Original Research

Impact of a Resistant Dextrin with a Prolonged Oxidation Pattern on Day-Long Ghrelin Profile

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Objectives: The effects of a new resistant dextrin ingested at breakfast on day-long metabolic parameters and ghrelin profile at subsequent lunch were investigated.

Methods: In this randomized, single-blinded, crossover study, 12 healthy men ingested a standardized breakfast with 50 g of NUTRIOSE 10, a resistant dextrin (RD), or of maltodextrin (Malto) and a standardized lunch 5 hours later. Both products (RD and Malto) were derived from corn naturally rich in ^{13}C to follow their metabolic fate (by using stable isotope analysis). Oxidation and fermentation patterns were assessed by simultaneous $^{13}CO_2/H_2$ breath testing. The appearance of exogenous ^{13}C-glucose in plasma, glycemia, insulinemia, nonesterified fatty acids (NEFAs), and ghrelin concentrations were measured for 10 hours following breakfast ingestion.

Results: With RD, H_2 excretion (fermentation) was significantly enhanced compared with Malto, whereas the appearance of $^{13}CO_2$ (oxidation) was significantly prolonged ($p < 0.0001$). Following breakfast, ghrelin secretion was significantly less inhibited and NEFA concentration was higher with RD ($p < 0.05$), but unexpectedly, both remained lower after lunch and up to T600 minutes. According to the reduced bioavailability of RD compared with Malto, the appearance of ^{13}C-glucose in plasma ($p < 0.0001$) and glycemic and insulinemic responses to breakfast ($p < 0.05$) were significantly reduced.

Conclusions: Ingestion of this new resistant dextrin at breakfast decreased ghrelin concentrations in response to the subsequent lunch, even if the caloric load ingested at breakfast was lower. This effect may be linked to the prolonged fermentation/oxidation pattern seen in the late postprandial phase (up to 10 hours after ingestion at breakfast), and thus prolonged energy release with the resistant dextrin.

INTRODUCTION

Current recommendations for the management of metabolic disorders such as obesity, type 2 diabetes, and cardiovascular diseases are in line with an increase in dietary fiber consumption. Thus dietary fibers have been extensively studied as dietary tools to improve metabolic control, particularly postprandial glucose and insulin profiles, as well as lipid metabolism [1–8], but also to decrease food intake [9,10]. Soluble dietary fibers, through their ability to form gels and to increase gastrointestinal viscosity that delays gastric emptying, reduce the rate of glucose absorption and thus decrease postprandial glycemic excursions [11,12].

Among other potential physiologic mechanisms of dietary fiber involved in improvement of glucose metabolism, the role of fermentation in the colon has been proposed through the production of short chain fatty acids (SCFAs) [13–16]. Similarly, if the bulking and viscosity-producing abilities of fibers have been identified as participating in their satietogenic effect [9], a potential role for fermentation has been identified [17]. The beneficial effects of dietary fibers on satiety [18–22] and body weight management [10] may be mediated by gut hormones regulating energy metabolism [23]. The gut peptide ghrelin, an orexigenic hormone secreted in the stomach, is a key factor in the regulation of food intake [24]. Ghrelin has been supposed to be involved in meal initiation, as its plasma

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concentration rises during fasting before a meal and decreases immediately afterward [25,26]. Modification of postprandial concentrations of ghrelin is dependent on dietary and/or postgastric and/or postabsorptive factors [27]. However, the effects of dietary fibers, particularly fermentable fibers, on ghrelin are still not fully understood [28].

Therefore, the aim of this study was to investigate the effects of a new, soluble, nonviscous resistant dextrin on metabolic parameters and satiety factors. NUTRIOSE 10 is a resistant dextrin (RD) from corn starch, incompletely hydrolyzed and absorbed in the small intestine because of a higher percentage of α-1,6 linkages and the presence of nondigestible glucoside linkages (e.g., α-1,2, α-1,3) [29]; it may be a potential tool for the modulation of postprandial metabolism and food intake regulation to improve metabolic risks. This RD is a naturally ^{13}C-enriched product, as corn plant has a natural enrichment of ^{13}C compared with most other plants [30]. Thus, the metabolic fate of this fiber can be traced through the measurement of $^{13}CO_2$ in breath excretion from the RD oxidation resulting from minor intestinal absorption, as well as from major colonic fermentation.

First, we determined the fermentation and oxidation pattern of the RD using a simultaneous $^{13}CO_2/H_2$ breath test to assess $^{13}CO_2$ origin (digestion and fermentation) [31,32]. Second, we investigated the effects of this RD on metabolic parameters and day-long ghrelin profile in response to breakfast and to a subsequent lunch. Thus, the appearance of exogenous ^{13}C-glucose from RD in plasma and the concentrations of plasma glucose, insulin, nonesterified fatty acids (NEFAs), and ghrelin were measured for 10 hours following test breakfast ingestion.

