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Applied nutritional investigation

Postprandial substrate use in overweight subjects with the metabolic syndrome after isomaltulose (Palatinose™) ingestion

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ABSTRACT

Objective: Dietary interventions with a low glycemic index have shown to be successful for the prevention and therapy of the metabolic syndrome. In the present study, we investigated the postprandial metabolic response at rest and during physical activity the low glycemic carbohydrate isomaltulose (Palatinose™) intake compared with a conventional carbohydrate (glucose syrup/sucrose [glc/suc]) with a higher glycemic index.

Methods: Twenty overweight or obese men (32–64 y old) with the metabolic syndrome and insulin resistance were enrolled in this double-blinded, randomized, cross-over study. In the morning, a breakfast consisting of a 250-mL drink and 140 g of cookies containing in a total of 50 g of Palatinose™ or glc/suc was consumed. Two hours after breakfast, subjects exercised at moderate intensity on a treadmill for 30 min. Thereafter, subjects ingested a standardized lunch consisting of a 250-mL drink with 10% Palatinose™ or glc/suc, mini pizzas, and an apple.

Results: Blood levels of glucose and insulin were measured and the postprandial substrate metabolism was determined. The glycemic and insulinemic responses were considerably lower after the ingestion of Palatinose™ (incremental area under the curve, $P < 0.05$). The total fat oxidation was significantly higher with Palatinose™ from breakfast to the beginning of lunch including the exercise and postexercise periods ($P < 0.05$). Fat oxidation with Palatinose™ was numerically higher throughout the entire examination period ($P = 0.09$).

Conclusion: In obese subjects with insulin resistance and the metabolic syndrome, the partial substitution of carbohydrates with a higher glycemic index in foods and drinks by Palatinose™ resulted in greater postprandial fat oxidation at rest and during physical activity. It is hypothesized that this increased fat oxidation may confer further benefits for long-term weight management and for an improvement in metabolic risk factors.

Introduction

Postprandial substrate use influences key metabolic factors such as whole-body energy balance, body composition, aerobic energy provision, and endurance performance. Carbohydrates and fats are the most important energy sources at rest and during exercise [1–4] and the organism has a distinct metabolic flexibility to switch between fat and carbohydrate use [3,5]. A major regulatory factor for substrate use is the presence or relative preponderance of one energy source over the other. Another pathway consists of the modulation of the glycemic index (GI) in the diet. Fat oxidation has been shown to increase after the consumption of foods with a low GI compared with a meal with a high GI [6–10].

Several investigations have demonstrated that dietary interventions with a low GI are successful for the prevention and therapy of insulin resistance and other components of the metabolic syndrome [11–13]. In part, this could be explained by a lower postprandial insulin response because high postprandial insulin levels inhibit lipolysis and switch energy consumption toward an increased carbohydrate use [8,14,15]. It has been proposed that a lower lipolysis and a decrease fatty acid use would favor extra adipocyte lipid accumulation and thus insulin resistance [16,17]. In addition, there is evidence that greater fat oxidation is responsible for an improved weight loss and

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Table 1
Anthropometric characteristics and laboratory findings in investigated subjects

Age (y)	50.7 ± 9.8
Height (cm)	179 ± 8.62
Weight (kg)	102 ± 15.1
BMI (kg/m^2)	32.1 ± 3.3
Waist circumference (cm)	112 ± 9.7
Total cholesterol (mg/dL)	201 ± 33.2
Triacylglycerol (mg/dL)	217 ± 144
HDL cholesterol (mg/dL)	46.2 ± 12.1
LDL cholesterol (mg/dL)	118 ± 23.4
SBP (mmHg)	149 ± 19.3
DBP (mmHg)	96.1 ± 8.2
Glucose (mg/dL)	105 ± 15.1
Insulin (μU/mL)	24.1 ± 17.6
HOMA-IR	6.23 ± 4.58

BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment for insulin resistance; LDL, low-density lipoprotein; SBP, systolic blood pressure
Values are presented as mean ± SD

long-term weight control [18]. Furthermore, it has been hypothesized that a lower insulin response would prolong satiety and fullness [19,20].

