Bioavailability of Quercetin From Berries and the Diet

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Abstract: Berries are a rich source of various polyphenols, including the flavonoid quercetin. In this article, the results of three intervention studies investigating the bioavailability of quercetin from berries are reviewed. In the first study, we investigated the short-term kinetics of quercetin after consumption of black currant juice and showed that quercetin is rapidly absorbed from it. In the second study, we showed that plasma quercetin levels increase up to 50% in subjects consuming 100 g/day of bilberries, black currants, and lingonberries as a part of their normal diets for 2 mo. In the third study, healthy subjects consumed a diet high or low in vegetables, berries, and other fruit for 6 wk. Quercetin concentrations nearly doubled in the high-vegetable, -berry, and –other fruit group and decreased by 30% in subjects consuming less of these foods than normally. The results showed that plasma quercetin is bioavailable from a diet containing berries and indicate that it may be a good biomarker of fruit and vegetable intake in general.

Introduction

Polyphenols exhibit a wide range of bioactivities in different in vitro models, including antioxidative and anti-inflammatory activities (1). Their bioavailability from the diet and particularly good food sources is therefore of interest. Berries are a rich source of various types of polyphenols (2). Quantitatively, the most important polyphenols are the anthocyanidins (for example, cyanidin), flavonols (for example, quercetin and myricetin), phenolic acids (for example, caffeic acid), and flavan-3-ols (for example, (+)-catechin).

Several factors affect the bioavailability of polyphenols (3,4). The most important determinants of bioavailability are the chemical structure of the aglycone and the type of glycoside. It is well known that polyphenols are rarely present in plants as aglycones (the basic polyphenol structure) but are usually bound to different sugars. Prior to absorption from the gastrointestinal tract, the glycosidic linkages are cleaved by enzymes originating from the small intestine or the colon (this the general rule, although some exceptions occur). The bioavailability of the different glycosidic forms of the same aglycone varies. Different glycosides are present in different plants, which results in marked variation in bioavailability of polyphenols from different dietary sources (5).

Little is known about the bioavailability of polyphenols from berries. Anthocyanins are an exception; several studies indicate that their bioavailability is relatively poor (4). We studied the bioavailability of the main berry flavonol (quercetin) in three human intervention studies. The first study investigated the short-term kinetics of the compound from black currant juice. The second and the third study investigated the bioavailability of quercetin during long-term consumption of diets containing different kinds of berries. The results of the first study are new and have not been published elsewhere. The two other studies have been published previously and are reviewed here with respect to quercetin (6–8).

Materials and Methods

Analytical Methods

Plasma quercetin was analyzed as previously described (9). The analytical method is based on solid-phase extraction and high-performance liquid chromatography with electrochemical detection. Electrochemical detection was performed with a Coularray detector from ESA, Inc. (Chelmsford, MA; Study 1) or a Coulochem 5100A detector (Studies 2 and 3). The between-day coefficient of variation was below 7% in all studies.

Subjects

Intervention 1: Human volunteers were recruited among students and employees from the Viikki campus of the University of Helsinki. The health status of the candidates was checked with a questionnaire and screening tests (body weight and height, blood pressure, and urinary glucose and protein). Twenty apparently healthy female volunteers were selected. Their baseline characteristics are
shown in Table 1. Two of the subjects dropped out during the study because of problems in blood sampling and one due to gastrointestinal problems. The study plan was accepted by the Ethics Committee of Faculty of Agriculture and Forestry, University of Helsinki, and the subjects gave their informed consent. The results presented here have not been published elsewhere.

**Intervention 2:** The study population consisted of male 60-yr-old volunteers. They were recruited among 523 men, who in 1994 participated in a health survey for men born in 1935 and living in the city of Turku. Exclusion criteria were use of regular medication, use of dietary supplements during the past month, and overweight (body mass index of >30 kg/m²). Twenty subjects were randomized into a berry group and 20 subjects were randomized into a control group. A third group receiving vitamin supplements was also included; however, samples from that group were not analyzed for quercetin. Details of the study have been published elsewhere (6,8).

**Intervention 3:** Healthy men and women, 19–52 yr of age, working or studying at the Viikki Campus at the University of Helsinki, were recruited. Their health status was checked through a questionnaire and screening tests (measurements of body weight and height, blood pressure, and urinary glucose and protein). Eighty subjects were randomly assigned to four treatment groups. Three subjects dropped out during the study. Nineteen subjects consuming their normal diets served as controls. Details of the study have been previously reported (7).

**Study Designs**

**Intervention 1:** The study was performed in partial crossover design. The subjects were divided into three groups. Groups 1 and 2 received different amounts of black currant juice, and group 3 received the same amount of black currant juice as group 2 but took it with a rice cake (Table 1). The control drink was sugar water for all groups. The subjects participated in the study on 2 days 1 wk apart. A baseline blood sample was collected into EDTA-containing tubes after an overnight fast, and after that the subjects drank black currant juice or the control drink. Additional blood samples were taken at 45, 90, 150, and 240 min. The subjects were not allowed to eat during this 4-h period. The subjects refrained from taking medication 1 wk before the first study day until the end of the study. They also refrained from consumption of berries and berry products as well as alcohol from 24 h before the study until the end of it. On the evenings preceding the study days the intake of tea, fruits, and fruit products was prohibited. Each subject received black currant juice or the control drink on one of the study days in randomized order. The juice was administered according to body weight (8 g/kg) and ingested within 10 min from the baseline blood sampling. The juice (produced with novel processing techniques at the Danish Technical University) was sweetened with sugar (16.7% wt/wt) and was diluted with water before ingestion. The intakes of undiluted black currant juice and flavonols are shown in Table 1.