SUBJECTS AND METHODS

Subjects

Fifteen healthy men were volunteered for the study, received written and oral information about the protocol, and signed an informed consent form. This study was approved by the Scientific Ethics Committee of Lyon (CPP Sud-Est II) according to the French "Huriet-Serusclat" Law and the Second Declaration of Helsinki. Prestudy screening tests were conducted wherein each subject gave a blood sample, was measured for height, was weighed, and was interviewed regarding general health. Eating habits, especially regarding usual fiber consumption, were explored by a trained dietitian through a dietary survey.

A lactulose breath test was performed to exclude subjects who were non–hydrogen producers. Subjects came to the Centre de Recherche en Nutrition Humaine Rhône-Alpes after an overnight 12-hour fast and ingested a solution containing 10 g of lactulose. Then, breath samples were collected for 240 minutes at 30-minute intervals. An increase of 10 ppm above baseline values of H_2 maintained for at least 3 successive time points was used as the inclusion criterion.

Other inclusion criteria for the study included men aged 20–65 years, body mass index (BMI) 20–25 kg/m^2, fasting glucose concentration <7.0 mmol/L, total cholesterol <7.0 mmol/L, stable body weight over the previous 3 months, normal results for preinclusion biological tests, sedentary or moderate physical activity, usual fiber intake, no history of metabolic or intestinal disorders, and no medication that could influence study outcomes.

Three men were excluded following the prestudy screening: 2 men detected as non–hydrogen producers and 1 man with BMI >25 kg/m^2. Finally, 12 men were included, aged 29 $\pm$ 1 year, weighing 71.7 $\pm$ 1.8 kg, with BMI 22.7 $\pm$ 0.5 kg/m^2, and with fasting glucose concentration of 4.49 $\pm$ 0.13 mmol/L and fasting total cholesterol concentration of 4.66 $\pm$ 0.24 mmol/L (mean $\pm$ standard error of the mean [SEM]).

Test Products and Experimental Meals

NUTRIOSE10 (Roquette Frères, Lestrem, France) is a resistant dextrin made from wheat or corn starch, using a highly controlled process of dextrinification, during which the starch undergoes a degree of hydrolysis followed by repolymerization. The repolymerization converted the starch into fiber by forming nondigestible glycosidic bonds. Dextrinification was followed by a separation step, ensuring the optimum molecular weight distribution. NUTRIOSE 10 tested in this study presented 75% fiber (average molecular weight, 4150 Da). A pure maltodextrin (Malto) (Glucidex 6, Roquette Frères) was selected as placebo. Corn starch was chosen as raw material for the NUTRIOSE 10 RD and Malto process, as corn is naturally enriched in stable isotope ^{13}C [30]. Potato starch (cultivated in a $^{13}CO_2$-enriched atmosphere) was added before processing to increase ^{13}C enrichment in test products and to allow optimal isotopic analysis conditions (1 g for 4 kg of RD or 1 g for 5 kg of Malto to obtain comparable enrichment levels for both test products).

Fifty grams of RD or Malto was mixed (powder) with 100 mL of water and was ingested in this form (limpid solution) as part of a standardized breakfast (without dietary fiber). The standardized breakfast consisted of 4 toasts, 20 g of butter, and a cup of coffee or tea (without sugar, each subject consumed the same beverage for the 2 test days). The standardized lunch consisted of 50 g of ham, 200 g of rice, 2 toasts, and 30 g of cheese. The composition of the test breakfasts and the standardized lunch is given in Table 1.

Experimental Design

This study was designed as a randomized, crossover, single-blinded trial. One month before investigations, subjects were asked to limit their consumption of food products that could affect the gastrointestinal tract microflora and alter the

Table 1. Macronutrient Composition of the 2 Test Breakfasts (RD and Malto) and the Standardized Lunch

	Serving Size (g)	Proteins (g)	Lipids (g)	Total CHO (g)	Fiber (g)	Energy (kcal)
NUTRIOSE 10 breakfast						
4 toasts	30	3.2	1.2	23.6	1.2	124
Butter	20	0.1	16.6	0.1	0	150
NUTRIOSE 10 (100 mL solution)	50	0	0	50	50	100
Total		3.3	17.8	73.7	51.2	374
Malto breakfast						
4 toasts	30	3.2	1.2	23.6	1.2	124
Butter	20	0.1	16.6	0.1	0	150
GLUCIDEX (100 mL solution)	50	0	0	50	0	200
Total		3.3	17.8	73.7	1.2	474
Standardized lunch						
Ham	50	9	0.6	0	0	57
Rice	200	4.6	0.4	52.6	1	238
2 toasts	15	1.4	1.1	11.4	0.6	62
Cheese	30	8.7	9.4	0	0	113
Total		23.7	11.5	64	1.6	470

