentation milk in middle east and India about 10,000 BC and in Egypt, Rome, Greece, and the rest of Europe about 7000-5000 BC, the first discovered of soy sauce in China, Japan and Korea about 4000-3000 BC, By 2000 BC, fermented rice was common in Asia. Fish sauce was discovered in North Africa and Southeast Asia around 1000 BC. Wine production began in North Africa around 3000 BC and later spread to the Middle East, Greece, Egypt, and Rome. Various probiotic bacteria like Lactobacillus*, Enterococcus, Streptococcus, Bacillus* and *Bifidobacterium*, as well as fungal genus such as Saccharomyces boulardii, were involved in these fermentation processes. Probiotics are utilised in poultry, livestock, aquaculture, and humans for the prevention and treatment of many disorders and diseases such as bacterial, viral, parasite, or fungal diseases, nervous system disorders, obesity, cancer, allergy difficulties, and in preoperative and postoperative care. (3).

Bacteriotherapy comprises three distinct agents: probiotics, prebiotics, and synbiotics. This review defines probiotics as live bacteria or fungi that provide a health benefit to the host. Prebiotics are indigestible substances that cause beneficial alterations in the gut microbiota, while synbiotics are products that include both probiotics and prebiotics. (4) Probiotics are living bacteria or fungi that are directly used and provide health benefits to the host, unlike prebiotics using prebiotics, probiotics, and synbiotics is still in its early stages compared to other alternative strategies(5).

1-1 Source of Probiotics:

Throughout history, microorganisms have continued to be significant in human nutrition, as they are consumed in great quantities through the fermentation of various food products rich in beneficial germs such fruits, juices, animal products, and other foods. The sources may come from human origins, such as the large intestine, small intestine and breast milk. Probiotic strains originated from the human microflora

that have been researched show higher adherence to the human intestinal epithelial barrier compared to other strains and are more likely to be safe (6). Probiotics can come from vegetables, pickles, or dairy fermentation products. Another source may be pharmaceutical products and healthy food. Some artificially produced prebiotics are, among others: lactulose, galactooligosaccharides, fructooligosaccharides, maltooligosaccharides, cyclodextrins and lactosaccharose (7). Both of Ogrodowczyk and Drabinska (2021) showed that an important feature of fermented fruits and vegetables is their effect on the human gut. Fermentation of plant-based products may be an alternative to probiotics for dairy and vegetarian people and individuals suffering from allergies. Modified kombucha, a fermented tea beverage made by fermenting black tea with tea fungus, yeasts and acetic acid bacteria, serves as another option to dairy probiotics(8).So exposure to microbes during birth and in the environment is key to the formation of the microbium; it is diagnosed in vaginal and fecal samples from adult mothers by caesarean section prevents the normal pattern of microbial colonization (9).

1-2Action of Probiotics

Various studies have demonstrated that probiotics can significantly impact immunological and inflammatory processes in both animals and humans. Nevertheless, the exact mechanisms remain unclear. Factors like diet, age, BMI (body mass index), drugs, and stress can influence the effectiveness of probiotic use. These drugs have influenced the establishment of the gut microbiome in addition to affecting host gut processes such as permeability and physiology (10) .In (11) referred the mechanisms of probiotics include : Colonization of intestinal microbial communities in children and adults, Replacement of pathogens and bacteriocin production, Activation of enzymes and volatile fatty acid production, Cell adhesion, cell antagonism and production of mucin, Modulation of the immune system and Interact with the brain-gut axis.

