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Fibre-enriched buckwheat pasta modifies blood glucose response compared to corn pasta in individuals with type 1 diabetes and celiac disease: Acute randomized controlled trial

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ABSTRACT

Aim: People with type 1 diabetes and celiac disease (T1D&CD) have high blood glucose variability. Processed gluten-free foods have shown to induce a worse metabolic profile whereas naturally gluten-free foods may represent healthier options. On the other hand, dietary fibre has shown to reduce postprandial glycemic excursions in individuals with diabetes. Thus, we evaluated the acute effect of fibre-enriched buckwheat (FBP) and corn pasta (CP) on postprandial blood glucose response (PP-BGR).

Methods: Ten adult patients with T1D&CD consumed two meals with the same amount of carbohydrate while differing only for pasta type (FBP or CP) preceded by the same insulin bolus. Participants utilized continuous glucose monitoring (CGM) and data over 6 h after meal were analyzed.

Results: PP-BGR differed between the two meals, being significantly lower in the first period (0–3 h) after the CP than the FBP meal (iAUC: -38 ± 158 vs. 305 ± 209 mmol/L · 180 min, $p = 0.040$), whereas significantly higher in the second period (3–6 h) after the CP than the FBP meal (iAUC: 432 ± 153 vs. 308 ± 252 mmol/L · 180 min, $p = 0.030$). Overall, a less variable postprandial profile was observed after FBP than CP consumption.

Conclusions: In individuals with T1D&CD, the acute consumption of FBP induces significant differences in PP-BGR compared with CP that may be clinically relevant.

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1. Introduction

Type 1 diabetes is often associated with celiac disease (gluten-sensitive enteropathy), an immune-mediated disorder trig-

gered by an adverse reaction to dietary gluten, a protein complex found in almost all cereals [1]. The frequency of celiac disease in individuals with type 1 diabetes is 1–16% compared with 0.3–1% in the general population [2].

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To date, the only therapy for celiac disease is the complete exclusion of gluten-containing foodstuff from the diet [3]. On the other hand, nutritional therapy is a cornerstone to achieving a good blood glucose control and preventing hypoglycemia in type 1 diabetic individuals [2,4].

The effect of gluten-free foods on glycemic response in individuals with type 1 diabetes and celiac disease is still controversial. It has been suggested that the lipid content and the high glycemic index of some gluten-free products may have detrimental effect on metabolic control [5].

Moreover, the gluten-free diet may lead to poor diet quality and nutritional deficiencies, especially in terms of micronutrients and fibre intake [3].

Hence, several efforts have been made to find alternative gluten-free foods that may be suitable from a metabolic point of view. In this context, naturally gluten-free foods as pseudocereals (i.e. buckwheat, amaranth, and quinoa) have been suggested as a healthier choice than the commercial gluten-free products. As a matter of fact, these foods are good sources of micronutrients (i.e. iron, zinc, copper, manganese, and magnesium) and dietary fibre [6].

In addition, it is well established that dietary factors such as soluble fibre content beneficially influence postprandial glycaemic excursions in individuals with either type 1 or type 2 diabetes mellitus [7,8]. Thus, the addition of soluble fibre to naturally gluten-free foods could represent a nutritional strategy to achieve a better blood glucose control in individuals with type 1 diabetes and celiac disease. In this regard, food industries are developing new types of products and, among them, a fibre-enriched buckwheat pasta has been produced.

Therefore, the aim of our study was to evaluate the acute impact of fibre-enriched buckwheat pasta on postprandial blood glucose in individuals with type 1 diabetes and celiac disease using corn pasta as control since it represents one of the most consumed gluten-free foods.

2. Subjects and methods

2.1. Participants

Ten individuals with type 1 diabetes and celiac disease (8 women and 2 men), treated with continuous subcutaneous insulin infusion or multiple daily injections of insulin according to a basal bolus regimen, and following a strict gluten-free diet since the diagnosis (18 ± 7 years), were recruited at the diabetes care unit of the Federico II University of Naples.

Exclusion criteria were positive serology for antibodies to tissue transglutaminase and endomysium in the previous 6 months, pregnancy/breast feeding, serious microvascular and macrovascular diabetes complications, and any other chronic or acute disease apart from diabetes seriously affecting health status.

