Rye whole-meal bread does not alter postprandial blood glucose response or gastric emptying in healthy subjects: a randomized blinded controlled trial

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Abstract

Background: Dietary fibre food intake is related to a reduced risk of developing diabetes mellitus. The aim of this study was to evaluate the effect of commercial rye whole-meal bread with a content of whole kernels (RWMB) compared to white wheat bread (WWB), on the rate of gastric emptying, and postprandial glucose response in healthy subjects.

Methods: Ten healthy subjects were assessed by using a blinded crossover trial. The subjects were examined regarding blood glucose levels and gastric emptying rate (GER) after ingestion of 150g WWB or 150g RWMB on two different occasions after an overnight fast. GER was measured using a standardized real time ultrasonography. GER was calculated as a percentage change in antral cross sectional area 15 and 90 minutes after the finished meal with WWB and RWMB.

Results: There was no statistical significance between the GER values or the blood glucose areas under the curve evaluated with the Wilcoxon signed rank sum test.

Conclusions: Postprandial blood glucose response or GER to grain products are not determined by the amount of fibre in the food.

Trial registration: NCT00779298

Background

Changing the diet can control the blood glucose level and help prevent the development of type 2 diabetes. The American Diabetes Association recommends increased intake of dietary fibre and whole grains to prevent the development of type 2 diabetes and cardiovascular disease [1].

Cereals are the most important source of dietary fibre throughout the world and bread is an essential part of the Swedish diet. The fibre in cereals is located mainly in the outer layer of the kernels. The term "whole grain" is often used for whole-meal products in which the structure of the kernel is destroyed in the flour containing the original dietary fibre, but also for cereal products in which a large proportion of whole cereal grains is intact. However, there seem to be a major difference in metabolic response between whole grain and whole-meal products. The amount of whole kernels is more effective in reducing glucose response than the fibre content [2, 3]. The preparation, cooking and particle size of the grain structures may also affect the metabolic response. The germ of the whole grain acts as a natural amylase inhibitor, which can be destroyed during the milling of wheat into whole-meal flour [4]. There are many definitions of dietary fibre, including a range of non digestible polysaccharides and lignin derived from cell walls that are poorly digested in the upper intestine. Dietary fibre has been divided into two groups, soluble and insoluble, in attempt to explain physiological effects to different types of fibre. Soluble fibres are considered partially but not entirely water-soluble, and include pectin, guar gum (galactomannan) and glucomannan (also known as konjac mannan), psyllium, β-glucan and arabinoxylans. Rye contains more of soluble fibre in the form of β-glucan and arabinoxylans than wheat [5]. Gastric emptying, together with other factors, regulates the postprandial blood glucose response, and a delay in the gastric emptying rate (GER) leads to a lower postprandial blood glucose concentration. It has been suggested that reduced postprandial glucose and insulin concentrations after the consumption

of different combinations of dietary fibre could be caused by delayed GER, mouth-to-cecum transit or delayed absorption of glucose in the small intestine. Previous studies on dietary fibres show divergent effects on GER [6-12]. Another hypothesis that has been proposed is that dietary fibre is fermented in the colon by the bacterial flora and leads to a release of short-chain fatty acids, lowering postprandial glucose levels [13]. It has been previously shown that whole-meal rye bread and rye bread with whole kernels lower postprandial insulin response but does not affect glucose response [13, 14] or GER in healthy subjects, when measured indirectly with paracetamol [14]. The paracetamol method is dependent on the release and absorption of paracetamol across the small intestine, which makes this method unreliable, as the pharmacokinetics of paracetamol vary within and between individuals [15, 16]. The aim of this study was to evaluate the effect of whole-meal rye bread with a content of whole kernels on the postprandial blood glucose and GER, measured directly using ultrasonography, in comparison with white wheat bread.