In the present study, we investigated the postprandial metabolic response after an intake of breakfast and lunch that contained 50 g of the low GI carbohydrate isomaltulose (Palatinose™) or a combination of glucose syrup and sucrose (1:1; glc/suc) with a higher GI and load, respectively.

Isomaltulose (Palatinose™) is a disaccharide with glucose and fructose linked by an α-1,6-glycosidic bond. The low GI of Palatinose™ of 32 [21] results from the slow hydrolysis of the α-1,6-glycosidic bond by the sucrase–isomaltase complex situated on the brush border membrane of the small intestinal cells [22]. Therefore, the rate of absorption of Palatinose™ is rather slow. Nevertheless, after hydrolysis, the resulting monosaccharides glucose and fructose are efficiently taken up, and it has been shown that Palatinose™ is a fully digestible carbohydrate [23]. In the present investigation, the most important target value was the postprandial and exercise-related substrate use, mainly the oxidation of fatty acids, as measured by indirect calorimetry. Compared with previous studies, we investigated the respective parameters in insulin-resistant subjects with the metabolic syndrome at rest and during moderate physical activity. The scientific background for this selection is based on various investigations suggesting that fat oxidation is impaired in insulin-resistant subjects, implying that interventions targeted to alter substrate use would be particularly important in this group as a risk panel for the development of, e.g., diabetes mellitus and cardiovascular diseases.

Materials and methods

The study was performed using a double-blinded, randomized, cross-over design. Twenty overweight or obese men 32 to 64 y old were enrolled in this 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, were overweight or obese (body mass index >25 kg/m^2), had a normal physical activity profile (no athletes or endurance-trained subjects), were able to carry out a physical activity protocol (specified below), fulfilled three of five of the National Cholesterol Education Program/Adult Treatment Panel III (NCEP/ATP III) criteria for the metabolic syndrome (National Institutes of Health, 2002; waist circumference >102 cm, triacylglycerol level >150 mg/dL, high-density lipoprotein cholesterol <40 mg/dL, blood pressure >130/85 mmHg, fasting blood glucose level >100 mg/dL), and were insulin resistant according to a homeostasis model assessment index higher than 2.5 (insulin [μU/mL] × blood sugar [mg/dL]/405). Exclusion criteria were generally accepted contraindications to physical exercise, type 1 diabetes, liver and kidney impairments, psychiatric disorders, other disorders of an acute or chronic nature (gastrointestinal, pulmonary, renal, cardiac, neurological, or psychiatric disorders), known allergies to foods or their ingredients, use of weight-reducing preparations or appetite suppressants, participation in a clinical study within 30 d before the beginning of this study or during this study, and use of β-blockers, oral antidiabetic medications, and insulin therapy. 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 09:00 h after an overnight fast (12 h), each subject consumed in a randomized fashion a breakfast (891 kcal, 110 g of carbohydrates, 46 g of fat, and 10 g of protein) consisting of a 250-mL drink with 25 g of Palatinose™ (Beneo GmbH, Mannheim, Germany) or glc/suc (1:1) and 140 g of cookies containing 60 g of carbohydrate, of which 25 g was from Palatinose™ or glc/suc. The drinks and the cookies were comparable in appearance, taste, and sweetness. Two hours after breakfast, subjects exercised at moderate intensity (4 km/h, inclination 5%) on a treadmill for 30 min followed by a 30-min post-exercise regeneration period. Thereafter, 180 min after breakfast, subjects ingested a lunch (640 kcal, 85 g of carbohydrates, 20 g of fat, and 18 g of protein) consisting of a 250-mL beverage with 25 g of Palatinose™ or glc/suc, a standardized mini pizza, and a medium-sized apple (~125 g). Combined, breakfast and lunch contained 195 g of carbohydrate, of which 75 g consisted of the test carbohydrates. The replacement of conventional sugars in the breakfast and lunch resulted in a decrease of the combined glycemic load by around one-third (from 145 to 100).

