The effects of apples and apple juice on acute plasma uric acid concentration: a randomized controlled trial

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ABSTRACT

Background: The consumption of large amounts of fructose from added sugars results in the hepatic production and export of uric acid into the circulation.

Objective: Our aim was to test whether fructose present in fruit is of sufficient quantity or in a form that will increase uric acid concentration.

Design: Seventy-three participants were randomly assigned to 1 of 3 groups to ingest small (205 g) and large (410 g) servings of apple segments, small (170 mL) and large (340 mL) servings of apple juice, or a glucose and a fructose control beverage. Within each group, participants ingested both treatments in a crossover design. The fructose control and the large servings of apple and juice contained 26.7 g fructose. Test foods were ingested within 10 min. Blood samples were taken at baseline and at 30 and 60 min after intake.

Results: Plasma uric acid concentrations increased after the intake of all fructose-containing treatments and decreased after the glucose beverage. The mean (95% CI) increase in uric acid at 30 min was 15 μmol/L (10, 21 μmol/L) for the fructose control and 19 μmol/L (8, 30 μmol/L) and 17 μmol/L (9, 24 μmol/L) for the large servings of apple and apple juice, respectively. There was no difference in change in uric acid between baseline and 30 min when comparing the apple (3 μmol/L; 95% CI: −8, 14 μmol/L) and apple juice (−7 μmol/L; 95% CI: −18, 5 μmol/L) with the fructose control. Blood pressure taken 70 min after ingestion was unaffected by any treatment ($P > 0.05$). There was no difference in change in satiety scores between the fructose and glucose control beverages ($P > 0.05$). Participants felt more satiated 30 min after ingesting whole apple than after apple juice. The glycemic response reflected the amount of glucose in each treatment.

Conclusions: The body acutely responds to fructose regardless of source. Longer-term studies are required to assess how small and transient increases in plasma uric acid contribute to health. This trial was registered with the Australian New Zealand Clinical Trials Registry at https://www.anzctr.org.au/trial/registration/trialreview.aspx?id=367974 as ACTRN12615000215527. *Am J Clin Nutr* 2018;107:165–172.

Keywords: fruit, fructose, uric acid, sugar, glycemia

INTRODUCTION

Fruit is recommended by health organizations worldwide as being a low energy–dense food rich in fiber and micronutrients (1). The World Cancer Research Fund and the WHO recommend that people consume 5 portions of nonstarchy fruit and vegetables each day to reduce the risk of a number of chronic diseases (1, 2). However, a sugar contained in fruit, fructose, has been the subject of current debate, with some arguing that fructose is toxic (3–5). A proposed reason for this statement is that the hepatic metabolism of fructose leads to the rapid depletion of ATP, resulting in the production of uric acid, a risk factor for hyperuricemia (6–9). Chronic hyperuricemia is a prerequisite of gout and is considered an independent risk factor for renal and cardiovascular disease (10).

The debate on fructose and hyperuricemia has been fueled by an increased use of added sugars, such as high-fructose corn syrup, and their association with an increase in obesity and the metabolic syndrome (11). Some argue that fructose is a key contributor to these chronic conditions and is implicated in the development of related diseases, including hyperuricemia (5, 11). Although the dietary intake of free fructose has been increasing since 1970 (11), many natural sources of free fructose are available in the diet, including fruit, some vegetables, and honey (12). This provides a contradiction within nutrition advice and guidelines in which fructose from added sugars is to be limited, whereas fruit, which contains fructose, is promoted. Johnson et al. (5) questioned whether "fructose is fructose" despite the source, suggesting that fructose from fruit may not have the same effects on reducing satiety and increasing uric acid and blood pressure as do added sugars due to the food matrix of whole fruit, which reduces the metabolic effects of fructose. Whether the structure of whole fruit has an effect on fructose metabolism is unclear, with Sievenpiper et al. (13) suggesting that there is little evidence to support this concept. However, it has been found that the acute

