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ORIGINAL CONTRIBUTION

An explorative study of in vivo digestive starch characteristics and postprandial glucose kinetics of wholemeal wheat bread

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Abstract *Background* Based on in vitro measurements, it is assumed that starch in wholemeal bread is rapidly digestible, which is considered to be less desirable for health. *Aim of the study* To evaluate the in vitro prediction, we characterized starch digestion of wholemeal wheat bread (WB) and postprandial glucose kinetics in healthy volunteers. *Methods* In a crossover study 4 healthy men ingested either intrinsically ^{13}C-enriched WB (133 g) or glucose (55 g) in water. Plasma glucose and insulin concentrations were monitored during 6 h postprandially. Using a primed continuous infusion of D-[6,6-$^{2}H_2$] glucose, the rate of systemic appearance of glucose was estimated (reflecting glucose influx) and the endogenous glucose production calculated. *Results* The glucose influx rate after WB was comparable with that after glucose in the early postprandial phase (0–2 h) ($P = 0.396$) and higher in the late postprandial phase (2–4 h) ($P = 0.005$). Despite the same initial glucose influx rate the 0–2 h incremental area under the curve (IAUC) of insulin after WB was 41% lower than after glucose ($P = 0.037$). Paradoxically endogenous glucose production after WB was significantly more suppressed than after glucose (0–2 h IAUC: $P = 0.015$, 2–4 h IAUC: $P = 0.018$). *Conclusions* Starch in WB seems to be partly rapidly and partly slowly digestible. Postprandial insulin response and endogenous glucose production after WB ingestion might not solely be determined by the digestive characteristics of starch; other components of WB seem to affect glucose homeostasis. In vitro measurements might not always predict in vivo starch digestion precisely.

Key words bread – starch digestion – glucose kinetics – stable isotopes

Introduction

Evidence is accumulating that the type of starchy foods plays a role in the prevention of chronic diseases. Associations are found between high intake of whole grain products and the protection against cardiovascular disease and type 2 diabetes [1, 12, 17]. Also, several studies [14, 17, 21], even though not always consistent [17, 18], have shown that diets that contain large amounts of foods which elicit relatively low postprandial blood glucose responses (low glycemic index foods) may protect against chronic diseases. It is generally assumed that the postprandial

blood glucose response to starchy foods is mainly determined by the rate of digestion of starch—thus products with slowly digestible starch features are considered to be beneficial. These features of starch digestion can be determined by in vitro assays. Postprandial blood glucose, however, is the net result of various postabsorptive processes and—besides absorption of starch derived glucose—endogenous glucose production and glucose disposal into various tissues determine blood glucose response. The contribution of these processes to postprandial blood glucose and how they are influenced by other food components has so far received little attention in nutritional studies.

In many societies bread is an important component of the diet. Bread made from refined flour and even wholemeal bread, if made from finely ground whole grains, has been shown in vitro to contain a high percentage of rapidly digestible starch (93% of total starch) [8] which implies that it is a less desirable food product. Yet so far, no information is available about the in vivo digestive characteristics of wheat bread starch in humans. Nor is there information on the underlying glucose kinetics which determine postprandial glucose response. Therefore, the purpose of our study was to characterize starch digestion of wholemeal wheat bread and postprandial glucose kinetics in healthy volunteers by comparing them to that of the readily absorbable monosaccharide glucose.

Subjects and methods

Subjects

Four healthy male subjects (age 23.0 ± 1.1 years, BMI of 21.4 ± 1.3 kg/m^2 (mean ± SEM)) were recruited by advertising. The criteria for exclusion were use of medications, use of antibiotics in the last 3 mo, gastrointestinal symptoms, diabetes mellitus and gastrointestinal surgery. Each subject gave written informed consent for the study, and approval was obtained from the Medical Ethics Committee of the University Medical Center in Groningen.