Material and Method

Ten healthy subjects, seven women and three men; mean age 26 ± 1 years [range 23-35 years]; mean BMI 24.1 ± 0.8 kg/m² [range 21.0-27.7 kg/m²], without symptoms or a prior history of gastrointestinal disease, abdominal surgery or diabetes mellitus, were included in the study. All subjects were recruited from the population in a southern county of Sweden. None of the subjects was a smoker or a snuff user. One of the subjects was taking hypertension medication and one levotyroxin. None of the subjects used any drugs on the day of the examination. The subjects were examined between 8:00 and 10:00 a.m. after an 8 hour fast. Each subject was required to have a normal fasting blood glucose level on the day of the study. If a subject showed gastrointestinal tract symptoms (diarrhea or constipation) the study was postponed.

Each test meal was planned to contain 50g carbohydrates from the test bread, ham and 300 ml FUN Light syrup (caloric value 3 kcal, 0.6 g carbohydrates) (Procordia Food AB, 241 81 Eslöv, Sweden) and was served and ingested gradually during the meal which lasted for 10 min. Because the analyzed nutrient compositions of the test breads were not available as the study started, the portions of the breads were calculated using data from the bakeries. The reference white wheat bread (WWB) (Storform, Cerealia Bakeries AB, 227 64 Lund, Sweden) contained 34.65% available carbohydrates and the rye whole-meal bread with a content of whole kernels (RWMB) (Danskt rågbröd, Hemköpskedjan AB, 171 78 Solna, Sweden) contained 41.8% available carbohydrates. The content of available carbohydrates was analyzed according to Holm et al [17]. The content of dietary fibre, fat and proteins were assumed to be the same as according to product information (Table 1). The meals were served in random order at intervals of 1 week. Randomization was performed using a table of random numbers. The total test duration did not exceed 2 months.

The GER was estimated using a previously described standardized ultrasound method [18]. The sonographic examination was performed using two different ultrasound machines (Siemens Acuson Sequoa 512 and Siemens Elegra, Siemens Medical Solutions, Mountains View, CA) with an abdominal 2.5-4 MHz transducer. However, the same machine was used to calculate values of the GER in every test occasion. The measurements of the gastric antrum were performed by the same radiologist, who was blinded with regard to the meals. The measurements were made 15 and 90 minutes after the end of meal ingestion. Gastric emptying was expressed as the percentage change of the antral cross-sectional area from 15 to 90 min. Finger-prick capillary samples were collected fasting and 40, 60, and 90 min after the end of the meal to measure blood glucose levels. Blood glucose concentrations were measured with a

HemoCue Glucose system (HemoCue AB, Ängelholm, Sweden). The study was performed according to the Helsinki declaration. All subjects gave written, informed consent before participating in the experiments.

Delta values of blood glucose levels were calculated as the difference between blood glucose levels before the meal (fasting value) and 40, 60 and 90 min after the end of the meal. The blood glucose was determined from the areas under the curves (AUCs), using the area above zero, for each subject (Graph Pad PRISM, version 4, San Diego). These values are presented as the mean ± SEM for the whole group. All statistical calculations were performed using SPSS for Windows (version 14.0, 2005). Differences in the GER, gastric antral cross-sectional area, and blood glucose levels were evaluated with the Wilcoxon signed rank sum test. Values of $p<0.05$ were considered significant.

Results

Postprandial blood glucose response

The mean fasting blood glucose level before ingestion of WWB was 4.4 ± 0.1 mmol/l compared to and was not significant different from that before ingestion of RWMB, which was 4.3 ± 0.1 mmol min/l. No significant differences were seen in blood glucose responses at different times, or in the incremental areas under the postprandial glucose curves between the different bread meals (Figure 1). The mean AUCs after ingestion of WWB, and RWMB were 121.1 ± 17.9, and 125.2 ± 21.2 mmol min/l, respectively.

