European Journal of Clinical Nutrition (2014) **68**, 980–986

www.nature.com/ejcn

ORIGINAL ARTICLE

Comparative effects of whey and casein proteins on satiety in overweight and obese individuals: a randomized controlled trial

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BACKGROUND/OBJECTIVE: Dairy protein seems to reduce appetite by increasing satiety and delaying the return of hunger and subsequently lowering energy intake compared with fat or carbohydrate. The aim of this study was to compare the effect of whey with that of casein proteins on satiety in overweight/obese individuals.

METHODS/SUBJECTS: This was a randomized, parallel-design 12-week-long study. Seventy subjects with a body mass index between 25 and 40 kg/m^2 and aged 18–65 years were randomized into one of three supplement groups: glucose control ($n=25$), casein ($n=20$) or whey ($n=25$) protein. Before commencing the study, at weeks 6 and 12 of the treatment, a Visual Analogue Scale (VAS) was used to measure subjective sensations of appetite before lunch and before dinner.

RESULTS: Rating for VAS (mm) at 6 and 12 weeks showed significantly higher satiety in the whey group compared with the casein ($P=0.017$ and $P=0.025$, respectively) or control ($P=0.024$ and $P=0.032$, respectively) groups when measured before lunch. Similarly, at 6 and 12 weeks, the score for fullness was also significantly higher in the whey group compared with both casein ($P=0.038$ and $P=0.022$, respectively) and control ($P=0.020$ and $P=0.030$, respectively) groups. However, these short-term effects on satiety from dairy whey proteins did not have any long-term effects on energy intake or body weight over 12 weeks compared with casein.

CONCLUSIONS: Collectively, whey protein supplementation appears to have a positive and acute postprandial effect on satiety and fullness compared with casein and carbohydrate supplementation in overweight and obese individuals.

European Journal of Clinical Nutrition (2014) **68,** 980–986; doi:10.1038/ejcn.2014.84; published online 7 May 2014

INTRODUCTION

Dietary proteins have been shown to reduce appetite[1,2] by increasing satiety[3–6] and delaying the return of hunger[2] and subsequently lowering energy intake[1] compared with fat or carbohydrate. Some of the mechanisms proposed to explain this apparent satiety hierarchy of macronutrients are the composition of dietary proteins,[7] higher thermogenic effect[5] and post-absorptive small intestinal gluconeogenesis.[8]

Interestingly, the type of proteins ingested may also affect postprandial responses and may differ in their satiating capacity.[9] Whey proteins account for 20% of the total protein in dairy and are rich in essential amino acids,[10] whereas casein is the major protein of milk accounting for ~80% of the total protein.[10] Whey and casein are both heterogeneous groups of proteins containing all amino acids and are especially rich in the essential ones, although in different proportions.

Whey proteins contain bioactive components such as lactalbumin and branched-chain amino acids[7] which are known for having a faster rate of digestion and absorption compared with other proteins, leading to a fast peak in plasma amino acids and may contribute to their effect on satiety[9,11] and insulinotropic effect.[12–16] Insulin is thought to be a satiety hormone that elicits a net catabolic response in the brain and consequently influences food intake regulatory mechanisms.[17]

Although dairy whey and casein proteins have been shown to influence appetite, most studies suggest that whey has a greater effect in suppressing hunger and reducing subsequent food intake compared with casein. However, these proteins may not necessarily have the same effect in lean[1,2,18] and overweight/obese subjects[19] because of differences in glucose metabolism, ghrelin (Ghr) regulation[20] and eating behavior.[18] In addition, most studies showing the effects of whey and casein on satiety and energy intake have been performed during the acute, postprandial period[11,18,21] with food intake and hunger levels measured 4 h after consumption, generally, at lunch. It is unknown whether hunger would be suppressed in a later meal setting, such as dinner, ~10 h after initial consumption.

Dietary proteins that cause short-term satiety may help the body to comply better with energy reduction and maintain the lower body weight obtained after weight loss.[22] However, there are mixed results from studies examining whether the short-term satiety effects of whey can translate to a reduction in total energy intake and reduction in body weight with long-term consumption.

Given the superior effects of dairy whey protein supplementation on appetite control in healthy adults in postprandial studies, the aim of the present study was to compare the effect of dairy whey and casein protein on satiety in overweight/obese individuals over 12 weeks of supplementation compared with carbohydrate supplementation.

