The effect of high-molecular-weight guar gum on net apparent glucose absorption and net apparent insulin and gastric inhibitory polypeptide production in the growing pig: relationship to rheological changes in jejunal digesta

BY P. R. ELLIS[1]*, F. G. ROBERTS[1,2], A. G. LOW[2] AND L. M. MORGAN[3]

[1] *Biopolymers Group, Division of Life Sciences, King's College London, Campden Hill Road, Kensington, London W8 7AH*

[2] *AFRC Institute for Grassland and Environmental Research, Shinfield, Reading RG2 9AQ*

[3] *Nutritional Metabolism Research Group, School of Biological Sciences, University of Surrey, Guildford GU2 5XH*

The present study was designed to determine the quantitative effects of starchy meals containing guar gum on rates of net apparent glucose absorption and net apparent insulin and gastric inhibitory polypeptide (GIP) production in growing pigs. The effects of these meals on the viscosity of jejunal digesta were also examined and correlated to changes in glucose absorption. Four growing pigs were each given either a low-fat semi-purified diet (control) or the same diet supplemented with a high-molecular-weight guar gum at concentrations in the diet of 20 or 40 g/kg. Blood samples were removed simultaneously via indwelling catheters from the mesenteric artery and the hepatic portal vein. Samples of jejunal digesta were removed via a T-piece cannula and used immediately for viscosity measurements at 39°. The 'zero-shear' viscosity of each sample was then calculated. Blood-flow measurements were made using an ultrasonic flow probe fitted to the hepatic portal vein. All measurements were made at intervals of 10 or 30 min during a 4 h postprandial period. Meals containing guar gum significantly increased ($P < 0.05$) the viscosity of jejunal digesta, an effect that was strongly dependent on the concentration of guar gum in the original diet. No significant differences in blood-flow rates were found between the control and guar-containing diets. Both concentrations of guar gum significantly reduced ($P < 0.05$) glucose absorption and insulin and GIP secretion rates over the 4 h postprandial period. An inverse relationship between the rate of glucose absorption and the 'zero-shear' viscosity of jejunal digesta was found. This study also provides direct evidence for the important role played by the entero-insular axis in modifying the glycaemic response to a meal containing guar gum.

Guar gum: Nutrient absorption: Viscosity: Pig

It is now well established that the addition of soluble non-starch polysaccharides (s-NSP), such as guar gum and pectin, to oral carbohydrate loads reduces postprandial blood glucose and plasma insulin levels. This has been observed in human subjects (Jenkins *et al.* 1978; Ellis *et al.* 1981; Jarjis *et al.* 1984) and experimental animal models such as the pig (Sambrook & Rainbird, 1985). Insulin is known to play a key role in the carbohydrate and lipid metabolism of man. The modification of insulin secretion by s-NSP may have

* For reprints.

important implications, therefore, for our understanding of the aetiology of diseases such as diabetes mellitus and atherosclerosis (Morgan *et al.* 1988). The beneficial effects of s-NSP on carbohydrate tolerance and lipid metabolism (i.e. reductions in plasma LDL-cholesterol) have important clinical applications, notably in the management of diabetes (Peterson *et al.* 1987).

Guar gum, an endosperm extract of the Indian cluster bean (*Cyamopsis tetragonoloba* (L.) Taub.), is frequently used as a 'model' polysaccharide in physiological and nutritional studies for a number of reasons. First, it can be isolated as a relatively pure form of s-NSP, consisting mainly of a high-molecular-weight galactomannan. Second, its physico-chemical properties have been well defined (Ellis & Morris, 1991) and can be easily modified, e.g. depolymerization of the galactomannan fraction (Robinson *et al.* 1982; Ellis *et al.* 1986).

The physiological mechanisms by which s-NSP improve carbohydrate tolerance and lipid metabolism are, as yet, incompletely understood. The postprandial effects of guar gum appear to depend on its capacity to increase the viscosity of digesta within the gastrointestinal tract, by the entanglement of fully hydrated chains of galactomannan. This in turn is thought to reduce the rate of digestion and absorption of carbohydrate and therefore attenuate the postprandial rise in blood glucose (Blackburn *et al.* 1984; Edwards & Read, 1990). However, there have been few studies on the relationship between the rheological properties of guar gum *in vivo* and subsequent postprandial changes in blood glucose and plasma hormone concentrations. This is due, in part, to the difficulty of measuring viscosity *in vivo* (Ellis *et al.* 1986). Preliminary studies in pigs given guar-containing meals indicated that maximum levels of digesta viscosity in the mid-jejunum (Roberts *et al.* 1990*a, b*) seem to correspond with reductions in postprandial hyper-glycaemia and plasma insulin levels seen in pigs (Sambrook & Rainbird, 1985) and human subjects (Jenkins *et al.* 1978; Morgan *et al.* 1985; Ellis *et al.* 1991). The reduction in postprandial insulin concentration is also attributed to a diminished stimulation of the entero-insular axis, notably the insulinotrophic gut hormone gastric inhibitory polypeptide (GIP; Morgan *et al.* 1979, 1985). The secretion of GIP is directly related to the rate and site of glucose absorption.

Although it is frequently stated that guar gum delays the rate of absorption of glucose and other nutrients (Jenkins *et al.* 1978), the evidence to substantiate this view has been obtained indirectly. Thus, in carbohydrate tolerance tests using human subjects, postprandial plasma glucose and insulin levels are normally determined at discrete time intervals on blood samples taken from the peripheral circulation (Ellis *et al.* 1991; Gatenby *et al.* 1991). However, measurements of glucose in the peripheral blood do not provide an accurate and direct quantitative index of the rate and degree of absorption of glucose. Nevertheless, some useful indirect measurements have been provided by both *in vitro* (Macagno *et al.* 1982; Edwards *et al.* 1988) and *in vivo* (Rainbird *et al.* 1984) modelling systems. A more reliable and direct quantitative method, using the pig as an animal model for man, is to measure the differences in glucose levels between the hepatic portal vein and the mesenteric artery, and, simultaneously, the flow rate of the portal blood (Rérat *et al.* 1977, 1979, 1988). Numerous methods are available for the measurement of blood-flow rate (e.g. thermal, dye and isotope dilution) and in earlier studies an electromagnetic blood-flow probe was used; however, the recent development of ultrasonic flow probes has enabled long-term measurements to be made on vessels which collapse or vary in diameter, such as veins (Barnes *et al.* 1983).

The present study was designed, therefore, to determine the quantitative effects of a well-characterized form of guar gum on rates of apparent glucose absorption and apparent insulin and GIP production. In addition, the viscosity of digesta collected from the small intestine of growing pigs was measured and correlated to changes in glucose absorption.

