

1 **Effect of commercial breakfast fibre cereals compared with corn flakes on postprandial**
2 **blood glucose, gastric emptying and satiety in healthy subjects: a randomized blinded**
3 **crossover trial**

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23 **Tables 3**

24 **Figures 3**

25

Abstract

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27
28 *Background:* Dietary fibre food intake is related to a reduced risk of developing diabetes
29 mellitus. However, the mechanism of this effect is still not clear. The aim of this study was to
30 evaluate the effect of commercial fibre cereals on the rate of gastric emptying, postprandial
31 glucose response and satiety in healthy subjects.

32 *Methods:* Gastric emptying rate (GER) was measured by standardized real time
33 ultrasonography. Twelve healthy subjects were assessed using a randomized crossover blinded
34 trial. The subjects were examined after an 8 hour fast and after assessment of normal fasting
35 blood glucose level. Satiety scores were estimated and blood glucose measurements were taken
36 before and at 0, 20, 30, 40, 60, 80, 100 and 120 min after the end of the meal. GER was
37 calculated as the percentage change in the antral cross-sectional area 15 and 90 min after
38 ingestion of sour milk with corn flakes (GER1), cereal bran flakes (GER2) or wholemeal oat
39 flakes (GER3).

40 *Results:* The median value was, respectively, 42% for GER1, 33 % for GER2 and 51% for
41 GER3. The GER after ingestion of bran flakes was significantly slower compared to wholemeal
42 oat flakes ($p=0.023$). The postprandial delta blood glucose level was significantly lower at 40
43 min ($p=0.045$) and 120 min ($p=0.023$) after the cereal bran flakes meal. There was no
44 significant difference between the areas under the curve (AUCs) of the cereals as far as blood
45 glucose and satiety were concerned.

46 *Conclusions:* The result of this study demonstrates that the intake of either cereal bran flakes or
47 wholemeal oat flakes has no effect on the total postprandial blood glucose response or satiety
48 when compared to corn flakes, but intake of cereal bran flakes slows the GER. Since these
49 products do not differ in terms of glucose response and satiety on healthy subjects, they should
50 be considered equivalent in this respect.

51 *Trial registration:* ISRCTN90535566

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Background

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55 In Sweden and worldwide the incidence of type 2 diabetes mellitus is increasing rapidly. To
56 prevent the development of diabetes mellitus, the American Diabetes Association recommends
57 a reduction in caloric intake and increased consumption of dietary fibre and food containing
58 whole grain [1]. An increased intake of fibre has been shown to reduce the risk of diabetes [2,
59 3]. Whether low-glycemic-index food in fact prevents diabetes mellitus is still unclear [2, 4-7].
60 However, a low-glycemic-index diet that reduces postprandial hyperglycemia is recommended
61 by the American Diabetes Association (ADA) to control glycemia in patients with diabetes [8-
62 9].

63 Fibre has been shown to delay gastric emptying rate, reduce the glycemic response and delay
64 the return of hunger in healthy subjects [10]. It has been assumed that fibre fermented in the
65 colon by the bacterial flora releases short chain fatty acids, thus lowering postprandial glucose
66 levels [11- 14]. Moreover, this fermentation has shown to result in a suppression of the
67 hepatic glucose production and serum-free fatty acids [15]. Colonic fermentation, measured
68 by breath hydrogen test, has been observed – after a meal consisting of ingestible
69 carbohydrates – to reduce the insulin and glucose response at the following meal. This effect
70 is called a second meal effect. [16]. However, another study showed that meals with what was
71 assumed to be fermentable carbohydrates did not improve glucose or insulin response at the
72 second meal [17]. A recently published study shows that an increased 3-day intake of
73 insoluble fibre in obese subjects improved whole-body insulin sensitivity [18].

