Milk Proteins in the Regulation of Body Weight, Satiety, Food Intake and Glycemia

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Abstract

Consumption of dairy products and their milk proteins increase satiety and reduce food intake and blood glucose response when consumed alone or with carbohydrate. Dairy proteins are of interest because proteins are more satiating than either carbohydrate or fat, and they regulate food intake and metabolic functions by the combined actions of the intact protein, encrypted peptides and amino acids on gastrointestinal and central pathways. As shown in this review, milk proteins have physiologic functions that contribute to the maintenance of a healthy body weight and control of factors associated with the metabolic syndrome through their effects on mechanisms regulating food intake and blood glucose. More recent reports show that these benefits can be achieved within the range of usual consumption of dairy. In addition, recent research points to an intrinsic value of small amounts of milk protein or dairy consumed shortly before a meal to reduce the glycemic response to carbohydrate and that this is not at the cost of increased demand for insulin.

Introduction

A role for dairy consumption and its physiologic functionality beyond the provision of nutrients in the management of obesity and metabolic syndrome is of interest because epidemiological studies have reported strong associations between higher dairy consumption and lower body weight [1]. Additionally, experimental studies show that consumption of dairy products and their milk proteins enhance satiety and reduce short-term food intake and blood glucose response when consumed alone or with carbohydrate.
Dairy proteins are of interest because proteins are more satiating than either carbohydrate or fat [2]. Milk proteins have received considerable investigation and have been shown to regulate food intake and metabolic functions through gastrointestinal and central pathways by the combined actions of the intact protein, encrypted bioactive peptides (BAPs) and amino acids [1, 3].

The following provides a review of the role of dairy in the regulation of body weight and the role of cow’s milk proteins in the regulation of satiety, food intake, blood glucose and their mechanisms of action.

**Dairy Consumption, Body Weight and the Metabolic Syndrome**

In recent years, numerous studies have associated milk and dairy consumption with favorable effects on body weight and metabolic control. Several epidemiological studies of adults have reported an inverse association between frequent dairy intake and adiposity as measured by the body mass index [1, 4]. In addition, a dietary pattern that included increased consumption of whole fruit and milk (skimmed and partly skimmed) were the two food patterns among 51 foods that were associated with the prevention of body weight increase in adults followed for 6 years in the Quebec Family Study [5].

Dietary patterns characterized by increased dairy consumption have also demonstrated a strong inverse association with insulin resistance, risk of type 2 diabetes and cardiovascular disease among overweight adults [1, 4, 6]. In the Health Professionals Follow-up Study, male participants with no history of diabetes, cardiovascular disease or cancer at baseline were followed for 12 years. Each serving per day increase in total dairy intake was associated with a 9% lower risk of type 2 diabetes and a corresponding relative risk of 0.88 for low-fat dairy intake [4, 7].

In a 10-year prospective study of dairy intake and the risk of type 2 diabetes in 37,183 middle-aged or older women, a dietary pattern that incorporated higher low-fat dairy products was inversely associated with the risk of type 2 diabetes [8]. Overall, daily consumption of dairy was associated with a 21% lower likelihood of the presence of the insulin resistance syndrome both in Blacks and Whites or men and women [6].

**Characteristics of Cow’s Milk Proteins**

Although the reasons for the observed benefits of increased dairy consumption and lower prevalence of obesity and chronic diseases remain unclear, the physiologic actions of their proteins, beyond providing essential amino acids for protein synthesis, has been offered as an explanation [1, 3, 9].
Physiologic Functions of Milk Proteins

Casein and whey proteins make up 80 and 20% of cow’s milk proteins, respectively, and each are made up of complex proteins of different characteristics [10]. Bovine casein consists of $\alpha_s^1$, $\alpha_s^2$, $\beta$, and $\kappa$-caseins, which represent 37, 10, 35 and 12% of whole casein, respectively. Bovine whey protein contains approximately 50% $\beta$-lactoglobulin, 20% $\alpha$-lactalbumin, 10% albumin and lactoferrin, and lactoperoxidase making up the remainder [10]. Both proteins have intense application as value-added ingredients in a wide range of food products [11].

