Nutrition 28 (2012) 35–39

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Applied nutritional investigation

# Fuel selection and appetite-regulating hormones after intake of a soy protein-based meal replacement

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ARTICLE INFO

*Article history:*
Received 10 September 2010
Accepted 11 February 2011

*Keywords:*
Obesity
Meal replacement
Weight loss
Metabolic syndrome
Fat oxidation

ABSTRACT

*Objective:* The present study investigated the postprandial glycemic and insulinemic responses, the levels of satiety-related proteins, and substrate use after a single dose of a meal replacement (MR) with a high soy protein content and a low glycemic index (GI). The results were compared with a standardized breakfast showing a high GI and a low protein content.

*Methods:* Eleven overweight or obese male subjects with the metabolic syndrome and insulin resistance were included in the study. In the morning, each subject consumed, in a randomized design, 65 g of a MR or an isocaloric standardized breakfast. Four hours after breakfast, all subjects consumed the same standardized lunch. Blood levels of glucose, insulin, ghrelin, protein YY(PYY), oxygen uptake, and carbon dioxide production were determined and the respiratory quotient and substrate use were calculated.

*Results:* The glycemic and insulinemic responses were considerably higher after the standardized breakfast. In addition, in these obese insulin-resistant subjects, the postprandial decease in fat oxidation was significantly less pronounced after intake of the MR. This effect was also detectable after lunch in terms of a second meal effect. Ghrelin levels were significantly lower 2 h after the intake of the MR and PYY levels tended higher.

*Conclusion:* Compared with the high GI/low-protein SB, a high soy protein MR with a low GI was associated with lower glycemia and insulinemia and relatively higher fat oxidation in the postprandial period. Together with a favorable course of appetite-regulating hormones, this could further help to explain the beneficial role of MR regimines high in soy protein for weight reduction and improvement of metabolic risk factors.



## Introduction

Therapeutic lifestyle changes are an effective treatment strategy against the increasing epidemic of obesity, the metabolic syndrome, and type 2 diabetes [1–3]. Among dietary interventions, meal replacement (MR) regimines have shown to be safe and appropriate for the induction and maintenance of weight loss [4–6]. Moreover, MRs have been associated with a rapid improvement in metabolic risk factors, mainly increased insulin sensitivity [7,8].

Several investigations have shown that dietary interventions with a low glycemic index (GI) are successful for the prevention and treatment of insulin resistance and other components of the metabolic syndrome [9–11]. In part, this could be explained by a lower postprandial insulin response; high postprandial insulin levels inhibit lipolysis and switch energy consumption toward glucose use [12,13]. It has been proposed that lower lipolysis and decreased fatty acid use would favor extra adipocyte lipid accumulation and thus insulin resistance [14,15]. In addition, there is evidence that higher fat oxidation is responsible for improved weight loss and long-term weight control [16]. Furthermore, it has been hypothesized that a lower insulin response would prolong satiety and fullness [17,18].

In the present study we investigated the postprandial glycemic and insulinemic responses after a single dose of an MR high in soy protein and a low GI. In addition, we used indirect calorimetry to measure postprandial fat oxidation. The metabolic response of this MR was compared with a high-glycemic low-protein standardized breakfast (SB) consisting of white toast with jam and fruit juice. Four hours after the start of the investigation, subjects consumed a standardized lunch to investigate the presence of a second meal effect. In addition, concentrations

This study was supported in part by Almased Wellness Corporation.
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doi:10.1016/j.nut.2011.02.008

**Table 1**
Baseline anthropometric characteristics and metabolic risk factors of subjects investigated*

| | |
|---|---|
| Age (y) | 56.4 ± 4.9 |
| Height (cm) | 180 ± 9.1 |
| Weight (kg) | 102 ± 11.9 |
| BMI (kg/m$^2$) | 31.6 ± 2.6 |
| Waist circumference (cm) | 113 ± 5.5 |
| Total cholesterol (mg/dL) | 201 ± 47.6 |
| Triacylglycerols (mg/dL) | 193 ± 148 |
| HDL cholesterol (mg/dL) | 49.6 ± 14.6 |
| LDL cholesterol (mg/dL) | 117 ± 31.1 |
| Systolic BP (mmHg) | 148 ± 18.3 |
| Diastolic BP (mmHg) | 95.1 ± 7.9 |
| Glucose (mg/dL) | 111 ± 20,7 |
| Insulin (pmol/L) | 165 ± 108 |
| HOMA-IR | 3.10 ± 1.3 |

BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment for insulin resistance; LDL, low-density lipoprotein

* Values presented as mean ± SD.

of satiety related proteins protein YY(PYY) and ghrelin were determined. Of special interest was whether the assumed decrease in postprandial insulinemia and glycemia with concomitantly increased fat oxidation was also present in obese subjects with the metabolic syndrome and insulin resistance.

### Materials and methods

Eleven male overweight or obese subjects 52 to 63 y old were enrolled in the investigation. All subjects completed a comprehensive medical examination and routine blood testing. Anthropometric data and baseline laboratory data are listed in Table 1. Subjects were included if they were free from acute diseases, fulfilled the criteria of the metabolic syndrome, and were insulin resistant according to the homeostasis model assessment index (insulin [microunits/milliliter] × blood sugar [milligrams/deciliter]/405) higher than 2.5. None of the subjects took an oral antidiabetic medication or insulin. Written informed consent was given by all subjects; the study protocol was approved by the ethical committee of the University of Freiburg.

In the morning at 8 o'clock after an overnight fast (12 h), each subject consumed, in a randomized design, 65 g (230 kcal) of an MR (high soy protein/low carbohydrate/low GI; total protein 34.6 g; soy protein 28.7 g; carbohydrate 19.8 g; fat 1.3 g) dissolved in 280 mL of water and 19 mL of linseed oil (170 kcal) or (after an interval of ≥3 d) an SB (low protein/high carbohydrate/high GI) consisting of 300 mL of skim milk (140 kcal), 50 g of jelly, and one bread roll (135 kcal). Thus, each time subjects consumed 400 kcal in the morning. The main difference was in the protein and carbohydrate contents and the GI of the test meals. The GIs of the MR and SB were tested according to the World Health Organization/FAO (Food and Agriculture Organization) protocol in healthy subjects and were 23 for the MR and 76 for the SB. Four hours after the start of the investigation, subjects consumed a standardized lunch (4 mini pizzas: 996 kcal, 40 g of protein, 208 g of carbohydrates, 44.4 g of fat; an apple; and a 150-mL glass of water).

Figure 1 shows the time flow of the investigation and the times when respective parameters were investigated. At each point in time, blood levels of glucose and insulin, oxygen uptake, and carbon dioxide production (ZAN 600 CPET, nSpire, Oberthulba, Germany) were determined. At baseline and every 2 h, blood levels of ghrelin and PYY were measured (enzyme-linked immunosorbent assay; BioVendor Laboratory Medicine, Heidelberg, Germany). The ratio of carbon dioxide production to oxygen consumption (respiratory quotient) was calculated, and resting energy expenditure was determined according the equation of Weir [19]; from the respiratory quotient and resting energy expenditure, fat oxidation was assessed.

#### *Statistical methods*

Statistical analysis was performed using SPSS 17.0 for Windows (SPSS, Inc., Chicago, IL, USA). Testing for changes between the two test meals was done by Wilcoxon rank-sum test; $P \leq 0.05$ was considered statistically significant.

## Results

The physical characteristics and the metabolic risk factors of subjects are listed in Table 1. All subjects were overweight or obese and fulfilled the Adult Treatment Panel III criteria for the metabolic syndrome.

In the first 2 h after breakfast, glucose levels (Fig. 2A) were significantly lower after the intake of the MR at most time points. Also, the area under the curve (AUC) for glucose (Fig. 2B) was significantly lower in the first 4 h after breakfast. After lunch, glucose concentrations increased comparably during the first postprandial hour but were significantly lower at 330 and 360 min. Because of this dichotomy in the course of glucose concentrations after lunch, the AUC was not different for the postprandial period after lunch or for the entire length of the investigation.

After the intake of the MR, insulin levels were lower at most time points of the examination; also, in the postprandial phase after lunch, insulin concentrations were still lower until 330 min, although the lunch was identical (Fig. 3). The AUC for insulin was also significantly lower after the MR intake in all time segments.

