The role of probiotics and indigestible carbohydrates in intestinal health

PL Conway[1], X Wang[1,2]

[1]CRC for Food Industry Innovation, School of Microbiology and Immunology, University of New South Wales, Sydney NSW 2052 and
[2]CSIRO Division of Food Science and Technology, Highett, VIC

Summary

The digestive tract of healthy individuals harbours a dense microbial population which contributes significantly to the health and well being of the host. These microbes are found in fairly low numbers in the upper regions of the tract and in very high numbers in the large bowel. Most of the microbes play a beneficial role, however, there are situations when constituents of the indigenous microbes are associated with disease. While the diversity and density of the microbial population are relatively stable, there is a dynamic equilibrium between the various components of the gastrointestinal system, namely the microbes, the diet and the host physiology. Consequently, the composition of the microbiota may be altered directly or indirectly by dietary modification. Manipulation of the microbiota by dietary means for the benefit of the host has been approached in two different ways, using probiotics and prebiotics. The term probiotics has evolved to describe preparations of microbes that induce a beneficial effect on intestinal health when ingested. Many of the early probiotic preparations were largely ineffective, but it is now well established that by carefully selecting the particular microbe to be used, intestinal health can be significantly improved using probiotic preparations eg reduction of diarrhoea, immunomodulation, competitive exclusion of pathogens. The term prebiotics has been coined to refer to carbohydrates which are not degraded by the host enzymes in the upper regions of the tract and hence reach the bowel intact where they are degraded and utilized by the colon microbes. It has been shown that some such indigestible carbohydrates (oligosaccharides and resistant starch granules with a high amylose content, eg Hi-maize™), promote the growth of the beneficial microbes in the colon and can thereby improve intestinal health.

The gastrointestinal microbiota

Composition of the microbiota

Table 1. Development of the major groups of microbes detectable in human faeces. Results are presented as the numbers of specific bacterial groups in faeces of 1 week old babies, 1-19 week old babies and adults and are expressed as the mean ± SD [3]

Bacterial group	Viable count (log CFU.g^{-1})					
	1 week[a]		1-19 weeks[b]		Adult[c]	
	BF	FF	BF	FF	Western diet	
Bifidobacterium	9.0 ± 1.1	7.8 ± 1.8	9.8 ± 2.9	9.7 ± 0.9	5.7 - 13.4	(10.4)
Bacteroides	7.3 ± 1.6	7.4 ± 1.0	7.5 ± 1.8	9.0 ± 0.8	9.0 - 13.5	(11.3)
Clostridium	3.5 ± 3.3	5.1 ± 1.5	4.9 ± 3.0	6.6 ± 0.8	6.5 - 13.1	(10.2)
Enterobacteria	7.5 ± 2.0	8.3 ± 1.1	8.1 ± 0.8	8.7 ± 0.9	4.9 - 12.4	(8.9)
Lactobacillus	ND	ND	7.2 ± 0.7	7.1 ± 0.7	3.6 -12.5	(9.3)
Streptococcus	7.1 ± 0.7	7.7 ± 0.7	7.3 ± 0.9	8.5 ± 0.9	5.1 - 12.9	(9.1)

[a]Calculated from data from 8 independant studies, representing 164 (BF) and 218 (FF) individuals, results for wet weight of feces. BF = breast fed; FF = formula fed; ND = no data available.

[b]Calculated from data from 17 independant studies, representing 325 (BF) and 182 (FF) individuals; results for wet weight of feces.

[c]Representing 62 individuals and expressed as the range (mean) in dry feces; not all bacterial groups detected are presented here, only those detected in babies are presented.

