

## Short Communication

# Dissociation of the glycaemic and insulinaemic responses to whole and skimmed milk

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In most carbohydrate-containing foods, the blood insulin response is predictable and is closely linked to the food's glycaemic index (GI). A single study, examining whole milk and fermented milk products made from whole milk, recently reported a large dissociation between the GI and insulinaemic index (II) in healthy normal adults. Because the fat component of a food may influence the GI and II, it is unclear if a similar dissociation may exist for skimmed milk in normal adults. We determined the GI and II of both skimmed and whole milk in nine healthy, male ( $n$  6) and female ( $n$  3) subjects (23.6 (SD 1.4) years). No significant ( $P > 0.05$ ) differences existed between GI and II for skimmed and whole milks. Significant ( $P < 0.05$ ) differences were observed between the actual and predicted areas under the insulin curves for both skimmed milk (predicted 1405 (SD 289) pmol  $\times$  min/l; actual 6152 (SD 1177) pmol  $\times$  min/l) and whole milk (predicted 1564 (SD 339) pmol  $\times$  min/l; actual 5939 (SD 1095) pmol  $\times$  min/l). Consequently, a large and similar dissociation of the GI and II existed for both whole milk (42 (SD 5) and 148 (SD 14)) and skimmed milk (37 (SD 9) and 140 (SD 13)). It is concluded that the dissociation of the GI and II in milk is not related to its fat content.

### Glycaemic index: Insulinaemic index: Whole milk: Skimmed milk

The glycaemic index (GI) was developed by Jenkins *et al.* (1981) to provide additional information to help diabetic patients make appropriate dietary decisions. The GI has important implications for controlling blood glucose concentrations in both diabetic and healthy individuals (Wolever *et al.* 1995; Björck *et al.* 2000), but has been criticized for overlooking the contribution of insulin to metabolic disorders (Hollenbeck *et al.* 1986). More recent studies have illustrated that the glucose response does not always predict the insulin response (Gannon *et al.* 1988; Holt *et al.* 1997). By contrasting the predicted and actual insulin response, the relative dissociation of the GI from the insulinaemic index (II) can be determined (Gannon *et al.* 1986). Dissociations of the insulin response from the glucose response have been demonstrated for oatmeal, kidney beans and lentils in type 2 diabetics (Krezowski *et al.* 1987) in which glucose was used as the reference food, as well as in beef and fish in healthy subjects (Holt *et al.* 1997) in which white bread was the reference food. Not all studies of diabetics have been able to show this effect (Aro *et al.* 1987). In most carbohydrate-containing foods, the blood insulin response is predictable and is closely linked to the food's glucose response (Holt *et al.* 1997). A single study, examining whole milk and fermented milk products made from whole milk, recently reported

a large dissociation between the GI and II for healthy normal subjects in which white bread was used as the reference food (Östman *et al.* 2001). Because the fat component of a food may influence the GI and II (Collier & O'Dea, 1983), it is unclear if a similar dissociation may exist for skimmed milk in normal subjects.

### Methods

Nine healthy subjects (six men, mean age 23.3 (SD 1.4) years, mean BMI 23.5 (SD 1.6) kg/m<sup>2</sup>; three women, mean age 24.3 (SD 1.2) years, mean BMI 24.3 (SD 1.3) kg/m<sup>2</sup>) were studied on three separate occasions separated by at least 2 d. Only eight subjects were reported for the skimmed milk trials. The subjects recorded their dietary and exercise patterns for 2 d prior to reporting to the laboratory following an 8–10 h fast. The subjects were asked to replicate their dietary and exercise patterns before each subsequent test. Upon arrival at the laboratory a catheter was placed in a forearm vein, and a baseline blood sample was drawn. The catheter was kept patent using normal saline after each blood draw. The subject then consumed one of three test foods (glucose, whole milk and skimmed milk) administered randomly. Each food contained 25 g available carbohydrate. Blood was