The inhibition of fat oxidation in the postprandial state was more pronounced after intake of the SB than after the MR (Fig. 4A). A relatively higher fat oxidation was also observed after lunch. Figure 4B shows that the AUC for fat oxidation was decreased significantly less after the SR than after the MR intake at all intervals.

The decrease in ghrelin concentration was significantly higher 120 min after breakfast (Fig. 5A) in the MR group. The decrease in ghrelin after lunch was identical in the two groups.

The PYY levels were not significantly different between groups, although a trend existed for higher levels throughout the investigation period in the MR group.

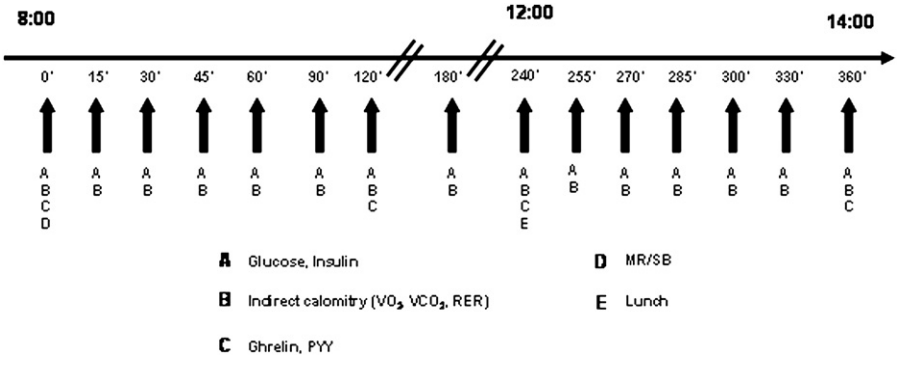


**Fig. 1.** Time flow of blood sampling and determination of $VO_2$ and $VCO_2$. MR, meal replacement; PYY, protein YY; RER, respiratory exchange ration; SB, standardized breakfast; $VCO_2$, carbon dioxide production; $VO_2$, oxygen uptake.