GER

No significant differences were observed between the meals with regard to gastric emptying rates (Figure 2). The median value of the GER after the reference meal was estimated to be 37% (q1=10%, q3=66%) compared with the corresponding value after RWMB meal, which was estimated to be 45% (q1=9%, q3=54%). The median values of the antral cross-sectional area after the ingestion of the reference meal were 963 mm^2 (q1=523 mm^2, q3= 1110 mm^2) and 523 mm^2 (q1=297 mm^2, q3=759 mm^2), 15 and 90 min, respectively after the end of the meal. After the ingestion of the RWMB the median values of the antral cross-sectional area were 660 mm^2 (q1=427 mm^2, q3= 957 mm^2) and 416 mm^2 (q1= 312 mm^2, q3= 585 mm^2), respectively, 15 and 90 min after the end of the meal. The median gastric antral cross-sectional areas were significantly larger after ingestion of the WWB than after the ingestion of the RWMB at 15 min (p=0.047). However, there was no significant difference between gastric antral cross-sectional areas at 90 min.

Discussion

The aim of this study was to elucidate the effect of dietary fibre and whole kernels present in rye-based bread products, on gastric emptying rate and glycemic response in healthy subjects. Our hypothesis was that an intake of dietary fibre would lower the postprandial blood glucose response due to delayed gastric emptying. We were not able to verify this hypothesis. The RWMB meal had the highest total available amount of carbohydrates, 62.7 g, compared to the WWB meal with 52.0 g. Unfortunately, the amount of available carbohydrates of the test breads were not available as the study started, and the portions of the breads were calculated using data from the bakeries. The meals were composed of commercial products and not our own manufactured test meals. It would be more practical to determine the test portions as grams of bread rather that based on available carbohydrates, since people usually eat a number of slices of bread. The RWMB had the lowest total caloric value, 390 kcal, compared

to the WWB with 435 kcal. An increased caloric value of a meal can delay the GER [19]. Still, the difference in the amount of fibre was essential. Despite their different fibre content and botanical structure, RWMB and WWB showed similar postprandial glycemic responses in this study. The rye kernels in the RWMB may have been disrupted during baking process, and thereby increase enzymatic accessibility of starch. Unfortunately, in the present study the structure of the bread or the amount of soluble fibre was not investigated. The lack of difference in GER [10] and postprandial blood glucose response between the breads is in agreement with studies performed by Juntunen et al and Leinonen et al, who compared whole-kernel rye bread and whole-meal rye bread to white wheat bread in healthy subjects [10, 14, 20]. Rye bread produces a lower postprandial insulin, and glucose-dependent insulinotropic polypeptide (GIP) than wheat bread [10, 20]. Furthermore, a lower C-peptide response after ingestion of rye bread indicates a diminished pancreatic secretion of insulin [20]. Unfortunately we did not measure insulin, GIP or C-peptide levels in this study. Despite the lack of difference in acute postprandial blood glucose response after ingestion of RWMB, there might be a second-meal effect not evaluated in the present study. Dietary fibre and resistant starch may ferment in the colon by the bacterial flora and lead to a release of short-chain fatty acids that may improve glucose tolerance of the following meal [13].

A relationship between antral area and satiety in healthy subjects has been observed by others [21-25]. A limitation of this study is that we did not evaluate the satiety. The median antrum area 15 min after the intake of the WWB meal was significantly larger than the 15 min antrum area after the intake of the RWMB meal. This is probably due to the larger volume of the WWB than the RWMB. The negative values of GER are caused by an increased gastric antral cross-sectional area at 90 min and this could be due to increased amount of gastric juices and saliva in the stomach.

Conclusions

The present study showed that there is no difference in postprandial blood glucose response or gastric emptying after ingestion of rye whole-meal bread. The results indicate that postprandial blood glucose response or GER to grain products are not determined by the amount of fibre in the food.

Competing interest

All authors declare that they have no competing interest.

