Probiotic bacteria: their properties and mode of action (Part 2 of 4)

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Introduction

Probiotic preparations are usually defined as live microbial dietary adjuvants which by improving nutritional and microbial balance in the intestinal tract beneficially affect the host's physiology[1,2]. This definition has recently been extended[3] to include the modulation of the mucosal and systemic immunity as one of the more important beneficial effects of probiotic preparations. *(SA Fam Pract 2003;45(3):36-38)*

These definitions and the research on which they are based, indicate that the benefits of probiotics extend beyond the maintenance of the correct microbial balance in the intestines and the positive effects on the digestive tract itself, and include other benefits to the general health of the host.

The microbial flora inhabiting the human intestinal tract is acquired gradually, starting just after birth. The digestive tract of an adult person is inhabited by over 400 species of various commensal microorganisms, *i.e.* bacteria, yeasts, viruses[4,5] and their approximate combined number is estimated[1,5] to be in the region of 10^{14}. The composition of the intestinal flora and the numbers of the individual types of microorganisms are not static, but undergo continuous changes influenced by the age, diet, life style, environment and/or pathological conditions[1,6,7,8]. The relationship between these microorganisms and the human body can be saprophytic, parasitic or symbiotic. Among the symbiotic microorganisms are those that have beneficial properties necessary to maintain a healthy digestive tract and which are believed to be responsible for the overall control of the balance in this part of the human body.

Two major groups of such probiotic microorganisms, naturally occurring in the intestines of a healthy person and generally acknowledged as being able to exert beneficial health effects are bacteria belonging to the genera *Lactobacillus* and *Bifidobacterium.*

Lactobacillus (microaerophilic) resides predominantly in the small intestine and *Bifidobacterium* (strictly anaerobic) resides in the large intestine.

Factors affecting probiotic microorganisms

The relationship between the various microorganisms (the beneficial, the saprophytic and the pathogenic) and their interactions are complex and the balance maintained between the various types is delicate and frequently critical. Numerous factors can affect the composition of the intestinal microflora. Changes in life style are probably responsible for the observation that the present day ecology of the human gastrointestinal tract is vastly different from that of the humans living in earlier times[9]. Among the factors which can deplete the beneficial bacteria are: frequent use of antibiotics, stress, incorrect diet, age, impaired peristalsis, compromised immune system and diarrhoea[6,8]. If the decrease in the numbers of the beneficial bacteria is large enough, the balance in the intestines is disturbed and pathogenic microflora may become dominant.

In order to be able to use probiotic preparations effectively, one needs to know their required properties, understand why these properties are needed, and also understand the mechanism through which these preparations exert their anticipated effects. A number of important criteria according to which the strains for the production of commercially available preparations should be selected, is outlined below.

Properties required of bacterial strains used in probiotic preparations

i. Safety

Safety of the selected strains should constitute an overriding consideration. According to the Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food[10], the strains:

- Should not possess pathogenic or virulence characteristics;
- Should not be capable of transferring antibiotic/drug resistance to pathogens and
- Should not become passively (through the process of lysis) a source of antibiotic resistance.

It should be mentioned that two *Enterococcus* species, used in the preparation of probiotic preparations, have been reported in the literature to be associated with the resistance to vancomycin, namely: *E. faecium* and *E. faecalis*[11,12,13,14], whereas *Lactobacillus reuteri* has been reported to be

associated with the resistance to erythromycin[15,16], chloramphenicol[17] and vancomycin[18].

ii. The ability to exert microbial interference

Production of anti-microbial substances

One of the most important mechanisms though which probiotic bacteria exert their effects on pathogens invading the human body, is the production of a range of compounds with strong anti-microbial properties.

During fermentation, lactic acid bacteria produce a range of short-chain fatty acids such as lactic, acetic, butyric and propionic acids which reduce the pH of the intestinal milieu and also have broad-spectrum inhibitory effects against Gram-positive and Gram-negative bacteria and some viruses[3,7]. Lactic and acetic acids are known to inhibit the growth of pathogens such as *Staphylococcus aureus*[19], *Salmonella typhimurium*[20], *Helicobacter pylori*[21] as well as of *Listeria*, *Campylobacter*, *Shigella*[22,23], *Clostridium difficile*[24,25] and *Yersinia*[26]. Rotavirus infections, frequently responsible for the infant diarrhoea were found to be effectively inhibited by probiotic strains[27].