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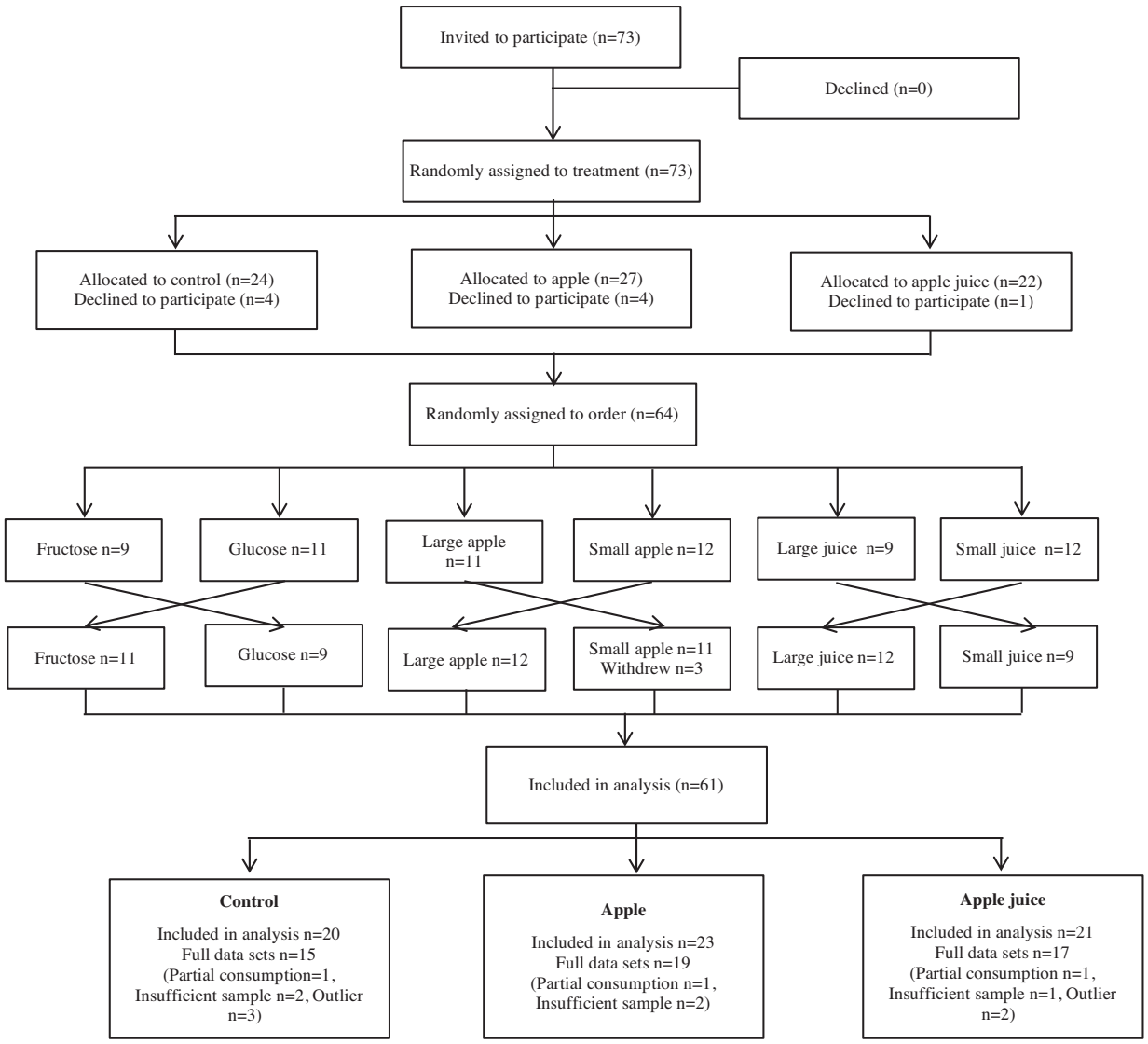

FIGURE 1 Participant flow diagram.

ingestion of 5 apples results in postprandial hyperuricemia (14). Five apples is a large amount of fruit to eat in one sitting, and our interest was to consider more realistic amounts of fruit in line with nutrition advice and guidelines. Therefore, the primary purpose of this study was to compare the acute effect of fructose from whole fruit and from fruit juice in typical serving sizes with a fructose monosaccharide beverage on plasma uric acid concentration. Secondary objectives were to measure satiety, glycemia, and blood pressure with these treatments.

