Short Communication

Berries modify the postprandial plasma glucose response to sucrose in healthy subjects

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Sucrose increases postprandial blood glucose concentrations, and diets with a high glycaemic response may be associated with increased risk of obesity, type 2 diabetes and CVD. Previous studies have suggested that polyphenols may influence carbohydrate digestion and absorption and thereby postprandial glycaemia. Berries are rich sources of various polyphenols and berry products are typically consumed with sucrose. We investigated the glycaemic effect of a berry purée made of bilberries, blackcurrants, cranberries and strawberries, and sweetened with sucrose, in comparison to sucrose with adjustment of available carbohydrates. A total of twelve healthy subjects (eleven women and one man, aged 25–69 years) with normal fasting plasma glucose ingested 150 g of the berry purée with 35 g sucrose or a control sucrose load in a randomised, controlled cross-over design. After consumption of the berry meal, the plasma glucose concentrations were significantly lower at 15 and 30 min ($P < 0.05$, $P < 0.01$, respectively) and significantly higher at 150 min ($P < 0.05$) compared with the control meal. The peak glucose concentration was reached at 45 min after the berry meal and at 30 min after the control meal. The peak increase from the baseline was 1·0 mmol/l smaller ($P = 0.002$) after ingestion of the berry meal. There was no statistically significant difference in the 3 h area under the glucose response curve. These results show that berries rich in polyphenols decrease the postprandial glucose response of sucrose in healthy subjects. The delayed and attenuated glycaemic response indicates reduced digestion and/or absorption of sucrose from the berry meal.

Berries: Polyphenols: Sucrose: Glucose response

Foods or meals high in available carbohydrate such as sucrose increase postprandial blood glucose concentrations. Regular consumption of diets with high glycaemic impact may increase risk for obesity, type 2 diabetes and CVD by promoting excessive food intake, pancreatic β cell dysfunction, dyslipidaemia and endothelial dysfunction[1]. Several *in vitro* and *in vivo* studies have suggested that polyphenols may influence carbohydrate digestion and absorption and thereby postprandial glycaemia. Polyphenols have inhibited intestinal α-glucosidase (maltase and sucrase) activity[2–8] and glucose transport[9–14] *in vitro*. They have also suppressed the elevation of blood glucose concentration after oral administration of glucose or maltose in animal models[7,11,14,15]. In human studies, beverages rich in polyphenolic compounds have shown beneficial effects on postprandial glycaemia. Delayed absorption of glucose after consumption of apple juice[16] and coffee[17] and attenuated glycaemic response to sucrose consumed in chlorogenic acid-enriched coffee[18] have been reported.

Berries are excellent sources of various polyphenols, such as anthocyanins, flavonols, phenolic acids, ellagitannins and proanthocyanidins[19–23]. Polyphenol-rich extracts of blueberries, blackcurrants, strawberries and raspberries have been shown to inhibit α-glucosidase activity *in vitro*[24,25]. In addition, consumption of cranberry juice sweetened with high-fructose corn syrup resulted in a different (but not statistically significant) pattern of postprandial glycaemia compared with the similar amount of the sweetener in water[26]. In the present study we investigated the glycaemic effect of a berry purée made of bilberries, blackcurrants, cranberries and strawberries, and sweetened with sucrose, in reference to sucrose alone.

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Experimental methods

Subjects

A total of twelve subjects (eleven women and one man) were recruited from the register of Foodfiles Ltd. At the screening visit, the health status of the subjects was checked by routine blood chemistry (fasting plasma glucose, blood count, serum thyroid-stimulating hormone, plasma creatinine, γ-glutamyl transferase and urate) and a structured interview on previous and current diseases, current medication, alcohol and tobacco consumption, physical activity and use of nutrient supplements. The mean age was 54·2 (SD 15·1; range 25–69) years, BMI 25·4 (SD 2·9; range 21·1–30·0) kg/m^2, and fasting plasma glucose concentration 5·3 (SD 0·4; range 4·5–6·0) mmol/l.

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the Research Ethics Committee of the Hospital District of Northern Savo (Finland). Written informed consent was obtained from all subjects.

Study design

The randomised, controlled, cross-over study was carried out single-blinded for the study nurse. Each subject was studied in two 3 h meal tests, on separate days, at least 5 d apart. The test meals were administered in a randomised order in an open-label design. The subjects were advised to keep their medication, lifestyles and body weight constant and to follow their habitual diet throughout the study. In the evening before the test, the subjects were instructed to avoid berries, and to consume a meal of choice and repeat that meal before the second test.