The study protocol was approved by the Federico II University Ethics Committee and registered at [ClinicalTrials.gov](https://clinicaltrials.gov), number NCT03380988. The present study was conducted according to the guidelines laid down in the Declaration of Helsinki. All participants gave their written informed consent to participate in the study.

2.2. Study design

The study was preceded by a 1-week run-in period during which participants underwent continuous glucose monitoring (CGM) and completed a 7-day dietary record to define the individual insulin-to-carbohydrate ratio. The study had a randomized crossover design with each subject studied on two occasions at least one week apart. Participants were assigned to consume, in random order, two test meals: a meal with fibre-enriched buckwheat pasta (FBP) or a meal with corn pasta (CP), used as control. Over the experimental period, participants underwent continuous glucose monitoring (CGM), wearing their sensors 7 days/week. They were instructed to calibrate 3 times/day using premeal blood glucose capillary tests.

On the morning of the test, subjects consumed the same standardized breakfast (30 g of carbohydrates), in order to avoid a second-meal effect bias, and had the usual insulin bolus. Then, the participants consumed the test meals at lunchtime. In case of premeal blood glucose levels outside the 5–8 mmol/L range or a rapid decrease/increase (3.3 mmol/L) of glucose levels during the last 60 min according to CGM measurement, the test meal was postponed.

Premeal insulin doses, injected just before eating, were based on the individual insulin-to-carbohydrates ratio determined during the run-in and, for each participant, were the same on the two occasions.

Moreover, blood was sampled before the test meal and over 3 h in the postprandial period (30, 60, 90, 120, 150 and 180 min) to evaluate plasma glucose concentrations.

2.3. Test meal

The two meals were composed by the two types of pasta containing 50 g of carbohydrates (FBP: 100 g or CP: 60 g) and tomato sauce (100 g tomato sauce, 5 g extra-virgin olive oil). The main difference between the meals was the fibre amount (FBP: 26.5 g or CP: 3.84 g; [Table 1](#)) due to the addition of pea fibre to the buckwheat pasta during the manufacturing process.

There were also small differences in total energy (due to the calculated energy from dietary fibre), and protein and fat intake due to some differences in the nutritional composition of the two types of pasta ([Table 2](#)).

The test meals were prepared by an expert dietitian with a standard procedure (1 L water, 8 g salt, cooking time after boiling: 5 min for FBP and 10 min for CP). Participants were asked to consume the meal together with 200 ml water within 15–20 min.

2.4. Measurements

Continuous glucose monitoring was performed by Enlite Sensor, Medtronic MiniMed, Inc., Northridge, CA ($n = 8$ participants) and Dexcom G4 sensor, San Diego, CA ($n = 2$ participants). The estimated mean absolute relative difference (MARD%) was 17.8% and 13.9%, respectively [9]. The subjects used the type of CGM they were accustomed to. Data from 6-h CGM after the test meals consumption and before

Table 1 – Nutritional composition of the two test meals.

	Control pasta meal	Fibre-enriched buckwheat pasta meal
Energy (kcal)	275	363
Carbohydrates (g)	53.1	53.7
Sugars (g)	3.14	3.61
Fibre (g)	3.84	26.5
Protein (g)	5.15	10.7
Total fat (g)	5.59	7.60
SFA (g)	0.81	1.24
MUFA (g)	3.65	3.65
PUFA (g)	0.38	0.38

MUFA: monounsaturated fatty acids, PUFA: polyunsaturated fatty acids; SFA: saturated fatty acids.

Table 2 – Composition of the two types of pasta expressed for 100 g.

	Control pasta	Fibre-enriched buckwheat pasta
Energy (kcal)	353	300
Carbohydrates (g)	78.3	47.6
Sugars (g)	0.24	0.61
Fibre (g)	3.90	25
Protein (g)	6.42	9.40
Fat (g)	0.66	2.40

the next meal were downloaded by dedicated informatics platforms.

Plasma glucose concentrations were assessed by enzymatic colorimetric methods (ABX Diagnostics, Montpellier, France; Roche Diagnostics, Milan, Italy) on a ABX Pentra 400 (HORIBA Medical, Montpellier, France).

2.5. Statistical analysis and calculation

The sample size was calculated on the primary outcome, i.e., postprandial blood glucose iAUC, on the basis of a previous study [10] where a 7 ± 6 mmol/L · 3h difference in postprandial blood glucose iAUC was detected in subjects with type 1 diabetes consuming test meals differing for glycemic index. This sample size would allow the detection of a difference of this magnitude in the postprandial blood glucose response with an 80% power and a 5% significance level.