METHODS

Participants

Participants were a convenience sample of University of Otago students (58 women, 15 men) recruited in February–March 2015 (**Figure 1**). Participants were required to be between 18 and 65 y of age and to have normal fasting blood glucose, defined by the WHO as a concentration <5.6 mmol/L (15). Exclusion criteria were as follows: diabetes, cancer, a digestive condition that may affect the absorption of fructose, a recent stroke, or current pregnancy. A unique study number with a code to identify sex was assigned to participants before randomization. By using a randomized list, the biostatistician (JJH) block-randomized participants by sex to groups and to the order in which they received the test foods. The biostatistician was not involved in the practical undertaking of the experiment. Randomization was undertaken with STATA (STATA/IC version 13.1; StataCorp) computer software.

Study foods

Royal Gala apples (*Malus domestica*) were chosen because they were in season during the study period. A Mill Orchard brand of apple juice was chosen, because it contained 100% apple juice with no added sugar, preservatives, colors, flavors, or concentrate. An accredited facility (Cawthron Laboratories Ltd.) assessed the free fructose, sucrose, and glucose contents of the apples and

the apple juice by HPLC. The apple group received unpeeled whole Royal Gala apples chopped into segments with the stalk, core, and seeds removed. Two apples yielded segments weighing 410 g, which contained a total of 26.7 g fructose (21.3 g free fructose, 4.5 g free glucose, and 10.7 g sucrose comprising 5.35 g glucose and 5.35 g fructose). The volume of apple juice containing this amount of fructose was 340 mL, which contained 25.2 g free fructose, 7.8 g free glucose, and 3.1 g sucrose comprising 1.55 g glucose and 1.55 g fructose. The smaller servings were half these amounts [1 apple (205 g), small serving of juice (170 mL)]. The control group received 26.7 g fructose or glucose monosaccharide dissolved in soda water and made up to a volume of 600 mL (4.45% solution).

Study design

Participants were randomly assigned to 1 of 3 groups: an apple group, an apple juice group, and a control group. Each participant tested 2 conditions. Within the apple and apple juice groups, participants ingested a large and a small serving. For the control group, there was a positive control (fructose beverage) and a negative control (glucose beverage). The study biostatistician allocated treatment regimens and had no involvement in the practical undertaking of the experiment. Within each group, the order in which each treatment was received was randomly assigned and testing was separated by a 1-wk washout period.

The day before each test, participants were asked to avoid alcohol, to eat a meal rich in carbohydrates the previous night, and to fast from 2200, with the exception of water. To monitor compliance with these instructions, participants filled out a questionnaire, with 96% deemed to be fully compliant. Baseline information on sex, age, family history of gout, smoking status, medication, supplement use, food allergy or intolerance, diagnosis of chronic disease, disease of the digestive system, and current pregnancy was collected; and participants' height and weight were measured. Before receiving the test food or beverages, 2 baseline capillary blood samples were collected. The start time of the experiment (time 0) was the commencement of the ingestion of the intervention food. On both test days, participants were required to ingest the randomly allocated food or beverage within 10 min. After the baseline collection, blood samples were taken at 30 and 60 min.

The study was conducted according to guidelines laid down in the Declaration of Helsinki, and all procedures involving human participants were approved by the University of Otago Human Ethics Committee (Health). Written informed consent was obtained from all participants. The trial was registered with the Australian New Zealand Clinical Trial Registry (ANZCTR; ACTRN12615000215527).

Laboratory measurements

Capillary blood samples (500 μL) were obtained by finger prick. Blood glucose concentration was measured by the average of 2 fasting samples at baseline to confirm that the participants had normal glucose tolernce. Uric acid concentrations were measured at baseline and at 30 and 60 min. Plasma was recovered from whole blood after centrifugation at 2850 × g at 20°C for 5 min then stored at −70°C. Uric acid analysis was conducted by using a Roche Hitachi Cobas c311 auto-analyzer (Roche Diagnostics). Plasma uric acid concentration was determined by enzymatic colorimetric assay with the use of a UA2 uric acid reagent test kit (Roche Diagnostics), according to the manufacturer's instructions. A 2-point calibration was conducted before analysis and when the UA2 uric acid reagent test kit was changed. Plasma uric acid concentrations are expressed in micromoles per liter. Analysis consistency was determined by using the manufacturer's normal and low controls and a pooled sample. The between-assay CVs for the pooled sample and normal and high controls were 2.56%, 2.31%, and 2.72% at mean concentrations of 260.8, 267.1, and 642.7 μmol/L, respectively. A priori, any samples that were >410 μmol/L were reassessed.