The differences in the physical and chemical properties of casein and whey are attributed to their physiological effects when ingested [1, 3]. Whey protein is rapidly digested (a fast protein), whereas casein is more slowly digested (a slow protein). The classification of casein and whey as ‘slow’ and ‘fast’ proteins is based on their contribution to protein synthesis and their effect on plasma amino acid concentrations [12]. In humans, consumption of whey (0.45 g/kg body weight) resulted in a fast, but short and transient, increase in plasma amino acids that peaked in 40 min to 2 h after its ingestion and returned to baseline values after 3–4 h. Casein, in contrast, and consistent with its slow gastric emptying, results in plasma amino acid concentrations that rose more slowly and are lower, but had sustained a plateau lasting for 7 h.

Amino acids released from milk proteins have a multitude of effects beyond their role in protein synthesis in the body. For example, they are a significant factor accounting for the insulinotropic effect of milk protein. Healthy subjects that ingested a mixture of branched-chain amino acids (BCAAs) including leucine, isoleucine, valine, lysine and threonine had glycemic and insulinemic responses similar to those with intact whey [13]. The high level of BCAAs, specifically the leucine content of milk proteins, may contribute to increased fat mobilization from adipose tissue observed in young obese subjects on high-dairy energy-restricted diet [14].

In addition to providing a high-quality source of amino acids, milk proteins are precursors of BAPs which are released either due to the separate or combined action of digestive, microbial and milk proteases during gastrointestinal digestion or dairy processing. Therefore, BAPs are generated in vivo after the ingestion of products containing milk proteins or externally, in the fermented dairy products such as yogurt, sour milk and cheese. At least 26 BAPs are encrypted in the primary structure of milk proteins and many of them have been isolated from dairy products, including sour milk, yogurts, and cheeses [15]. During digestion, the caseins produce numerous BAPs. The casokinins originate from major subunits of casein, $\alpha_s^1$, and $\beta$-caseins and inhibit angiotensin I-converting enzyme (ACE), reducing blood pressure [16]. Opioid peptides known as $\beta$-casomorphins are also derived from casein and are involved in the regulation of various physiological processes, including food intake regulation, gastrointestinal motility, and plasma insulin concentrations [17]. During cheese-making, $\kappa$-casein is hydrolyzed by chymosin into para-$\kappa$-casein
and caseinomacropeptide (CMP), which includes the glycosylated form of CMP called glycomacropeptide (GMP). As a result, CMP becomes an ingredient of commercially available whey protein products with its content between 12 and 28% [18].

Peptides derived from whey have physiological functions including the modulation of blood pressure, inflammatory processes, blood glucose and systems regulating food intake. Whey proteins (α-lactalbumin and β-lactoglobulin) are precursors of ACE-inhibitory peptides called lactokininns [16], which have antihypertensive activities.

Many BAPs from milk proteins possess numerous physiologic activities and are considered to be multifunctional peptides. For example, whey-derived α-lactorphin and casein-derived β-casomorphin-7 have both opioid and ACE-inhibitory activities [16].

**Milk Proteins, Satiety and Food Intake**

Many studies show that milk proteins increase satiety, but not necessarily later food intake. However, the variability in results can be explained in part by the protein source, quantity and time of measurements used in the studies [19]. For example, a randomized, single-blind study of 25 healthy adults found that a breakfast with 25% of energy from casein was more satiating than a breakfast with 10% of energy from casein to lunch (3–4 h later) [20]. However, there were no differences in energy intake at lunch. Similarly, whey has been shown to suppress appetite in a number of short-term studies, but the effects on energy intake are inconsistent.

