Letters to the Editors

Polyols, breath hydrogen and fermentation

I was pleased to see our Society Journal published the paper 'Breath hydrogen after ingestion of the bulk sweetener sorbitol, isomalt and sucrose in chocolate' by Lee, Zumbe and Storey of Salford University Lee *et al.* (1994). It has become increasingly clear in recent years that the gastro-intestinal behaviour of polyols in humans is complex and partly dependent on the medium in which they are ingested. As exemplified in this paper, polyol behaviour ought to be investigated by its incorporation into the type of food expected to be available to the consumer; in this instance chocolate. As considered by the authors, a drawback to the use of polyols is their fermentation in the large bowel, which may result in discomfort. It is often believed that breath H_2 measurements can be used to quantify or semi-quantify the extent of fermentation and, together with information on intake, the extent of digestion of a carbohydrate in the small intestine. Lee *et al.* appear to support a lesser degree of small-intestinal absorption of sorbitol than of isomalt on the basis of breath H_2 data. Early evidence would support such a belief but recent evidence offers a different interpretation, making such support imprudent.

Supporting, though not proving, the interpretation of the breath H_2 response (BHR) as a semi-quantitative index of fermentation were the linear relationships between varying dosage of fermentable carbohydrates and varying breath H_2 responses (Fritz & Siebert, 1985; Flourie *et al.* 1988; Rumessen *et al.* 1990). Further supporting evidence was the production of similar amounts of H_2 from similar amounts of true carbohydrates $[C(H_2O)_n]$ during fermentation *in vitro* (Bond & Levitt, 1972, 1976; Fritz & Siebert, 1985). However, more recent findings on BHR and H_2 production *in vitro* do not support the use of BHR even as a semi-quantitative index. Such findings are: (a) differences in H_2 production among certain complex carbohydrates and simple sugars fermented *in vitro* (Christl *et al.* 1992); (b) differences in H_2 production among differing bulking agents and bulk sweeteners fermented *in vitro* (Livesey *et al.* 1993); and (c) interactions between bulking agents in mixtures that affect the stoichiometry of H_2 production from them, both *in vitro* and *in vivo* (Livesey *et al.* 1993). Further, *in vitro* tests of stoichiometry do not always allow calibration of BHR because the composition of small-intestinal hydrolysis products entering the large intestine may be unknown. For example, after ingestion of isomalt the substrate entering the large intestine will be a five-component mixture comprising unknown proportions of the three hydrolysis products (glucose, sorbitol, mannitol) and ingested two-mixture disaccharide alcohol. Each component has its own and different stoichiometry for H_2 production and to complicate matters there may be interactions between the components of the mixture and, possible, other dietary components that reach the large intestine.

The mass of evidence against the utility of BHR for comparing different substrates, it should be noted, was not available to Lee *et al.* at the time they submitted their paper to the *British Journal of Nutrition*. However, it is important that the difficulties of interpretation of BHR are appreciated in order to avoid attaching too much significance, in terms of small-intestinal absorption and extent of fermentation, to differences in BHR amongst alternative bulk sweeteners.

The low BHR response to isomalt in humans may be explained either by its digestion and absorption in the small intestine or by a low production of H_2 from this polyol. Of sixteen bulking agents and their mixtures examined recently (Livesey *et al.* 1993), isomalt gave the

least amount of H_2. Thus it appears that information on BHR after isomalt ingestion may have been wrongly interpreted resulting in an underestimate of the extent to which it escapes small-intestinal digestion. By contrast, sorbitol, as a mixture with Polydextrose, gives rise to large amounts of H_2 *in vitro* (Livesey *et al.* 1993), and so it seems that information on BHR to sorbitol may have overestimated the extent to which it is fermented *in vivo*. Further evidence supporting a higher small-intestinal absorption of sorbitol than isomalt has been discussed previously (Livesey, 1992).

While caution may be advised on the interpretation of BHR, particularly when comparing different bulking agents, the closing conclusion of Lee *et al.* that isomalt has advantages over sorbitol as a bulking agent is independent of the interpretation of the relative extents of fermentation of these polyols. The lower BHR from isomalt is consistent with the milder adverse symptoms from the lower intestinal tract and the low conversion of isomalt to H_2 during fermentation. Eventually it may become evident that such symptoms relate not only to the extent of fermentation but also to the stoichiometry of the process.

G. LIVESEY
Institute of Food Research,
Norwich Laboratory,
Norwich Research Park,
Colney,
Norwich NR4 7UA

REFERENCES

Bond, J. H. & Levitt, M. D. (1972). Use of pulmonary hydrogen (H_2) measurements to quantitate carbohydrate absorption. Study of partially gastrectomised patients. *Journal of Clinical Investigation* **51**, 1219–1225.