74 The β -glucan effect is not fully understood. Products enriched with β -glucan have been shown
75 to reduce postprandial glucose and insulinemic responses in healthy subjects [19-21] and in

76 type 2 diabetes patients [22-24]. Reduced postprandial glucose and insulin concentrations after
77 consumption of viscous types of fibre have been discussed to be caused by delayed mouth-to
78 caecum transit and delayed absorption of glucose in the small intestine [25]. The viscosity of
79 oat gum, an oat extract composed of β -glucan, has been shown to cause a reduction in plasma
80 glucose and insulin levels [26]. However, lower postprandial glucose and insulin concentrations
81 have not been shown to be caused by the fermentation of β -glucan in the colon [27]. Another
82 mechanism discussed is that β -glucan delays gastric emptying.
83 Healthy subjects are recommended to consume products with fibre to prevent the
84 development of diabetes mellitus. Also, patients with diabetes consume commercial products
85 with fibre and low glycemic food to control the blood glucose levels. This study was designed
86 to determine whether there is a delay in gastric emptying in healthy subjects, thus affecting
87 postprandial blood glucose levels and satiety, after consumption of commercially popular
88 fibre cereals.

89

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Methods

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92 Twelve healthy subjects (six men and six women; mean age 28 ± 4 years [range 23 - 36
93 years]; mean BMI 22 ± 2 kg/m² [range 19 – 24 kg/m²], without symptoms or a prior history of
94 gastrointestinal disease, abdominal surgery or diabetes mellitus were included in the study.
95 One subject had been appendectomized. None of the subjects used any drugs on the
96 examination day. Three of the women, including one with polycystic ovary syndrome, had
97 birth control medication. The subject with the polycystic ovary syndrome had a BMI 21 kg/m²
98 and previously underwent a glucose tolerance test which proved normal. All subjects were
99 recruited from the population of a southern county of Sweden. Four of the subjects were
100 smokers and two were snuff users. The subjects were examined between 8:00 and 10:00 am

101 after an 8 hour fast. Smoking and snuff-taking were prohibited for 8 h before the test as well
102 as during the test. Each subject was checked for normal fasting blood glucose concentration
103 on the day of the examination. For subjects with symptoms from the gastrointestinal tract
104 (diarrhoea or constipation) on the examination day, the examination was postponed. The test
105 meals consisted of 300 g sour milk (Skånemejerier, 205 03 Malmö, Sweden) (caloric value
106 135 kcal) and 50 g cereal bran flakes (Kellogg's All-Bran, Kellogg's, Sverige
107 Konsumentkontakt, Box 742, 194 27 Upplands Väsby, Sweden) (caloric value 163 kcal) or
108 wholemeal oat flakes (Frebaco Fullkorns Havreringsar, Frebaco Kvarn AB, Box 878, 531 18
109 Lidköping, Sweden) (caloric value 185 kcal). The reference meal, consisting of 50 g corn
110 flakes (Kellogg's Corn Flakes, Nordisk Kellogg's, Sverige Konsumentkontakt, Box 742, 194
111 27 Upplands Väsby, Sweden) (caloric value 185 kcal), had the same brand and quantity of
112 sour milk as the test meal (Table 1). The meals were served in a random order more than one
113 week apart. Each meal was ingested within 5 minutes.

114 GER was estimated using a previously described standardised ultrasound method [28]. The
115 sonographic examination was performed using two different ultrasound machines (Siemens
116 Acuson Sequoia 512 and Aloka Prof. Sound) with an abdominal transducer multi-MHz. For
117 every single calculation of GER the same machine was used. The measurements of the gastric
118 antrum were performed by the same radiologist who was blinded with regard to the meals. At
119 each observation of the gastric antrum the abdominal aorta and the left lobe of the liver were
120 used as internal landmarks. The subjects were examined lying down, but they were in upright
121 position between examinations. Measurements were taken 15 and 90 min after the end of
122 meal ingestion. Gastric emptying was expressed as the percentage change of the antral cross-
123 sectional area from 15 to 90 min. At each examination three measurements of the longitudinal
124 (d1) and anteroposterior (d2) diameters were performed and mean values were used to
125 calculate the cross-section area of the gastric antrum using the following formula:

126

127 Antrum area = $\pi \times r^2 = \pi \times d1 / 2 \times d2 / 2 = \pi \times d1 \times d2 / 4$

128

129 The gastric emptying (GER) was calculated using the following formula:

130

131 $GER = [1 - (\text{Antrum area } 90 \text{ min} / \text{Antrum area } 15 \text{ min})] \times 100$

132

133 Finger-prick capillary samples were taken before and at 0, 20, 30, 40, 60, 80, 100 and 120 min
134 after the end of the meal to measure glucose. Blood glucose concentrations were measured with
135 HemoCue Glucose system (HemoCue AB, Ängelholm, Sweden). A validated satiety score
136 numerical scale was used according to the method of Haber et al on the basis of a scoring
137 system with grades from -10 cm (extreme hunger) to 10 cm (extreme satiety) [29]. Satiety score
138 was estimated before the meal and at 0, 20, 30, 40, 60, 80, 100 and 120 min after the end of the
139 meal.

