

PROBIOTICS: A NOVEL APPROACH IN IMPROVING THE VALUES OF HUMAN LIFE

PRAVEEN KUMAR VEMURI*, RAMYA HARI PRIYA VELAMPATI AND SRI LAASYA TIPPARAJU

Centre for Genomics & Proteomics, Department of Biotechnology, K L University, Green Fields, Vaddeswaram, Guntur Dist, Andhra Pradesh, India. Email: vemuripraveen_bt@kluniversity.in

Received: 02 Nov 2013, Revised and Accepted: 24 Nov 2013

ABSTRACT

Probiotics improves the values of human life since the intestinal tract is a diverse microenvironment where more than 500 species of bacteria thrive. A single layer of epithelium is all that separates these microorganisms and pathogens from the underlying immune cells and thus epithelial barrier function is a key component in the defense mechanisms required to prevent infection and inflammation. This is a large quantity of working bacteria, which perform very important functions in our body - from the mouth all the way down to the rectum. The term probiotic generally used to describe the living beneficial bacteria that support digestion as well as vaginal and urinary tract health. The good friendly bacteria or probiotics promote the body's natural immunity and keep us healthy. We live in harmony with them and they provide us with an excellent service if they are given a reasonable diet and kept in good health. These probiotics were well exploited in food, medical and aquaculture industries. This review summarizes the evidence about effects of the many available probiotics with an emphasis on functionality, applications in various fields and the mechanisms affected by probiotics.

Keywords: Probiotics, Gastrointestinal tract, *Lactobacillus*, Hypertension, Vaginosis.

INTRODUCTION

A probiotic is currently defined as a live microbial food supplement with a proved beneficial effect on human health. Probiotics is a Greek word meaning "for life". This contrasts with antibiotics[1] meaning "against life", these are a class of "good" or "friendly" bacteria that are normal inhabitants of the intestinal tract, helping with digestion. Although the word "bacteria" is usually associated with germs and illness, there are in fact a number of strains of friendly bacteria that help the human body to function, maintain health and fight illness and disease. Probiotics are live microorganisms that occur naturally in the human digestive system. Probiotics[2] aim to produce a beneficial on the host by

administration of viable microorganisms such as those found in traditional yogurts and other fermented foods as well as powders, tablets, liquid suspensions and lyophilized forms in capsules. Probiotics exhibit strain-specific differences in their resistance to acid and bile, ability to colonize gastrointestinal tract, clinical efficacy, and benefits to the health of the host. Probiotics may have antimicrobial, immunomodulatory, anticarcinogenic, antidiarrheal, antiallergenic and antioxidant activities. One of the major problems when trying to identify and evaluate candidate probiotic strains is our lack of knowledge about their mode of action; several modes of action have been hypothesized or proven. The following are microorganisms [3] considered to be human probiotics, listed in table 1.

Table 1: Summary of the most widely studied types of probiotics

Microorganisms	Strains used as probiotics
<i>Lactobacillus</i> species	<i>L. acidophilus</i> , <i>L. amylovorus</i> , <i>L. brevis</i> , <i>L. casei</i> , <i>L. casei</i> subsp. <i>rhamnosus</i> (<i>Lactobacillus GG</i>), <i>L. caucasicus</i> , <i>L. crispatus</i> , <i>L. delbrueckii</i> subsp. <i>bulgaricus</i> (<i>L. bulgaricus</i>), <i>L. fermentum</i> (<i>L. fermenti</i>), <i>L. gasseri</i> , <i>L. helveticus</i> , <i>L. johnsonii</i> , <i>L. lactis</i> , <i>L. leichmannii</i> , <i>L. paracasei</i> , <i>L. plantarum</i> , <i>L. reuteri</i> , <i>L. rhamnosus</i> .
<i>Bifidobacterium</i> species	<i>B. adolescentis</i> , <i>B. bifidum</i> , <i>B. breve</i> , <i>B. infantis</i> , <i>B. lactis</i> (<i>B. animalis</i>), <i>B. licheniformis</i> , <i>B. longum</i> , <i>B. coagulans</i> .
<i>Streptococcus</i> species	<i>S. oralis</i> KJ3, <i>EvoraPlus</i> , <i>S. uberis</i> KJ2, <i>S. rattus</i> JH145, <i>S. salivarius</i> TOVE-R, <i>S. salivarius</i> K58, <i>S. zooepidemicus</i> , <i>S. oligofermentans</i> .
Other lactic acid bacteria	<i>Enterococcus faecium</i> , <i>Lactococcus lactis</i> , <i>Leuconstoc mesenteroides</i> , <i>Pediococcus acidilactici</i> , <i>Streptococcus thermophilus</i> .
Nonlactic acid bacteria	<i>Bacillus subtilis</i> , <i>Escherichia coli</i> strain nissle, <i>Saccharomyces boulardii</i> , <i>Saccharomyces cerevisiae</i> .

