

## The effect of guar gum on the viscosity of the gastrointestinal contents and on glucose uptake from the perfused jejunum in the rat

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1. Male Wistar rats were meal-fed for at least 10 d a control semi-synthetic diet containing no guar gum, or one of three similar test diets containing 3, 10 or 20 g dry guar gum/kg.
2. Rats were killed 6 h after feeding, and contents of stomach, small and large intestine were collected separately. The apparent viscosities of stomach and small intestine contents from animals fed on diets containing 10 and 20 g guar gum/kg were increased relative to control animals, but large intestine contents were unchanged.
3. In the second part of this study, male Wistar rats were anaesthetized and two consecutive lengths of jejunum were perfused, initially with Ringer only (control) or Ringer plus 5 or 6 g guar gum/l (test). Following this pre-perfusion, both segments were perfused with Ringer containing glucose (10 mM), [<sup>3</sup>H]glucose and [<sup>14</sup>C]inulin, and the rate of glucose absorption was determined.
4. The rate of glucose absorption was decreased relative to control values in segments pre-perfused with both 5 and 6 g guar gum/l solution, but this reduction was significant only in the instance of the 6 g/l solution ( $P < 0.001$ ).
5. These results provide evidence to support previous assumptions that ingestion of guar gum will increase the apparent viscosity of the contents of the stomach and small intestine. We propose that a possible mechanism by which guar reduces post-prandial glycaemia is a reduction of glucose absorption from the small intestine, resulting from an increase in viscosity of the contents.

Guar gum, a soluble galactomannan and classed as dietary fibre (as defined by Trowel *et al.* (1976)) has been shown to reduce post-prandial glycaemia in normal and diabetic humans (Jenkins *et al.* 1976; Jenkins, Leeds & Gassul, 1977; Morgan *et al.* 1979; Wahlqvist *et al.* 1979). It has been suggested that the mechanism of this action is related to the capacity of guar gum to form viscous solutions (Jenkins, Leeds, Gassul, Cochet *et al.* 1977; Jenkins *et al.* 1978; Wolever *et al.* 1978; Leeds *et al.* 1979), but it is not clear how this reduces the rate of glucose absorption.

A delay in gastric emptying has been suggested as an explanation (Holt *et al.* 1979), but Taylor (1979) and Leeds (1979), while agreeing that a delay in gastric emptying is important in the mechanism of action of guar gum, suggest that some other mechanism is involved in the reduction of post-prandial glycaemia, possibly involving absorption of glucose in the small intestine. This twofold action of guar gum has also been proposed by Jenkins *et al.* (1978).

Johnson & Gee (1980) demonstrated a reduction in glucose transport in everted sacs of rat jejunum incubated with guar gum *in vitro*, and propose that this effect is due to an increased thickness of the unstirred layer at the mucosal surface. However, the studies on the effect of guar gum on absorption in the intact rat are contradictory. Förster & Hoos (1977) showed no reduction in active sugar transport, whereas Elsenhans *et al.* (1980) have reported a reversible inhibition of solute transport in the rat both *in vitro* and *in vivo*.

The aims of the present study were as follows. Although it has been previously assumed that ingestion of guar gum will increase the viscosity of the gut contents, this has never been demonstrated *in vivo*. The first part of this study was designed to determine the magnitude of the effects of ingested guar gum on the viscosity of the gastrointestinal contents. In the second part of this study, a perfused intestinal preparation was used to examine the effects of guar gum on glucose absorption in the intact animal, and thus explore the significance of the *in vitro* work of Johnson & Gee (1980).

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

Diet . . . Ingredients	Test			
	Control	1	2	3
Starch*	290	287	280	270
Sucrose	290	290	290	290
Casein†	200	200	200	200
Maize oil	80	80	80	80
Cellulose‡	80	80	80	80
Mineral mix	40	40	40	40
Vitamin mix§	20	20	20	20
Guar gum¶	—	3	10	20

\* 'Snoflake' corn flour; Corn Products Ltd, Manchester.

† Edible casein; Glaxo Farley Foods, Plymouth.