fermentation pattern. Thus, consumption of food products containing high amounts of dietary fiber (including whole grains) or prebiotics or probiotics was limited to once a week (dairy products with added cultures, chicory, artichoke, rhubarb, plum, light food products, legumes). Moreover, subjects were asked to avoid nutrients known to be enriched in ^{13}C (corn starch and oil, cane sugar, tropical fruits, tinned foods). Twenty-four hours before the study, they were asked to limit their physical activity and to not drink alcohol-containing beverages. Dietary advice was given to each subject to standardize the dinner menu (rice, fish, toasts, cheese) on the day before the investigation began.

Each subject came to the Centre on 2 separate days, with a washout of 3 weeks in between. They arrived at the Centre at 6:30 AM on the exploration day following a 12-hour overnight fast and had either the breakfast with RD test solution or the breakfast with Malto test solution, selected at random. Body weight was measured with a calibrated scale (Seca, Birmingham, United Kingdom). At T0, subjects ingested the test solution together with the standardized breakfast in 15 minutes. Blood samples were collected at baseline and sequentially every 15 minutes until 60 minutes, then every 30 minutes until 180 minutes following ingestion of breakfast, and finally every 60 minutes between 240 minutes and 600 minutes. The standardized lunch was served and ingested at T300 minutes. Blood was collected in tubes maintained at 4°C and was immediately centrifuged at 4500 rpm for 10 minutes at 4°C and then stored at −20°C until assay. Blood samples were used to determine plasma concentrations of glucose, insulin, NEFA, ghrelin, and ^{13}C-glucose isotopic enrichments. Breath samples were also collected at baseline and then every hour until T600 for breath hydrogen analysis, as well as for $^{13}CO_2$ isotopic enrichment measurements.

Analytical Procedures

Breath Hydrogen Analysis. After mouth rinsing (antibacterial mouthwash) at arrival, subjects were instructed to breathe out deeply, and end-expiratory breath samples were collected directly in a modified bag (Quintron Instruments, Milwaukee, WI). Samples of collected air were injected into a Quintron Model DP Microlyzer gas chromatograph (Quintron Instruments). Hydrogen concentration was measured with a detected accuracy of ±2 ppm.

Isotope Analysis. Plasma glucose isotopic enrichments were determined on neutral fractions of deproteinized plasma samples, partially purified over sequential anion-cation exchange resins, as previously described [33]. Plasma ^{13}C glucose enrichment was measured by gas chromatography-combustion-isotope ratio mass spectrometry (GC-C-IRMS, Isoprime, GV Instruments, Lyon, France) after derivatization to pentaacetylaldonitrile glucose [34]. Breath sample $^{13}CO_2$ to $^{12}CO_2$ ratios were measured on a continuous-flow inlet system connected to an Isoprime isotope ratio mass spectrometer (GV Instruments).

The ^{13}C isotopic enrichment of test products (RD and Malto) was determined by 2 procedures as previously described [35]. The ^{13}C isotopic enrichment of the test products measured was 2.56 $\partial^{13}C‰$ (1.11405 atom%^{13}C) and 6.15 $\partial^{13}C‰$ (1.11799 atom%^{13}C) for RD and Malto, respectively. Moreover, test products underwent an acid hydrolysis using chlorhydric acid at 100°C for 45 minutes, and the glucose obtained was purified by sequential anion-cation exchange chromatography before derivatization as glucose pentaacetylaldonitrile and was analyzed as previously described [35] to determine the ^{13}C enrichment of the derivatized glucose: 1.81 $\partial^{13}C‰$ (1.11322 atom%^{13}C) and 5.75 $\partial^{13}C‰$ (1.11755 atom%^{13}C) for RD and Malto, respectively.

Metabolites and Hormones. Glucose and NEFA concentrations were measured with an enzymatic colorimetric method on a Cary 50 Bio spectrophotometer (Varian Medical System, Palo Alto, CA) using, respectively, a BioMérieux Glucose RTU kit (BioMérieux, Marcy l'Etoile, France) and a Wakochemicals NEFA-C kit (Wako, Freiburg, Allemagne). Plasma insulin and ghrelin concentrations were determined by radioimmunoassay using a Medgenix Diagnostics kit (Medgenix, Rungis, France, and Immunotech, Marseille, France) and a ghrelin (total) radioimmunoassay (RIA) kit, respectively.

Calculations

^{13}C-glucose enrichment in plasma and $^{13}CO_2$ enrichment in expired air were expressed as Atom% Excess (APE). The measured Atom%, AP of plasma glucose after ingestion was transformed in APE by the formula:

$$APE = AP_s - AP_b$$

where AP_s is the AP of the sample, and AP_b the AP of the plasma glucose at baseline.