drawn 15, 30, 45, 60, 90 and 120 min after completion of the meal and was analysed for plasma glucose and insulin concentrations. Glucose was analysed using the hexokinase/glucose-6-phosphate dehydrogenase method, and insulin was measured using the DSL-10-1600 ACTIVE Insulin ELISA Kit (Diagnostic Systems Laboratories, Inc., Webster, TX, USA). Incremental area under the curve (AUC) above baseline was calculated for both glucose and insulin (Wolever *et al.* 1991). Glucose was set as 100 and the GI and II of whole and skimmed milk were presented as a percentage of the glucose and insulin AUC after 25 g glucose. Prior to data collection the project was approved by the Human Subjects Committee at Colorado State University. Data were analysed using SPSS version 11.5 (Statistical Package for Social Science, SPSS Inc., Chicago, IL, USA). Paired *t* tests were employed to evaluate dependent variable differences between whole and skimmed milks and  $\alpha$  was set at 0.05. The relative dissociation of the GI from the II for both skimmed and whole milks was calculated using a previously described procedure (Gannon *et al.* 1986). With this procedure the insulin response to a test food is algebraically derived using the glycaemic response to the test food and the glycaemic and insulinaemic response to glucose by the same subjects. The derived value is compared with the actual insulin AUC to show the dissociation of the II from the GI.

## Results

The results of the experiment are shown in Table 1 and Fig. 1. Values are reported as means and standard deviations. No significant differences existed between GI and II for skimmed and whole milks. Significant ( $P < 0.05$ ) differences were observed between the actual and predicted areas under the insulin curves for both skimmed milk (predicted 1405 (SD 289) pmol  $\times$  min/l; actual 6152 (SD 1177) pmol  $\times$  min/l) and whole milk (predicted 1564 (SD 339) pmol  $\times$  min/l; actual 5939 (SD 1095) pmol  $\times$  min/l). Consequently, a large and similar dissociation of the GI and II existed for both whole milk (42 (SD 5) and 148 (SD 14)) and skimmed milk (37 (SD 9) and 140 (SD 13)).

## Discussion

The novel finding of this experiment was that skimmed milk elicited a disproportionately large insulinaemic response

relative to its low glycaemic response in healthy normal subjects. Our results expand upon Gannon and colleagues' work showing skimmed milk to be a potent insulin secretagogue in type 2 diabetic patients (Gannon *et al.* 1986) and corroborate a previous study demonstrating a similar effect in healthy normal subjects with whole milk and fermented products made from whole milk (Östman *et al.* 2001).