**Intervention 2:** Subjects consumed 100 g/day of berries in addition to their normal diets for 8 wk. The control group consisted of subjects consuming their normal diets. The subjects in the berry group were given deep-frozen black currants, lingonberries, and bilberries packed into 100-g portions. The subjects were instructed to eat one portion per day fresh and to eat the different berries in turns. The control group received 500 mg of calcium gluconate daily. Blood samples were obtained 2 wk prior to the study, at baseline, and at 2, 4, and 8 wk.

The subjects filled out 3-day dietary records at the beginning of the study and at 8 wk. The average daily intakes of quercetin were calculated with the Nutrica computer program. Quercetin data from the Fineli database (kindly provided by M.-L. Ovaskainen from the National Public Health Institute) were added to the Nutrica database.

**Intervention 3:** The study was a strictly controlled dietary intervention study with a random parallel design (7). Ninety percent of daily energy was obtained from the experimental diets provided to the subjects. The 80 subjects that were recruited for the study were assigned to four groups. Each group consumed the diet they had been assigned to for 6 wk. Two diets contained high amounts of vegetables, berries, and other fruits, and two diets contained low amounts of them (that is, consumption was closer to normal amounts consumed by the Finnish population). The two high diets, as well as the two low diets, differed in their fatty acid composition, but, because this did not affect plasma quercetin con-

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**Table 1. Characteristics of the Volunteers and Intakes of Undiluted Black Currant Juice in Intervention 1**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n = 5)</th>
<th>Group 2 (n = 5)</th>
<th>Group 3 (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>31.2 (21–48)</td>
<td>27.8 (24–32)</td>
<td>27.3 (19–38)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>61.6 (9.6)</td>
<td>59.3 (5.0)</td>
<td>61.7 (4.7)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.2 (3.5)</td>
<td>22.0 (1.9)</td>
<td>23.5 (2.6)</td>
</tr>
<tr>
<td>Undiluted black currant juice intake (ml)</td>
<td>251 (39)</td>
<td>145 (12)</td>
<td>151 (11)</td>
</tr>
</tbody>
</table>

a: Group 1 received 4.4 g/kg body weight of undiluted black currant juice; group 2 received 2.7 g/kg body weight of undiluted black currant juice; group 3 received 2.7 g/kg body weight of undiluted black currant juice and a rice cake. Values are means with range or SD in parentheses. The groups were compared by Kruskall-Wallis analysis of variance, and no differences were seen in the baseline characteristics of the subjects.
centrations, the results for the high and the low groups were combined for this article. The high diets contained 440 g of fresh or frozen vegetables, 204 g of frozen berries, and 166 g of other fruits daily per 10 MJ. The low diets contained 167 g of vegetables, 0 g of berries, and 54 g of other fruits daily per 10 MJ. Of the high diets, the most abundant vegetables and fruits (other than berries) were unpeeled apple, carrot, tomato, cabbage, cucumber, broccoli, onion, and French beans. Berries that were consumed included strawberry, raspberry, bilberry, black currant, and lingonberry. Of the low diets, the most abundant fruits and vegetables were banana, peeled apple, carrot, cabbage, cucumber, Chinese cabbage, and tomato. In addition, both diets contained 144 g/10 MJ of juice (orange juice in high diets and apple or pear juice in low diets); high diets contained 151 g/10 MJ of processed fruit or berry products (jams, soups, and canned fruits) and low diets contained 106 g/10 MJ.

Results

Short-Term Kinetics of Quercetin from Black Currant Juice (Intervention 1)

The plasma concentrations of quercetin after consumption of two doses of black currant juice, with or without a rice cake, are shown in Fig 1. Quercetin concentrations were significantly higher after juice consumption compared with baseline in all groups (P < 0.05, GLM for repeated measures, contrast analysis). In the group consuming 4.4 ml of juice, the concentrations appeared to be higher compared with the group consuming 2.7 ml of juice (the result was statistically nonsignificant, likely because of the small number of subjects). Consumption of the juice with a rice cake had no effect on serum quercetin concentrations. No changes in plasma quercetin were observed after intake of the control drink (data not shown).

Bioavailability of Polyphenols from Mixed Berries (Intervention 2)

Fasting plasma quercetin concentrations in men consuming bilberries, black currants, and lingonberries for 8 wk, and in the control group, are shown in Table 2. Plasma quercetin was significantly higher in the berry group compared with the control group during berry consumption (for P values see Table 2). The increase was 32–51% depending on the time point. The calculated intake of quercetin was 12.3 ± 1.4 mg in the berry group at the end of the berry consumption period, which was twice as high as in the control group, which had an intake of 5.8 ± 0.6 mg/day at 8 wk. The intake of quercetin in the control group was practically the same at baseline (5.5 ± 0.5 mg/day) and at the end of the study.