Most often, dairy proteins are consumed in food form. Satiety has been reported after consumption of dairy foods such as nonfat milk [21], chocolate milk [22], high protein cheese [23], and low-fat yogurt [24]. While increased satiety translated into reduced ad libitum energy intake in some of these studies [21]; it failed to do so in others [22, 24], but did not result in higher energy intake compared to control conditions [23]. These observations can be attributed to the amount of preload, protein content and time of measurement of food intake. Consumption of 600 ml of milk (21 g protein) at breakfast prior to lunch 4 h later resulted in reduced food intake at lunch [21], and a cheese snack (22 g protein) containing either casein or a mixture of casein and whey proteins 1 h before lunch resulted in partial energy compensation at lunch and full energy compensation over 24 h [23]. However, a study investigating the effects of 200-kcal preloads consisting of semisolid yogurt (17.1 g protein), liquid yogurt (17.1 g protein), dairy fruit beverage (2.6 g protein) and fruit drink (0 g protein) prior to a lunch 90 min later did not lead to energy compensation [24]. Similarly, 500 ml of a chocolate milk drink compared with 500 ml of a sugar-sweetened carbonated beverage did not result in a reduction in ad libitum food intake 30 min later [22].
Of the milk proteins, whey protein preloads of 45–50 g have been shown to decrease food intake more than casein at meals consumed 30–90 min later [2], while casein reduced food intake more at 180 min [25]. These early studies used treatment doses well above that which may be obtained from usual serving sizes, and thus provided little evidence that dairy consumed in usual amounts contribute to food intake regulation. However, more recent studies indicate that protein intake from milk in the range of usual serving sizes, defined as 250 ml (9 g protein), but often consumed in larger amounts of 360–500 ml (18 g protein), is of functional significance for food intake control through the combination of the effects of whey in early, and casein in later, satiety. The consumption of 600 ml (21 g protein) of milk, compared with a fruit-based beverage, and served with a toast and jam breakfast reduced measures of hunger and increased fullness over 4 h to lunch time and reduced food intake [21]. A decrease in subjective appetite ratings was found after consumption of approximately 15 g of whey providing 10% of the energy content of breakfast, compared with casein or soy protein [20]. Although the lowest dose of whey protein (15% GMP) found to suppress food intake when consumed 30 min prior to a meal was shown to be 20 g based on a sample size of 16 healthy individuals (fig. 1) [26], the reduction of 78 kcal at the meal following 10 g whey protein was predicted to be statistically significant in a sample size of 40 subjects.
Milk Proteins and Satiety Mechanisms

To explain protein-induced satiety, several mechanisms have been proposed based on their release of amino acids, encrypted BAPs and satiety hormones [3].

There is a long history of the study of intake regulation based on amino acid-sensing systems in the brain [27]. Imbalances in the essential amino acid content of dietary proteins are readily sensed by the brain and lead to reduced food intake. Other amino acids including tryptophan and tyrosine provide precursor control of serotonergic and catecholaminergic systems which also are involved in food intake regulation. Finally, the brain uses BCAAs as fuel, which may also be a satiety signal [28]. Milk proteins are high in BCAAs and neurotransmitter precursors [29].

The role of BAPs in control mechanisms regulating food intake and metabolism has received relatively little investigation. However, the importance of BAPs in food intake regulation is suggested based on the following observations: (1) BAPs from casein reduce food intake via peripheral opioid and cholecystokinin (CCK)-A receptors in the gut in rats [30] and stimulate glucagon-like peptide-1 (GLP-1) release [31]; (2) A mixture of free amino acids fails to stimulate the effect of intact whey on incretin secretion in the gut hormones [13]; (3) The ingestion of milk proteins stimulates the release of the gut hormones including CCK, GLP-1, glucagon inhibitory peptide (GIP), peptide tyrosine tyrosine (PYY) and of insulin, while reducing ghrelin [1, 3], all known to be involved in appetite and food intake regulation. Although whey protein, compared to casein, has a stronger effect on these hormones and contains a higher content of BAPs, the results reported may be due also to the duration of measurement which may not have been extended long enough to show the complete effect of the more slowly digested casein [19]; (4) GMP stimulates satiety hormones (e.g. CCK) and has been suggested to be a factor accounting for the effects of milk proteins or commercial whey proteins on satiety. Unfortunately, much confusion on the efficacy of GMP arises from the failure of studies to report the GMP content of whey protein [3]. For example, GMP (0.8 g) was not found to be of importance in pre-meal whey-induced satiety or later food intake [32]. However, in 25 healthy adults, ad libitum energy intake was 10% lower 3 h later at lunch after a breakfast containing both 10% (15 g protein) or 25% (37.5 g of protein) of energy from whey protein containing GMP compared to a breakfast with whey protein without GMP [33]. Although the GMP content of the treatments was not described, it is possible that the whey protein with GMP contained 15% GMP [3]. If so, the amounts of GMP consumed would have been substantially more than that provided in the experiments of Burton-Freeman [32]. A dose-response study with defined quantities of GMP compared with GMP-free whey is required to resolve this issue.
Milk Proteins and Glycemic Control

Short-term experimental studies support the hypotheses that dairy consumption before or as part of a meal offers benefits in metabolic control. Milk consumption decreases the glycemic response to carbohydrate ingestion [34, 35]. Lower glycemic responses have been found after high milk breakfasts compared with high fat breakfasts or high fiber breakfasts in both healthy participants and individuals with type 2 diabetes [36]. When milk or whey were added to either high or low glycemic index carbohydrate meals, there were markedly lower glycemic responses [34, 35, 37]. An insulinotropic effect of milk is seen with both whole and skim milk indicating that insulin release is due to its protein content [4, 34].