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Received 24 April 2013; revised 4 March 2014; accepted 4 March 2014; published online 7 May 2014

MATERIALS AND METHODS

Subjects

Overweight and obese individuals with body mass indices between 25 and 40 kg/m^2 and aged between 18 and 65 years were recruited from the community through the local newspapers and TV in Perth, Australia. Potential participants were screened by telephone and were attended personally at the Curtin University to assess their suitability for the study, at which time the details of the study were explained. Exclusion criteria included smoking, lipid-lowering medication, use of steroids and other agents that may influence lipid metabolism, use of warfarin, diabetes mellitus, hypo- and hyperthyroidism and cardiovascular events within the last 6 months. Briefly, of the 380 responses to the study advertisement, 97 were considered eligible and 89 women and men commenced the study (30 in the glucose group; 29 in the casein group; and 30 in the whey group). Seventy participants completed the 12-week study, as 19 dropped out before baseline or within 4 weeks of baseline because of noncompliance for several reasons: five because of illness, three because of travel, eight because of personal reasons unrelated to diet and three were lost to follow-up (five in the control, nine in the casein and five in the whey group). The selection criteria included both men and women; however, we had a greater number of female participants interested in the study. We decided to keep the male participants even though there was a smaller percentage of them.

The study was approved by the Curtin University Human Research Ethics Committee (approval number HR 149/2007) and all subjects gave informed consent.

Study design

This was a randomized, parallel-design study over a 12-week period with a 4-week washout period before commencement during which participants were asked to avoid consumption of dairy products in order to reduce whey and casein intake. Seventy subjects completed the 12-week study and were randomized into one of the following three groups (using a computer-generated list of random numbers from http://www.randomization.com): control group: $n=25$, 22 women and 3 men; casein group: $n=20$, 17 women and 3 men; whey protein group: $n=25$, 21 women and 4 men. Participants were blinded in regard to the type of supplement received, as supplements were controlled for taste, smell, texture, palatability and appearance. A small sensory study was performed with 10 staff members from the Curtin University before the commencement of the study. The staff members consumed the supplements and completed a sensory questionnaire, which evaluated the supplements for taste, smell, texture, palatability, acceptability and appearance. They were asked to rate these supplements as either poor, good, very good or excellent. All supplements were rated as very good and/or excellent by all staff. The silver packaging of the glucose, casein and whey protein supplements was visually identical. Patients were allocated to their groups by a research assistant (RA). The RA also distributed the supplements to the participants. The supplement sachets were numerically coded so that the RA distributing the supplements could not decode. The subjects receiving the treatments and the investigators assessing the outcomes and analyzing the data were blinded to the supplement assignment. Subjects were asked to consume one of the following coded supplement packages mixed with 250 ml water twice a day for 12 weeks: whey protein isolate, sodium caseinate (both containing 27 g protein) or glucose control (27 g glucose; MG Nutritionals, Koroit, Victoria, Australia). Glucose was chosen as the non-protein control, as it added equal calories to the daily energy intake as the two protein interventions (525 kJ per sachet). The supplementation dose used was based on previous similar studies.[9,23–25] The whey and casein content is shown in Table 1. Subjects were instructed to take one sachet within 30 min before breakfast and one within 30 min before their evening meal, and then their consumption of the sachets was recorded by marking tailored calendar tick boxes as well as by keeping empty sachets to monitor compliance. The empty (taken) and full (not taken) sachets were delivered to the RA on the day of the visits and were counted for compliance.

Food records were completed every 2 weeks of the study (weeks 2, 4, 6, 8 and 12, on two week days and one weekend day) in conjunction with analysis of the food records on FoodWorks 2007. All subjects were instructed to refrain from taking any multivitamins or herbal supplements during the study period and to limit alcohol to two or less standard drinks for men and one or less standard drinks for women, to limit any confounding metabolic effects from alcohol, following the recommendation of our NHMRC guidelines.[26] All other aspects of their dietary intake were to remain unchanged, as previous reported.[27,28] Energy expenditure was calculated from a 3-day physical activity questionnaire (short version of the self-administered International Physical Activity Questionnaire). The Harris–Benedict equation was used to estimate the basal metabolic rate of the subjects so that total energy expenditure could be calculated.