Accordingly, the pigs were surgically modified by the insertion of two indwelling catheters in the hepatic portal vein and the mesenteric artery and an ultrasonic blood-flow probe was attached to the hepatic portal vein to measure instantaneous blood-flow rate. The pigs were also fitted with a simple T-piece cannula, located in the mid-jejunum, to allow removal of digesta samples for subsequent viscosity determinations.

MATERIALS AND METHODS

Animals and housing

Four Large White × Landrace boar pigs initially of 35 kg live weight were used. The animals were kept in a single room but housed individually in metabolism crates, with a floor area of 1·8 m², and kept at a constant temperature of $20 \pm 1°$.

Surgical modifications

Each pig was prepared with two indwelling catheters, one in the hepatic portal vein and a second in the mesenteric artery. The animals were also fitted with a 12 mm Transonic® blood-flow probe (Transonic Systems Ltd, Ithaca, NY, USA). The probe was attached to the hepatic portal vein as close to the catheter site as was possible without interfering with blood-flow measurements. The probe flex was exteriorized through the body wall on the left flank slightly below the catheters. Both the probe flex and catheter tubing were held in place with elastic bandage. Finally, a simple T-piece cannula of the type described by Rainbird (1983) was fitted in the mid-jejunum of each pig, 2·0 m distal to the pylorus of the stomach. The insertion of the catheters and the blood-flow probe was carried out according to the basic surgical details described earlier by Rérat et al. (1980). The animals were kept in dorsal recumbency and all modifications were carried out through a mid-line incision extending from xiphisternum to prepuce.

Post-operative care

The catheters were flushed daily with a solution of heparinized physiological saline (50 IU/ml in a 9 g NaCl/l solution). The area around the exit site for the probes and catheters was carefully washed and dried and sulphanilamide powder applied. Bandages were changed every 3–4 d and the sutures removed after 7 d. The area around the cannula was washed daily with a weak veterinary antiseptic solution and a water-resistant barrier cream (Sudocrem, Tosara Products (UK) Ltd, Liverpool, Merseyside) applied to the surrounding skin. Attention to post-operative care was of great importance because of the complexity of the surgical procedures involved.

Diet composition

The animals received a control basal, low-fat, semi-purified (SP) diet based on wheat starch and casein, fed wet on a 1:2·5 w/v basis. The composition of the diet is presented in Table 1.

Guar gum

Guar-gum flour (Meyprogat 150 flour; Meyhall Chemicals (UK) Ltd, Wirral, Merseyside), consisting mainly of high-molecular weight (M_w) galactomannan (about 847 g/kg guar gum), was incorporated into the control SP diet at concentrations of 20 or 40 g/kg. The guar gum was added to the SP diet as an aqueous solution by dispersing it in tap water (e.g. 2·5 litres for a 50 kg pig receiving 1 kg SP diet/feed) for 12 h to allow it to hydrate as fully

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

Ingredients	g/kg
Wheat starch	680·9
Maize oil	30·0
Casein	180·0
Solka floc	60·0
Trace mineral mix*	10·0
Vitamin mix†	2·0
Dicalcium phosphate	31·0
Choline hydrochloride	1·1
Sodium chloride	5·0
Total B-group vitamins (mg)	30·0

* Supplied (/kg diet): K_2CO_3 4·47 g, $MgCO_3.H_2O$ 1·73 g, $FeSO_2.7H_2O$ 0·33 g, $MnSO_4.4H_2O$ 80 mg, $ZnCO_3$ 0·10 g, NaF 8 mg, $CuSO_4.5H_2O$ 17·5 mg, $CoCl_2$ 6 mg.

† Supplied (/kg diet): retinol 12·5 mg, cholecalciferol 0·6 mg, riboflavin 3·25 mg, thiamin 2·0 mg, nicotinic acid 15·75 mg, pantothenic acid 16·0 mg, pyridoxine 3·25 mg, DL-α-tocopherol acetate 4·0 mg, biotin 5·0 mg, pteroylmonoglutamic acid 1·0 mg, τ-inositol 195 mg, ascorbic acid 30·0 mg, menadione 2·0 mg, p-aminobenzoic acid 20·0 mg.

as possible. This resulted in guar-gum concentrations in the diet equivalent to 8 and 16 g guar gum/l solutions respectively. Each solution was then mixed (5 min) with the control diet 15 min before feeding. A Kenwood hand blender was used to homogenize the feed.

Animal weighing and feeding

The animals were weighed every 7 d and fed on a scale based on 40 g/kg body weight per d (e.g. 2 kg SP diet/d for a 50 kg pig). Food was offered twice daily in equal meals (by weight) at 08.00 and 16.00 hours. Before the onset of the first treatment period all animals had been conditioned to eat each feed within 10 min; this was done to minimize variations in the time course of nutrient absorption. Each pig received each of the three diets for a week. The diets were allocated on a random basis and were changed on the Thursday evening of each week to allow 3 d adaptation before sampling.

Blood and digesta sampling

Blood sampling. After 3 d adaptation to the diet, blood samples were taken on the 4th and 7th day of each of the control and guar-gum diet periods. Sampling was carried out on conscious, unrestrained animals at the following times: − 10 and 0 min, then at 10, 20, 30, 40, 50 and 60 min after the start of the morning feed and then at 30 min intervals up to 4 h post-feeding. A 6 ml blood sample was removed from each catheter and immediately centrifuged for 15 min at 9000 g. A 2 ml sample of plasma was used for subsequent insulin and GIP assays. A further 2 ml of plasma was deproteinized (using 2 ml 10 g trichloroacetic acid/l, BDH Chemicals Ltd, Poole, Dorset) overnight at 4°, centrifuged at 9000 g for 15 min and the supernatant fraction used for glucose analysis.

Blood-flow recordings. Continuous pre- and postprandial portal blood-flow-rate measurements were made on the days of blood sampling. The ultrasonic blood flow probe located in the pig was linked directly to a recorder (Transonic Systems Ltd) which automatically produced a value for integrated flow rate.

