Effect of cinnamon and turmeric on urinary oxalate excretion, plasma lipids, and plasma glucose in healthy subjects¹–³

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ABSTRACT

Background: High oxalate intake resulting from consuming supplemental doses of cinnamon and turmeric may increase risk of hyperoxaluria, a significant risk factor for urolithiasis.

Objective: This study assessed urinary oxalate excretion from supplemental doses of cinnamon and turmeric as well as changes in fasting plasma glucose, cholesterol, and triacylglycerol concentrations.

Design: Eleven healthy subjects, aged 21–38 y, participated in an 8-wk, randomly assigned, crossover study that involved the ingestion of supplemental doses of cinnamon and turmeric for 4-wk periods that provided 55 mg oxalate/d. Oxalate load tests, which entailed the ingestion of a 63-mg dose of oxalate from the test spices, were performed after each 4-wk experimental period and at the study onset with water only (control treatment). Fasting plasma glucose and lipid concentrations were also assessed at these time points.

Results: Compared with the cinnamon and control treatments, turmeric ingestion led to a significantly higher urinary oxalate excretion during the oxalate load tests. There were no significant changes in fasting plasma glucose or lipids in conjunction with the 4-wk periods of either cinnamon or turmeric supplementation.

Conclusions: The percentage of oxalate that was water soluble differed markedly between cinnamon (6%) and turmeric (91%), which appeared to be the primary cause of the greater urinary oxalate excretion/oxalate absorption from turmeric. The consumption of supplemental doses of turmeric, but not cinnamon, can significantly increase urinary oxalate levels, thereby increasing risk of kidney stone formation in susceptible individuals. Am J Clin Nutr 2008;87:1262–7.

INTRODUCTION

About 75% of all kidney stones are composed primarily of calcium oxalate (1), and hyperoxaluria is a primary risk factor for this disorder (2). Urinary oxalate, derived from a combination of exogenous and endogenously synthesized oxalate, is a primary determinant of the level of calcium oxalate saturation (3). Although it had been accepted that dietary oxalate contributes no more than 10% to 20% of the oxalate excreted in the urine under normal conditions (1, 4), recent work (5, 6) suggests that even in the absence of gastrointestinal disorders, intestinal absorption of dietary oxalate can make a more significant contribution to urinary oxalate. Thus, high oxalate intake may increase risk of hyperoxaluria, a significant risk factor for urolithiasis.

Oxalate is a common component in food, including nuts, fruits, vegetables, grains, and legumes, and is a salt or ester of oxalic acid: (COO)₂H₂ (4). In food, oxalic acid is typically found in its salt form, primarily as either sodium or potassium oxalate, which are water soluble, or calcium oxalate, which is insoluble. The propensity of a specific food to raise urinary oxalate is dependent both on oxalate content and efficiency of absorption because it is well established that little oxalate catabolism occurs after absorption and >90% of absorbed oxalate can be recovered in the urine within 24 to 36 h (7).

Oxalate absorption in the small intestine occurs via active transport, and there is passive absorption along the gastrointestinal tract (8). Oxalate solubility within the small intestine appears to be a critical factor as evidenced by the propensity of concomitant calcium ingestion to reduce oxalate absorption (5, 9), presumably by chelating with oxalic acid in the small intestine. An unanswered question is whether the solubility of oxalate in a specific food source is an important predictor of efficiency of oxalate absorption. The assertion that the amount of soluble oxalate in food is a major determinant of oxalate absorption is supported by some (10, 11) but not all studies (12).

Spices such as cinnamon and turmeric are currently being consumed in supplemental doses because of their purported health benefits (13, 14), which include improvements in glycemic (15, 16) and lipid profiles (15, 17, 18). However, no studies to date have reported the oxalate content and oxalate solubility of these spices or assessed the efficiency of oxalate absorption. Because previous unpublished work in our laboratory suggested that cinnamon and turmeric are high-oxalate spices, their supplementation could have a significant influence on total oxalate absorption and urinary excretion, an important consideration for individuals predisposed to the formation of calcium oxalate-containing kidney stones. Thus, the primary objectives of this study were to quantify the total and soluble oxalate content of cinnamon and turmeric and to assess and compare the change in urinary oxalate excretion from these 2 spices. A secondary objective was to assess fasting plasma glucose, cholesterol, and triacylglycerol responses to 4-wk periods of cinnamon and turmeric supplementation in a healthy, nonobese population.