Figure 1 shows the time flow of the investigation and the times when the respective parameters were investigated. At each time point, blood levels of glucose, oxygen uptake, and carbon dioxide production (ZAN 600 CPET, nSpire, Oberthulba, Germany) were determined. The sampling duration at each time point for oxygen uptake and carbon dioxide production was 5 min. Insulin concentrations were determined at each time point until lunch. Triacylglycerols, cholesterols (total, low-density lipoprotein, high-density lipoprotein, very low-density lipoprotein), cortisol, and non-esterified fatty acids were analyzed from

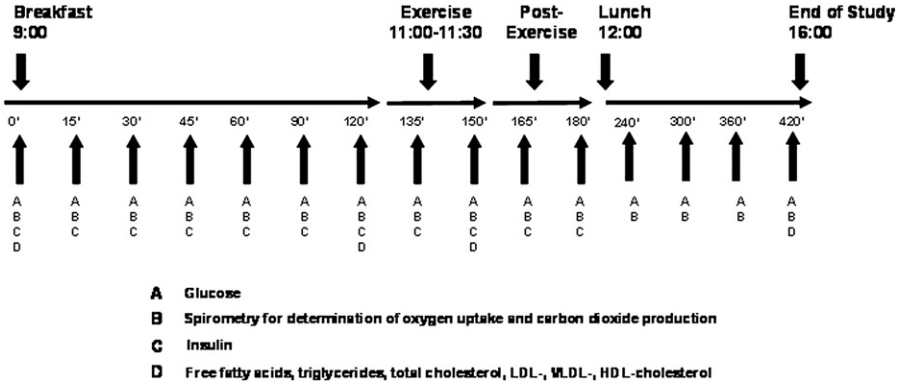

Fig. 1. Time flow of blood sampling and the determination of oxygen uptake and carbon dioxide expiration. HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein.

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venous blood samples at fasting (0 min), 120 min after breakfast (120 min), after exercise (150 min), and 3 h after the standardized lunch meal (360 min) The ratio of carbon dioxide production to oxygen consumption (respiratory quotient, respiratory exchange ratio) was calculated, and the energy expenditure and fat oxidation were determined according the equation of Weir [24]. The total fat oxidation over the test periods was derived from the area under the curve calculated by the trapezoid method.

Statistical methods

Statistical analysis was performed using the SPSS 17.0 for Windows (SPSS, Inc., Chicago, IL, USA). Data are presented as mean ± standard deviation. The testing for differences between the two test meals was done by the Wilcoxon rank-sum test; $P \leq 0.05$ was considered statistically significant.

Results

The baseline anthropometric characteristics and biochemical findings in subjects are listed in Table 1. All subjects were overweight or obese and fulfilled the NCEP/ATP III criteria for the metabolic syndrome. All 20 subjects participated in the two test sessions. No adverse or unintended effect was observed.

Postprandial blood glucose levels (Fig. 2) were lower after the breakfast with Palatinose™, with significant differences at individual time points in the first hour after breakfast and a lower incremental area under the curve compared with glc/suc for the complete 2-h postprandial period ($P = 0.002$). Blood glucose levels decreased at the start of physical activity similarly with the two interventions and remained below the fasting levels during exercise. In the postexercise period, the blood glucose level increased again, reaching a maximum 1 h after lunch in the two groups. The subsequent decrease of the blood glucose level was less pronounced and slower in the Palatinose group, with a significantly higher glucose value late in the second postprandial period 3 h after lunch. Insulin levels were lower in the Palatinose group at all time points (significant differences after 30, 45, and 90 min; Fig. 3) and