Table 1. Components of whey and casein protein supplements

Component (60 g daily intake)	*Whey protein isolate*	*Sodium caseinate*
Protein (TN × 6.38) (g)	54.0	54.3
Amino-acid profile % w/w		
Alanine	4.8	2.8
Arginine	2.0	3.8
Aspartic acid	9.3	6.8
Cystine	1.8	0.3
Glutamic acid	17.5	21.0
Glycine	1.1	1.9
Histidine[a]	1.1	2.9
Isoleucine[b]	6.8	4.8
Leucine[b]	9.5	8.2
Lysine[a]	8.5	7.1
Methionine[a]	2.3	3.0
Phenylalanine[a]	2.5	4.9
Proline	2.5	1.0
Serine	4.1	5.7
Threonine[a]	6.6	4.0
Tryptophan[a]	2.1	0.9
Tyrosine	2.6	5.5
Valine[b]	5.8	6.0
Fat (g)	0.30	0.72 g
Carbohydrate-lactose (g)	0.30	0.12
Sodium (g)	0.42	0.78
Calcium (g)	0.09	0.06
Phosphorus (g)	0.18	0.46
Moisture (g)	1.32	0.78
Ash (g)	2.20	2.20
Sweetener (sucralose) (g)	0.04	0.04
Flavoring (g)	1.80	1.80

Abbreviation: TN, total nitrogen. [a]Essential amino acids. [b]Branched-chain essential amino acids.

Assessments

Subjects were asked to come to the Curtin University for measurements in a fasted state and wearing light clothing on three occasions: at baseline, week 6 and week 12. Body weight (UM-018 Digital Scales, Tanita, Tokyo, Japan) was recorded in light clothing without shoes. Height was measured to the nearest 0.1 cm using a stadiometer (26SM 200 cm SECA, Hamburg, Germany) without shoes. Waist circumference was measured in the standing position at the narrowest area between the lateral lower rib and the iliac crest. Hip measurement was taken at the largest circumference of the lower abdomen. The average at each time point was then reported. Body fat was assessed with whole-body dual-energy X-ray absorptiometry (Lunar Prodigy; Lunar, Madison, WI, USA) as previously described.[28]

Appetite rating by Visual Analogue Scale (VAS)

Participants completed the VAS ratings of their appetite immediately before lunch and dinner ($t=0$) as previously reported[29] on three different occasions: at baseline, week 6 and week 12, representing a single measurement from each participant. VAS consisted of 100-mm lines anchored at each end with opposing statements. Participants placed an 'x' on the line to indicate their feeling at that point in time and the score was calculated by measuring the distance in millimeters from the beginning of the line to the position of the 'x' (from left to right).

A score of zero represented that the subjects were 'not full at all' and a score of 100 represented that the subjects were 'very full', with higher scores meaning more fullness. Subjective appetite was assessed using five visual scales that measured hunger, fullness and prospective food

consumption[30] through the following questions: 'How hungry do you feel?' (I have never been more hungry—I am not hungry at all), 'How satisfied do you feel?' (I am completely empty—I cannot eat another bite), 'How full do you feel?' (Not at all full—Totally full), 'How strong is your desire to eat?' (A lot—Nothing at all) and 'How much do you think you could eat now?' (A lot—Nothing at all).

Statistical analysis

A sample size of 16 participants per group was predicted to provide sufficient power (80%) at the 5% significance level to detect a 15% difference; however, we aimed to recruit 20 participants per group to accommodate for a 20% attrition rate.

Statistical analysis was undertaken using SPSS 17 for Windows (SPSS Inc, Chicago, IL, USA). Data were expressed as the means with their s.e.'s[31] and assessed for normality to ensure that the assumptions of the analysis were met. The data for appetite responses were analyzed using the General Linear Model to assess the effects of the groups after adjusting for baseline values. When significant between-group effects were present, *post hoc* comparisons were made using the Tukey's test. Analysis of variance was used to determine significant differences between dietary treatments at a given time point. Statistical significance was considered at $P < 0.05$.

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects/patients were approved by the Curtin University Human Research Ethics Committee (approval number HR 149/2007). Written informed consent was obtained from all subjects. This clinical trial has been registered with the Australian New Zealand Clinical Trials Registry. The registration number is ACTRN12609000175279, and trial Web address is http://www.ANZCTR.org.au/ACTRN12609000175279.aspx.

RESULTS

Subjects

Out of 89 men and women who were randomly assigned to either casein or whey protein supplements or control group, 70 participants completed the 12-week study (control group: $n = 25$ (11 overweight and 14 obese), casein group: $n = 20$ (7 overweight and 13 obese), whey protein group: $n = 25$ (10 overweight and 15 obese)). Characteristics of participants between the three groups at baseline were not significantly different (Table 2). All groups finished their sachets by the end of the study and intake of supplement sachets was similar in all three groups.