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Received August 21, 2007.
Accepted for publication December 13, 2007.
SUBJECTS AND METHODS

Subjects

The study protocol was approved by the University of Wyoming Institutional Review Board. Twelve healthy non–stone formers (7 women and 5 men) were recruited from the university community. Subjects were recruited without regard to sex because previous work had suggested no significant sex difference in oxalate absorption from food sources (9). Written informed consent was obtained from all participants. One participant (man) dropped out of the study following the control test day for personal reasons. Thus, all statistical analyses were based on an n value of 11. Overall, subjects were judged to be healthy based on a preexperimental screening questionnaire that assessed their general health status. There were no reports of any intestinal or renal problems that could have modified oxalate absorption or excretion.

Study design

The study was a randomly assigned, crossover design with 6 subjects starting on the cinnamon treatment and the remaining 5 subjects starting on turmeric, each treatment of 4-wk duration. Subjects were asked to maintain their normal dietary and exercise patterns throughout the entire 8-wk experimental period with the exception of consuming supplemental doses of cinnamon and turmeric.

Subjects were given a supplemental dose of 3.0 g (6 capsules) cinnamon or 2.8 g (7 capsules) turmeric (Puritan’s Pride, Oakland, NY) for 4 wk. This provided ≈55 mg of oxalate per day. The selected number of capsules approximated the doses used by previous studies that assessed blood lipid or glucose responses to cinnamon supplements (15, 16, 19). Subjects were directed to take 2 capsules with breakfast, 2 with lunch, and the remaining capsules with dinner. Subjects were given a 2-wk supply of the assigned spice and asked to return any unconsumed capsules to the researchers.

Oxalate load tests were performed and blood samples were obtained at baseline, at 4 wk, and at 8 wk. The initial oxalate load test entailed the ingestion of water only (control treatment). The latter oxalate load tests were administered to coincide with the completion of the 4-wk, randomly assigned cinnamon and turmeric treatments. The amount of cinnamon and turmeric used in the oxalate load tests was adjusted to provide an ≈63-mg dose of oxalate, which was either 7 capsules (3.5 g) of cinnamon or 8 capsules (3.2 g) of turmeric.

Subjects were provided with detailed lists of oxalate-rich foods and were instructed to avoid these foods starting the day before the oxalate load tests and for 24 h post–oxalate ingestion. Subjects fasted overnight for a minimum of 12 h before each data-collection day. Subjects were also given 360 mL of bottled water to drink on the test days after their first urine voiding in the morning to ensure adequate urine production. They were instructed to arrive at the lab within 2 h after their first urine voiding at which time fasting blood samples were drawn into evacuated tubes containing EDTA. Samples were centrifuged at 2500 × g for 10 min and plasma samples were frozen at −25 °C for subsequent analyses. At the 2-h time point, subjects emptied their bladders and the urine samples were collected. These initial urine samples were designated as the baseline (B-2) urine samples.

Right after the initial 2-h urine collection period, subjects ingested water (for the control oxalate load test) or the appropriate oxalate-containing spice in capsule form at the 4- and 8-wk time points. Each hour for 6 h post–oxalate ingestion, 150–200 mL of distilled, deionized water was consumed to ensure adequate urine production. Urine samples were collected at 2-h intervals for 6 h, after which subjects were allowed to leave the laboratory but continued to collect all urine samples to complete a 24-h urine collection period. These urine samples were designated S-2, S-4, S-6, and S-22 to correspond to the urine collection timing in hours post–oxalate/water ingestion. Forty-five minutes after the ingestion of cinnamon or turmeric capsules or water (control treatment), a standardized low-oxalate, low-calcium meal was provided as subjects were allowed to choose from sausage, scrambled eggs, a cold rice cereal with rice milk, apple, grapes, and apple juice. Ten minutes after their third (S-4) urine samples, subjects were given a low-oxalate snack that included rice cakes, cheese, yogurt, apple, and grapes. Subjects kept a detailed food record on the test day and were required to consume the same type and amounts of food for the provided meal and snack on all 3 test days to minimize any potential confounding effects.