Data are expressed as means \pm SD unless otherwise stated. Postprandial glucose incremental areas were calculated by the trapezoidal method.

Differences in postprandial blood glucose profiles were evaluated by two-tailed Student's *t* test for paired samples. Statistical analysis was performed according to standard methods using the Statistical Package for Social Sciences software version 21.0 (SPSS/PC; SPSS, Chicago, IL, USA).

3. Results

3.1. Participants' characteristics

The participants were 32 ± 8 years old and had a BMI of 22.7 ± 3 kg/m². Mean diabetes duration was 23 ± 6 years and they

had an acceptable blood glucose control (HbA1c $7.3 \pm 1.0\%$). As for insulin therapy, 5 participants used continuous subcutaneous insulin infusion, whereas 5 participants used multiple daily injections of insulin according to a basal bolus regimen. No patient had signs or symptoms of autonomic neuropathy.

3.2. Postprandial Glycemia

The 6-h CGM profile showed rather different shapes for the two meals (Fig. 1a). In fact, after CP meal, glucose concentrations were lower in the first part of the curve, in particular from 60 to 220 min, with values that bordered hypoglycemia (3.89 mmol/L) and registered hypoglycemic events in four participants. In two cases, the reduction of glucose concentrations resulted in symptomatic hypoglycemic events. On the contrary, in the second part of the postprandial period (3–6 h), glucose concentrations increased with mean values above 8.89 mmol/L.

A less variable postprandial profile was observed after the FBP meal: a higher glucose response was observed in the first period (from 60 to 220 min), whereas lower values were detected in the second part of the curve (from 220 to 360 min), with mean glucose concentrations that did not exceed 8.89 mmol/L over the whole 6-h period.

The differences in postprandial profile between the two meals were particularly evident evaluating postprandial glucose response as iAUC. As a matter of fact, in the first 3 h of the postprandial response (Fig. 1b) glucose iAUC was significantly lower after the CP meal (CP meal: -38 ± 158 vs. FBP: 305 ± 209 mmol/L · 180 min, $p = 0.040$ by two-tailed Student's *t* test for paired samples).

In the second part of the curve (3–6 h; Fig. 1c) the glycemic response reversed with significantly higher glucose values for the CP meal compared to FBP meal (432 ± 153 vs. 308 ± 252 mmol/L · 180 min, $p = 0.030$).

As for the overall 6-h response, the difference between the two meals was less marked, even if lower iAUC values were detected for CP than FBP meal (425 ± 24 vs. 597 ± 33 mmol/L · 360 min, $p = 0.017$; Fig. 1d).

Measurement of plasma glucose concentrations over the first 3 h (Fig. 2a) were in line with CGM results, with significantly lower levels after CP than FBP at 90 min ($p = 0.043$) and as iAUC was significantly lower after the CP meal than FBP meal (217 ± 208 and 545 ± 236 mmol/L · 180 min, $p = 0.026$; Fig. 2b).

All CGM-derived results remained similar when the two participants treated for the symptomatic hypoglycemic events were excluded from the analyses.

4. Discussion

The main result of this study is that CGM clearly reveals that the shape of the 6-h postprandial blood glucose response to fibre-enriched buckwheat pasta is different from that induced by corn pasta, after the injection of the same dose of insulin, in individuals with type 1 diabetes and celiac disease. The shape of the postprandial response to fibre-enriched buckwheat pasta seems to be more stable with lower risk of