There are many reports of the effect of whey protein, consumed alone, in beverage form or when consumed with carbohydrate on increasing plasma insulin as the mechanism by which the reduction in blood glucose occurs [13, 37, 38]. Addition of whey (total 18 g) to a meal containing rapidly digested and absorbed carbohydrates, stimulated greater plasma insulin concentrations (+57% after lunch) and reduced postprandial blood glucose (~21% over 120 min response) in subjects with type 2 diabetes [38]. Whey protein has been suggested to be the primary insulinotropic factor because a 50% greater increase in insulin response was found after preloads of 25 g carbohydrate with 18 g of whey protein than with the same amount of protein from milk or cheese [37]. Although it has been suggested that the insulinotropic effect of whey protein [1, 3, 9] arises from its rapid digestion and high content of BCAAs [37], the comparison of its effect with milk or cheese high in casein may be attributed as well to food form and rate of stomach emptying and digestion.

More recent evidence suggests that the explanation for the effect of whey consumption on glycemic control is not solely dependent on its insulinotropic effects. A BCAA mixture was found to mimic the glycemic and insulinotropic responses after whey protein but did not reproduce the effect of the intact whey protein on gut hormones in humans [13], suggesting that postprandial glucose reduction occurs by mechanisms in addition to insulin action. Furthermore, a recent study has shown that a lower blood glucose following a meal of fixed size occurs without an overall increase in insulin requirement in response to the 10–40 g of whey preloads consumed 30 min prior to a meal of fixed size given to healthy young men and women [26]. A lower post-meal blood glucose with increasing doses of whey protein (15% GMP) was achieved in the presence of a lower, not higher, post-meal insulin AUC and a similar cumulative (0–170 min) insulin AUC (table 1). When the cumulative AUC for blood glucose was divided by the cumulative AUC for insulin to evaluate the efficacy of insulin action, the ratio was decreased, in a dose-dependent manner, to 50% of the control after pre-meal consumption of intact whey protein of 40 g (fig. 2). In contrast to 10 g of intact protein, 10 g
of whey protein hydrolysate did not result in a lower cumulative blood glucose than the control even though it increased the post-meal and cumulative insulin AUC similarly, suggesting that noninsulinotropic mechanisms require stimulation arising from the digestion of intact proteins, perhaps due to the release of encrypted BAPs.

Although the mechanism by which pre-meal whey protein brings about improved post-meal glucose control with a lower requirement for insulin is unclear, the most probable explanation for the insulin-independent actions of pre-meal consumption of whey protein on blood glucose control resides in the

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**Table 1.** Pre- and post-meal blood glucose and insulin responses after the doses of whey protein and whey protein hydrolysate (WPH)

<table>
<thead>
<tr>
<th>Preload</th>
<th>Blood glucose, mmol×min/l</th>
<th>Insulin, µIU×min/ml</th>
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<tr>
<td><strong>Pre-meal AUC (0–30 min)</strong></td>
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<tr>
<td>Control</td>
<td>-1.6 ± 1.5&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.0 ± 4.5&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>Whey protein, 5 g</td>
<td>1.5 ± 1.3&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>48.5 ± 11.0&lt;sup&gt;b,c&lt;/sup&gt;</td>
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<tr>
<td>WPH, 10 g</td>
<td>5.6 ± 1.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>95.1 ± 11.5&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>Whey protein, 10 g</td>
<td>-1.4 ± 1.4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>107.9 ± 12.9&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>Whey protein, 20 g</td>
<td>4.3 ± 1.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>185.5 ± 25.6&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>Whey protein, 40 g</td>
<td>4.2 ± 1.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>217.5 ± 32.6&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>p</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
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<tr>
<td><strong>Post-meal AUC (30–170 min)</strong></td>
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<tr>
<td>Control</td>
<td>232.9 ± 21.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3,593.4 ± 510.5&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>Whey protein, 5 g</td>
<td>207.1 ± 17.4&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>2,720.2 ± 313.6&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
<td>WPH, 10 g</td>
<td>196.6 ± 17.8&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>2,173.3 ± 272.2&lt;sup&gt;b,c&lt;/sup&gt;</td>
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<td>Whey protein, 10 g</td>
<td>162.5 ± 12.9&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>1,995.8 ± 271.3&lt;sup&gt;b,c&lt;/sup&gt;</td>
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<td>Whey protein, 20 g</td>
<td>121.6 ± 8.9&lt;sup&gt;cd&lt;/sup&gt;</td>
<td>1,502.6 ± 253.5&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>Whey protein, 40 g</td>
<td>82.2 ± 13.9&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1,578.1 ± 303.7&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>p</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
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<tr>
<td><strong>Cumulative AUC (0–170 min)</strong></td>
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<tr>
<td>Control</td>
<td>214.6 ± 22.7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3,593.7 ± 507.0</td>
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<td>Whey protein, 5 g</td>
<td>210.8 ± 22.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3,221.6 ± 354.4</td>
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<td>WPH, 10 g</td>
<td>234.4 ± 24.1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3,154.9 ± 348.5</td>
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<td>Whey protein, 10 g</td>
<td>149.9 ± 20.6&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3,110.5 ± 374.0</td>
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<td>Whey protein, 20 g</td>
<td>146.9 ± 14.3&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3,419.6 ± 384.5</td>
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<tr>
<td>Whey protein, 40 g</td>
<td>112.3 ± 17.1&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3,826.0 ± 426.5</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.0001</td>
<td>n.s.</td>
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Mean ± SEM blood glucose AUC (mmol × min/l) and insulin AUC (µIU × min/ml) after the whey protein and WPH preload consumption were calculated for pre-meal (0–30 min) and post-meal (30–170 min) and cumulative (0–170 min; n = 21). One-factor repeated-measures ANOVA followed by Tukey’s post-hoc was used to compare the effect of preloads (means with different superscripts at pre- and post-meal and cumulative AUC are different, p < 0.0001).
Physiologic Functions of Milk Proteins