Bond, J. H. & Levitt, M. D. (1976). Quantitative measurement of lactose absorption. *Gastroenterology* **76**, 1058–1062.

Christl, S. U., Murgatroyd, P. R., Gibson, G. R. & Cummings, J. H. (1992). Production, metabolism and excretion of hydrogen in the large intestine. *Gastroenterology* **102**, 1269–1277.

Flourié, B., Florent, C., Etanchaud, F., Evard, D., Franchisser, C. & Rambaud, J.-C. (1988). Starch absorption by healthy man evaluated by the lactulose hydrogen breath test. *American Journal of Clinical Nutrition* **47**, 61–66.

Fritz, M. & Siebert, G. (1985). Dose dependency of the breath hydrogen and methane in healthy volunteers after ingestion of a commercial disaccharide mixture, Palatinit®. *British Journal of Nutrition* **54**, 389–400.

Lee, A., Zumbe, A. & Storey, D. (1994). Breath hydrogen after ingestion of the bulk sweeteners sorbitol, isomalt and sucrose in chocolate. *British Journal of Nutrition* **71**, 731–737.

Livesey, G. (1992). The energy values of dietary fibre and sugar alcohols for man. *Nutrition Research Reviews* **5**, 61–84.

Livesey, G., Johnson, I. T., Gee, J. M., Smith, T., Lee, W. E., Hillan, K. A., Meyer, J. & Turner, S. C. (1993). 'Determination' of sugar alcohol and Polydextrose® absorption in humans by the breath hydrogen (H_2) technique: the stoichiometry of hydrogen production and the interaction between carbohydrates assessed *in vivo* and *in vitro*. *European Journal of Clinical Nutrition* **47**, 419–430.

Rumessen, J. J., Hamberg, O. & Gudman-Hoyer, E. (1990). Interval sampling of end-expiratory hydrogen (H_2) concentrations to quantify carbohydrate malabsorption by means of a lactulose standard. *Gut* **31**, 37–42.

Reply from Storey et al.

It was pleasing to see that our recent paper (Lee, Zumbe & Storey, 1994) has stimulated the interest of others working in the field and we were interested to read the comment of Dr Livesey and his co-workers. In the context of events occurring in the intestinal lumen, Livesey refers to the stoichiometry of different polyols for H_2 production and also to interactions between components of the mixture and possibly other dietary components reaching the large intestine. We would not disagree. We also agree with Livesey that the gastrointestinal behaviour of polyols is complex and, *in vivo*, depends upon the medium in which they are ingested. However, it also depends to a large part upon the inherent sensitivity of the individuals ingesting the bulk sweetener, as well as the dose and the

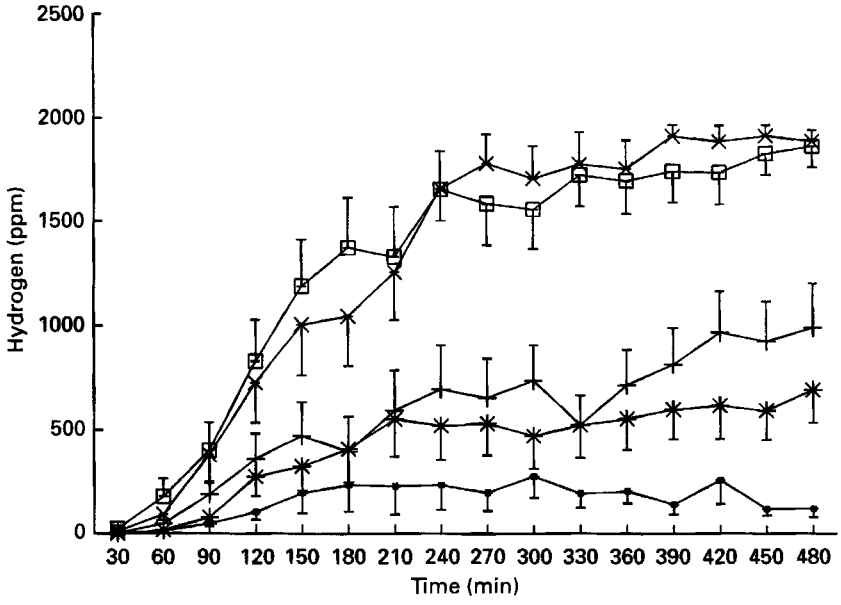

Fig. 1. H_2 concentrations (ppm) after an anaerobic *in vitro* fermentation of the sugar alcohols lactitol (×), sorbitol (□), maltitol (+) and isomalt (*) and a control (■) mixture. Each incubation contained 0·5 g polyol, 100 ml sterile growth medium and faecal bacteria (50 g/l stool homogenate). The control mixture contained no polyol. Values are means and standard errors represented by vertical bars for fourteen determinations.

frequency with which the polyol is ingested. Further complications to the provocation of intolerance symptomatology are whether or not the product containing the polyol is consumed acutely or chronically and whether it is consumed with or without fasting. Without a completely adequate *in vitro* model to mimic conditions occurring *in vivo*, the best that can be achieved is informed speculation as to what actually happens in the normal, non-intubated intact gut.