Because ^{13}C enrichment of the derivatized glucose molecule from the 2 test products (RD and Malto) differed, a correction was applied to take into account test product enrichment at baseline.

APE_{cor}, representing the % of plasma ^{13}C-glucose from ingested test product, was calculated as follows:

$$APE_{cor} = (APE_t/APE_p) \times 100$$

where APE_t is the APE of plasma ^{13}C-glucose at time t and APE_p is the APE of the test product.

Peaks of glucose, insulin, and APE_{cor} were calculated as the maximum concentration or APE following breakfast for each subject (consequently, they do not correspond to the same time points for each subject). Areas under the curve (AUCs) were calculated using the trapezoidal method and were integrated throughout the experiment (0–600 minutes) and between 0 and 300 minutes and 300 and 600 minutes.

Statistical Analysis

Results at specific time points and AUCs were expressed as mean ± SEM.

A power calculation was performed using as the study primary endpoint the difference in appearance of exogenous glucose in plasma; this calculation was based on a previous study examining fermentation of a resistant dextrin through breath hydrogen excretion in healthy subjects [36]. According to previous studies, 12 subjects per group provided >80% power to detect a significant difference in the total quantity of exogenous glucose appearing in the plasma between the 2 groups when differences in postprandial glucose kinetics were investigated at the $p < 0.05$ level [37,38].

For each parameter, normality was checked before testing. Significant differences between products for AUCs, kinetics, and peaks were assessed using a paired-sample t test for normally distributed data. To compare the response to test meals, an analysis of variance (ANOVA) for repeated measures with product and time as within-participant factors was used to determine differences between products over a time course and for the meal × time interaction, with post hoc Bonferroni corrections to assess statistical differences between meals at specific time points when appropriate. For one studied parameter, a significant meal × time interaction means that the time effect is different between the 2 meal conditions (RD and Malto), that is, the kinetics of the studied parameters is different.

Statistical significance was inferred at $p < 0.05$. All statistical analyses were performed using the SAS statistical package, version 9.2 (SAS Institute, Cary, NC).

RESULTS

Combined $^{13}CO_2/H_2$ Breath Test Analyses

Fig. 1 shows the breath hydrogen excretion profile for 10 hours following RD or Malto ingestion. Little H_2 excretion occurred after Malto consumption, when ingestion of RD induced an increase in breath H_2 (excretion peak 36 ± 6 ppm for RD vs 20 ± 3 ppm for Malto; $p = 0.05$). The AUC for breath hydrogen was also significantly higher with RD (10358 ± 1556 ppm/600 min with RD vs 5818 ± 975 ppm/600 min with Malto; $p = 0.008$).

Fig. 1 also presents the kinetics of APE_{cor} CO_2, which represents the % of $^{13}CO_2$ from oxidation of ingested test product that appears in expired CO_2. Following test breakfast ingestion, the appearance of $^{13}CO_2$ increased for the 2 products, but the appearance was twice lower after RD (main product effect $p < 0.0001$; peak of APE_{cor} CO_2: 7.86 ± 0.43% with RD vs 17.43 ± 0.42% with Malto; $p < 0.0001$). After lunch ingestion at T300 minutes, the pattern of APE_{cor} CO_2 significantly differed: APE_{cor} CO_2 still decreased after Malto until T600 minutes, whereas it remained steadier after RD (significant interaction × time and main product effect, $p < 0.0001$).

Metabolites Concentration Kinetics in Plasma

Fig. 2 shows the kinetics of APE_{cor} plasma glucose, which represents the % of plasma ^{13}C-glucose from ingested test product that appears in plasma following test breakfast ingestion. The appearance of exogenous ^{13}C-glucose from the test product first increased as a result of glucose intestinal absorption, and then rapidly decreased after T60 minutes. When the kinetics of the 2 products were compared, the RD curve was seen to be significantly lower throughout the