‡ 'Solka-floc'; Johnson, Jørgensen, Wettre Ltd, London.

|| Mineral mix produced the following levels of minerals in the diet (g/kg diet): CaHPO<sub>4</sub> 13, CaCO<sub>3</sub> 8.2, KCl 7.03, Na<sub>2</sub>HPO<sub>4</sub> 7.4, MgSO<sub>4</sub> · H<sub>2</sub>O 4.0, MnSO<sub>4</sub> · H<sub>2</sub>O 0.18, ZnCO<sub>3</sub> 0.03, FeSO<sub>4</sub> · 7H<sub>2</sub>O 0.144, CuSO<sub>4</sub> 0.015, KIO<sub>3</sub> 0.001.

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

¶ Sigma Chemical Co., St Louis, USA.

## MATERIALS AND METHODS

### *Viscosity study*

Male Wistar rats (150–200 g) were used in all experiments. The animals were housed individually in wire-bottomed cages, and trained to mealfeed (09.00–10.00 hours) on one of the semi-synthetic diets detailed in Table 1.

The rats consumed the appropriate diet for at least 10 d before the experiment. The daily food intake of each rat was recorded, and only those maintaining a regular feeding pattern were used.

Rats were killed by a blow to the head followed by cervical dislocation 6 h after removal of the food, this interval having been found to be optimal for recovery of the digesta. The whole gastrointestinal tract was excised; the stomach contents were collected by opening the stomach and gently scraping out the contents, and those of the small and large intestine by squeezing from 150 mm segments. The samples from three animals were pooled and centrifuged for 15 min (approximately 1000 g). The liquid fractions from stomach, small and large intestine were then decanted off into stoppered vials, re-warmed to 37° and their apparent viscosities were determined on a Contraves Rheomat 15 using the cone and plate measuring system type KPI. A 5 g guar gum/l solution was centrifuged as described previously, to determine whether centrifugation changed the measured viscosity. All apparent viscosity values are presented as milliPascal seconds (mPa · s). One mPa · s is equal to one centipoise (cP).

### *Glucose transport study*

Male Wistar rats between 250 and 400 g in weight, fed on standard laboratory diet (Labsure Animal Diets, Christopher Hill Group Ltd, Poole) were used in all experiments.

The animals were anaesthetized by an intraperitoneal injection (0.4–0.6 ml) of pentobarbitone sodium ('Sagatal'; May and Baker Ltd, Dagenham), administered as a single or divided dose according to response. The small intestine was exposed by a mid-line ventral

incision, and a length (approximately 350 mm) of jejunum from the duodeno-jejunal flexure was isolated. An incision was made at both ends of this segment, two glass cannuli (internal diameter 2 mm) were tied in place in the incisions, and the contents were flushed out using Krebs bicarbonate Ringer, pH 7.4 (McDowall, 1960) at 37°, pre-gassed with oxygen-carbon dioxide (95:5, v/v). Two adjacent incisions were then made midway along the isolated loop, and two further glass cannuli were inserted to produce two consecutive lengths of jejunum for perfusion. The intestine was then returned to the abdominal cavity, and the cannuli connected to a Technicon multi-channel peristaltic pump producing a flow in the oral-anal direction (1 ml/min) in both segments.

One segment (control) was perfused for 12 min with bicarbonate Ringer at 37° and the other (test) perfused for 10 min with Ringer plus 5 or 6 g guar gum/l (Sigma Chemical Co., St Louis, USA), followed by a 2 min perfusion with Ringer only. Segments used for test and control were alternated.

After this initial perfusion, both segments were perfused with an identical Ringer solution containing glucose (10 mM) and radiotracer levels of D-[<sup>3</sup>H]glucose (2.8 mCi/mg, 2  $\mu$ Ci in 60 ml perfusate) and [<sup>14</sup>C-carboxylic acid] inulin (1.3  $\mu$ Ci/mg, 1  $\mu$ Ci in 60 ml perfusate). The preparation was allowed to equilibrate for 8 min, after which the outflows were collected separately over time-intervals of 2 min (pre-perfusion with 6 g guar gum/l solution) or 3 min (pre-perfusion with 5 g guar gum/l solution), directly into pre-weighed polyethylene scintillation vials, for a total of 21 min (20 min for pre-incubation with 6 g guar gum/l). All perfusions were performed under an infra-red lamp (ambient temperature approximately 37°) and the abdomen covered with a gauze moistened with Ringer solution.