There were no significant differences within or between groups in body composition as assessed by body weight, body mass index, waist and hip circumference and percentage of body fat by dual-energy X-ray absorptiometry as described in Table 3 and previously reported.[28] The participants also self-reported their dietary intake by the 3-day food diaries. Briefly, there were no significant differences in total energy intake and total fat (Table 3), saturated fat, monounsaturated fat, polyunsaturated fat (data not shown) between control, casein and whey protein groups. However, at week 6, the percentage of carbohydrates in the total energy intake was significantly lower in the casein and whey groups (all $P < 0.0001$) compared with the control group. Consequently, at week 6, protein intake was significantly higher in subjects in the casein and whey groups (all $P < 0.0001$) compared with the control group.

Energy expenditure was calculated from a 3-day physical activity questionnaire (short version of the self-administered International Physical Activity Questionnaire). Results showed that there was no significant difference in physical activity between groups at 12 weeks: control group, 12 763 ± 533.4 kJ/day; whey, 11 987 ± 632.3 kJ/day; casein, 12 985 ± 527.3 kJ/day.

VAS analyses

The rating for satiety in absolute value (mm) following the question 'how satisfied do you feel?' before lunch was significantly higher in the whey group at 6 ($P = 0.25$) and 12 ($P = 0.035$) weeks of intervention compared with baseline (within group analysis).

Table 2. Subject characteristics at baseline

	Control (n = *25*)	*Casein* (n = *20*)	*Whey* (n = *25*)
Gender (female/male)	22/3	17/3	21/4
Age (years)	48.4 ± 1.5	48.0 ± 2.1	48.5 ± 2.0
Weight (kg)	84.1 ± 1.8	82.9 ± 3.1	90.5 ± 3.4
BMI (kg/m^2)	30.6 ± 0.8	31.3 ± 0.9	32.0 ± 0.8
Body fat (%)	35.4 ± 1.1	35.1 ± 2.1	37.6 ± 1.9
Waist circumference (cm)	93.7 ± 1.5	92.1 ± 2.1	95.9 ± 1.7
Waist:hip ratio	0.83 ± 0.01	0.81 ± 0.02	0.82 ± 0.01

Abbreviation: BMI, body mass index. Data are means ± s.e.m. ($n = 70$). There were no differences between the groups at baseline.

Similarly, the rating for fullness (how full do you feel?) before lunch was significantly higher in the whey group at 6 ($P = 0.008$) and 12 ($P = 0.015$) weeks of intervention compared with baseline (within group analysis; Table 4).

VAS at 6 weeks showed a significantly higher satiety in the whey group compared with the casein ($P = 0.017$) and control ($P = 0.024$) groups when measured before lunch. In addition, an increased rating of satiety in the whey group was observed compared with the casein ($P = 0.025$) and control ($P = 0.032$) groups at week 12 (Table 4 and Figure 1a). Similarly, the score for fullness was also significantly higher in the whey group compared with both casein ($P = 0.038$) and control ($P = 0.020$) groups at 6 weeks. At week 12, the score for fullness was also significantly higher in the whey group compared with both casein ($P = 0.022$) and control ($P = 0.030$) groups (Table 4 and Figure 1b). There was no effect of the three different interventions on other appetite ratings before dinner at 6 or 12 weeks.

Adverse events

The participants did not report any important harm or unintended adverse effect related to the consumption of the supplements during the time of the study.

DISCUSSION

Protein intake strongly influences satiety and energy intake[3,21,32–34] leading to a greater satiation compared with carbohydrate and fat.[6] The protein source may be a determinant of the effects of protein on satiety and fullness; however, evidence in this regard is still inconsistent.

Our study results showed that whey protein supplementation in the morning was more effective than casein or glucose (control) in significantly increasing satiety and fullness ~4 h later, just before lunch, at 6 and 12 weeks. However, this effect did not persist 10 h after consumption. In addition, we previously showed that there were no changes in energy intake and body weight with long-term consumption of whey or casein for 12 weeks in these participants.[28]

Previous studies[32] showed that both whey and soy proteins (45–50 g) but not egg protein suppressed food intake at a pizza meal consumed 1 h later in young men compared with water (control), with suppression lasting for 2 h. Moreover, a previous study of our group investigating the acute postprandial effects of four different protein meals on satiety and energy intake observed that healthy men presented a significantly lower rating of hunger with the whey meal compared with the tuna ($P = 0.033$), turkey ($P = 0.001$) and egg ($P = 0.001$) meals.[29] Whey suppressed energy intake at the *ad libitum* meal at lunch, 4 h later ($P = 0.001$), compared with the other three meals.[29] Whey protein meal also produced a greater insulin response than the other proteins. Interestingly, a postprandial study[9] observed a reduction in food intake after whey protein intake, beyond the greater satiety rating