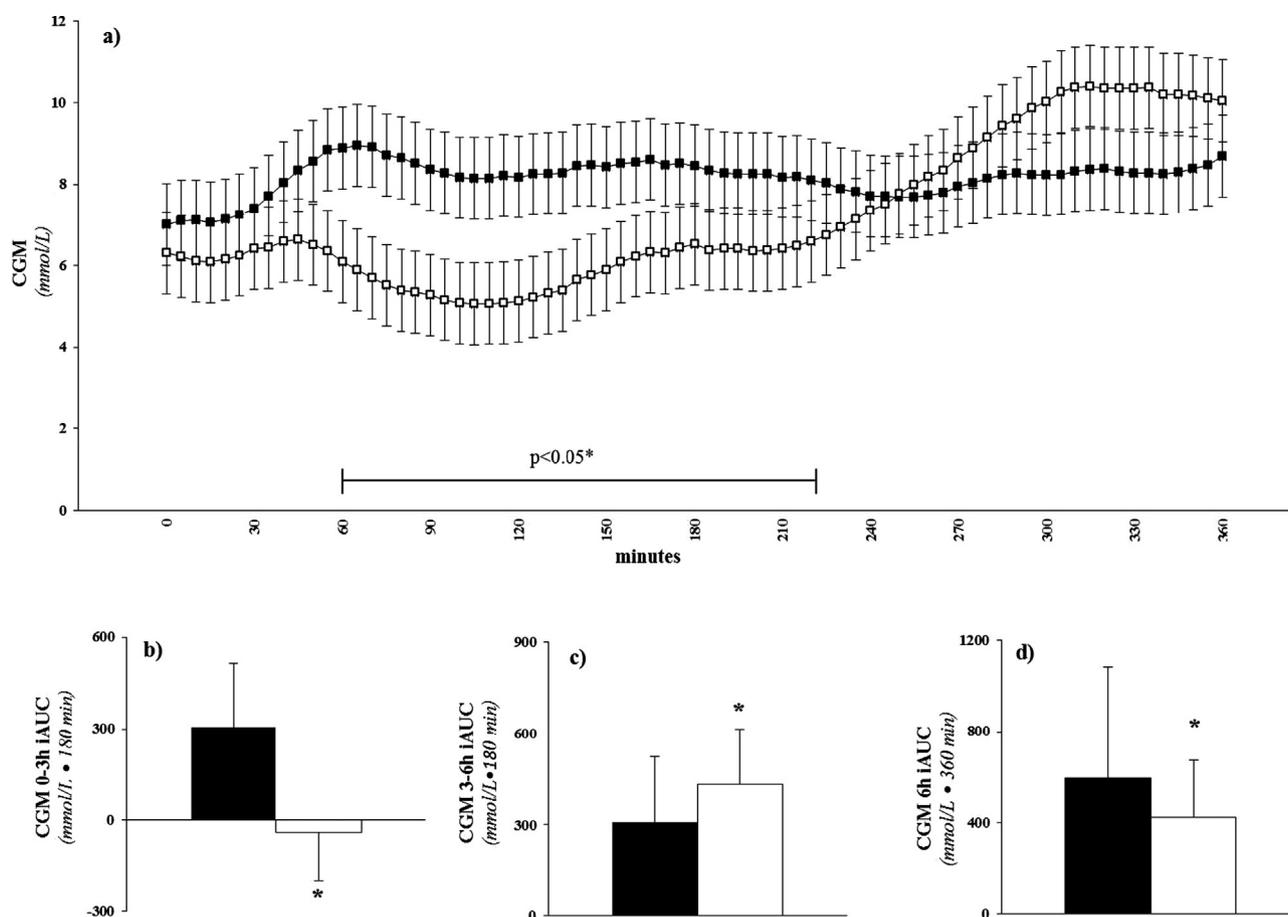


Fig. 1 – (a) CGM profiles after the corn pasta meal (white square) and fibre-enriched buckwheat pasta meal (black square). (b, c, d) CGM response after the two test meals expressed as 0–3 h iAUCs (b), 3–6-h iAUCs (c), and 6-h iAUCs (d). Data are shown as mean \pm SEM. * $p < 0.05$ from 60 to 220 min by two-tailed Student's *t* test for paired samples.

hypoglycemia during the first 2–3 h, and with lower blood glucose concentrations during the late postprandial phase (3–6 h) being constantly lower than 8.89 mmol/L.

On the contrary, after corn pasta intake the risk of hypoglycemia was substantial, with four participants having blood glucose concentrations below 3.89 mmol/L in the first postprandial phase, and two of them having symptomatic hypoglycemia. Of course, with corn pasta there was a greater rebound of blood glucose response in the late postprandial period, with mean blood glucose concentrations above 8.89 mmol/L.

Therefore, although the overall 6-h postprandial glucose response was lower after corn pasta consumption, there was a higher stability after fibre-enriched buckwheat pasta - especially with a lower risk of hypoglycemia in the first postprandial period. This reduction in postprandial glucose variability could mean, in the long-term, a better blood glucose control that is very challenging in individuals with diabetes and celiac disease.

