

Effect of dietary supplements of guar gum and cellulose on intestinal cell proliferation, enzyme levels and sugar transport in the rat

BY I. T. JOHNSON, J. M. GEE AND R. R. MAHONEY*

AFRC Food Research Institute, Colney Lane, Norwich NR4 7UA

(Received 27 April 1984 – Accepted 11 June 1984)

1. Male Wistar rats (approximately 200 g) were given fibre-free semi-synthetic diets containing either sucrose (S) or a sucrose-starch mixture (SS) as the carbohydrate component, or a diet similar to SS containing 40 g guar gum/kg (G), or 100 g cellulose/kg (C). The animals remained healthy, and weight gain after 30 d was similar in all groups.
2. The small intestines of the animals given diet G were significantly longer than those of the other groups, and showed signs of increased mitotic activity and mucosal growth.
3. No significant differences in mucosal enzyme activity were detected between the two fibre-free control groups. Lactase (*EC* 3.2.1.23) and alkaline phosphatase (*EC* 3.1.3.1) activities were significantly lower than controls in group G, but were higher in group C.
4. Kinetic analysis of 3-O-methyl glucose uptake by isolated intestine indicated that the maximum transport rate (V_{max}) of tissue from group G tended to be lower than from the fibre-free group SS and group C.
5. It is concluded that materials which are classed as dietary fibre but which differ markedly in their physical properties may also differ in the functional changes to which they give rise in the small intestine. These changes may be at least partially mediated by effects on mucosal cell proliferation.

It is now well established that the ingestion of guar gum and other viscous, non-absorbable polysaccharides improves glucose tolerance in experimental animals and man. This potentially useful effect is the result of delayed absorption in the small intestine and requires that the viscous material is present in the lumen, intimately mixed with the food bolus (Blackburn *et al.* 1984). Apart from this acute effect, a few reports have suggested that the long-term consumption of various types of dietary fibre leads to a persistent improvement in glucose tolerance which does not require that the fibre is present in the test meal (Munoz *et al.* 1979; Cannon *et al.* 1980; Mahalko *et al.* 1984). Such an effect could be brought about by an adaptive change in the rate of gastric emptying, a slowing of intestinal absorption, or by increased insulin secretion. Firm evidence for an adaptive reduction in the rate of intestinal glucose transport has been advanced by Schwartz & Levine (1980), who reported that feeding a supplement of either cellulose or pectin to rats resulted in improved glucose tolerance and slower glucose absorption compared with control animals fed on a fibre-free diet. In more recent publications they have shown that the same dietary regimen led to a reduction in trans-mucosal ion flux and reduced uptake of glucose and leucine in vitro (Schwartz *et al.* 1982, 1983). Other groups who have fed dietary fibre to rats for long periods have, however, failed to observe any reduction in intestinal absorption rates (Brown *et al.* 1979; Ebihara & Kiriyaama, 1982).

In a previous report, we described the absence of any significant change in glucose uptake from perfused loops of intestine in rats which had been fed on guar-gum-supplemented diets (Gee *et al.* 1983). In the present study we have explored this area in more detail. Groups of rats were fed on diets which were fibre-free, or contained either guar gum or cellulose supplements, and an in vitro method was used to determine the kinetics of carrier-mediated sugar uptake in the jejunum. In addition, similar groups of animals were used to examine

* Present address: Department of Food Science and Nutrition, University of Massachusetts, Amherst MA, USA.

the effect of the diets on mucosal cell proliferation and enzyme activities, with the aim of achieving a more detailed understanding of the effect of dietary fibre on small intestinal structure and function.

MATERIALS AND METHODS

Animals

Male Wistar rats (approximately 200 g) were randomly allocated to experimental groups, caged in pairs and provided with water and a semi-synthetic diet *ad lib*. Body-weight was measured at twice-weekly intervals throughout the feeding period and food intakes were recorded daily for the first 12 d of the study.