Table 3. Changes in body composition and dietary consumption of subjects

	Baseline	*Week 6*	*Week 12*
Weight (kg)			
Control	84.1 ± 1.8	83.9 ± 1.8	83.8 ± 1.9
Casein	82.9 ± 3.1	82.1 ± 3.1	82.0 ± 3.1
Whey	90.5 ± 3.4	90.3 ± 3.8	89.7 ± 3.2
BMI (kg/m^2)			
Control	30.6 ± 0.9	30.6 ± 1.5	30.5 ± 1.5
Casein	31.3 ± 0.9	31.0 ± 0.9	30.9 ± 0.9
Whey	32.0 ± 0.8	32.0 ± 0.7	31.8 ± 0.8
Waist circumference (cm)			
Control	93.7 ± 1.5	95.1 ± 1.7	93.7 ± 1.6
Casein	92.1 ± 2.1	93.7 ± 2.6	91.2 ± 2.1
Whey	95.9 ± 1.7	97.6 ± 2.0	95.5 ± 1.9
Waist:hip ratio			
Control	0.83 ± 0.01	0.84 ± 0.01	0.84 ± 0.01
Casein	0.81 ± 0.02	0.83 ± 0.01	0.82 ± 0.02
Whey	0.82 ± 0.01	0.83 ± 0.01	0.83 ± 0.01
Body fat (%)			
Control	35.4 ± 1.1		35.1 ± 1.1
Casein	35.1 ± 2.1		34.1 ± 2.1
Whey	37.6 ± 1.9		37.6 ± 1.8
Total energy intake (kJ)[a]			
Control	7535.9 ± 373.9	7385.0 ± 1197.8	7244.9 ± 337.9
Casein	7072.6 ± 212.4	6564.7 ± 263.3	6721.9 ± 235.8
Whey	7770.4 ± 415.5	7353.2 ± 447.0	7507.0 ± 385.1
Carbohydrate % of EI			
Control	45.7 ± 1.3	50.5 ± 0.9^{*,a}	51.5 ± 1.1$^{\#,a}$
Casein	41.6 ± 1.5	37.2 ± 1.2^{*,b}	35.3 ± 1.3$^{\#,b}$
Whey	43.7 ± 1.1	36.5 ± 0.9^{*,b}	34.9 ± 1.3$^{\#,b}$
Protein intake % of EI			
Control	18.3 ± 0.7	16.4 ± 0.6^{*,a}	15.8 ± 0.7$^{\#,a}$
Casein	20.5 ± 0.8	33.4 ± 1.1^{*,b}	32.9 ± 0.8$^{\#,b}$
Whey	19.9 ± 0.8	31.3 ± 0.9^{*,b}	31.9 ± 0.8$^{\#,b}$
Fat intake % of EI			
Control	33.0 ± 1.0	31.0 ± 0.9	30.1 ± 0.9
Casein	34.9 ± 1.1	30.4 ± 1.1	29.3 ± 1.0
Whey	33.7 ± 1.1	31.4 ± 1.0	29.7 ± 0.9

Abbreviations: BMI, body mass index; EI, energy intake. Data are means ± s.e.m. (control $n = 25$, casein $n = 20$, whey $n = 25$, total $n = 70$). Dietary data were recorded from the 3-day food diaries.[28] Significant difference ($P < 0.001$) between groups at 6 and 12 weeks is indicated by different letters. $^{*}P < 0.001$ within groups (baseline versus 6 weeks). $^{\#}P < 0.001$ within groups (baseline versus 12 weeks). [a]1 kcal = 4.186 kJ.

compared with casein protein. However, other studies have found no differences in either appetite or food intake when comparing whey with casein and lactose,[23] or whey protein versus maltodextrin.[35] In a recently published review,[19] we observed that the effects of whey protein on satiety and energy intake could be related to the body weight of participants, as ~50 g of whey protein seems to suppress hunger in lean[3,25,32,36] but not in overweight/obese individuals.[12–14]