Diet records were started the day before the oxalate load tests and continued through 24 h post–oxalate ingestion. Diet records were reviewed for compliance to the low-oxalate diet and adherence to the overall experimental protocol. Subjects were given a written questionnaire on the last oxalate load test day to assess whether there were any feelings of discomfort or gastrointestinal symptoms in relation to taking the capsules either on a test day or at any time during the 8-wk study.

Sample analyses

All urine volumes were recorded, samples were acidified with HCl to a pH < 2.0, and aliquots frozen for subsequent analysis. Urine oxalate, as well as oxalate in cinnamon, turmeric, and the foods provided for the breakfast and snack, was analyzed with use of an oxalate kit purchased from Trinity Biotech (Berkeley Heights, NJ). This method is based on the oxidation of oxalate by oxalate oxidase followed by measurement of hydrogen peroxide by a peroxidase-catalyzed reaction. Urinary creatinine was analyzed with use of the picric acid method (20). Urinary oxalate was expressed in absolute values (mg) and relative to creatinine excretion (mg oxalate/g creatinine). Total oxalate and soluble oxalate from cinnamon and turmeric were extracted according to the method described by Ross et al (21), which involved extracting weighed amounts in a shaking water bath at 80 °C for 30 min followed by centrifugation (10 min at 3000 × g) and filtration. The spics were extracted in 2 mol/L H3PO4 for total oxalate and in distilled, deionized water for soluble oxalate. Plasma glucose, total cholesterol, and triacylglycerol concentrations were analyzed in duplicate with use of a portable Micro-Stat Multi-Assay Analyzer (Analox Instruments, Lunenburg, MA). The calcium content of cinnamon and turmeric as well as the foods provided for the breakfast and snack were obtained from the US Department of Agriculture food composition database (22).

An estimation of net oxalate excretion is required to approximate oxalate absorption. Net oxalate excretion represents the difference between total urinary oxalate and that portion of total urinary oxalate that can be attributed to endogenous oxalate synthesis. The B-2 urinary oxalate excretion on the test days can be considered an approximation of endogenous oxalate.
endogenous oxalate excretion was assumed to be constant throughout the day. The 6- and 22-h endogenous oxalate was computed by multiplying the B-2 urinary oxalate by 3 and 11 for 6 and 22 h, respectively. The original intent was to use the B-2 from each treatment to compute net oxalate over 6- and 22-h postoxalate time periods. However, the mean CV across all subjects for B-2 urinary oxalate on the 3 test days was high (17.6%). Thus, a more accurate estimate of 2-h endogenous oxalate could be obtained through the use of the average B-2 across the 3 treatments for each subject. The average B-2 urinary oxalate was used to approximate each subject’s 6- and 22-h endogenous oxalate excretion, which in turn was used to compute net oxalate excretion (ie, net oxalate = total oxalate – endogenous oxalate). Finally, net oxalate was used to approximate oxalate absorption (ie, percentage absorbed = net oxalate/63 mg, with 63 mg representing the amount of oxalate provided by cinnamon and turmeric on the test days).

Statistical analysis

The initial statistical analysis made use of a crossover experimental design to test the hypothesis that the cinnamon/turmeric treatment order did not influence the results. When no treatment order effect was detected, subsequent statistical analyses tested for treatment effects without regard to treatment order. Treatment differences in oxalate load urinary volume, oxalate, creatinine, and ratio of oxalate to creatinine were tested with use of a repeated-measures analysis of variance in which both treatment and time (with time representing the different time periods of urine collection during the oxalate load tests) were entered into the model. When a significant treatment effect, but no significant treatment-by-time interaction, was observed, the interpretation was that the treatment effect was essentially consistent over the different time periods of urine collection during the oxalate load tests. In this case, differences were not presented across treatments at specific time points. In instances for which both significant treatment and treatment-by-time interactions were observed, treatment differences at specific time points were determined with use of the Tukey post hoc test. Treatment differences in plasma glucose, cholesterol, and triacylglycerols were tested with use of a repeated-measures analysis of variance. Statistical calculations were based on the general linear model procedure of SAS (version 8.1, SAS Institute Inc, Cary, NC). Values of P < 0.05 were considered to designate statistical significance. Data are reported as means ± SD.

