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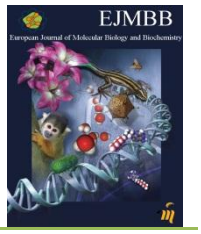

PROBIOTICS – THE MODULATOR OF GUT HEALTH

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ABSTRACT
The gastrointestinal microflora is a very complex community. Within the gastrointestinal tract, different habitats have to be recognized, e.g. mouth, stomach, small intestine (especially lower jejunum and ileum) large intestine (caecum, colon) and rectum. More than 400 species within the intestinal microflora can be identified and may attain population levels nearly as high as 10^{12}/g in the colon. Microflora of the gastrointestinal tract plays a crucial role in the anatomical, physiological, and immunological development of the host. It stimulates the immune system to respond rapidly to infection with pathogens and through bacterial antagonism it inhibits the colonisation of the gut by harmful or pathogenic bacteria. It consists of species belonging to the families *Bacteroides, Fusobacterium, Butyrivibrio, Clostridium, Bifidobacterium, Eubacterium* and *Lactobacillus. Enteroccocus* and *Escherichia coli* constitute less than 1% of all intestine microorganisms. Anaerobes dominate upon facultative anaerobes and micro aerophiles at the ratio of 1000:1. A dominant flora represents 90% of the population, essentially composed of bifidobacteria and lactobacilli. The residual or fluctuating flora (less than 0.01%) of the population is more diversified and contains the potentially pathogenic species.

INTRODUCTION

The gastrointestinal tract of the newborn is inoculated by the mother's vaginal and fecal flora during birth [1]. Initially, a predominance of facultative anaerobic strains such as *Escherichia coli or enterococci exists* [2, 3]. These bacteria may therefore create a highly reduced environment that then allows the growth of strict anaerobes. The fecal flora of breast fed infants is dominated by populations of bifidobacteria, with only -1% enterobacteria. After weaning (>2 y of age), a pattern that resembles the adult flora becomes established. Information regarding the composition of the gut microbiota has shown that numerically predominant anaerobes were Gram negative rods of the genus Bacteroides.

These microorganisms can constitute to 30% of the total fecal flora. Probiotics are dietary preparations of live, nonpathogenic microbes which benefit the host by improving the 'balance' of gut bacteria perceived as either beneficial or harmful [4].The probiotics that are marketed as nutritional supplements and in functional foods, such as yogurts, are principally commensals like the *Bifidobacterium* and *Lactobacillus* species. Probiotics are sometimes called colonic foods. Most of the presently available probiotics are bacteria. *Saccharomyces boulardii* is an example of probiotic yeast. Some of the bacteria that serve as probiotics are

Bifidobacterium

Bifidobacteria are normal inhabitants of the human and animal colon. Newborns, especially those that are breast-fed, are colonized with bifidobacteria within days after birth. Bifidobacteria were first isolated from the feces of breast-fed infants. The population of these bacteria in the colon appears relatively stable until advanced age, when it seems to decline. They are saccharolytic organisms that produce acetic and lactic acids without generation of CO_2, except during degradation of gluconate. They are also classified as lactic acid bacteria (LAB).

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Lactobacillus, Lactococcus and Streptococcus thermophilus

Lactobacilli are normal inhabitants of the human intestine and vagina. *Lactococcus lactis* (formerly known as *Streptococcus lactis*) is found in dairy products and is commonly responsible for the souring of milk. *Steptococcus thermophilus* is also found in milk and milk products. It is a probiotic and used in the production of yogurt.

Saccharomyces

Saccharomyces belongs to the yeast family, which include *Saccharomyces cerevisiae*, also known as bakers' yeast. The principal probiotic yeast is *Saccharomyces boulardii. S. boulardii* is normally nonpathogenic yeast, which has been used to treat diarrhea associated with antibiotic use.

Criteria for the use of probiotics in humans

1. Identified at the genus, species, and strain level
   - The gold standard for species identification is DNA–DNA hybridization; 16S rRNA sequence determination is a suitable substitute, particularly if phenotypic tests are used for confirmation
   - Strain typing should be performed by pulsed-field gel electrophoresis
   - Strain should be deposited in an international culture collection
2. Safe for food and clinical use
   - Nonpathogenic
   - Not degrading the intestinal mucosa
   - Not carrying transferable antibiotic resistance genes
   - Not conjugating bile acids
   - Susceptible to antibiotics
3. Able to survive intestinal transit
   - Acid and bile tolerant
4. Able to adhere to mucosal surfaces
5. Able to colonize the human intestine or vagina
6. Producing antimicrobial substances
7. Able to antagonize pathogenic bacteria.
8. Possessing clinically documented and validated health effects.
9. Stable during processing and storage.

Probiotics and Immunity

Gut-associated lymphoid tissue (GALT) is the largest lymphoid tissue of the human body. Its earliest and largest exposure to microbial antigens occurs during the initial intestinal colonization, which starts at birth. A fairly stable configuration of permanently colonizing bacteria is reached in children by approximately 4 years of age. The stimuli provided by colonization with commensal bacteria are essential for the development of a fully functional and balanced immune system, including not only homing of B and T cells to the lamina propria and expansion and maturation of IgA plasmocytes and IgA production but also the induction of tolerance toward innocuous food and microbial antigens.

