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Viscosity of gums *in vitro* and their ability to reduce postprandial hyperglycemia in normal subjects

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Abstract

Experiments were carried out *in vitro* with three viscous polysaccharides (guar gum, pectin, and carboxymethylcellulose (CMC)) of similar initial viscosity submitted to conditions that mimic events occurring in the stomach and duodenum, and their viscosity in these situations was compared to their actions on postprandial hyperglycemia in normal human subjects. Guar gum showed greater viscosity than the other gums during acidification and/or alkalinization and also showed larger effects on plasma glucose levels (35% reduction in maximum rise in plasma glucose) and on the total area under the curve of plasma glucose (control: 20,314 ± 1007 mg dl^{-1} 180 min^{-1} *vs* guar gum: 18,277 ± 699 mg dl^{-1} 180 min^{-1}, $P<0.01$). Pectin, which showed a marked reduction in viscosity at 37°C and after events mimicking those that occur in the stomach and duodenum, did not have a significant effect on postprandial hyperglycemia. The performance of viscosity and the glycemia response to CMC were at an intermediate level between guar gum and pectin. In conclusion, these data suggest that temperature, the process of acidification, alkalinization and exposure to intestinal ions induce different viscosity changes in gums having similar initial viscosity, establishing a direct relationship between a minor decrease of gum viscosity *in vitro* and a reduction of postprandial hyperglycemia.

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- Pectin

It is well established that the addition of viscous polysaccharides to carbohydrate-rich meals or oral glucose loads reduces postprandial hyperglycemia in normal and diabetic humans (1-5). The action of the polysaccharides in reducing postprandial hyperglycemia is thought to be related to their viscosity, determined *in vitro* before ingestion (6-10). However, using different fiber preparations, Edwards et al. (8) were unable to demonstrate a correlation between viscosity measured *in vitro* and the glycemic response to a meal. In rats, Cameron-Smith et al. (11) showed that the large differences in viscosity of the gastrointestinal contents following ingestion of diets containing soluble fibers were not predictive of the postprandial glycemic responses. In these studies (8,11) the solutions of various polysaccharides were administered at the same concentration for the evaluation of the effects of this rheological property in reducing postprandial hyperglycemia. One way of studying the real effect of gum viscosity in reducing postprandial glycemic responses is to use different gums with similar initial viscosity.

We carried out experiments *in vitro* with three viscous polysaccharides of similar ini-

tial viscosity which have been submitted to conditions that mimic events occurring in the stomach and duodenum and we compared their viscosity in these situations to their actions on postprandial hyperglycemia in normal human subjects.

The following commercially available viscous polysaccharides were studied: guar gum (G), pectin (P) and carboxymethylcellulose (CMC). For each type of experiment, both *in vitro* and *in vivo*, the gums were dissolved by stirring the solution vigorously at 22ºC.

The viscosity of the polysaccharides in 20% glucose solutions was measured with a Brookfield cone viscometer (Brookfield Engineering Lab, Inc., Stoughton, MA) at shear rates of 1.0, 2.5, 5.0, 10, 20, 50, and 100 rpm at pH 4.5 by citric acid addition at 22ºC (step 1) and then at 37ºC (step 2). We varied the concentrations of the polysaccharides so that all of them would have identical viscosity at a shear rate of 10 rpm. The concentrations (v/v) were 2.5% guar, 2.91% CMC and 7.5% pectin.

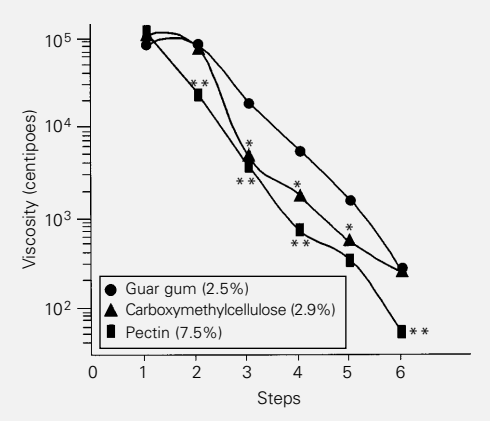

Figure 1 - Effect of temperature, hydration, acidification and reneutralization at a shear rate of 10 rpm on the viscosity measurements of the viscous polysaccharides guar gum, carboxymethylcellulose and pectin. Step 1: 22ºC; step 2: 37ºC; step 3: one hour acidification with 200 ml of a 0.1 M HCl, 54 mM KCl solution; step 4: second hour acidification with 400 ml of a 0.1 M HCl, 54 mM KCl solution; step 5: third hour acidification with 600 ml of a 0.1 M HCl, 54 mM KCl solution; step 6: one hour reneutralization with a 120 mM $NaHCO_3$ + 5 mM KCl + 30 mM NaCl solution. *P<0.01 and **P<0.001 compared to guar gum (*t*-test for unpaired samples).