Capillary blood glucose was measured at baseline and at 30 and 60 min after the ingestion of the test foods by using a calibrated HemoCue Glucose 201+ meter (HemoCue America). Systolic and diastolic blood pressure was measured at baseline and at 70 min after the ingestion of the test foods by using an Omron digital automatic blood pressure monitor (model Hem907; Omron). A standardized procedure was adopted whereby participants were seated in a relaxed upright position with their feet on the floor and the arm to be measured positioned palm upward with the monitor's cuff at heart level. Satiety was assessed by using 100-mm visual analog scales at baseline and at 30 and 60 min after ingestion of the test foods. The questions and anchoring statements in accordance with previously published methodology (16) were as follows: "How hungry do you feel? (I am not hungry at all/I have never been more hungry)," "How satisfied do you feel? (I am completely empty/I cannot eat another bite)," "How full do you feel? (Not at all full/Totally full)," and "How much do you think you can eat? (Nothing at all/A lot)."

Statistical analysis

In a parallel design, 16 persons/group would have 80% power to detect a difference of 1 SD in plasma uric acid response to treatment at an α of 0.05; therefore, it was decided that 22 participants/group would be recruited to allow for dropout. Although a difference of 1 SD is relatively large, our study was designed to investigate acute effects, which would need to be large if they were to have an impact on health. A small difference between the acute uric acid response to glucose and fructose would be of little clinical significance.

To determine the effect of apples (410 g) or apple juice (340 mL) on plasma uric acid response compared with fructose or glucose (parallel design), mixed-effects regression models were generated for plasma uric acid with a random effect for participant and an interaction term between treatment and time. Adjustments for sex, order of intervention (small serving followed by the large serving or vice versa), time of intervention (morning or afternoon), and family history of gout were made. Mean differences in change in uric acid (and 95% CIs) between baseline and 30 min and between 30 and 60 min were calculated. To determine the effect on plasma uric acid of a large serving of apples or juice compared with a small serving of apples (crossover design), mixed-effects regression models were generated for plasma uric acid with participant ID as a random effect and an interaction term between time and size of serving (large or small), adjusted for randomized order. The same analyses were also undertaken with blood glucose and satiety responses as the outcomes.

TABLE 1
Participant characteristics at baseline

Characteristic	Control group ($n = 20$)	Apple group ($n = 23$)	Juice group ($n = 21$)
Age, y	21 ± 2[1]	22 ± 6	24 ± 7
Male sex, *n* (%)	5 (25)	5 (22)	5 (24)
BMI, kg/m^2	23 ± 2	23 ± 4	23 ± 3
Family history of gout, *n* (%)	3 (15)	2 (9)	4 (19)
Blood glucose, mmol/L	5.0 ± 0.4	4.9 ± 0.5	4.8 ± 0.4
Systolic blood pressure, mm Hg	108 ± 8	110 ± 11	111 ± 11
Diastolic blood pressure, mm Hg	61 ± 5	62 ± 7	63 ± 8
Visual analog scale,[2] mm			
How hungry do you feel?[3]	56 ± 17	52 ± 22	51 ± 19
How satisfied do you feel?[4]	31 ± 14	27 ± 20	31 ± 16
How full do you feel?[4]	24 ± 18	25 ± 22	24 ± 16
How much do you think you can eat?[3]	65 ± 12	65 ± 22	66 ± 17

[1] Mean ± SD (all such values).
[2] Score on a 100-mm visual analog scale on which a participant indicates his or her subjective feeling.
[3] A high value indicates feeling hungry and wanting to eat.
[4] A low value indicates feeling less satisfied and less full.

Differences in the change in blood pressure (both diastolic and systolic) from baseline to 70 min between consumption of apples or juice and glucose or fructose (parallel design) were determined by using a linear regression model adjusted for baseline blood pressure and randomized order. When comparing between differing amounts of food (large compared with small; crossover design), a mixed-effects regression model was used with participant ID as a random effect.

All of the analyses were completed with the use of Stata 15.0 (StataCorp). Residuals of all models were checked for homogeneity of variance and normality.