At the end of the perfusion the animals were killed, the segments were drained, removed, then dried to constant weight at 80°. The perfusate samples were weighed to determine volume, scintillant was added to each vial (triton-toluene X (2:1, v/v) with 4 g PPO/l), then <sup>14</sup>C and <sup>3</sup>H activities were determined using a liquid-scintillation counter (Phillips liquid scintillation analyser model PW 4500) at the appropriate settings for dual-labelled samples. The initial activity of the labelled perfusate was also determined in this way. These activities were used to calculate the rate of glucose disappearance from the perfused loops of jejunum.

## RESULTS

### *Viscosity study*

A total of nine control animals and six animals for each test diet were used. Once accustomed to the semi-synthetic diets, animals ate between 12 and 16 g food/d, and no significant differences in food intake were observed between any of the groups of animals.

*Rheological properties of guar gum.* A solution of guar forms a non-Newtonian fluid which demonstrates shear-thinning properties i.e. apparent viscosity is reduced as shear rate increases. This is illustrated in the rheogram shown in Fig. 1. On centrifugation of a 5 g guar gum/l solution, a sediment appeared, but the apparent viscosity remained unchanged at all shear rates.

*Stomach contents.* Test diet no. 1 produced stomach contents of a watery consistency similar to those found in control animals and with no significant difference in apparent viscosity. Test diets nos. 2 and 3 yielded stomach contents in the form of a solid mass, with a sticky exterior but almost dry interior, from which no liquid could be separated by centrifugation. It was therefore not possible to make any viscosity measurements on such samples, but obvious that feeding guar gum at these levels changed the nature of the stomach contents.

*Small intestine contents.* Liquid was collected from all samples after centrifugation. The results from viscosity measurements are shown in Fig. 2. All test diets caused an increase

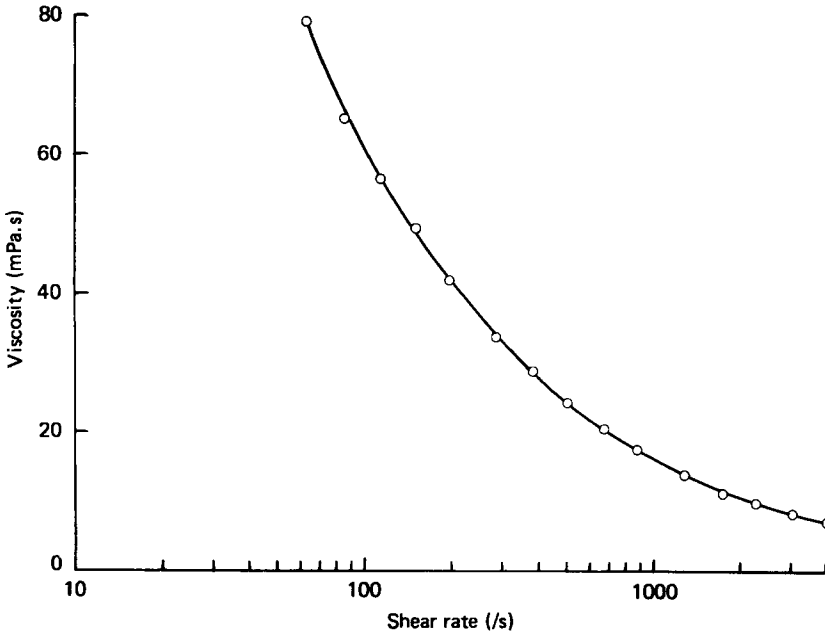


Fig. 1. Viscosity (mPa.s) of 5 g guar gum/l solution at different shear rates/s.