To mimic events occurring in the stomach and duodenum, the viscosity of the gum solutions was also measured after they had been acidified to pH 2.0 for 1 h with a mixture of 200 ml 0.1 M HCl and 54 mM NaCl (step 3), after a second hour of acidification with 400 ml (step 4) and a third hour of acidification with 600 ml of this mixture (step 5). The acidified gums were then reneutralized for 1 h with a solution containing 120 mM $NaHCO_3$, 5 mM KCl and 30 mM NaCl (step 6). Gums diluted with equivalent volumes of 154 mM NaCl served as controls (C). The viscosities were measured with a Brookfield viscometer with numbers 6 and 7 spindles at shear rates of 1, 2.5, 5, 10, 20, 50 and 100 rpm.

Studies were performed on a total of 16 healthy volunteers (14 men and 2 women) aged 21 to 39 years, after obtaining their written informed consent. The study was approved by the Ethics Committee of the University Hospital, UNICAMP. Female subjects were studied only if they were in the first 10 days of the menstrual cycle. All subjects took part in two or more experiments, one of which was a control, performed in a randomized order at least two days apart. The meals were taken over an 8-min period in the morning after an overnight fast, with the basic meal consisting of 75 g glucose in 400 ml water. In the test experiments, 10 g guar gum (10 subjects), 40 g pectin (10 subjects) or 11.65 g methylcellulose (11 subjects) was added to the basic meal.

Venous blood samples were taken under fasting conditions and 15, 30, 45, 60, 90, 120 and 180 min after the beginning of the meal for analysis of plasma glucose and serum insulin as previously described (12). The area under the curve for the insulin and glucose profiles was calculated by planimetry.

The viscosity of each gum was inversely related to the shear rate, although the slopes of the relationships varied with each preparation at 22ºC (Figure 1). All preparations

were less viscous at 37ºC, but pectin showed the most pronounced fall. The effects of diluting the gums with acidic and neutralizing solutions to mimic the actions of the gastrointestinal tract are shown in Figure 1. In all stages guar gum showed a higher viscosity than CMC, which in turn showed higher viscosity than pectin.

Plasma glucose levels were significantly lower than controls at 30 ($P<0.001$), 45 ($P<0.001$), 60 ($P<0.001$), 90 ($P<0.01$) and 120 ($P<0.05$) min after guar gum ingestion, at 30 ($P<0.01$), 45 ($P<0.02$) and 60 ($P<0.002$) min after methylcellulose ingestion, and at 30 ($P<0.05$) min after pectin ingestion. It can be seen from Figure 2 that guar gum was more effective than CMC as a modifier of plasma glucose levels, and CMC was more effective than pectin. All the gums reduced the area under the 3-h glucose profiles, but only in the case of guar gum was this result statistically significant (C: 20,314 ± 1007 mg dl^{-1} 180 min^{-1} *vs* G: 18,277 ± 699 mg dl^{-1} 180 min^{-1}, $P<0.01$). Guar gum decreased the percentage maximum rise in plasma glucose by 35%, CMC decreased this percentage by 20% while no reduction was observed with pectin.

The serum insulin levels were reduced at 60 min (C: 93 ± 13 µU/ml *vs* G: 58 ± 9 µU/ml, $P<0.002$) and 120 min (C: 75 ± 13 µU/ml *vs* G: 39 ± 6 µU/ml, $P<0.005$) after guar gum, at 30 min (C: 70 ± 10 µU/ml *vs* CMC: 45 ± 5 µU/ml, $P<0.005$), at 60 min (C: 80 ± 16 µU/ml *vs* CMC: 42 ± 10 µU/ml, $P<0.002$) and at 120 min (C: 57 ± 9 µU/ml *vs* CMC: 36 ± 5 µU/ml, $P<0.05$) after CMC, and at 60 min (C: 84 ± 11 µU/ml *vs* P: 52 ± 10 µU/ml, $P<0.002$) after pectin ingestion.