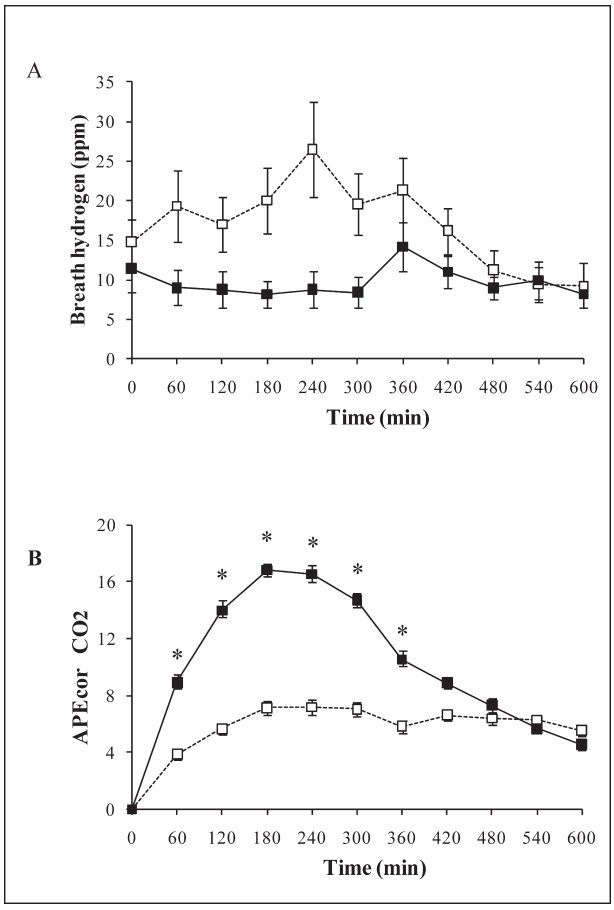

Fig. 1. Kinetics of breath hydrogen (H_2) and APE_{cor} CO_2 (% of $^{13}CO_2$ from oxidation of ingested test product) after consumption of RD breakfast (white squares) or Malto breakfast (black squares). Data are presented as means ± SEM. * represents a significant difference at specific time points after Bonferroni correction. A standardized lunch was ingested at t = 300 minutes. H_2 excretion was significantly increased by RD ingestion (significant difference in $AUC_{0\text{-}600min}$; $p = 0.008$). APE_{cor} CO_2 was significantly reduced after consumption of RD (main product effect; $p < 0.0001$) and then remained steadier after T300, but it decreased after consumption of Malto (significant interaction × time and main product effect; $p < 0.0001$).

experiment (significant product × time interaction and main product effect; $p < 0.0001$). The peak of APE_{cor} plasma glucose was also significantly lower (26.36 ± 1.74% with RD vs 61.32 ± 1.65% with Malto; $p < 0.0001$).

The glycemic response was significantly lower over the 300 minutes after ingestion of RD breakfast (Fig. 2). A significant product × time interaction ($p = 0.03$) and a significant product effect ($p < 0.0001$) were noted. The postbreakfast glucose peak was also significantly lower after RD (7.60 ± 0.25 mmol/L with RD vs 9.50 ± 0.44 mmol/L after Malto; $p = 0.01$). Consequently, early AUC glycemia was also significantly lower after RD ($AUC_{0\text{-}150min}$ 896 ± 32 mmol/L/150 min with RD vs 1036 ± 52 mmol/L/150 min with Malto; $p = 0.03$).