RESULTS

Participants were healthy adults, most of whom were in their early 20s. Nine participants who reported a family history of gout were distributed among the groups. All of the participants were nonsmokers. The flow of participants through the study is shown in Figure 1. Of the 73 persons randomly assigned to the treatment, 9 declined to participate. The remaining 64 participants were randomly assigned to the order in which they received their allocated treatment. Three participants, who were all assigned to the apple group, withdrew before completing the study, citing unwillingness to repeat eating apple pieces. Data from the 61 participants who completed the study were analyzed.

There were instances of missing data. Insufficient plasma volume for the laboratory assay occurred 5 times. Three participants could not finish 1 of their assigned test foods ($n = 1$, large apple; $n = 1$, large apple juice; $n = 1$, fructose beverage). There were 3 instances in which uric acid assay values were considered outliers—that is, when the difference from the previous measure was greater than the 75th percentile + 1.5 times the IQR of the group difference. Including the outlying values in the analysis did not substantially change the results. In total, 61 individuals were included in the analysis, with 51 having complete sets of data from both treatments, which exceeded the required minimum number of participants determined by the power calculation.

Participant characteristics are given in **Table 1**. By design, the ratio of males to females was the same in each group. Participants were not stratified by family history of gout, but by chance, small numbers of participants were distributed among the groups. There was no change in uric acid concentration after ingestion

TABLE 2
Baseline uric acid concentration and uric acid response to 410 g apples and 340 mL apple juice compared with glucose and fructose[1]

Mean (SD) baseline uric acid concentration, μmol/L					Difference in change (95% CI) in uric acid concentration between test food and comparison,[2] μmol/L			
Test food	Value	Comparison	Value	*n*	Baseline to 30 min	*P*	30–60 min	*P*
Apple	279 (67)	Glucose	268 (50)	41	25 (15, 35)	<0.001	−7 (−17, 4)	0.206
Apple	279 (67)	Fructose	268 (46)	37	3 (−8, 14)	0.594	−7 (−18, 5)	0.248
Apple juice	265 (57)	Glucose	268 (50)	37	22 (14, 30)	<0.001	2 (−7, 10)	0.681
Apple juice	265 (57)	Fructose	268 (46)	33	0 (−9, 9)	0.976	2 (−7, 11)	0.710

[1] Comparisons are for participants with complete data (baseline and 30 and 60 min); the inclusion of participants with missing data did not substantially change the results. The large serving of apple and apple juice and the fructose control beverage contained 26.7 g fructose. The glucose control beverage contained 26.7 g glucose.
[2] Mixed-effects regression with a time and treatment interaction and with participant as a random effect, adjusted for treatment order, time of day, sex, and family history of gout.