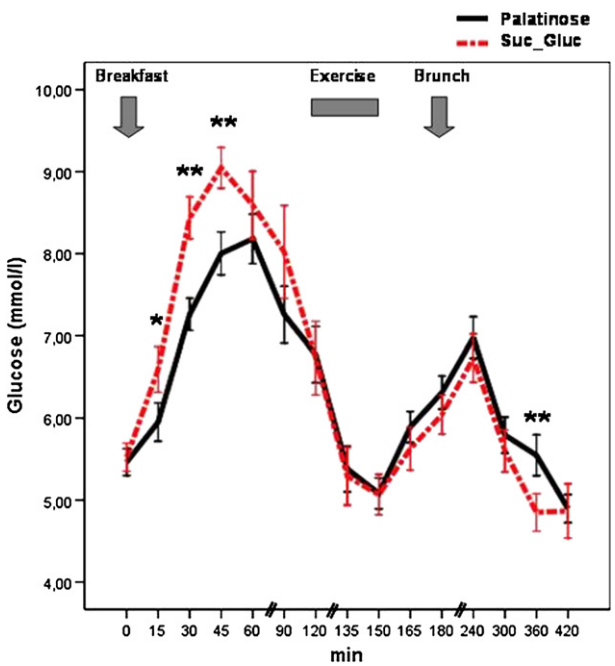

Fig. 2. Glucose levels after ingestion of the two different test meals (solid line, breakfast and lunch with Palatinose™; dotted line, breakfast and lunch with Suc_Gluc). $^{*}P < 0.05$, Palatinose™ versus Suc-Gluc; $^{**}P < 0.01$, Palatinose™ versus Suc-Gluc. Suc_Gluc, sucrose and glucose syrup.

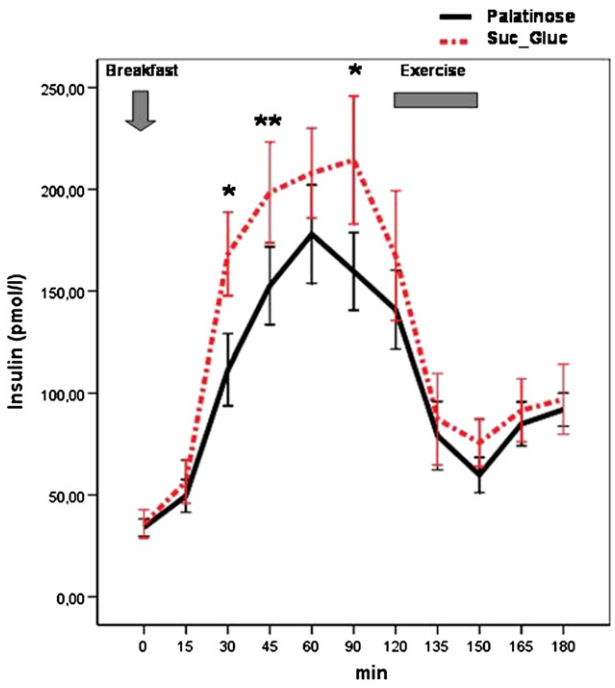

Fig. 3. Insulin levels after ingestion of the two different test meals (solid line, breakfast and lunch with Palatinose™; dotted line, breakfast and lunch with Suc_Gluc). $^{*}P < 0.05$, Palatinose™ versus Suc_Gluc; $^{**}P < 0.01$, Palatinose™ versus Suc_Gluc. Suc_Gluc, sucrose and glucose syrup.

for the incremental area under the insulin curve during the 120-min period after breakfast ($P = 0.002$). In contrast to the glucose concentrations, insulin levels were higher than baseline levels for the entire examination period.

Breakfast ingestion resulted in a decrease of fasting non-esterified fatty acid levels, which was significantly more pronounced after 120 min with the glc/suc product ($P = 0.03$) (Table 2). The non-esterified fatty acid levels returned to about 0.34 to 0.36 mmol/L until the test end, yet remained below the fasting levels and was lower with the glc/suc intervention (not significant).