At birth the gastrointestinal tract is virtually devoid of microbes and is subsequently successively colonised by microbes which originate from the mother and the surrounding environment. There is a fairly typical pattern of development until a stable microbial population is established (Table 1). In both the developing gut of the infant and that of the adult, the composition of the microbiota is influenced by the diet. In addition, the microbiota can be influenced by the host physiology since secretions from the host are released into the lumen and can either directly or indirectly impact on the microbes eg digestive enzymes, immunoglobulins and bile acids. Environmental stresses can also induce an alteration in the host secretions. A dynamic equilibrium exists between these various factors including diet, host physiology, external stresses and the microbes of the digestive tract. An alteration in one such parameter can induce a shift in the metabolism or composition of the microbiota, which in turn can have ramifications on the health of the host as outlined below [1] [2].

Role of the microbiota

The microbes of the gastrointestinal tract contribute to the health of the host in a number of ways as summarised in Table 2. While some harmful effects have been reported, the microbes generally contribute to the well being of the host. This has been well demonstrated using germ free mice which were particularly susceptible to the intestinal pathogen, Salmonella. In contrast mice that had a stable microbial population in the digestive tract were considerably more resistant to the estalishment of the pathogen [4], a situation referred to as colonisation resistance [5]. The indigenous intestinal microbes also contribute to the nutrition of the host since they can synthesise vitamins and produce metabolites such as butyrate which is utilized by the enterocytes of the colon as a metabolic fuel. Unfortunately, some components of the microbiota can be opportunistic pathogens and emerge as a threat to the host should there be a shift in the diversity of the microbiota. For example, *Clostridium difficile* is detectable in low levels in the faeces of healthy adults. Antibiotic treatment, however, reduces levels of other indigenous microbes and can favour proliferation of *C. difficile* and result in diarrhoea. Severe intestinal discomfort and flatulence are linked to microbial fermentation in the intestine and often associated with specific dietary components. The microbes have also been shown to play a role in tumour formation and carcinogen levels within the intestine. Antibiotics have been shown to induce some improvement in a number of physiological diseases eg arthritis, irritable bowel syndrome, ulcerative colitis and Crohn's disease. Consequently, it has been proposed that microbes could also be involved in these conditions, but the causative agents have not yet been identified.

Table 2. Influences of the gastrointestinal microbes on the host

Beneficial effects	Harmful effects
Inhibition of pathogens	Constipation
Immunomodulation	Diarrhoea
Synthesis of vitamins	Infection
Metabolic fuel for enterocytes	Tumour incidence
Mucosal permeability	Arthritis*
Stabilize the ecosystem	Irritable bowel syndrome*
Colonization resistance	Crohn's disease*
Contributes to digestion	Ulcerative colitis*

* Speculative since no causative agent has been identified

Probiotics

Probiotics are preparations of live microorganisms which induce a beneficial effect on the host by influencing the indigenous microbes[6] .

The concept of including probiotic microbes in foods dates back to the turn of the century when the Russian scientist Metchnikoff proposed that the Bulgarians lived longer because they consumed fermented milk products and that one could prevent intestinal putrefaction by consuming these beneficial bacteria. Interest in probioitcs has been sporadic since the time of Metchnikoff because there were frequently non-conclusive or conflicting results presented. Interest focused largely on the lactic acid bacteria and in particular the lactobacilli (Table 3). By the 1980s, it became apparent that alternatives to antibiotics or preparations for use in combination with antibiotics were required. It was proposed that if one paid strict attention to the particular strain of probiotic used, one would be able to improve the intestinal health of the host by oral dosage of probiotic preparations [6, 7, 8]. In particular, it was suggested that the probiotic strain should be of host origin, be able to grow and colonize the intestinal tract, be stable and be biologically active against the target [6, 7, 8]. There is now increasing demand from the scientific and medical professions for validation of claims of efficiacy of probiotics using scientifically controlled clinical studies.

Today, a number of probiotic strains that have been isolated using these selection criteria have emerged and the future of probiotics usage for improving intestinal health appears promising[9]. Consistent with the early studies these strains are largely lactic acid bacteria. It is well established that specific probiotic strains can reduce lactose intolerance, diarrhoeal disease and bacterial enzymes [9] as well as trigger the immune system for the benefit of the host [10, 11]. In addition, it is proposed that probiotics have the potential to reduce cholesterol, competitively exclude intestinal pathogens and prevent cancer, however, additional studies are required to verify these benefits.