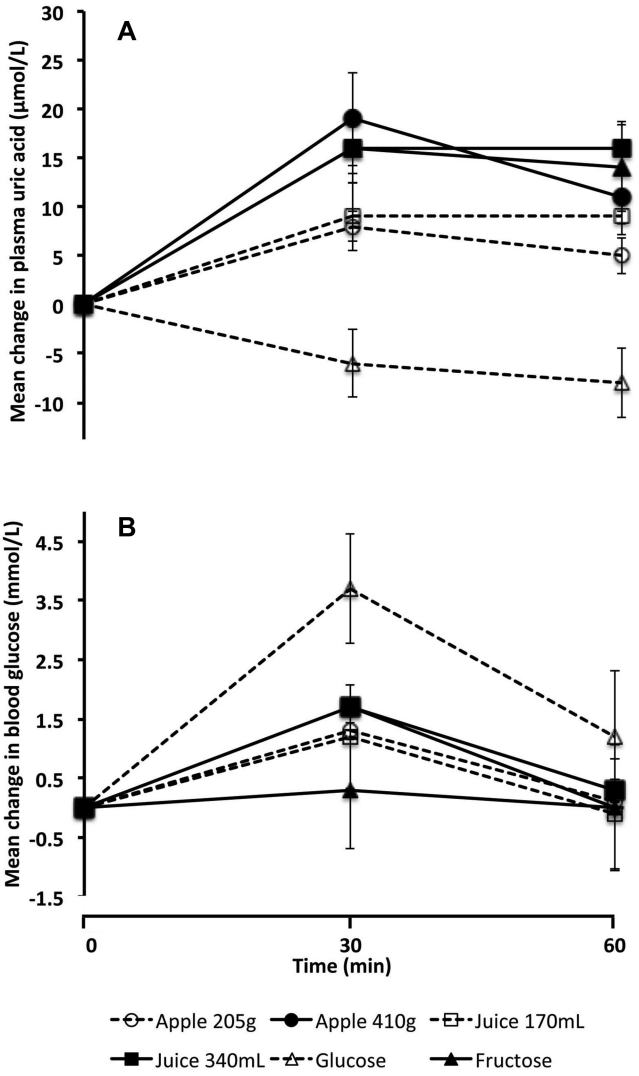

FIGURE 2 Change from baseline in plasma uric acid (A) and blood glucose (B) concentrations after the ingestion of test foods and beverages. The large servings of apple (n = 21) and juice (n = 18) and the fructose beverage (n = 15) contained 26.7 g fructose; the small servings of apple (n = 19) and juice (n = 20) contained 13.55 g fructose. The large servings of apple and juice contained 9.85 and 9.35 g glucose, respectively; the small servings contained half those amounts. The glucose beverage (n = 19) contained 26.7 g glucose. The fructose and glucose control beverages had a concentration of 4.45% sugar. Vertical bars represent SEMs. (A) An increase in uric acid concentrations was found for all fructose-containing treatments and a decrease was shown for the glucose control. There was no difference in change in uric acid concentration between the large servings of apple and juice and the fructose control (all containing 26.7 g fructose). (B) Blood glucose concentrations increased significantly from baseline for all treatments at 30 min. The glycemic response to the glucose beverage at 30 min was larger than for all other treatments.

of the glucose beverage, either at 30 min (P = 0.124) or between 30 and 60 min (P = 0.436). In contrast, plasma uric acid concentrations significantly increased 30 min after the ingestion of small and large servings of apple and apple juice and after the fructose control beverage. The mean increase in uric acid at 30 min was 15 μmol/L (95% CI: 10, 21 μmol/L) for the fructose control and 19 μmol/L (95% CI: 8, 30 μmol/L) and 17 μmol/L (95% CI: 9, 24 μmol/L) for the large servings of apple and apple juice, respectively. There was a decrease in uric acid concentration of 6 μmol/L (95% CI: 0.4, 13.0 μmol/L) after the ingestion of the glucose beverage. Differences in change in uric acid concentration between the large servings of apples and juice (26.7 g fructose) and the glucose and fructose control treatments (26.7 g of the respective monosaccharide) over time are shown in **Table 2**. The largest differences occurred between the test treatments and the glucose control over the first 30-min period. There was no difference in change in uric acid concentration over either time period between the test treatments and the fructose control beverage. **Figure 2**A shows change over time after treatments.

Comparisons of change in uric acid between the large and small servings of test foods are shown in **Table 3**. Uric acid concentrations increased to a greater extent after the ingestion of the large serving of apple than after the small serving (P = 0.013), but were no different between the large and small apple juice beverages (P = 0.112). There was little change in relative terms in uric acid concentration between 30 and 60 min.

As depicted in Figure 2B, blood glucose increased significantly at the 30 min time point after the ingestion of all treatments. The greatest increase from baseline was 3.7 mmol/L (95% CI: 3.2, 4.2 mmol/L) after the glucose treatment (26.7 g glucose) and the smallest increase was 0.3 mmol/L (0.05, 0.6 mmol/L) after fructose ingestion (0 g glucose). Compared with the small serving, the large apple serving resulted in a greater increase in blood glucose at 30 min (0.6 mmol/L; 95% CI: 0.1, 1.0 mmol/L; P = 0.007). Comparison of the change in blood glucose between the small and large servings of apple juice at 30 min (0.6 mmol/L; 95% CI: −0.01, 1.2 mmol/L) did not show a significant difference (P = 0.054).

There was no significant difference in diastolic or systolic blood pressure between baseline and at 70 min after the ingestion of the test foods. Similarly, there was no difference in change in blood pressure over the same time period when comparing apple or juice with either of the control foods (glucose or fructose beverages).

Satiety data have been expressed comparing feelings of hunger, fullness, satisfaction, and how much people can eat. The data given in **Table 4** represent subjective visual analog scale scores over the first 30 min and indicate greater satiety after the ingestion of whole apple compared with apple juice. There were no significant differences in change in scores between 30 and 60 min for any of the comparisons (data not shown). There was no difference in change in satiety scores between the fructose and glucose control beverages, with mean (95% CI) differences from baseline to 30 min for hunger, satisfaction, fullness, and how much a person can eat of 6 (−6, 18), −13 (−24, 20), 9 (−3, 22), and −3 (−12, 5) mm, respectively.