Diets

The compositions of the diets used are given in Table 1. The first and second diets included no added source of fibre, but contained either a mixture of starch and sucrose (SS) or sucrose alone (S) as the carbohydrate component. The third and fourth diets were based on the first (SS) but differed in that they contained either guar gum (G) or cellulose (C) substituted for a proportion of the starch as shown in Table 1.

Mucosal cell proliferation

The mucosal-cell birth-rate was estimated by the metaphase-arrest technique; estimates of the ratio, crypt: villus were obtained from the same sample of tissue (Wimber & Lamerton, 1963; Clarke, 1970). Ten animals were given an intraperitoneal injection of vincristine sulphate (Sigma, Poole, Dorset) in distilled water (1 mg/kg body-weight) and killed in succession at 12-min intervals by stunning and cervical dislocation. The entire small intestine was removed, flushed with saline (9 g sodium chloride/l), everted and placed on the bench. The extended but unstretched intestine was measured, and 10% of the total length was discarded from the proximal end. A further 100 mm sample was then removed and transferred to fixative (ethanol-acetic acid; 75:25 v/v). After removal of the most distal ileum (approximately 150 mm) the remaining intestine was slit open, laid mucosa uppermost and scraped with a microscope slide. The isolated mucosa was then transferred to a pre-weighed glass vial, frozen over solid carbon dioxide and stored at -20° for subsequent enzyme assay.

Samples of intestine (5–10 mm), fixed for 24 h, were passed through ethanol-water (50:50 v/v; 10 min), stained in bulk by the Feulgen reaction (Clarke, 1970), rinsed once more in distilled water and transferred to glacial acetic acid-water (45:55, v/v).

Ten crypts were obtained from each sample by microdissection, transferred to a drop of glacial acetic acid-water on a microscope slide and squashed by gentle pressure with a coverslip. The total number of blocked metaphases was counted under the compound microscope. The numbers of crypts and villi per mm^2 serosal surface were estimated using a dissecting microscope fitted with a calibrated eyepiece.

Uptake of 3-O-methyl glucose

After the 30 d feeding period, ten animals from each group were killed by a blow to the head followed by cervical dislocation. The entire small intestine was removed and rinsed with saline, everted and extended on the bench as described previously. After removal of the first 10% of the total length, the following 40% was cut into rings (2–3 mm) and placed in saline. A further 50 mm length was removed from the remaining half of the intestine, the mucosa and serosa were separated by scraping with a microscope slide and the samples were placed in pre-weighed vials.

The everted rings were distributed at random amongst twelve 25 ml conical flasks containing 5 ml substrate in Krebs-bicarbonate-buffered saline. Nine of the flasks contained

Table 1. Composition of the diets (g/kg diet)

Diet... Ingredients	Fibre-free		Guar gum G	Cellulose C
	SS	S		
Starch*	360	—	320	260
Sucrose	300	660	300	300
Casein†	200	200	200	200
Maize oil	80	80	80	80
Cellulose‡	—	—	—	100
Guar gum§	—	—	40	—
Mineral mix	40	40	40	40
Vitamin mix¶	20	20	20	20
Dietary fibre**	0.4	0.7	39.4	102.4

* 'Snoflake' maize flour; Corn Products Ltd, Manchester.

† Edible casein; Glaxo Farley Foods, Plymouth.

‡ Solkafloc; Johnson, Jorgensen, Wettre Ltd, London.

§ Sigma Chemical Co., St Louis, MO, USA.

|| Produced the following levels of minerals in the diet (g/kg diet): CaHPO₄ 13, CaCO₃ 8.2, KCl 7.03, Na₂HPO₄ 7.4, MgSO₄·H₂O 4.0, MnSO₄·H₂O 0.18, ZnCO₃ 0.03, FeSO₄·7H₂O 0.144, CuSO₄ 0.015, KIO₃ 0.001.

¶ Contained all necessary vitamins at levels equal to, or above, those recommended by the (US) National Research Council (1972) for growth and reproduction.

