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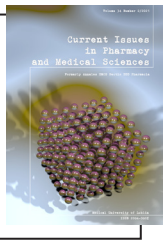

An educational review on Probiotics

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ABSTRACT

Probiotics are live microorganisms that appear to provide health benefits when swallowed or introduced to the body. They are present in dairy and other fermented foods, as well as in dietary supplements and cosmetics. While many people still believe bacteria and other microorganisms are harmful "germs", many are beneficial. Certain bacteria aid in the digestion of food, destroy disease-causing cells and absorb vitamins. Some of the microorganisms found in probiotic products are similar to or identical to those found naturally in our bodies. This article provides sufficient data to support the use of probiotics in a variety of uncommon clinical diseases, including skin disorders, Parkinson's disease, psychiatric disorders, liver transplantation, diabetic foot and periodontal care.

INTRODUCTION

This article presents significant evidence for the benefit of probiotics in uncommon health issues such as skin illnesses, Parkinson's disease, psychiatric issues, liver transplantation, diabetic foot and periodontal treatment. Probiotics have shown promising benefits in reducing skin sensitivity, protecting against UV radiation, immunomodulation, and in preventing and treating dermatitis. Additionally, they contribute to the maintenance of the skin's pH by inhibiting pathogenic microorganisms selectively. Probiotics have been shown to reduce inflammatory responses and enhance anti-inflammatory responses in Parkinson's disease. Additionally, they demonstrate antioxidant action and enhanced gut integrity. Because the gut microbiota is involved in the creation of key neurotransmitters necessary for mood, cognition, and behavior, supplementing with probiotics aids in the recovery of mental health in individuals suffering from psychiatric disorders such as schizophrenia, depression and others. Patients administered probiotics who have undergone liver transplantation, have experienced significant decreases in post-operative infections, ICU stay and hospitalization, non-bacterial infectious sequelae, bilirubin concentrations and AST/ALT levels. Although there are insufficient trials to demonstrate the efficacy of probiotics in treating diabetic foot infection, this article discusses treatment options for diabetic foot infection. Periodontal disease has also been historically difficult to treat due to antibiotic resistance, hence, this paper discusses the treatment of a specific bacterium that causes periodontal disease. Alternative therapies have proven critical in the fight against antibiotic resistance. Probiotics are one such treatment modality.

Probiotics in Indian scenario

In India, the prevalence of non-communicable diseases and lifestyle disorders such as type 2 diabetes mellitus, fatty liver disease and coronary artery disease has risen alarmingly, paving the way for alternative preventive therapies such as probiotics [1]. Probiotics, it is believed, have a larger application in the prevention and management of a variety of common health problems [2-4]. India holds less than 1% of the worldwide probiotic market, with Amul, Mother Dairy, Yakult Danone and Nestle making significant contributions. Probiotic research and probiotic foods are gaining traction as a result of growing consumer awareness [5]. Probiotic research has long been regarded as a highly specialized field of study on a global scale. In India, major pharmaceutical companies are attempting to develop novel probiotic products and supplements [6]. The Indian Council of Medical Research (ICMR)/Department of Biotechnology (DBT) has taken the lead in formulating guidelines for the use of probiotics in food, their safety and efficacy assessment, their health claims and their labeling [7].

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Probiotics in skin disorders

Probiotics have proven effectiveness against a variety of infections by competing for survival resources and generating antimicrobials that aid in wound healing in individuals with multidrug-resistant bacteria infected skin lesions [8]. Numerous studies have demonstrated that oral treatment of probiotics in conjunction with antibiotics enhances wound healing prior to and following surgery [9]. Probiotics have a variety of beneficial effects on the skin, including reducing irritation, acting as a screen against UV radiation, promoting immune system regeneration and preventing atopic dermatitis [10]. Additional information is presented in (Figure 1).