Test meals

The test meals were either 133 g of wholemeal wheat bread (WB) and 250 ml of tap water or 55 g glucose (90% carbohydrates) (glucose-monohydrate, Natufood, Natuproducts BV, Harderwijk, The Netherlands) which was dissolved in 250 ml of tap water. Each test meal provided 50 g available carbohydrates.

Glucose was corn derived and therefore naturally labeled with ^{13}C, which is necessary to be able to apply the dual isotope technique. The ^{13}C abundance of glucose was 1.09824 atom % ^{13}C. ^{13}C-labelling of wheat (Durum wheat *var Lloyd*) was achieved by subjecting plants to a $^{13}CO_2$ enriched atmosphere. For preparation of WB 11.00 g ^{13}C-enriched wheat grains (3.034 atom % ^{13}C) and 355 g unlabelled wheat grains (1.085 atom % ^{13}C) of the same variety were milled in an electric household grain mill (SAMAP Elsasser grain mill F 100) on the finest grade. The wholemeal flour, 320 g lukewarm water, 6.4 g dry yeast and 6.4 g salt was used to bake bread in a Panasonic home bread maker with the wholemeal bread program of 5 h. After cooling, the bread was sliced and the crusty ends removed. Portions of 133 g bread were frozen. To measure the level of ^{13}C-enrichment of the bread starch was isolated and hydrolysed. The ^{13}C abundance of starch in bread was 1.1176 atom % ^{13}C. One portion of bread consisted of 50 g available carbohydrates, 11.5 g protein, 2.1 g fat, 54.8 g water and 14.6 g fiber.

In vitro analysis

In vitro carbohydrate analysis of WB was conducted according to the method of Englyst [9].

Study protocol

The study was performed in a crossover manner, with each subject studied on two occasions at least 1 week apart. The subjects were asked to refrain from consuming foods enriched in ^{13}C, like cane sugar, corn products and pineapple, for 3 days preceding the experiments. The subject's food intake after 1700 h the day before each experiment was individually standardized. Subjects refrained from alcohol and strenuous exercise for 24 h before each study day. They fasted and drank only water, coffee or tea without sugar and milk from 2200 h the night before the study. Subjects arrived at 0800 h and cannulas were inserted into veins in both forearms, one for collection of blood, kept patent with heparin (50 IE/ml), and the other for infusion of D-[6,6-$^2H_2$]glucose (98% ^{2}H APE) (Isotec Inc, Miamisburg, OH, USA). Throughout the 8-h study period subjects relaxed by reading or watching videos. A primed-continuous infusion of D-[6,6-$^2H_2$]glucose (prime: 342 mg, continuous infusion: 3.5 mg/min (9.5 mg/ml)) was started at time minus 120 min. 120 min after the beginning of the infusion (t = 0) the test meal was ingested.

Sample collection

Blood and breath samples were collected every 30 min for 90 min, every 15 min for the following 150 min

and every 30 min thereafter. Blood was collected into tubes containing sodium fluoride and potassium oxalate. After centrifugation (3,000×*g*; 7 min) at 4°C, the plasma samples were stored at −20°C until assayed.

Analytical procedures

Glucose was measured with an ECA-180 glucose analyzer (Medingen, Dresden, Germany). The inter-assay and intra-assay coefficient of variation was 3 and 1%, respectively. Insulin concentrations were measured in duplicate using a commercially available RIA (Diagnostic Systems Laboratories, Webster, Texas, USA). The inter-assay and intra-assay coefficient of variation was 9.9 and 4.5%, respectively. The sample preparation procedure for the analysis of the isotopic enrichment of plasma glucose is described in detail elsewhere [26, 27]. The $^{13}C/^{12}C$ isotope ratio measurement of the glucose penta-acetate derivative was determined by GC/Combustion/Isotope Ratio MS [25] and the ^{2}H enrichment in the derivative by GC/MS [26].