Digesta sampling and viscosity measurements. Digesta samples (10 ml) were taken from the jejunal cannula at − 10 and 0 min and then at 10, 20, 30, 40, 50 and 60 min followed by intervals of 30 min up to 4 h post-feeding. The 'zero-shear' viscosity of each sample was

determined immediately (Morris, 1990). 'Zero-shear' viscosities of guar-gum solutions (8 and 16 g guar gum/l) were also measured before they were added to SP diets. A Brookfield DV-II rotoviscometer (Brookfield Instrumentation, Stoughton, MA, USA) fitted with a small-sample adaptor was used. A full description of maximum 'zero-shear' viscosity and shear-thinning behaviour of reasonably polydisperse random-coil polysaccharides at concentrations above the onset of coil-overlap and entanglement (the so-called c*; Robinson *et al.* 1982) can be characterized by using equation 1:

$$\eta = \eta_0/(1 + (\dot{\gamma}/\dot{\gamma}_{\frac{1}{2}})^{0.76}), \tag{1}$$

where η at any shear rate ($\dot{\gamma}$) can be characterized by two variables: the maximum 'zero shear' viscosity (η_0) and the shear rate ($\dot{\gamma}_{\frac{1}{2}}$) at which viscosity is reduced to $\eta_0/2$. The values of η_0 and $\dot{\gamma}_{\frac{1}{2}}$ can be derived from, respectively, the intercept and the slope of a simple linear plot of η v. $\eta\,\dot{\gamma}^{0.76}$ (Morris, 1990). Viscosity measurements were taken at 39° within 60–90 s of removal of the digesta samples from the animal. In contrast to earlier studies (Roberts *et al.* 1990*a, b*) the sample could not then be returned to the small intestine because the animals were fitted with T-piece as opposed to re-entrant cannulas. This resulted in a total loss of sample of approximately 120 ml over the whole sampling period. This amount (less than 3% of the total flow volume) is unlikely to produce a feedback effect on gastric emptying.

Biochemical assays

Glucose. Plasma glucose in the deproteinized samples was determined using a glucose oxidase–peroxidase (*EC* 1.11.1.7) procedure (Boehringer Mannheim, Mannheim, Germany) with a fully automated system ('Encore' Baker Instruments Corp., Pennsylvania 18001, USA).

Insulin. A double-antibody radioimmunoassay procedure was used (kit method supplied by Guildhay Antisera, Guildford, Surrey). The plasma sample was initially incubated with the primary reagents, i.e. assay buffer, insulin antiserum, normal guinea-pig serum, test plasma and ^{125}I-labelled insulin (Amersham International, Amersham, Bucks) for 16–24 h. This was followed by a 2 h phase separation with polyethyleneglycol (PEG)-accelerated second antibody (BDH Chemicals Ltd). After the final spin and aspiration, the remaining pellets were counted on an Inter-Technique CG 4000 gamma sample counter.

Gastric inhibitory polypeptide. A double-antibody radioimmunoassay procedure was used for the determination of GIP (Morgan *et al.* 1979), using an antiserum directed against porcine GIP and porcine-GIP standards. The main procedure of the assay involved a 48 h incubation of primary reagents and sample, followed by a phase separation with PEG-accelerated second antibody.

Calculation of glucose absorption and hormone secretion

Glucose absorption and apparent insulin and GIP production were calculated from veno–arterial differences in the mesenteric artery and hepatic portal vein, and portal blood-flow rate determinations. Insulin and GIP concentrations can only be described as 'apparent' due to the pulsatile secretion and hepatic extraction effects in the former and variable half-life values for both. Calculations were done by using equations (2) and (3) from the method of Rérat *et al.* (1980):

$$q = (C_p - C_a)\,F(\mathrm{d}t), \tag{2}$$

$$Q = q \sum_{t_0}^{t_1}, \tag{3}$$

where q is the quantity of glucose absorbed or hormone produced during the short time

(e.g. dt, 10 min) during which each factor was considered to be constant; C_p is the portal concentration; C_a is the arterial concentration; F is the instantaneous blood-flow rate; and Q is the quantity of glucose absorbed or hormone produced during the postprandial period between times t_0 and t_1.

Statistical analysis

Control and guar-gum diets were allocated to each pig in a repeated measures design; each pig received each diet twice, giving a measure of within- and between-pig variation. Repeated measures ANOVA was used to make comparisons between control and guar-gum diets for 'zero-shear' viscosity, portal blood-flow rates and plasma glucose, insulin and GIP. Analysis was carried out on values for postprandial concentrations, time to reach peak value and glucose absorption and hormone production. The statistical programme used throughout was GENSTAT V (Rothamsted Experimental Station, 1989). Correlation analysis was done to determine the relationship between glucose absorption and 'zero-shear' viscosity of digesta, and also between glucose absorption and the production of either insulin or GIP. Statistically significant differences were accepted at $P < 0.05$.

RESULTS

In general, no practical difficulties were experienced in ensuring that the pigs ate the appropriate quantities of diet containing 20 or 40 g guar gum/kg. All the diets were palatable to the pigs and there were no significant differences in the time taken to eat each diet (mean value 8 (SEM 1·5) min). All results are presented as mean values (n 8).

'Zero-shear' viscosity of digesta

Postprandial changes in 'zero-shear' viscosity of the jejunal digesta over 4 h in response to control or guar-gum diets are presented in Fig. 1 and Table 2. Table 2 also includes 'zero-shear' viscosity values of guar-gum solutions and information about statistical differences. The viscosity of jejunal digesta was significantly increased ($P < 0.05$) in pigs given SP diets containing high M_w guar gum and this was strongly dependent on the concentration of guar gum in the original diet (Table 2). However, the differences in digesta viscosity between the two concentrations of guar gum were significantly smaller than the difference in viscosity between the corresponding concentrations of guar gum in solution. Peak postprandial viscosity after each of the guar-gum treatments was reached within 1 h, although the time to reach a peak value after the meal containing 40 g guar gum/kg was approximately 20 min later than that seen after the 20 g guar gum/kg meal (Table 2).

Portal blood-flow rates

The addition of guar gum to the diet had no significant effect on blood-flow rate at any point up to 4 h postprandially (Fig. 2). After each diet there was a slight increase in blood flow following the morning feed. This was quickly followed by establishment of a steady-state blood-flow rate (pooled mean of all animals) of 1·36 (SEM 0·30) litres/min or 38·8 ml/min per kg live weight, which was slightly higher than initial pre-feeding values.