Prebiotics

Prebiotics are non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon and thus improve host health. Food ingredients that are degraded by the host enzymes fail to reach the colon and hence the microbes at this site would fail to thrive and contribute to the wellbeing of the host in the absence of these non-digestible food ingredients. The most well studied of the prebiotics are the oligosaccharides, especially the fructooligosaccharides. It has been shown that oligofructose and inulin can selectively stimulate the beneficial bifidobacteria of the human colon [12, 13].

Table 3. Microbes used as probiotics for humans

Lactobacillus acidophilus	*Bifidobacterium bifidum*
L. plantarum	*B. infantis*
L. casei	*B. adolescentis*
L. fermetnum	*B. longum*
L. reuteri	*B. breve*
Saccharomyces boulardii	*Enterococcus faecalis*
Lactococcus lactis	*Entero. faecium*

More recently, it has been shown that high amylose starch granules are not degraded in the upper regions of the small intestine [14, 15, 16, 17]. It was consequently of interest to determine which colonic microbes could hydrolyse the starch granules. Using high amylose starch granules, it was shown (Wang et al, unpublished observations) that they were selectively hydrolysed in vitro by many *Bifidobacterium* species and by some bacteroides as well as *Clostridium butyricum.* (Table 4). When this concept was tested in vivo using Hi-maize™ as the high amylose starch granules and mice (Wang et al unpublished observations), an elevation of the faecal bifidobacterium numbers was noted. In addition, the faecal concentration of butyrate was also elevated in Hi-maize™ fed animals. An additional advantage of Hi-maize™ was noted. *Bifidobacterium* cells adhered to the starch granules and when grown in the presence of Hi-maize™ or mixed together with Hi-maize™, the *Bifidobacterium* cells were more resistant to low pH (Table 5). This could ensure better survival of the *Bifidobacterium* cells in vitro as well as in vivo.

Table 4 In vitro hydrolysis of high amylose starch granules by colonic microbes (Wang et al. manuscript 1)

Test bacteria	Hydrolysis	Test bacteria	Hydrolysis
Bif. infantis	+	*L.fermentum A*	-
Bif. adeloscentis	+	*Lactobacillus sp*	-
Bif. longum	+	*L.murinus*	-
Bif. bifidum	+	*L.fermentum B*	-
Bif. pseudolongum	+	*L.fermentum C*	-
Bif. breve	+	*L.fermentum D*	-
Bact. fragilis	±	*L. casei*	-
Bact. vulgatus	±	*L.acidophilus*	-
Bact. thetaitaomicron	-	*L.plantarum*	-
Bact. distasonis	-	*L. rhamnosus*	-
Bact. ovatus	-	*L. brevis*	-
Cl. difficile	-	*L. salivarius*	-
Cl. butyricum	+	*Strept. thermophilus*	-
Cl. tyrobutyricum	-	*Strept. salivarius*	-
Cl. sporogenes	-	*P. acne*	-
F. gonadoformons	-	*P. fredenreichii*	-
F. montiferum	-	*E. linosum*	-
F. necrogenes	-	*Staphyl. aureus*	-
F. necrophorum	-	*Lacto. lactis*	-

Table 5 Protective effect of Hi-maize™ on Bifidobacterium grown in the presence of either glucoseor Hi-maize™ and exposed to low pH buffered solutions (Wang et al, manuscript 2)

Time (h)	Viable count (log CFU per ml)					
	pH 6.5		pH 3.5		pH 2.3	
	Glucose	Hi-maize™	Glucose	Hi-maize™	Glucose	Hi-maize™
0	6.1	7.8	6.4	7.8	6.1	6.9
3	6.0	7.6	3.5	6.7	<2	<2
6	5.5	7.9	<2	5.2	<2	<2