Calculations

The enrichment of [6,6-$^{2}H_2$]glucose (in mole% excess) and ^{13}C (expressed in atom % excess) were calculated as previously described [26], and smoothed using the Optimized Optimal Segments program developed by Bradley et al. [2]. The rate of total (endogenous and exogenous) glucose appearance (RaT) in plasma was estimated using the non-steady state equation of Steele as modified by De Bodo [7, 22]. Identical behavior of labeled and unlabeled glucose molecules was assumed. The effective volume of distribution was assumed to be 200 ml/kg and the pool fraction value 0.75 [24]. The RaEx was calculated according to Tissot et al. [24] and endogenous glucose production (EGP) by subtracting RaEx from RaT [24].

To describe postprandial kinetics the time to peak, the peak values and the incremental areas under the postprandial curves (IAUCs) were used and compared. The time to peak was defined as time period between the intake of the test meal and the appearance of peak plasma concentration or rate. Using the trapezoidal rule [11] the IAUCs for all parameters were calculated for 2-h time periods (0–120, 120–240, 240–360 min) for the periods before values stayed at baseline levels. For the IAUC calculations of RaT and RaEx values were multiplied by body weight and for RaEx expressed as percentage of the administered dose of glucose equivalents (cum dose %). EGP was expressed as % suppression of the mean of the baseline values and IAUC values calculated for the time periods 0–120, 120–240 and 240–360 min.

Statistics

Data are presented as mean ± SEM. Rates are expressed as milligrams per kilogram total body weight per minute. Differences between the results of the test meals were assessed with the two-tailed paired Student's *t* test. All analyses were performed with the statistical program SPSS 11.0 for Windows software (SPSS inc., Chicago, IL). $P < 0.05$ was considered to be significant.

Results

Test meals

In vitro determination showed that 90.5% of the total amount of carbohydrates in wholemeal wheat bread (WB) was rapidly available glucose (RAG), 3.6% slowly available glucose (SAG) and 5.9% resistant starch (RS).

Postprandial plasma glucose and insulin response

Fasting plasma glucose concentrations did not differ on the glucose (5.1 ± 0.2 mmol/l) and WB (4.9 ± 0.1 mmol/l) study days ($P = 0.607$). Neither the peak glucose concentrations nor the IAUC of the WB differed significantly ($P = 0.239$ and $P = 0.078$, respectively) from that of glucose (Fig. 1, Table 1).

Fasting insulin concentrations did not differ on the glucose (36.7 ± 4.3 pmol/l) and WB (27.0 ± 1.8 pmol/l) study days ($P = 0.178$). After WB a lower insulin peak concentration than after glucose was observed (168.2 ± 37.6 and 251.6 ± 36.2 pmol/l, respectively; $P = 0.01$) as well as a 41% lower 0–120 min IAUC ($P = 0.037$) (Fig. 2, Table 1).

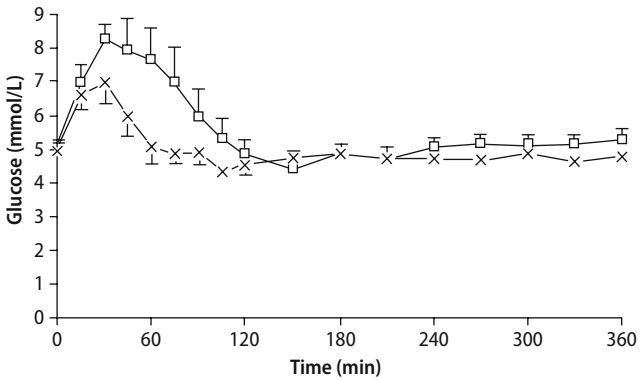

Fig. 1 Postprandial plasma glucose concentrations in healthy men after ingestion of 55 g ^{13}C-enriched glucose (*open square*) and 133 g ^{13}C-enriched wholemeal wheat bread (*multi symbol*). Values are means ± SEM, $n = 4$. The 0–120 min incremental area under the curve was not significantly ($P = 0.078$) lower after WB than after glucose

Table 1 Incremental areas under the curve of glucose, insulin, RaT, RaEx and EGP after ingestion of 55 g of glucose and 133 g of wholemeal wheat bread in healthy men[a]