Bioavailability of Quercetin from a Diet Containing High Amounts of Fruits, Vegetables, and Berries (Intervention 3)

Fasting plasma quercetin concentrations of subjects consuming diets high or low in vegetables, berries, and other fruits for 6 wk are shown in Fig 2. After 6 wk on the high-vegetable, -berry, and -fruit diet, plasma quercetin con-

Figure 1. Plasma quercetin concentrations 0–4 h after consumption of black currant juice. Group 1 (n = 4) consumed 4.4 ml/kg of juice, group 2 (n = 5) consumed 2.7 ml/kg of juice, and group 3 (n = 7) consumed 2.7 ml/kg of juice together with a rice cake. Values are mean ± 5D. Data points for group 3 have been slightly offset.
Concentrations increased to 170% compared with baseline \((P < 0.05)\). In subjects consuming the low-vegetable, -berry, and -fruit diet, the concentrations decreased to 70% of the baseline values \((P < 0.05)\). The intake of quercetin, calculated from 3-day food records, was 2.6 mg/day on the low diet and 24.1 mg/day on the high diet (7).

### Discussion

Several short-term studies have previously shown that quercetin is bioavailable from its main dietary sources, that is, onions (10), tea (11), and red wine (11), and from capsules containing pure quercetin aglycone or quercetin glycosides (12,13). In our laboratory, we investigated the bioavailability of quercetin during long-term consumption of so-called normal diets, that is, diets resembling those of the general population, with or without berries. In this article, we review the results of those studies. We also present new results from a short-term kinetic study with black currant juice.

Our studies included the most commonly consumed berries in Finland. Lingonberries (Vaccinium vitis idaea), which are like small cranberries, and bilberries (V. myrtillus), closely related to blueberries, are sold frozen in supermarkets all year and are picked by people residing in rural areas. Black currants, strawberries, and raspberries, which are widely consumed, are cultivated but are also grown by many people in their own gardens.

Quercetin is mainly present in plants as glycosides. The types and quantities of different quercetin glycosides vary greatly between berries from different families and genera. The subject has been investigated thoroughly by Määttä-Riihinen et al. They quantitated the quercetin glycosides in different types of berries and reported that black currants, for instance, contain about half and half of quercetin-3-glucoside and quercetin-3-rutinoside and small amounts quercetin hexoside-malonate (14). The total quercetin amount, expressed as milligrams aglycone per kilogram of fresh weight of berry, was 47 for black currant. The total quercetin content in lingonberries and bilberries was reported to be 131 and 81 mg/kg, respectively (2). The quercetin content of strawberries and raspberries was much lower (15).

In the short-term kinetics study, quercetin was clearly bioavailable from black currant juice. Quercetin concentr-
tions appeared to be higher in the group consuming the 60% higher amount of juice (4.4 ml/kg vs. 2.7 ml/kg), although the difference was not statistically significant due to the low number of subjects. Consumption of the juice with a rice cake (containing protein) clearly had no effect. The quercetin found in plasma within 4 h likely originates from the quercetin-3-glucoside present in black currant juice. It has been shown that quercetin is rapidly absorbed (peak plasma value at approximately 30 min) from capsules containing pure quercetin glucosides (5,12). Quercetin from quercetin-3-rutinoside, on the other hand, appears in plasma several hours after ingestion (peak plasma values are achieved between 5 and 10 h) (5,13).

In subjects consuming 100 g/day of black currants, lingonberries, and bilberries, plasma quercetin levels were significantly higher compared with baseline or the control group. In this study, it was not possible to estimate how much the different berries contributed to the increase. Of the berries in question, the highest concentrations of quercetin are found in lingonberries (2). According to pilot studies performed in our laboratory, the compound is bioavailable from all of the berries included in the study.

In the strictly controlled dietary intervention study (intervention 3), plasma quercetin was nearly doubled after 6 wk on a diet rich in vegetables, berries, and other fruits. A considerable part of the total quercetin intake originated from the approximately 200 g of frozen berries consumed daily. In the subjects consuming less fruits and vegetables than usual, and no berries, plasma quercetin decreased by 30% from baseline. It should be noted that the low diet was not a “deprivation diet” but contained enough fruits and vegetables to ensure an adequate intake of vitamin C (100 mg/day). The intake of vitamin C was on average 23% lower during the low diet compared with the habitual diets.

In conclusion, results from our short-term kinetic study show that quercetin is rapidly absorbed after single ingestion of black currant juice and that absorption is not decreased when the juice is ingested together with a rice cake. Results from the two long-term interventions, on the other hand, show that quercetin is bioavailable from berries when they are consumed as part of a normal diet as well as from normal diets not containing berries. Furthermore, the results indicate that fasting plasma quercetin concentration may be a good biomarker of a diet rich in fruits and vegetables in general.

Acknowledgments and Notes

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References