** Determined by a modification of the Southgate method (Southgate, 1969).

3-O-methyl glucose at a range of concentrations up to 120 mmol/l; the remaining three contained 3-O-methyl glucose at 20, 60 or 120 mmol/l together with phloridzin (phloretin-2-β-D-glucoside; Sigma) at a concentration of 0.5 mmol/l. All of the flasks were labelled with ³H-3-O-methyl glucose (Amersham International plc, Amersham, Bucks).

Flasks were incubated for 4 min at 37°, gassed continuously with oxygen-CO₂ (95:5, v/v), and shaken at 120 cycles/min. The tissue was collected on a Buchner filter, rinsed with ice-cold saline, placed in glass vials and dried overnight at 85°. The dried residues were dissolved in concentrated nitric acid (0.4 ml) and mixed with 0.75 M-Trizma base (3.6 ml). Portions of this solution (0.5 ml) were diluted to 2 ml with distilled water, added to 18 ml scintillation fluid (Cocktail T, Scintran; BDH, Poole, Dorset) and counted on a Philips PW4700 liquid-scintillation spectrometer.

Analytical methods

Maltase (EC 3.2.1.20), *lactase* (EC 3.2.1.23) and *sucrase* (EC 3.2.1.48). Brush border disaccharidase activities in the scraped mucosa were determined by a modification of the methods of Dahlqvist (1964, 1968) and Asp & Dahlqvist (1972). Homogenates were prepared in saline, diluted, and incubated with the appropriate substrate for 50 min at 37° in maleate buffer (0.1 M, pH 6.0). After incubation the samples were diluted with distilled water to a volume of 1 ml, placed for 3 min in a boiling water-bath, cooled and centrifuged (10000 g; 1 min). The supernatant fractions were assayed directly for glucose by the glucose oxidase (EC 1.1.3.4) method (GOD-Perid; Boehringer, Mannheim, FDR). Blanks were prepared by boiling the homogenate and substrate before incubation.

Alkaline phosphatase (EC 3.1.3.1). Mucosal homogenates were assayed for alkaline phosphatase activity by a modification of the Sigma method for serum (Sigma Chemical Co., 1980). Diluted homogenate was incubated with substrate in glycine buffer (0.05 M, pH 10.5) for 30 min at 37°. The reaction was stopped by the addition of 20 mM-sodium hydroxide, and the absorbance at 400 nm recorded.

Protein. The protein content of mucosal homogenates was determined by a method based

Table 2. *Food consumption and growth of rats fed on control or fibre-supplemented diets*
(Values are means with their standard errors for twenty animals, or ten pairs)

Diet...	SS		S		G		C		Statistical significance of differences		
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	SSv.G	SSv.C	Gv.C
Food consumption (g/pair per 12 d)	550	13	522	7	513	10	530	13	NS	NS	NS
Body-wt gain (g/animal per 12 d)	78.3	4.1	81.7	1.9	68.5	3.8	68.4	4.1	NS	NS	NS
Food conversion† (per pair)	28.6	0.8	31.3	0.5	26.5	0.8	25.7	0.7	*	**	NS
Final body-wt (g)	372	34	381	15	355	28	365	36	NS	NS	NS

SS, control diet with sucrose and starch; S, control diet without starch; G, guar-gum diet; C, cellulose diet; NS, not significant.

* $P < 0.05$, ** $P < 0.01$.

† Body-wt gain $\times 100$ /food intake.

on that described by Lowry *et al.* (1951). The dry-matter content was determined by oven-drying samples of homogenate to constant weight, a correction being made for the contribution of the saline.

DNA. The DNA contents of the mucosal homogenates and oven-dried scrapes were measured by the method of Fiszar-Szarfarz *et al.* (1981), using the equivalent of 0.2–0.3 g fresh tissue for the assay.