140

141 All subjects provided written informed consent. The study was approved by the Ethics
142 Committee at Lund University and performed according to the Helsinki Declaration.

143

144 Median values with quartiles (q1 to q3) are presented for the antral cross-sectional areas and the
145 GER. Delta values of blood glucose and satiety scores are calculated as changes at 0, 20, 30, 40,
146 60, 80, 100 and 120 min after the end of the meal from a fasting value. The AUCs for each
147 subject were determined for the delta blood glucose and satiety (Graph Pad PRISM, version 4,
148 San Diego). The AUCs were calculated above zero. The AUCs values are presented as means \pm
149 SEMs. All statistical calculations were performed in SPSS for Windows. Significant differences

150 of GER, gastric antral cross-sectional areas, delta blood glucose and AUCs were evaluated with
151 the Wilcoxon t-test. Values of $P < 0.05$ were considered significant.

152

153

Results

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Postprandial blood glucose response

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157 Ingestion of cereal bran flakes resulted in a significantly lower blood glucose response in the
158 initial postprandial phase (40 min) than did the reference meal of corn flakes ($p=0.045$) (**Figure**
159 **1**). Ingestion of cereal bran flakes resulted in a significantly lower blood glucose response in the
160 late postprandial phase (120 min) than did wholemeal oat flakes ($p=0.023$) (Figure 1).
161 However, the blood glucose AUCs did not differ significantly between cereal bran flakes,
162 wholemeal oat flakes and corn flakes (**Table 2**).

163

164

Gastric emptying rate

165

166 The median values of the antral cross-sectional area after ingestion of the cereal bran flakes
167 meal were $641 \pm 197 \text{ mm}^2$ (range 418 to 1035 mm^2) ($q_1= 524 \text{ mm}^2$, $q_3= 824 \text{ mm}^2$) and $331 \pm$
168 253 mm^2 (range 137 to 924 mm^2) at 15 and 90 min, respectively, after the end of the meal. In
169 the same subjects the median values of the antral cross-sectional area after the ingestion of the
170 wholemeal oat flakes meal were $743 \pm 240 \text{ mm}^2$ (range 498 to 1188 mm^2) ($q_1= 568 \text{ mm}^2$, $q_3=$
171 1003 mm^2) and $331 \pm 226 \text{ mm}^2$ (range 149 to 852 mm^2) ($q_1= 205 \text{ mm}^2$, $q_3= 626 \text{ mm}^2$) at 15 and
172 90 min after the end of the meal. In the same subjects the median values of the antral cross-
173 sectional area after the ingestion of the corn flakes meal were $716 \pm 187 \text{ mm}^2$ (range 170 to 740
174 mm^2) ($q_1= 436 \text{ mm}^2$, $q_3= 905 \text{ mm}^2$) and $481 \pm 227 \text{ mm}^2$ (range 380 to 1008 mm^2) ($q_1= 251$

175 mm², q3= 495 mm²) at 15 and 90 min after the end of the meal. There were no significant
176 differences between gastric antral cross-sectional at 15 or 90 min between the different meals.
177 The median value of GER after the cereal bran flakes meal was estimated at 28% (range -8% to
178 73%) (q1= 15%, q3= 56%) compared to the median value of GER after the wholemeal oat
179 flakes meal which was estimated at 50 % (range 25% to 73 %) (q1= 38%, q3= 70%). The
180 median value of GER after the corn flakes meal was estimated at 39 % (range 21% to 73 %) (q1= 31%, q3= 49%). The cereal bran flakes meal had a significantly lower GER compared to
182 wholemeal oat flakes meal (p=0.023) (**Figure2**). There were no significant differences between
183 cereal bran flakes or wholemeal oat flakes compared to corn flakes with regard to GERs
184 (Figure2).

185

186 **Satiety**

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188 Ingestion of cereal bran flakes or wholemeal oat flakes did not result in a significantly higher
189 satiety compared to the reference corn flakes meal (**Table 3, Figure 3**).

