



Original Communication

Milk as a supplement to mixed meals may elevate postprandial insulinaemia

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Objective: The objective was to evaluate the impact of milk added to a high-glycaemic index (GI) white bread meal vs a low-GI spaghetti meal, respectively, on postprandial glucose and insulin responses in healthy subjects.

Design: The volunteers were served the bread or spaghetti meals with either milk (200 or 400 ml, respectively) or water (400 ml) following an overnight fast. Capillary blood samples were collected before and during 3 h after the meals.

Setting: The study was performed at the Department of Applied Nutrition and Food Chemistry, Lund University, Sweden.

Subjects: Ten healthy volunteers, seven men and three women, aged 22–30 y, with normal body mass indices, were recruited.

Results: There was no difference in postprandial glucose area under curve (AUC) with and without added milk in the case of the high-GI bread meals. As could be expected, glucose AUC after the bread meal + water was higher than after the spaghetti meal + water. Milk added at 200 or 400 ml to the spaghetti meal did not affect glucose AUC. However, a significantly higher insulin AUC was seen with the bread meal with 400 ml milk (+65%) and the spaghetti meal with 200 ml or 400 ml milk (+300%), respectively, compared with corresponding test meal with water.

Conclusions: The addition of milk to a low-GI spaghetti meal may significantly increase the postprandial insulinaemia. Even an ordinary amount of milk (200 ml) increased the insulin AUC to a low-GI spaghetti meal to the same level as seen with white bread. The mechanism for the insulinotropic effect of milk is not known, and the potential long-term metabolic consequences need to be elucidated.

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Descriptors: glycaemic index; insulinaemic index; milk; healthy subjects; carbohydrates; insulinotropic
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Introduction

In a FAO/WHO document focused on carbohydrates in human nutrition, an increased consumption of low glycaemic index (GI) foods is emphasised (FAO/WHO, 1998). The GI concept was introduced in the early 1980s as a method for assessing and classifying the postprandial

glucose response after a carbohydrate meal (Jenkins *et al*, 1981). Accumulating documentation has since shown that the glycaemic response to different carbohydrate foods is related to different food factors rather than to the carbohydrate component *per se*. Food factors that have been shown to modify the GI of starchy foods are for example a preserved botanical integrity (Liljeberg & Björck, 1994), the presence of viscous dietary fibre (Liljeberg *et al*, 1996), an elevated amylose/amylopectin ratio of the starch (Åkerberg *et al*, 1998), and the presence of organic acids produced upon fermentation processing (Liljeberg *et al*, 1995).

There are many studies showing a therapeutic potential of low-GI diets in individuals with diabetes (Järvi *et al*, 1999; Wolever *et al*, 1992) as well as in dyslipidaemia (Jenkins *et al*, 1985, 1987). In addition, recent data indicates a preventive role of a low-GI diet against development of type II diabetes (Salmerón *et al*, 1997a, b) and cardiovascular disease (Frost *et al*, 1998), respectively. Consequently, a low-GI diet should be recommended in

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subjects suffering from insulin resistance, or other disturbances (eg dyslipidaemia, hypertension) connected with the metabolic syndrome.

Data from our laboratory have shown a high correlation between GI and calculated insulinaemic index (II), for a range of starchy foods in healthy subjects (Björck *et al*, 2000). The same observation has been made by others for certain carbohydrate foods (Miller *et al*, 1995; Holt *et al*, 1996). However, in a recent study based on milk products (Östman *et al*, 2001), a discrepancy between GI and II was noted. Consequently, despite extremely low GIs (GI = 15–30), high IIs were found (II = 90–98). From this study it was concluded that the insulinotropic effect was not related only to the carbohydrate component of milk, but also to some yet unidentified food component. The literature comparing GI and II of food products is scarce. Moreover, the impact of milk as part of a mixed meal on postprandial metabolic responses has not been studied.

The aim of this study was to evaluate the impact of milk added to a high-GI white bread meal vs a low-GI spaghetti meal, respectively, on postprandial blood glucose and insulin responses in healthy subjects. The bread and spaghetti meals were served with either milk at two levels (200 or 400 ml, respectively) or water (400 ml).

Materials and methods

Food products included in test meals

Milk. Commercial milk (3% fat) produced by Skåne-mejerier (Malmö, Sweden) was bought locally.

Spaghetti. Spaghetti was obtained from Kungsörnen AB (Järna, Sweden). This pasta product was made from 100% durum wheat flour with addition of monoglycerides, and subjected to high-temperature drying following mixing/forming in a pasta extruder. Before being served, the spaghetti was boiled for 12 min in 1 l of water containing 1 g of NaCl.