Effect of protein on gastric emptying [26]. Even a modest change in gastric emptying affects the magnitude and timing of postprandial blood glucose and insulin increase and is decreased by protein ingestion consumed either with carbohydrate or alone or when consumed before a meal. Furthermore, slower stomach emptying would be expected because whey protein and other proteins release CCK, GLP-1, glucagon inhibitory peptide and peptide tyrosine tyrosine from the intestinal enteroendocrine cells [1].

Fig. 2. Ratio of cumulative blood glucose/insulin AUCs following consumption of whey protein (a) Ratio (mean ± SEM) of cumulative blood glucose/insulin AUCs after whey protein consumption (n = 21). One-factor repeated-measures ANOVA followed by Tukey’s post-hoc was used to compare the effect of preloads (means with different superscripts are different, p < 0.05). (b) Association (r = −0.33, p < 0.001) between whey protein doses and ratio of cumulative (0–170 min) blood glucose/insulin AUC after consumption (Pearson’s correlation coefficient).
Conclusions

Milk proteins have physiologic functions that contribute to the maintenance of a healthy body weight and control of factors associated with the metabolic syndrome through their effects on mechanisms regulating food intake and blood glucose. Recent reports show that these benefits can be achieved within the range of usual consumption of dairy. In addition, more recent research points to an intrinsic value of small amounts of milk protein or dairy consumed shortly before a meal to reduce the glycemic response to carbohydrate and that this is not explained by its insulinotropic effect alone.

References

Physiologic Functions of Milk Proteins

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Discussion

Dr. Gibson: You talked about studies in which casein and whey fractions are being compared, and I often read in the literature this sort of thing. Is there a comparison
between whey proteins and non-bovine milk proteins such as soy proteins or other animal proteins? Are there comparative studies?

Dr. Anderson: In the first slide I showed, soy protein did not suppress food intake as much as whey. Also, it was surprising that egg albumin didn’t have any effect at all. This may be due to its low solubility over that time and slow release from the stomach. Margriet Westerterp and her group in Holland have done a lot of studies looking for biomarkers of satiety with different proteins. They reported different effects on PYY, CCK, insulin, and other hormones, but found that outcome depends on dose and meal timing, and what the meal consists of. These biomarkers generally fail to associate with subjective measures of satiety. I guess the only thing I could offer is that generally whey keeps coming out as more efficacious in short-term studies.

Dr. Melnik: I would like to know whether you have also looked at ghrelin response after whey feeding. After milk ingestion, we observed a strong insulin response and a decrease in ghrelin levels.

Dr. Anderson: Ghrelin goes down after whey consumption, also in rats, not just in humans.

Dr. Clemens: Would you like to speculate on the impact some of these hydrolytic enzymes that are used in food processes might have on satiety and stimulation of IGF-I?