190

191 **Discussion**

192

193 The results of this study show that the presence of fibre in a semisolid meal does not affect
194 total postprandial blood glucose or satiety responses in healthy subjects, despite the delay in
195 gastric emptying for the product containing the higher amount of fibre (cereal bran flakes).

196 This study was designed to evaluate the effect of commercial cereals on blood glucose, satiety
197 and GER. The postprandial glucose response was reduced at the initial postprandial phase
198 after the cereal bran flakes meal compared to the corn flakes meal. Similar results have
199 previously been presented showing a lower early postprandial blood glucose response after

200 the intake of cereal bran flakes when compared to corn flakes [30]. In the same study it was
201 shown that this lower postprandial blood glucose response was related to a higher initial
202 postprandial plasma insulin response after a meal composed of 119.2g cereal bran flakes
203 compared to a meal of 60.9g corn flakes [30]. However, the total postprandial insulin AUC
204 was identical for the two meals and gastric emptying was not measured [30]. It is obvious that
205 healthy subjects have a sufficient insulin response, thus giving a normal blood glucose
206 response. Consequently, we have had similar total postprandial blood glucose AUCs for the
207 products in our study. Moreover, the cereal bran flakes meal had a smaller amount of
208 carbohydrates than that of the corn flakes meal. However, if we had used the same amount of
209 carbohydrates from each cereal brand in our study, we would have had a larger difference in
210 energy, which, in turn, could potentially have influenced the GER results. An increased
211 caloric value of a meal can delay the GER [31]. The cereal bran flakes meal had the lowest
212 total caloric value, 298 kcal, compared to the other meals with 320 kcal, respectively. Still,
213 the difference in GER was only significant between the cereal bran flakes meal and the
214 wholemeal oat flakes, probably due to the higher amount of fibre in the cereal bran flakes
215 meal. Also, the glucose response was reduced at the end of the postprandial phase after the
216 cereal bran flakes meal compared to the wholemeal oat flakes meal (Figure 1), which could be
217 related to the lower GER (Figure 3). However, in patients with type 2 diabetes, oat bran flour
218 containing 9.4 g β -glucan lowered the postprandial glycemia [24]. In the same study on type 2
219 diabetes patients using oat bran crisps containing 3.0g β -glucan, the postprandial glycemia
220 was also reduced, although the reduction was only half as large as compared to oat bran flour
221 containing 9.4 g β -glucan [24]. It has previously been shown in type 2 diabetes patients that
222 each gram of β -glucan in food can lower the GI by four GI units [23]. The wholemeal oat
223 flakes meal contained only 0.5 g β -glucan. Probably the amount of β -glucan was too small to
224 affect the blood glucose response. In this study we could not show any significant difference

225 in satiety despite a delayed gastric emptying after the cereal bran flakes meal compared to the
226 wholemeal oat flakes meal. A delay in GER has previously been shown to increase satiety
227 [32]. However, despite a difference in postprandial blood glucose and satiety hormones –
228 such as ghrelin and plasma peptide YY (PYY) – after consumption of oat and wheat fibre, no
229 difference was found with regard to satiety in healthy subjects [33].

230 The American Diabetes Association (ADA) recommends a daily intake of 14g fibre/1.000
231 kcal and foods with whole grains to prevent diabetes [1]. The intake of total dietary fibre,
232 particularly insoluble and cereal fibre, has been shown to have an inverse association with
233 diabetes type 2 [2]. Insoluble fibre and fibre from fruit, vegetables, or legumes have been
234 shown to be unrelated to diabetes [2]. It is unclear whether low glycemic index food prevents
235 diabetes mellitus. Still, the ADA recommends low glycemic index foods that are rich in fibre
236 [1]. However, the composition of the commercial product should be more important than the
237 fibre content alone. Several studies have shown that there was no difference in postprandial
238 blood glucose response directly after the intake of fibre, whereas a beneficial effect on
239 glucose metabolism was observed on the second meal test due to colonic fermentation [14,
240 34- 35].