In addition, while gluten-free diet is considered to be a sufficient therapeutic intervention for treating celiac disease, patients simultaneously feel that it is difficult to comply with a strict, gluten-free diet. This feeling is associated with a poorer quality of life and a worse glycemic control [11]. In this

light, having more dietetic options would increase dietary compliance thus improving general health status and quality of life [12].

On the other hand, no side effects have been reported with the use of the fibre-enriched buckwheat pasta.

Since the two test meals used in this acute experiment had the same amount of carbohydrates, the different blood glucose response may be due only to the type of pasta: corn pasta or fibre-enriched buckwheat pasta. There was also a small difference in protein content between the two test meals (5.15 g in corn pasta and 10.7 g in fibre-enriched buckwheat pasta). Although a higher protein intake could induce an increase in insulin secretion, this could not be the case in this study because of the lack of insulin secretion in these type 1 diabetes patients. However, it is known that dietary protein may also delay gastric emptying rate and reduce chyme pH, thus reducing carbohydrates digestion and absorption in healthy subject [13,14] as well as in individuals with diabetes [15,16]. As a consequence, even if the difference in protein intake between the two meals was small, a possible effect of protein on postprandial glucose response cannot be totally excluded.

Buckwheat has showed to be a good source of dietary fibre and micronutrients (i.e. iron, zinc, copper, manganese, and

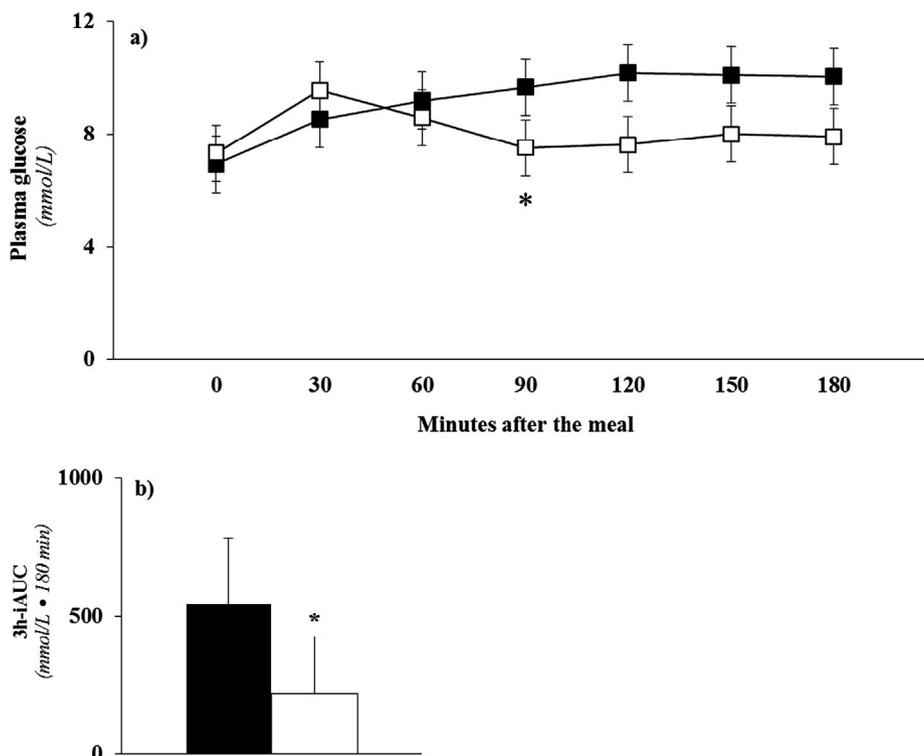


Fig. 2 – (a) Postprandial plasma glucose profiles after the corn pasta meal (white square) and fibre-enriched buckwheat pasta meal (black square). (b) Postprandial plasma glucose response expressed as 3-h iAUC. Data are shown as mean \pm SEM. * $p < 0.05$ by two-tailed Student's *t* test for paired samples.

magnesium) [6,17]. Therefore, buckwheat-based products may represent a suitable tool to increase fibre and micronutrients intake, thus contributing to the improvement of dietary quality in individuals with type 1 diabetes and celiac disease.