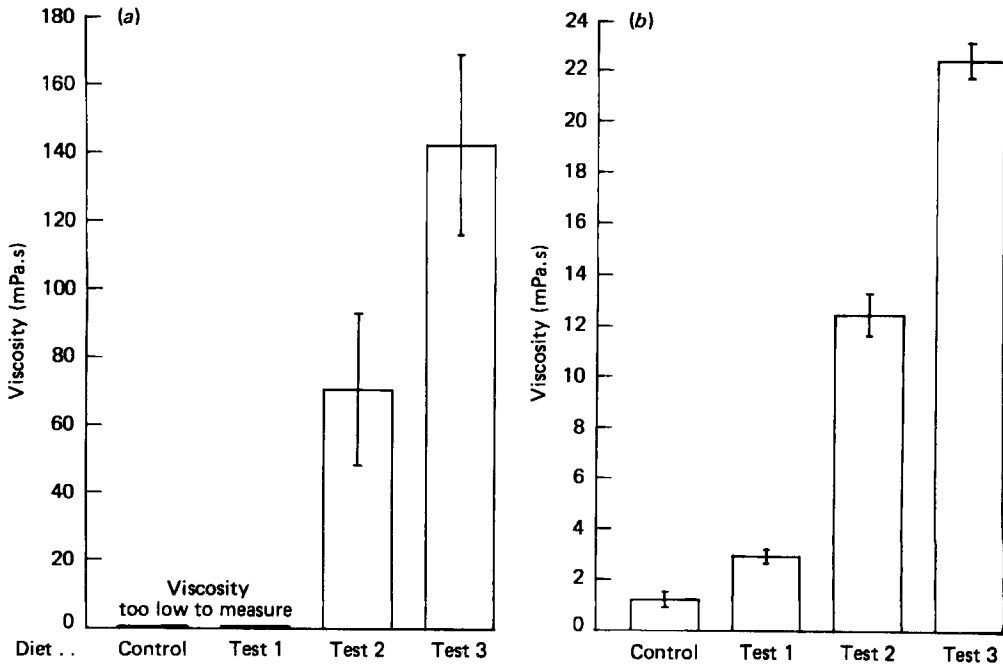


Fig. 2. Viscosity (mPa.s) of rat small intestine contents after ingesting various levels of guar gum at shear rates of (a) 149/s (b) 3010/s. Values are means of three (control) or two (test) results, each resulting from combined samples from three animals, with the range of determination represented by vertical bars. For details of diets, see Table 1.

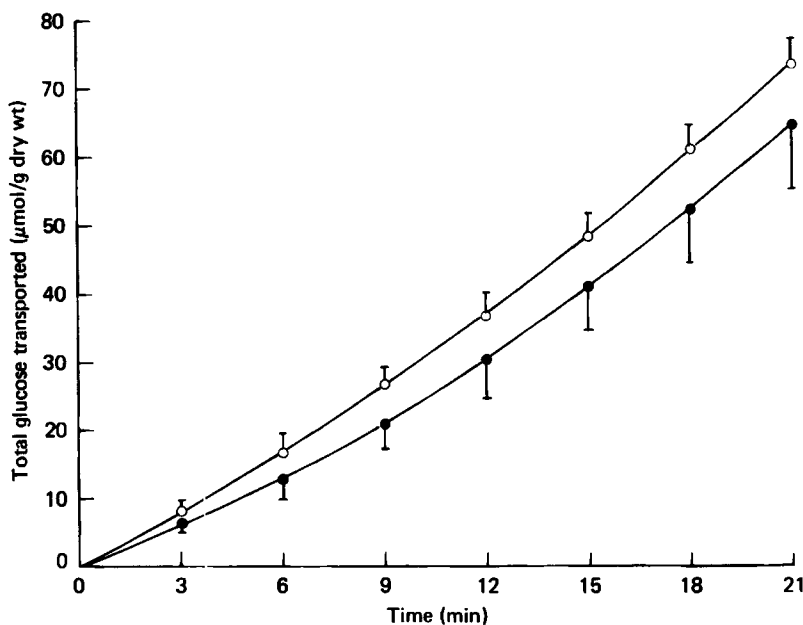


Fig. 3. Total glucose transported ( $\mu\text{mol/g}$  dry weight tissue) v. time (min) for segments of rat jejunum pre-perfused with Ringer solution only (○) or Ringer solution with 5 g guar gum/l (●). Points are mean values, with their standard errors represented by vertical bars, for five animals.

in the apparent viscosity of the contents of the rat small intestine relative to the control diet, the increase being proportional to the amount of guar ingested.