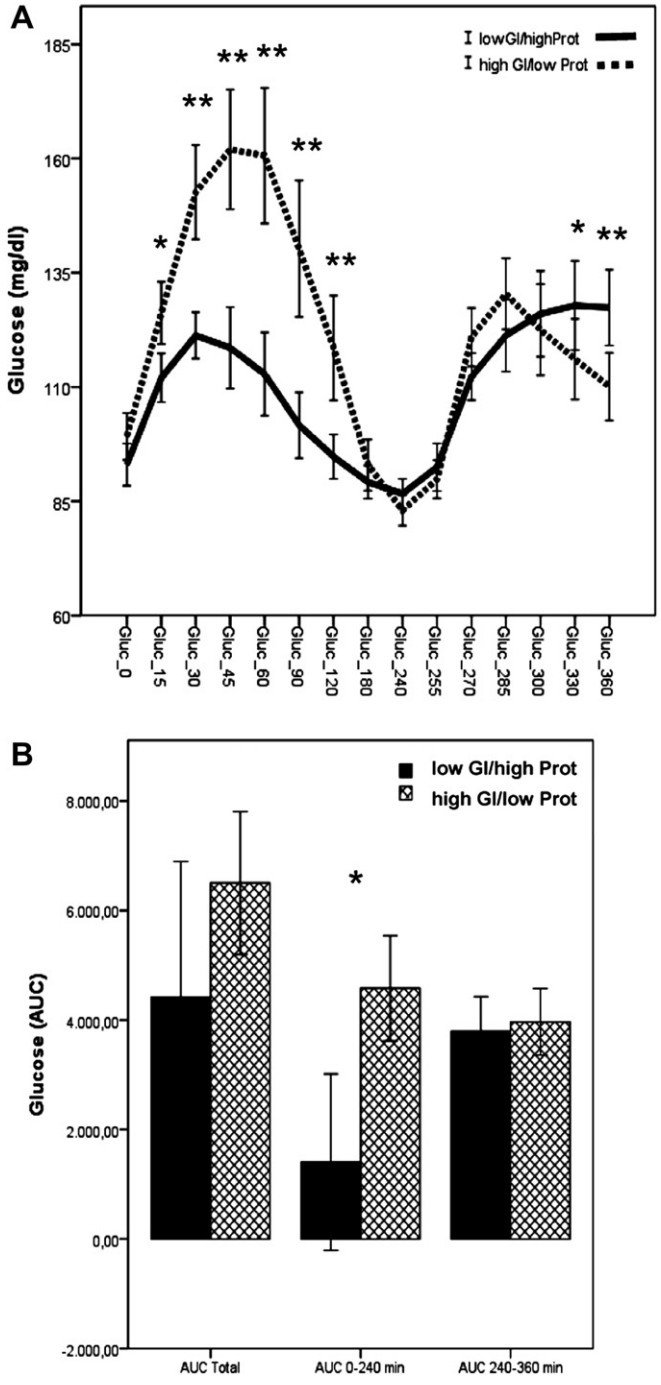


**Fig. 2.** (A) Glucose levels after the two different breakfast meals (solid line, meal replacement with a low GI and high protein content; dotted line, standardized breakfast with a high GI and low protein content) and the lunch after 240 min. Numbers at bottom indicate the time in minutes after the start of the investigation. (B) AUC for glucose for the entire examination period (AUC Total), the period before lunch (AUC 0–240 min), and the period after lunch (AUC 240–360 min); meals (solid bars, meal replacement with a low GI and high protein content; hatched bars, standardized breakfast with a high GI and low protein content). * $P < 0.05$; ** $P < 0.01$. AUC, area under the curve; Gluc, glucose; GI, glycemic index; Prot, protein.