Authors' contributions

The authors' contributions were as follows: JMJ, GD, JH, and LOA contributed to the design of the study; JMJ was responsible for recruiting the subjects and carried out the practical aspects of the study. OB performed the ultrasound examinations; JH, SL, and JMJ conducted the statistical calculations; JH created the graphs. JH wrote the first draft of the manuscript and, GD, JMJ, SL, OB, and LOA made critical revisions of the manuscript. All authors read and approved the final manuscript. None of the authors had any personal or financial conflict of interest.

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References

1. Bantle JP, Wylie-Rosett J,, Albright AL, Aprovian CM, Clark NG, Franz MJ, Hoogwef BJ, Lichtenstein AH, Mayer-Davis E, Mooradian AD, Wheeler ML: **Nutrition recommendations and interventions for diabetes: a position statement of the American Diabetes Association.** *Diabetes care* 2007, **30**:S48-S65.
2. Jenkins DJ, Wolever TM, Jenkins AL, Giordano C, Giudici S, Thompson LU, Kalmusky J, Josse RG, Wong GS: **Low glycemic response to traditionally processed wheat and rye products: bulgur and pumpernickel bread.** *Am J Clin Nutr,*1986, **43**(4):516-520.
3. Liljeberg H, Granfeldt Y, Björck I: **Metabolic responses to starch in bread containing intact kernels versus milled flour.** *Eur J Clin Nutr*,1992, **46**(8):561-575.
4. Snow P, O´Dea K: **Factors affecting the rate of hydrolysis of starch in food.** *Am J Clin Nutr* 1981, **34**:2721-2727.
5. Åman P, Nillson M, Andersson R: **Positive health effects of rye.** *Cereal Foods World* 1997, **42**:684-688.
6. Benini L, Castellani G, Brighenti F, Heaton KW, Brentegani MT, Casiraghi MC, Sembenini C, Pellegrini N, Fioretta A, Minniti G, et al: **Gastric emptying of a solid meal is accelerated by the removal of dietary fibre naturally present in food**. *Gut* 1995, **36**:825-830.
7. Ray TK, Mansell KM, Knight LC, Malmud LS, Owen OE, Boden G: **Long-term effects of dietary fibre on glucose tolerance and gastric emptying in noninsulin-dependent diabetic patients.** *Am J Clin Nutr* 1983, **37**(3):376-381.
8. Hagander B, Scherstén B, Asp NG, Sartor G, Agardh CD, Schrezenmeir J, Kasper H, Ahrén B, Lundquist I: **Effect of dietary fibre on blood glucose, plasma immunoreactive insulin, C-peptide and GIP responses in non insulin dependent (type 2) diabetics and controls.** *Acta Med Scand* 1984, **215**(3):205-213.

9. Hlebowicz J, Lindstedt S, Höglund P, Björgell O, Almér LO, Darwiche G: **The botanical integrity of wheat products influences the gastric distension and satiety in healthy subjects** *Nutr J* 2007, **7:**12

10. Juntunen KS, Niskanen LK, Liukkonen KH, Poutanen KS, Holst JJ, Mykkänen HM: **Postprandial glucose, insulin, and incretin responses to grain products in healthy subjects**. *Am J Clin Nutr* 2002, **75**:254-262.

11. Jenkins DJ, Wolever TM, Leeds AR, Gassull MA, Haisman P, Dilawari J, Goff DV, Metz GL, Alberti KG: **Dietary fibres, fibre analogues, and glucose tolerance: importance of viscosity.** *Br Med J* 1978, **1**:1392-1394.

12. Hlebowicz J, Wickenberg J, Fahlström R, Björgell O, Almér LO, Darwiche G: **Effect of commercial breakfast fibre cereals compared with corn flakes on postprandial blood glucose, gastric emptying and satiety in healthy subjects: a randomized blinded crossover trial.** *Nutr J* 2007, **17**;6:22.

13. Wang H, Weening D, Jonkers E, Boer T, Stellaard F, Small AC, Preston T, Vonk RJ, Priebe MG: **A curve fitting approach to estimate the extent of fermentation of indigestible carbohydrated.** *Eur J Clin Invest* 2008, **38**(11):863-868.