DISCUSSION

The primary finding of this study is that plasma uric acid concentrations increased after fructose ingestion, regardless of whether the sugar was contained in apples, apple juice, or as a solution of the monosaccharide itself. The increase in uric acid concentration was dependent on the amount of fructose in the food, with twice the amount of food practically doubling the uric acid response. Postprandial increases in uric acid concentration were previously shown with the consumption of 5 apples (14), but, to our knowledge, our findings are novel in the use of

TABLE 3
Uric acid response to a large serving of apples and apple juice compared to a small serving[1]

Mean ± SD baseline uric acid concentration, μmol/L					Difference in change (95% CI) in uric acid concentration between serving sizes,[2] μmol/L			
Test food (large)	Baseline	Test food (small)	Baseline	*n*	Baseline to 30 min	*P*	30–60 min	*P*
Apple (410 g)	279 ± 67	Apple (205 g)	276 ± 75	19	13 (−12, 38)	0.314	−7 (−32, 19)	0.600
Apple juice (340 mL)	265 ± 57	Apple juice (170 mL)	268 ± 46	17	7 (−10, 24)	0.451	2 (−15, 19)	0.855

[1]Comparisons are for participants with complete data (baseline and 30 and 60 min); the inclusion of participants with missing data did not substantially change the results. The large serving of apple and apple juice contained 26.7 g fructose; the small servings contained 13.35 g fructose.
[2]Mixed-effects regression with a time and treatment interaction and with participant as a random effect, adjusted for treatment order.

realistic amounts of fruit and fruit juice containing relatively small amounts of fructose. The findings of this study are consistent with our previous work in sugar-sweetened beverages containing 16 g fructose in which a uric acid response was found (17). However, our findings differ from those of Lecoultre et al. (18), who concluded that uric acid is only produced when fructose intakes are abnormally high after observing no change in plasma uric acid to repeated hourly doses of fructose (equivalent to 12 g fructose/h). The reason for this difference may be the timing of the blood sampling relative to fructose ingestion. In our experiment, an increase in uric acid concentration occurred within the first 30 min after fructose ingestion, and in another trial, serum urate had peaked by 60 min and declined thereafter (19). Lecoultre et al. took blood samples at 2-h intervals, perhaps missing an initial increase. Another explanation may be that our participants were required to ingest test foods and beverages within 10 min, whereas the time taken for ingestion by the participants in the study by Lecoultre et al. (18) was unstated. Sipping beverages over an extended period may enable the timely metabolism of fructose without the production of uric acid. In a practical sense, our specified protocol of eating within a period of 10 min was a realistic time frame for people to ingest the fruit and fruit drinks.

In longer-term research, chronic increases in uric acid have been found after overweight and obese adults drank 1 L of a sugar-sweetened beverage containing ~50 g fructose daily for 6 mo (20). Other metabolic changes, including increased liver fat, fasting triglycerides, and insulin, have been attributed to fructose (21). Sugar-sweetened beverage intake has also been associated with increased risk of insulin resistance in adolescents, again mediated through a proposed link between fructose intake and uric acid production (22). Evidence of this type suggests that fructose from added sugars that results in hepatic production of uric acid is metabolically detrimental (23). Although our data indicate that fructose intake increases uric acid concentrations regardless of the food source, it has been argued that fructose contained in whole fruit is not harmful because fruit contains nutrients such as vitamin C that may inhibit any adverse effects due to fructose (5). In support of this contention, fruit consumption was found to be inversely associated with the risk of cardiovascular disease (24). The cardiovascular benefit of fruit is possibly mediated through lower adiposity or the provision of antioxidant activity provided by vitamins, polyphenols, flavonoids, and uric acid (24, 25). The postprandial appearance of uric acid after fruit intake has been found to increase the antioxidant load in blood (14), potentially offering health benefits (26, 27).