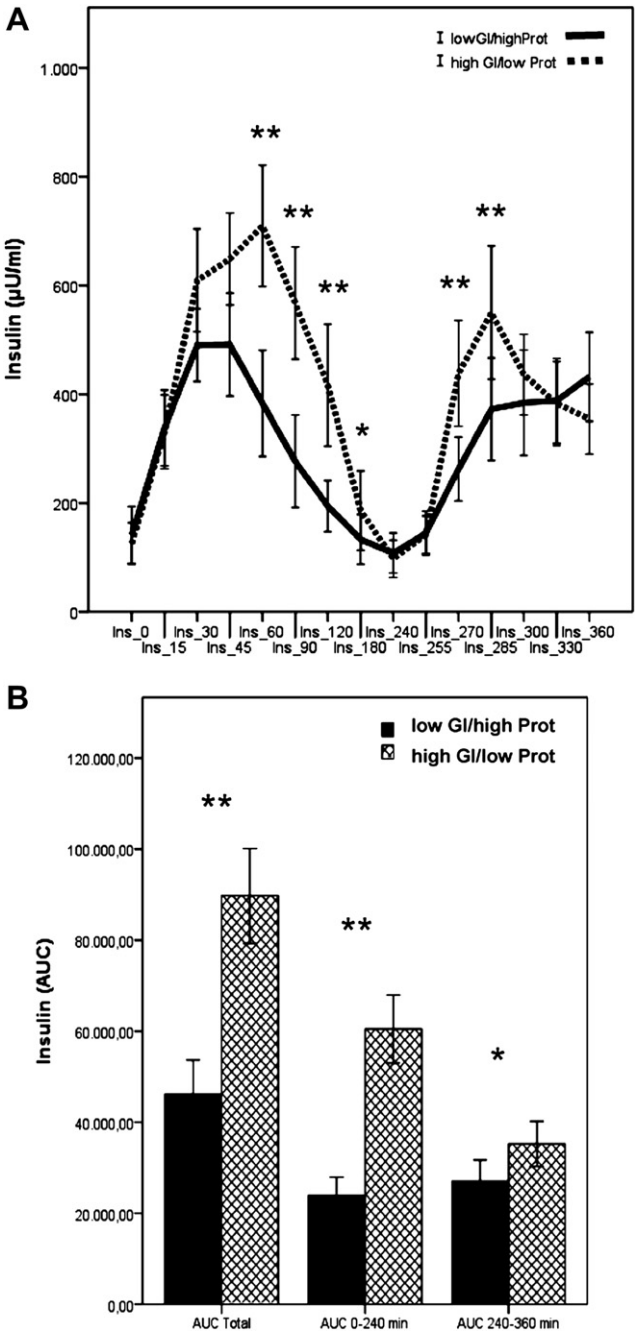


**Fig. 3.** (A) Insulin levels after the two different breakfast meals (solid line, meal replacement with a low GI and high protein content; dotted line, standardized breakfast with a high GI and low protein content), and the lunch after 240 min. Numbers at bottom indicate the time in minutes after the start of the investigation. (B) AUC for insulin for the entire examination period (AUC Total), the period before lunch (AUC 0–240 min), and the period after lunch (AUC 240–360 min); meals (solid bars, meal replacement with a low GI and high protein content; hatched bars, standardized breakfast with a high GI and low protein content). * $P < 0.05$; ** $P < 0.01$. AUC, area under the curve; GI, glycemic index; Ins, insulin; Prot, protein.

## Discussion

The most important finding of the present investigation was that, in obese insulin-resistant subjects, fat oxidation was significantly higher after the intake of an MR with a low GI and high soy protein content compared with an SB with a high GI and low protein content. This effect was also detectable after lunch in terms of a second meal effect.

From the difference in glucose and insulin levels depending on the type of breakfast, it is very likely that the lower insulin

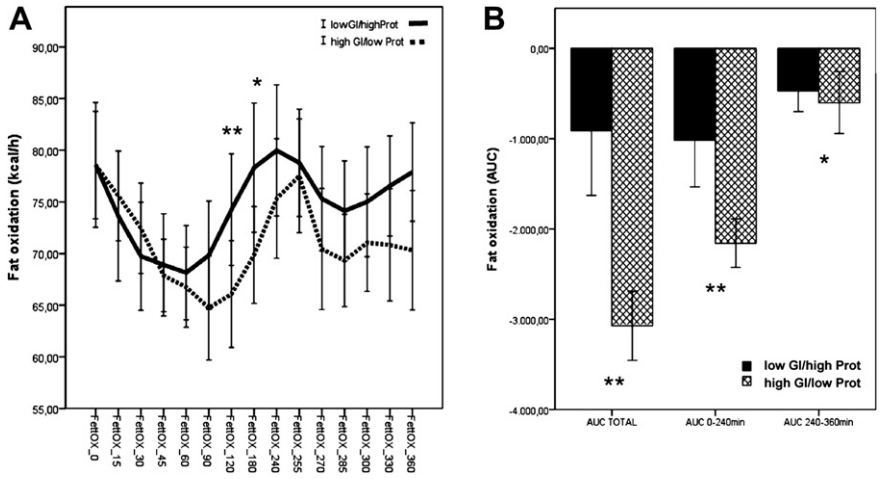


**Fig. 4.** (A) Fat oxidation after the two different breakfast meals (solid line, meal replacement with a low GI and high protein content; dotted line, standardized breakfast with a high GI and low protein content), and the lunch after 240 min. Numbers at bottom indicate the time in minutes after the start of the investigation. (B) AUC for fat oxidation for the entire examination period (AUC Total), the period before lunch (AUC 0–240 min), and the period after lunch (AUC 240–360 min); meals (solid bars, meal replacement MR with a low GI and high protein content; hatched bars, standardized breakfast with a high GI and low protein content). $^{*}$ $P < 0.05$; $^{**}$ $P < 0.01$. AUC, area under the curve; FettOX, fat oxidation; GI, glycemic index; Prot, protein.