White wheat bread. Commercial white wheat flour (Kungsörnen AB, Järna, Sweden) was bought locally, and a standardised white bread was baked in a baking machine as fully described previously (Liljeberg & Björck, 1994). After cooling, the bread was sliced (the crust removed),

wrapped in aluminium foil, put into plastic bags and stored in a freezer until use.

Chemical analysis

The contents of lactose, glucose and galactose in the milk product were determined by use of an enzymatic kit (Boehringer Mannheim, Germany). A portion of bread or boiled spaghetti was dried and milled (Cyclotec, Tecator Sweden) prior to analysis. The products were analysed for starch according to Holm *et al* (1986).

Test meals

The composition of the test meals is shown in Table 1. Three test meals based on white bread (70.2 g) and three test meals based on spaghetti (44.9 g dried pasta) were included in the study. The bread and spaghetti meals were served with either milk (200 or 400 ml, respectively) or water (400 ml). To standardise the liquid volume in the test meals, 200 ml water was added to the meal containing 200 ml milk. The test meals were served with 4 g butter and 25 g smoked ham. Also, 150 ml coffee or tea was included in each meal. The subjects were served the meals as a breakfast in random order after an overnight fast. The tests were performed approximately one week apart and commenced at the same time in the morning.

Subjects

Ten healthy volunteers, seven men and three women, aged 22–30 y, with normal body mass indices (BMI; $24.1 \pm 3.0 \text{ kg/m}^2$) and without drug therapy, participated in the study.

Blood analyses

Finger-prick capillary blood samples were taken prior the meal (0) and at 15, 30, 45, 70, 95, 120 and 180 min after the meal for analysis of glucose, and after 15, 30, 45, 95 and 120 min for analysis of insulin. The blood glucose concentrations were analysed with a glucose oxidase-peroxidase reagent. The serum insulin levels were determined with an enzyme immunoassay kit (Mercodia Insulin ELISA, Mercodia AB, Uppsala, Sweden) on an integrated immunoassay analyzer, CODA™ Open Microplate System (Bio-Rad Laboratories, Hercules, CA, USA).

Approval of the study was given by the Ethic Committee at the Faculty of medicine at Lund University, Sweden.

Table 1 Composition of the test meals

Test meals	Carbohydrates from bread or spaghetti (g)	Carbohydrates from milk (g)	Total carbohydrates in the test meal (g)
Bread + water	30.0	—	30.0
Bread + milk (200 ml)	30.0	9.8	39.8
Bread + milk (400 ml)	30.0	19.6	49.6
Spaghetti + water	30.0	—	30.0
Spaghetti + milk (200 ml)	30.0	9.8	39.8
Spaghetti + milk (400 ml)	30.0	19.6	49.6

Calculations and statistical methods

The 95 min glucose and insulin areas under the curves (AUC) were calculated by use of GraphPad Prism[®], version 2.0. The results are expressed as mean \pm s.e.m., and the statistical significance of differences was assessed by general linear model (ANOVA), followed by Tukey's multiple comparisons test. The MINITAB[™] advanced statistic program (release 13 for Windows) was used. A value of $P < 0.05$ was considered statistically significant.

Results

No significant differences in postprandial blood glucose levels were found between the bread meals supplemented with water or milk (200 and 400 ml), respectively (Figure 1). With the spaghetti meals, a significantly higher glucose increment at 30 min was found with the test meal based on spaghetti + milk (200 ml), compared with the meal based on spaghetti + water ($P < 0.05$; Figure 2). However, the calculated glucose AUC, did not differ between the spaghetti meals with and without added milk (Table 2). The glucose AUC with the bread + water meal was significantly higher than the corresponding area with the spaghetti + water meal. No difference in glucose AUC was found between the meals based on bread + milk (200 ml) and spaghetti + milk (200 ml), respectively. In contrast, a significantly higher glucose AUC was observed with the bread + milk (400 ml) meal, compared with the spaghetti + milk (400 ml) meal.

The postprandial insulin responses after the bread meal supplemented with milk (400 ml) were significantly higher ($P < 0.05$) at 15 and 95 min, compared with the bread + water meal (Figure 3). Also, the insulin AUC was significantly higher (+65%) with the bread + milk (400 ml) meal as compared to the bread meal without milk (Table 2). Supplementation of the spaghetti meal with milk (200 or 400 ml, respectively) increased the insulin concentrations at 0–30 min, compared with the spaghetti + water meal (Figure 4). Moreover, the insulin AUC with the two spaghetti meals with added milk (200 and 400 ml, respectively), were significantly higher (+300%) than the corresponding AUC with the meal based on spaghetti + water. The insulin AUC with the bread + water meal was significantly higher than the corresponding area with the spaghetti + water meal. No difference in insulin AUC was found between the meals based on bread + milk (200 ml) and spaghetti + milk (200 ml), respectively. In contrast, a significantly higher insulin AUC was observed with the bread + milk (400 ml) meal, compared with the spaghetti + milk (400 ml) meal.