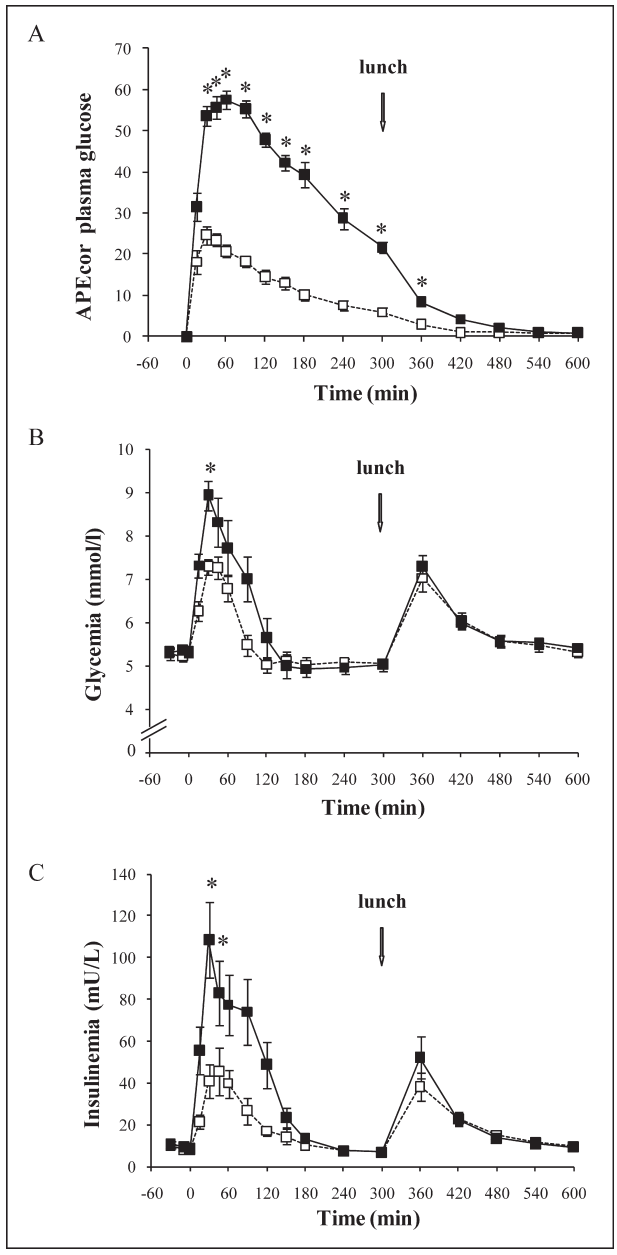

Fig. 2. Kinetics of APE_{cor} plasma glucose (% of ^{13}Cglucose from ingested test product) (A) after consumption of RD breakfast (white squares) or Malto breakfast (black squares). Data are presented as means ± SEM. * represents a significant difference at specific time points after Bonferroni correction. A standardized lunch was ingested at t = 300 minutes. APE_{cor} plasma glucose was significantly reduced after consumption of RD (significant product × time interaction and main product effect; $p < 0.0001$). Mean (±SEM) plasma glucose (B) and insulin (C) responses after consumption of RD breakfast (white squares) or Malto breakfast (black squares). A standardized lunch was ingested at t = 300 minutes. Glycemic and insulinemic responses to breakfast were significantly lower with RD compared with Malto (peaks and AUC, $p < 0.05$). No significant difference between products was detected for glycemic and insulinemic responses to lunch ingestion.

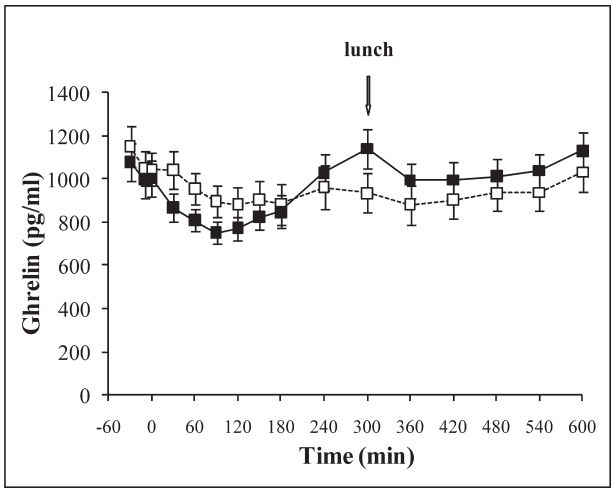

Fig. 3. Mean (±SEM) plasma ghrelin responses after consumption of RD breakfast (white squares) or Malto breakfast (black squares). A standardized lunch was ingested at t = 300 minutes. Ghrelin concentration decreased to a lesser extent following RD breakfast and remained steadier until T600 (significant product × time interaction; $p < 0.0001$).

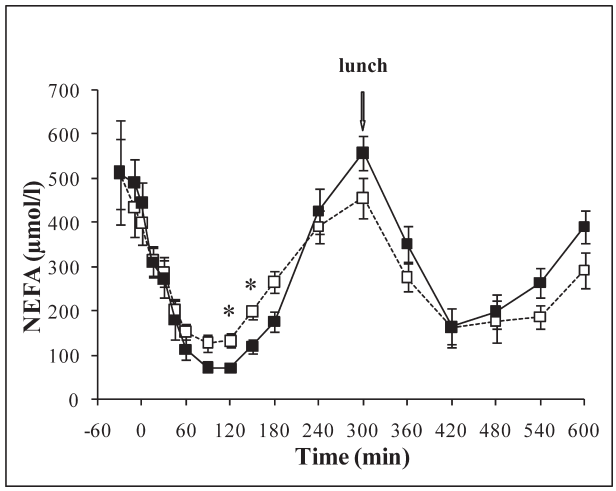

Fig. 4. Mean (±SEM) plasma NEFA responses after consumption of RD breakfast (white squares) or Malto breakfast (black squares). * represents a significant difference at specific time points after Bonferroni correction. A standardized lunch was ingested at t = 300 minutes. NEFA concentration was less inhibited following RD breakfast ($p < 0.0001$), then was lower at lunch ($p = 0.09$) and remained steadier until T600.

Plasma insulin response was significantly lower after ingestion of RD breakfast (Fig. 2), with a significant product × time interaction ($p < 0.0001$), a significant product effect ($p = 0.0004$), a lower insulinemic peak (58.5 ± 10.6 mU/L with RD vs 118.0 ± 17.5 mU/L after Malto; $p = 0.0002$) and a lower $AUC_{0\text{-}300min}$ (5440 ± 711 mU/L/300 minutes with RD vs 11171 ± 1644 mU/L/300 minutes with malto; $p = 0.002$). No difference was noted between products in terms of insulinemic response to lunch (T300 minutes).

