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Wholegrain barley ß-glucan fermentation does not improve glucose tolerance in rats fed a high-fat diet

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ABSTRACT

Fermentation of oat and barley *β*-glucans is believed to mediate in part their metabolic health benefits, but the exact mechanisms remain unclear. In this study, we sought to test the hypothesis that barley *β*-glucan fermentation raises circulating incretin hormone levels and improves glucose control, independent of other grain components. Male Sprague-Dawley rats (n = 30) were fed a high-fat diet for 6 weeks and then randomly allocated to 1 of 3 dietary treatments for 2 weeks. The low– (LBG, 0% *β*-glucan) and high– (HBG, 3% *β*-glucan) *β*-glucan diets contained 25% wholegrain barley and similar levels of insoluble dietary fiber, available carbohydrate, and energy. A low-fiber diet (basal) was included for comparison. Immediately prior to the dietary intervention, gastric emptying rate (using the ^{13}C-octanoic breath test) and postprandial glycemic response of each diet were determined. At the end of the study, circulating gut hormone levels were determined; and a glucose tolerance test was performed. The rats were then killed, and indices of cecal fermentation were assessed. Diet did not affect live weight; however, the HBG diet, compared to basal and LBG, reduced food intake, tended to slow gastric emptying, increased cecal digesta mass and individual and total short-chain fatty acid pools, and lowered digesta pH. In contrast, circulating levels of glucose, insulin, gastric-inhibitory peptide, and glucagon-like peptide-1, and glucose tolerance were unaffected by diet. In conclusion, wholegrain barley *β*-glucan suppressed feed intake and increased cecal fermentation but did not improve postprandial glucose control or insulin sensitivity.

1. Introduction

The incidence of type 2 diabetes (T2D) continues to increase globally. Current recommendations target diet and lifestyle modification along with annual screening for T2D as the best approach for preventing and treating impaired glucose tolerance (prediabetes) [1].

Systematic reviews and meta-analyses of large, prospective studies consistently demonstrate that frequent consumption of wholegrain foods improves metabolic homeostasis and prevents or delays the development of T2D and its complications in a variety of cohorts [2,3]. In particular, wholegrain foods improve indices of diabetes risk, including glycemic control, fasting plasma insulin and glucose, and insulin sensitivity, and

Abbreviations: GIP, gastric inhibitory peptide; GLP-1, glucagon-like peptide-1; HBG, high *β*-glucan; LBG, low *β*-glucan; Bgl, *β*-glucan less; PYY, polypeptide-YY; SCFA, short-chain fatty acid; T2D, type 2 diabetes.

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Table 1 – Ingredient composition of the diets fed to rats

	Basal	Wholegrain barley	
		LBG	HBG
Ingredients, g/kg			
Wholegrain barley flour, *bgl*	0	252	0
Wholegrain barley flour, Him977	0	0	252
Wheat bran	50	60	0
Maize starch	214.5	191.5	250
Sucrose	220	35.1	35.1
Maltodextrin10	75	75	75
Casein	190	135.9	137.4
Anhydrous milk fat	180	180	180
Sunflower seed oil	20	20	20
L-Cystine	3	3	3
Choline bitartate	2.5	2.5	2.5
Vitamin mix AIN-93G	10	10	10
Mineral mix AIN-93G	35	35	35
Composition of diets, g/kg			
Protein	170	166	165
Fat	204	215	199
β-Glucan	0	0.2	30
Insoluble NNSP	8.9	30.3	28.0
Soluble NNSP	0.7	3.3	23.7
Total NNSP	9.5	33.6	51.7
Total carbohydrate [a]	490	420	396
Glycemic impact [b]	413	408	383
Energy, kJ/g [c]	19.0	18.3	18.3

NNSP = neutral nonstarch polysaccharide.
[a] Total carbohydrate is the sum of all carbohydrates provided by each ingredient.
[b] Glycemic impact is calculated in the same way as total carbohydrate; however, only 65% of the carbohydrate from sugar is included [24].
[c] Energy content of each diet was calculated based on energy values provided by the manufacturer for individual ingredients. The energy content of the wholegrain cereals was calculated based on macronutrient composition.

also aid in the management of those individuals with or at high risk of developing T2D [4–8]. The metabolic health benefits of wholegrains are attributable to many grain constituents, including dietary fiber, vitamins, minerals, and phytochemicals [9]; however cereal fiber appears to account for much of the reduction in diabetes risk [3,10]. There is mounting evidence that, of the many different types of fiber, the soluble fiber β-glucan may be effective in reducing T2D risk [11].