1-3 Probiotics' effects on health and disease

Probiotic products offer a variety of nutritional and therapeutic benefits, influenced by factors such as the strain's genetic makeup, probiotic quantity, intended use, and shelf life. Bacterial strains have distinct properties: some are beneficial for obesity treatment, others for diabetes mellitus and some for chronic kidney disease. Probiotics impact bone health by aiding in vitamin production and influencing bone mass through their effect on the gut microbiome. They also have favorable effects on gut health and can help with skin issues like burns, scars, infections, and sores. Probiotics act by influencing the gut microbiota, which is linked to unbalanced neuro-developmental diseases like autism. A prebiotic is a beneficial food item that promotes the growth of helpful bacteria that alter the gut microbiota. To alleviate pain, vomiting, nausea, and gastrointestinal syndrome, support gut pH balance, promote the generation of antimicrobial peptides, enhance mucus production, modulate host immune system response, and alter gut microbiota. Irritable bowel syndrome is associated with a disruption in intestinal balance, leading to an uncontrolled immune response to the gut microbiota by intestinal immune cells and epithelial cells. This can lead to complications like ulcers and fibrosis. Lactobacilli supplements may help reduce stone formation and lower the risk of urolithiasis. Probiotic strains have shown promise in preventing eczema. Dysbiosis, also known as dysbacteriosis, is an imbalance in the body's microorganisms, especially the disrupted microbiota. This is often linked to conditions like IBD, colon cancer, metabolic syndrome, and allergic reactions (12). The efficacy of probiotics in treating and preventing urinary tract infections. Research is expanding on their potential utility as an initial approach to managing the urine microbiota to lower the risk of certain urinary diseases (13) . Mei and Li, 2022, found that Lactobacillus to be the predominant bacteria in the vagina and is associated with the vaginal mucosal barrier(14). Lactobacillus attaches to the vaginal epithelium and competes against pathogen colonization. Lactobacillus produces substances, including bacteriocin and hydrogen peroxide (H2O2), that can hinder the growth of harmful germs and sustain the acidic pH of the vagina and crucial for stabilizing the vaginal milieu, enhancing the immunological response, and preventing the advancement of cervical cancer(14).

1-4 Effect of probiotics on gastrointestinal metabolism

Probiotic bacteria restore the gut ecosystem and reduce gut resistance and AR gene carriers (15). In clinical trials, researchers have found a small group of prebiotics, probiotic strains, and synbiotics that can effectively prevent or ease the symptoms of a number of conditions, including irritable bowel syndrome, diabetes, necrotizing enterocolitis in babies born with very low birth weight, hepatic encephalopathy, and diarrhea caused by infections or antibiotics. Research indicates that probiotics alter the composition of gut bacteria, resulting in the production of compounds that impact health through several processes, such as antibacterial properties, strengthening of the intestinal barrier, and regulation of the immune system. Introducing probiotics to restore the balance of gut flora can be advantageous for human health in preventing and treating diseases (4). Another instance includes researching the use of a commercial probiotic formula including B. bifidum and Streptococcus thermophiles to lessen antibiotic-associated

diarrhoea in newborns by oral therapy (16). Probiotics can improve the bacteria that live in the gut in a number of ways, including by making more mucus and lowering the amount of lipopolysaccharides (LPSs) that are present so that tight junction proteins don't break down. When LPS binds to toll-like receptors 2 and 4 on endothelial cells, it turns on dendritic cells and macrophages, which causes inflammatory markers to rise (10).

1-5 Effect of probiotics on food preservation

Lactic acid bacteria (LAB) offer several key benefits when used in food preservation and active packaging:

1- Acid Production: LABs are known for their ability to produce lactic acid as a metabolic byproduct. This environmental acidification helps inhibit the growth of harmful bacteria, extending the shelf life of food products.

2- Antimicrobial Compounds: LAB can produce various antimicrobial compounds, such as peroxide and bacteriocins, which further contribute to food preservation by inhibiting the growth of spoilage and pathogenic microorganisms.

3- Contribution to Flavor: LAB plays a crucial role in the fermentation process, contributing to the development of unique flavors and textures in fermented foods. This enhances the sensory appeal of the products.

4- LAB produces lactic acid, which synthesizes biodegradable polymers like poly-lactides. These polymers are suitable for use in active packaging, providing an environmentally friendly alternative to traditional packaging materials.