Discussion

The inconsistency between glycaemic and insulinaemic responses to fresh milk and two fermented milk products in healthy subjects was recently addressed by Östman *et al* (2001). In an earlier observation by Gannon *et al* (1986), it was found that milk was a potent insulin secretagogue in

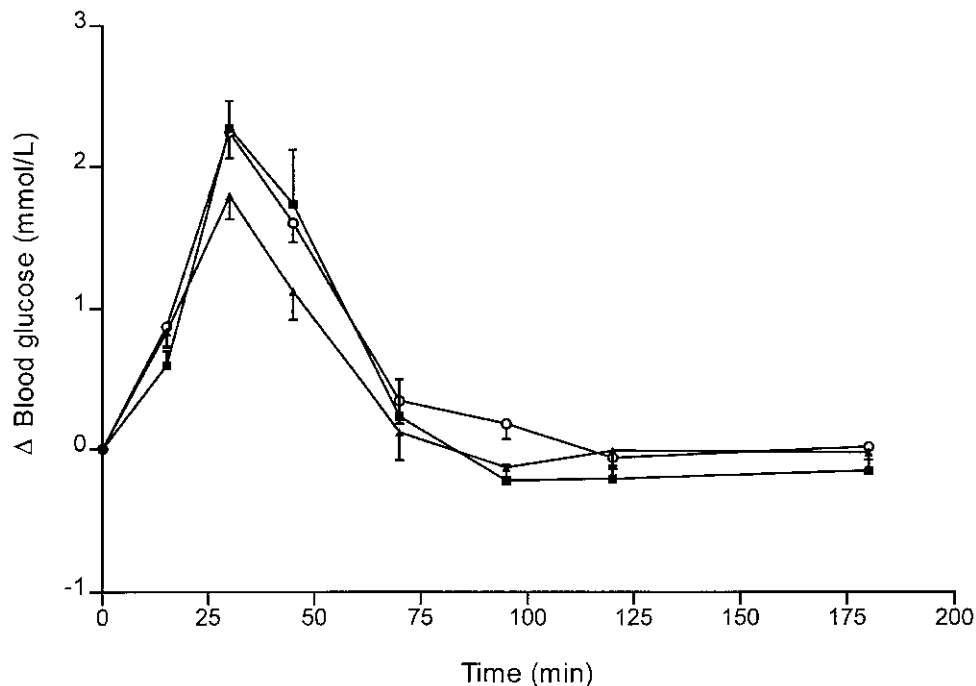


Figure 1 Mean incremental blood glucose responses in healthy subjects following ingestion of breakfast meals with white bread + water (square), white bread + milk (200 ml) (triangle) and white bread + milk (400 ml) (circle). Values are means \pm s.e.m., $n = 10$.