*Large intestine contents.* Test diets nos. 1, 2 and 3 produced liquid fractions with apparent viscosities not significantly different from those of the control animals.

#### Glucose transport study

In five animals, test loops were pre-perfused with 5 g guar gum/l, and although the rate of glucose uptake appeared to be lower than in the control loops (see Fig. 3), paired *t* tests performed on data from the separate samples from each 2 min period (as opposed to the cumulative data plotted in Figs. 3 and 4) indicated this difference was not statistically significant.

Eight animals were pre-perfused with 6 g guar gum/l solution (see Fig. 4). There was a marked reduction in the rate of glucose absorption in test segments compared to control segments, and paired *t* tests (as described previously) indicate this reduction to be significant at all sampling times ( $P < 0.001$ ).

#### DISCUSSION

There is now clear evidence for the effectiveness of guar gum and other soluble polysaccharides as means of controlling blood glucose levels in humans, whether taken as a large dose in solution (Jenkins *et al.* 1976; Jenkins, Leeds & Gassul, 1977; Abele *et al.* 1978; Wahlqvist *et al.* 1979; Holt *et al.* 1979) or as a component of soup, or a solid food such as bread (Wolever *et al.* 1978; Morgan *et al.* 1979).

Though opinions differ as to mechanism, it is generally accepted that the effect stems from a reduction in the rate of glucose absorption, and that this is due to the presence of a viscous

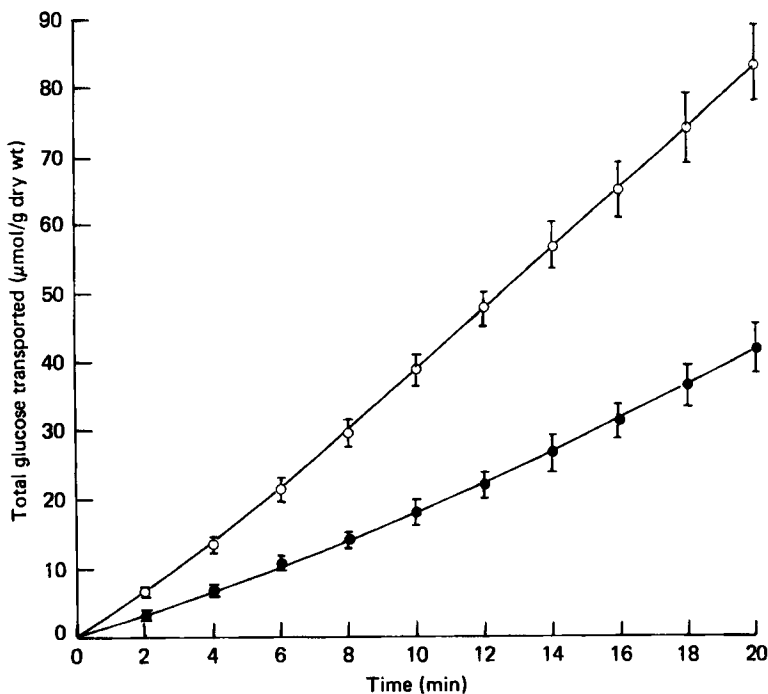


Fig. 4. Total glucose transported ( $\mu\text{mol/g}$  dry weight tissue) v. time (min) for segments of rat jejunum pre-perfused with Ringer solution only ( $\circ$ ) or Ringer solution with 6 g guar gum/l ( $\bullet$ ). Points are mean values, with their standard errors represented by vertical bars, for eight animals.

polysaccharide dispersion in the gastrointestinal tract. However, no previous studies of the rheological behaviour of guar gum within the gut have been reported.

