

REVIEW

Review of human studies investigating the post-prandial blood-glucose lowering ability of oat and barley food products

SM Tosh

Oat and barley foods have been shown to reduce human glycaemic response, compared to similar wheat foods or a glucose control. The strength of the evidence supporting the hypothesis that the soluble fibre, mixed linkage β -glucan, reduces glycaemic response was evaluated. A search of the literature was conducted to find clinical trials with acute glycaemic response as an end point using oat or barley products. Of the 76 human studies identified, 34 met the inclusion and exclusion criteria. Dose response and ratio of β -glucan to available carbohydrate as predictors of glycaemic response were assessed. Meals provided 0.3–12.1 g oat or barley β -glucan, and reduced glycaemic response by an average of 48 ± 33 mmol \cdot min/l compared to a suitable control. Regression analysis on 119 treatments indicated that change in glycaemic response (expressed as incremental area under the post-prandial blood-glucose curve) was greater for intact grains than for processed foods. For processed foods, glycaemic response was more strongly related to the β -glucan dose alone ($r^2 = 0.48$, $P < 0.0001$) than to the ratio of β -glucan to the available carbohydrate ($r^2 = 0.25$, $P < 0.0001$). For processed foods containing 4 g of β -glucan, the linear model predicted a decrease in glycaemic response of 27 ± 3 mmol \cdot min/l, and 76% of treatments significantly reduced glycaemic response. Thus, intact grains as well as a variety of processed oat and barley foods containing at least 4 g of β -glucan and 30–80 g available carbohydrate can significantly reduce post-prandial blood glucose.

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INTRODUCTION

It has long been established that post-prandial glucose response to carbohydrate meals is not determined by the amount of available carbohydrate alone.^{1,2} The proportions of different nutrients, particularly protein and fat, as well as food microstructure can affect the rate of glucose absorption. The presence of soluble dietary fibre in carbohydrate foods also influences the glycaemic response after a meal. Oat and barley β -glucans have been widely studied for their health benefits, including their ability to reduce post-prandial glucose alone and in a wide variety of food formats.³

The mechanism of action has been well established. Oat and barley β -glucans, in their native state, are very high molecular-weight polysaccharides that exhibit high viscosities at low concentrations.⁴ Consumption of viscous polysaccharides increases the viscosity of the meal bolus in the stomach,⁵ which reduces mixing of the food with digestive enzymes and delays gastric emptying. Increased viscosity also retards the absorption of glucose.^{6,7} *In vitro* digestion studies demonstrate that β -glucan slows the rate of starch digestion.^{8–10} Owing to its solubility, β -glucan is easily fermented by the gut microbiota, which produces short-chain fatty acids, including acetate, propionate and butyrate.^{11,12} A study designed to keep viscosity in the small intestine constant, while the β -glucan was fermented in the large intestine, showed that slowed glucose absorption by viscosity development in the gut was responsible for acute effects.¹³ However, fermentation products may affect post-prandial glucose at subsequent meals. After evening meals containing barley, post-prandial glucose response to a standardized breakfast was

reduced and inversely correlated with colonic fermentation as indicated by increased breath hydrogen.¹⁴ It was also inversely related to plasma butyrate and acetate concentrations.¹⁵

Recently, the European Food Safety Authority, Panel on Dietetic Products, Nutrition and Allergies issued an opinion that 'reduction of post-prandial glycaemic responses (as long as post-prandial insulinaemic responses are not disproportionately increased) may be a beneficial physiological effect'.¹⁶ The panel recognized that a cause and effect relationship between consumption of oat and barley β -glucans and a reduction of post-prandial glycaemic responses has been established. Based on six studies, the panel concludes that 'in order to obtain the claimed effect, 4 g of β -glucans from oat or barley for each 30 g of available carbohydrates should be consumed per meal'. This condition of use is likely to be difficult for food processors to meet.

To aid in elaborating the strength of the evidence, a summary of the human trials that have been undertaken, focusing on glycaemic responses in relation to the β -glucan and available carbohydrate doses, is presented here.

METHODS

Outcome measures

Post-prandial glucose response is generally measured by determining blood-glucose concentration several times over a 2 h interval after a test meal is consumed and calculating the incremental area under the curve (AUC). In two studies, the AUC was measured over 1 h¹⁷ or 4 h,¹⁸ but as blood glucose returned to base line after 1 h in the first instance, it was felt that the difference in time interval did not affect the measurement greatly,

and for the second study a 2 h value was calculated. Although the physiological response most frequently reported was area under the post-prandial blood-glucose curve (AUC), some studies reported glycaemic index (GI), which is AUC as a percentage of response to a standard glucose drink or white bread test ($GI = AUC_{\text{test meal}}/AUC_{\text{standard meal}} \times 100$).

Another useful measurement is the peak blood-glucose rise. Oat β -glucan and other viscous soluble polysaccharides tend to slow the initial blood-glucose absorption, resulting in a flatter peak and sustained glucose uptake. Therefore, even when AUC is not decreased, the blood-glucose uptake may be blunted, avoiding large fluctuations in blood glucose and insulin.

Search strategy

A search of the literature was conducted on 14 November 2012 using the search string '(oat* or barley) and (glycaem* or glycem* or (blood and glucose))' using the PubMed and SCOPUS search engines. The searches returned 437 matches from PubMed and 602 matches from Scopus. From this list, 79 human studies, published in English, were extracted based on the titles and abstracts.

Inclusion criteria

Studies were included if they were controlled, randomized, blinded, crossover or parallel human studies, which included information on available carbohydrate dose, β -glucan or soluble fibre dose and post-prandial blood-glucose response.