Triacylglycerol and cholesterol levels (total, low-density lipoprotein, high-density lipoprotein, very low-density lipoprotein) analyzed from the venous blood samples at fasting (0 min), 120 min after breakfast (120 min), after exercise (150 min), and 3 h after lunch (360 min) were similar with the two interventions (Fig. 2).

The respiratory exchange ratio (Fig. 4) was lower with Palatinose compared with glc/suc throughout the entire testing period (significant differences after 45, 60, and 165 min). Fat oxidation (Fig. 5) also was higher in the Palatinose group at all time points (significant after 30 and 60 min). Figure 6 shows the differences in the area under curve for fat oxidation between the two groups. A significantly greater fat oxidation was observed for the first 2-h postprandial period, i.e., from breakfast to the beginning of exercise and from breakfast to the beginning of lunch including the exercise and postexercise periods. Fat oxidation with Palatinose was approximately 18% greater than with glc/suc throughout the entire examination period ($P = 0.09$). There was a trend for greater total energy expenditure with Palatinose™ compared with glc/suc (1176 ± 42 versus 1126 ± 43 kcal, $P = 0.06$). The total carbohydrate oxidation was comparable ($P = 0.68$).

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Table 2
FFA, TG, TC, LDL cholesterol, HDL cholesterol, and VLDL cholesterol before and breakfast, after exercise, and at the end of the investigation period

	Palatinose		Glucose syrup/sucrose	
	Mean	SEM	Mean	SEM
FFA				
0 h	0.46	0.02	0.48	0.02
120 min	0.27*	0.02	0.24	0.01
150 min	0.32	0.02	0.31	0.02
420 min	0.36	0.02	0.34	0.03
TG				
0 h	210	35.9	199	29.7
120 min	270	34.1	255	30.8
150 min	300	32.8	306	36.1
420 min	302	39.1	311	44.7
TC				
0 h	203	8.15	205	6.57
120 min	202	7.93	203	6.27
150 min	203	7.93	205	6.64
420 min	204	7.59	206	6.83
LDL				
0 h	116	6.57	117	5.09
120 min	111	5.64	111	4.85
150 min	112	6.07	110	4.33
420 min	108	5.46	109	4.65
VLDL				
0 h	40.4	4.41	41.1	4.94
120 min	43.9	4.04	45.1	4.98
150 min	46.6	3.79	48.6	4.77
420 min	54.3	4.28	53.6	5.27
HDL				
0 h	45.4	2.32	46.2	2.56
120 min	45.3	2.46	45.6	2.61
150 min	43.6	2.31	45.7	2.57
420 min	40.8	2.04	42.8	2.16

FFA, free fatty acid; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triacylglycerol; VLDL, very low-density lipoprotein
Levels were measured before breakfast (0 h), after breakfast (120 min), after exercise (150 min), and at the end of the investigation period (420 min)
* $P < 0.05$, Palatinose™ versus glucose syrup/sucrose.