RESULTS

Eleven subjects (7 women, 4 men) completed the study. The mean participant age was 27 ± 6 y (range: 21–38 y) and the mean BMI was 24.7 ± 2.5 kg/m² (range: 21.0–28.2 kg/m²). Overall compliance with taking the cinnamon and turmeric supplements was judged to be excellent on the basis of the return of empty vials that had contained the daily allotment of capsules. Two subjects missed taking 9 capsules during the 8-wk supplementation period, and 1 subject missed 5 complete days during the turmeric supplementation period because of illness. The return of empty vials suggested that the remaining subjects consumed all the provided supplements.

Four subjects reported experiencing eructation in association with taking cinnamon either on the oxalate load test day or during the 4 wk of daily ingestion. One subject reported experiencing a headache in association with taking cinnamon on the test day. Another subject reported an occasional burning stomach during the 4 wk of cinnamon consumption. There were no other reported symptoms with either cinnamon or turmeric consumption.

Total and soluble oxalate content of cinnamon and turmeric

The total oxalate content of cinnamon and turmeric, analyzed in duplicate on 4 occasions, was 1789 ± 54 and 1969 ± 56 mg/100 g, respectively. The percentage of oxalate that was water soluble differed markedly between cinnamon (107 ± 8 mg/100 g, 6% of total) and turmeric (1788 ± 1 mg/100 g, 91% of total).

Oxalate and calcium content of the provided breakfast and snack

An attempt was made to provide similar breakfasts and snacks for each subject for the 3 treatments to minimize the potentially confounding effect of differing nutrient intakes, especially oxalate and calcium. The breakfast was designed to be low in both oxalate and calcium. Computed oxalate intakes (± SD) for this meal were 8.3 ± 4.1, 6.4 ± 3.8, and 6.8 ± 5.0 mg for the control, cinnamon, and turmeric treatments, respectively; the corresponding calcium intakes from breakfast for the same order of treatments were 77 ± 25, 67 ± 21, and 60 ± 29 mg. Mean oxalate intakes from the snack ranged from 21.2 to 22.8 mg for the 3 treatments. Because the snack was provided >4 h after the oxalate loads were ingested, calcium consumed at this time would not be expected to interfere with oxalate absorption from the oxalate loads. Thus, these calcium intakes were not strictly controlled with mean intakes for the 3 treatments ranging from 380 to 420 mg.

Oxalate absorption from cinnamon and turmeric

Baseline as well as postoxalate load urine volumes and oxalate and creatinine levels are presented in Table 1. There were no significant treatment differences for either urine volumes or creatinine levels. The statistical analysis indicated a significant main effect of treatment but no significant treatment-by-time interaction for postload urinary oxalate levels. The Tukey separation test of treatment means, averaged over the 5 separate time points, indicated a significantly higher mean urinary oxalate for the turmeric compared with the control treatment, whereas the control and cinnamon treatments were not significantly different. The total 6- and 22-h urinary oxalate parameters represent the total oxalate excretion accumulated after B-2 for 6 and 22 h. The significantly higher urinary oxalate for turmeric, compared with both the control and cinnamon treatments, for the total 6-h parameter appeared to largely account for the similar finding for the total 22 h parameter. There were no significant differences between the cinnamon and control treatments for either total 6-h or total 22-h urinary oxalate levels.

