



Probiotics — how functional are they?

Probiotics have become a topic of great interest to the medical world. There is considerable scientific evidence of their potential and real benefits in *in vitro* and animal experiments and to a lesser extent in humans.¹⁻⁶ There are, however, also concerns about the validity of much of the research as applied to human health, while aggressive commercialisation of probiotics backed by exaggerated or unsubstantiated claims often reduces probiotics to 'a very naïve and simplistic level in order to market products'.⁷

Various definitions of a probiotic have been proposed but it is in essence 'a live microbial food ingredient that is beneficial to health'.⁶ The best known and studied probiotics are the lactic acid bacteria and bifidobacteria, which are widely used in yoghurts and other dairy products. They retain viability during storage and survive passage through the stomach and small bowel and are generally regarded as safe, i.e. non-pathogenic and non-toxic.

Closely linked to probiotics are dietary substances known as prebiotics, which are not digested in the upper intestinal tract and reach the large bowel where they selectively stimulate the growth or metabolism of lactobacilli or bifidobacteria. They are usually in the form of the oligosaccharides present in onions, chicory, garlic, lectins, artichokes and cereals and are selectively utilised by these micro-organisms, resulting in their enhanced growth.

Effector mechanisms required for the control of a balanced intestinal microflora exerted by probiotic bacteria include low molecular metabolites such as formic acid, propionic acid, CO₂, ammonia, ethanol, hydrogen peroxide, diacetyl and acetaldehyde, as well as bacteriocins and antimicrobial substances with broad-spectrum activity (reuterin produced by *Lactobacillus reuteri* and other unidentified agents produced by *Lactobacillus GG*, *L. acidophilus* LAI and some strains of bifidobacteria.^{1,3,5} Soluble vitamins are also synthesised by some but not all strains of bifidobacteria.¹

Potentially beneficial effects of probiotics are numerous. They include antimutagenic properties based on, for example, binding of pyrolysates produced during cooking at high temperatures, degradation of N-nitrosamines by lactobacilli and antitumour activities of purified bifidobacterial cell walls.^{1,5} Co-administration of prebiotics such as lactulose or fructo-oligosaccharides with specific *Bifidobacterium* strains has also been shown to have antitumour activity in *in vitro* and animal experiments.^{1,3,5}

Probiotics affect mucosal and systemic immunity through interaction with intestinal epithelial cells, B and T lymphocytes and accessory cells of the immune system. Lipopolysaccharide (endotoxin), peptidoglycan and lipoteichoic acids of probiotic bacteria associate with epithelial cell membranes and can serve as antigen carriers to target tissues where immune reactions may be provoked.¹ Probiotics also stimulate cytokine production, mononuclear cell proliferation and macrophage phagocytosis and killing.^{1,5} Relatively few studies on the

immune modulating properties of probiotics have been performed in humans, but *Lactobacillus GG* administration to 31 infants with cow's milk allergy and atopic eczema resulted in clinical improvement with reduced excretion of tumour necrosis factor α .¹

The role of probiotics in lactose intolerance has been studied extensively. Subjects with low β -galactosidase (lactase) activity absorb lactose from yoghurt or milk containing *L. acidophilus* concentrate better than from milk. In two double-blind randomised controlled studies the administration of a rose-hip drink containing *L. acidophilus* 299V reduced flatulence and pain in patients with irritable bowel syndrome significantly, but in another similarly designed study milk containing *L. acidophilus* did not appreciably improve the condition.³

Probiotics have also been studied in intestinal infections with varying results. *Lactobacillus GG* proved beneficial in antibiotic-associated colitis in a small study of 5 patients but no such effect could be demonstrated when *L. acidophilus* NCDO 1748 was administered in freeze-dried form.¹ Different groups of investigators have found that probiotics shorten episodes of rotavirus diarrhoea or reduce the risk of disease.^{6,8}

Another entity in which the effects of probiotics proved to be controversial is cardiovascular disease. *L. plantarum* in a Swedish fruit juice with fermented oat flour significantly lowered concentrations of low-density lipoprotein (LDL) cholesterol and fibrinogen in persons with moderately raised cholesterol levels, while in another study involving heavy smokers the authors found a significant decrease in systolic blood pressure, leptin and fibrinogen, as well as significant decreases in plasma interleukin-6 and plasma F₂ isoprostanes and significantly reduced adhesion of monocytes to native and stimulated human endothelial cells. No significant changes were observed in the plasma concentration of total cholesterol and only moderate reductions in LDL cholesterol (12%) and similarly low increases in high-density lipoprotein (HDL) cholesterol (10%) levels were found.⁹ Taylor and Williams could not demonstrate a probiotic-mediated hypocholesterolaemic effect.¹⁰

It is clear from many studies that specific strains of lactobacilli and bifidobacteria and adequate organism loads are required for the beneficial effects attributed to probiotics. Stringent quality control and labelling standards are therefore required for the rational use of probiotics based on reliable information supplied by manufacturers. The study on the evaluation of probiotics available in South Africa recently published in the *SAMJ* is therefore opportune.¹¹ With regard to the technology used to detect and identify probiotics in the formulations tested, the principle of PCR amplification using primers directed at the 16S rDNA genes of bacteria is well established and its specificity depends on the choice of primers. Temmerman *et al.*,¹² who described the method based on the abovementioned principle and performed the test on the South African samples, validated his approach by means of



suitable control strains and the use of conventional identification technology.

Despite the numerous studies claiming good results with probiotics, more well-designed studies are required in humans to substantiate earlier findings. In a recent critical evaluation of pre- and probiotics, Roberfroid indicated that, based on the strength of available evidence, a strong case could be made for the use of probiotics in lactose intolerance and that the scientific status of immunostimulation, faecal mutagenesis and colonic microflora is at this time still preliminary and should be investigated further in human subjects.⁶ Prebiotics in their own right may also confer benefit and their role in promoting calcium bioavailability is promising.⁶ More human trials are required to validate the many potential benefits of pre- and probiotics.

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