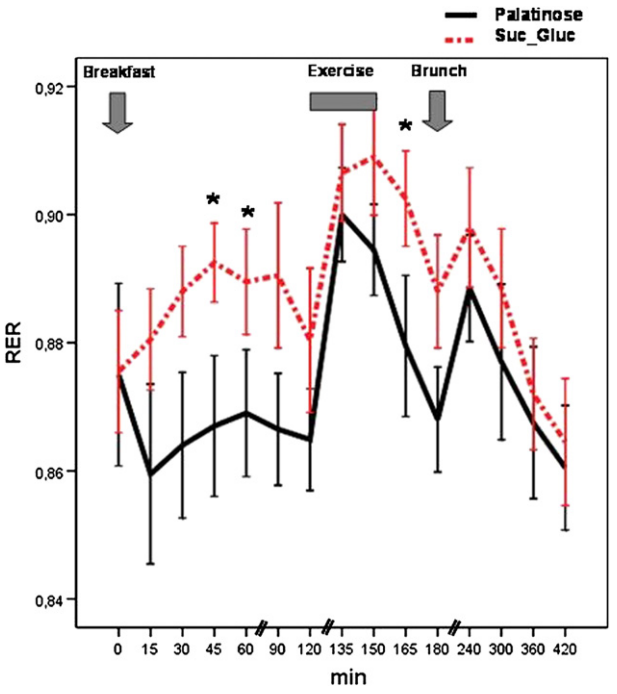

Fig. 4. Respiratory exchange ratio after ingestion of the two different test meals (solid line, breakfast and lunch with Palatinose™; dotted line, breakfast and lunch with Suc_Gluc). *$P < 0.05$, Palatinose™ versus Suc_Gluc. RER, respiratory exchange ratio; Suc_Gluc, sucrose and glucose syrup.

Discussion

The most important finding in the present investigation was that, in obese subjects with insulin resistance and the metabolic syndrome, the partial substitution (~40%) of conventional higher GI carbohydrates in foods and drinks by Palatinose™ resulted in a shift in postprandial substrate use to a greater postprandial fat oxidation. This effect was apparent over the full course of the study day but was most pronounced in the morning after the breakfast, which could perhaps be explained by the different compositions of the meals. From the difference in glucose and insulin levels, it is very likely that the lower glycemic and insulinemic responses are responsible for the greater fat oxidation after the ingestion of Palatinose™.

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 [25–27]. Evidence has suggested that intracellular fat accumulation is responsible for the insulin resistance and the development of metabolic risk factors [14,16,28,29]. Despite an ongoing discussion of which processes are responsible for the accumulation of fat in skeletal muscle cells (and other organs such as the liver or pancreas), there is widespread consensus that an increased fat oxidation, particularly in the postprandial period, would be beneficial for an improvement in insulin resistance [14, 30–34]. It has been shown that an improved capacity for mitochondrial fatty acid uptake and oxidation leads not only to a decrease in muscle lipid content but also to a change in the saturation status of lipids, which may, at least in part, provide a mechanism for the increased insulin action observed with endurance training in obese individuals [35,36]. Therefore, an increased fat oxidation in the postprandial phase may account

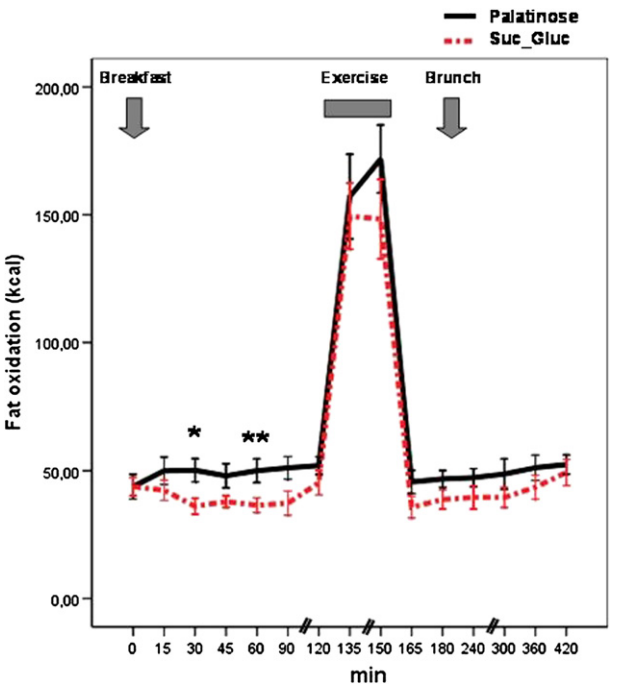

Fig. 5. Fat oxidation (kilocalories per hour) after ingestion of the two different test meals (solid line, breakfast and lunch with Palatinose™; dotted line, breakfast and lunch with Suc_Gluc). *$P < 0.05$, Palatinose™ versus Suc_Gluc. Suc_Gluc, sucrose and glucose syrup.