241

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Conclusions

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244 The result of this study demonstrates that the intake of equal amounts of either cereal bran
245 flakes and wholemeal oat flakes has no effect on the total postprandial blood glucose response
246 or satiety when compared to corn flakes. Furthermore, this study shows that the intake of
247 cereal bran flakes slows the GER when compared to wholemeal oat flakes and corn flakes,
248 probably due to a higher content of fibre. Since these products do not differ in terms of
249 glucose response and satiety on healthy subjects, they should be considered equivalent in this

250 respect. However, this study does not exclude a potential difference between the meals with
251 regard to a delayed second meal effect.

252

253 **Competing interest**

254

255 All authors declare that they have no competing interest.

256

257 **Authors' contributions**

258

259 JH participated in the design of the study, performed the statistical calculations and the graphs
260 and drafted the manuscript. RF and JW participated in the design of the study, recruited
261 subjects, collected the data and drafted the manuscript. GD participated in the design of the
262 study, performed the statistical calculations and the graphs, paid for the study and participated
263 in drafting the manuscript. OB participated in the design of the study and performed the
264 ultrasound examinations. LOA participated in the design of the study and in drafting the
265 manuscript. All authors read and approved the final manuscript. All authors lacked any
266 conflict of interest.

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395 **Table 1.** Nutrient composition of the test product portions.

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	Sour Milk	Frebaco Wholemeal Oatflakes	Kellogg's All-Bran Regular Flakes	Kellogg's Cornflakes
	300 g	50g	50g	50g
Total energy (kcal)	135	185	163	185
Total protein (g)	12	6	5	3.5
Total fat (g)	1.5	2	1	0.35
Total Carbohydrate (g)	18	35.5	33.5	42
Sugar (g)	15	0.75	11	4
Total Fibre (g)		4	7.5	1.5
β -glucan (g)		0.5		

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410 **Table 2.** Postprandial blood glucose areas under the curve (AUCs) after ingestion of meals
 411 consisting of wholemeal oat flakes, cereal bran flakes or corn flakes in twelve healthy
 412 subjects ¹. Significant differences of postprandial blood glucose AUCs were calculated with
 413 the Wilcoxon t-test. There were no significant differences between the AUCs.
 414

AUC	Wholemeal Oat Flakes <i>mmol * min/ L</i>	Cereal Bran Flakes <i>mmol * min/ L</i>	Corn Flakes <i>mmol * min/ L</i>
0 – 5 min	0.3 ± 0.1	1.3 ± 0.1	0.3 ± 0.1
0 - 25 min	21.2 ± 2.8	19.3 ± 1.4	19.3 ± 3.4
0 – 45 min	58.9 ± 7.1	53.8 ± 3.9	59.2 ± 10.2
0 - 65 min	83.0 ± 12.4	76.9 ± 7.7	93.8 ± 16.9
0 - 85 min	97.8 ± 16.3	88.7 ± 9.9	116.8 ± 21.8
0-105 min	110.1 ± 18.9	96.0 ± 10.4	124.4 ± 26.4
0 - 125 min	120.6 ± 21.5	106.8 ± 12.9	143.0 ± 26.3

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 416 ¹ Mean ± SEM; n= 12

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425 **Table 3.** Satiety areas under the curve (AUCs) after ingestion of meals consisting of
 426 wholemeal oat flakes, cereal bran flakes or corn flakes in twelve healthy subjects ¹.
 427 Significant differences of satiety AUCs were calculated with the Wilcoxon t-test. There were
 428 no significant differences between the AUCs.
 429

AUC	Wholemeal Oat Flakes <i>cm²</i>	Cereal Bran Flakes <i>cm²</i>	Corn Flakes <i>cm²</i>
0 – 5 min	14.0 ± 2.1	16.4 ± 2.4	12.5 ± 2.5
0 - 25 min	128.1 ± 18.7	148.5 ± 19.4	112.9 ± 21.1
0 – 45 min	244.0 ± 34.7	275.6 ± 34.2	206.2 ± 38.0
0 - 65 min	359.8 ± 45.8	386.4 ± 46.9	289.4 ± 52.6
0 - 85 min	459.8 ± 56.6	466.6 ± 56.1	363.5 ± 65.8
0-105 min	542.3 ± 66.1	544.9 ± 64.9	418.1 ± 75.0
0 - 125 min	602.4 ± 74.6	600.8 ± 12.9	454.6 ± 80.1

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 431 ¹ Mean ± SEM; n= 12

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440 **Figure 1.** Means (\pm SEM) incremental blood glucose concentrations in twelve healthy subjects
441 after ingesting meals consisting of sour milk with cereal bran flakes (■), corn flakes (◆) or
442 wholemeal oat flakes (▲). Significant differences calculated with the Wilcoxon t-test. * Cereal
443 bran flakes significantly different in response compared to corn flakes ($p < 0.05$). Z Cereal bran
444 flakes significantly different from response compared to wholemeal oat flakes ($p < 0.05$).