As can be seen in Fig. 3, following breakfast, ghrelin concentrations decreased to a lesser extend with RD than with Malto and remained steadier (significant product × time interaction; $p < 0.0001$). As a consequence, the ghrelin concentration curve remained lower after RD from T300 (lunch) to T600 minutes ($AUC_{300\text{-}600min}$ 278337 ± 25730 pg/mL with RD vs 310605 ± 24270 pg/mL with Malto; $p = 0.03$).

Concomitantly, NEFA concentration was higher following RD breakfast, as can be seen on Fig. 4 (nadir of NEFA concentration: 65 ± 5 µmol/L with Malto vs 110 ± 12 µmol/L with RD; $p = 0.001$). NEFA concentration rebound was less pronounced with RD just before lunch ($p = 0.09$) and remained lower until T600 minutes.

DISCUSSION

This study demonstrated that NUTRIOSE 10, a resistant dextrin, presented a prolonged oxidation pattern that was parallel to its fermentation in colon. Thanks to ^{13}C-labeling of test products, this phenomenon has been highlighted by the simultaneous use of 2 breath markers: $^{13}CO_2$ as a marker of test product oxidation and H_2 as a marker of test product fermentation. It is interesting to note that this late oxidation was parallel to a reduction in ghrelin level at lunch, although the caloric content of the RD breakfast was lower (100 kcal). This could be one potential link between fermentation of dietary fibers and their satietogenic effects.

As indicated by breath H_2 levels, colonic fermentation was significantly increased after the RD breakfast compared with the Malto breakfast. This is in accordance with results from a previous study using supplementation of 30 and 45 g/d of resistant dextrin for 4–5 weeks [36]. In another previous study using lower doses of resistant dextrin (10–15 g/d), the authors attributed the absence of a significant difference in breath H_2 levels between the fiber and maltodextrin to the low amount of product consumed at each meal (total quantity split daily between the 3 meals) [39].

When measuring the appearance of $^{13}CO_2$ from oxidation of test products, we first observed a larger increase in APE_{cor} CO_2 for Malto, which reflected Malto intestinal digestion and further oxidation. At the same time, the increase in APE_{cor} CO_2 for RD was significantly lower; only about 20% of the fiber is digested in the small intestine [29]. This was confirmed by the reduced appearance of exogenous ^{13}C-glucose in plasma from test products. Then, the oxidation of Malto decreased, while the oxidation of RD remained steady and prolonged until T600 minutes. At the same time, the kinetics of volume of CO_2 expired was not different between products, indicating that the observed difference in product oxidation could not be allocated to a difference in CO_2 production rate (data not shown).

Maintenance of $^{13}CO_2$ excretion from RD oxidation was parallel to the H_2 increase because of fermentation of the fiber.

Colonic bacterial fermentation results in the production of SCFAs (acetate, butyrate, and propionate) together with gazes and heat [40,41], with the proportion of different SCFAs depending on the substrate and eventually on gut microflora [42]. Colonic epithelial cells use SCFAs for their metabolism, particularly butyrate [43]. Once absorbed in the colon, residual butyrate, acetate, and propionate are extracted from the portal circulation by the liver. Acetate is then taken up by peripheral tissues such as muscles to be metabolized [44]. Propionate could have a neoglucogenic effect in the liver [15,45,46], as demonstrated in hepatocytes [47] and in ruminants [43]. In the present study, the prolonged appearance of $^{13}CO_2$ was of particular interest. We hypothesized that SCFAs produced by the fermentation of RD (^{13}C-labeled) in the colon could be used as neoglucogenic substrates before being oxidized. Another possible explanation could be that ^{13}C-labeled SCFAs produced could be oxidized in colonocytes or other tissues. Thus, the colonic fermentation of RD provided a more sustained energy supply for oxidation.

One of the main findings of the present study was the significant smoothing of the day-long ghrelin profile after RD ingestion. Several gastrointestinal hormones (ghrelin, cholecystokinin, glucagon-like peptide 1 [GLP-1], peptide YY) regulate satiety and appetite [48], and dietary fiber action on satiety may be mediated via these actors. Recently, Cani observed that a 2-week fructan supplementation induced an increase in gut microbial fermentation, which was associated with an increase in GLP-1 and peptide YY concentrations, along with a reduction in hunger sensation [49]. Following RD ingestion, postbreakfast ghrelin concentration was decreased to a lesser extend than after Malto. Then, ghrelin concentration was significantly lower just before lunch ingestion and remained lower throughout the day. Ingestion of maltodextrin or complex carbohydrates has been shown to decrease ghrelin concentrations [50], in proportion to their energy content [51]. Indeed, Callahan showed that the decline in ghrelin was all the more strong and prolonged when the ingested meal was high in calories [51]. This is in accordance with the present results, as RD supplied twice fewer calories than Malto and induced an acutely weaker decrease in ghrelin response at breakfast. Because the caloric content of the RD breakfast was lower than that of the Malto breakfast, a greater rebound in ghrelin level was expected 5 hours following breakfast ingestion. However, actually, with the RD breakfast, ghrelin concentration was still not back to its baseline level at lunch. This suggested a late effect of RD that may be related to the fermentation process that took place up to 6 hours following fiber ingestion.