The experiments began in the morning after a 12 h overnight fast. The fasting blood samples were obtained from a fingertip capillary blood drop using a lancing device.
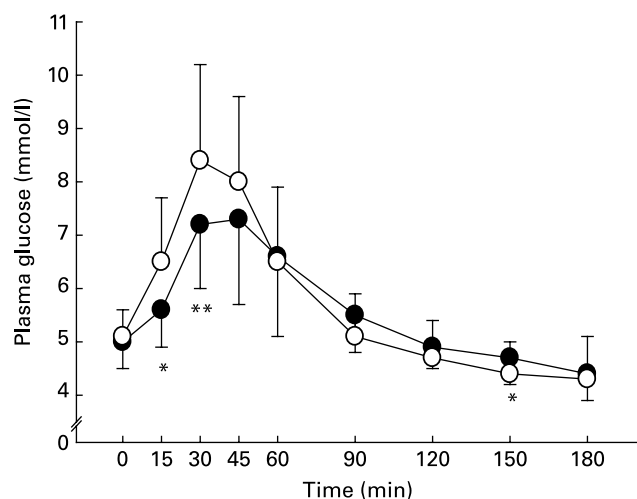

Fig. 1. Plasma glucose concentrations after ingestion of the berry meal (●) and the control meal (○) in healthy subjects (n 12). Values are means, with standard deviations represented by vertical bars. Mean value was significantly different from that of the control meal: *P<0·05, **P<0·01 (paired-samples t test with Bonferroni correction).

The subjects were advised to consume the test meal within 15 min. The first bite in the mouth was set as time 0 and the following blood samples were taken after 15, 30, 45, 60, 90, 120, 150 and 180 min. Blood glucose was analysed using a HemoCue Glucose 201 + analyser (HemoCue AB, Angelholm, Sweden) calibrated to plasma-equivalent glucose concentrations.

Test meals

The test meal was a mixed berry purée (150 g) with 35 g sucrose. It consisted of equal amounts (37·5 g) of black currants (Ribes nigrum), bilberries (wild European blueberries, Vaccinium myrtillus), European cranberries (Vaccinium oxycoccos) and strawberries (Fragaria x ananassa). The natural sugar composition of the purée was 3·0 % glucose (4·5 g/portion) and 3·4 % fructose (5·1 g/portion), as analysed by HPLC. Water (120 ml) was served with the berry purée. The control meal included 250 ml water, 35 g sucrose, 4·5 g glucose and 5·1 g fructose, to achieve the similar profile and amounts of available carbohydrates.

Statistical analysis

The data were analysed with the SPSS 15·0 for Windows statistical program (SPSS, Inc., Chicago, IL, USA). Normal distribution of variables was checked with the Shapiro–Wilk test. The statistical significance of the overall difference in plasma glucose concentrations between the meals was assessed with a general linear model (GLM) for repeated measures followed by paired-samples t tests with Bonferroni correction to analyse the differences between the test meals at different timepoints. In addition, the maximum increase from baseline was calculated and the difference between the test meals was analysed by paired-samples t tests with Bonferroni correction. The 0–180 min areas under the glucose response curve were calculated using Canvas 8·0·2 (Deneba Software, Miami, FL, USA), ignoring the area below the baseline concentration, and the statistical significance was assessed with paired-samples t tests. Statistical significance was obtained at P<0·05.

Results

The mean body weight of the study subjects remained stable during the study: 68·6 (SD 9·7) kg at screening, 68·5 (SD 9·9) kg at visit 1 and 68·3 (SD 9·9) kg at visit 2. The ingestion order of the berry meal and the control meal had no effect on the results. The fasting plasma glucose concentrations did not differ between the test meal occasions. The berry meal was ingested in 9·9 (SD 0·7) min and the control meal in 10·0 (SD 1·0) min.

The plasma glucose concentrations at 15 and 30 min after the berry meal were significantly lower than those after the control meal (P<0·05, P<0·01, respectively) (Fig. 1). In addition, the glucose response at 150 min after the berry meal was higher than after the control meal (P<0·05). The peak glucose concentration was reached at 45 min after the berry meal and at 30 min after the control meal. The maximum increase in plasma glucose concentration from the baseline was smaller (P=0·002) after ingestion of the berry meal

(2·3 (SD 1·3) mmol/l) than after ingestion of the control meal (3·3 (SD 1·5) mmol/l). The 0–180 min areas under the glucose response curve tended to be lower after the berry meal (133 (SD 58) min × mmol/l) than after the control meal (149 (SD 74) min × mmol/l; $P = 0.29$).