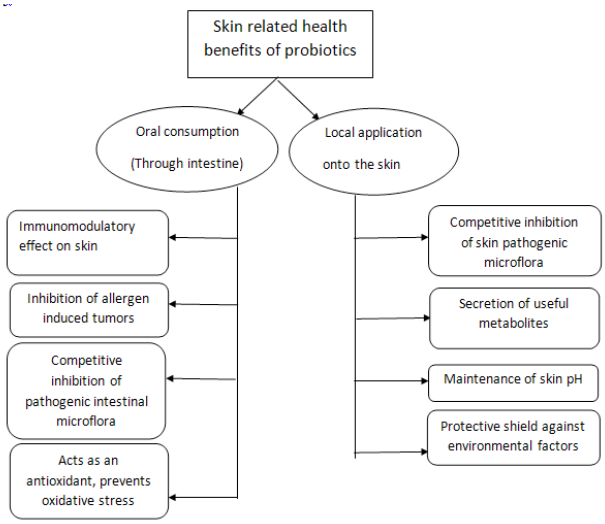

Figure 1. Mechanism of probiotics in skin disorders

Probiotics and Parkinson's disease [11]

Research in rat models and human subjects have established a possible link between changed gut microbiome and the development of Parkinson's disease. Such work provides overviews of how changed gut microbiota may contribute to the development of Parkinson's disease. Induced Parkinson's disease mice have a higher ratio of Enterobacteriaceae, which is associated with postural instability and gait [12], and lower counts of Prevotellaceae, which are important for the production of the folate and thiamine that are required for intestinal homeostasis.

Benefits [13]

In a study of 80 Italian patients (40 Parkinson disease + 40 controls), 20 ml of blood was drawn and peripheral blood mononuclear cells (PBMC) were isolated using normal procedures. These cells were co-cultured with bacterial probiotic strains belonging to the genus Lactobacillus and Bifidobacterium. Inflammatory (Interleukin-6,17A and TNF-α) and anti-inflammatory cytokines (IL-4, 10) as well as Reactive Oxygen Species (ROS) were investigated. Certain tests were undertaken, including the effects on intestinal membrane integrity and pathogenicity inhibition, and encoding of the gene tyrosine decarboxylase. The research showed the efficacy of *Lactobacillus Plantarum* (LP01) and *Lactobacillus rhamnosus* (LR06) against pathogenic bacteria like *Escherichia coli* and *Klebsiella pneumonia* inhibition. In male and female Parkinson disease patients treated with *Lactobacillus rhamnosus* (LR06) and *Bifidobacterium animalis* subsp, ROS development was also found to be lower, as for Lactis (BS01).

Probiotics and psychiatric disorders [14]

Good microbes play a key role in controlling amino acids that serve as building blocks for multiple neurotransmitters such as GABA, glutamate, norepinephrine, serotonin, melatonin and dopamine. Changes in mood, cognition, and actions may be the crippling result of gut microbial disruption.

Probiotics and liver transplantation [15]

Probiotic bacteria have immunological advantages, as well as non-immunological effects that are as follows:

1. Immunologically, local macrophages have been shown to increase the antigen pin in the body, increase local and systemic development of secretory immunoglobulin A (IgA), which prevents bacterial adhesion to mucosal epithelial cells, and alters the release of cytokines in response to inflammatory stimuli.
2. Probiotics can also establish an unfavorable environment for pathogens through multiple mechanisms that ultimately reduce secondary-infection downstream complications.
3. Non-immunological benefits include detoxification of xenobiotics, biosynthesis of vitamin K and improvement of peristalsis of the intestines. The following clinical trials were performed using robust methods including randomization, blinding, and placebo control, supporting the use of probiotics as a prevention technique for infections.

Study 1: 95 patients on liver transplantation received a retrospective, randomized research performed in Germany. They were classified into three groups as follows: the first group was treated with enteral nutritional antibiotics and antifungals, but not probiotics (n = 32); the second group was treated with *Lactobacillus plantarum* 299, along with oat fiber supplementation; and the third group was treated with heat-inactivated Lactobacillus, along with oat fiber. All patients were treated with different immunosuppressive drugs, calcineurin inhibitor and prednisolone, and a total of 60 patients received additional treatment steps, including IL-2 inhibitors, sirolimus and Mofetil Mycophenolate. Intra-abdominal infections were mainly due to enterococcus and other enteric bacteria.

Study 2: 66 patients following liver transplantation were treated with synbiotics. All patients were treated with low-fibre enteral nutrition, prophylactic antibiotics and immunosuppressants, including prednisolone, calcineurin inhibitor, IL-2 inhibitor, and H2 receptor antagonist antihistamines. The isolated bacteria have been identified as having enteric roots.

Study 3: Patients were diagnosed with dual or triple immunosuppressant treatment, which involves medications of the following class: corticosteroid (prednisolone), calcineurin inhibitor, Mycophenolate Mofetil, in a study performed in around 50 adults undergoing liver transplantation.