	IAUC 0–120 min		IAUC 120–240 min		IAUC 240–360 min	
	Glucose	WB	Glucose	WB	Glucose	WB
Glucose (mmol/l/2 h)	196 ± 51	81 ± 28				
Insulin (pmol/l/2 h)	13,994 ± 3,725	8,272 ± 2,294[b]				
RaT (g/2 h)	32.6 ± 1.1	18.2 ± 0.8[b]	3.2 ± 0.6	4.0 ± 1.6		
RaEx (%dose/2 h)	62.4 ± 4.3	64.9 ± 4.0	11.4 ± 1.5	29.6 ± 1.8[2]	0.3 ± 1.0	9.9 ± 1.4[b]
EGP (%supp/2 h)[c]	−4,887 ± 892	−7,751 ± 787[2]	−2,171 ± 749	−6,398 ± 648[2]	−975 ± 387	−4,370 ± 476[b]

[a] *RaT* systemic rate of appearance of total glucose, *RaEx* systemic rate of appearance of exogenous glucose, *EGP* endogenous glucose production, mean ± SEM; $n = 4$
[b] Significantly different from glucose, $P < 0.05$ (Student's t test)
[c] % suppression of mean baseline values

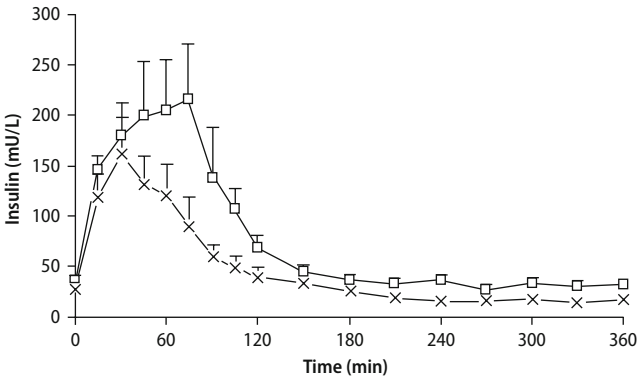

Fig. 2 Postprandial plasma insulin concentrations in healthy men after ingestion of 55 g ^{13}C-enriched glucose (*open square*) and 133 g ^{13}C-enriched wholemeal wheat bread (WB) (*multi symbol*). Values are means ± SEM, $n = 4$. The 0–120 min incremental area under the curve was significantly ($P = 0.037$) lower after WB than after glucose

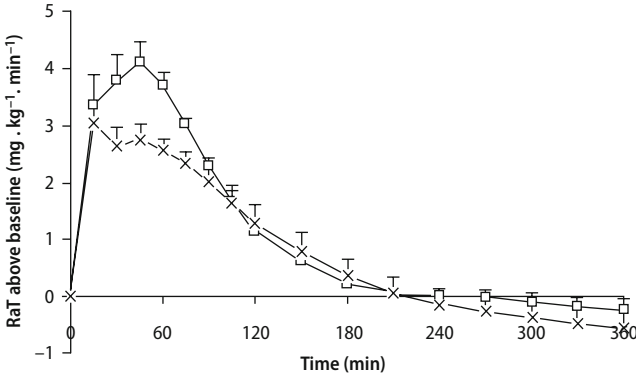

Fig. 3 Rate of systemic appearance of total glucose above baseline in healthy men after ingestion of 55 g ^{13}C-enriched glucose (*open square*) and 133 g ^{13}C-enriched wholemeal wheat bread (*multi symbol*). Values are means ± SEM, $n = 4$. The 0–120 min incremental area under the curve (IAUC) was significantly ($P = 0.038$) lower after WB than after glucose. The 120–240 min IAUC were the same

Rate of systemic appearance of total glucose (RaT)

The basal RaT was different on the glucose and the WB study day (2.2 ± 0.2 and 2.6 ± 0.2 mg/kg · min, respectively; $P = 0.010$). The RaT increased to a maximum above baseline of 3.0 ± 0.4 mg/kg min after WB at 15 ± 0 min and of 4.3 ± 0.4 mg/kg min after glucose at 34 ± 7 min (Fig. 3). Peak RaT and time to peak was not statistically different ($P = 0.058$ and $P = 0.080$, respectively) nor was the 120–240 min IAUC ($P = 0.640$). The 0–120 min IAUC was significantly higher after glucose than after WB ($P = 0.038$) (Fig. 3, Table 1).