Where it was available, information concerning peak blood-glucose response and insulin response was extracted from either graphs or tables. Information on number of subjects, food format and food processing was also collected.

Exclusion criteria

Studies were excluded if they did not have an appropriate control, used subjects with type 2 diabetes (including non-insulin-dependent diabetes mellitus), used low viscosity extracts or the β -glucan was deliberately depolymerized.

It has been demonstrated that depolymerization of β -glucan affects its efficacy as related to post-prandial blood-glucose reduction.¹⁹ Therefore, 10 treatments where the β -glucan molecular weight (MW) was reduced deliberately to <250 kDa, either to demonstrate loss of efficacy or to produce a low viscosity extract, were excluded from further analysis.^{7,10,19,20} One paper included six treatments with high levels of resistant starch in addition to β -glucan.²¹ Only the treatments with low levels of resistant starch were considered.

Data analysis

Extracted data were used to calculate change in AUC or GI compared to an appropriate control. For 12 studies, AUC was calculated from tables or graphs.^{6,21–28} Data extracted from the papers were tabulated. Ranges, averages and s.d.'s were calculated. Various plots and regressions were produced to represent the relationships among the parameters. Where a glucose drink was used as a control for solid foods,^{21,28–31} the data were adjusted to simulate a hypothetical control of white bread with a GI of 71.

Statistical analysis

Statistical analyses were performed using Graph Prism v. 5.0 (GraphPad Software, La Jolla, CA, USA). Regression analysis was performed to determine significant relationships among β -glucan dose or β G/AC (mixed linkage cereal β -glucan/available carbohydrate) ratio and the post-prandial glucose response measures. One data point, with the highest β -glucan dose, 14.1 g per serving and the highest ratio of β G/AC, was excluded because it was an outlier and the dose was too high to be of commercial interest.⁸

RESULTS

Of the 76 studies reviewed in full, 34 studies that comply with inclusion and exclusion criteria were included in the analysis: 18 on oat products, 10 on barley products and 6 including both oats and barley foods. Thus, the analysis was conducted on a total of 119 treatments from these 34 studies. The treatments included 55 oat products and 64 barley products.

A solution containing 50 g of glucose was included as a control in 15 of the studies. The mean AUC for the standard glucose solutions was 184 ± 31 mmol \cdot min/l (range 122–240 mmol \cdot min/l).

Glycaemic response in relation to available carbohydrate dose

Between 5 and 20 participants were recruited to determine the post-prandial response. Table 1 summarizes the data extracted from the studies that comply with the inclusion and exclusion criteria. The dose of β -glucan in the treatments ranged from 0.3–12.1 g per meal and the dose of available carbohydrate ranged from 25 to 100 g per meal. Of the 119 treatments, 74 used 50 g of available carbohydrate and the change in glycaemic response ranged from -1.4 to -147 mmol \cdot min/l for these treatments. This large variation shows that available carbohydrate dose is not the dominant factor determining glycaemic response. The range of β -glucan to available carbohydrate ratios (β G/AC) was 0.004–0.305 with an average of 0.101 ± 0.063 .

For oats, 69% of treatments (38/55) reported significant reduction in AUC and/or GI, and 71% of treatments (29/41) reporting information on peak blood-glucose rise indicated a significant reduction. One data set (four treatments) reported significant differences in peak blood-glucose rise and insulin, but did not specify for AUC or GI changes.²⁶ For barley, 64% of treatments (41/64) demonstrated significant reductions in AUC and/or GI, and 68% (21/31) of treatments reporting peak rise data showed significant reductions. Oat and barley products were not significantly different in terms of the average reduction in AUC ($P=0.17$) or GI ($P=0.19$), therefore the data for oats and barley were combined for the regression analyses.

Typically, foods with a GI >70 are considered high GI, whereas those with GI <55 are considered low GI.² Therefore, for the purposes of this paper, a reduction equivalent to the difference, or change in GI >15 units, will be considered of biological relevance. Back-calculating for a control glucose solution with an average AUC of 184 mmol \cdot min/l, 15 GI units corresponds to a change in AUC of 27 mmol \cdot min/l. For oat and barley combined, the average reductions in AUC and GI were 48 ± 33 and 31 ± 17 mmol \cdot min/l, respectively. These values represent substantial reductions and reinforce the certainty that oat and barley β -glucans consistently reduce post-prandial glucose. The treatments represented a wide range of oat and barley formats using a number of food-processing technologies. These products could serve as prototypes of functional foods for the consumer market.

In Figure 1, each treatment was plotted on a grid, indicating their relative β -glucan and available carbohydrate composition, and whether there was a significant lowering of AUC. An assumption was made by the EFSA Panel on Dietetic Products, Nutrition and Allergies¹⁶ that there is a linear relationship between β G/AC and efficacy. A dot is plotted to represent the condition of use recommended by the panel. A product containing 4 g β -glucan per 30 g of available carbohydrate and presumably any product with a β G/AC ratio ≥ 0.133 shown by the dashed line could make a claim. If efficacy was dependent on β G/AC ratio, a diagonal pattern would be observed with non-significant treatments falling below the line and significant treatments above the line. This pattern is not apparent in the data; moderate doses of β -glucan appear to be effective at higher available carbohydrate doses.

All 29 of the treatments that are plotted above the dashed line were effective in reducing post-prandial blood glucose. Additionally, 51 products which also exhibited significant reduction fell below the line. This suggests that the recommendation is overly restrictive.