As for glucose metabolism, buckwheat-based food intake has been shown to induce a lower or more stable blood glucose response in healthy [18,19] and type 2 diabetic individuals [19–21]. However, no information was available in type 1 diabetic subjects with or without celiac disease. On the other hand, the beneficial effect of fibre-rich foods or fibre-enriched supplements on blood glucose response is well documented in healthy subjects and in diabetic individuals. In particular, the addition of pea fibre to a mixed meal induced prolonged lower blood glucose concentrations in the postprandial period in healthy volunteers [22,23]. No information was available on the combination of the two components, buckwheat and pea fibre, and, to our knowledge, this is the first study evaluating alternative gluten-free foods enriched in soluble fibre for celiac subjects with type 1 diabetes.

Due to the high amount of fibre added to the buckwheat pasta (26.5 g), we would have expected a greater reduction of glucose response. Likely, food processing may have affected the physical state of pea fibre, thus, reducing its glucose-lowering activity, as reported in previous studies [24–26]. As a matter of fact, it has been demonstrated that physical disruption and heat exposure are the main determinants of fibre degradation in fibre-containing foods [24]. Thus, it can be hypothesized that the fibre-enriching process may have deeply modified the physical form of pea fibre thus reducing its potential biological effect. On the other hand, it

is possible that isolated pulses-derived fibres are not as effective as those naturally contained in pulses. Indeed, it is well known that food matrix influences the biological activity of bioactive compounds [27].

Our study is an acute experiment as participants consumed the fibre-enriched buckwheat pasta in one occasion; therefore, our results should be confirmed by evidence from medium/long-term clinical trials. However, our results suggest that fibre-enriched buckwheat pasta may induce a more stable postprandial blood glucose profile as compared to corn pasta, one of the most used food by individuals with celiac disease. In particular, fibre-enriched buckwheat pasta reduces the risk of hypoglycemia in the first hours after the meal and the subsequent rebound of blood glucose concentrations in the late phase of the postprandial period.

Of course, our finding cannot be directly transferred to other populations (i.e. healthy individuals, patients with celiac disease without type 1 diabetes, and patients with type 1 diabetes without celiac disease) due to some specific features of our study group (patients with type 1 diabetes and celiac disease) that could have affected the glucose response. In particular, increased intestinal permeability to carbohydrates is a major trigger of postprandial glucose variability in patients with type 1 diabetes [28] and, even more, in patients with both type 1 diabetes and coeliac disease [29].

In addition, patients with type 1 diabetes or celiac disease showed differences in the composition of the gut microbiota compared to healthy controls [30] associated with worse glycaemic control [31].

Nevertheless, to the best of our knowledge, there are no studies comparing microbiota composition between individuals with type 1 diabetes or celiac disease and those presenting both diseases and we did not perform any measurement of microbiota composition and intestinal permeability. Hence, we have no information about how these two factors might have affected our results.

In conclusion, the consumption of fibre-enriched buckwheat pasta may represent a useful strategy to induce a more stable glucose response in the postprandial period in subjects with type 1 diabetes and celiac disease. Further studies are necessary to evaluate the medium/long-term effects and to investigate possible mechanisms behind these effects.

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Conflicts of interest

C.V., L.B., M.G., A.G., L.C., E.D.M., P.C., A.M., G.A. and A.A.R. declare that there is no conflict of interest regarding the publication of this paper.

A.T. and G.I. work at Andriani SpA, Gravina di Puglia, Bari, Italy.

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C.V. and L.B. wrote the manuscript, designed the experiment, collected and analyzed data, and contributed to discussion. M.G. and A.G. prepared the test meals and provided dietary counseling. L.C. and E.D.M. collected and analyzed data on continuous glucose monitoring. P.C. and A.M. performed biochemical measurements. A.T. and G.I. provided the two pasta types. G.A. contributed to the discussion, and reviewed and edited the manuscript. A.A.R. designed the experiment and wrote the manuscript. A.A.R. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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REFERENCES