14. Leinonen K, Liukkonen K, Poutanen K, Uusitupa M, Mykkänen H: **Rye bread decreases postprandial insulin response in healthy Finnish subjects.** *Eur J Clin Nutr* 1999, **53**(4):262-267.

15. Holm J, Björck I, Drews A, Asp NG: **A rapid method for the analysis of starch.** *Starch/Stärke* 1986, **38**;224-226.

16. Darwiche G, Almér L, Björgell O, Cederholm C, Nilsson P: **Measurement of Gastric Emptying by Standardized Real-Time Ultrasonography in Healthy Subjects and Diabetic Patients.** *J Ultrasound Med* 1999, **18**:673-682.

17. Rawlins MD, Henderson DB, Hijab AR: **Pharmacokinetics of paracetamol (acetaminophen) after intravenous and oral administration.** *Eur J Clin Pharmacol* 1977, **11**(4):283-286.

18. Sanaka M, Kuyama Y, Yamanaka M: **Guide for judicious use of the paracetamol absorption techniques in a study of gastric emptying rate of liquids.** *J Gastroenterol* 1998, **33**(6):785-791.

19. Calbet JA, MacLean DA: **Role of caloric content on gastric emptying in humans.** *J Physiol* 1997, **498**(2):553-559.

20. Juntunen KS, Laaksonen DE, Autio K, Niskanen LK, Holst JJ, Savolainen KE, Liukkonen KH, Poutanen K, Mykkänen H: **Struktural differences between rye and wheat breads but not the total fibre content may explain the lower postprandial insulin response to bread.** Am J Clin Nutr 2003, **78**:957-964.

21. Jones KL, Doran SM, Hveem K, Bartholomeusz FD, Morley JE, Sun WM, Chatterton BE, Horowitz M: **Relation between postprandial satiation and antral area in normal subject**. *Am J Clin Nutr* 1997, **66**:127-132.

22. Santangelo A, Perracchi M, Conte D, Fraquelli M, Porrini: **Physical state of meal gastric emptying, cholecystokinin release and satiety.** *Br J Nutr* 1998, **80**:521-527.

23. Bergmann JF, Chassany O, Petit A, Triki R, Caulin C, Segrestaa JM: **Correlation between echographic gastric emptying and appetite: influence of psyllium.** *Gut* 1992, **33**:1042-1043.

24. Sturm K, Parker B, Wishart J, Feinle-Bisset C, Jones KL, Chapman I, Horowitz M: **Energy intake and appetite are related to antral area in healthy young and older subjects.** *Am J Clin Nutr* 2004, **80**:656-667.

25. Hveem K, Jones KL, Chatterton BE, Horowitz M: **Scintigraphic measurment of gastric empying and ultrasonographic assessment of antral area: relation to appetite**. *Gut*

1996, **38**:816-821.

Figure 1. Gastric emptying rate following the ingestion of rye whole-meal bread (RWMB) and white wheat bread (WWM), in ten healthy subjects. The median, minimum (Min), and maximum (Max) values and the values of the first (q1) and the third (q3) quartiles are shown. No significant differences were found between the GERs evaluated with the Wilcoxon signed rank sum test.

Figure 2. The mean incremental blood glucose concentration in ten healthy subjects after the ingestion of meals consisting of rye whole-meal bread (triangle), and white wheat bread (square). No significant differences were found between the incremental blood glucose concentrations following the various meals evaluated with the Wilcoxon signed rank sum test.

Table 1. Nutrient composition of the test bread portions.