The short-term effects of whey protein on satiety do not appear to have any effect on energy intake and body composition over 12 weeks.[28] The body of evidence from studies of dietary protein on hunger and satiety suggests that high-protein meals have the potential to suppress hunger to a greater degree and result in enhanced sensations of satiety.[37] However, most studies have not controlled for dietary factors other than proteins that have the potential to influence hunger and satiety, including fiber and fat content, glycemic index, energy density, variety and palatability.[37] Although our study has been controlled for those confounding factors, we observed no difference on body weight and energy intake.[28] A study by Stubbs *et al.*,[38] one of the most tightly controlled for dietary factors, identified a greater satiety effect of protein but noted no difference in subsequent energy intake. This result is important as much attention has been given to high-protein diets in weight management.[3,6,37]

According to a recent review,[39] some other studies have explored the relationship between dairy product consumption and alterations in body weight and fat mass in overweight and obese populations during energy restriction.[36,40–43] Two studies[41,42] demonstrated that high-dairy diets promote greater weight and fat loss, whereas three other studies showed no evidence that a diet high in dairy products enhanced weight loss by overweight and obese individuals during periods of energy restriction.[36,40,43] Whey and casein similarly affected body weight and fat in healthy subjects who underwent a 5- to 6-week energy restriction period followed by a weight maintenance period of 12 weeks, receiving maltodextrin (HC group) or protein (HP group) (casein (HPC subgroup) or whey (HPW subgroup)) supplements (2 × 25 g per day).[44] Subjects in both the HP diet groups showed significantly better weight maintenance after weight loss (−2.3 kg difference, $P = 0.04$) and fat mass reduction (−2.2 kg difference, $P = 0.02$) compared with subjects in the HC control group. Although these results suggest that low-fat high-casein/whey protein diets are more effective for weight control than low-fat HC diets, there appears to be no difference in the type of protein used.[44] The driving mechanisms in such weight loss trials may be due to changes in satiety related to high-protein diets; however, satiety levels were not measured.[44] Whey and casein seem to have a similar effect on body weight, as a lack of differences in body weight between whey and casein groups has been shown in previous studies.[28,44,45]

The differential acute effects of casein and whey on satiety at lunch may be related to their digestive properties and in accordance with the denomination of whey as 'fast protein' and casein as 'slow protein'.[11] Whey seems to have a stronger effect on short-term food intake in humans compared with casein, soy protein and egg albumin.[32] Consumption of whey (0.45 g/kg body weight) leads to a fast, but sudden and provisory, increase in plasma amino acids that peaks in 40 min to 2 h after ingestion and returns to baseline values 3–4 h later. Evidence shows that whey proteins reach the jejunum as intact proteins, and their peptides are slowly hydrolyzed in the small intestine. Compared with other proteins, whey is digested and absorbed over a greater length of the intestine,[11,46] whereas casein has been shown to have slower gastric emptying that results in a slower and lower increase in plasma amino-acid concentrations.[11,47]

The beneficial effects of whey on satiety and fullness may also be related to its amino-acid content. Whey supplement used in this study had higher amount of tryptophan compared with casein supplement (Table 1), which has been shown to have a potent effect on suppressing appetite.[48] Whey proteins also contain high concentrations of branched-chain amino acids[7] such as leucine, isoleucine, valine, lysine and threonine, which seem to have a faster rate of digestion and absorption than other proteins, such as casein, leading to a rapid peak in essential plasma amino acids[14] that might contribute to their effect on satiety[9,11] and insulinotropic effect.[12,14–16,49] Although whey and casein proteins contain several common and essential amino acids, in the present study the differences in appetite 4 h after consumption (before lunch) between the two diet protein supplements may be related to the proportion of their amino-acid content.

Despite the long-term consumption of whey protein over 12 weeks, ingestion of whey supplement at breakfast only seemed

Table 4. Sensations of appetite measured by the Visual Analogue Scales in overweight/obese and control subjects