Baseline as well as postoxalate load urine ratios of oxalate to creatinine are presented in Table 2. The statistical analysis indicated a significant treatment effect as well as a significant treatment-by-time interaction. There were no significant treatment differences for B-2 and S-22. The ratio of oxalate to creatinine for the turmeric treatment was significantly higher than the corresponding ratios for the control and cinnamon treatments for S-2, S-4, and S-6.
An estimation of net oxalate, the difference between total urinary oxalate and that portion of total urinary oxalate that can be attributed to endogenous oxalate synthesis, is required to approximate oxalate absorption. The computed estimate of endogenous oxalate excretion was used to compute net oxalate excretion (ie, net oxalate = total oxalate – endogenous oxalate), which in turn was used to approximate oxalate absorption (ie, percentage absorbed = net oxalate/63 mg, with 63 mg representing the amount of oxalate provided by cinnamon and turmeric on the test days). The estimates of net oxalate excretion and absorption were significantly higher for the turmeric compared with the cinnamon treatment for both the 6- and 22-h time periods (Table 3).

### Fasting glucose and lipids

Fasting plasma glucose, total cholesterol, and triacylglycerols for the control, cinnamon, and turmeric treatments are summarized in Table 4. At the initial (control) time point, all subjects had normal fasting blood glucose (<100 mg/dL) and total cholesterol (<200 mg/dL) concentrations. Four subjects had elevated fasting triacylglycerol concentrations (>150 mg/dL).

### DISCUSSION

Supplemental doses of cinnamon and turmeric have been shown to be beneficial in decreasing blood lipids in patients with hyperlipidemia and in improving glycemic control in diabetic patients (15–17). Because these supplements are widely available, their very high oxalate content should be taken into consideration. The primary purpose of the current study was to determine whether ingestion of high doses could increase the risk of kidney stone formation in susceptible individuals. The cinnamon and turmeric supplements used in this study had oxalate contents of 1798 and 1969 mg/100 g, respectively. It has been recommended that kidney stone patients limit dietary oxalate intake to no more than 50 mg of oxalate per day (23), a level which would likely be exceeded with cinnamon or turmeric supplementation. For example, cinnamon supplementation at a level of 3 g/d would provide an additional 51 mg of oxalate.

The amount of urinary oxalate is dependent on both the oxalate content of the diet and oxalate bioavailability. Oxalate absorption rates from different foods have been estimated to range from 2% to 15% (24, 25). Oxalate absorption appears to depend on a number of factors, including absorptive properties of the intestine, gut transit time, presence of divalent cations such as calcium, and gut transit time, presence of divalent cations such as calcium.
and magnesium that can bind oxalate within the gastrointestinal tract, and presence of oxalate-degrading bacteria (26, 27). There is a lack of consensus as to whether oxalate absorption is dependent on the amount of soluble compared with insoluble oxalate in food (27, 28). Our data support the contention that the relative amount of soluble and insoluble oxalate plays a role in determining efficiency of oxalate absorption. There was a significantly higher computed 6-h oxalate absorption rate from turmeric ingestion (8.2%) than from cinnamon ingestion (2.6%), which was most likely explained by the 91% soluble oxalate content of turmeric compared with 6% for cinnamon. This difference in oxalate solubility could likely be attributed to the higher calcium content of cinnamon than turmeric (1002 compared with 183 mg/100 g), which resulted in computed calcium/oxalate molar ratios of 1.3 and 0.2 for cinnamon and turmeric, respectively. A previous study by Chai and Lieberman (11) also suggested that the relative amount of soluble and insoluble oxalate in food has an important role in the determination of oxalate absorption. Oxalate absorption from almonds (5.9%) was significantly higher than that from black beans (1.8%). Soluble oxalate accounted for ≈31% of total oxalate from almonds whereas black beans had a soluble content of 5%.

There was no significant change from baseline in urine oxalate excretion after cinnamon consumption, possibly because of the low soluble oxalate content (6%). For those predisposed to kidney stones, cinnamon can be considered a low-oxalate food in terms of absorption, and its ingestion would not be expected to increase risk for kidney stone formation.

Hyperoxaluria has been defined as urine oxalate excretion that exceeds 40 mg/24 h (26). Twenty-four-hour oxalate excretion increased from 19.9 mg (control treatment) to 24.9 mg (turmeric treatment). Thus, even with the computed 6-h oxalate absorption rate of 8.2% from turmeric, total 24-h oxalate excretion remained well below the cutoff that designates increased risk. There is some evidence that kidney stone formers have an increased rate of endogenous oxalate synthesis (29) and may absorb a higher percentage of dietary oxalate (30). Most kidney stone formers are also likely to have higher oxalate intakes than those imposed in the present study on test days. For these reasons, the ingestion of supplemental doses of turmeric by some stone formers may raise 24-h urinary oxalate levels close to or above the 40 mg threshold.