Patients with impaired renal function were given an IL-2 inhibitor. Prior to surgery, incompatible recipients of the blood group were provided with Rituximab. As per hospital practice, all patients obtained perioperative prophylaxis through surgery.

Study 4: 67 recipients of adult hepatic transplantation were tested for post-operative bacterial infection. Patients were tested for signs of infection, including fever > 38°C, C reactive protein elevation and other clinical symptoms of infection. Bacterial culture was performed and the isolated bacteria mainly detected were enterococci, *Escherichia coli* and *Enterobacter spp.*

Study 5: 55 recipients of liver transplants were recruited and a double-blind placebo-controlled study was conducted. The patients were tested for mortality and postoperative infection. The study's secondary objectives included measuring aspartate, AST, ALT, bilirubin, INR after 5 days of surgery, as well as wait-list mortality, MELD (Mayo End-stage Liver Disease) score, changes in child-Turcotte-Pugh and rate of pretransplantation infections. *Enterococcus faecium* was the most commonly isolated pathogen and was preceded by *Klebsiella pneumonia*.

Probiotics and diabetic foot [16]

Damage to the skin may occur due to underlying health conditions, such as diabetes. This in effect causes extra cost with regard to patient's health care and impairs the individual's quality of life. Biofilm forming bacteria such as *Staphylococcus aureus*, *Pseudomonas aeruginosa, Enterococcus faecalis, Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* spp., *Peptostreptococcus* spp. are common. In treatments, probiotics serve as an important alternatives to antibiotics for the following reasons:

- stimulation of the production of immune cells;
- competitor development;
- function as a signaling receptor in the skin's epidermis and dermis layers against pathogens by activating beta-defensins that provide additional immunity to the skin.

Like other cases, clinical trials specifying the benefits of probiotics in diabetic foot infection are not available, but as a point of interest, the probiotics used against the aforementioned pathogens in various clinical settings can be reasonably considered to provide a rough overview of the treatment of diabetic foot-related infections. More description is given below in (Table. 1).

Probiotics in periodontal disease [17]

Periodontal disease is divided into two groups, namely gingivitis and periodontitis. The former induces gingiva inflammation, while the latter affects all the supporting tissue that surrounds the teeth. Popular pathogenic species responsible for this condition include: *Porphyromonas gingivalis*, *Treponema denticola*, *Tannerella forsythia*, and *Aggregatibacter actinomycetemcomitans*. Probiotics work against these species through direct pathogen inhibition and/or activation of pathways for host defense. Probiotics function by means is explained in (Table 2), with benefits listed.

Table 1. Probiotics whose use could be extended to diabetic foot infection management