Generally, foods containing barley or oat β-glucan have lower glycemic impact; and prolonged consumption of these foods improves insulin sensitivity. β-Glucan slows available carbohydrate assimilation and dampens postprandial glycemic and insulinemic responses [12] in healthy subjects and those with T2D or metabolic syndrome [11]. The reduction in glycemia is commonly attributed to the highly viscous nature of β-glucan, which is known to slow gastric emptying and digesta transit rate in the small intestine, and impede the actions of starch and other hydrolases and, consequently, rate of nutrient absorption in the upper gut [13,14]. Liatis and colleagues [15] showed that chronic consumption of β-glucan reduced fasting glucose and insulin levels and improved insulin sensitivity; however, the underlying mechanisms were not clarified in that study. Long-term studies in rats also show an improvement in insulin sensitivity after consumption of a diet containing β-glucan for 12 weeks [16,17]. However, concomitant reductions in body weight and adiposity may have been responsible for the observed improvements in insulin sensitivity [16,17]. Fermentation of β-glucan in the large bowel may also play a role in improving insulin sensitivity through stimulation of gut hormones, but evidence for this is less clear. The major products of β-glucan fermentation are short-chain fatty acids (SCFAs) [18,19]. These microbial metabolites stimulate secretion of hormones from colonic enteroendocrine cells, including glucagon-like peptide-1 (GLP-1), which acts systemically to increase pancreatic β-cell growth, glucose-dependant insulin secretion, and satiety via the hypothalamus, as well as decreasing glucagon secretion [20].

There is limited understanding of how fermentation of β-glucan by large bowel microbiota may influence circulating gut hormone levels. Wholegrain cereals rich in β-glucan also contain other types of fermentable dietary fiber, such as fructans and arabinoxylan [21,22]. High intakes of insoluble cereal fibers are associated with protection against T2D in observational studies [23].

The objective of the study was to determine whether fermentation of β-glucan in a wholegrain barley modulates circulating levels of glucoregulatory hormones (gastric-inhibitory peptide [GIP] and GLP-1) to improve glucose homeostasis. It was hypothesized that barley β-glucan fermentation would raise circulating incretin hormone levels and improve glucose control, independent of other grain components. We used 2 different novel barley varieties, one high in β-glucan and the other a novel barley mutant with negligible β-glucan content. This enabled us to negate possible confounding factors such as components in the grain other than β-glucan. An obese rat model was chosen because it allowed us to investigate the metabolic actions of β-glucan per se in animals with insulin resistance and increased adiposity.

2. Methods and materials

2.1. *Rats and diets*

Nine-week-old, male Sprague-Dawley rats (331 ± 2 g, mean ± SEM, n = 30), obtained from Laboratory Animal Services, University of Adelaide, were housed in wire-bottomed cages in a room with controlled heating and lighting (23°C with a 12-hour light/dark cycle, light phase commenced at 09:00) and had free access to food and water. After arrival, the rats were adapted to a nonpurified commercial diet for 1 week and then fed a basal diet for 6 weeks (Table 1). Rats were then allocated randomly to 1 of 3 dietary treatment groups. One group remained on the high-fat diet (basal), whereas the other 2 groups were fed high-fat diets that also contained 25 g/100 g wholegrain barley flour that provided either 0.02% β-glucan (LBG) or 3% β-glucan (HBG) (Table 1). The wholegrain barley flours were betaglucanless (*bgl*) [25] and a high–β-glucan barley mutant *Him977* obtained by screening an EMS Himalaya barley population (Zhongyi Li, Commonwealth Scientific & Industrial Research Organisation unpublished). The barley grains were milled to a sieve size of 1 mm. Low-amylose maize starch (Avon

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