The ability of the gastrointestinal tract to dramatically alter the viscosities of ingested soluble fibers may be mediated either by dilution by secretions entering the gastrointestinal tract or by pH, when solutions approxi-

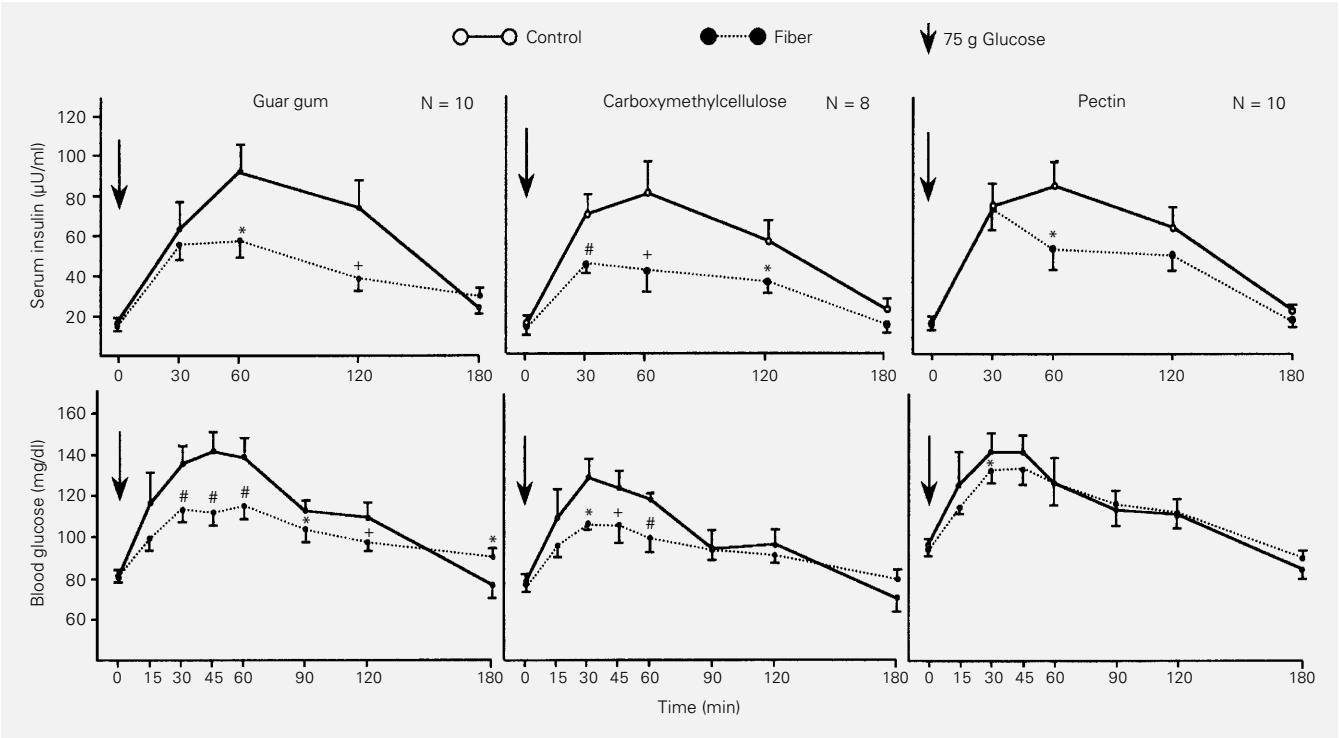

Figure 2 - Effect of a fiber-containing test meal on plasma glucose and serum insulin concentrations of volunteers after taking 75 g glucose (test meal) and fiber-containing test meals. *$P<0.01$, +$P<0.05$ and #$P<0.001$ compared to control (*t*-test for paired samples).

mating the pH of gastric and duodenal secretions are used (13). We investigated the influence of these processes on the viscosity of the gums (ingested at similar viscosity) using an HCl-NaCl mixture and an $NaHCO_3$-KCl-NaCl mixture to simulate gastric and duodenal secretions. Guar gum had the highest viscosity in each of these steps, followed by CMC and pectin, respectively. It is interesting that guar gum also had the greatest effect in reducing the postprandial glycemic response *in vivo*, as demonstrated by the ability to decrease the percentage of maximum rise in plasma glucose and/or reduction in the area under the plasma glucose levels. On the other hand, pectin, which showed a marked reduction in viscosity at 37°C and after events mimicking those that occur in the stomach and duodenum, did not have an important action on postprandial hyperglycemia. The performance of viscosity and the glycemic response to CMC were at intermediate levels between guar gum and pectin.

The mechanism responsible for this *in vivo* action possibly involves the effects of gums on convection in the small intestine. A more viscous solution (guar gum) may markedly reduce the access of nutrients to the epithelium by inhibiting convective solute movement within the intestinal lumen (14).

These data suggest that, starting from similar initial viscosity of three gums before ingestion, the temperature, the process of acidification, alkalinization and exposure to ionic intestinal constituents induce changes in gum viscosity *in vitro* and fibers that maintain higher viscosity during these steps have more important effects on the reduction of postprandial plasma glucose and serum insulin levels in human subjects.

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