British Journal of Nutrition (1999), **81**, 83–84

Invited commentary

Gut fermentation and health advantages: myth or reality?

In this issue of the *British Journal of Nutrition*, Van Loo and colleagues summarize the findings of a pan-European research project (Van Loo *et al*. 1999). The ENDO (European Non-Digestible Oligosaccharides) project has explored the functional properties of dietary oligosaccharides that are not metabolized in the upper gastrointestinal tract. The authors have collated a large amount of data which show both the prebiotic (stimulation of potentially beneficial gut microflora in the bowel) and systemic (e.g. improved mineral absorption, reduction in blood lipid levels) effects of non-digestible oligosaccharides (NDO). Through their article, the authors have produced a consensus report in an area of nutritional sciences currently attracting much interest and debate.

The bowel has not always been a prime focus of attention for the thinking nutritionist. Indeed, it is thought that around 400BC Hippocrates was responsible for the phrase 'death sits in the bowel', thus formulating the hypothesis that the intestines, in particular the colon, contributed little towards human nutrition. It has long been thought that this organ's main benefits lie in the storage and excretion of waste material ingested in the diet, with some absorptive capacity. As the residence time of material in the hindgut is long, certain disorders may arise through the accumulation of various toxins. These include chronic gut diseases like bowel cancer, ulcerative colitis, intestinal putrefaction and antibiotic-associated colitis, as well as motility disorders such as diarrhoea and constipation (Gibson & Macfarlane, 1994). Moreover, the large gut is the preferred site of infection for bacteria, viruses and parasites which are often transmitted in food. This includes the deadly food poisoning micro-organism *Escherichia coli* 0157 which was responsible for over twenty fatalities in Wishaw, Scotland, in 1996. Just to compound the issue, it is believed that irritable bowel syndrome contributes more towards demands upon general practitioners' time than any other common disorder. With food intolerance and allergies also linked with disturbances in gut function, it is no surprise that the organ has received such a bad press!

Against this background it is difficult to appreciate evidence for potentially positive aspects of colonic metabolism and particularly the concept that this ecosystem plays a vital role in human nutrition and perhaps health. This is developed in the consensus ENDO report published in the present issue (Van Loo *et al*. 1999). Although most papers published in the *British Journal of Nutrition* contain findings from single research studies, the value of the ENDO review lies in its comprehensive summary of this rapidly developing area of nutritional science.

The enormous metabolic activity of the large bowel has, seemingly, been seriously underestimated. We harbour an intense bacterial microflora in our lower intestine which can reach up to 10^{14} prokaryote cells in total. This equates to about 95 % of all the cells in the body. Other pertinent estimations are that:

one person has more colonic bacteria than the number of people that there has ever been on the planet,
adults can carry over 1 kg of gut bacteria,
we all excrete our own weight in faecal bacteria per annum,
there are thought to be at least 500 bacterial species in the colon,
over 60 % of faecal solids is bacteria.

Whilst these 'soundbites' are hard to imagine (and impossible to prove!), the fact is that the human colon is an intensively colonized area. In fact, life without these bacteria would be extremely unpleasant, if not impossible. A further truth is that the majority of these residents are in fact benign and may even offer some health-promoting value (Table 1). Lactic acid-excreting bacteria, such as the lactobacilli and bifidobacteria, are thought to belong to the latter category, hence their very common use as probiotics.

Metchnikoff (1907) was one of the earliest scientists to recognize the biological significance of the colon and, noting the longevity of Bulgarian peasants, he attributed this to a high intake of milks 'soured' by bacteria. It was this early observation which developed into the modern concept of probiotics. Conventionally, these are lactic acid bacteria added to yoghurts (e.g. 'live', 'active', 'bio', 'bifidus'). Most products contain between one million and one billion bacteria per teaspoon. Other more recently developed vehicles for human consumption include lyophilized forms given in capsules or tablets, and soft drinks, including infant formulas, containing probiotic bacteria.

Table 1. Postulated health advantages associated with human gut bacteriology (largely unproven in volunteer trials)

Maintenance of gut homeostasis
Prevention of pathogen colonization
Metabolism of procarcinogens
Stimulation of gut immunity
Reduced gas distension
Improved energy yield (through the generation of short-chain fatty acids and their systemic metabolism)
Metabolism of xenobiotic materials
Reduced translocation
Formation of vitamins
Reduced blood lipid levels
Improved bowel motility
Production of digestive enzymes

One difficulty with probiotics is that their survival, both in the product and after ingestion, is difficult to guarantee. These (usually anaerobic) micro-organisms have a number of barriers to their survival such as gastric acidity, bile secretions and competition with over 500 resident bacterial species. As an adjunct, or alternative approach, the prebiotic concept has been developed (Gibson & Roberfroid, 1995). This takes the view that lactic acid bacteria are present in everyone's gut and advocates that fortification of these components of the microbiota can be achieved through ingestion of non-viable, non-digestible food ingredients which are susceptible to selective fermentation in the large bowel. As such, a prebiotic is a dietary fibre-like material. But it has a much more tailored fermentation in that selective metabolism occurs in the mixed culture environment of the hindgut. Clearly, the selectivity should be towards desirable micro-organisms. Oligosaccharides are the commonest and most extensively researched form of prebiotic.