Statistical methods

In most cases the results for the four groups were compared using a one-way analysis of variance and by calculation of the least significant difference where the *F* test suggested an inequality of the means (Cochran & Cox, 1964). For the comparison of crypt-cell division rates, the significance of differences between the slopes of the lines of best-fit were assessed by means of a *t* test utilizing pooled sums of squares (Bailey, 1959).

For the estimation of parameters of the curves of best-fit in the transport study, the Michaelis–Menten equation was fitted to the data using the non-linear regression program of Dugleby (1981).

RESULTS

For most of the measurements carried out in the present study there was close agreement between the two fibre-free control groups; therefore, the significance of differences between means has been tabulated for only four of the six possible comparisons, and any exceptions mentioned.

The four diets were readily accepted by the rats, all of which appeared to thrive throughout the 4-week feeding period. Details of food consumption and growth for four groups of twenty animals are given in Table 2, together with their average body-weights after 30 d. During the first 12 d of the feeding period there was a tendency for the control groups to gain weight more quickly than the fibre-supplemented groups, and this was reflected in their significantly higher levels of food conversion (Table 2). There was no significant difference in the average weights of the groups after 30 d however.

Table 3. Numbers of crypts and villi, and rates of crypt-cell division in the mucosae of rats fed on control or fibre-supplemented diets
(Values are means with their standard errors for ten animals per group)

Diet...	SS		S		G		C		Statistical significance of differences			
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	SS _v :G	SS _v :C	G _v :C	G _v :C
Length of small intestine (mm)	1050	22	1060	15	1154	19	1017	20	**	NS	**	**
Villous density (no./mm ²)	7.4	0.2	7.2	0.2	6.6	0.3	7.6	0.4	NS	NS	NS	NS
Crypt density (no./mm ²)	241	7.2	219	10.5	201	11.0	239	7.2	**	NS	**	**
Crypt: villi	32.6	0.8	30.2	0.8	30.7	1.7	31.5	1.0	NS	NS	NS	NS
Cell division rate (Divisions/crypt per h)	16.3	1.4	17.3	1.0	24.8	6.1	13.3	1.6	NS	NS	NS	NS
Net villous influx†	531	48	523	32	761	192	419	52				

SS, control diet with sucrose and starch; S, control diet without starch; G, guar-gum diet; C, cellulose diet; NS, not significant.

* $P < 0.05$, ** $P < 0.01$.

† The product of the cell division rate and crypt: villi.

Intestinal growth and mucosal cell proliferation

The small intestines from the guar-gum-supplemented animals were significantly longer than those of any other group. The villi of these intestines were less densely packed, but as this was associated with a reduction in the numbers of crypts per unit area, the ratio, crypt: villus did not differ significantly from that for the other groups (Table 3).

The crypt-cell production rate was estimated from the slope of the line obtained by plotting the number of blocked metaphases per crypt, for each animal, against the time-interval from administration of vincristine to death. Good linear relationships were obtained for each of the groups, although the values for the guar-gum-supplemented animals were more scattered than those of the others. In consequence, although the estimated crypt-cell production rate for the guar-gum group was markedly higher than that for the others, the precision of the estimate was poor. Comparison of the slopes of the regression lines for the guar-gum- and the cellulose-supplemented groups, using a conventional *t* test, indicated that they differed significantly ($P < 0.05$), but since the estimated variances about these lines also differed significantly ($F 11.5$), such a test is not strictly valid. The results in Table 3 are therefore presented only as means with estimated standard errors.

Mucosal enzyme activities

There were no significant differences between the two fibre-free groups for any of the enzymes measured (Table 4). When expressed in terms of mucosal protein, the activities of lactase and alkaline phosphatase were significantly lower in the guar-gum-supplemented group than in the controls, whilst the activities of all three disaccharidases and alkaline phosphatase were significantly higher in the cellulose-supplemented group than in the controls. The general pattern of these differences was retained when the enzyme activities were expressed in terms of mucosal DNA, although the magnitude and significance of the differences decreased. This was partly due to a higher DNA:protein value in the guar-gum-supplemented group (Table 4).

