M. E. Sanders
Dairy and Food Culture Technologies
Littleton
Colorado
USA
and
Dairy Products Technology Center
California Polytechnic State University
San Luis Obispo
California
USA

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Functional food properties of non-digestable oligosaccharides

We were very interested to read the papers by Gibson *et al.* (1999) and the ENDO project group (Van Loo *et al.* 1999) in the February issue of the *British Journal of Nutrition*. They give a useful introduction to the field and list over a dozen different potential health advantages of altered gut bacteriology. When we last attempted to prepare a list of physiological actions of fermentable substrates on the hindgut we gave up after thirty. One of these actions, which was not mentioned in the two papers, was the stimulation of cell proliferation in the intestinal mucosa by the production of short-chain fatty acids (SCFA). There is substantial confusion on the actions of the SCFA, as *in vitro* studies have shown them to be powerful stimulators of differentiation and apoptosis; however, *in vivo* they are clearly powerful mitogens (Goodlad *et al.* 1989), moreover there is poor evidence for pro-apoptotic effects *in vivo*. The implications of this significant proliferative effect are as yet still unclear, but increased proliferation is traditionally regarded as a potential risk factor in the development of carcinogenesis (Wasan *et al.* 1996). Fermentation in the colon also has other biological–cellular actions on the process of crypt fission (McCullough *et al.* 1998), which we have implicated as a critical event in the initiation–development of colorectal carcinogenesis (Wasan *et al.* 1997).

It would appear that this consensus paper is somewhat biased towards the positive evidence, and one must be clearly aware that most clinical dietary interventions have not had the intended beneficial outcomes. This is especially worth stressing in light of the unanticipated results of most of the randomized human β-carotene studies, vitamins C and E and fibre-polyp prevention studies. In these human clinical trials, either no benefits were seen or, more worryingly, detrimental, (i.e. pro-carcinogenic) effects were observed, which led to the early closure of some of the studies (ATBC, 1994). Thus no prospective human clinical study has ever confirmed the purported theoretical benefits. Indeed, worryingly, a fair proportion of dietary fibre studies in animals have also shown pro-carcinogenic effects (Hill *et al.* 1996).

A further complication may be that the addition of fermentable substrate supplements to a 'Western' diet may result in a feast or famine pattern of fermentation (McBurney *et al.* 1987) in which there are sudden surges in bacteriological activity followed by a lack of substrate, in which case the colonic flora must either ferment each other (cannibalism) or the colonic epithelial mucosa and mucins.

We therefore agree with the ENDO group that there is a great need for more in-depth research, but would caution against over enthusiasm in instigating human trials based on the currently available scientific data.

Robert A. Goodlad
Principal Scientific Officer
Imperial Cancer Research
Fund and Senior Lecturer
Imperial College of Science, Technology and Medicine
DuCane Road
London W12 0NN
United Kingdom

Harpreet Wasan
Senior Lecturer and Honorary Consultant in Medical Oncology
Imperial College of Science, Technology and Medicine
DuCane Road, London W12 0NN
United Kingdom

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