However, 76% of the treatments (48/63) with 4 g or more β -glucan showed significant reduction in post-prandial glucose, independent of their available carbohydrate content (Table 3). The average carbohydrate dose for these 63 treatments was

Table 1. Included studies using oat or barley products

First author	Food format	Subjects n	β G dose (g)	AC dose (g)	Change in AUC (mmol · min/l)	sig. ^a	Change in GI values	Peak Change sig. ^a	Insulin change sig. ^a
Aldughpassi ^{32,33}	Whole grain boiled barley	10	3.0	50	-104	Yes	-41		
	Pearled boiled barley	10	2.8	50	-80	Yes	-30		
	Whole grain pasta	10	3.0	50	-10	No	-5		
	Pearled barley pasta	10	2.8	50	-24	No	-14		
	Whole grain boiled barley	10	3.7	50	-92	Yes	-35		
	Whole grain boiled barley	10	3.8	50	-102	Yes	-43		
	Whole grain boiled barley	10	3.4	50	-100	Yes	-42		
	Whole grain boiled barley	10	3.1	50	-98	Yes	-42		
	Whole grain boiled barley	10	4.3 ^b	50	-118	Yes	-46		
	Pearled boiled barley	10	4.2 ^b	50	-101	Yes	-38		
	Whole grain boiled barley	10	8.4 ^b	50	-128	Yes	-49		
	Pearled boiled barley	10	8.9 ^b	50	-111	Yes	-41		
	Whole grain boiled barley	10	5.7 ^b	50	-105	Yes	-45		
	Whole grain boiled barley	10	4.9 ^b	50	-111	Yes	-47		
	Whole grain pasta	10	4.3 ^b	50	-14	No	-5		
	Pearled barley pasta	10	4.2 ^b	50	-36	No	-14		
	Alminger ²⁹	Oat tempe	13	1.8	25	-79	Yes	-37	Yes
Barley tempe		13	1.7	25	-147	Yes	-70	Yes	Yes
Behall ³⁰	Pudding with oat flour	10	3.23 ^{b,c}	73.7 ^d	-62	Yes		Yes	No
	Pudding with oatmeal	10	3.23 ^{b,c}	73.7 ^d	-49	Yes		Yes	No
	Pudding with barley flour	10	12.1 ^b	76.1 ^d	-101	Yes		Yes	Yes
Behall ²¹	Pudding with barley flakes	10	12.1 ^b	76.1 ^d	-111	Yes		Yes	Yes
	Oat bran muffins	18	0.3 ^c	72 ^d	3	No		No	No
	Oat bran muffins	18	0.9 ^c	72 ^d	5	No		No	No
Braaten ⁶	Oat bran muffins	18	3.7 ^c	72 ^d	-26	No		Yes	Yes
	Oat β -glucan isolate gel	10	11.3 ^b	50	-64	Yes	-48	Yes	Yes
Brummer ³⁴	Oat bran cereal (high MW)	12	8.6 ^b	31	-56	Yes	-56	Yes	
	Oat bran cereal (medium MW)	12	8.3 ^b	31	-46	Yes	-46	Yes	
	Oat bran cereal (medium MW)	12	8.7 ^b	31	-64	Yes	-44	Yes	
Casiraghi ³⁵	Oat bran cereal (medium MW)	12	8.4 ^b	31	-65	Yes	-27	Yes	
	Barley crackers	10	3.6	40	-15.9	No	-25.3	No	Yes
Cavallero ²²	Barley cookies	10	3.5	40	-32.8	Yes	-47.8	Yes	Yes
	Bread with barley fraction	8	1.8	50	-18.7	No	-0.8		
Chillo ²⁰	Bread with barley fraction	8	3.3	50	-37.9	No	-18.3		
	Bread with barley fraction	8	4.9 ^b	50	-41.9	Yes	-27.8		
	Bread with barley fraction	8	4.9 ^b	50	-41.9	Yes	-27.8		
De Angelis ²³	Pasta with barley concentrate	9	1.5	50	-21.4	No	-19.3		
	Pasta with barley concentrate	9	3.0	50	-28.5	No	-25.7		
	Pasta with barley concentrate	9	4.4 ^b	50	-35.4	No	-31.9		
Finocchiaro ²⁴	Pasta with barley concentrate	9	6.1 ^b	50	-47.2	No	-42.6		
	Pasta with barley concentrate	9	7.7 ^b	50	-57.1	Yes	-51.6		
Granfeldt ³⁶	Sourdough bread with oat fibre	15	3.9	50	-35.	Yes	-18.3	Yes	
	Bread 40% waxy barley flour	9	5.3 ^b	50	-22.9	No	-12.7		
Granfeldt ⁹	Bread 40% non-waxy barley flour	9	4.8 ^b	50	-46.1	Yes	-25.6		
	Oat bran muesli	9	3.3 ^c	50	-23.6	No	-11	No	No
	Oat porridge	9	3.3 ^c	50	-11.5	No	-7	No	No
Granfeldt ³⁷	Boiled oat kernels	9	3.5 ^c	50	-80.0	Yes	-40	Yes	No
	Boiled barley kernels	10	4.5 ^{b,c}	50	-73.6	Yes	-35	Yes	Yes
	Boiled barley flour	9	4.7 ^{b,c}	50	-36.2	Yes	-61	Yes	Yes
	Boiled barley kernels	10	6.6 ^{b,c}	50	-68.5	Yes	-34	Yes	Yes
	Boiled barley flour	9	6.8 ^{b,c}	50	-45.3	Yes	-55	Yes	Yes
Hallfrisch ³¹	Boiled barley kernels	10	6.2 ^{b,c}	50	-79.9	Yes	-29	Yes	Yes
	Oat bran muesli	19	3	50	-16.7	No		No	No
Hätönen ³⁸	Oat bran muesli	13	4 ^c	50	-29.3	Yes		Yes	Yes
	Oat bran	20	3.7	83.9 ^d	-71	Yes		No	Yes
	Oat extract	20	3.8	83.9 ^d	-44	Yes		No	Yes
	Barley flour	20	7.4 ^b	83.9 ^d	-49	Yes		No	Yes
Hlebowicz ³⁹	Barley extract	20	5.2	83.9 ^d	-60	Yes		Yes	Yes
	Oatmeal porridge	12	4 ^b	50	-29.4	Yes	-24		
Hlebowicz ¹⁷	Wholemeal oatflakes	12	0.5	31.5	-23	No		No	
	Oat bran muesli	12	4 ^b	32.7	-15.5 ^e	Yes		Yes	
Juntunen ⁴¹	Oat bran fettucini	10	5.2 ^b	54.2	-4.5	Yes			Yes
	Rye bread with oat β -glucan concentrate	10	5.4 ^b	50	-48	Yes		Yes	Yes
Lan-Pidhainy ⁴²	Oat bran muffin	11	8 ^b	50	-79	Yes		Yes	
	Previously frozen oat bran muffin	11	8 ^b	50	-66	Yes		Yes	
	Previously frozen oat bran muffin	11	8 ^b	50	-48	Yes		Yes	
	Oat bran muffin	11	12 ^b	50	-73	Yes		Yes	
	Previously frozen oat bran muffin	11	12 ^b	50	-68	Yes		Yes	
	Previously frozen oat bran muffin	11	12 ^b	50	-63	Yes		Yes	
Liljeberg ⁸	Bread with coarse boiled oats	10	2.1 ^c	50	-15.6	Yes	-6.7	Yes	Yes
	Wholemeal barley bread	10	2.8 ^c	50	-13.7	No	-5.1	No	No
	Bread with coarse boiled barley	10	2.4 ^c	50	-29.5	Yes	-16.7	Yes	Yes
	Bread with coarse scalded barley	10	2.5 ^c	50	-38.5	Yes	-26.3	Yes	Yes
Liljeberg ⁴³	Barley bread (80% scalded kernels)	8	4.5 ^{b,c}	50	-92.6	Yes	-66.8	Yes	Yes
	Barley bread (40% scalded kernels)	8	2.8 ^c	50	-54.4	Yes	-34.4	No	No
	Wholemeal barley bread	8	4.1 ^{b,c}	50	-11	No	1.2	No	Yes
	Sourdough wholemeal barley bread	8	4.0 ^{b,c}	50	-29.2	No	-15.8	No	Yes
	Scalded wholemeal barley bread	8	3.8 ^{b,c}	50	-3	No	10.1	No	Yes
Liljeberg ²⁵	Oat porridge	9	2.1 ^c	35.5	-7.1	No	5.8	No	No
	Barley porridge	9	2.3 ^c	35.5	-2.5	No	-3	No	No
	Barley porridge (50% PW ^f)	9	7.6 ^{b,c}	35.5	-18.2	Yes	-22.3	Yes	Yes
	Barley bread (50% PW ^f)	9	8.0 ^{b,c}	31.5	-23.7	Yes	-29	Yes	Yes
	Barley bread (80% PW ^f) excluded	9	14.1 ^c	31.5	-31.9	Yes	-39.1	Yes	Yes