All subjects maintained a low-oxalate diet starting the day before a data collection day by avoiding a detailed list of oxalate-containing foods during this period. This allowed the supplemental doses of either cinnamon or turmeric given on an oxalate load day to be the major source of exogenous oxalate. It also allowed an approximation of the subjects’ endogenous 2-h baseline oxalate excretion. Although it was assumed that endogenous oxalate synthesis occurred at a constant rate throughout the 22-h postoxalate load periods, there is the possibility that a component of the cinnamon or turmeric supplement could have altered endogenous oxalate synthesis. Another study limitation relates to the possible effect of chronic oxalate feeding on adaptation by colonic oxalate-degrading bacteria, a phenomenon that has been well established (31). However, this factor was thought to be of only minor significance because the 4-wk cinnamon and turmeric supplementation periods added only an additional 55 mg of oxalate to the subjects’ normal daily diets. Providing the test oxalate loads (63 mg) as a single dose rather than having the cinnamon and turmeric supplements spread throughout the day, as was done during the 4-wk experimental periods, could have altered the efficiency of oxalate absorption. Previous work documented a marked decrease in absorptive efficiency as dietary oxalate was increased from very low levels up to ≈50 mg (6). All of these considerations highlight the inherent assumptions that should be acknowledged with respect to the presently reported estimates of oxalate absorption.

The finding that the increase in urinary oxalate occurred primarily during the initial 6 h after oxalate ingestion is in agreement with previous studies (5, 11) and suggested only a small colonic contribution to overall oxalate absorption. After 6 h of consumption, there was a similar oxalate excretion for the 3 treatments.

The ratio of oxalate to creatinine was also computed to compare the 3 treatments. Expressing urinary oxalate relative to creatinine helps normalize the data for irregularities in urine flow and for any urine which was inadvertently not collected. Thus, the ratio of oxalate to creatinine can be more accurate than the absolute amount of oxalate, especially when a subject fails to collect all the 24-h urine. Only turmeric ingestion led to a marked increase in the ratio of oxalate to creatinine for the S-2, S-4, and S-6 samples, thus further supporting the finding of a significantly higher oxalate absorption from turmeric than from cinnamon.

The secondary objective of the study was to determine whether 4 wk of supplementation with cinnamon or turmeric would affect fasting glucose and lipid concentrations. Previous studies (15, 16) have found that supplementation with 1 to 6 g cinnamon/d for 40 to ~120 d modestly improved both blood glucose and lipids in individuals with type 2 diabetes, although this finding has not been universally reported (19). A recent study (32) in nondiabetic subjects also found that 6 g of cinnamon added to rice pudding significantly reduced the postprandial blood glucose response. Supplementation with turmeric has also been shown (17, 18) to improve the lipid profile in experimental animals with hyperlipidemia. Our findings extend previous research and show that supplementation with ~3 g of cinnamon or turmeric does not alter blood glucose or plasma lipid concentrations in healthy, young nondiabetic men and women. Whereas it is not surprising that the hypolipidemic benefit of these spices is experienced only in those with elevated lipid levels, it is important to note that hypoglycemia is not a potential side effect of supplementation in healthy subjects who may supplement with these spices to gain other health benefits (13, 14).

In summary, the estimated 6-h oxalate absorption from turmeric (8.2%) was significantly higher than the corresponding value for cinnamon (2.6%). The difference in soluble oxalate content appeared to be the primary cause of the significantly greater urinary oxalate excretion/oxalate absorption from turmeric. Neither cinnamon nor turmeric supplementation affected fasting blood glucose or lipid concentrations.
We thank Kentz Willis for his help with the plasma glucose and plasma lipid analyses. We also thank all the volunteers who participated in the study. The authors’ contributions were as follows—MT and ML: design; MT, ML and DEL: data collection, analysis, and article preparation; ML: principal investigator. None of the authors had any financial or personal conflicts of interest.

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