Need of probiotics

The vast majority of the total cells in the body are present as bacteria in the colon help us with digestion by breaking foods down into their component parts for absorption into the body. "Bad" or "pathogenic" bacteria on the other hand, can cause intestinal microflora imbalances and lead to illness and disease[4]. While human beings usually start life with a relatively healthy intestinal tract, lifestyle and other physical factors can greatly reduce the number of friendly bacteria allowing pathogenic bacteria to take hold and cause problems. Supplementing our diets with an effective probiotic re-populates the intestinal tract with friendly strains to reverse this trend, improve intestinal health and guard against disease.

Action of Probiotics

The mechanism of action of probiotics has been described for decades. They include the treatment and the prevention of gastrointestinal diseases, urinary and vaginal infections and

allergies. Probiotics have been shown to decrease the risk of airway infections, immune activity and bowel infections. The main mechanisms[5] whereby probiotics exert protective or therapeutic efforts are not fully elucidated but several mechanisms have been postulated. Scientific evidence is based on a limited number of *in vivo* studies and reductions from well founded *in vitro* studies that had involved adults and children with intestinal disorders. Furthermore, results obtained in probiotic clinical trials suggest beneficial effects over placebo in the relief of irritable bowel syndrome symptoms. The functionality for probiotic organism is by their, antimicrobial activity, colonization resistance, adjuvant effects, cytokine expression, stimulation of phagocytosis by peripheral blood leucocytes, secretory IgA, antimutagenic effects, antigenotoxic effects, influence on enzyme activity, enzyme delivery.

Molecular mechanisms of probiotics are mainly manifested in the following ways:

- Protective functions through modulation of immune activity and epithelial function in both large and small intestine
- Modulation of nuclear factor- κ B pathway in response to TNF- α
- Alter action signal transduction pathways in the presence or absence of pathogenic bacteria and cytokines with epithelial and immune cells.
- Enhanced phosphorylation of actinin and occluding in the tight junction region epithelial cells.
- Prevent cytokine induced apoptosis in intestinal epithelial cells by inhibiting tumor necrosis factor.

Probiotics in food industry

Probiotic bacteria are typically, but not always, chosen from bacteria that normally inhabit the gastrointestinal system of humans, and belong to a species that is known to be safe. These bacteria are purified, grown to large numbers, concentrated to high doses and preserved. They are provided in products in one of three basic ways,

- As a culture concentrate added to a food (usually a dairy product) at medium levels, with little or no opportunity for culture growth.
- Inoculated into a milk-based food (or dietary supplement) and allowed to grow to achieve high levels in a fermented food.
- As concentrated and dried cells packaged as dietary supplements such as powders, capsules, or tablets.

Probiotic bacteria have a long history of association with dairy products[6]. This is because some of the same bacteria that are associated with fermented dairy products also make their homes in different sites on the human body, including the mouth, the gastrointestinal tract and the vagina. Some of these microbes, therefore, can play a dual role in transforming milk into a diverse array of fermented dairy products and contributing to the important role of colonizing bacteria. Dairy products[7] can provide a desirable "probiotic delivery vehicle" for several reasons.

Probiotics in health

Probiotics are described as live microbial food ingredients that are beneficial to health[8] of the host, especially by improving intestinal microbial balance. As our population ages, the importance of the prevention of disease has been recognized a new and our entire society has become health-oriented. Following that trend, product development based on beneficial bacteria including lactobacilli is now in full bloom. While there is a scientifically proven benefit to effective probiotics, there is also some confusion amid the wide range of supplements available and the claims made for them. There has also been some disappointment for some of these products not resulting in any noticeable change or decrease in symptoms of an intestinal problem.