Table 1. (Continued)

First author	Food format	Subjects <i>n</i>	β G dose (g)	AC dose (g)	Change in AUC (mmol · min/l)	sig. ^a	Change in GI values	Peak Change sig. ^a	Insulin change sig. ^a
Mäkeläinen ²⁶	Oat bran drink	10	2	50	-26.9	?	-16.3	Yes	No
	Oat bran drink	10	4 ^b	50	-68.8	?	-41.7	Yes	No
	Previously frozen oat bran drink	10	4 ^b	50	-58.9	?	-35.7	Yes	No
Nilsson ⁴⁴	Oat bran drink	10	6 ^b	50	-60.6	?	-36.7	Yes	No
	Boiled oat kernels	12	2.9 ^c	50	-40.4	No	-15		
	Boiled barley kernels	12	2.9 ^c	50	-76.8	Yes	-51		
	Bread with barley fibre	12	6.3 ^{b,c}	50	-29.4	No	-7		
Östman ²⁷	Barley porridge	12	2.6 ^c	50	-10.8	No	12		
	Barley bread (50%)	10	1.1	30	-15.2 ²	No	-16.8		No
Panahi ⁷	Barley bread (35% PW ^f)	10	2.9	30	-18.6 ²	No	-25.2		Yes
	Barley bread (50% PW ^f)	10	4.6 ^b	30	-17.8 ²	Yes	-35.5		Yes
	Barley bread (75% PW ^f)	10	9.2 ^b	30	-26 ²	Yes	-45.3		Yes
	Glucose drink with oat extract	11	6 ^b	75	-39	Yes			
Regand ⁴⁵	Oat porridge (high MW)	12	4 ^b	43	-37	No		Yes	
	Oat crisp bread (medium MW)	12	4 ^b	64	-11	No		No	
	Oat granola (high MW)	12	4 ^b	44	-29	No		Yes	
	Oat pasta (medium MW)	12	4 ^b	42	-7	No		No	
Regand ¹⁰	Oat grannola product (high MW)	12	6.2 ^b	38	-35	Yes		Yes	
	Oat grannola product (medium MW)	12	6.2 ^b	38	-28	Yes		Yes	
	Oat grannola product (high MW)	12	6.3 ^b	60	-33	Yes		Yes	
	Oat grannola product (medium MW)	12	6.3 ^b	60	0	No		No	
Threndre ⁴⁶	Barley chapattis	8	2	50	-1.4	No	0	No	No
	Barley chapattis	8	4.1 ^b	50	-40.9	Yes	-43	Yes	No
	Barley chapattis	8	6 ^b	50	-16.3	No	-16	No	No
	Barley chapattis	8	7.8 ^b	50	-48.3	Yes	-47	Yes	No
Threndre ²⁸	Barley porridge (high fibre)	10	2.7	50	-112	Yes	-61	Yes	
	Barley porridge (medium fibre)	10	2.7	50	-105	Yes	-57	Yes	
Tosh ¹⁹	Oat bran muffin (medium MW)	10	4 ^b	50	-26	No			
	Oat bran muffin (medium MW)	10	4 ^b	50	-44	Yes			
	Oat bran muffin (high MW)	10	4 ^b	50	-50	Yes			
	Oat bran muffin (medium MW)	10	8 ^b	50	-49	Yes			
	Oat bran muffin (medium MW)	10	8 ^b	50	-74	Yes			
Ulmius ⁴⁷	Oat bran muffin (high MW)	10	8 ^b	50	-76	Yes			
	Beverage with oat bran	18	5 ^b	75	-40	No	-40		Yes
Wood ⁴⁸	Oat bran porridge	9	8.8 ^b	60	-54	Yes	-38		
	Cream of wheat + oat β -glucan isolate	9	8.6 ^b	60	-57	Yes	-40		
Yokohama ¹⁸	Barley pasta	5	12 ^b	100	-92	Yes		Yes	No

