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COMMUNICATIONS

The effect of pectin on the gastric emptying rates and blood glucose levels after a test meal

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Abstract—This study was designed to evaluate the effect of pectin given in a palatable form on the gastric emptying rates of the solid and liquid phases of a test meal and to ascertain whether pectin affected blood glucose levels in ten healthy male and female volunteers. Gastric emptying was measured using dual isotope gamma scintigraphy. Allocation to the treatment group was double-blind and randomized. Sequential blood sampling was used to measure blood glucose levels. The times for the stomach to empty half the radiolabelled meal were similar after both pectin and placebo; however, a significant difference was seen between the AUC values of the meal between the two treatments. This can be attributed to the divergence of the emptying curves after the time point at which 50% of the meal had emptied, as pectin delayed the emptying of the last 20% of the meal. The initial phase of emptying for both pectin and placebo was significantly faster than the meal. No significant difference was found between blood glucose levels when either pectin or placebo was administered.

Dietary fibres such as pectin, a gel forming carbohydrate, and guar gum, which resist digestion in the alimentary tract, have been shown to reduce post-prandial blood glucose levels in healthy volunteers and insulin requirements in diabetics (Jenkins et al 1976, 1977). Dietary manipulation with fibre has also been found to slow the rapid gastric emptying associated with dumping syndrome, which results from abnormally rapid gastric emptying of nutrients, especially hyperosmolar carbohydrates (Leeds et al 1981; Lawaertz et al 1983). Fibre supplementation has been used in morbidly obese subjects to produce increased satiety and delayed gastric emptying (Di Lorenzo et al 1988).

Although dietary fibre supplementation has a wide variety of such applications, the amount of pectin administered with a meal is critical; 5 g pectin was insufficient to delay emptying of a 2048 kJ meal, but 10–15 g significantly decreased the rate at which water and carbohydrates emptied (Flourie et al 1985). However, this quantity of pectin made the meal unpalatable. The formulation used in the present study contained a much lower dose of pectin (2 g). The rationale of the present study was to determine if a lower dose of pectin, formulated as a palatable drink which would gel on contact with gastric acid, would produce a delay in gastric emptying of the digestible solid phase of a test meal. The post-prandial blood glucose profiles were also measured to ascertain whether a significant amount of liquid became entrapped within the gelled pectin, thus delaying delivery of the glucose to the site of absorption.

Materials and methods

The pectin, placebo and randomization treatment codes were all provided by Farma Food A/S (Denmark). The study medication was supplied in individual volunteer treatment packs. Each sachet contained 2 g pectin, whereas this had been replaced by microcrystalline cellulose in the placebo. The active and placebo formulations were matched for taste and texture.

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Radiolabelling the placebo and pectin. Due to the double-blind design of the trial, a method had to be designed in which the placebo and pectin could both be radiolabelled using an identical procedure. The pectin could not be labelled by direct addition of indium and hence a suitable carrier for the label was identified which did not change the pH or rate of gelation of the formulation in-vitro. 1 MBq ^{111}In chloride was added to 50 mg sodium alginate. One millilitre of 0·04 M HCl was added to gel the alginate. One sachet of either the placebo or active formulation was slowly introduced to the gel, mixing continuously to ensure an even distribution.

The rate of loss of the radiolabel from the pectin and placebo was measured in-vitro. The labelled formulations were reconstituted with 150 mL tap water and left to stand for 2 min. These were then incubated with 125 mL simulated gastric acid (USP formulation) at 37°C, which was well stirred. At 30-min intervals a 1-mL sample was removed and centrifuged at 2500 rev min^{-1} for 10 min. The supernatant and pellet were counted for ^{111}In activity. The experiment was repeated a minimum of four times to check the uniformity of results.

Gastric-emptying study. The study was performed in ten normal, healthy non-patient volunteers recruited from the Nottingham University student population. Approval for the study was obtained from the Nottingham University Ethical Committee and permission to administer isotopes was obtained from the Department of Health. The subjects were given a medical examination before entry into the trial. Information concerning the trial was given both verbally and in written form. The subjects gave their written consent to participate in the trial.