The ENDO consensus report summarizes evidence for beneficial systemic and prebiotic effects of dietary oligosaccharides. However, the authors make it clear that there remain some important unanswered questions. Of paramount importance are the real health values associated with foods that target gut bacteria. This necessitates the use of modern methodologies applied towards well-controlled human studies. It is our opinion that conventional laboratory animals do not appropriately reflect the human gut microbiota composition and activities, nor in most cases do they act as suitable models for human lipoprotein metabolism and immunology. To address these research issues, effective *in vitro* models of the human hindgut should be used and the results applied in volunteer trials.

One major difficulty lies in the accurate determination of the gut microflora composition and its response to diet. However, new approaches in molecular characterization of gut microflora will help alleviate this problem. Our (unpublished) data, using direct community analysis of faecal DNA, indicate that round 60 % of the gut flora remains to be characterized. Nevertheless, 16SrRNA sequencing combined with gene probing of important bacterial groups are highly applicable to large-scale volunteer trials in multiple-centre studies. Such application will help identify the outcomes of prebiotic (including oligosaccharide) feeding to volunteers.

It is probable that certain populations may derive different health benefits from others. For example, age-related differences may be important. Breast- and formula-fed infants, children at the weaning stage, adults, and the elderly are thought to have a varied gut flora composition. Similarly, geographical differences are likely and probably driven by dietary change. Hospitalized and institutionalized subjects may respond differently to persons on less-controlled diets. New molecular probing techniques offer unprecedented opportunities to characterize the variability of human gut microflora, and evaluate the impact of dietary change, using non-invasive and socially acceptable techniques.

Whilst the use of molecular probing techniques constitutes an essential step forward in the demonstration of unequivocal prebiotic effects of NDO, well-controlled human trials are also needed to provide clear-cut evidence of beneficial local and systemic effects of these dietary constituents. The ENDO consensus report illustrates the current paucity of evidence linking ingestion of NDO to improvements in markers of human health. We have previously discussed limitations in the design of studies which have investigated effects of probiotics on blood lipids in volunteers (Taylor & Williams, 1998). Studies on the systemic effects of prebiotics in humans are also very limited in number (Williams, 1998). A recent human trial has provided evidence of modest triacylglycerol-lowering effects of the NDO inulin, thus supporting the findings obtained from a number of animal studies (KG Jackson, GR Taylor, AM Clohessy and CM Williams, unpublished results). Further work is needed to ascertain whether or not these effects are reproducible in subjects of varying ages, fasting lipid values and background diets. Mechanisms underlying putative actions of prebiotics on human systemic metabolism require elucidation.

The next few years will see important developments in human gut microbiology and the effects, on colonic bacteria, of feeding selected dietary constituents. Time will tell whether the early hypotheses of Hippocrates, Metchnikoff and others are valid or not. Happily, the tools are now available to identify this and determine whether the huge potential that exists can be realized.

Glenn R. Gibson
Christine M. Williams
Department of Food Science and Technology
The University of Reading
Whiteknights
Reading RG6 6AP
United Kingdom

References

Gibson GR & Macfarlane GT (1994) Intestinal bacteria and disease. In *Human Health – the Contribution of Micro-organisms*, pp. 53–62 [SAW Gibson, editor]. London: Springer-Verlag.

Gibson GR & Roberfroid MB (1995) Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. *Journal of Nutrition* **125**, 1401–1412.

Metchnikoff E (1907) *The Prolongation of Life*. London: William Heinemann.

Taylor GR & Williams CM (1998) Effects of probiotics and prebiotics on blood lipids. *British Journal of Nutrition* **80**, Suppl. 2, S225–S230.

Van Loo J, Cummings J, Delzenne N, Englyst H, Franck A, Hopkins M, Kok N, Macfarlane G, Newton D, Quigley M, Roberfroid M, van Vliet T & van den Heuvel E (1999) Functional food properties of non-digestible oligosaccharides: a consensus report from the ENDO project (DGXII AIRII-CT94-1095). *British Journal of Nutrition* **81**, 121–132.

Williams CM (1998) Effects of inulin on blood lipids in man. *Journal of Nutrition* (In the Press).