Abbreviations: AC, available carbohydrate; β G, mixed linkage cereal β -glucan; MW, molecular weight. The italicized row indicates the excluded data point. ^aYes means significant reduction detected ($P < 0.05$). ^bTreatment included in table 3. ^cSoluble fibre measured. ^d1 g AC/kg body weight, average given. ^e1 h AUC data reported. ^fPW—high β -glucan, prowashonupana variety. The italicized row indicates the excluded data point.

51.1 ± 13.6g, much higher than the recommended 30g of available carbohydrate. In fact, nearly half (43%) of products with 2–4g β -glucan per meal showed significant reduction in post-prandial blood glucose as well.

Regression analysis

To compare the predictive value of the ratio of β -glucan to available carbohydrate versus β -glucan dose alone, regression analyses against AUC were performed.

When the data were considered as a whole, neither the ratio nor the dose data set passed the D'Agostino and Pearson omnibus test of normality performed within the statistical software. Examination of the data indicated that the whole boiled grains gave markedly lower values than the processed foods, therefore the data were divided into two sets. Subsequently, both the processed and intact grain groups passed the normality tests. A test for non-linear behaviour showed that the data did not exhibit significant curvature, therefore a linear model was employed. There was a large scatter in the data, but significant slopes of relationships were observed. Statistical parameters are reported in a Supplementary Table available at the European Journal of Clinical Nutrition's website.

Figure 2a shows the data for β G/AC plotted against glycaemic response. The β G/AC ratio for processed foods was weakly correlated with the AUC ($P < 0.0001$, $r^2 = 0.24$). The low r^2 values mean that there is a small chance that post-prandial glycaemic response can be reliably predicted by the β G/AC ratio for a given product. For all processed food treatments, the average β G/AC ratio was 0.137 ± 0.065. The intact grains had a much lower AUC

than the processed foods, including porridge. There was a significant relationship between AUC and the β G/AC ratio ($P = 0.011$, $r^2 = 0.26$) and average change in AUC of the intact grains was -83 ± 29.

The dashed line shows where products containing 4g β -glucan and 30g available carbohydrate (β G/AC = 0.133) would fall. All 29 treatments (27 processed and 2 intact kernels), with a β G/AC > 0.133 significantly reduced glycaemic response. However, 55% (16 processed and 23 intact kernels) of treatments with β G/AC < 0.133 also showed significant reductions in post-prandial blood glucose. Moreover, this suggests that the recommended condition of use may be too stringent.

Figure 2b shows the dependence of glycaemic response on β -glucan dose. The data for processed products show a significant ($P < 0.0001$) drop in AUC with increasing dose. Compared to β G/AC ratio, β -glucan dose showed a stronger association with AUC ($r^2 = 0.48$). The regression predicts a reduction in AUC of 5.2 ± 0.6 mmol · min/l for each gram of β -glucan included in a meal. The physiologically relevant reduction of 27 mmol · min/l was attained with a dose of 4.0g β -glucan. On the graph, a dashed line indicates a dose of 4.0g β -glucan. To the right of the line, 75% of the processed treatments (45/60) and 95% (21/22) of the intact boiled barley treatments demonstrated a significant reduction in AUC with an average reduction of 51 ± 29 mmol · min/l.