Lactose Intolerance: The inability of adults to digest lactose, or milk sugar, is prevalent worldwide. People of northern European descent are unique in retaining the ability to produce the lactose-digesting enzyme, lactase, into adulthood. Consumption of lactose by those lacking adequate levels of lactase produced in the small intestine can result in symptoms of diarrhea, bloating, abdominal pain and flatulence. These symptoms are due to the undigested lactose reaching the large intestine and being fermented by the colonic microbes. These microbes can produce gases i.e.; H₂ and products that lead to watery stool. It has been documented scientifically that many lactose intolerant individuals are better able to consume fermented dairy products, such as yogurt, with fewer symptoms than the same amount of unfermented milk, even though yogurt contains about the same amount of lactose as milk. Yogurt was found to aid digestion of lactose because the lactic acid bacteria used to make yogurt produce lactase and digest the lactose before it reaches the colon. In addition to yogurt starter bacteria[9], *L. acidophilus* and bifidobacteria have been shown by several studies to improve digestion of lactose, although generally to a lesser extent than the yogurt starter cultures, *Lactobacillus bulgaricus* and *Streptococcus thermophilus*.

Hypertension: About 50-60 million people in United States are estimated to have hypertension, or elevated blood pressure. Antihypertensive[10] effects have been documented in animal models and in mildly hypertensive adults for three compounds derived from the growth of certain lactobacilli: 1) fermented milk containing two tripeptides derived from the proteolytic action of *L. helveticus* on casein in milk; 2) bacterial cell wall components from cell extracts of lactobacilli; and 3) fermented milk containing fermentation-derived gamma amino butyric acid. Systolic blood pressure was decreased on the order of 10-20 mm Hg. These results suggest that consumption of certain lactobacilli, or products made from them, may reduce blood pressure in mildly hypertensive people.

Cancer: The fight against cancer is one of the biggest challenges faced by humanity[11]. Research suggests that the consumption of probiotic cultures may decrease cancer risk. Researchers testing the effect of the consumption of fermented milks, probiotic bacteria and components of bacteria or extracts of bacteria have found that enteropathogens such as *E. coli* and *Clostridium perfringens* produce enzymes such as beta-glucuronidase, and nitroreductase. Beta-glucosidase and urease can convert procarcinogens to proximate carcinogens. The colonising cells of bifidobacterium produce lactic acid and lower the intestinal pH and create a bactericidal environment for these putative enteropathogens, and thus develop a favourable microenvironment which modulates the bacterial enzymes. Purified bifidobacterial has cell wall antitumour activities and induces activation of phagocytes to destroy growing tumour cells. RAS activation represents one of the earliest and most frequently occurring genetic alterations associated with human cancers, especially carcinoma of colon[12]. Probiotics also stimulate apoptosis through end-product formation.

Immune System Stimulation: The immune system provides the primary defense against microbial pathogens that have entered our bodies. The immune system is extremely complex, involving both cell-based and antibody-based responses to potential infectious agents. Immunodeficiency can result from certain diseases (e.g., cancer, AIDS, leukemia) or, to a lesser extent, from more normal conditions such as old age, pregnancy, or stress. Autoimmune diseases (e.g., allergies, rheumatoid arthritis, inflammatory bowel diseases) also can occur due to misdirected immune system activity. Probiotic cultures have been shown in a variety of test systems to stimulate[13] certain cellular and antibody functions of the immune system[14]. The colonic microflora affects mucosal and systemic immunity in the host. Intestinal epithelial cells, blood leucocytes, B and T lymphocytes, and accessory cells of the immune system are all complicated targets for probiotics. The effect is produced either by absorption of a soluble antigen or by translocation of 'lactobacilli' through the gut wall into the blood stream. Lactobacilli which adhere to human intestinal epithelial cells are capable of activating macrophages or factors like cytokines, immunoglobulins, interferons etc. An exciting area of research has been documenting the ability of certain probiotic bacteria to modulate immune dysregulation.