Dr. Anderson: Let’s just step back. If you compare soy-based diet with a milk-based diet, antioxidant capacity is improved and blood lipid oxidation is decreased with the milk-based diet. If you hydrolyze proteins, then of course depending on which enzymes are used you will get different peptide fractions. It’s very hard to determine if they reflect normal digestive processes or, even if they don’t, what lengths of the peptides are left in the process. Some will expose proteins to digestive enzymes for 30 min and then separate the peptides, and others let the process go for much longer. Unfortunately, authors often fail to give details about how the hydrolysates were prepared or their composition. I am not aware of reports of their effects on IGF-I, but I am sure that would depend on the degree of hydrolysis. Perhaps Dr. Haschke would like to comment?

Dr. Haschke: I can only comment on infant formulas. We have formulas with partial or extensive protein hydrolysis. Producers of those formulas have to specify the enzymes that are used and the exact profile of peptides in the hydrolysate. The reason for that is that the molecular size of the peptide fractions is very important for allergy prevention or treatment. As already mentioned, at 6 years of age growth (weight, height, BMI) of children who were fed three different hydrolysates (Nutramigen, Pepti-Junior, NAN-HA) during infancy was similar to that of children who were exclusively breastfed during infancy [1]. However, one cannot conclude that long-term growth of children who were fed other hydrolysates would be similar.

Dr. Anderson: I think that the point that I want to make, going back to the formulas, is that we don’t have any metabolic measures on infants being fed different formulas to the extent that you could make the comparison, and to the extent that that would be possible I think it would be worthwhile doing.

Dr. Haschke: We have very limited data, I agree with you. For example, we have data which are published on one partially hydrolyzed formula in terms of IGF-I secretion and insulin secretion, and the reference is again the breastfed infant. The data have been shown earlier during the meeting, and it’s clear that it’s the amount of protein that determines insulin secretion and IGF-I levels – the higher the protein the higher the IGF-I levels. But I agree with you, we don’t have data comparing extensively hydrolyzed and partially hydrolyzed intake formulas; as far as I know, this cannot be found in the literature.
Physiologic Functions of Milk Proteins

Dr. Anderson: One of the points going back to the question of bodybuilders and some of the adverse effects suggested to be due to the huge amounts of whey they consume, my concern is that we might throw the baby over the bath water. I am trying to give the message that dairy products in the amounts that are normally consumed and within our dietary guidance of three servings a day provide whey in amounts much below the large amounts consumed by bodybuilders. There is no evidence that normal consumption levels are a problem.

Dr. Lönnédal: I would like to emphasize what you discussed regarding extensively hydrolyzed infant formulas. Dr. Hernell and I did a clinical study in which we compared regular infant formula, breastfeeding and extensively hydrolyzed formula based on either 100% casein or 100% whey, starting from 1 month of age up to 6 months of age, but it was not sized to look at growth. As you may know, the daily volume consumed by formula-fed infants is higher than that of breastfed infants. The intakes of the extensively hydrolyzed formulas were even higher, so I wonder what this did to appetite control once these peptides had broken down to a very small size. I am coming back to Dr. Haschke’s comment that we have to be a bit cautious about growth studies on infants fed especially extensively hydrolyzed formulas because very often they are given to compromised infants with allergies that always have poor growth and need to catch up. In this Swedish study, we compared healthy normal infants with regular formula controls and breastfed infants.

Dr. Anderson: I agree. If you take the branched-chain amino acids alone or hydrolyzed whey and compare them with intact whey you get a very different endocrine and food intake responses. There is good evidence that you need the intact protein to get the full benefits from gut and metabolic hormones. But I just want to make another point that arose from Dr. Melnik’s presentation, where he provided an example of feeding adults with infant formula. We know little about how this compares to cow’s milk or soy beverage.

Dr. Dehbi: I wonder if all these findings may be applied to diabetes in children; maybe this will prepare for a formula for children with diabetes because it’s difficult to control diabetes in childhood.

Dr. Anderson: Yes, absolutely. In Canada, as in the US, we are now into bariatric surgery for teenagers and young children, and of course we see diabetes in children. The question is which is the chicken and which is the egg in the etiology of energy imbalance and diabetes? Has the obese child lost the physiologic signals or is the problem all environmental, or can you still make use of the physiological signals in order to help them lose weight? If so, then the high-satiety foods may be of value for appetite control. That’s why we are studying milk because we think milk and whey are highly satiating. However, I also showed that whey consumed before a meal by adults results in blood glucose control through mechanisms in addition to insulin. If so, then a practical approach to glycemic controls may be to encourage a child with obesity and diabetes to have a glass of milk or a beverage with 5–10 g whey before eating. This possibility is being investigated.

Reference