Peak blood-glucose rise

The development of viscosity in the gut caused by oat and barley β -glucan tends to slow the absorption of glucose. As the post-prandial blood-glucose curves tend to be low broad peaks, after

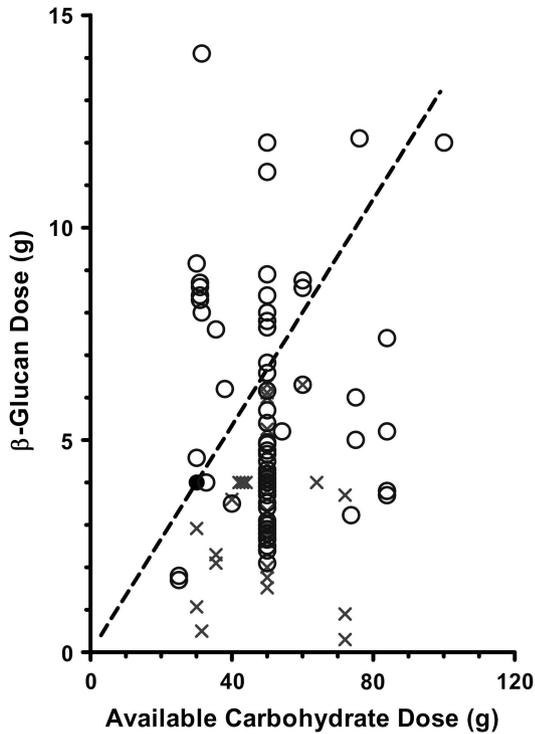


Figure 1. Plot of β -glucan dose against available carbohydrate dose for included treatments. Whether a treatment significantly reduced AUC or GI (O), or not (X) is indicated. Dot represents β -glucan and available carbohydrate ratio recommended in condition of use, and the line shows the cutoff for products with a ratio of 4 g β -glucan per 30 g of available carbohydrate (0.133).

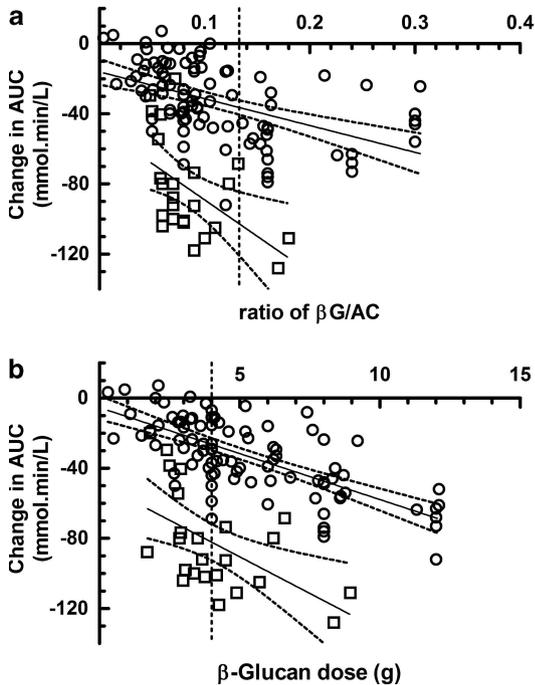


Figure 2. Relationship between (a) ratio of β -glucan/available carbohydrate (β G/AC) or, (b) β -glucan dose and post-prandial blood-glucose responses (AUC). Processed (O) and intact grain (square) treatments are indicated. The solid line is a trendline with the 95% confidence limits shown as dotted lines. The dashed line represents the cutoff point for (a) ratio 4 g β G/30 g AC = 0.133, or (b) 4 g β -glucan.

consumption of oat and barley foods, peak blood-glucose rise is often a more sensitive measure of efficacy than AUC or GI. Peak blood-glucose rise was reported for 72 treatments (41 for oat and 31 for barley) (Table 2). In these studies, 69% of the treatments had a peak blood-glucose rise significantly smaller than the control meal.

Of the 43 treatments with at least 4 g of β -glucan where peak rise was reported, 81% (35/43) significantly reduced the peak blood-glucose rise (Table 3). The available carbohydrate dose ranged from 30 to 100 g. This result is further evidence of the ability of moderate doses of oat and barley β -glucan to modulate glucose absorption, independent of available carbohydrate dose.

Insulinaemic response

Information concerning the insulin response was given in tables or graphs for 56 of the 119 treatments. The insulin did not rise significantly in any of the measurements. This shows that 'post-prandial insulinaemic responses are not disproportionately increased'.¹⁶ For treatments using 4 g β -glucan or more, 72% (18/25) processed foods and all four intact barley treatments confirmed a significant reduction in area under the insulin curve (Table 3).

Table 2. Attributes of oat and barley foods included in analysis

	Oats	Barley	Combined
Average β -glucan dose (g)	5.4 \pm 2.9	4.7 \pm 2.5	5.0 \pm 2.7
Average AC (g)	51.7 \pm 13.6	49.1 \pm 12.8	50.3 \pm 13.2
Average β G/AC ratio	0.113 \pm 0.072	0.090 \pm 0.052	0.101 \pm 0.063
Treatments (no. reported)	55	64	119
No. of significant reductions	38 (69%)	41 (64%)	79 (66%)
Non-significant treatments	17 (31%)	23 (36%)	40 (34%)
AUC change			
Range (mmol · min/l)	7.1 – – 80	– 1.4 – – 147	7.1 – – 147
Average (mmol · min/l)	41 \pm 24	– 54 \pm 39	48 \pm 33
GI change (no. reported)	18	47	65
Range	6 – – 48	10 – – 70	10 – – 70
Average	27 \pm 14	33 \pm 19	31 \pm 17
Peak rise (no. reported)	41	31	72
No. of significant reductions	29 (71%)	21 (68%)	50 (69%)
Non-significant treatments	12 (29%)	10 (32%)	22 (31%)
Insulin Change (no. reported)	23	33	56
No. of significant reductions	10 (43%)	24 (73%)	34 (61%)
Non-significant treatments	13 (57%)	9 (27%)	22 (39%)

Abbreviations: AUC, area under the curve; β G, mixed linkage cereal β -glucan; GI, glycaemic index. Treatments containing 0.3–12.1 g β -glucan per meal.