Rate of systemic appearance of exogenous glucose (RaEx)

The peak values of RaEx did not differ between the WB meal and the glucose meal (4.8 ± 0.5 and 5.1 ± 0.2 mg/kg min, respectively, $P = 0.397$) nor did the time to peak (45 ± 12 and 41 ± 4 min respectively, $P = 0.718$) (Fig. 4). The 0–120 min IAUC after WB was the same as after glucose ($P = 0.396$), however after 120 min the RaEx after WB declined significantly slower than after glucose. The differences in RaEx kinetics resulted in a higher 120–240 and 240–360 min IAUC after WB as compared to glucose ($P = 0.005$ and $P = 0.001$) (Table 1).

Endogenous glucose production (EGP)

Maximum suppression after WB did not differ from that after glucose (76 ± 6 and 68 ± 8%, respectively; $P = 0.239$) nor did the time to maximum suppression (71 ± 21 and 53 ± 14%, respectively; $P = 0.137$). In the 0–120, 120–240, 240–360 min period EGP was more suppressed after ingestion of WB than after glucose ($P = 0.015$, $P = 0.018$ and $P = 0.005$, respectively)

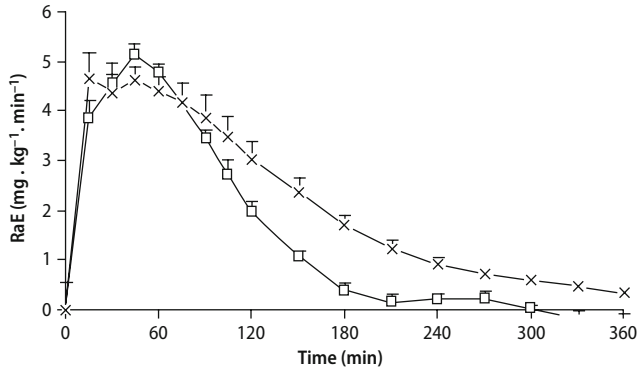

Fig. 4 Rate of systemic appearance of exogenous glucose in healthy men after ingestion of 55 g ^{13}C-enriched glucose (*open square*) and 133 g ^{13}C-enriched wholemeal wheat bread (*multi symbol*). Values are means ± SEM, $n = 4$. The 0–120 min incremental area under the curve (IAUC) after WB and glucose were the same. The 120–240 and 240–360 min IAUC were significantly ($P < 0.05$) higher after WB than after glucose

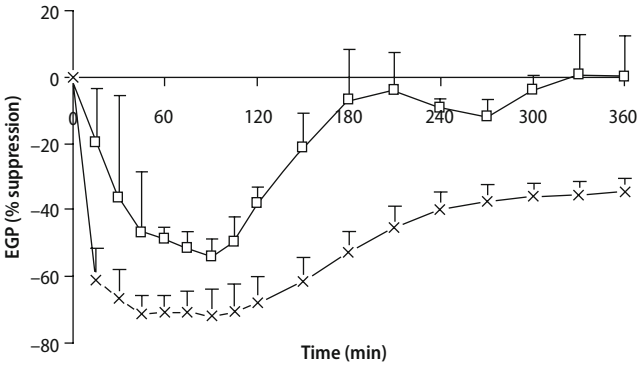

Fig. 5 Percentage suppression from baseline of endogenous glucose production in healthy men after ingestion of 55 g ^{13}C-enriched glucose (*open square*) and 133 g ^{13}C-enriched wholemeal wheat bread (*multi symbol*). Values are means ± SEM, $n = 4$. The 0–120, 120–240 and 240–360 min incremental areas under the curve were significantly ($P < 0.05$) higher after WB than after glucose

(Fig. 5, Table 1). Endogenous glucose production returned to near baseline values at 180 min after glucose whereas it remained still suppressed 6 h after WB.