- [1] Leonard MM, Cureton PA, Fasano A. Managing coeliac disease in patients with diabetes. *Diabetes Obes Metab* 2015;17:3–8. <https://doi.org/10.1111/dom.12310>.
- [2] American Diabetes Association. *Standards of medical care in diabetes*. *Diabetes Care* 2017;40:S105–13.
- [3] Vici G, Belli L, Biondi M, Polzonetti V. Gluten free diet and nutrient deficiencies: a review. *Clin Nutr* 2016;35:1236–41. <https://doi.org/10.1016/j.clnu.2016.05.002>.
- [4] Authors/Task Force Members, Rydén L, Grant PJ, Anker SD, Berne C, Cosentino F, Danchin N. ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). *Eur Heart J* 2013;34:3035–3087. <http://doi.org/10.1093/eurheartj/eh1108>.
- [5] Scaramuzza AE, Mantegazza C, Bosetti A, Zuccotti GV. Type 1 diabetes and celiac disease: the effects of gluten free diet on metabolic control. *World J Diabetes* 2013;4:130–4. <https://doi.org/10.4239/wjcd.v4.i4.130>.
- [6] Alvarez-Jubete L, Arendt EK, Gallagher E. Nutritive value and chemical composition of pseudocereals as gluten-free ingredients. *Int J Food Sci Nutr* 2009;60:240–57. <https://doi.org/10.1080/09637480902950597>.
- [7] Franz MJ, MacLeod J, Evert A, Brown C, Gradwell E, Handu D, et al. Academy of nutrition and dietetics nutrition practice guideline for type 1 and type 2 diabetes in adults: systematic review of evidence for medical nutrition therapy effectiveness and recommendations for integration into the nutrition care process. *J Acad Nutr Diet* 2017;117:1659–79. <https://doi.org/10.1016/j.jand.2017.03.022>.
- [8] Anderson JW, Randles KM, Kendall CW, Jenkins DJ. Carbohydrate and fiber recommendations for individuals with diabetes: a quantitative assessment and meta-analysis of the evidence. *J Am Coll Nutr* 2004;2:5–17.
- [9] Matuleviciene V, Joseph JJ, Andelin M, Hirsch IB, Attvall S, Pivodic A, et al. A clinical trial of the accuracy and treatment experience of the Dexcom G4 sensor (Dexcom G4 system) and Enlite sensor (guardian REAL-time system) tested simultaneously in ambulatory patients with type 1 diabetes. *Diabetes Technol Ther* 2014;16:759–67. <https://doi.org/10.1089/dia.2014.0238>.
- [10] Parillo M, Annuzzi G, Rivelles AA, Bozzetto L, Alessandrini R, Riccardi G, et al. Effects of meals with different glycaemic index on postprandial blood glucose response in patients with Type 1 diabetes treated with continuous subcutaneous insulin infusion. *Diabet Med* 2011;28:227–9. <https://doi.org/10.1111/j.1464-5491.2010.03176.x>.
- [11] Pham-Short A, Donaghue KC, Ambler G, Garnett S, Craig ME. Quality of life in type 1 diabetes and celiac disease: role of the gluten-free diet. *J Pediatr* 2016;179(131–138). <https://doi.org/10.1016/j.jpeds.2016.08.105> e1.
- [12] Kurien M, Trott N, Sanders DS. Long-term care for patients with coeliac disease in the UK: a review of the literature and future directions. *J Hum Nutr Diet* 2016;29:617–23. <https://doi.org/10.1111/jhn.12379>.
- [13] Karamanlis A, Chaikomin R, Doran S, Bellon M, Bartholomeusz FD, Wishart JM, et al. Effects of protein on glycemic and incretin responses and gastric emptying after oral glucose in healthy subjects. *Am J Clin Nutr* 2007;86:1364–8. <https://doi.org/10.1093/ajcn/86.5.1364>.
- [14] Stanstrup J, Schou SS, Holmer-Jensen J, Hermansen K, Dragsted LO. Whey protein delays gastric emptying and suppresses plasma fatty acids and their metabolites compared to casein, gluten, and fish protein. *J Proteome Res* 2014;13:2396–408. <https://doi.org/10.1021/pr401214w>.
- [15] Ma J, Stevens JE, Cukier K, Maddox AF, Wishart JM, Jones KL, et al. Effects of a protein preload on gastric emptying, glycemia, and gut hormones after a carbohydrate meal in diet-controlled type 2 diabetes. *Diabetes Care* 2009;32:1600–2. <https://doi.org/10.2337/dc09-0723>.
- [16] Bell KJ, Smart CE, Steil GM, Brand-Miller JC, King B, Wolpert HA. Impact of fat, protein, and glycemic index on postprandial glucose control in type 1 diabetes: implications for intensive diabetes management in the continuous