445
446 **Figure 2.** Gastric emptying of sour milk with cereal bran flakes, wholemeal oat flakes or corn
447 flakes, estimated as gastric emptying rate (GER), in twelve healthy subjects. The median,
448 minimum (Min), and maximum (Max) values and the values of the first (q1) and the third (q3)
449 quartiles are shown. Significant differences were calculated with the Wilcoxon t-test. Cereal
450 bran flakes significantly different in response compared to wholemeal oat flakes ($p < 0.05$)

451
452 **Figure 3.** Means (\pm SEM) incremental satiety scores in twelve healthy subjects after ingesting
453 meals consisting of sour milk with cereal bran flakes (■), corn flakes (◆) or wholemeal oat
454 flakes (▲). Significant differences calculated with the Wilcoxon t-test. There were no
455 significant differences between the mean incremental satiety scores.

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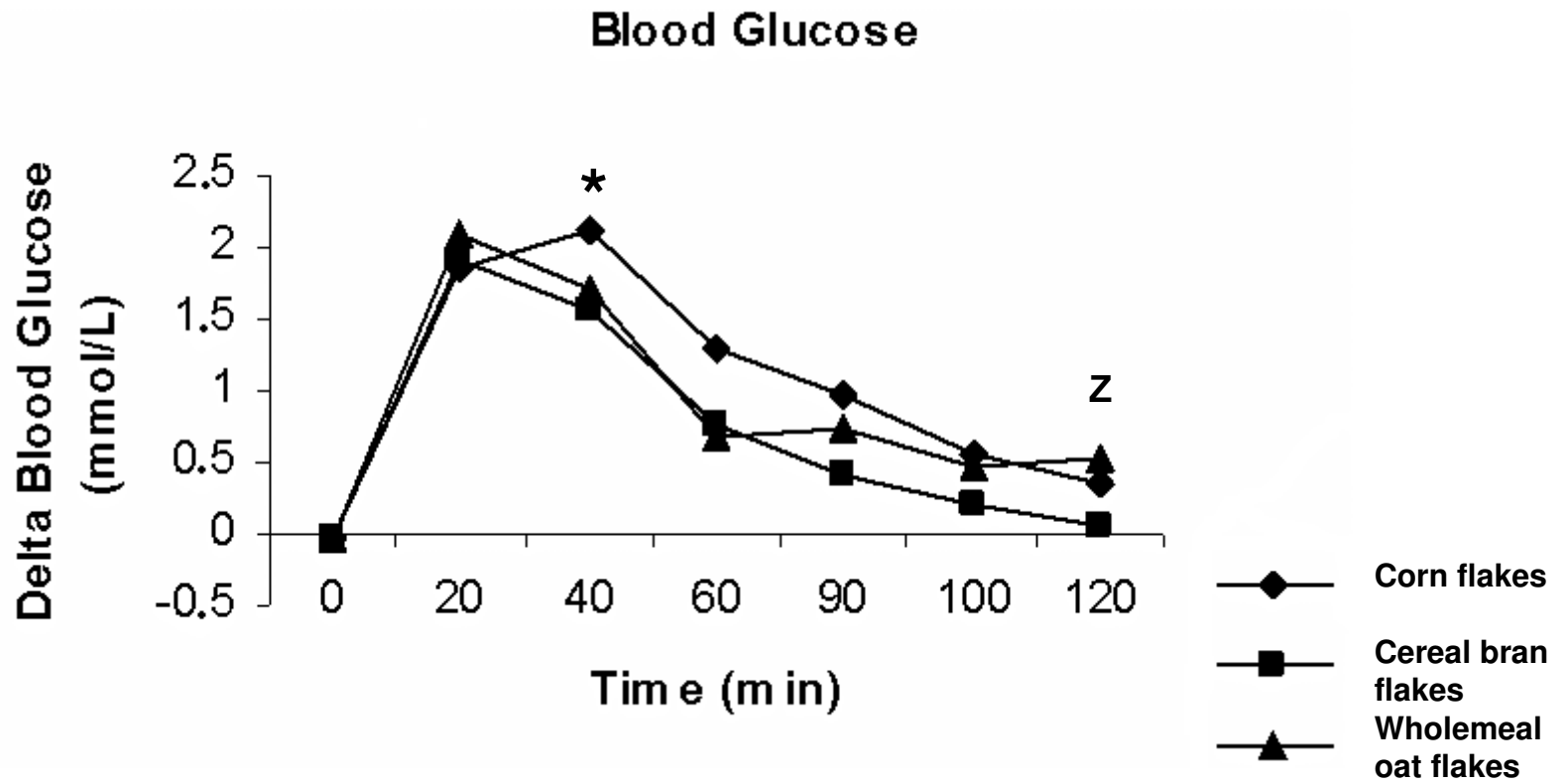