Conclusions

It is established that the microbes residing in the gastrointestinal tract play an important role in the health and well being of the individual and that these microbes can be manipulated by dietary means using probiotics and prebiotics. The probiotic concept involves the oral administration of beneficial bacteria and the prebiotic concept involves the oral consumption of non-digestible carbohydrates which are specifically utilized by the host. By careful selection of the probiotic strain and the prebiotic which may be preferentially utilized by the probiotic, one envisages that functional foods can improve intestinal health.

References

1. Savage DS. Microbial ecology of the gastrointestinal tract. Annu Rev Microbiol 1977;31: 107-33.
2. Conway PL. Microbial ecology of the human large intestine. In: Macfarlane GT, Gibson GR, eds Human colonic bacteria: Role in nutrition, physiology, and pathology. Boca Raton: CRC Press Inc, 1995:1-24.
3. Conway PL. Acquisition and succession of the gut microflora In: Mackie RI, Bryan AW, Isaacson RE eds.The gastrointestinal microflora. New York: Chapman and Hall, 1997: 2:1-13

4. Freter R. Interactions between mechanisms controlling the intestinal microflora. Amer J Clin Nutr 1974;27:1409-16.
5. Hentges DJ. Gut flora and disease resistance. In: Fuller R, ed. Probiotics, the scientific basis. London: Chapman & Hall,1992: 87-110.
6. Havenaar H, Ten Brink B, Huis Int Veld J. Selection of strains for probiotic use. In: Fuller R, ed. Probiotics: The scientific basis. London: Chapman and Hall, 1992:209-24.
7. Conway PL. Lactobacilli: fact and fiction. In: Grubb R, Midtvedt T, Norin E, eds. The regulatory and protective role of the normal microflora. London: The MacMillan Press LDT, 1989: 263-82.
8. Conway PL, Henriksson A. Strategies for the isolation and characterization of functional probiotics. In: Gibson, SAW, ed. Human health: the contribution of microorganisms. London: Springer-Verlag, 1994: 75-94.
9. Lee, Y-K, Salminen, S. The coming of age of probiotics. Trends in Food Science and Technology 1995; 6:219-51.
10. De Simone C, Vesely R, Bianchi Salvadori B, Jirillo E. The role of probiotics in modulation of the immune system in man and animals. Int J Immunotherapy 1993;9:23-8.
11. Schiffrin EJ, Rochat F, Link-Amster H, Aeschlimann JM, Donnet-Hughes A. Immunomodulation of human blood cells following the ingestion of lactic acid bacteria. J Diary Sci 1995;78:491-7.
12. Wang, X, Gibson, GR, Effects of the in vitro fermentation of oligofructose and inulin by bacteria growing in the human large intestine. J Appl Bacteriol 1993;75:373-80.
13. Tanaka, R, Takayama, H, Morotomi, M, Kuroshima, T, Ueyama, S, Matsumoto, K, Kuroda, A, Mutai, M Effects of administration of TOS and Bifidobacterium breve 4006 on the human fecal flora. Bifid Microflora 1983;2:17-24.
14. Muir JG, Young GP, O'Dea K, Cameron-Smith D, Brown IL, Collier GR Resistant starch - the neglected 'dietary fibre'? Implications health. Dietary Fibre Bibliography and Reviews 1993;1:33-47.
15. Muir JG, Birkett A, Brown IL, Jones G, O'Dea K. Food processing and maize variety affects levels of starch escaping digestion in the small intestine. Am J Clin Nutr 1995;61:82-9.
16. Brown I, McNaught K, Moloney E (1995) Hi-maize: new directions in starch technology and nutrition. Food Aust 1995; 47:272-5.
17. Brown I. Complex carbohydrates and resistant starch. Nutr Reviews 1996 ;54 :S115-9.