3-O-methyl glucose transport

In the absence of phloridzin, there was a curvilinear relationship between the uptake of 3-O-methyl glucose and its concentration in the incubation medium. In the presence of phloridzin, which is a specific inhibitor of intestinal sugar transport, the uptake was much reduced and was linearly related to concentration. By subtracting this linear component from the uptake in phloridzin-free media, an estimate of the carrier-mediated component of transport was obtained for each animal. The kinetics of this process were analysed by fitting the Michaelis-Menten equation to the values; the means of the parameters for the curves of best fit were then compared between the groups and are given in Table 5. There was no evidence of differences in carrier-affinity (K_m) between the groups, but the estimated maximum transport rate (V_{max}) for the cellulose-supplemented animals was significantly higher than that for the guar-gum-supplemented group ($P < 0.05$) and for the sucrose (S) control group ($P < 0.01$).

Differences in V_{max} for transport rates expressed in terms of dry weight of whole intestinal wall may arise because of differences in the numbers of absorptive cells present per unit weight of tissue. Both mucosal mass and mucosal DNA levels were higher in the guar-gum-supplemented animals, and the estimated V_{max} values were corrected accordingly and are included in Table 5. When thus expressed, the average V_{max} for the guar-gum-supplemented group was significantly lower than that for both the cellulose group and the sucrose-starch control group.

Table 4. Mucosal enzyme activities and protein and DNA contents in rats fed on control or fibre-supplemented diets
(Values are means with their standard errors for ten animals per group)

Diet...	SS		S		G		C		Statistical significance of differences			
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	SSv.G	SSv.C	Gv.C	
Enzyme activity (munits/mg protein):												
Sucrase (<i>EC</i> 3.2.1.48)	101	7	104	5	114	5	136	8	NS	**	*	
Maltase (<i>EC</i> 3.2.1.20)	582	24	538	28	509	7	756	58	NS	**	**	
Lactase (<i>EC</i> 3.2.1.23)	28	2	26	1	17	2	33	1	**	*	**	
Alkaline phosphatase (<i>EC</i> 3.1.3.1)	110	3	115	3	76	4	129	6	**	*	**	
Enzyme activity (munits/mg DNA):												
Sucrase	2.4	0.23	2.6	0.12	2.5	0.31	3.1	0.31	NS	*	NS	
Maltase	13.8	1.06	12.6	0.69	11.8	1.99	17.7	2.59	NS	NS	*	
Lactase	0.7	0.05	0.6	0.03	0.4	0.10	0.7	0.05	*	NS	**	
Alkaline phosphatase	2.6	0.14	2.6	0.18	1.8	0.30	2.9	0.27	*	NS	**	
DNA:protein†	0.043	0.001	0.043	0.002	0.051	0.005	0.046	0.003				

SS, control diet with sucrose and starch; S, control diet without starch; G, guar-gum diet; C, cellulose diet; NS, not significant.

* $P < 0.05$, ** $P < 0.01$.

† Ratio, DNA: protein in mucosal homogenate used for enzyme assay.

Table 5. Kinetic indices for the uptake of 3-O-methyl glucose by everted rings of jejunum from rats fed on control or fibre-supplemented diets

(Values are means with their standard errors for ten animals per group)

Diet...	SS		S		G		C		Statistical significance of differences			
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	SSv.G	SSv.C	SSv.C	Gr.C
V_{max} :												
$\mu\text{mol}/4 \text{ min per g}$	19.8	3.0	13.7	1.6	15.6	2.3	26.1	3.5	NS	NS	NS	*
$\mu\text{mol}/4 \text{ min per mg DNA}$	1.64	0.29	1.02	0.12	0.96	0.17	2.10	0.30	*	NS	NS	**
K_m	32.5	7.4	39.0	12.3	28.6	3.4	31.4	5.4	NS	NS	NS	NS
Mucosal mass (mg/g dry wt)	417	15	472	20	543	18	446	16	**	**	NS	**
Mucosal DNA (mg/g dry wt)	12.7	0.5	13.9	0.7	16.9	0.8	12.7	0.4	**	NS	NS	**

SS, control diet with sucrose and starch; S, control diet without starch; G, guar-gum diet; C, cellulose diet; V_{max} , maximum transport rate; K_m , carrier affinity; NS, not significant.

