An increase in renal dopamine does not stimulate natriuresis after fava bean ingestion1–3

Emily M Garland, Tericka S Cesar, Suzanna Lonce, Marcus C Ferguson, and David Robertson

ABSTRACT

Background: Fava beans (Vicia faba) contain dihydroxyphenylalanine (dopa), and their ingestion may increase dopamine stores. Renal dopamine regulates blood pressure and blood volume via a natriuretic effect.

Objective: The objective was to determine the relation between dietary fava beans, plasma and urinary catechols, and urinary sodium excretion in 13 healthy volunteers.

Design: Catechol and sodium data were compared by using a longitudinal design in which all participants consumed a fixed-sodium study diet on day 1 and the fixed-sodium diet plus fava beans on day 2. Blood was sampled at 1, 2, 4, and 6 h after a meal, and 3 consecutive 4-h urine samples were collected.

Results: Mean (±SD) plasma dopa was significantly greater 1 h after fava bean consumption (11.670 ± 5440 compared with 1705 ± 530 pg/mL; \( P = 0.001 \)) and remained elevated at 6 h. Plasma dopa increased nearly 15-fold during this period. Fava bean consumption also increased urinary dopamine excretion to 306 ± 116, 360 ± 235, and 159 ± 111 \( \mu \)g/4-h urine sample compared with 45 ± 21, 54 ± 29, and 44 ± 17 \( \mu \)g in the 3 consecutive 4-h samples after the control diet (\( P \leq 0.005 \)). These substantial increases in plasma and urinary dopa and dopamine were unexpectedly associated with decreased urinary sodium.

Conclusion: The failure of fava bean consumption to provoke natriuresis may indicate that dopa concentrations in commercially available beans do not raise renal dopamine sufficiently to stimulate sodium excretion, at least when beans are added to a moderate-sodium diet in healthy volunteers. This trial was registered at clinicaltrials.gov as NCT01064739.

INTRODUCTION

Fava beans are a broad bean and have potential clinical relevance in patients with Parkinson disease because they contain high concentrations of the dopamine precursor dihydroxyphenylalanine (dopa) (1–3) and have the potential to increase the striatal dopamine content. Fava beans have, in fact, been used as complementary medicine by patients with Parkinson disease (4, 5). Ingestion increases plasma dopa concentrations and improves motor skills in patients with Parkinson disease, similar to L-dopa administration (3, 5–7).

In addition to the central nervous system functions of dopamine that are compromised in Parkinson disease, renal dopamine has vasodilatory and natriuretic activities (8). Infusion of low- or renal-dose dopamine raises plasma dopamine to ng/mL concentrations and enhances renal blood flow, the glomerular filtration rate, and natriuresis (9). On the other hand, renal dopamine is synthesized endogenously in the proximal tubule cells after uptake and decarboxylation of filtered dopa and reduces sodium reabsorption, mainly by the inhibition of Na+, K+-ATPase, and the Na+/H+ exchanger. Elevated urinary dopamine, however, does not consistently correlate with increased urinary sodium excretion (10–14), and there are conflicting opinions over the conditions under which renal dopamine might regulate sodium balance. To our knowledge, only one study has shown that consumption of fava seedlings stimulates sodium excretion in healthy participants, but plasma dopa concentrations in that study were far higher than in other studies with fava beans, and sodium excretion was stimulated to a much lesser extent than renal dopamine formation (15).

Studies with plant-based interventions infrequently occur in a well-controlled clinical setting. Historically, botanical studies lack clear controls for interventions and include incomplete information not only about the dosage of the product, but also about its mechanisms of action (16). By conducting this study using strict dietary control of sodium and a more traditional clinical trial approach, we avoided deficiencies common in other assessments of plant-based therapy that may confound results and limit validation.