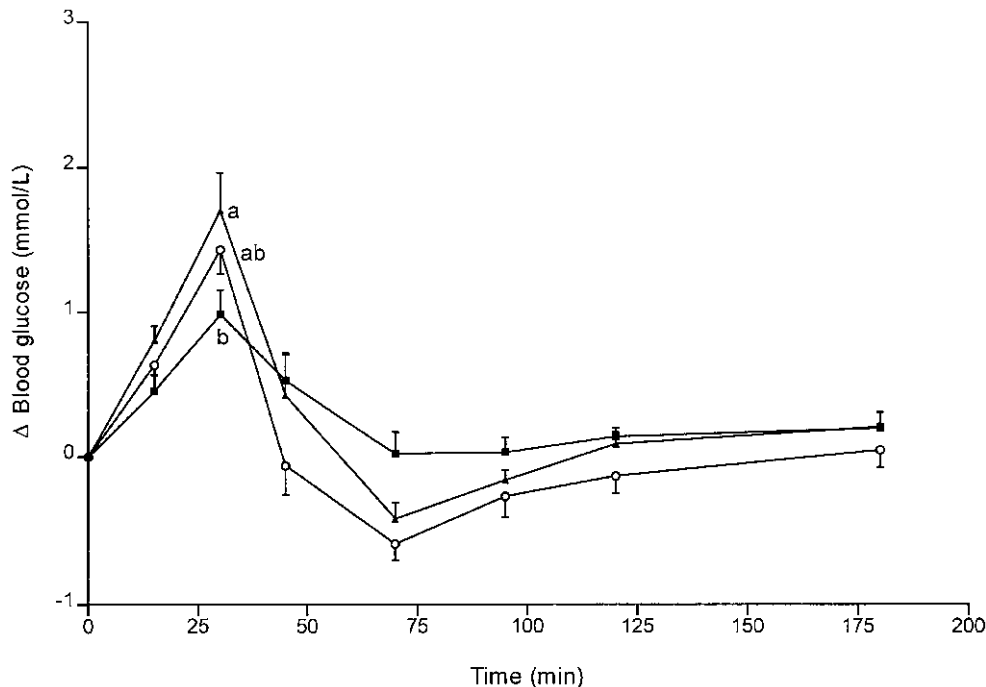


Figure 2 Mean incremental blood glucose responses in healthy subjects following ingestion of breakfast meals with spaghetti + water (square), spaghetti + milk (200 ml) (triangle) and spaghetti + milk (400 ml) (circle). Values are means \pm s.e.m., $n = 10$. Values not sharing the same letters are significantly different ($P < 0.05$).

Table 2 Postprandial blood glucose and serum insulin areas in healthy subjects after different starchy meals supplemented with water or milk (200 and 400 ml, respectively)¹

Test meals	Glucose AUC (0–95 min)	Insulin AUC	
		(0–95 min)	$\Delta\%$
Bread + water	86.5 \pm 13.3 ^a	13.5 \pm 1.7 ^a	
Bread + milk (200 ml)	68.8 \pm 8.1 ^{a,c}	16.7 \pm 3.0 ^{a,b}	+24 ²
Bread + milk (400 ml)	90.0 \pm 7.3 ^a	22.3 \pm 3.4 ^b	+65 ²
Spaghetti + water	37.1 \pm 9.0 ^b	3.5 \pm 1.0 ^c	
Spaghetti + milk (200 ml)	47.5 \pm 7.9 ^{b,c}	11.6 \pm 1.7 ^{a,b}	+331 ³
Spaghetti + milk (400 ml)	34.0 \pm 5.2 ²	10.9 \pm 2.0 ^{a,b}	+311 ³

¹X \pm s.e.m.; $n = 10$. Values within the same column with different superscript letters are significantly different, $P < 0.05$.

²Increase in postprandial serum insulin AUC, percentage of the bread + water meal.

³Increase in postprandial serum insulin AUC, percentage of the spaghetti + water meal.

type II diabetic individuals. Moreover, according to Schrenzenmeir *et al* (1989), the postprandial glucose and insulin responses after a milk containing breakfast did not correlate in healthy subjects. This inconsistency has not been acknowledged, and milk products appear to be an exception in that the II cannot be predicted from the GI.

In the present study the aim was to evaluate the impact of milk supplementation to a mixed meal on postprandial glucose and insulin responses in healthy subjects. The high

glucose and insulin concentrations after the white bread meal were not affected by an addition of 200 ml milk. However, a supplementation of the bread meal with 400 ml milk further increased the insulin demand. The spaghetti product used in the present study has previously been characterised regarding the postprandial glycaemic and insulinaemic responses, and was found to have a low GI and II (GI = 52, II = 42; Liljeberg *et al*, 1999). These favourable characteristics could be seen in the present study when comparing the bread + water and spaghetti + water meals (Table 2). However, when adding 200 or 400 ml milk to the spaghetti meal, the insulin levels were comparable to the levels after the bread meal + water. Consequently, the addition of milk to a low-GI starchy meal may elevate the postprandial insulinaemia.

When comparing the bread and spaghetti meals supplemented with milk, there was no difference in glucose and insulin AUC between the bread + milk (200 ml) meal and the spaghetti + milk (200 ml) meal. However, a higher glucose and insulin AUC were seen with the bread meal supplemented with 400 ml milk, compared with the spaghetti meal added the same amount of milk.