Table 3. Attributes of oat and barley foods with at least 4 g β -glucan

	Processed	Intact grain
Number of treatments	63	9
β -glucan dose (g)	6.6 \pm 2.5	6.0 \pm 1.7
AC dose (g)	51.1 \pm 13.6	50.0
β G/AC ratio	0.137 \pm 0.060	0.078 \pm 0.030
<i>Change in AUC (mmol · min/l)</i>	– 45 \pm 24	– 99 \pm 20
Significant treatments	48 (76%)	9 (100%)
Non-significant treatments	15 (24%)	0
<i>Peak rise</i>		
Significant treatments	31 (79%)	4 (100%)
Non-significant treatments	8 (21%)	0
<i>Insulinaemic response</i>		
Significant treatments	18 (72%)	4 (100%)
Non-significant treatments	7 (28%)	0

Abbreviations: AC, available carbohydrate; AUC, area under the curve; β G, mixed linkage cereal β -glucan.

DISCUSSION

The 119 treatments included in the review used 92 processed products bread, pasta, hot and cold breakfast cereals, beverages and other food products as β -glucan sources, and represented a wide variety of processing conditions, as well as 25 intact oat and barley grains.

The regression analysis indicates that for processed products glycaemic response is more strongly dependent on β -glucan dose than the ratio of β G/AC. Although there is evidence that glycaemic response depends on the amount of starch in a meal,^{10,37,43} it also depends on the characteristics of the starch. Resistant starch can lower the glycaemic responses²¹ as does an increase in slowly digestible starch¹⁰ or an increase in the amylose to amylopectin ratio.^{9,24} Thus, simply considering the β G/AC ratio is too simplistic and adds error to the model.

The statistical analysis predicts a reduction of 5.2 \pm 0.6 mmol · min/l in AUC for each gram of β -glucan added to a processed product, or 8.4 \pm 2.7 mmol · min/l for intact oat and barley treatments as indicated by the slopes of the trendlines in Figure 2b. The dose at which the model predicts a physiologically relevant decrease of 27 mmol · min/l (equivalent to 15 GI units) was 4.0 g β -glucan for processed products. All of the intact oat and barley treatments reduced AUC by more than 27 mmol · min/l compared to the control.

Table 3 shows the characteristics of the 72 treatments from 27 studies, which contain at least 4 g of β -glucan. Products containing at least 4 g of oat or barley β -glucan significantly reduced glycaemic response in 76% of the treatments tested. Peak blood-glucose rise was significantly reduced in 79% of the reported observations. The average reduction in AUC was – 45 \pm 24 mmol · min/l for processed products and – 99 \pm 20 mmol · min/l for intact boiled grains. The products considered had an average carbohydrate dose of 51.1 \pm 13.6 g (range 30–100 g).

Implications for persons with type 2 diabetes

Although studies conducted on subjects with type 2 diabetes were not included in the statistical analysis, the outcomes of those studies suggest that type 2 diabetics would benefit from consuming oat and barley foods as well. A study where type 2 diabetics consumed 3 g of β -glucan in muesli containing extruded oat bran⁴⁹ resulted in a 204 mmol · min/l reduction in AUC ($P < 0.01$) compared to a whole wheat cereal. Research

conducted on a commercial oat bran breakfast cereal (3.7 g β -glucan per serving), a β -glucan-enriched breakfast cereal (7.3 g β -glucan per serving) and a cereal bar (6.2 g β -glucan per serving) showed that they had significantly lower GI values compared to white bread.⁵⁰ The β -glucan in the oat products tested reduced the AUC (180 min) of type 2 diabetic subjects by 74, 372 and 332 mmol · min/l when they consumed the oat bran breakfast cereal, high β -glucan cereal and bar, respectively. A dose-response study using extruded breakfast cereals with 4.0, 6.0 or 8.4 g β -glucan per serving showed significant reductions in both glucose and insulin response.⁵¹ The 4.0 g dose reduced the AUC and peak blood-glucose rise by 33% ($P < 0.05$) compared to a whole wheat-based continental breakfast, whereas the 6.0 and 8.4 g of doses reduced glycaemic response by 60% ($P < 0.001$). Therefore, although incorporating more β -glucan into the diets of healthy individuals is effective in maintaining healthy blood-glucose levels, it appears that it also ameliorates blood-glucose levels in persons with type 2 diabetes.

Food formats

Intact boiled kernels were used in six studies, as is, fermented, pearled or baked into wheat bread.^{9,29,32,36,43,44} Where the integrity of the kernel was maintained, 96% (21/22) treatments showed efficacy with an average reduction in AUC of 99 \pm 20 mmol · min/l. The glycaemic response to intact boiled barley was shown to be related to total dietary fibre and slowly digestible starch, rather than β -glucan content.³² This difference from processed products suggests that, for cooked kernels, the intact cell walls act as a physical barrier to starch-degrading enzymes.