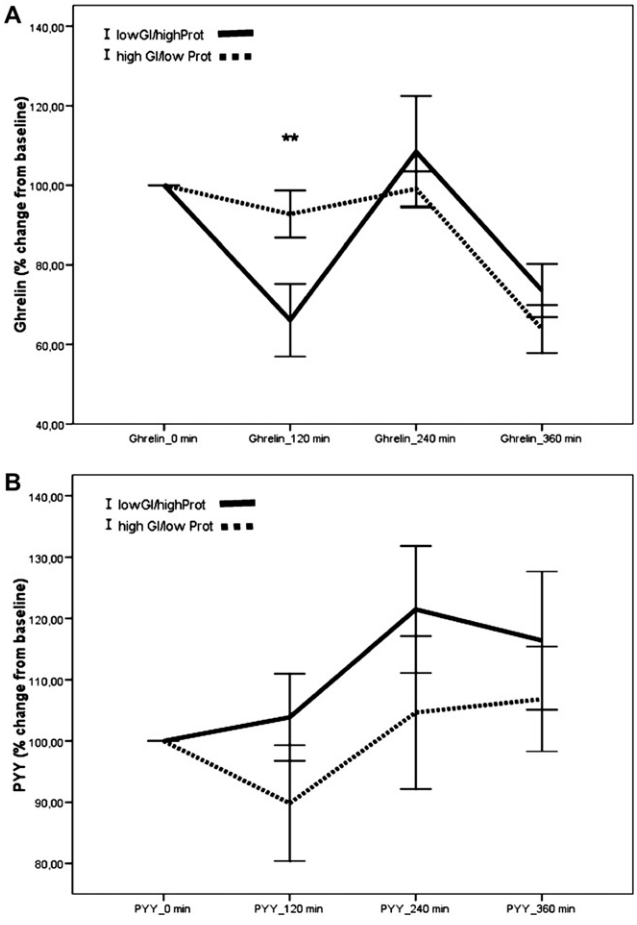


**Fig. 5.** Changes in (A) ghrelin and (B) PYY levels after the two different breakfast meals (solid line, meal replacement with a low GI and high protein content; dotted line, standardized breakfast with a high GI and low protein content), and the lunch after 240 min. * = $P < .05$; ** = $P < .01$. GI, glycemic index; Prot, protein; PYY, protein YY.

concentrations are responsible for the higher fat oxidation after the MR [20]. It has been speculated that fat transport across the cell membrane is increased and fat oxidation is decreased in obese subjects and particularly in those with the metabolic syndrome [21,22]. Although the hypothesis is not supported by all findings, there is evidence that the decreased fat oxidation is responsible for intracellular fat accumulation, lipo-toxicity, and eventually for insulin resistance [12,14,23–25]. Therefore, it could be speculated that the increased fat oxidation after the intake of an MR could account not only for better weight loss but also for the observed rapid improvement in metabolic risk factors [7,26].

In addition, the results demonstrate that in insulin-resistant subjects, the amount of fat oxidation can be influenced by the GI and insulinemic index of a meal. Although the role and importance of the GI in daily nutrition is still under debate, more studies have demonstrated its role in the pathogenesis and prevalence of the metabolic syndrome [11]. The low GI and insulinemic index of the MR (soy–yogurt–honey preparation) is mainly determined by the amino acid pattern, but the isoflavones genistein and daidzein have also been shown to contribute to the lower pancreatic insulin secretion and the lower expression of transcription factors associated with lipo-toxicity such as sterol regulatory element binding protein-1 [21,27].

Another important aspect that has been described by some investigators concerns the greater and longer satiety after the intake of a protein-based MR with a low GI [17]. We found that ghrelin concentrations were significantly lower 2 h after intake of the MR compared with the SB. After lunch, the decrease in ghrelin levels was almost identical. The reason for the greater decrease in ghrelin after the MR cannot be answered conclusively. In some investigations, ghrelin levels have been correlated with insulin levels, whereas others could not establish such a relation [28]. Data regarding how far the amino acid composition could have influenced the postprandial course of ghrelin and PYY are still lacking. Nevertheless, the significantly greater decrease in ghrelin levels and the trend toward higher PYY concentrations in the postprandial period likely contribute to the greater and longer satiety found after the intake of MRs [17].

It should be mentioned, however, that the number of subjects investigated was rather small. The results need to be reproduced in a larger cohort and in subjects differing in age, body mass index, and gender.

In conclusion, compared with the high GI/low protein SB, a high soy protein MR with a low GI was associated with lower glycemia and insulinemia and a relatively higher fat oxidation in the postprandial period. Together with a favorable course of appetite-regulating hormones, this could further explain the success of this MR regimine for weight reduction and improvement of metabolic risk factors.

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