Bread	Portion Size g	Available CHO g	Dietary fibre g	Protein g	Fat g	Energy Content kJ
White wheat	150	52.0	0	13.5	0	435
Rye whole-meal	150	62.7	3.75	12.75	4.5	390

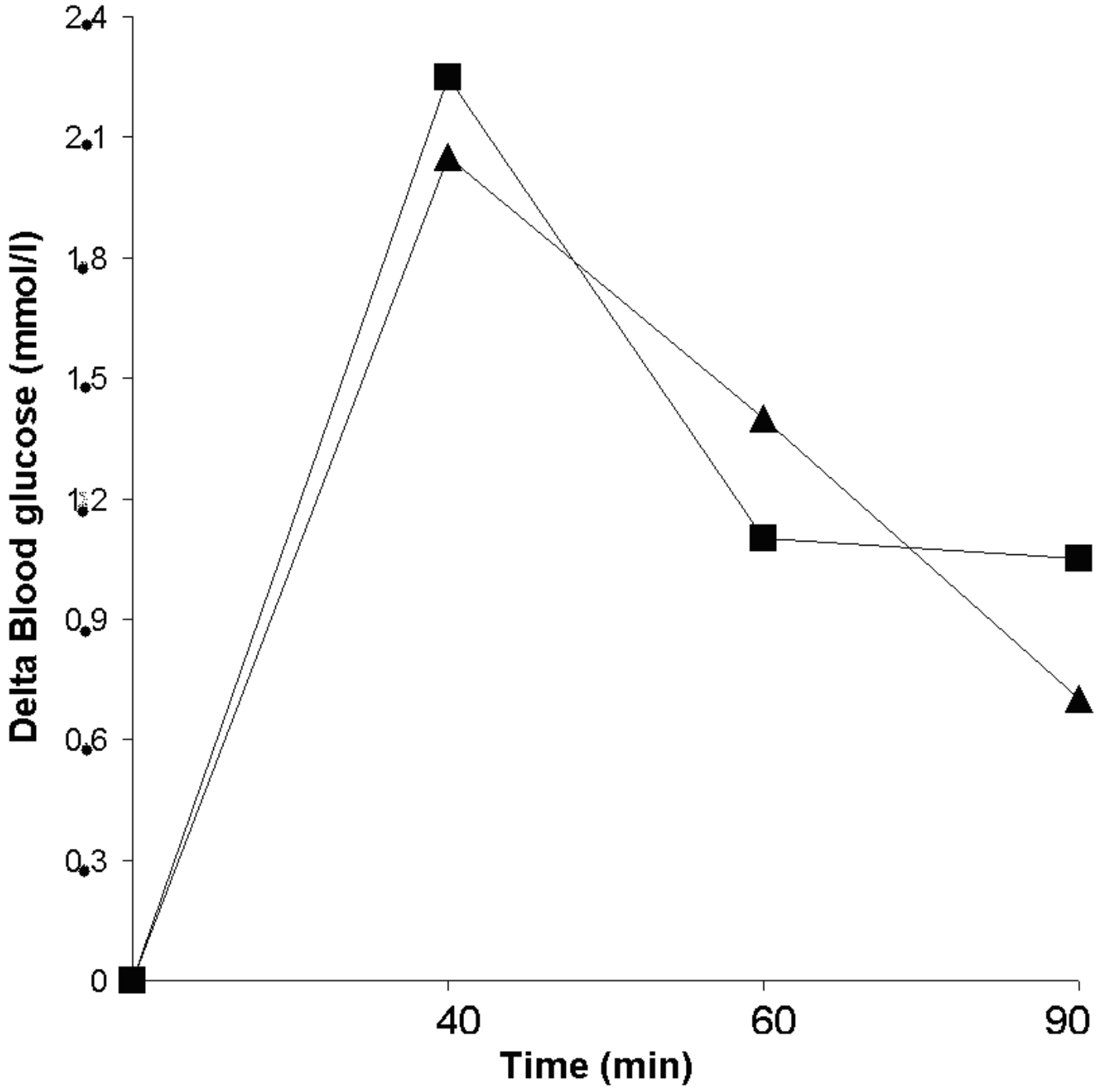
Delta Blood glucose (mmol/l)
2.4
2.1
1.8
1.5
1.2
0.9
0.6
0.3
0
40
60
90
Time (min)