Figure 1

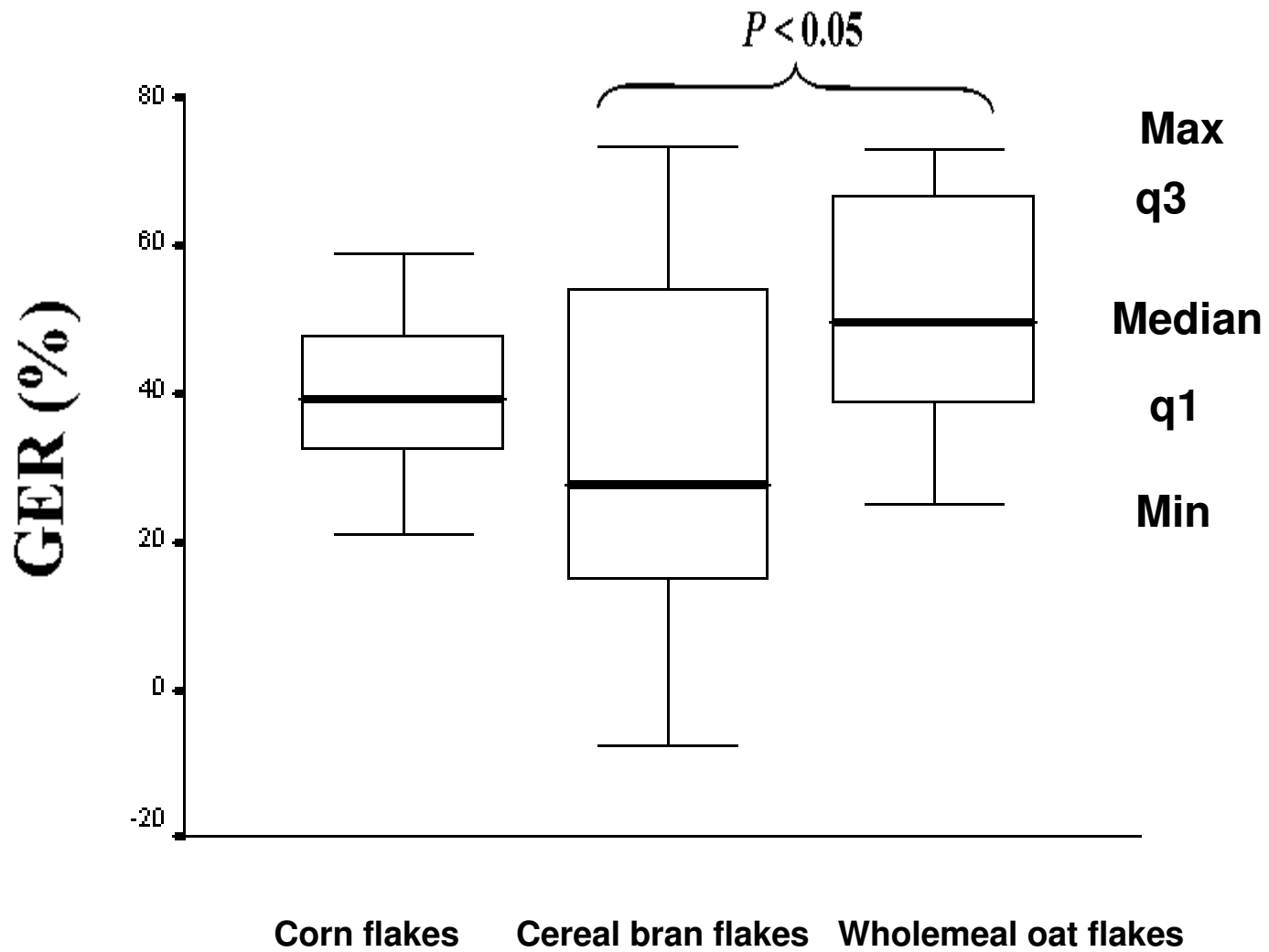