Postprandial changes in blood glucose, insulin and GIP concentrations

At each sampling time point during the 4 h postprandial period the effects of control and guar-gum diets on plasma glucose and hormone concentrations were determined in both the portal and arterial blood (Fig. 3). Diets containing guar gum consistently produced significant reductions ($P < 0.05$) in plasma glucose, GIP and, to a lesser extent, insulin
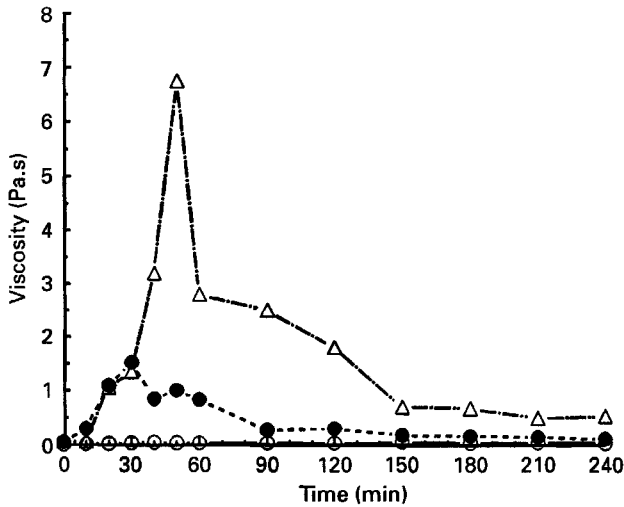
Fig. 1. Effect of guar-gum supplementation on 'zero-shear' viscosity of digesta from the mid-jejunum of growing pigs: (○) control semi-purified (SP) diet; (●) SP diet supplemented with 20 g guar gum/kg; (△) SP diet supplemented with 40 g guar gum/kg. Values are means for four pigs. For SED and statistical differences see Table 2. For details of composition of SP diet see Table 1.

concentrations in the portal blood compared with the control. The magnitude of each response was dependent on the concentration of guar gum in the diet. The glucose- and insulin-lowering properties of guar gum were greatest during the first 30–40 min postprandially, although significant reductions in glucose level were sustained throughout the entire postprandial sampling period. Only the highest concentration of guar gum (40 g/kg) significantly reduced plasma insulin levels at some of the later postprandial times (150–210 min). The 20 g/kg guar gum diet had little or no insulin-lowering effect at the later postprandial times. Following an initial rise to a peak value in the first hour, GIP concentrations in the portal blood in response to all the diets remained, more or less, at a plateau until 150 min, at which point there was a slight but steady decline. The presence of guar gum in the diet produced a significant ($P < 0.05$) attenuation of the GIP response throughout the 4 h sampling period, although no reductions were seen after the lowest concentration of guar gum in the first 30 min postprandially.

The effects of guar gum on arterial concentrations of glucose, insulin and GIP at each time point were often less marked than for the corresponding portal values. Nevertheless, in response to the diet containing the highest concentration of guar gum (40 g/kg) there were significant reductions ($P < 0.05$) in glucose, insulin and GIP concentrations in arterial blood at most of the postprandial times compared with the control diet. The reductions in arterial blood GIP levels at most postprandial times were of a similar magnitude to those observed in the portal blood. Significant reductions ($P < 0.05$) in arterial blood levels of glucose and insulin were also found after feeding the pigs on the diet containing the lowest concentration of guar gum (20 g/kg), but only in the early postprandial phase ($\leqslant$ 60 min). No reductions in GIP levels in arterial blood were found after the 20 g/kg diet in the first 30 min postprandial phase, but some significant reductions ($P < 0.05$) were observed at later postprandial times.

Table 2. 'Zero-shear' viscosity of jejunal digesta in pigs at fasting and twelve postprandial time intervals after start of consumption of diets without or with guar gum (20 or 40 g/kg)*

(Mean values for four pigs. Equivalent in vitro mean values (n 2) are shown for pure solutions of guar gum (8 and 16 g/l))

Diet	Viscosity (Pa.s) at fasting and twelve postprandial times (min)													ΔAUC† (Pa.s × min)	In vitro‡ (Pa.s)
	0	10	20	30	40	50	60	90	120	150	180	210	240		
Control	0·01[a]	0·02[a]	0·02[a]	0·03[a]	0·05[a]	0·04[a]	0·03[a]	0·03[a]	0·03[a]	0·06[a]	0·04[a]	0·04[a]	0·04[a]	6·1	—
20 g guar gum/kg	0·06[b]	0·30[b]	1·09[b]	1·52[b]	0·85[b]	1·00[b]	0·83[b]	0·27[b]	0·30[b]	0·18[b]	0·17[b]	0·15[b]	0·12[a]	84·0	3·1
40 g guar gum/kg	0·07[b]	0·07[b]	1·06[b]	1·35[b]	3·2[c]	6·75[c]	2·80[c]	2·50[c]	1·80[c]	0·70[c]	0·68[c]	0·50[c]	0·54[c]	357·0	44·7

[a,b,c] Values with different superscript letters within a column were significantly different ($P < 0.05$); standard error of difference between means = 0·05 (df 7).

* For details of diets and procedures, see Table 1 and pp. 541–543.

† Incremental area under the curve (integrated 'zero-shear' viscosity).

‡ Diets containing 20 and 40 g guar gum/kg are equivalent to solutions of guar gum containing 8 and 16 g guar gum/l; for explanation see pp. 541–542.

Table 3. Total apparent postprandial glucose absorption (g) in pigs during periods of 10 or 30 min after start of consumption of diets without or with guar gum (20 or 40 g/kg)*

(Mean values for four pigs)

Diet	Sampling time (min after meal)												
	0	10	20	30	40	50	60	90	120	150	180	210	240
Control	0·9[a]	6·4[a]	8·9[a]	9·1[a]	9·1[a]	6·3[ab]	6·6[a]	25·9[a]	26·1[a]	21·9[a]	21·5[a]	22·7[a]	22·2[a]
20 g guar gum/kg	0·3[a]	3·4[b]	6·2[b]	7·5[ab]	9·3[a]	7·7[a]	6·5[a]	21·2[b]	16·8[b]	17·2[b]	17·4[b]	15·3[b]	18·4[b]
40 g guar gum/kg	0·8[a]	1·8[b]	4·6[b]	5·4[b]	6·6[b]	5·3[b]	2·5[b]	19·0[c]	17·8[b]	14·1[c]	11·6[c]	7·7[c]	12·3[c]

[a,b,c] Values with different superscript letters within a column were significantly different ($P < 0.05$); standard error of difference between means = 2·2 (df 7).