The study was performed as a double-blind, randomized, cross-over design. The subjects abstained from alcohol for 24 h before the study and were fasted overnight. On the morning of the trial the subjects arrived at 0800 h at the study unit. Female volunteers were given a pregnancy test and were only accepted if the result was negative. The subjects then had a cannula inserted in a superficial vein in the back of the hand which was maintained patent by the continuous slow infusion of sterile saline (150 mM NaCl). This was attached to a saline drip to keep the vein patent. Heparin-saline was not used since this would have altered plasma fatty acids and thus could possibly have interfered with blood glucose measurements. The cannulated hand was warmed in a heating device which served to increase and standardize peripheral blood flow and to keep the vein dilated to allow easy blood sampling. An initial blood sample was taken and stored on ice in a fluoride oxalate tube.

The meal for the study day was standardized and given to the subject to take at the specified time. The test meal consisted of 2 eggs (60 g), 30 mL milk, 25 g butter, 2 slices of toast and 300-mL high-glucose drink (Lucozade, SmithKline Beecham) (61·5 g carbohydrate). This was served as scrambled eggs with the high-glucose drink and provided a total energy value of 2738·5 kJ (654·5 kcal). The scrambled eggs were labelled by the

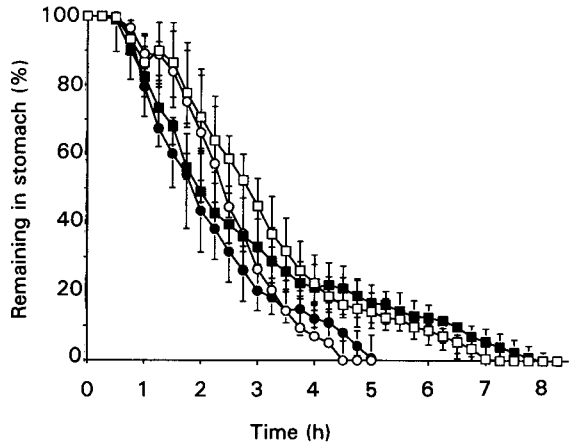

FIG. 1. Gastric-emptying curves of the pectin (■), placebo (□) and their respective meals (●, ○) (median values and interquartile ranges, n = 10).

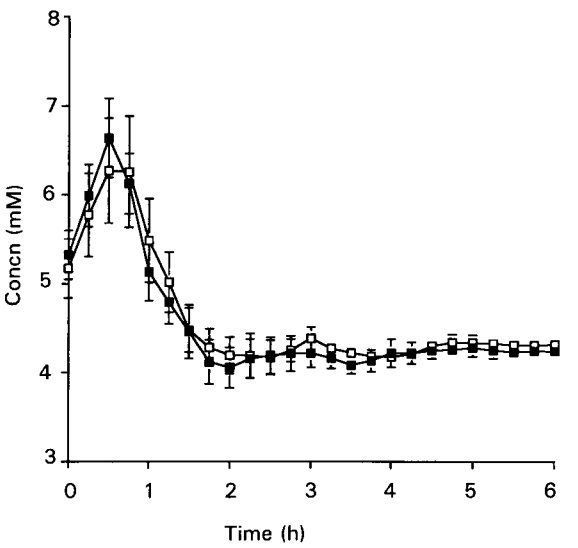

FIG. 2. Concentration of glucose in the blood with time (mean ± s.e.m., n = 10).

addition of 3 MBq ^{99m}Tc tin colloid to the ingredients before cooking using the method of Feldman et al (1984).

Gamma camera images (anterior and posterior) were recorded for a period of 30 s every 20 min for up to 6 h after the treatment. Technetium and indium images were recorded simultaneously, but stored separately in the computer for subsequent analysis. Further blood samples were also taken every 20 min and stored on ice for the glucose analysis carried out at the end of each study day.

To assess gastric emptying, two regions of interest were created on the computer, one around the whole stomach and the second to assess background activity. The stomach counts were corrected for background radiation and decay of the isotope. Counts from the technetium channel were corrected for overlap from the indium channel. The geometric mean of the counts from the anterior and posterior pair of images was calculated. The counts were normalized to calculate the percentage of radiolabel remaining in the stomach with time. The individual curves were interpolated to obtain a mean graph. The significance of differences in the time for the stomach to half empty (T50) were calculated using a Wilcoxon signed-rank sum test.