- glucose monitoring era. *Diabetes Care* 2015;38:1008–15. <https://doi.org/10.2337/dc15-0100>.
- [17] Li SQ, Zhang QH. Advances in the development of functional foods from buckwheat. *Crit Rev Food Sci Nutr* 2001;41:451–64. <https://doi.org/10.1080/20014091091887>.
- [18] Skrabanja V, Liljeberg Elmståhl HG, Kreft I, Björck IM. Nutritional properties of starch in buckwheat products: studies in vitro and in vivo. *J Agric Food Chem* 2001;49:490–6.
- [19] Gabriel SG, Shakib MR, Gabriel GN. Effect of pseudocereal-based breakfast meals on the first and second meal glucose tolerance in healthy and diabetic subjects. *Open Access Maced J Med Sci* 2016;4:565–73. <https://doi.org/10.3889/oamjms.2016.115>.
- [20] Stringer DM, Taylor CG, Appah P, Blewett H, Zahradka P. Consumption of buckwheat modulates the post-prandial response of selected gastrointestinal satiety hormones in individuals with type 2 diabetes mellitus. *Metabolism* 2013;62:1021–31. <https://doi.org/10.1016/j.metabol.2013.01.021>.
- [21] Su-Que L, Ya-Ning M, Xing-Pu L, Ye-Lun Z, Guang-Yao S, Hui-Juan M. Effect of consumption of micronutrient enriched wheat steamed bread on postprandial plasma glucose in healthy and type 2 diabetic subjects. *Nutr J* 2013;12:64. <https://doi.org/10.1186/1475-2891-12-64>.
- [22] Smith CE, Mollard RC, Luhovyy BL, Anderson GH. The effect of yellow pea protein and fibre on short-term food intake, subjective appetite and glycaemic response in healthy young men. *Br J Nutr* 2012;108:74–80. <https://doi.org/10.1017/S0007114512000700>.
- [23] Mollard RC, Luhovyy BL, Smith C, Anderson GH. Acute effects of pea protein and hull fibre alone and combined on blood glucose, appetite, and food intake in healthy young men—a randomized crossover trial. *Appl Physiol Nutr Metab* 2014;39:1360–5. <https://doi.org/10.1139/apnm-2014-0170>.
- [24] Scazzina F, Siebenhandl-Ehn S, Pellegrini N. The effect of dietary fibre on reducing the glycaemic index of bread. *Br J Nutr* 2013;109:1163–74. <https://doi.org/10.1017/S0007114513000032>.
- [25] McRorie Jr JW, McKeown NM. Understanding the physics of functional fibers in the gastrointestinal tract: an evidence-based approach to resolving enduring misconceptions about insoluble and soluble fiber. *J Acad Nutr Diet* 2017;117:251–64. <https://doi.org/10.1016/j.jand.2016.09.021>.
- [26] Meng H, Matthan NR, Ausman LM, Lichtenstein AH. Effect of prior meal macronutrient composition on postprandial glycemic responses and glycemic index and glycemic load value determinations. *Am J Clin Nutr* 2017;106:1246–56. <https://doi.org/10.3945/ajcn.117.162727>.
- [27] Aggett PJ, Antoine JM, Asp NG, Bellisle F, Contor L, Cummings JH, et al. PASSCLAIM: consensus on criteria. *Eur J Nutr* 2005;44:5–30. <https://doi.org/10.1007/s00394-005-1104-3>.
- [28] Damci T, Nuhoglu I, Devranoglu G, Osar Z, Demir M, Ilkova H. Increased intestinal permeability as a cause of fluctuating postprandial blood glucose levels in Type 1 diabetic patients. *Eur J Clin Invest*. 2003;33:397–401.
- [29] Uibo R, Panarina M, Teesalu K, Talja I, Sepp E, Utt M, et al. Celiac disease in patients with type 1 diabetes: a condition with distinct changes in intestinal immunity? *Cell Mol Immunol* 2011;8:150–6. <https://doi.org/10.1038/cmi.2010.66>.
- [30] Cohn A, Sofia AM, Kupfer SS. Type 1 diabetes and celiac disease: clinical overlap and new insights into disease pathogenesis. *Curr Diab Rep* 2014;14:517. <https://doi.org/10.1007/s11892-014-0517-x>.
- [31] Murri M, Leiva I, Gomez-Zumaquero JM, Tinahones FJ, Cardona F, Soriguer F, et al. Gut microbiota in children with type 1 diabetes differs from that in healthy children: a case-control study. *BMC Med* 2013;11:46. <https://doi.org/10.1186/1741-7015-11-46>.