Hydrogen peroxide (H_2O_2), produced by the lactic acid bacteria is known to have an inhibiting effect on a number of microorganisms[28,29] and is most frequently used in the control of the overgrowth of *Candida albicans*[5,25].

A detailed discussion of numerous bacteriocins (antibiotic-like substances and bactericidal proteins) is included in the review by Naidu et al.[3].

Competitive exclusion of pathogen binding and competition for nutrients

In addition to the ability to produce a range of anti-microbial substances, probiotics' ability to compete for space and for nutrients constitutes the second group of mechanisms through which they may antagonize pathogenic microflora within the human body[3,6].

It should be emphasised that the competitive exclusion and competition for nutrients occur simultaneously with the production of anti-microbial compounds.

iii. Colonization of the human intestinal tract

Resistance to acid and bile

For the successful colonization of the gastrointestinal tract, it is essential for probiotic bacteria to be resistant to the gastric juices in order to survive the passage through the harsh milieu of the stomach and also to be resistant to the strongly antibacterial properties of the bile[3,10].

Ability to adhere to various types of mucosal cells

It is not clear whether the ability of probiotic bacteria to adhere to the intestinal mucosal cells and thus avoid/prevent their rapid removal by contraction of the gut, is essential for optimum

effects[5]. It should be mentioned that transient microbes such as dairy strains present in yoghurt can induce short-term beneficial effects, such as lowering the pH and the production of organic acids, without being able to reside in the gut[5].

Probiotic strains intended for use in the urogenital therapy should have the ability to adhere to the vaginal and uroepithelial cells[30] and thus be able to interfere with the adhesion of vaginal or uro-pathogens[30,31] and re-colonize the vagina.

Similarly, probiotic strains that are used in the treatment of oral pathogens, should be able to adhere effectively to the mucosal cells in the mouth[32].

iv. Ability to modulate the human immune system

Increasing attention has recently been given to the effects of probiotics and probiotic products on the mucosal immune system and the mucosa-associated lymphoid tissue[33,34,35,36,37,38]. As the intestinal mucosa is the major habitat of these bacteria, they are in intimate contact with the gut-associated lymphoid tissue (GALT). GALT constitutes the largest lymphoid tissue in the human body[37] and therefore the naturally occurring probiotic bacteria play a fundamental role in the functioning of the mucosal immune system[34,35,36,37]. In a recent publication[38], an outline of the mechanisms through which probiotic bacteria modulate the human immune system is presented.

v. Production of β-galactosidase

The inability to digest lactose (lactose intolerance) is a problem affecting up to 75% of the world's adult population[39]. In order to avoid the unpleasant symptoms of the intestinal distress, the affected individuals, with too low levels of the enzyme β-galactosidase necessary for the degradation of lactose, typically restrict the intake of dairy products. This in turn may lead to the development of nutritional deficiencies, predominantly of calcium[5]. As the lactic acid bacteria are efficient producers of β-galactosidase, it is frequently a matter of a sufficient number of them being present in the digestive tract to produce sufficient amounts of the enzyme. The administration of probiotic bacteria and also of the dairy strains of lactic acid bacteria should prevent or at least reduce the symptoms of lactose intolerance[5,6,40,41].

vi. The ability to reduce the level of serum cholesterol and lipids

As a substantial body of evidence is accumulating relating to the beneficial effects of probiotic bacteria on the reduction of serum and lipids, the strains used commercially should be able to offer these benefits. Although the mode of action through which lactic acid bacteria can reduce cholesterol and lipid levels is not fully understood, several mechanisms have been postulated, namely: direct assimilation of cholesterol, deconjugation of bile salts, reduced transport of cholesterol to plaque deposits and the inhibition of low-density lipoproteins formation[1,42,43,44]. The decrease in the level of β-hydroxy-β-methylglutaryl-Coenzyme A reductase in the liver observed with the consumption of probiotics, is considered to be an indication of the decrease of cholesterol synthesis and constitutes another possible mode of action[45].

With the growing antibiotic resistance within the human pathogenic microflora and with the increasing emphasis on preventative approaches, the potential for the prophylactic and therapeutic use of probiotic seems to be enormous.❐

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