Discussion

We determined the starch digestive characteristics of WB and compared the postprandial glucose kinetics with that of glucose dissolved in water.

We found that in the early postprandial phase (0–120 min) the influx rate of glucose derived from WB starch was comparable to that of glucose from the glucose solution. Despite of this the insulin response was significantly lower after WB and paradoxically the EGP was significantly more suppressed after WB. This indicates that in the case of WB consumption suppression of EGP is largely insulin independent. The same glucose influx rate accompanied by enhanced suppression of EGP after WB resulted in lower RaT as compared to glucose.

The comparison of the physiological responses to the ingestion of glucose with that of a starchy food with a comparable glucose influx rate makes it possible to identify which responses are related to either starch characteristics or other food components. Decreased insulin response after bread as compared to glucose can not be explained by a slower influx rate of starch derived glucose in our study. Therefore, the effect of other components present in bread on insulin concentrations need to be considered. WB contains yeast, fiber and a small amount of protein as well as a wide range of micronutrients and phytochemicals. Protein is capable of enhancing insulin response which would be the opposite effect of what we have observed. Dietary viscous fiber have been described to be able to blunt insulin response but are unlikely to be responsible in our case since wheat fiber is predominantly non-viscous fiber [20]. *Indirect* effects of those components on the insulin response have also to be taken into account since more than 50% of the increase in plasma insulin concentrations after a glucose load is accounted for by incretin release [19]. Glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 are incretin hormones which are released from the gut after ingestion of a meal. It is therefore possible that less pronounced concentrations of these hormones are responsible for the reduced insulin concentrations after WB as compared to glucose. Other factors than the glucose influx rate need then to be responsible for the difference of effect. For GIP this would be in contrast to the results of our recent study [27] in which we showed that the influx rate of glucose was correlated to GIP plasma concentrations after ingestion of glucose, corn pasta and uncooked cornstarch. However, these test meals were much simpler in composition and did not contain a comparable variety of nutrients and phytochemicals nor did they contain dietary fiber. So far very limited information [28] is available about the effects of cereal fiber—which are *independent* from the glucose influx rate - on incretin concentrations. Only one study [28] investigated the effect of insoluble fiber on incretin response. Insoluble oat fiber added to bread accelerated GIP response whereas added insoluble wheat fiber did not. GLP-1 plasma concentrations were not affected by the addition of fiber.

Until now measures aimed to decrease postprandial insulin concentrations were to decrease the load of carbohydrates or to slow down the rate of absorption by inhibitors or by choosing low GI foods [29]. Based on the results of this study it seems that

food characteristics other than the digestion rate also should to be considered. In view of the adverse health effects of high insulin concentrations [13, 16], investigating which factors are responsible is highly relevant.

EGP in this study is not measured directly but derived from the RaT and RaEx values. The apparently insulin-independent effect on EGP is very intriguing. Insulin is regarded as the primary determinant of EGP which exerts its effect in humans mainly in a direct manner [4]. However, indirect actions also play a role which comprise inhibition of glucagon secretion, decrease in release of nonesterified fatty acids and glycerol from adipose tissue and gluconeogenic precursors from skeletal muscles as well as changes in neural signalling to the liver [3]. Furthermore, EGP might also be influenced by adipokines (e.g. adiponectin [5, 23]) and gastrointestinal hormones (e.g. GLP-1 [6]) either directly or by their insulin-sensitizing effects on the liver. In view of the complexity of the regulation of EGP, identifying food components involved in modulation of EGP is very challenging.