Figure 2

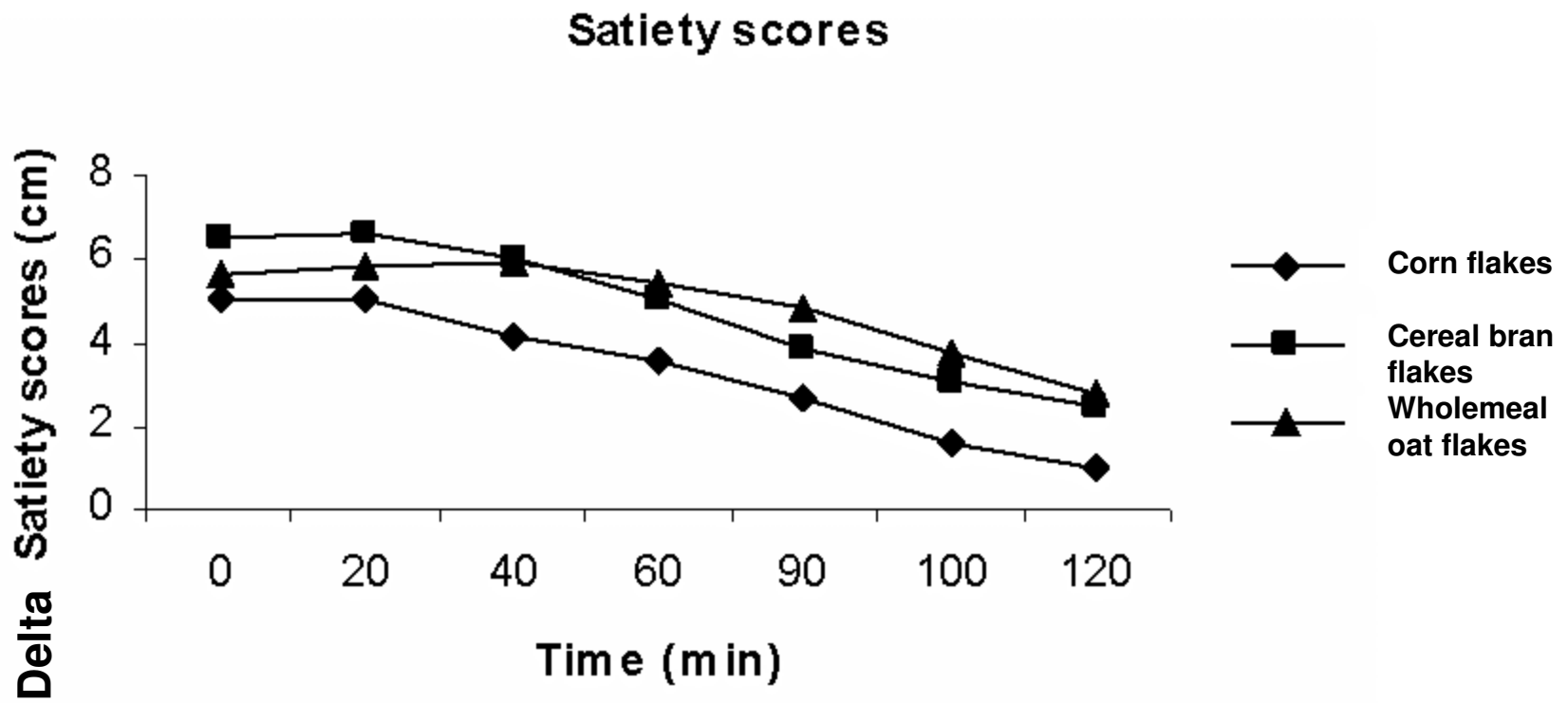


Figure 3