Despite differences in carbohydrate contents between the test meals (30.0–49.6 g), there were no differences in calculated postprandial glucose AUC to the bread meals with and without added milk. This was also true for the spaghetti meals with and without milk. These observations and the fact that the spaghetti meals supplemented with

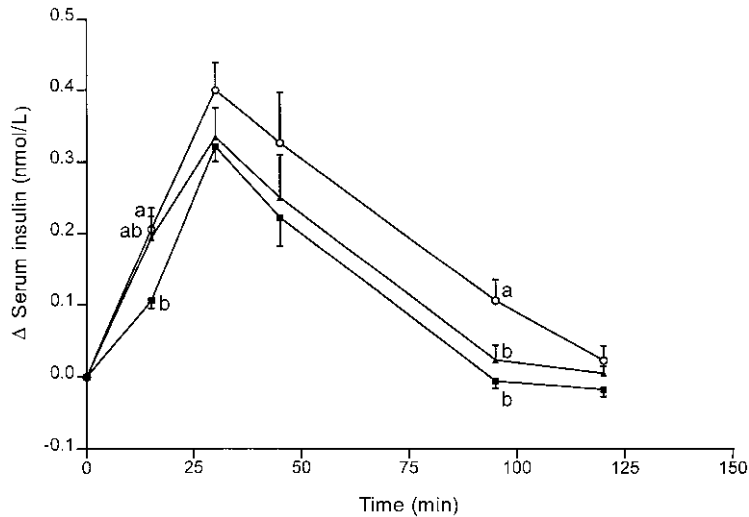


Figure 3 Mean incremental serum insulin responses in healthy subjects following ingestion of breakfast meals with white bread + water (square), white bread + milk (200 ml) (triangle) and white bread + milk (400 ml) (circle). Values are means \pm s.e.m., $n = 10$. Values not sharing the same letters are significantly different ($P < 0.05$).

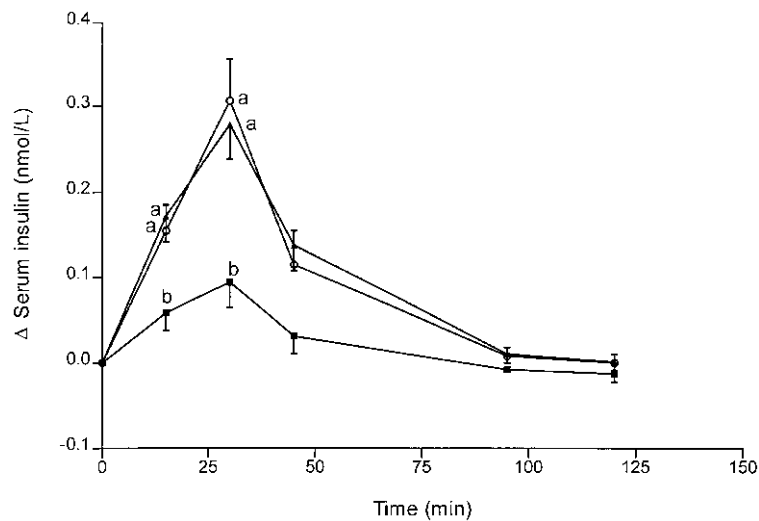


Figure 4 Mean incremental serum insulin responses in healthy subjects following ingestion of breakfast meals with spaghetti + water (square), spaghetti + milk (200 ml) (triangle) and spaghetti + milk (400 ml) (circle). Values are means \pm s.e.m., $n = 10$. Values not sharing the same letters are significantly different ($P < 0.05$).

milk resulted in a slight hypoglycaemia, could probably be explained by the insulinotropic effect of milk.

The high insulin responses following milk as a component of mixed meals is not communicated in dietary recommendations to healthy or diabetic individual, and the potential metabolic consequences of the insulinotropic effect have not been studied. In healthy adults an increased insulin release is considered unfavourable, and it is known that even a short duration of unphysiologically high insulin levels will reduce insulin sensitivity (DelPrato *et al*,

1994)—a key factor involved in etiology of the metabolic syndrome. However, it cannot be excluded that the stimulated insulin release seen with milk is favourable for certain groups of individuals, eg those with type II diabetes where normoglycaemia is a key factor.

The mechanism for the insulinotropic effect of milk is not known, and in our previous study (Östman *et al*, 2001) it was concluded that some milk components, in addition to lactose, are responsible for the increased insulin release. Several essential amino acids have been found to stimulate

the postprandial release of insulin as well as of glucagon and pancreatic polypeptide (Schmid *et al.*, 1989), and it could be hypothesized that the insulinotropic effect is related to the protein fraction in milk. Another explanation to the unexpectedly high insulin responses seen with milk could be that milk products have the capacity to stimulate the incretin hormones. According to Habener (1993), the incretin peptides GIP and GLP-1 are strongly linked to insulin secretion.

It should be noted that even an ordinary amount of milk (200 ml) added to a spaghetti meal increased the insulin AUC to the same level seen with bread. When added to a low-GI meal, milk may thus importantly increase postprandial insulin levels. Milk products are by tradition an important staple food in Sweden, as well as in many other countries. Consequently, the potential metabolic consequences of this insulinotropic capacity of milk need to be elucidated.

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