Groups	*Before lunch*			*Before dinner*		
	Baseline	*Week 6*	*Week 12*	*Baseline*	*Week 6*	*Week 12*
How hungry do you feel?						
Control	58.0 ± 2.9	53.7 ± 4.0	59.0 ± 3.7	69.6 ± 2.4	58.8 ± 4.3	55.4 ± 4.1
Casein	55.9 ± 4.0	56.4 ± 3.9	55.8 ± 3.4	61.7 ± 3.5	53.9 ± 4.1	57.9 ± 4.1
Whey	57.8 ± 4.1	58.4 ± 3.1	64.0 ± 3.1	63.8 ± 3.2	62.8 ± 3.3	59.9 ± 3.3
How satisfied do you feel?						
Control	55.0 ± 3.3	50.1 ± 4.0[a]	54.6 ± 4.3[a]	61.3 ± 3.7	57.6 ± 4.6	52.4 ± 4.4
Casein	55.5 ± 3.3	53.9 ± 4.6[a]	52.3 ± 3.7[a]	53.2 ± 4.0	52.0 ± 4.1	51.2 ± 4.1
Whey	53.4 ± 3.2	64.7 ± 3.5[b,*]	62.8 ± 3.0[b,*]	57.0 ± 3.3	56.3 ± 4.0	56.9 ± 3.2
How full do you feel?						
Control	57.7 ± 3.3	51.4 ± 4.6[a]	56.7 ± 3.9[a]	62.3 ± 3.7	59.5 ± 4.9	53.6 ± 4.7
Casein	54.7 ± 3.7	58.8 ± 4.0[a]	52.3 ± 3.6[a]	53.7 ± 4.4	51.8 ± 4.2	50.2 ± 4.4
Whey	49.2 ± 4.8	66.5 ± 2.9[b,*]	62.8 ± 3.2[b,*]	51.3 ± 3.8	58.7 ± 4.4	57.3 ± 2.9
How strong is your desire to eat?						
Control	57.8 ± 4.0	49.9 ± 4.1	57.6 ± 4.0	62.8 ± 5.2	55.1 ± 4.9	51.0 ± 4.6
Casein	55.1 ± 5.4	52.1 ± 4.8	59.7 ± 4.1	56.8 ± 5.4	55.5 ± 4.6	47.3 ± 4.8
Whey	55.2 ± 4.6	57.3 ± 3.7	64.7 ± 3.4	60.2 ± 4.8	58.6 ± 4.2	55.4 ± 3.2
How much do you think you could eat now?						
Control	51.8 ± 3.9	47.2 ± 3.9	54.1 ± 3.9	56.0 ± 4.1	45.6 ± 4.6	51.4 ± 4.5
Casein	55.3 ± 4.6	51.0 ± 4.8	48.5 ± 4.1	53.9 ± 5.2	45.7 ± 4.5	49.7 ± 4.8
Whey	52.9 ± 4.4	55.9 ± 2.6	60.2 ± 3.1	58.4 ± 5.1	56.1 ± 4.2	55.8 ± 4.3

Data are means ± s.e.m. (control $n = 25$; casein $n = 20$; whey $n = 25$) of various questions of the absolute values (mm) from the VAS (Visual Analogue Scale) at baseline, week 6 and week 12. Statistical significance between groups is indicated by different letters at $P < 0.05$. *Indicates within group significant difference from baseline. Data were analyzed using the general linear model and difference was assessed by the Tukey's test.

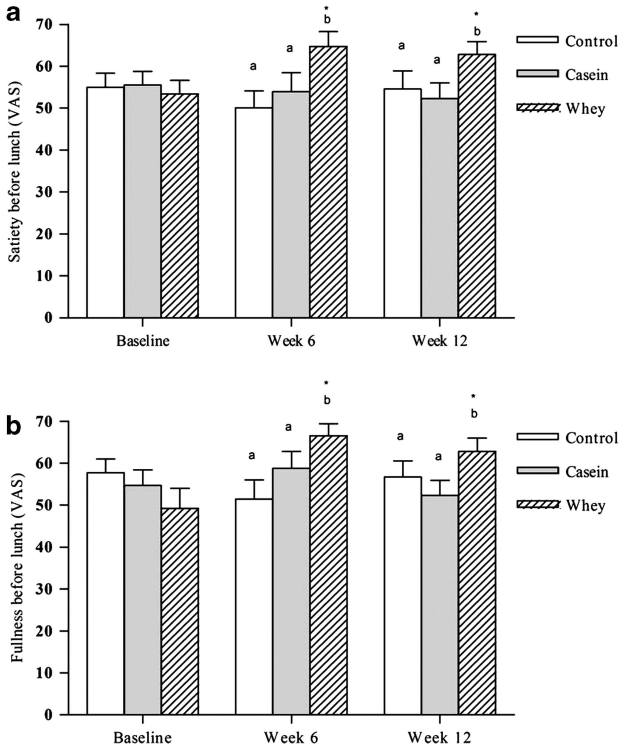

Figure 1. Self-report information from the VAS. (**a**) Response rating for the question: *How satisfied do you feel (before lunch)?* (**b**) Response rating for the question: *How full do you feel (before lunch)?* Data are means ± s.e.m.; statistical significance between groups is indicated by different letters at $P < 0.05$. *Indicates within group significant difference from baseline.