* $P < 0.05$, ** $P < 0.01$.

DISCUSSION

In previous reports we have shown that the inclusion of guar gum in the diet of rats leads to important changes in the physical properties of their gastrointestinal contents, coupled with a probable slowing of nutrient absorption (Blackburn & Johnson, 1981, 1983). The present study demonstrates that the ingestion of guar gum has other, long-term consequences for intestinal growth and function, and serves to emphasize that materials which are frequently classed under a common heading as dietary fibre may, nevertheless, differ markedly in their physiological effects.

In common with other workers who have fed guar gum and other viscous polysaccharides to rats, we observed a significant increase in small intestinal length as well as increased mucosal mass and DNA content (Brown *et al.* 1979; Elsenhans *et al.* 1981; Jacobs, 1983), coupled with a marked increase in the estimated rate of crypt-cell division. Although the unusual variation between animals in the guar-gum-supplemented group led to a loss of precision in this estimate, this combination of observations strongly suggests an increased rate of mucosal proliferation in these animals. This is consistent with the recent report of Jacobs (1983) who described increased crypt-cell proliferation and faster migration of enterocytes in guar-gum-supplemented rats. It is interesting to note that Jacobs (1983) also reported signs of a decrease in proliferative activity in the jejunal crypts of oat-bran-supplemented rats, compared with controls fed on a fibre-free diet. In the present study the estimated cell-division rate in the cellulose-supplemented animals was lower than that of the fibre-free groups, although the difference was not significant.

Further studies will be necessary to determine the mechanism by which guar gum stimulates growth in the small intestine of rats, but two possibilities deserve comment. It is well established that the presence of nutrients in the lumen exerts a trophic effect on the intestinal mucosa, and it has been suggested that the normal proximal-to-distal gradient of morphology and physiological activity seen in the intestine is a response to a similar gradient of nutrient concentration in the lumen (Diamond & Karasov, 1983).

A slowing of absorption in the proximal lumen might be expected to displace the lumen concentration gradient, and give rise to a corresponding increase in the trophic stimulus exerted on the distal mucosa. This mechanism provides a satisfying explanation for the increased intestinal length seen in guar-gum-supplemented rats since, from a teleological point of view, it can be seen as an adaptive response to the possibility of malabsorption. However, as an explanation of the increased cell-division rates seen in these animals it is less satisfactory, as there is no evidence of a proximal-to-distal decline in the rate of cell-divisions per crypt in the normal intestine (Clarke, 1970).

Another possibility is that the presence of guar gum in the gut acts as a stimulus for the secretion of one or more gastrointestinal hormones with trophic activity. Of the many possibilities, gastrin has a particularly well-established role as a stimulus to growth in the stomach and duodenum, although its importance in the remainder of the small bowel is less certain (Sircar *et al.* 1983).

Whatever the mechanism underlying the changes in mucosal growth seen in our fibre-supplemented animals, it is evident that they are accompanied by functional differences as well. In general, the activities of the mucosal enzymes were below those of the controls in the guar-gum-supplemented animals and higher in the cellulose-supplemented group. This divergence of the two fibre-supplemented groups from one another persisted, even when the enzyme activities were expressed in terms of mucosal DNA, suggesting the existence of real differences in the average enzyme levels of individual mucosal cells. No differences in enzyme activity between the two control groups, which differed widely in their sucrose content, were observed.