As a component of the diet, fruit intake has been found not to correlate with fasting serum uric acid concentration (28). Consistent with the observational data, a diet rich in fruit and vegetables consumed for 30 d has been associated with lower serum uric acid concentrations compared with a control diet (29). Indeed, a high intake of fruit and vegetables, as characterized by the Dietary Approaches to Stop Hypertension (DASH) diet, is associated with a lower risk of incident gout (30). One explanation is that uric acid is cleared from the circulation more effectively by the consumption of a fruit- and vegetable-rich diet via the alkalization of urine (31). By this mechanism, fruit could produce a transient postprandial increase in uric acid while, over the longer term, predisposing to lower circulating uric acid concentrations. A high fruit and soybean diet has been used as a treatment for asymptomatic hyperuricemic adults over 3 mo, resulting in the lowering of fasting uric acid concentrations (32).

TABLE 4
Acute changes in visual analog scale ratings from baseline to 30 min[1]

	Small serving (205 g apple, 170 mL juice), mm				Large serving (410 g apple, 340 mL juice), mm			
Question	Apple[2] (*n* = 19)	Juice[2] (*n* = 20)	Mean difference (95% CI) (apple vs. juice) (*n* = 39)	*P*	Apple[2] (*n* = 19)	Juice[2] (*n* = 18)	Mean difference (95% CI) (apple vs. juice) (*n* = 37)	*P*
How hungry do you feel?[3]	−18 ± 38	4 ± 25	−13 (−30, 3)	0.112	−18 ± 38	8 ± 23	−16 (−33, 1)	0.072
How satisfied do you feel?[4]	26 ± 31	3 ± 14	16 (2, 29)	0.028	26 ± 31	2 ± 14	17 (3, 32)	0.021
How full do you feel?[4]	32 ± 33	2 ± 16	25 (10, 39)	0.001	32 ± 33	0 ± 16	28 (13, 42)	<0.001
How much do you think you can eat?[3]	−14 ± 33	6 ± 8	−18 (−30, −5)	0.007	−14 ± 33	6 ± 8	−19 (−32, −6)	0.007

[1]The visual analog scale is a 100-mm line on which a participant indicates his or her subjective feeling in units of millimeters.
[2]Mean ± SD.
[3]A negative value indicates feeling less hungry and wanting to eat less.
[4]A positive value indicates feeling more satisfied and full.

It has been suggested that a high fructose intake is associated with high blood pressure (33). Indeed, an increase in blood pressure over a period of weeks has been attributed to chronically induced hyperuricemia (34). Observationally, sugar-sweetened beverage intake has been positively associated with blood pressure (35), whereas an inverse association has been found with fruit intake (36). In a very-high-fruit-diet intervention, the inclusion of 20 portions fruit/d into individuals' diets was associated with a reduction in systolic blood pressure (37). Thus, relations found between fructose, uric acid, and blood pressure are variable. Under our acute study conditions, the ingestion of fructose-containing food and beverages at the servings provided had no significant effect on blood pressure.

In a review of fructose and appetite, evidence was put forward that high-fructose diets increase appetite via a number of peripheral and hypothalamic signaling peptides (38). In our study, postprandial responses to satiety questions did not differ between glucose and fructose beverages, possibly reflecting the relatively small amount of sugars or the subjective nature of measuring satiety. Nevertheless, the questions were sufficiently sensitive to detect greater satiety between apples in their whole form and juice, consistent with previous research (39).

In summary, the satiating effect of whole apples was greater than that of the various beverages, the glycemic response reflected the amount of glucose in the test foods and beverages, blood pressure was unaffected by any of the treatments 70 min after ingestion, and the uric acid response was independent of the source of fructose. A limitation of this work is that 3 groups were used for comparisons between the test foods rather than a full crossover design. This was done because of financial and logistical constraints, but the fact that the uric acid responses were similar among the groups with the same amount of fructose strengthens generalizability. This work was carried out in healthy young adults, and it is unknown if persons with gout or compromised kidney function would respond in the same way. A further limitation is that we are unable to state if small and transient increases in plasma uric acid contribute to chronic hyperuricemia and disease risk, which would increase the translation of our findings into practice. These data indicate that uric acid increases in the circulation with small intakes of fructose regardless of source. Longer-term studies are required to assess how small and transient increases in plasma uric acid affect health.

The authors' responsibilities were as follows—BJV: conceived the study; BJV, SJW, ELC, and ANR: designed the study and collected the data; SJW, ELC, and ANR: analyzed blood samples; JJH: performed statistical analysis; and all authors: contributed to writing and editing the manuscript, and read and approved the final manuscript. None of the authors had a financial or personal conflict of interest to declare.

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