Pathogen	Probiotic Strain	Treatment Duration	Clinical Condition
Staphylococcus aureus	*Lactobacillus casei* Shirota *Bifidobacterium* Breve Yakult/2*108 cfu	Oral for 14 days after surgery	Biliary cancer surgery
	Pediococcus pentosaceus LMG P-20608, *Leuconostoc mesenteroides* LMG P-20607, *Lactobacillus paracasei* subsp. Paracasei LMG p-17806, *L. plantarum* LMG P-20606 1010 cfu	Oral from the day of surgery up to 2 weeks	Liver Transplantation Surgery
	L. plantarum ATCC 10241 105 cfu	Daily – topical application for 10 days	Second and third degree burns and chronic infected leg ulcers
	*Bifidobacterium bifidum** 3.3*109 cfu	Oral – 7 days before and 5 to 10 days after surgery	Colorectal Cancer Surgery
Pseudomonas aeruginosa	*L. plantarum* ATCC 10241 105 cfu	Daily – topical application for 10 days	Second and third degree burns and chronic infected leg ulcers
	*Bifidobacterium bifidum** 3.3*109 cfu	Oral – 7 days before and 5 to 10 days after surgery	Colorectal Cancer Surgery
	L. acidophilus LA-5, *L. plantarum**, *B. Lactis* BB-12, *Saccharomyces boulardii**/5.5*109 cfu	Oral – 1 day prior to operation and 14 days after surgery	Colorectal Cancer surgery
Enterococcus faecalis	*Lactobacillus casei* Shirota *Bifidobacterium* Breve Yakult/2*108 cfu	Oral for 14 days after surgery	Biliary cancer surgery
	L. plantarum ATCC 10241 105 cfu	Daily – topical application for 10 days	Second and third degree burns and chronic infected leg ulcers
	L. acidophilus LA-14, *L. plantarum* LP-115, *Bifidobacterium lactis* BBL-04, *L.Casei* LC -11, *Lactobacillus rhamnosus* LR-32, *Lactobacillus brevis* LBr-35/2.75* 1010 cfu	Oral – at least 7 days after oral fluid tolerance post operation	Liver Transplantation Surgery
	*Bifidobacterium bifidum** 3.3*109 cfu	Oral – 7 days before and 5 to 10 days after surgery	Colorectal Cancer Surgery
Acinetobacter baumannii	L. acidophilus LA-5, *L. plantarum*, *B. Lactis* BB-12, Saccharomyces boulardii/5.5*109 cfu	Oral – 1 day prior to operation and 14 days after surgery	Colorectal Cancer surgery
Escherichia coli	*L. acidophilus* LA-14, *L. plantarum* LP-115, *Bifidobacterium lactis* BBL-04, *L. Casei* LC -11, *Lactobacillus rhamnosus* LR-32, *Lactobacillus brevis* LBr-35/2.75* 1010 cfu	Oral – at least 7 days after oral fluid tolerance post operation	Liver Transplantation Surgery
	*Bifidobacterium bifidum** 3.3*109 cfu	Oral – 7 days before and 5 to 10 days after surgery	Colorectal Cancer Surgery
Klebsiella pnemoniae	*L. plantarum* ATCC 10241 105 cfu	Daily – topical application for 10 days	Second and third degree burns and chronic infected leg ulcers
Enterobacter spp	*L. acidophilus* LA-14, *L. plantarum* LP-115, *Bifidobacterium lactis* BBL-04, *L. Casei* LC-11, *Lactobacillus rhamnosus* LR-32, *Lactobacillus brevis* LBr-35/2.75* 1010 cfu	Oral – at least 7 days after oral fluid tolerance post operation	Liver Transplantation Surgery

* Lactic acid *Bacteria-Pediacoccus pentosaceus*, *Leuconostoc mesenteroides*, *Lactobacillus paracasei*, *L. plantarum* and bioactive fibres-betaglucan, inulin, pectin and resistant starch. In study 2, despite the fact that patients in the true intervention group had higher rates of non-infectious complications which were inevitably associated with infections, the incidence rate of bacterial infection was significantly less

Table 2. Pathogens with probiotics along with its benefits

Pathogen	Probiotic	Potential benefits
Porphyromonas gingivalis	*Lactobacillus rhamnosus Lactobacillus paracasei*	Strongly binds to saliva coated surfaces and survives in the bacterial biofilm
Streptococcus mutans	*Lactobacillus rhamnosus GG Lactobacillus casei*	Prevents adherence of other bacteria and modifies the protein composition of salivary pellicle
Gram positive bacteria	*Weissella cibaria*	Secretes hydrogen peroxide and bacteriocin that act against gram positive bacteria
Fusobacterium nucleatum	*Weissella cibaria*	Effective colonization of oral cavity through coaggregation with pathogen and epithelial cell adherence

DISCUSSION

The purpose of this research is to demonstrate the beneficial effects of diverse bacterial strains under varied clinical situations for reducing resistance generated by antibiotic treatment and minimizing drug-related side effects. Although probiotics have been shown to be useful in the majority of research, conventional clinical recommendations for their employment are needed because their protection against systemic infections, harmful metabolic activity, gene transfer and harmful immunomodulation is highly unknown. Studies indicate that lozenges with probiotics are preferred over chewing gums containing standard oral medications. Additional research, however, is needed to determine whether the beneficial benefits of probiotic bacteria are the same when processed or added to food products. Dried probiotics that have been properly prepared and processed will survive the travel through the intestines. In contrast, heat kills active crops. The development of recommendations for the use of probiotics in food, their safety and efficacy assessment, health claims, and probiotic product labeling is a goal shared by all scientists, businesses and health institutes.

CONCLUSION

The medical community recognizes the potential health benefits of probiotic diets. Still, additional effort is required to solidify the arguments. While the medical community recognizes the potential health benefits of probiotic diets, additional effort is required to solidify the arguments. At this stage, the best we can say is that they will not cause harm and may even be beneficial.

CONFLICT OF INTEREST

The authors declare none.

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