The presence of an undispersed mass of diet in the stomachs of animals consuming guar gum at levels of 10 and 20 g/kg in the diet suggests that guar gum can slow the mechanical disruption of food in the stomach, and thereby impede the delivery of nutrients to the small intestine. Though none of the animals in this study showed evidence of ill-effects or a decline in food consumption, there may be a danger of gastric obstruction following the ingestion of large quantities of dry guar gum. A recent report has suggested the possibility of gastric bezoar in human diabetics consuming a high-fibre diet, and this point requires further study (Canivet *et al.* 1980).

The present results establish that the ingestion of guar gum as a dry component of the food gives rise to an increase in the apparent viscosity of the small intestinal contents of the rat. Owing to the non-Newtonian behaviour of guar gum solutions, absolute viscosity values cannot be quoted, but the results indicate distinct differences in the apparent viscosities of small intestinal contents from test and control groups, over a range of shear rates. Though no information is available as to shear rates within the intestine, it is perhaps relevant to note that values of 50 to a few hundred/s have been suggested for the mouth during mastication (Sherman, 1976).

No increase in the apparent viscosity of the large intestinal contents was observed at any level of guar gum in the diet. This is presumably due to degradation of guar gum by the action of microflora in the large bowel. It has been previously shown that in the rat, guar gum is degraded to a certain extent in the large bowel (Booth *et al.* 1963) and Stephen &

Cummings (1980) refer to unpublished observations suggesting guar gum is digested by the bacteria of the human colon.

Several previous workers have suggested that the presence of a viscous polysaccharide solution in the gut lumen may slow the diffusion of solutes to the absorptive surface (Southgate, 1973; Jenkins *et al.* 1976). In a separate report from this laboratory (Johnson & Gee, 1981) it was shown that the transport of glucose by everted intestinal sacs was slowed by a pre-incubation in the presence of guar gum. This effect was accompanied by an increase in the apparent thickness of the mucosal unstirred layer, and tissue from such sacs exhibits traces of adherent guar gum when examined by scanning electron microscopy (I. T. Johnson & J. M. Gee, unpublished observations). The two-stage-perfusion design used in this present study indicates that guar gum need not be present in the bulk mucosal solution in order to exert a rate-limiting effect on absorption *in vivo* and is thus consistent with the proposal of Johnson & Gee (1981) that the material slows glucose diffusion by increasing the viscosity of the fluid layer adjacent to the mucosa. The importance of viscosity is again emphasized by the fact that an increase in guar gum concentration of only 1 g/l, which is accompanied however by an increase in apparent viscosity of 100% (70 mPa.s at 85/s) greatly increased the rate-limiting effect of the treatment.

The results from this study are in agreement with the report of Elsenhans *et al.* (1980) but contradict those of Förster & Hoos (1977), who observed no reduction in glucose uptake from ligated loops containing solutions of various gums.

Clearly then the consumption of guar gum, and by implication other forms of soluble polysaccharide, can dramatically alter the rheological properties of the gut contents, and hence influence the absorption of nutrients in at least two ways. A slowing of the dispersion of solid food, and of gastric emptying will reduce the rate at which nutrients enter the small intestine. Furthermore, we have shown that under the conditions of the present study the inclusion of guar gum in the diet at a level of 20 g/kg gave rise to a solution in the small intestine having an apparent viscosity well in excess of that which significantly slowed glucose absorption in perfused jejunal loops. This supports the suggestion that the ingestion of guar gum by human subjects may have a dual effect on glucose uptake (Jenkins *et al.* 1978; Leeds, 1979; Taylor, 1979) and is consistent with the observations of Levy & Jusko (1965), who showed that the absorption of salicylic acid and ethanol in the rat was reduced by methylcellulose, which both slowed gastric emptying and diminished the diffusion of drugs to the stomach wall.

The relative importance of these effects in slowing the uptake of nutrients is likely to depend to a large extent on the form and frequency with which guar gum is administered, and these factors should be born in mind when incorporating guar gum in the diet, and perhaps in seeking alternative materials that enhance viscosity for nutritional use.

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