Probiotics in Clinical Practice

Inflammatory diseases of the bowel *Crohn's* disease (CD) and ulcerative colitis (UC) are two distinct clinical forms of inflammatory bowel disease (IBD. Decreased levels of *Bifidobacterium* and *Lactobacillus* strains have been described in fecal samples, whereas raised counts of *Enterococcus* and *Bacteroides* species are found in inflamed mucosa of patients with IBD [5].

Diarrhoea

Many types of diarrhoeal illnesses, with many different causes, disrupt intestinal function. The ability of probiotics to decrease the incidence or duration of certain diarrhoeal illnesses is perhaps the most substantiated health effect of probiotics. Probiotics can prevent or ameliorate diarrhea through their effects on the immune system. Moreover, probiotics might prevent infection because they compete with pathogenic viruses or bacteria for binding sites on epithelial cells. In the pediatric population, probiotics appear to benefit viral diarrhoea, possibly by increasing the antibody secretory IgA and decreasing viral shedding, suggesting an immunological mechanism [6].

Cancer

Cancer-causing chemicals (carcinogens) can be ingested in a normal diet or generated by metabolic activity of microbes that live in the gastrointestinal system. It has been hypothesized that probiotic cultures might decrease the exposure to chemical carcinogens by

(a) Detoxifying ingested carcinogens;

(b) Altering the environment of the intestine and thereby decreasing populations or metabolic activities of bacteria that may generate carcinogenic compounds;

(c) Producing metabolic products (e.g., butyrate) which improve a cell's ability to die when it should die (a process known as apoptosis or programmed cell death);

(d) Producing compounds that inhibit the growth of tumor cells; or

(e) Stimulating the immune system to better defend against cancer cell proliferation

Immune System Stimulation

Probiotic cultures have been shown in a variety of test systems to stimulate certain cellular and antibody functions of the immune system. Animal and some human studies have shown an effect of yogurt or lactic acid bacteria on enhancing levels of certain immunoreactive cells (e.g. macrophages, lymphocytes) or factors (cytokines, immunoglobulins, interferon)]. Results accumulated so far suggest that probiotics may provide an additional tool to help your body protect itself.

Allergy

Allergy is on the rise in industrialized nations. 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. It is suggested that the exposure of infants to microbes before the age of six months helps the immune system mature to better tolerate allergens later in life (http://www.usprobiotics.org/basics 2006)

Lactose Intolerance

The inability of adults to digest lactose, or milk sugar, is prevalent worldwide which is due to the undigested lactose reaching the large intestine and being fermented by the colonic microbes, which can produce gases and products that lead to watery stool (http://www.usprobiotics.org/basics2006)The consumption of dairy products – important for supplying calcium and preventing osteoporosis – by people with lactose intolerance can be facilitated by probiotic bacteria

Hypertension

Antihypertensive effects have been documented in animal models and in mildly hypertensive adults for three compounds derived from the growth of certain lactobacilli:

i) fermented milk containing two tripeptides derived from the proteolytic action of L. *helveticus* on casein in milk

ii) Bacterial cell wall components from cell extracts of lactobacilli

iii) Fermented milk containing fermentation-derived gamma amino butyric acid.

(http://www.usprobiotics.org/basics 2006)

Antibiotic therapy disease

The purpose of antibiotics is to kill harmful bacteria. Unfortunately, they frequently kill normal bacteria as well, often resulting in disruption of the bacterial flora, leading to diarrhea and other intestinal disturbances. Replenishing the flora with normal bacteria during and after antibiotic therapy seems to minimize disruptive effects of antibiotic use.

Vaginosis

The vagina and its microbiota form a finely balanced ecosystem. Disruption of this ecosystem can lead to a microbiological imbalance and symptoms of vaginosis. Lactobacilli predominate in the healthy vagina, and a lack of lactobacilli (especially those producing hydrogen peroxide) 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. Intravaginal applications of lactobacilli have been somewhat effective in treating bacterial vaginosis.

Helicobacter pylori

Helicobacter pylori is a bacterium which colonizes the stomach. 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 and conclude that antibacterial substances including organic acids produced by some lactobacilli inhibit the growth and survival of this pathogen.

CONCLUSION

Most yogurt manufacturers have been adding probiotics to yogurt for years, with cultures such as L. acidophilus, L. casei, L. reuteri commonly found on their labels. Probiotics represent a potentially significant therapeutic advance. The industry as a whole will gradually respond to consumer requests and expectations regarding strains and levels of probiotics contained in their products, as well as what information is included on labels. As the demand grows and the consumer gains an understanding of the health benefits of probiotics, other foods will undoubtedly also be used as a "base" for delivering probiotics. Research will need to verify the efficacy of the benefits when probiotics are added to these food products. The beneficial effects of probiotics will depend upon a number of factors including the strain chosen, level of consumption, duration and frequency of exposure, and the physiological condition of the individual. It will be important to consider the desired health effect (for example, alleviating lactose intolerance versus improving immune function). Clients should be counseled to not consider probiotics the latest "magic pill" but instead to integrate probiotics consumption into other healthy dietary and lifestyle strategies. The natural and historical association of probiotics with dairy foods allows the individual to capitalize on the taste and availability of dairy products as well as nutrients such as calcium, vitamin D, magnesium and more recently identified components such as sphingolipids, conjugated linoleic acid and functional peptides. It will be imperative to stay informed, in both the research and application areas of probiotics, in order to provide consumers with advice based on the most current knowledge available.

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