Several groups of workers have recently reported on the effects of various components of dietary fibre on mucosal enzymes in the rat, but the results have not been entirely consistent. Brown *et al.* (1979), who compared the effects of a pectin-supplemented diet with those of a fibre-free and a pellet diet, described a decline in alkaline phosphatase and leucyl- β -naphthylamidase (leucine amino-peptidase; EC 3.4.11.1) activities, associated with a rise in mucosal protein, and histological evidence of increased cellular proliferation. Similarly, Thomsen & Tasman-Jones (1982) reported a decline in disaccharidase levels in rats fed on pectin-, tannin- or galactomannan-supplemented diets, although in subsequent work it was shown that the effect was dependent on the strain of rat employed (Thomsen *et al.* 1983). In contrast, Farness & Schneeman (1982) observed an increase in leucine amino-peptidase activity in rats fed on pectin- or cellulose-supplemented diets, and Schwartz *et al.* (1983) have recently reported increased disaccharidase levels in rats fed on a pectin supplement, but no change in animals fed on a cellulose-supplemented diet.

The 3-O-methyl glucose uptake study provided some evidence of adaptive changes in the capacity for intestinal transport in our four groups. As with alkaline phosphatase and lactase activity, the maximum rate of sugar uptake by the jejunum of the guar-gum-supplemented animals was significantly less than that of the sucrose-starch control group, whilst that of the cellulose group tended to be higher. This result is consistent with previous reports suggesting that prolonged consumption of guar gum and other viscous polysaccharides leads to a persistent improvement in glucose tolerance in rats (Cannon *et al.* 1980; Schwartz & Levine, 1980), although it contradicts the additional claim by Schwartz & Levine (1980) that dietary cellulose has a similar effect.

To summarize the findings of the present study, the addition of guar gum to a semi-synthetic rat diet stimulated the growth of the mucosa, but tended to reduce the activities of some mucosal enzymes, and the maximum transport rate for glucose, when these were expressed in terms of DNA. The implication of this is that average cellular levels of both enzymes and glucose carriers were reduced in the guar-gum-supplemented rats. The addition of cellulose to the diet tended to produce the opposite effects, so that the two groups supplemented with dietary fibre diverged significantly from one another in terms of most of their measured features. A simple working hypothesis to explain these observations is that increased cellular proliferation gives rise to a shorter villus transit time, and hence a reduction in the average lifespan of the mucosal cells. Since both enzyme levels and transport capacity increase with cell maturity (Kinter & Wilson, 1965; de Both *et al.* 1975), a reduction in the average age of the mucosal cells might lead directly to the results we have obtained. Although this model should provide a useful basis for further experimental work, it must be pointed out that the inter-relationship of cellular proliferation and tissue function is unlikely to prove to be so simple. The increased mucosal growth seen, for example, during pregnancy and lactation in the rat, is associated with higher rates of nutrient absorption (Cripps & Williams, 1975).

We conclude that the present study provides some support for the view that the prolonged consumption of guar gum may improve glucose tolerance by reducing the rate of digestion and absorption of sugars, even when guar gum is absent from the intestine, although the nutritional significance of this for man remains to be adequately tested. It is clear too that this conclusion cannot be generalized to all non-available polysaccharides, and further work is necessary to unravel the inter-relationships which exist between diets containing these materials and the growth and function of the small intestinal mucosa.

The authors are grateful to Mrs J. Cooke and Mr P. Muddel for animal care, and to Miss J. Brown for technical assistance.

