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# Mechanism of action of pre-meal consumption of whey protein on glycemic control in young adults $\stackrel{\leftrightarrow}{\prec}, \stackrel{\leftrightarrow}{\prec} \stackrel{\leftrightarrow}{\prec}$

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#### Abstract

Whey protein (WP), when consumed in small amounts prior to a meal, improves post-meal glycemic control more than can be explained by insulindependent mechanisms alone. The objective of the study was to identify the mechanism of action of WP beyond insulin on the reduction of post-meal glycemia. In a randomized crossover study, healthy young men received preloads (300 ml) of WP (10 and 20 g), glucose (10 and 20 g) or water (control). Paracetamol (1.5 g) was added to the preloads to measure gastric emptying. Plasma concentrations of paracetamol, glucose, and  $\beta$ -cell and gastrointestinal hormones were measured before preloads (baseline) and at intervals before (0–30 min) and after (50–230 min) a preset pizza meal (12 kcal/kg). Whey protein slowed pre-meal gastric emptying rate compared to the control and 10 g glucose (P<.0001), and induced lower pre-meal insulin and C-peptide than the glucose preloads (P<.0001). Glucose, but not WP, increased pre-meal plasma glucose concentrations (P<.0001). Both WP and glucose reduced post-meal glycemia (P=.0006) and resulted in similar CCK, amylin, ghrelin and GIP responses (P<.05). However, compared with glucose, WP resulted in higher post-meal GLP-1 and peptide tyrosine-tyrosine (PYY) and lower insulin concentrations, without altering insulin secretion and extraction rates. For the total duration of this study (0–230 min), WP resulted in lower mean plasma glucose, insulin and C-peptide, but higher GLP-1 and PYY concentrations than the glucose preloads. In conclusion, pre-meal consumption of WP lowers post-meal glycemia by both insulin-dependent and insulin-independent mechanisms. © 2014 Elsevier Inc. All rights reserved.

Keywords: Whey protein consumption; Blood glucose; Insulin; GLP-1; Gastric emptying

### 1. Introduction

When consumed with carbohydrate (CHO), proteins in general [1,2] and milk proteins specifically [3,4] reduce glycemic response compared with CHO alone. This effect has been attributed to the insulinotrophic effect of milk proteins [5,6], and more specifically to whey protein (WP) [7]. The addition of WP [3,8] or whey peptides [4] to a glucose drink or CHO meal reduces glycemic response, which has been attributed to its rapid digestion [9], and release of amino acids and bioactive peptides during digestion stimulate release of insulin [10], and many gastrointestinal hormones [7].

Proteins are known to be insulinotrophic but whether WP is more so, as has been suggested, and it is the only cause of the lowered glycemia after its consumption is unclear. A breakfast and lunch, each containing 28 g of WP and 50 g CHO served to adults with type II diabetes (T2D) resulted in higher blood insulin concentrations after both breakfast and lunch and lower glucose after the lunch than when the meals contained lean ham [3]. Additionally, 50 g WP in a meal lowered glycemia more than a similar amount of protein from turkey or egg albumin, and resulted in higher insulin concentrations than the meals with turkey, egg albumin and tuna over 240 min [11].

However, the reduced glycemia after protein consumption either with CHO [2] or alone [9,12] may be due to increased insulin release but also to release of gut hormones that delay stomach emptying and to the release of incretins that increase efficacy of insulin [7]. Small amounts (as low as 9–10 g) consumed 30 min prior to a meal [13] reduce post-meal concentrations of both glucose and insulin, indicating that insulin cannot be the only cause of the reductions. Only one study has related decreased post-meal glycemia to slower gastric emptying. Pre-meal consumption of 55 g WP increased glucagon-like peptide-1 (GLP-1) and delayed gastric emptying more than when consumed with a small CHO meal [14].

Therefore, the hypothesis of this study was that WP consumed alone prior to a meal improves post-meal glycemic control by both

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insulin-dependent and -independent mechanisms. The objective was to describe and compare the effect of WP and glucose consumed 30 min before a fixed meal in healthy men on pre- and post-meal plasma concentrations of glucose, insulin, gastrointestinal hormones regulating stomach emptying and incretins involved in potentiating insulin efficacy and on pre-meal gastric emptying rate.

#### 2. Methods and materials

#### 2.1. Participants

In a randomized crossover design, 10 men (18–29 y, 18.5–29.4 kg/m<sup>2</sup>) received preloads (300 ml) of WP (10 and 20 g), glucose (10 and 20 g) or water (control).

Paracetamol (1.5 g) was added to the preloads to measure gastric emptying. Plasma concentrations of paracetamol, glucose,  $\beta$ -cell hormones and gastrointestinal hormones were measured before preloads (baseline) as well as at intervals before (0–30 min) and after (50–230 min) a preset pizza meal (12 kcal/kg).

Participants were recruited through advertisements posted on the University of Toronto campus. At initial contact by phone or e-mail, eligibility requirements were described to the potential subjects and they were asked for their age, body weight, height, if they smoke or were taking any medications. Breakfast skippers, smokers, dieters and individuals with diabetes or other metabolic diseases were ineligible to participate in the study. Individuals who fulfilled eligibility requirements were asked to come to the Department for a second screening to complete questionnaires regarding food habits, food preference and dietary restraint [15] and to read and sign the consent form. Their height and weight were measured to calculate their body mass index (BMI). Qualified subjects were invited to participate in the study. Subjects were financially compensated for completing the study. The procedures of the study were

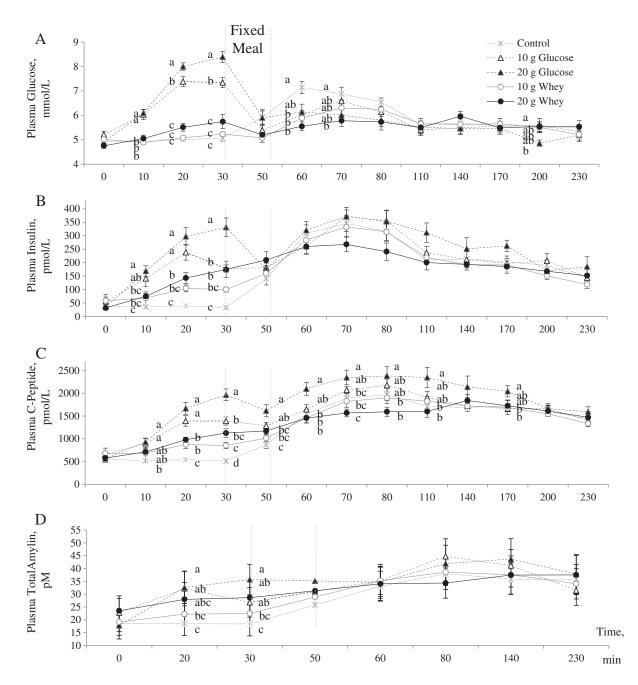


Fig. 1. Mean ( $\pm$ S.E.M.) pre- and post-meal plasma concentrations of glucose (A), insulin (B), C-peptide (C) and amylin (D) in 8 healthy men after intake of water (... $\times$ ...), 10 g glucose (... $\wedge$ ...), 20 g glucose (... $\wedge$ ...), 10 g whey protein (-O-), and 20 g whey protein (-O-). Different superscripts at each measured time are different between preloads (one-way ANOVA, Proc Mixed, followed by Tukey's post hoc, *P*<.05).

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