Figure 1

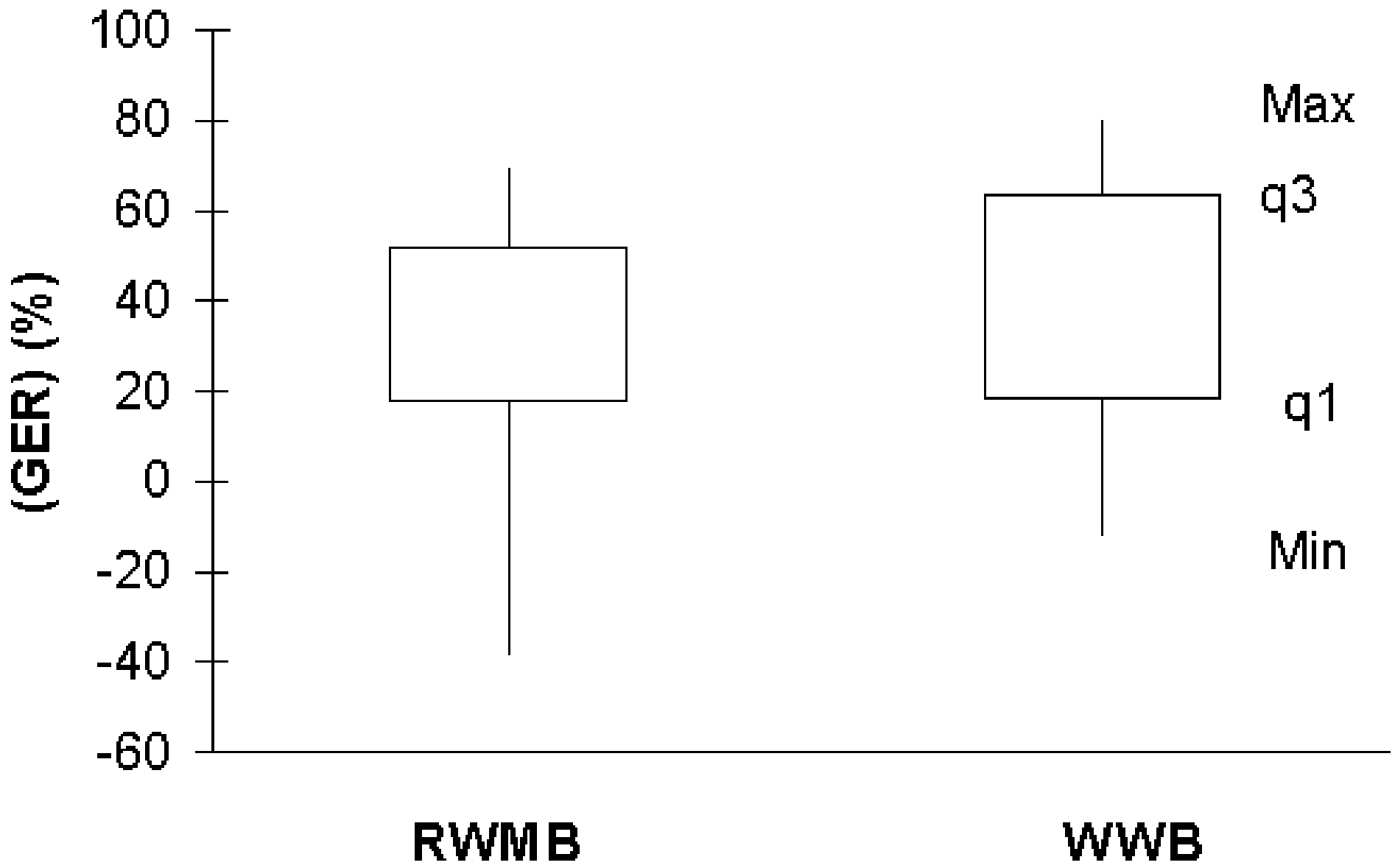

Figure 2