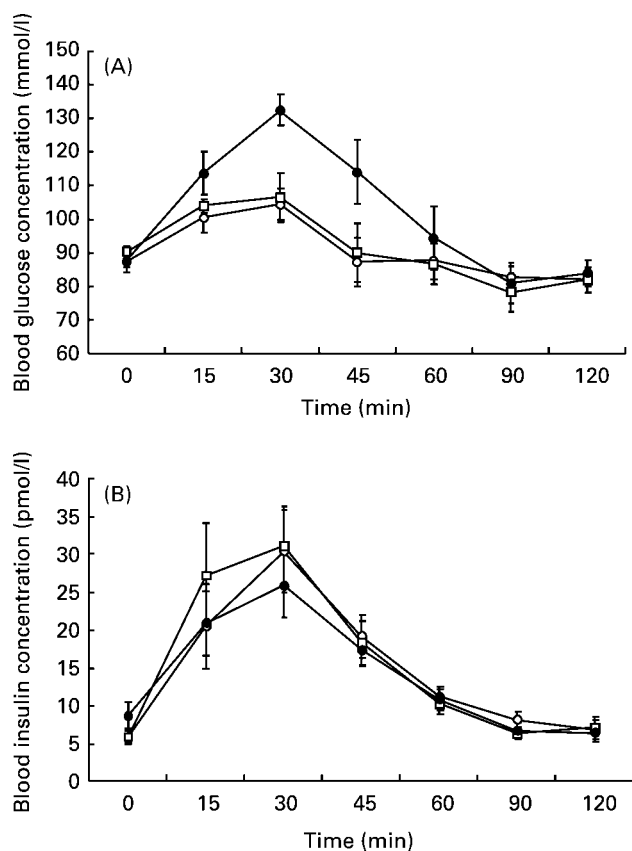
Östman *et al.* (2001) established that insulinaemia was greater after their subjects consumed milk products than after an equivalent amount of lactose and water, indicating that some milk component in addition to lactose stimulates insulin secretion. Although these authors suggested that a lipid component in milk may have been responsible, the present results effectively rule out this possibility and suggest that some factor within the protein fraction was responsible for milk's insulinotropic effect. Certain amino acids (tryptophan, leucine, isoleucine and glutamine) are insulinogenic (Schmid *et al.* 1989). Hence, it has been hypothesized that elevated concentrations of these amino acids in milk may underlie its insulin-stimulating capabilities (Östman *et al.* 2001). However, the insulinogenic amino acid profile of beef and milk are quite similar (Nutritionist V, Firstdatabank, Indianapolis, IN, USA), and beef has an insulin score of 51 (Holt *et al.* 1997), whereas the insulin scores for milk products have been reported to range from 89 to 115 (Holt *et al.* 1997; Östman *et al.* 2001). Lactose alone has an II of 50 (Östman *et al.* 2001). Taken together, these data suggest that an additive effect of lactose and amino acids likely underlie milk's insulin-stimulating effects. In support of this notion are data showing that when healthy subjects consumed 50 g protein as lean beef together with 50 g glucose, the insulin response was additive (Krezowski *et al.* 1986). Nonetheless, we cannot rule out other potential insulin secretagogues in the protein fraction of milk including specific peptides or even endogenous bovine hormones (Koldovský, 1995).

Except for cheese with an insulin score of 45 (Holt *et al.* 1997) all dairy products (whole milk, skimmed milk, yoghurt, ice cream, cottage cheese and fermented milk products) have been shown to have potent insulinotropic properties that may have far-reaching health effects, given the hypothesis that insulinaemia is a modulator of insulin resistance (Ludwig, 2002). Our data (Fig. 1) confirm the observation of Östman *et al.* (2001) that consumption of milk induces a reactive hypoglycaemia. Four of our

**Table 1.** Glycaemic index, insulinaemic index, predicted and actual area under the insulin curve (AUC) for whole and skimmed milk

(Mean values and standard deviations)

	Whole milk		Skimmed milk		<i>t</i> Score	<i>p</i> -Value
	Mean	SD	Mean	SD		
Glycaemic index	41	5	37	9	0.56	0.592
Insulinaemic index	148	14	140	13	0.53	0.612
	Predicted AUC (pmol $\times$ min/l)		Actual AUC (pmol $\times$ min/l)		<i>t</i> Score	<i>p</i> -Value
Whole milk	1564	339	5939	1095	5.72	0.000
Skimmed milk	1405	289	6152	1177	4.03	0.005



**Fig. 1.** Area under the glucose (A) and insulin (B) curves for glucose, whole and skim milks. (●) glucose; (□) skimmed milk; (○) whole milk.

subjects' blood glucose concentrations had dropped below baseline within 60 min after consuming milk. This response is similar to, high glycaemic load carbohydrates, which have been implicated as an underlying cause of certain diseases of insulin resistance (Ludwig, 2002). Even the addition of milk to low GI mixed meals elicits an insulinotropic effect (Liljeberg Elmstahl & Björck, 2001). Despite these potentially adverse acute effects, a recent epidemiological report demonstrated dairy consumption to be associated with a lower risk for type 2 diabetes (Pereira *et al.* 2002). Nevertheless, until well-controlled interventions can corroborate epidemiological associations, our data suggest caution is warranted in recommending higher milk consumption for adults, particularly those at risk for diseases of insulin resistance. Clearly, further research is needed to elucidate milk's potential to influence insulin metabolism adversely.

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