Food allergy: Allergy is on the rise in industrialized nations. It is estimated that the incidence of asthma in the United States doubled between 1980 and 2000. Scientists have proposed a hypothesis known as the 'hygiene hypothesis' to explain the rise in allergic conditions such as asthma and eczema. This hypothesis is based on observations that lower allergy incidence is associated with environments that have greater numbers of microbes, such as day care centers, farms, or in homes with siblings or pets. Sanitary living environments and the consumption of processed foods have limited the number of microbes in the diet. Probiotics, by their potentiating effect on the non-immunologic and immunologic defense barrier of the gut, alleviate the inflammatory response in food allergy[15]. Bifidobacteria and lactobacilli have been shown to enhance IgA production in Peyer's patches, and potentiate IgA response to potentially harmful antigens. Probiotics reduce the secretion of Th2 cytokines which are IL-4, IL-5, IL-6, IL-9, IL-10 and IL-13. These cytokines are responsible for strong antibody especially IgG and IgE responses and eosinophils found in helminthic infections and allergic disorders. Probiotics induce the secretion of IL-12 by activated macrophages. IL-12 increases resistance to intracellular

bacteria and parasites. Lactobacilli modify the immunomodulatory properties of native food protein. Thus, probiotics influence the immune system by activating the lymphoid cells of the gastrointestinal lymphoid tissue.

Vaginosis: Vaginosis used to be considered a mere annoyance, but now is being examined for a role in serious conditions including pelvic inflammatory disease, pregnancy-related complications and increased susceptibility to AIDS infection. Vaginosis can be caused by several different organisms, and in many cases, the causative agent may not be identified. What is known is that lactobacilli predominate in the healthy vagina, and a lack of lactobacilli is a risk factor for vaginosis. The lactobacilli are thought to maintain a favorable vaginal pH in the acidic range and to inhibit pathogens, possibly through the production of hydrogen peroxide and other antimicrobial factors. Essentially, bacterial vaginosis is considered as an overgrowth of anaerobic organisms combined with a loss of the protective lactobacilli normally found in the healthy vagina. The mode of action might compromise increased ascension of probiotic and/or indigenous lactobacilli from the rectal skin to the vagina and enhancement of the intestinal mucosal immunity which effects vaginal immunity rendering the environment less receptive to bacterial vaginosis organisms. Intravaginal applications of lactobacilli have been somewhat effective in treating bacterial Vaginosis[16].

Helicobacter pylori Infection: *Helicobacter pylori* are a bacterium which colonizes the gastric mucosa[17]. Its presence is associated with gastric ulcers and gastric cancer, although its role in the etiology of these diseases is still under investigation. The effect of probiotics on *Helicobacter pylori* has been studied. Most evaluations have been done either in laboratory assays or in animal models. The studies on these lines showed that antibacterial substances including organic acids produced by some lactobacilli inhibit the growth and adhesion to epithelial cells and an effect on the human immune system. The following is a list of some other disorders, which can be cured by Probiotics - Pancreatitis, Pouchitis, Alcoholic liver disease, Juvenile chronic arthritis, Hepatic encephalopathy and Non-alcoholic fatty liver disease

Aquaculture: Aqua industry is facing a problem to export the aqua products because of the presence of antibiotic residues. The solution for the problem is derived by application of probiotics in this industry. Some Photosynthetic bacteria when added into the water, they could eliminate the $\text{NH}_3\text{-N}$, H_2S , organic acids, and other harmful materials rapidly thus improve the water quality and balance the pH. The heterotrophic probiotic bacteria may have chemical actions such as oxidation, ammonification, nitrification, denitrification, sulphurification and nitrogen fixation. When these bacteria were added into the water, they could decompose the excreta of Shrimps[18], fish or prawns, remaining food materials, remains of the plankton and other organic materials to CO_2 , Nitrate and Phosphate. These inorganic salts provide the nutrition for the growth of micro algae, while the bacteria grow rapidly and become the dominant group in the water, inhibiting the growth of the pathogenic microorganisms. The photosynthesis of the micro algae provide dissolved oxygen for oxidation and decomposition of the organic materials and for the respiration of the microbes and cultured animals. This kind of cycle may improve the nutrient cycle, and it can create a balance between bacteria and micro algae, and maintaining a good water quality environment for the cultured animals.