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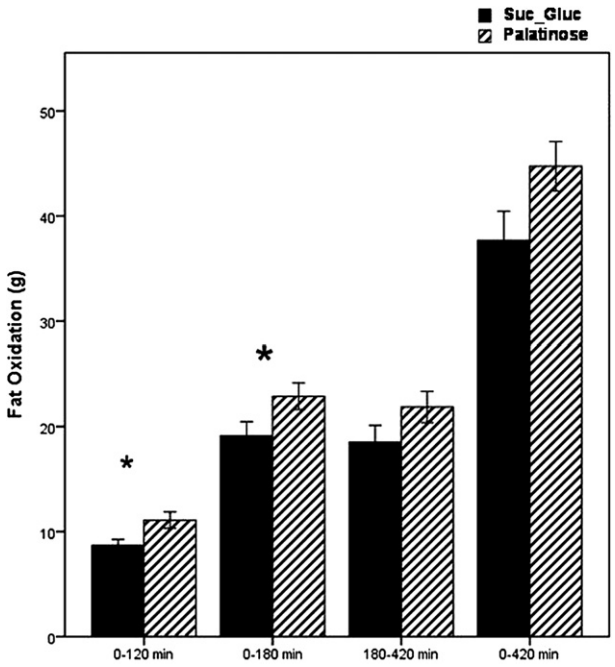

Fig. 6. Total fat oxidation (area under curve) in the 2-h postprandial period after breakfast (0–120 min), 3-h period from breakfast until the beginning of lunch including the exercise and postexercise periods (0–180 min), the postprandial 4-h period after lunch (180–420 min), and the complete testing period (0–420 min) with the Palatinose™ (striped bars) or the Suc_Gluc (black bars) intervention. $^{*}P < 0.05$, Palatinose™ versus Suc_Gluc. Suc_Gluc, sucrose and glucose syrup.

for not only better weight loss but also an improvement in metabolic risk factors [37,38].

Although the role and importance of the GI in daily nutrition are still under debate, an increasing number of studies has investigated its role in the prevention and therapy of the metabolic syndrome and type 2 diabetes mellitus [13]. However, data comparing the acute metabolic effects of a diet exhibiting a low versus high GI in subjects with overweight or insulin resistance are still scarce. Several investigations in healthy subjects have convincingly demonstrated that fat oxidation is greater after the ingestion of low GI carbohydrates compared with high GI carbohydrates [6–10]. Isomaltulose has been shown to decrease postprandial glycemic and insulinemic responses and improve glycemic control in patients with type 1 and 2 diabetes mellitus and has been associated with a lower respiratory exchange ratio and an increased fat oxidation in healthy and type 1 diabetic subjects during resting conditions and during exercise [23, 39–46]. Animal experiments with normal and diabetic mice have found a lower fat accumulation and a lower respiratory quotient with the isomaltulose-based formula than with a dextrin-based formula [41]. Feeding diets with isomaltulose or sucrose to Zucker fatty (*fa*/*fa*) rats for 8 wk resulted in decreases in visceral fat mass, adipocyte cell size, hyperglycemia, and hyperlipidemia [47].

Data from human and animal studies have shown that the effect of the GI on body composition is mediated by changes in substrate oxidation, not by energy intake [48]. In addition, it has been demonstrated that a decreased fat oxidation after a meal with a high GI has been associated with an obese, insulin-resistant, and metabolically inflexible phenotype [49]. Therefore, there is a rationale to consider increased fat oxidation as a beneficial metabolic effect in obese, insulin-resistant subjects.

In conclusion, the results of this investigation have shown lower glycemic and insulinemic responses and increased fat oxidation after ingestion of Palatinose™ in overweight, insulin-resistant subjects at rest and during physical activity. To our knowledge, this is the first such study. The favorable metabolic characteristics of Palatinose™ were thus confirmed for a risk panel for the development of, e.g., diabetes and cardiovascular diseases. The effect of an attenuated glycemic and insulinemic response and the greater contribution of fat oxidation in energy metabolism may be favorable in the long term for weight management and the improvement of metabolic risk factors.

Acknowledgments

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