Up until now, the direct effects of dietary fibers on appetite and gut peptide such as postprandial ghrelin suppression have not been fully clarified, mainly because scarce studies have been performed, with numerous different dietary fibers presenting different properties leading to discrepancies between study results [28]. Indeed, in Juvonen's study, the decrease in postprandial ghrelin (0–180 min) was greater with a high-viscosity oat bran beverage than with a low-viscosity beverage. However, ghrelin concentration just before lunch and food intake and appetite ratings at the subsequent lunch were not affected [52]. In a previous study using Nutriose, supplementation with 30 or 45 g of the resistant dextrin daily for 4–5 weeks did not significantly influence satiety as measured by visual analogue scale [36]. However, in this study, which was designed to assess gastrointestinal tolerance, the number of subjects in each group in this parallel trial may have been not sufficient to detect a significant effect on food intake or satiety because of high variability between subjects in terms of such subjective parameters. Soluble arabinoxylan (6 g) in breakfast induced a shorter postprandial decrease in ghrelin compared with the control breakfast [53], but soluble psyllium fiber (23 g) added to a 300 kcal meal did not alter the postprandial ghrelin profile [28]. When added to bread matrix, 10 g of insoluble wheat fiber blunted the postprandial decrease in ghrelin when 10 g of soluble oat fiber did not; again postprandial hunger scores were not altered [23]. Another insoluble fiber, carob pulp, did not decrease total ghrelin concentration but affected the active form of acylated ghrelin [54].

In a recent study, 3 g of beta-glucan added to bread reduced hunger and energy intake and increased satiety and fullness at lunch. In parallel, ghrelin concentration was reduced at lunch as can be seen in the present study [55]. Such discrepancies may be related to the type of ghrelin measured (active acylated form or total ghrelin) and/or the types of fibers. As previously shown, postprandial ghrelin concentration may require post-gastric feedback [50], and an inhibitory effect of insulin on ghrelin response has been proposed [56]. Presently, because the insulin response to breakfast was decreased with RD, the inhibitory effect of insulin on ghrelin may have been consequently reduced. This effect is still discussed and supported by some authors [50,56–58] but not all [59,60]. Together, these results suggest a potential effect of resistant fiber on ghrelin levels that may be mediated through prolonged energy release by fermentation.

A possible limitation of the present results analysis is that we did not perform satiety scores in parallel to ghrelin concentration measurement. However, to acutely characterize satiety feelings, such ratings of satiety remained subjective and could have been highly altered by experimental conditions (clinical research context).

Ingestion of RD significantly decreased glycemic as well as insulinemic responses to breakfast. This blunted plasma glucose response at breakfast compared with Malto was consistent with the reduced appearance of exogenous ^{13}C-glucose in plasma, reflecting a diminution of glucose absorption from RD in the small intestine caused by many nondigestible glucoside linkages [29]. This effect was in accordance with the findings of previous intervention studies investigating soluble fiber effects on postprandial glucose

metabolism [4,5–7,51–64]. As for resistant starches, the reduced glycemic response to breakfast could be linked to the reduced digestibility of RD in the small intestine. We also observed that the decrease in NEFA level was less pronounced after RD breakfast, as expected in view of the reduced insulin response. Unexpectedly, NEFA concentrations tended to be lower at lunch after RD, when at the same time insulin levels were similar between tests. However, the acutely lower glycemic response at breakfast was not predictive of a lower glycemic response at the subsequent lunch, although it has been reported that such a second-meal effect could be due to improved insulin sensitivity induced by reduced NEFA levels as induced by prolonged glucose and insulin responses [64]. The reduced NEFA concentration at lunch could be the result of an inhibitory effect on lipolysis of SFCAs produced by fiber fermentation, as has been previously suggested [46].

CONCLUSION

In conclusion, the present results demonstrate that oxidation of a highly resistant dextrin was prolonged over 10 hours following its ingestion at breakfast. Such prolonged energy release from resistant dextrin may be linked to its colonic fermentation, resulting in production of SCFAs that can act as neoglucogenic substrates for late oxidation.

It is interesting to note that RD ingestion at breakfast induced in parallel a significant reduction of satiety-related ghrelin levels at the subsequent lunch, even if the caloric load ingested at breakfast was lower. Fermentation of dietary fiber may be involved in modulating ghrelin, possibly through prolonged energy release from fermentation.

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