Results

In-vitro labelling efficacy. Initial studies had attempted to label pectin directly with ^{111}In, but the labelling efficiency was less than 20%, possibly due to charge effects. Addition of the small quantity of ^{111}In-alginate to the formulation did not affect the rate of pH of gelation of the pectin in-vitro. Labelling efficiencies of 68 and 76% were achieved when the respective pectin and placebo formulations were labelled with alginate. A 250-min incubation in simulated gastric juice at 37°C demonstrated no further dissociation of the label from the pectin, but approximately 10% was lost from the placebo formulation.

The gastric emptying curves for the meal and the formulations are shown in Fig. 1. The median times and interquartile ranges for the stomach to half empty (T50) and the area under the gastric emptying curves (AUC) are shown in Table 1. The post-prandial blood glucose curves are shown in Fig. 2 and the median time and interquartile range for peak height and time to peak to be attained are shown in Table 2.

Pectin did not significantly affect the T50 of the meal when compared with the placebo. However, a significant difference ($P = 0.008$) was seen between the AUC values of the meal after the two treatments, which was due to the divergence of the curves after the T50 point as pectin only delayed the emptying of the last 20% of the meal.

Discussion

The first 50% of both the pectin and placebo emptied from the stomach significantly faster than their co-administered meal ($P = 0.006$ at T50 for both). It is probable that the placebo and the pectin in solution emptied from the stomach with the liquid phase of the meal, which would be faster than the digestible solid phase labelled with ^{99m}Tc.

Table 2. Blood glucose data.

	Placebo	Pectin
Peak concn (mM)	6·98 ± 1·91	6·94 ± 1·22
Time to peak (h)	0·69 ± 0·27	0·71 ± 0·28

Mean ± s.d.

Table 1. Median and interquartile ranges of the area under the gastric emptying-time curves (AUC) (% h) and the time for the stomach to half empty (T50) (h).

	Meal + placebo	Placebo	Meal + pectin	Pectin
AUC median	3·35	2·80	4·54	3·71
interquartile range	3·01–3·87	2·32–3·20	3·75–5·04	3·03–4·77
T50 median	2·38	1·84	2·88	1·88
interquartile range	2·09–2·81	1·48–2·25	2·66–3·19	1·59–2·19

The mechanism by which pectin slows the terminal phase of gastric emptying appears to be complex. Pectin does not change the osmolality of pH of the gastric contents. It is thought that pectin delays gastric emptying by forming a gel and thus increasing the viscosity of the gastric contents (Holt et al 1979). This gel formation would entrap the water and any soluble nutrients, this retarding their emptying. It is possible that the pectin did not gel in the stomach until the pH fell to a suitably low level, as pectin gel formation is pH dependent. A large volume of liquid was ingested with the test meal and formulation, which would have had the effect of diluting the intra-gastric hydrogen ion concentration. Although the protein content of the food stimulates gastric acid secretion, it would initially buffer the acid, thus also contributing to a high pH in the first 2 h of the study. With test meals of this type, the pH rises from a baseline of 1·75 to 3·5 on ingestion of food and only returns to basal levels after 2–3 h when a significant part of the gastric contents has emptied (Washington et al 1993). Pectin has a pK_a of 3·3 and is completely gelled at pH 2 (Michel et al 1982). For the first 2 h the pectin empties at the same rate as the non-gelling placebo; the pectin only shows gastric retention relative to placebo after 2·5 h, when $\sim$ 30% of the material remains in the stomach. Again, only after 2·5 h does the meal adminstered with pectin start to be gastrically retained relative to the meal administered with placebo. This suggests that the pH changes affect the pectin gelation, which further controls the emptying of the meal.

The glucose administered in this study was given in the form of a drink. It appeared to empty from the stomach and be absorbed very quickly, within the first hour after administration. If the pectin only gelled the stomach contents after 2 h, by which time a significant proportion of the liquid phase of the meal had been emptied, this would explain why no significant changes in glucose levels due to pectin administration were seen during the study. It is possible that if the pectin formulation had been consumed 10–15 min before the test meal it would have gelled in the acidic conditions of the fasted stomach.

This study demonstrates that a small dose of pectin formulation can significantly delay the rate at which the terminal phase of the digestible component of the test meal was emptied from the stomach. It appears that the pH sensitivity of pectin gelation, coupled with the gastric pH profile, is responsible for this effect. Consequently, the pectin did not affect blood glucose levels when the glucose load was administered in liquid form. This highlights the need for a thorough understanding of gastric pH and the relevant carbohydrate chemistry if such materials are to be used as dietary control agents.

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