* For details of diets and procedures, see Table 1 and pp. 541–543.
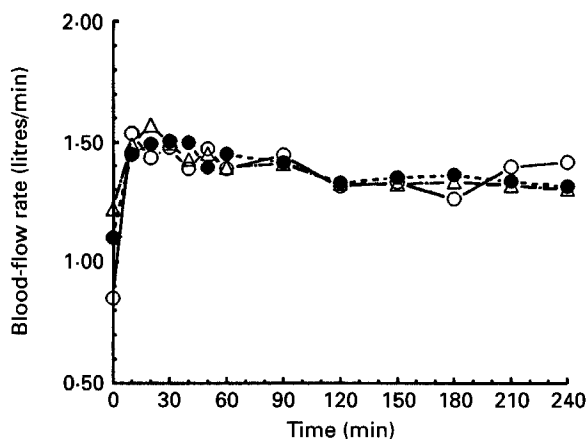
Fig. 2. Effect of guar-gum supplementation on blood-flow rate (litres/min) in the hepatic portal vein in growing pigs; (○) control semi-purified (SP) diet; (●) SP diet supplemented with 20 g guar gum/kg; (△) SP diet supplemented with 40 g guar gum/kg. Values are means for four pigs. For details of composition of SP diet see Table 1.

Net apparent postprandial glucose absorption, insulin and GIP secretion

Net apparent glucose absorption, and insulin and GIP secretion rates were determined over the 4 h postprandial period on the basis of the veno–arterial differences and instantaneous blood-flow rate measured in the hepatic portal vein (Rérat *et al.* 1980). Results showing total apparent glucose absorption and hormone production in response to control and guar-gum diets are presented in Tables 3, 4 and 5. Diets containing guar gum (at both concentrations) significantly reduced ($P < 0.05$) the rate of glucose absorption. The 20 g/kg guar-gum diet suppressed cumulative glucose absorption to approximately 87 and 78 % of the control values during the 1 h and 4 h postprandial phases respectively. The 40 g/kg guar-gum diet reduced postprandial glucose absorption still further, to about 56 and 58 % of the control value during the 1 h and 4 h periods respectively. Apparent net insulin production was significantly reduced ($P < 0.05$) after the guar-gum diets, although this effect, which was much less than that seen for glucose absorption, appeared to be biphasic (early and late postprandial periods). Thus, the 20 and 40 g/kg guar-gum diets reduced insulin production to approximately 87 and 89 % of the control value respectively, over the 4 h postprandial period. Significant reductions ($P < 0.05$) in apparent GIP production were also observed following the guar-containing diets. These reductions were significantly more pronounced than those seen for insulin production and were similar to the percentage changes seen for glucose absorption. Thus, both the 20 and 40 g/kg guar-gum diets attenuated GIP production to about 53 % of the control value during the 4 h period.

Correlation analysis between net apparent glucose absorption and concentration of guar gum in diet or 'zero-shear' viscosity

Correlation analysis was performed on mean values of glucose absorption during 30 min and 4 h periods (Table 3) using Q values of equation (3) on p. 543 and 'zero-shear' viscosity values at 30 min periods and integrated values over 4 h (Table 2). Integrated 4 h values were calculated from areas under the viscosity curve (Fig. 1).

A strong correlation was found between the amount of glucose absorbed during a 4 h period and the concentration of guar gum in the pig diet (r^2 0·999, $P < 0.02$, df 1), indicating a close negative linear relationship between these two variables (Fig. 4(a)). However, correlation analysis did not indicate a close linear relationship between glucose absorption and 'zero-shear' viscosity (r^2 0·898, not significant, df 1; Fig. 4(b)). A much
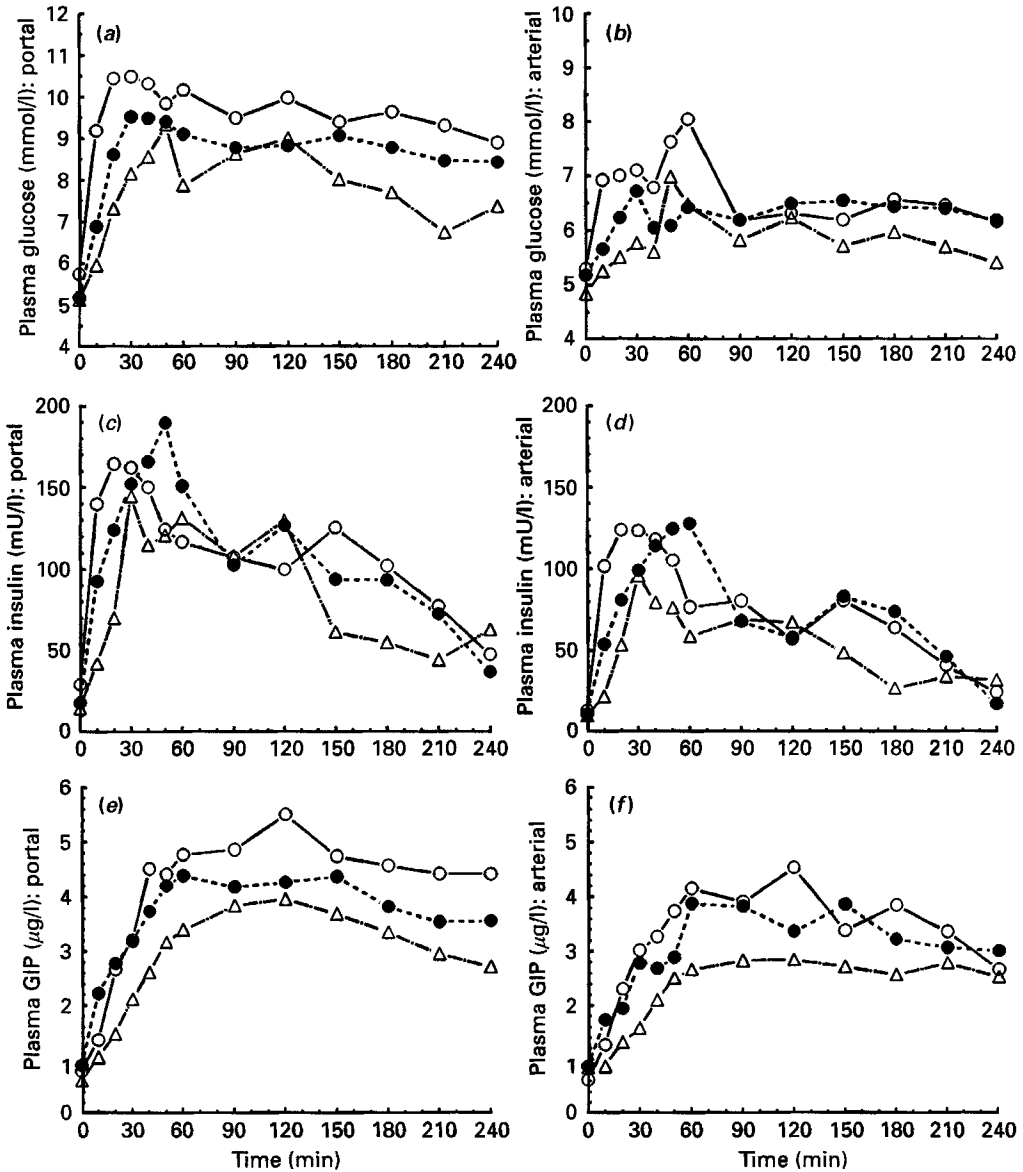
Fig. 3. Effect of guar-gum supplementation on plasma glucose concentrations (mmol/l) in (a) the hepatic portal vein (SED 0·3, df 7) and (b) the mesenteric artery (SED 0·2, df 7); plasma insulin concentrations (mU/l) in (c) the hepatic portal vein (SED 8·5, df 7) and (d) the mesenteric artery (SED 7·0, df 7); and plasma gastric inhibitory polypeptide (GIP) concentrations (μg/l) in (e) the hepatic portal vein (SED 0·22, df 7) and (f) the mesenteric artery (SED 0·175, df 7), in growing pigs; (○) control semi-purified (SP) diet; (●) SP diet supplemented with 20 g guar gum/kg; (△) SP diet supplemented with 40 g guar gum/kg. Values are means for four pigs. For details of composition of SP diet see Table 1.