The dynamics of the gastrointestinal response to polyols are somewhat more complex than Livesey suggests and depend upon factors which include: (1) the extent of digestion of the native polyol, (2) the extent of absorption of the products of hydrolysis, (3) the inherent fermentability of the residual polyol and its hydrolysis products, (4) the fermentative capacity of the particular colon under consideration, (5) the extent of colonic absorption of fermentation products, (6) the osmotic properties of the polyol–hydrolysis products mixture, (7) the 'sensitivity' of the large bowel *muscularis externa*. One aspect of our paper (Lee *et al.* 1994) was to attempt to correlate the breath H_2 response (BHR) with the incidence of gastrointestinal symptomatology in non-intubated subjects, thus taking all the above considerations into account.

Livesey refers to the mass (*sic*) of evidence against the utility of the BHR for comparing different substrates but cites only two papers, his own (Livesey *et al.* 1993) and that of Christl *et al.* (1992). The point surely is that BHR data should not be used alone but, as suggested in our paper (Lee *et al.* 1994), should be taken together with information relating to the incidence of intolerance symptoms in the individuals providing the breath samples. Used in this way it can be a useful tool to overview the degree of digestion and fermentation of ingested polyol. Whilst we accept that the interpretation of BHR is difficult and must be made with circumspection, we maintain that it gives a useful insight into the events

occurring in the intact gut and we are not yet prepared to confine it to the back-burner in our attempts to understand fully the gastrointestinal response to the ingestion of polyols.

Livesey also refers to the low (*sic*) production of H_2 from isomalt compared to other polyols and polyol mixtures after *in vitro* faecal fermentation. We have also performed such studies and one relevant data set is presented above (Fig. 1). Differences between our protocol and that of Livesey *et al.* (1993) are that that in their work each substrate was incubated once only whereas in ours there were fourteen replicates, and our H_2 collections were sequential over 8 h whereas those of Livesey *et al.* (1993) were shown as total gas accumulations per vessel over 168 h. Despite these differences our data from *in vitro* faecal fermentation studies confirm that isomalt appears to be inherently less fermentable than some other sugar alcohols such as sorbitol and lactitol. The same, incidentally, is also true of crystalline maltitol. It must be borne in mind, however, that the confines of an inert *in vitro* fermentation vessel cannot replicate the conditions within a human colon. *In vitro* faecal fermentation is a useful technique, but much remains to be defined in terms of its suitability to predict what might happen in the colon of a person ingesting polyol. Like breath H_2 monitoring, it should be used with caution along with data from consumption studies to explain the gastrointestinal response to polyols.

D. M. STOREY, Z. ZUMBE AND A. LEE
Department of Biological Sciences,
Science Research Institute,
University of Salford,
Salford,
M5 4WT

Christl, S. U., Murgatroyd, P. R., Gibson, G. R. & Cummings, J. H. (1992). Production, metabolism and excretion of hydrogen in the large intestine. *Gastroenterology* **102**, 1269–1277.

Lee, A., Zumbe, A. & Storey, D. (1994). Breath hydrogen after ingestion of the bulk sweeteners sorbitol, isomalt and sucrose in chocolate. *British Journal of Nutrition* **71**, 731–737.

Livesey, G., Johnson, I. T., Gee, J. M., Smith, T., Lee, W. E., Hillan, K. A., Meyer, J. & Turner, S. C. (1993). 'Determination' of sugar alcohol and polydextros® absorption in humans by the breath hydrogen (H_2) technique; the stoichoiometry of hydrogen production and the interaction between carbohydrates assessed *in vivo* and *in vitro*. *European Journal of Clinical Nutrition* **47**, 419–430.

Bioavailability '93: Different aspects of 'bioavailability' in perspective

The understanding of the term 'bioavailability' differs, at least in part, between human nutrition, animal nutrition, and medicine. In human nutrition 'bioavailability' marks the efficiency with which nutrients are utilized. It encompasses the digestion of food as well as its absorption and metabolic utilization. Mutual interactions among nutrients and between nutrients and other food components have a great impact on digestion and absorption. Anabolic and endocrine adaptation to growth, pregnancy and different age leads to different metabolic requirements which influence the utilization of a nutrient by various feed-back mechanisms. Therefore, the bioavailability of a nutrient is likely to differ among individuals. The complexity of these interactions was reflected by the broad scope of contributions to the Bioavailability '93 meeting in Ettlingen on 9–12 May, 1993.