to affect satiety before lunch (4 h after consumption) and did not carry over to the dinner meal 10 h later. The acute effect of whey on satiety may also be partially explained by its influence on short-lived satiety hormones, which suppress appetite in the post-prandial period and shortly thereafter and is the likely mechanism by which whey exerts its satiety effects. Several anorexigenic hormones in the gut that are known to increase satiety (glucose-dependent insulinotropic polypeptide, glucagon-like peptide-1, cholecystokinine, peptide YY[9,13–15] and inhibititing Ghr[50,51]) seem to be stimulated by whey proteins; however, studies in this area are still conflicting. Studies have found milk proteins to increase cholecystokinine concentrations in plasma, peaking initially at 15–20 min, then falling and increasing again to ~ 90 min.[9,25] Whey protein has been found to increase cholecystokinine more than casein in some studies[9] but not others.[25] Human studies found consumption of whey protein rather than casein to greatly increase plasma concentrations of glucagon-like peptide-1 for up to 3 h.[9] The orexigenic gut hormone Ghr[24] is released into circulation and reaches a peak concentration immediately before meals. Ghr is suppressed by food ingestion,[52] and by whey protein isolate[23] and calcium caseinate in humans only over 3 h;[25] this effect was related with a major decrease in subsequent food intake.[25] Collectively, there appears to be no carry over effect at dinner time from the morning supplement or from long-term consumption of whey protein for 12 weeks.

The effect of whey on satiety and fullness may be related to its effect on postprandial insulin secretion. Insulin is thought to be a satiety hormone, with increased insulin levels in the brain eliciting a net catabolic response influencing food intake regulatory mechanisms.[17] Studies suggest that the sources of proteins may stimulate insulin release differentially[51] as well as the rate at which the amino acids are released during digestion and absorbed into the circulation.[51] Milk products have been shown to be powerful acute stimulants of insulin secretion[16] and insulin response.[53]

Although whey protein induces marked short increases in plasma amino acids, which act as direct insulin secretagogues,[8,15] enhancing insulin response,[54] casein also leads to a slower prolonged increase in amino-acid concentrations; however, plasma insulin concentrations were not different between the two meals.[11] Whey protein also stimulates incretin release[55] necessary for insulin-mediated amino-acid uptake into cells, which may also explain its effect on satiety. Incretins are gut-derived hormones that are secreted in response to oral ingestion of nutrients and enhance insulin secretion by stimulation of specific receptors on the β cells. Whey proteins may be acting through the two major incretin hormones, glucagon-like peptide-1 and glucose-dependent insulinotropic polypeptide, which are both important insulinotropic intestinal peptide messengers.[56] Despite the favorable effects of whey on satiety in humans observed in the majority of the studies, the mechanism by which whey act remains unclear.

Energy intake was underestimated by the participants, as the instruments available to estimate self-reported energy intake (24-h food record, food frequency questionnaire are 3-day dairy record) are not very reliable. The difference between calculated total energy expenditure and measured energy intake is as large as 4000–6000 kJ. As the body weight of the subjects did not change, this major difference between intake and expenditure can only be explained by a too-low reported energy intake. The literature suggests that 10–54% of people in the most diverse groups (independent of age, gender, ethnicity and socioeconomic background) under-report their food intake.[57–63] Our study did not investigate the postprandial amino-acid profiles and satiety hormone responses, which may have provided greater insights into the effects of whey protein on appetite suppression when compared with casein and glucose-supplemented diets. In addition, it is unclear whether the effects of liquid protein on appetite and energy intake would be similar if solid forms of food were used instead. Future studies should explore whether these findings can be extrapolated to whole foods rather than to liquids. Participant's body weight should also be taken into consideration when investigating satiating effects in humans.

Collectively, whey protein supplementation appears to have a positive and acute postprandial effect on satiety and fullness compared with casein and carbohydrate supplementation in overweight and obese individuals.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

This trial was funded by the Dairy Australia.

DISCLAIMER

Dairy Australia has not participated in the study design, data collection and analysis or in the preparation of the manuscript and the decision to publish it.

AUTHOR CONTRIBUTIONS

SP conceived and designed the study, supervised the study and the statistical analysis, and mentored the script. SR-B had input into the writing and reviewing of the manuscript. VE coordinated the trial, conducted data collection and statistical analysis, and provided input in the manuscript.

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