REFERENCES

- Asp, N. G. & Dahlqvist, A. (1972). *Analytical Biochemistry* **47**, 527–538.
- Bailey, N. T. J. (1959). *Statistical Methods in Biology*, p. 99. London: English Universities Press.
- Blackburn, N. A. & Johnson, I. T. (1981). *British Journal of Nutrition* **46**, 239–246.
- Blackburn, N. A. & Johnson, I. T. (1983). *Pflügers Archiv* **397**, 144–148.
- Blackburn, N. A., Redfern, J. S., Jarjis, H., Holgate, A. M., Hanning, I., Scarpello, J. H. B., Johnson, I. T. & Read, N. W. (1984). *Clinical Science* **66**, 329–336.
- Brown, R. C., Kelleher, J. & Losowsky, M. S. (1979). *British Journal of Nutrition* **42**, 357–365.
- Cannon, M., Flenniken, A. & Track, H. S. (1980). *Life Sciences* **27**, 1397–1401.
- Clarke, R. M. (1970). *Journal of Anatomy* **107**, 519–529.
- Cochran, W. G. & Cox, G. M. (1964). *Experimental Designs*, p. 76. New York: John Wiley.
- Cripps, A. W. & Williams, V. J. (1975). *British Journal of Nutrition* **33**, 17–32.
- Dahlqvist, A. (1964). *Analytical Biochemistry* **7**, 18–25.
- Dahlqvist, A. (1968). *Analytical Biochemistry* **22**, 99–107.
- de Both, N. J., van der Kamp, A. W. M. & van Dongen, J. M. (1975). *Differentiation* **4**, 175–182.
- Diamond, J. M. & Karasov, W. H. (1983). *Nature* **304**, 18.
- Dugleby, R. G. (1981). *Analytical Biochemistry* **110**, 9–18.
- Ebihara, K. & Kiriyaama, S. (1982). *Nutrition Reports International* **26**, 193–201.
- Elsenhans, B., Blume, R. & Caspary, W. F. (1981). *American Journal of Clinical Nutrition* **34**, 1837–1848.
- Farness, P. L. & Schneeman, B. O. (1982). *Journal of Nutrition* **112**, 1315–1319.
- Fizar-Szarfarz, B., Szarfarz, D. & Guevara de Murillo, A. (1981). *Analytical Biochemistry* **110**, 165–170.
- Gee, J. M., Blackburn, N. A. & Johnson, I. T. (1983). *British Journal of Nutrition* **50**, 215–224.
- Jacobs, L. R. (1983). *American Journal of Clinical Nutrition* **37**, 954–960.
- Kinter, W. B. & Wilson, T. H. (1965). *Journal of Cell Biology* **25**, 19–39.
- Lowry, O. H., Roseborough, N. J., Farr, A. L. & Randall, R. J. (1951). *Journal of Biological Chemistry* **193**, 265–275.
- Mahalko, J. R., Sandstead, H. H., Johnson, L. K., Inman, L. F., Milne, D. B., Warner, R. C. & Haunz, E. A. (1984). *American Journal of Clinical Nutrition* **39**, 25–34.
- Munoz, J. M., Sandstead, H. H. & Jacob, R. A. (1979). *Diabetes* **28**, 496–502.
- National Research Council (1972). *Nutrient Requirements of Laboratory Animals*, 2nd ed., p. 64. Washington, DC: National Academy of Sciences.
- Schwartz, S. E. & Levine, G. D. (1980). *Gastroenterology* **79**, 833–836.
- Schwartz, S. E., Levine, G. D. & Starr, C. M. (1982). *American Journal of Clinical Nutrition* **36**, 1102–1105.
- Schwartz, S. E., Starr, C., Backman, S. & Holtzapple, P. G. (1983). *Journal of Lipid Research* **24**, 746–752.
- Sigma Chemical Co. (1980). *Sigma Technical Bulletin* no. 104. St Louis, Missouri: Sigma Chemical Co.
- Sircar, B., Johnson, L. R. & Lichtenberger, L. M. (1983). *American Journal of Physiology* **244**, G327–G335.
- Southgate, D. A. T. (1969). *Journal of the Science of Food and Agriculture* **20**, 331–335.
- Thomsen, L. L. & Tasman-Jones, C. (1982). *Digestion* **23**, 253–258.
- Thomsen, L. L., Tasman-Jones, C. & Maher, C. (1983). *Digestion* **26**, 124–130.
- Wimber, D. R. & Lamerton, L. F. (1963). *Radiation Research* **18**, 137–146.