Discussion

The present study shows that ingestion of sucrose with berries produced a different postprandial glycaemic response compared with the control without berries but with a comparable profile of available carbohydrates. The shape of the plasma glucose curve, with reduced concentrations in the early phase and a slightly elevated concentration in the later phase, indicates a delayed response due to berry consumption. Berries also significantly decreased the peak glucose increment.

We did not analyse the polyphenol content of the berry meal, but the contents of several classes of polyphenols have been extensively reported for Finnish berries[19–23]. According to the data published previously[23], the total amount of polyphenols in the berry meal was nearly 800 mg, with anthocyanins and proanthocyanidins as the major groups. Due to the dark-coloured bilberries and blackcurrants, the anthocyanin content was high. Based on our previous data[22], we estimate that the berry meal provided approximately 300 mg anthocyanins. It has been reported that the extent of *in vitro* inhibition of α-glucosidase by berry extracts is related to their anthocyanin content[24]. The two anthocyanins cyanidin-3-rutinoside[27] and cyanidin-3-galactoside[28] were *in vitro* inhibitors of α-glucosidase. Cyanidin-3-rutinoside is one of the major anthocyanins in blackcurrants[29], and it showed inhibitory activity comparable with voglibose[27]. Cyanidin-3-galactoside is present in bilberries[29] and cranberries[26], and showed a synergistic effect with acarbose[28]. Acarbose and voglibose are inhibitors of α-glucosidase used in the treatment of diabetes. Also proanthocyanidins have shown potent α-glucosidase inhibitory activity[8]. It is thus possible that at least part of the reduced postprandial glycaemia observed in the present study can be explained by inhibition of α-glucosidase, the enzyme responsible for the digestion of sucrose to glucose in the intestinal epithelium, by berry polyphenols.

Intestinal absorption of glucose is mediated by active Na-dependent transport via sodium glucose co-transporter 1 (SGLT1) and facilitated Na-independent transport via GLUT2[30]. The Na^+-dependent SGLT1-mediated glucose uptake was inhibited in a competitive manner by several phenolic acids (chlorogenic, ferulic and caffeic acids)[9] as well as by glucosides of quercetin[12], whereas the galactoside and glucorhamnoside and the aglycone quercetin itself were ineffective. The glucose transport by GLUT2 was inhibited by the flavonols quercetin and myricetin[11,13]. These phenolic acids and flavonols with inhibitory activity against intestinal glucose uptake are common polyphenolic constituents of berries[19–21] and were present in our berry meal.

A similar postprandial glucose response as observed in the present study has also been reported after consumption of a 25 g glucose load in commercial apple juices[16]. The mean plasma glucose concentrations were significantly lower at 15 and 30 min after ingestion of clear apple juice, and significantly lower at 15 min but significantly higher at 45 and 60 min after ingestion of cloudy apple juice compared with the control drink (glucose load). The effects of apple juices with high levels of polyphenols (chlorogenic acid and phloridzin) on plasma glucose, insulin, glucose-dependent insulinotropic peptide and glucagon-like peptide-1 concentrations were consistent with the delayed absorption of glucose.

Soluble dietary fibre attenuates postprandial glucose responses after carbohydrate-rich meals[31]. Based on the Finnish food composition database[32], our berry meal contained 5·4 g dietary fibre, of which approximately 70 % was insoluble. Since the amount of soluble fibre provided by the berry meal was no more than 1·5 g, it is unlikely that the reduced glycaemic response could be solely explained by the fibre content of the berry meal.

The peak glucose increase was 1·0 mmol/l smaller after ingestion of the berry meal with sucrose compared with the control sucrose load. In addition, the difference in glucose values at 30 min was even bigger, being 1·2 mmol/l. The reduction in the postprandial glucose concentrations was of the same magnitude as previously detected with 4–11 g oat fibre, β-glucan[33–35], and it can be considered clinically significant.

In conclusion, a mixture of berries rich in polyphenols decreased the postprandial glucose response of a sucrose load in healthy subjects. Reduced rates of sucrose digestion and/or absorption from the gastrointestinal tract are the most probable mechanisms underlying the delayed and attenuated glycaemic response. For better understanding of the role of berries in the regulation of glucose metabolism, further studies assessing their effects on insulin and other hormonal responses are needed.

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