In animal nutrition there is a similar understanding of 'bioavailability'. The term describes the nutritive value of the feed to support growth and maintenance of the animals. For this purpose the concept of 'total utilization' defines the fraction of a dietary nutrient that is ultimately used in intermediary metabolism (Kirchgessner *et al.* 1993). This fraction is determined by the absorption of a nutrient and its metabolic utilization. In addition, the interest of the animal nutritionist focuses on how to supply animals with food at minimum

costs. So, in animal nutrition 'bioavailability' is closely related to the economic aspects of food production.

In pharmacology 'bioavailability' characterizes the fraction of a dose that reaches the systemic circulation after oral administration. This fraction is usually defined by changes in a drug's plasma concentration over time as indicated by the 'area under the curve' (Benet & Sheiner, 1985). Contrary to the nutritionist's approach, this definition does not deal with the utilization of a drug or nutrient. The pharmacodynamic and toxic effects are investigated separately. However, the desired and undesired effects of a drug clearly depend on the dose and on the bioavailability of a drug. Therefore, according to this concept, a drug's bioavailability is optimized under health aspects.

Under which aspects is the bioavailability of a nutrient optimized in human nutrition? In underdeveloped countries the economic aspect and the health aspect may be identical: a high bioavailability of nutrients helps to avoid famine and starvation in situations of scarcity. However, in an affluent society it is not necessarily healthy simply to increase the bioavailability of a nutrient. To improve the supply with fat and sugar could hardly be a recommendation to the majority of people in industrialized countries. To optimize health effects in a mixed western diet the availability of some nutrients may have to be compromised. For instance, high-fibre diets, especially those rich in phytate, may inhibit the intestinal absorption of Fe and Zn, on the one hand. On the other hand, dietary fibre or fibre components may decrease the risk of colon cancer and of arteriosclerosis. Rapidly growing infants and pregnant or lactating women have a high demand for essential minerals. The decreased bioavailability of essential trace metals from diets rich in fibre and phytate can be compensated either by supplementation or, as in the case of Fe, by addition of ascorbate. Vitamin C competitively inhibits the formation of insoluble Fe–phytate complexes, thereby improving the bioavailability of Fe even in mixed diets rich in phytate.

There can be no doubt that increasing the bioavailability of minerals and vitamins is highly effective in fighting deficiencies and restoring health. An oversupply of food and decreasing levels of physical activity in industrialized countries are related to high occurrence of obesity and diabetes. To support health in type II diabetes, fast increases of the postprandial glucose concentrations have to be avoided in order to economize the remaining activity of endogenous insulin. Guar and acarbose serve this purpose by delaying intestinal glucose absorption which modulates glucose bioavailability in favour of health benefits. Oral administration of cholestyramine reduces the enterohepatic circulation of bile acids which results in a decrease of plasma LDL concentrations and in a lower risk of arteriosclerosis. This is another example for a modification of bioavailability with a positive health effect, in which 'bioavailability' is defined according to the concept of 'total utilization' taken from animal nutrition. Prospective epidemiological studies are needed to show whether changes in the bioavailability of nutrients produce health benefits in humans.

The examples show that there are positive and negative effects on health when the bioavailability of a nutrient is modified. The goal of future research should be to tailor the bioavailability of nutrients in a mixed diet to the health problems of special subgroups of the population. The next Bioavailability conference, to be held in Wageningen, The Netherlands, in 1997, will show to what extent the nutritional sciences can succeed in linking their research to such perspectives.

KLAUS SCHÜMANN AND BERND ELSENHANS
Walther Straub-Institute für Pharmakologie und Toxikologie,
Ludwig-Maximilians-Universität,
Nussbaumstr. 26, 80336 München, Germany
AND DENNIS GORDON

Department of Food Science and Human Nutrition,
University of Missouri,
122 Eckles Hall, Columbia, Missouri 65211
AND ULRICH SCHLEMMER
Bundesforschungsanstalt für Ernährung,
Institut für Ernährungsphysiologie,
Engesserstr. 20, 76131 Karlsruhe, Germany

REFERENCES

Benet, L. Z. & Sheiner, L. B. (1985). Pharmacocinetics: the dynamics of drug absorption, distribution, and elimination. In *The Pharmacologic Basis of Therapeutics*, 7th ed., pp. 3–34 [A. Goodman-Gilman, L. S. Goodman, T. W. Rall and F. Murad, editors]. New York, Toronto, London: Macmillan Publishing Company.

Kirchgessner, M., Windisch, W. & Weigand, E. (1993). The bioavailability of zinc and manganese by isotope dilution technique. In *Bioavailability '93 Proceedings*, part 1, pp. 213–222 [U. Schlemmer, editor]. Karlsruhe, Germany: Bundesforschungsanstalt für Ernährung.

Printed in Great Britain