The goal of our study was to clarify the natriuretic effect of fava beans obtained from a source that serves patients with Parkinson disease. In an earlier study (17), we found reduced mean upright blood pressure in 23 patients with Parkinson disease in sodium balance with 150 mEq Na/d at the Vanderbilt Clinical Research Center. The reduced blood pressure was associated with lower plasma renin activity, likely because of reduced sympathetic activation. Because the orthostatic hypotension experienced by many patients with Parkinson disease (18) could be exacerbated during diuresis and natriuresis, we also assessed orthostatic blood pressure changes after fava bean consumption. We proposed that dietary dopa ingested as fava

1 From the Autonomic Dysfunction Center (EMG, TSC, SL, MCF, and DR), the Division of Clinical Pharmacology (EMG, SL, MCF, and DR), and the Departments of Medicine (EMG, SL, MCF, and DR) and Pharmacology (DR), Vanderbilt University School of Medicine, Nashville, TN.

2 Supported in part by Vanderbilt Clinical and Translational Science Award grant UL1 RR024975 and grant R01 HL071784 to DR.

3 Address correspondence to EM Garland, Autonomic Dysfunction Center, AA3228 Medical Center North, Vanderbilt University, Nashville, TN 37232-2195. E-mail: emily.garland@vanderbilt.edu.

Received July 30, 2012. Accepted for publication February 13, 2013. First published online April 3, 2013; doi: 10.3945/ajcn.112.048470.
beans would increase plasma dopa, urinary dopamine, and urinary sodium in a healthy population (Figure 1).

SUBJECTS AND METHODS

Study subjects

The study was approved by the Vanderbilt University Institutional Review Board, and written informed consent was obtained from all participants. Procedures were in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 2008. This study was registered at clinicaltrials.gov as NCT01064739.

Thirteen individuals aged 34.4 ± 12.9 y (77% female; 11 whites, 2 blacks, and 2 Hispanics) from the Nashville, TN, area enrolled in the study between November 2009 and November 2010. They underwent a complete history and physical examination, including assessment of blood chemistry, a complete blood count, and an electrocardiogram. During screening, participants consumed a sample of the fava beans to ensure that the taste was tolerable and that the beans elicited no adverse reaction. Exclusion criteria included significant cardiovascular, pulmonary, hepatic, or hematologic disease based on history or screening results; pregnancy; hypertension defined as a blood pressure >145/95 mm Hg (off medications) or the need for antihypertensive medications; food allergies to favas; Parkinson disease; glucose-6-phosphate dehydrogenase deficiency based on a family or personal medical history; or a Mediterranean heritage.

Protocol

Participants underwent testing while on a methylxanthine-free diet providing 150 mEq Na/d and 75 mEq K/d. The study involved a longitudinal design in which the participants served as their own controls. Subjects consumed the standard fixed-sodium diet for ≥2 d before the study day and on study day 1 during an inpatient stay at the Vanderbilt Clinical Research Center. On study day 2, participants ate 100 g puréed fava beans and pods with the study diet at breakfast (0800) and lunch (1200). We purchased fresh fava beans in bulk from International Gourmet—a source of beans for patients with Parkinson disease and froze them in their pods at −40°C until needed. Beans and pods were prepared before breakfast by microwaving them for 2 min and then blending them in a food processor with 50 mL water and 15 g of a salt-free seasoning blend (Mrs. Dash; B&G Foods Inc). Aliquots of all samples were saved for catechol analysis.

We recorded single blood pressure and heart rate measurements with an automated oscillometric blood pressure device (Critikon Dinamap) (19) while participants were supine immediately before and hourly for 6 h after breakfast. We also collected standing data 2 and 6 h after breakfast. Blood was sampled for catechol assays before and 1, 2, 4, and 6 h after breakfast. Three consecutive 4-h urine samples were collected for electrolyte and catechol contents.