5- LAB can convert food waste and other complex substrates into valuable compounds such as lactic acid, which various industries, including food, chemicals, and packaging, can utilize. This contributes to the concept of a circular economy by reducing waste and promoting sustainability.

Overall, the use of lactic acid bacteria in food preservation and active packaging not only enhances the safety and quality of food products but also aligns with sustainable practices in the food industry (17,18,19).

1-6 Effect of probiotics on pathogenic bacteria

There are numerous in vitro studies examining the impact of probiotics on foodborne pathogens. Lactic acid and other antibacterial compounds produced by Lactobacillus rhamnosus GG affect the survival of Listeria monocytogenes on fruit during storage as well as its viability during gastrointestinal simulation. (20). Many lactobacilli exhibited antagonistic effects against the Campylobacter jejuni pathogen. The study results revealed a reduction in the expression of specific genes related to invasion, motility, and AI-2 production.This supplementation also reduced infection severity, Escherichia coli colonization, and TNF-a downregulation in infected mice. Lactobacillus kefiranofaciens treatment stopped the symptoms caused by Escherichia coli infection, including bacterial translocation, Shiga toxin penetration, intestinal damage, and higher IgA responses specific to Escherichia coli in the mucosa. Lactobacilli inhibit various virulence factors, such as biofilm formation, toxin production, host cell adhesion, and invasion. Lactobacilli inhibit virulence genes, including those involved in the quorum sensing system, which is crucial for bacterial virulence. This system produces autoinducers that stimulate gene expression. Studies have demonstrated the effectiveness of lactobacilli in preventing complications, such as those caused by Clostridium difficile. It has been found that S-layer proteins from different strains of Lentilactobacillus kefiri can protect Vero cells from damage caused by clostridial toxins. It seems that S-layer proteins and clostridial toxins work directly with each other because strains that gathered had higher activity than strains that didn't assemble. Lpb. plantarum was tested for its impact on P. aeruginosa acyl-homoserine-lactones, elastases, and biofilm virulence factors. Results indicated that lactobacilli from the human vagina exhibited significant inhibitory effects on T. vaginalis, N. gonorrhoeae, and G. vaginalis. But it was seen that Lpb. plantarum also made Serratia marcescens (a pathogen that causes hospital-acquired infections) and Bacillus cereus (a pathogen that causes food poisoning) more dangerous. (21). Lactic acid bacteria (LAB) decreasing pH and producing organic acids (acetic and lactic acids) affected the inhibitory action of probiotics on S. aureus culture broth in the study by (22). Inhibited-resistant and sensitive S. aureus isolates affected the study results. A study (23) found that the LAB treatment from Lactobacillus delbreuckii, Lactobacillus paracasei, and Lactobacillus rhamnosus changed genes important for adhesion in all Salmonella species, including Salmonella Typhimurium, Salmonella Enteritidis, and Salmonella Heidelberg(23). Similarly,a significant reduction in the expression of sipA, sipB, and sopB was also observed in epithelial cells (CEC), which was variable. The treated supernatant of both lactobacilli strains with trypsin and catalase can stop S. marcescens from swarming at concentrations between 4 and 2%, but concentrations lower than 1% have no effect (24). Other study found that the presence of oxygen reduced the pathogenicity of L. monocytogenes, the bacteria that causes listeriosis, in cabbage. It also found that the sigB and hly genes were less expressed (25). According to (26), Lactobacillus casei strain

Shirota (LcS) secreted compounds and promoted swimming motility loss in H. pylori 1101 strains and S. Typhimurium SL1344(19).