closer relationship between these variables was indicated when a non-linear model was applied (e.g. r^2 0·948 for a power law fit). Indeed, a similar relationship was found when the same non-linear analysis was performed on glucose absorption and viscosity data taken at 30 min intervals rather than over 4 h (r^2 0·349, df 22). Linear analysis of the same data produced an r^2 of only 0·098 (df 22).

Table 4. *Total apparent postprandial insulin production (mU) in pigs during periods of 10 or 30 min after start of consumption of diets without or with guar gum (20 or 40 g/kg)**

(Mean values for four pigs)

Diet	Sampling time (min after meal)												
	0	10	20	30	40	50	60	90	120	150	180	210	240
Control	137[a]	604[a]	562[a]	631[a]	515[a]	300[a]	573[a]	1135[a]	1735[b]	1835[a]	1466[a]	1476[a]	1183[a]
20 g guar gum/kg	73[a]	563[a]	591[a]	730[a]	699[b]	923[b]	352[b]	1281[b]	2617[b]	485[b]	632[b]	887[b]	651[b]
40 g guar gum/kg	61[a]	200[b]	242[c]	760[a]	513[b]	648[c]	999[c]	1746[c]	2382[c]	524[b]	1095[c]	408[c]	1213[a]

[a,b,c] Values with different superscript letters within a column were significantly different ($P < 0.05$); standard error of difference between means = 130 (df 7).

* For details of diets and procedures, see Table 1 and pp. 541–544.

Table 5. *Total apparent postprandial gastric inhibitory polypeptide production (µg) in pigs during intervals of 10 or 30 min after start of consumption of diets without or with guar gum (20 or 40 g/kg)**

(Mean values for four pigs)

Diet	Sampling time (mean after meal)												
	0	10	20	30	40	50	60	90	120	150	180	210	240
Control	1·9[a]	1·5[a]	6·7[ab]	2·9[a]	19·6[a]	10·6[ab]	9·8[a]	42·3[a]	39·0[a]	63·9[a]	33·5[a]	48·5[a]	83·6[a]
20 g guar gum/kg	−0·6[a]	6·8[a]	10·7[a]	5·3[a]	14·2[a]	16·4[a]	5·4[a]	14·0[b]	32·0[b]	17·6[b]	21·7[b]	23·2[b]	22·9[b]
40 g guar gum/kg	−3·8[a]	1·8[a]	0·8[b]	7·7[a]	7·3[b]	8·5[b]	9·0[a]	40·5[a]	40·6[a]	34·6[a]	28·9[c]	5·1[c]	5·1[c]

[a,b,c] Values with different superscript letters within a column were significantly different ($P < 0.05$); standard error of difference between means = 6·8 (df 5).

* For details of diets and procedures, see Table 1 and pp. 541–544.
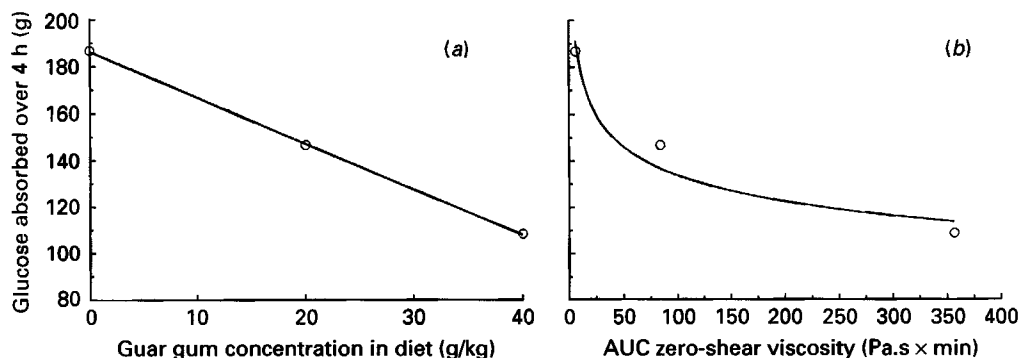
Fig. 4. (a) Glucose absorbed over 4 h (g) v. guar gum concentration (g/kg) in a semi-purified diet fed to growing pigs. Experimental points are mean values (n 8 observations). Correlation analysis of linear model, r^2 0·999, $P < 0.02$, df 1). (b) Glucose absorbed over 4 h v. area under the curve (AUC) 'zero-shear' viscosity (mPa.s × min) of digesta of pigs after consumption of diets with or without guar gum (20 or 40 g/kg). Values are means for four pigs. Correlation analysis of non-linear model (power law), r^2 0·948, df 1. For details of composition of diet see Table 1.

DISCUSSION

'Zero-shear' viscosity

The results of the present study clearly show that the liquid SP diets containing guar gum, when fed to conscious growing pigs, produced substantial increases in digesta viscosity in the mid-jejunum over a 4 h postprandial period (Fig. 1; Table 2), an effect that was strongly dependent on the concentration of guar gum in the original diet. Thus, diets containing 20 and 40 g guar gum/kg produced 14- and 60-fold increases in integrated viscosity levels respectively, relative to the viscosity level produced after the control diet (Table 2). Measurements of 'zero-shear' viscosity were made on the whole jejunal digesta and no assessment was made, therefore, of the effects of insoluble particulate material on the rheological behaviour of guar gum in the digesta samples. Recent work in our laboratory has shown that this is of considerable importance when interpreting, for example, the contribution made by guar galactomannan to the viscosity of complex biopolymer mixtures, such as those found in human and pig digesta (Rayment et al. 1994). Such studies are of crucial importance if we are to understand more precisely the mechanism of action of guar gum and other s-NSP in the gastrointestinal tract.