In the late postprandial phase (120–240 min) the influx rate of starch derived glucose was significantly higher after WB than after glucose and suggests that wheat starch in bread is in part slowly digestible. Data of the influx rate of slowly digestible starch (uncooked corn starch) of our previously study [27] support this suggestion. After consumption of uncooked corn starch we found a similar 120–240 min influx rate of 34.6 ± 2.7 cum % dose/2 h, whereas the 0–120 min influx rate was lower than that of wheat bread (35.4 ± 3.9 cum % dose/2 h)—as expected. Even though release of ^{13}C-glucose that has initially been taken up by the liver could contribute to the late ^{13}C-appearance, this contribution has been shown to be quantitatively very small (<3%, [15]).

The high influx rate in the late postprandial phase amounted to 30% of the dose ingested. This was not expected based on the in vitro data which predicted a very low amount of SAG (4% of total carbohydrates). So far studies evaluating the predictive value of in vitro measurement of RAG and SAG have been based on total blood glucose concentrations during the first two postprandial hours since it is generally assumed that blood glucose concentrations directly reflect the rate of digestion and influx of exogenous glucose into the systemic circulation. For a number of cereal products the glycemic index values could be explained by the RAG or SAG content of the product [10]. However, our study implies that blood glucose concentrations do not adequately reflect in vivo digestion rate because influx of exogenous glucose from a starchy meal can be ongoing after blood glucose concentrations are back to basal levels after 2 h. Therefore in vitro measurements can be useful for predicting glucose response but the predictive value for the in vivo rate of digestion seems to be limited.

In conclusion, our data suggest that WB starch is partly rapidly and partly slowly digestible which could not be derived from in vitro determinations.

Furthermore, our data suggest that decreased insulinemic response is not necessarily caused by a lower intestinal rate of starch digestion and absorption. The physiological response after whole meal bread consumption seems not only be determined by the characteristics of the starch but also by other components of the bread. If our observations can be confirmed with other starchy products this will have implications for the classification of food products which is currently focused on starch characteristics.

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References

1. Anderson JW, Hanna TJ, Peng X, Kryscio RJ (2000) Whole grain foods and heart disease risk. J Am Coll Nutr 19:291S–299S
2. Bradley DC, Steil GM, Bergman RN (1995) OOPSEG: a data smoothing program for quantitation and isolation of random measurement error. Comput Methods Programs Biomed 46:67–77
3. Cherrington AD (2005) The role of hepatic insulin receptors in the regulation of glucose production. J Clin Invest 115:1136–1139
4. Cherrington AD, Edgerton D, Sindelar DK (1998) The direct and indirect effects of insulin on hepatic glucose production in vivo. Diabetologia 41:987–996
5. Combs TP, Berg AH, Obici S, Scherer PE, Rossetti L (2001) Endogenous glucose production is inhibited by the adipose-derived protein Acrp30. J Clin Invest 108:1875–1881
6. D'Alessio D, Vahl T, Prigeon R (2004) Effects of glucagon-like peptide 1 on the hepatic glucose metabolism. Horm Metab Res 36:837–841
7. De Bodo RC, Steele R, Altszuler N, Dunn A, Bishop JS (1963) On the hormonal regulation of carbohydrate metabolism: studies with C14 glucose. Recent Prog Horm Res 19:445–448
8. Englyst HN, Kingman SM, Cummings JH (1992) Classification and measurement of nutritionally important starch fractions. Eur J Clin Nutr 46(Suppl 2):S33–S50