1-7 Effect of probiotics on immune response:

Probiotics modulate the host's immunological response and limit the expression of pro-inflammatory cytokines, therefore reducing inflammation. Taking supplements with probiotics raises the production of antibodies and B cells by increasing IL10 levels when Salmonella, Staphylococcus aureus, and E. coli are present. Lactobacillus spp. also reduces the S. Typhimurium count in feces. The study demonstrated a decrease in the spread of the bacteria in the liver, spleen, and intestine of mice, leading to improved overall health. Researchers found that L. rhamnosus, L. fermentum, and L. acidophilus modulate the immune response of host cells, reducing their pro-inflammatory reaction to H. pylori. Additionally, S. boulardii, a yeast strain, showed potential as a probiotic against clostridial toxins. Probiotics treat and manage Staphylococcus infections. L. casei (BL23) lowers inflammation in the mammary glands when S. aureus is present. It does this by stopping the production of cytokines like IL8, IL6, TNF-α, IL1², and IL1α. Researchers used multiple probiotics to combat the L. monocytogenes infection. Limiting the adaptive and innate immune responses of rats during an infection with L. monocytogenes is part of treating L. salivarius (BGHO1) host infection(3). The unique characteristics of the gut immune system include its ability to differentiate between commensal bacteria and dangerous pathogens. Immunological tolerance ensures that the immune system does not react against harmless bacteria that share similarities with harmful germs. Oral tolerance is a complex process that includes immune exclusion and immunosuppressive mechanisms against harmless food antigens. PRRs, including Toll-like receptors (TLRs), facilitate these tasks through a sophisticated system of receptors. Key immune cells in the intestines, such as macrophages and dendritic cells, have TLRs on their surface. (26).

The main findings concerning probiotics' immunomodulatory effects on cell profiles are as follows: Probiotics have the ability to regulate, stimulate, and modulate immune responses by influencing the production of proinflammatory and anti-inflammatory cytokines and different probiotic strains exhibit immunostimulatory or immunoregulatory effects, impacting the balance between proinflammatory and anti-inflammatory cytokine also probiotics can change the gut barrier by telling B cells to make IgA and changing how antigen-presenting cells (APCs) make cytokines [T3]. The immunomodulatory effects of probiotics on cytokine profiles play a crucial role in enhancing the defense system against various pathogens and maintaining intestinal health. The studies have shown that probiotics influence the production of cytokines like IL-10, which possesses anti-inflammatory properties and aids in inhibiting proinflammatory cytokines that cause intestinal inflammation, these findings highlight the intricate relationship between probiotics, the cytokine regulation, underscoring the potential to support immune function and overall health (27).

1-8 Effect of probiotics on animals

Researchers are investigating the effects of probiotics on weight gain, illness resistance in young calves, and milk production in lactating animals during peak lactation to counter negative energy balance. Probiotics can impact the gut's microbial ecology, leading to improvements in rumen function that can ultimately enhance milk quality and output. The precise molecular and metabolic alterations induced by probiotic feed additives remain incompletely understood. Probiotics, as living biotherapeutic agents, can modify animals' gene expression profiles by initiating the signalling cascade in host cells. This research examines the direct and indirect aspects of probiotic techniques aimed at improving the production of dairy cows. The study also investigates the preventive effects of probiotics against different ailments. Parasitic sickness and bacterial infection are prevalent in dairy animals (28), elucidates the function of probiotics enhanced the growth, nutrient absorption, and immune system of various farm animals such as cows, sheep, goats, pigs, aquacultures, and poultry. They also improved immune response, milk production, food digestion, and weight gain, especially in ruminants facing stressful environments. S Probiotics, comprising Ent. faecium and Sacc. cerevisiae, boost milk production by 2.3 litres per dairy cow daily, research indicates that cows given a diet enriched with probiotics demonstrate a rise in milk production. Probiotics positively impact immunological responses in fish. (29). Other study looked at how the dietary supplement Saccharomyces cerevisiae culture (SC) affected the pH of the rumen, the levels of volatile fatty acids (VFAs), inflammatory cytokines, and the milk production of high-yielding dairy cows. Supplementing high-production nursing cows with 100 g/d of the specific carbohydrate enhances milk yield, milk fat content, and milk lactose content without impacting protein content. Supplementing with sodium bicarbonate affects the total concentration of volatile fatty acids in the rumen, resulting in a significantly higher ruminal pH. It can boost rumen bacterial development and reduce inflammation. Our research indicates that supplementing with SC has a beneficial impact on the productivity and health of dairy cows (30). Utilizing various microorganisms such as bacillus, lactic acid bacteria, Bifdobacteria, yeast, and Enterococcus to avoid subclinical necrotic enteritis (SNE) and exploring the molecular pathways that enhance the benefits of probiotics on SNE. Clostridium perfringens (CP) induces subclinical necrotic