The 'zero-shear' viscosity profiles (Fig. 1) of control and guar-containing digesta seen in the present pig study were similar to those observed in our earlier studies (Roberts et al. 1990a, b), in which pigs were fitted with re-entrant rather than T-piece cannulas. Thus, it would seem that reliable results can be obtained from using the simple T-piece cannula, even though the re-entrant cannula is a more useful preparation in that it allows total digesta collection and ensures, therefore, that the measurements of digesta viscosity are more representative of results in the mid-jejunum.

Although both concentrations of guar gum in the pigs' diet (20 and 40 g/kg) generated large increases in digesta viscosity, the differences in viscosity between these two concentrations were small when compared with the in vitro measurements of viscosity of the guar-gum solutions added to the original diet (Table 2). A possible explanation for this is that there are substantial differences in total volume of digesta passing through the jejunum as a result of changes in the flux of endogenous secretions and/or fluid absorption in the gut (Roberts et al. 1990a, b; Roberts, 1991). Thus, the 40 g/kg guar-gum diet appeared to be diluted by the presence of additional fluid in the digesta. This is also thought to be part

of the explanation for recent observations in pigs showing small differences in 'zero-shear' viscosity between digesta samples containing low- and high-M_w guar gum (Roberts et al. 1990a). Changes in the rate of gut secretions are not unique to meals containing s-NSP; variations in the amount and content of pancreatic secretions in response to cereal-based meals have been reported in earlier studies in pigs (Zebrowska & Low, 1987).

Plasma glucose, insulin and gastric inhibitory polypeptide concentrations

Postprandial glucose concentrations in both portal and arterial blood were significantly reduced by the guar-containing diets (Fig. 3(a) and (b)). The greatest reductions were seen in the early postprandial phase. The reductions in arterial blood glucose levels in pigs given the highest concentration of guar gum (40 g/kg) are consistent with the glucose-lowering effects seen in earlier studies in which pigs were given similar concentrations of guar gum (Sambrook & Rainbird, 1985; Malmlöf et al. 1989). In our present study the glucose-lowering effect of guar gum was more marked in the portal vein than in the mesenteric artery, a finding that confirms earlier observations by Malmlöf et al. (1989). No comparable results are available from human studies, however, since for obvious practical and ethical reasons measurements of glucose concentrations in the portal blood are difficult to obtain.

It is well known that fasting and postprandial blood glucose concentrations vary according to site of sampling (i.e. vein, artery, capillary) and this is clearly an important factor when interpreting an individual's glycaemic response to a meal (Burrin & Alberti, 1990). Moreover, measurements of glucose concentrations in the peripheral venous blood over a stipulated time period are unlikely to give a reliable indication of the rate of glucose absorption. Accordingly, in some studies of healthy human subjects guar-containing meals have been shown to have negligible effects on postprandial hyperglycaemia, whilst at the same time significantly reducing plasma insulin and GIP levels (Morgan et al. 1985; Ellis et al. 1988, 1991). These results are based on measurements taken from the peripheral blood alone, which represent the net effect of a number of post-absorptive processes. In such studies, changes in plasma GIP levels in peripheral venous blood may provide a more reliable indicator of the rate of glucose absorption, as indicated in the present study (see p. 553).

Reductions in arterial and portal plasma insulin levels were seen after the 40 g/kg guar-gum diet, mainly in the early and late postprandial periods, whereas reductions were seen after the 20 g/kg guar-gum diet in the early phase only. This insulin-reducing effect, which was less marked than the hypoglycaemic effect of guar gum, is, nevertheless, similar to that reported in earlier pig studies (Sambrook & Rainbird, 1985; Malmlöf et al. 1989) using guar-containing diets. Recent studies in humans (Morgan et al. 1985; Ellis et al. 1991) have demonstrated similar insulin-sparing effects in subjects given guar-containing meals. However, Ellis et al. (1991) have shown that the insulin-sparing effect of guar gum is negligible in healthy subjects who produce a small insulin response postprandially.

A substantial proportion of the total insulin secreted from the pancreas is 'lost' during the first passage through the liver via hepatic extraction. Thus, concentrations of insulin in the peripheral blood will be much lower than in the portal blood, as seen in the present study (Fig. 3(c) and (d)) and in a similar study by Malmlöf et al. (1989). However, although postprandial insulin concentrations in the portal blood were higher than in the arterial blood, the insulin-lowering effect of guar gum was found to be only slightly greater in the former than in the latter (Fig. 3(c) and (d)). In agreement with a previous study in pigs (Sambrook & Rainbird, 1985), guar gum also significantly delayed the time taken to reach a peak insulin concentration. This delay, and the reduction in the rise of plasma insulin in response to the guar-gum diet, is assumed to be due to a slower rate of glucose absorption

from the small intestine. However, glucose absorption is not the only factor determining postprandial insulin concentrations. It is known that the stimulation of the entero-insular axis, a notable component of which is the insulinotrophic hormone GIP, also has an important role to play (Morgan *et al.* 1979, 1985). The addition of guar gum to the diet of growing pigs significantly reduced postprandial GIP concentrations in portal and arterial blood by about the same degree as the reductions in plasma glucose levels, consistent with a role for GIP in the control of insulin secretion (Fig. 3(e) and (f)). The importance of GIP in mediating the glycaemic response has also been shown recently in piglets (Ponter *et al.* 1991), and these results are similar to those in earlier studies in human subjects (Morgan *et al.* 1979, 1985).

Blood-flow rate

An indication of the rate and extent of digestion and absorption of starchy foods can be obtained from measurements of the changes in blood glucose concentrations. To obtain quantitative measurements of glucose absorption and hormone production, however, it is necessary to monitor the flow rate of blood in the hepatic portal vein. Methods to determine blood-flow rate, which have been routinely available for use in pigs to date include isotope dilution (Braude *et al.* 1970), indicator dilution (Anderson, 1974), thermal dilution (White *et al.* 1974) and the electromagnetic probe which is attached as a cuff around the blood vessel (Rérat *et al.* 1977, 1979, 1980; Giusi-Perier *et al.* 1989). Although the latter method appears to be both sensitive and accurate, it only allows reliable measurements to be made for 2–4 weeks after surgery. The general principle of employing a 'cuff' surrounding the vessel to measure blood-flow rates instantaneously was employed in the present study, but an ultrasonic flow probe was selected for testing rather than the electromagnetic preparation.