9. Englyst KN, Englyst HN, Hudson GJ, Cole TJ, Cummings JH (1999) Rapidly available glucose in foods: an in vitro measurement that reflects the glycemic response. Am J Clin Nutr 69:448–454
10. Englyst KN, Vinoy S, Englyst HN, Lang V (2003) Glycaemic index of cereal products explained by their content of rapidly and slowly available glucose. Br J Nutr 89:329–340
11. Food and agriculture organization of the United Nations (1998) Carbohydrates in human nutrition: report of a joint FAO/WHO expert consultation. Nutrition Paper no. 66. Food and agriculture organization of the United Nations, Rome
12. Jacobs DR Jr, Meyer KA, Kushi LH, Folsom AR (1998) Whole-grain intake may reduce the risk of ischemic heart disease death in postmenopausal women: the Iowa women's health study. Am J Clin Nutr 68:248–257
13. Kopp W (2003) High-insulinogenic nutrition–an etiologic factor for obesity and the metabolic syndrome? Metabolism 52:840–844
14. Liu S, Willett WC, Stampfer MJ, Hu FB, Franz M, Sampson L, Hennekens CH, Manson JE (2000) A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. Am J Clin Nutr 71:1455–1461
15. Livesey G, Wilson PD, Dainty JR, Brown JC, Faulks RM, Roe MA, Newman TA, Eagles J, Mellon FA, Greenwood RH (1998) Simultaneous time-varying systemic appearance of oral and hepatic glucose in adults monitored with stable isotopes. Am J Physiol 275:E717–E728
16. Ludwig DS (2002) The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. JAMA 287:2414–2423
17. McKeown NM, Meigs JB, Liu S, Wilson PW, Jacques PF (2002) Whole-grain intake is favorably associated with metabolic risk factors for type 2 diabetes and cardiovascular disease in the Framingham offspring study. Am J Clin Nutr 76:390–398
18. Meyer KA, Kushi LH, Jacobs DR Jr, Slavin J, Sellers TA, Folsom AR (2000) Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. Am J Clin Nutr 71:921–930
19. Nauck MA, Homberger E, Siegel EG, Allen RC, Eaton RP, Ebert R, Creutzfeldt W (1986) Incretin effects of increasing glucose loads in man calculated from venous insulin and C-peptide responses. J Clin Endocrinol Metab 63:492–498
20. Ramulu P, Rao PU (1997) Effect of processing on dietary fiber content of cereals and pulses. Plant Foods Hum Nutr 50:249–257
21. Salmeron J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC (1997) Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. JAMA 277:472–477
22. Steele R, Wall JS, De Bodo RC, Altszuler N (1956) Measurement of size and turnover rate of body glucose pool by the isotope dilution method. Am J Physiol 187:15–24
23. Stefan N, Stumvoll M, Vozarova B, Weyer C, Funahashi T, Matsuzawa Y, Bogardus C, Tataranni PA (2003) Plasma adiponectin and endogenous glucose production in humans. Diabetes Care 26:3315–3319
24. Tissot S, Normand S, Guilluy R, Pachiaudi C, Beylot M, Laville M, Cohen R, Mornex R, Riou JP (1990) Use of a new gas chromatograph isotope ratio mass spectrometer to trace exogenous ^{13}C labelled glucose at a very low level of enrichment in man. Diabetologia 33:449–456
25. Vonk RJ, Hagedoorn RE, de Graaff R, Elzinga H, Tabak S, Yang YX, Stellaard F (2000) Digestion of so-called resistant starch sources in the human small intestine. Am J Clin Nutr 72:432–438
26. Vonk RJ, Stellaard F, Priebe MG, Koetse HA, Hagedoorn RE, De Bruijn S, Elzinga H, Lenoir-Wijnkoop I, Antoine JM (2001) The ^{13}C/2H-glucose test for determination of small intestinal lactase activity. Eur J Clin Invest 31(3):226–233
27. Wachters-Hagedoorn RE, Priebe MG, Heimweg JA, Heiner AM, Englyst KN, Holst JJ, Stellaard F, Vonk RJ (2006) The rate of intestinal glucose absorption is correlated with plasma glucose-dependent insulinotropic polypeptide concentrations in healthy men. J Nutr 136:1511–1516
28. Weickert MO, Mohlig M, Koebnick C, Holst JJ, Namsolleck P, Ristow M, Osterhoff M, Rochlitz H, Rudovich N, Spranger J, Pfeiffer AF (2005) Impact of cereal fiber on glucose-regulating factors. Diabetologia 48:2343–2353
29. Wolever TM, Campbell JE, Geleva D, Anderson GH (2004) High-fiber cereal reduces postprandial insulin responses in hyperinsulinemic but not normoinsulinemic subjects. Diabetes Care 27:1281–1285