CONCLUSION

Probiotics have long been used as an alternative to traditional medicine with the goal of maintaining enteric homeostasis and preventing disease. However, the actual efficacy of this treatment is still debated. In a very short period of time, many studies have been conducted to validate the concept of probiotics[19] as a viable therapeutic modality in the treatment of gastrointestinal disease. However, a number of issues need to be resolved regarding the use

of probiotics. Basic research must provide more detailed data on the mechanism of probiotic action on the molecular level, after which clinical trials must be undertaken to find the probiotic strain and dosage with optimal results for each clinical situation. The probiotic organisms are playing a vital role in improving the living standards of human beings[20]. The application area of this probiotics is enormous, each and every field related to human having a good scope. Many kinds of the organisms were explored to derive their probiotic capacity. In food, medical and aqua industries significant number of commercial products of probiotic origin were available and new products are being launched by the reputed companies by their constant R&D efforts. The coming of age of probiotics[21] this field is one of the promising areas for providing opportunities as well as for revenue generation.

REFERENCES

1. Parker RB. Probiotics, the other half of the antibiotic story. *Animal Nut. Health.* 1974; 29:4-8.
2. Havenaar R, and J H J Huis in't Veld. Probiotics: a general review. *The Lactic Acid Bacteria*, 1992; 1:151-170.
3. Havenaar R, Ten Brink B and Huis in't Veld J H J. Selection of strains for probiotic use. Chapman and Hall, London. 1992; 1:209-224.
4. Anuradha S and Rajeshwari K. Probiotics in health and disease. *JACM* 2005; 6:67-72.
5. Ng SC Hart AL, Kamm MA, Stagg AJ and Knight SC. Mechanisms of action of probiotics: recent advances. *Inflamm Bowel Dis.* 2009; 15(2):300-10.
6. Fuller R. Probiotic foods: Current use and future developments. *Int Food Ingred.* 1993; 3:23-6.
7. Adnan Tamime, Rajka Bozanic and Irena Rogelj. Probiotic fermented dairy products. *Portal of scientific journals of Croatia.* 2003; 53:111-134.
8. Semih Otles, Ozlem Cagind and Eren Akcicek. Probiotics and Health. *Asian Pacific J Cancer.* 2003; 4:369-372.
9. Fernandez M F, S Boris and C Barbes. Probiotic properties of human lactobacilli strains to be used in the gastrointestinal tract. *J. Appl. Microbiol.* 2003; 94:449-455.
10. Min-Tze Liong. Probiotics: A Critical Review of Their Potential Role as Antihypertensives, Immune Modulators, Hypocholesterolemic, and Perimenopausal Treatments. *Nutrition Reviews.* 2007; 65: 316-328.
11. Kumar V Praveen, S Prasanthi, V R S Lakshmi and M V Sai Santosh. Cancer vaccines: a promising role in cancer therapy. *Ac. J. of Cancer Research.* 2010; 3(2):16-21.
12. Wollowski I, Rechkemmer G and Pool-Zobel BL. Protective role of probiotics and prebiotics in colon cancer. *Am J Clin Nutr.* 2001; 73:451-455.
13. Perdigon G, Alvarez S, Rachid M, Agüero G and Gobato N. Immune stimulation by probiotics. *J Dairy Sci.* 1995; 78:1597-1606.
14. Dugas B, Mercenier A, Lenoir-Wijnkoop I et al. Immunity and probiotics. *Immunol Today.* 1999; 57:387-390.
15. Majamaa M and Isolauri E. Probiotics: a novel approach in the management of food allergy. *J Allergy Clin Immunol.* 1997; 99:179-85.
16. Falagas M E, Betsi G I and Athanasiou S. Probiotics for the treatment of women with bacterial vaginosis. *Clinical Microbiology and Infection.* 2007; 13:657-664.
17. Felly C. Probiotics and *Helicobacter pylori*. *Clinical Gastroenterology.* 2003; 17:785-79.
18. Ali Farzanfar. The use of probiotics in shrimp aquaculture. *FEMS Immunology & Medical Microbiology.* 2006; 48(2):149-158.
19. Vanderhoof J A. Probiotics: Future directions. *Am J Clin Nutr.* 2001; 73:1152-1155.
20. Gill H S and Guarner F. Probiotics and human health: a clinical perspective. *Postgrad Med J* 2004; 80:516-526.
21. Lee Y-K and Salminen S. the coming age of Probiotics. *Trends Food Sci Technol.* 1995; 6:241-5.