In the current study the surgically-modified animals remained viable for 6 weeks enabling repeated measurements of blood-flow rates within the same animal; this period compares favourably with that of 18 d quoted by Rérat *et al.* (1980) who used an electromagnetic flow probe. Mean blood-flow rate following each meal (pooled values for all animals) was 1·36 litres/min or 38·8 ml/min per kg live weight (Fig. 2). This compares closely with a value of 37·4 ml/min per kg live weight recorded by Rérat *et al.* (1988). In both the present study and the earlier studies of nutrient absorption (Rérat *et al.* 1988) there was no correlation between mean blood-flow rate and the composition of the meal ingested; blood flow seems to be more dependent on the behaviour of the animal on the day of sampling. This point has been reiterated in the most recent study by Simões Nunes & Malmlöf (1992). Following an initial rise at the onset of feeding, mean blood-flow rate remained steady throughout the postprandial sampling period. In this present study the animals were generally quiescent and recumbent. However, clinical studies in man (Brown *et al.* 1989) have shown that the blood-flow rate is significantly reduced when an individual moves from an upright to a supine position. Thus, postural effects need to be taken into account when extrapolating results from pigs to humans, particularly when accurate measurements of portal blood flow are required for quantitative studies of nutrient absorption.

Net apparent glucose absorption and insulin and gastric inhibitory polypeptide production

Combined measurement of veno–arterial differences with blood-flow rates in the hepatic portal vein enabled the calculation of net apparent glucose absorption and production of insulin and GIP. Diets containing guar gum (at both concentrations) reduced significantly the amount of glucose absorbed postprandially relative to the control (Table 3). Thus, in pigs fed on diets containing guar gum at concentrations of 20 and 40 g/kg, there were reductions of about 22 and 42 % respectively in the amount of glucose absorbed over a 4 h

period. These results, in addition to similar findings recently reported by Simões Nunes & Malmlöf (1992), provide the first direct evidence, albeit in an experimental animal, that guar gum added to starch-rich diets reduces the rate of glucose absorption from the small intestine. The glucose absorption data presented in the present paper should only be regarded as 'apparent absorption' because the technique provides no estimation of the amount of glucose immediately metabolized by the mucosa of the small intestine. It is possible, also, that a proportion of dietary starch, and/or hydrolysed products of starch, remains unabsorbed in the small intestine in the presence of guar gum, thus providing a potential substrate for microbial enzymes in the large intestine. Early human studies (Jenkins *et al.* (1978) have provided little evidence of this, although recent studies in pigs using various sources of NSP have demonstrated decreased glucose absorption over a 24 h period leading to an increase in the proportion of the available carbohydrate reaching the large intestine for subsequent fermentation (Giusi-Perier *et al.* 1989). A useful future experiment would be, therefore, to quantify the production of short-chain fatty acids (e.g. butyrate) using the same technique employed in the present study, based on the assumption that the portal blood is the main route of absorption for these colonic metabolites. It would also be useful to extend the sampling period over which glucose absorption can be measured to account for all the wheat starch fed to the pigs.

In view of the effect of guar gum on glucose absorption seen in the current study, the reduction in apparent insulin production following each of the guar-gum meals is not unexpected (Table 4). However, the magnitudes of these reductions over 4 h, about 11–13 % of that produced after the control, were smaller than we would have expected from the glucose-reducing effect of guar gum. Moreover, the results of a recent pig study have shown that a diet containing guar gum at a concentration of 60 g/kg reduces insulin production by as much as 30 % of that produced for the control over a 8 h postprandial period (Simões Nunes & Malmlöf, 1992). In the present study the insulin-reducing effect of guar gum appeared to be biphasic (i.e. early and late phases of the postprandial curve), so that in the last 2 h of the postprandial period guar gum reduced insulin production by between 45 and 55 % of the control value.

Diets containing guar gum also reduced apparent production of GIP (Table 5) by about the same proportion seen for the reduction of glucose absorption after the 40 g/kg guar-gum meal (Table 3). Moreover, the reductions in glucose absorption at different postprandial times followed more closely the reductions in GIP production than the corresponding insulin values. Thus, correlation analysis of values in the first 60 min postprandial period showed a stronger linear relationship between glucose absorption and GIP production (Spearman rank correlation r^2 0·302, $P < 0·01$, df 20) than between glucose absorption and insulin production (Spearman rank correlation r^2 0·232, $P < 0·05$, df 20). The closer relationship between GIP production and glucose absorption is perhaps indicative of the steady secretion of GIP, the release of which is directly stimulated by the rate of absorption of glucose in the small intestine. In contrast, the secretion of insulin in response to glucose absorption and stimulation of the entero-insular axis is pulsatile and biphasic (Matthews *et al.* 1983), a pattern of release that is unlikely to correlate closely with the rate of glucose absorption.

Relationship between glucose absorption and digesta viscosity

Correlation analysis revealed an inverse linear relationship between glucose absorption during the 4 h postprandial period and the concentration of guar gum in the original pig diet (Fig. 4(a)). However, the same analysis did not indicate a similar relationship between glucose absorption and 'zero-shear' viscosity of jejunal digesta. A stronger relationship between glucose absorption and average viscosity levels, either during intervals of 30 min

or during the whole 4 h period (i.e. area under the curve), was indicated when a non-linear model was applied (Fig. 4(b)). Although at this stage there are insufficient data to attempt to utilize either of these models for predictive purposes, the results do provide the first direct evidence of the importance of viscosity in determining the physiological activity of guar gum. If an inverse, non-linear relationship between glucose absorption and digesta viscosity proves to be an appropriate model, then this would indicate that reductions in glucose absorption are proportionately greater at low levels of viscosity than at high levels.

Conclusions

We have demonstrated that a liquid SP diet containing high-M_w guar gum increased digesta viscosity significantly in the mid-jejunum and reduced the rate of glucose absorption and apparent insulin and GIP production in growing pigs. The rate of glucose absorption after a meal was found to be inversely related to the 'zero-shear' viscosity of digesta in the small intestine. The modification of the entero-insular axis is strongly implicated in the mechanism of action by which guar gum improves glycaemic control. An ultrasonic blood-flow probe, a novel technique for measuring blood-flow rates instantaneously, was used successfully to quantify glucose absorption and hormone secretion far more directly than is possible at present with human subjects. This again serves to highlight the benefits and the suitability of using the pig as an animal model for studies of this nature (Leeds *et al.* 1980; Miller & Ullrey, 1987).

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