The effects of food processing are frequently questioned in regard to maintaining the efficacy of soluble fibre in oat and barley products. A wide variety of food formats were used in the clinical studies considered here. Foods were divided into different categories based on the type of processing they received and treatments, which provided at least 4 g of oat or barley β -glucan, were assessed. Raw flours, flakes and bran mixed into beverages or puddings were used in four of the experiments^{30,31,47} and 75% demonstrated effectiveness with an average change in AUC of 75 \pm 33 mmol · min/l (Table 1). All seven of the treatments that used > 4 g β -glucan from isolates or extracts, significantly reduced the glycaemic response with an average reduction of 58 \pm 39 mmol · min/l.^{6,7,26,31,48} This may be because it is easier to achieve higher concentrations of β -glucan in a meal. The dose for these studies was 4–11.3 g per meal. Porridge is considered a minimally processed food, and often thought to be better than more highly processed foods. However, 6 of the 12 porridge products studied contained less than 4 g β -glucan. Of those that contained at least 4 g β -glucan, 83% significantly lowered the glycaemic response, with an average reduction in AUC of 38 \pm 10 mmol · min/l.^{25,36,38,45,48} Thus, porridges were not particularly better than other products. Granola, muesli and breakfast cereal are products where the moisture content is kept relatively low during processing, and hydration of the β -glucan may be inhibited. For cereal products containing at least 4 g β -glucan, 82% of test meals showed significant results with an average change in AUC of – 32 \pm 15 mmol · min/l.^{10,17,34,36,37,45} Muffin batter has a higher water content allowing β -glucan to better solubilize, and disperses through the crumb.^{42,52} For muffins with at least 4 g β -glucan, 92% (11/12) of the treatments significantly reduced blood glucose with an average reduction of 60 \pm 16 mmol · min/l.^{19,42} There were 26 tests run on oat and barley breads, which was the largest group of food products. Despite concerns that β -glucan may be partially degraded by enzyme activity during bread production,^{45,53} 64% of bread products containing at least 4 g β -glucan (9/14) showed significant decreases in glycaemic response with an average AUC reduction

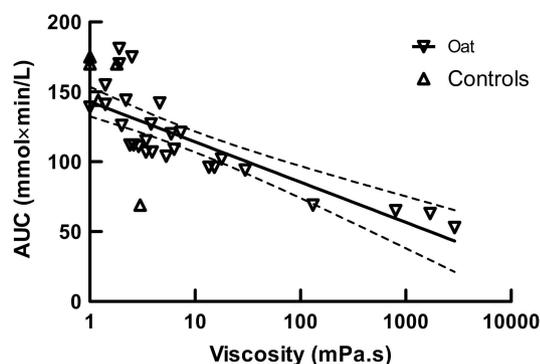


Figure 3. Relationship between post-prandial glucose responses (AUC) and the viscosity of an *in vitro* digestion extract demonstrates that viscosity development in the gut has a role in the reduction of post-prandial blood glucose. Oat and barley test products (∇) and control wheat products (Δ) are indicated. The solid line is a trendline ($P < 0.0001$, $r^2 = 0.69$) with the 95% confidence limits shown as dotted lines.

of 29 ± 13 mmol \cdot min/l.^{22,24,25,27,41,43,46} In pasta products, where depolymerization has also been observed,⁴⁵ three of the eight tests showed significant reductions.^{18,20,32,40} Therefore, the main concern with regard to the effects of processing on efficacy is maintaining the MW of the β -glucan.

Relation to viscosity development in the gut

Five of the studies reported viscosity of an *in vitro* digestion extract in addition to physiological data.^{10,19,34,42,45} Samples of the foods used in the clinical trials were treated with digestive enzymes, with appropriate pH changes at 37 °C in a shaking water bath. The liquid containing the soluble β -glucan was removed by centrifugation and the viscosity of the extract was measured. The sample to buffer ratio was doubled in Regand experiments.^{10,45} To account for this difference in concentration, the 4.4th root of viscosity values was used because Ren *et al.*⁴ showed that a doubling in concentration results in an exponential increase in viscosity of that order.

The control whole wheat products (muffins, crispbread, pasta, granola and cereal) all had low viscosity extracts (Figure 3). The oat products were modified to change the β -glucan content, solubility, MW and processing conditions which resulted in a range of extract viscosities from 1.2 to 2900 mPa \cdot s. The glycaemic response for the control and oat pastas was lower than for the other test foods, 96 and 89 mmol \cdot min/l, respectively. Pasta is known to have lower GI than other food products,⁵⁴ possibly because of its compact microstructure, which restricts enzyme access to starch.⁵⁵ For the other 33 meals, the AUC ranged from 175 mmol \cdot min/l for whole wheat muffins and granola to 53 mmol \cdot min/l for extruded oat bran cereal, with 8.6 g high MW β -glucan per meal. A significant linear relationship was found between AUC and log(viscosity) ($r^2 = 0.69$, $P < 0.0001$). For each decade of increase in viscosity, the model predicts a decrease in AUC of 32 ± 4 mmol \cdot min/l. This correlation between viscosity and reduction in glycaemic response supports the hypothesis that β -glucan influences blood-glucose concentrations by increasing viscosity in the upper gut.

Summary

The results of 119 treatments from 34 publications were reviewed to determine the dose of oat or barley β -glucan necessary to achieve a consistent post-prandial blood-glucose lowering effect. The β -glucan content ranged from 0.3 to 12.1 g, and the available carbohydrate content ranged from 30 to 100 g, resulting in a β G/AC range of 0.004–0.305. The statistical analysis, as indicated

by the correlation coefficients (r^2 values), shows that efficacy was more strongly related to β -glucan content alone than to the ratio of β G/AC. This is reassuring, as oat and barley foods are often eaten as part of a meal including additional carbohydrates. Based on the data analysed, it is suggested that intact cooked or fermented grains containing at least 3 g β -glucan per meal is sufficient to significantly lower glycaemic response. Processed oat or barley foods, where the β -glucan is soluble and has a MW $> 250\,000$ g/mol, containing at least 4 g β -glucan per meal is sufficient to reduce post-prandial by AUC 27 ± 3 mmol \cdot min/l for meals with ~ 30 –80 g of available carbohydrate. This reduction in glycaemic response is sufficient to be considered a physiologically relevant effect.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Supplementary Information accompanies the paper on European Journal of Clinical Nutrition website (<http://www.nature.com/ejcn>)