enteritis (SNE). Probiotics decrease the likelihood of SNE by boosting the body's immune system, strengthening the gut microbiota, and promoting metabolism. Several suggested modes of action for bacterial and yeast probiotics exist. These include the production of organic acids, bacteriocins, and H2S, nutritional competition, anti-inflammatory properties, and the prevention of pathogen attachment to the epithelium (31). The experimental group showed an increase in egg production. Moreover, yeast supplementation impacted positively on birds' immune systems (32). Probiotics are good microbes that help maintain a balanced gut microbiota, improve nutrient absorption, and prevent harmful germs, reducing the need for antibiotics in poultry farming. Nutritionists and veterinary specialists have shown significant interest in utilizing nutrients and probiotics to promote poultry growth. (33).

1-9 Effect of probiotics on plants and soil:

Microbial-based biofertilizers play a crucial role in enhancing crop productivity and supporting sustainable agro-ecosystems. These microbial groups may possess Plant Growth Promoting (PGP) traits like phytohormones, siderophores, amino acids, and polysaccharides, which could further enhance crop growth(34). Utilizing favorable plant-microbe interactions and microbiome integration could offer a sustainable way to enhance agricultural production. Addressing several difficulties is necessary to achieve extensive commercial usage of plant-beneficial bacteria. A systems approach using microscale information technology for reconstructing microbiome metabolism could make it easier to use microbes in natural settings again and again(35). There are four kinds of biofertilizer: those that break down phosphate, those that add nitrogen, those that break down organic matter, and those that kill pests and encourage plant growth (36). Probiotics enhanced the agrochemical qualities of soil, including total and nitrate nitrogen, humic acid, total and accessible phosphorus, organic carbon, and humus content. Plant probiotics serve as an ecological option for cultivating cereals and enhancing soil agrochemical properties(37). *Bacillus spp*. is the most notable plant growth-boosting rhizobacteria because of its capacity to produce enduring, stress-resistant spores. Metabolites that form chemical signals influence Bacillus-plant interactions, leading to enhanced plant growth and defense mechanisms. Bacillus spp. also creates siderophores that aid in extracting iron from minerals and organic substances in the rhizosphere. Small siderophores like enterobactin, pyochelin, alcaligin, and rhizoferin can chelate iron, making it difficult for other microorganisms to obtain iron. Bacillus spp. makes volatile organic chemicals, lipopeptides, polyamines, phytohormones, and acyl homoserine lactose. Plants produce low-molecular-weight compounds such as phytohormones, organic acids, and flavonoids. The effectiveness of microbial biostimulants depends on how well the beneficial microorganisms can colonize the roots. Dynamic molecular communication between bacteria and plants in the rhizosphere plays a key role in the complex process of root colonization, which remains not fully understood(37).

2-CONCLUSION:

Probiotics have physiological effects with a definitive mechanism. so, the exact mechanism of how they work to enhance health and prevent different diseases must be explored. Evidence from clinical trials has revealed that probiotics can potentially alleviate different GI and other disorders. Although our understanding of some molecular mechanisms underlying beneficial aspects of probiotics, we are still far from clinically proven efficacy in many autoimmune and inflammatory diseases. Moreover, many studies have been done on the animal model, so there is an emergent need to translate these results into humans. Currently, genetically modified commensal lactic acid bacteria are being used to deliver special health-interest compounds. But most of the work regarding recombinant bacteria is related to vaccines. More consistent and reproducible clinical trials are required to reveal probiotics efficacy, limitations, and safety, determining their effects on immune system.

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