Catechol analysis

Catechols were measured with batch alumina extraction followed by separation and quantification by HPLC and electrochemical detection (20). Concentrations of sulfon conjugated catechols were assayed by the same method after incubation of the alumina supernatant fluid with sulfatase (100 mU/10 μL Sulfatase type VI; Sigma Aldrich) at 37°C for 30 min (21). For measurement of dopa in the fava beans, 1 g blended bean/pod mixture was extracted with 5 mL of 0.1 mol perchloric acid. The sample was homogenized and sonicated on ice. After centrifugation, the supernatant fluid was removed and saved. The precipitate was extracted with perchloric acid and centrifuged another 2 times. The precipitate was then extracted with 5 mL ethanol until no dopa could be detected in the supernatant fluid. All supernatant fluid was analyzed for dopa by HPLC, and the total dopa content of the bean/pod mix was calculated.

Statistical analysis

The primary outcome was urinary sodium excretion. Because most hormone and hemodynamic variables were not normally distributed, we used Wilcoxon’s matched-pairs signed-rank test for differences between data obtained with and without fava beans. This test was also used to assess the influence of posture, ie, the difference between supine values and those obtained after standing. We used the Friedman test to compare data collected at different times within the control or fava bean group. A general linear model analysis for repeated measures determined whether changes over time differed significantly between the control and fava bean interventions (treatment × time interaction). In the absence of a significant interaction, but when the main effect of treatment (diet) was significant, we included the results of Wilcoxon’s matched-pairs signed-rank tests. We evaluated the relation between dietary dopa and plasma and urinary catechol concentrations using linear regression. Statistical analyses were carried out by using the SPSS statistical software for Windows, version 17.0 (SPSS Inc). Reported P values are 2-tailed, and P < 0.05 was considered significant. The results are expressed as means ± SDs or with 95% CIs, as indicated. On the basis of an SD of 35 mEq for urinary sodium excretion in a group of 87 normal volunteers on our 150-mEq Na/d diet, a sample size of 13 subjects has a >90% power to detect a difference of 35 mEq with a paired design (22).

RESULTS

Fava bean dopa concentrations

The mean dopa content of the fava beans and pods was 59 (95% CI: 47, 70) mg for breakfast and 69 (95% CI: 56, 81) mg for lunch.

FIGURE 1. Proposed effect of fava bean ingestion on urinary sodium excretion. We proposed that dietary dopa ingested as fava beans would increase plasma dopa, urinary DA, and urinary sodium. DA, dopamine; dopa, dihydroxyphenylalanine.
No nausea or other adverse events occurred with fava bean consumption. The higher the dietary dopa content, the higher the plasma dopa concentration (Figure 2): 1 h after breakfast ($R^2 = 0.462, P = 0.011$) and 2 h after breakfast ($R^2 = 0.424, P = 0.011$). Furthermore, a higher fava bean dopa content was associated with greater urinary dopamine: for breakfast fava dopa content and 4–8 h postbreakfast urinary dopamine excretion in $\mu$g/4 h ($R^2 = 0.398, P = 0.021$) and for lunch dopa content and 8–12 h postbreakfast urinary dopamine excretion ($R^2 = 0.328, P = 0.041$).

**Plasma catechols**

The treatment $\times$ time interaction was significant ($P < 0.013$) for dopa, dopamine, and norepinephrine by repeated-measures ANOVA. Baseline plasma catechol concentrations were similar before breakfast on the 2 study days (Figure 3). Plasma dopa was significantly elevated 1 h after the fava bean breakfast when compared with the control diet ($11,670 \pm 5440$ compared with $1705 \pm 530$ pg/mL; $P = 0.001$) and remained higher for the next 5 h. Plasma dopamine increased nearly 15-fold during this period (at 1 h: $90 \pm 47$ compared with $6 \pm 3$ pg/mL; $P = 0.001$). Both plasma dopa and dopamine dipped before rising again after the fava bean lunch. Plasma norepinephrine increased with time after fava beans, peaking at $380 \pm 332$ compared with $159 \pm 89$ pg/mL ($P = 0.005$) 6 h after breakfast.

Plasma samples collected before the fava bean breakfast and 2 h after breakfast were assayed for sulfoconjugated catechols. Conjugated forms of norepinephrine and adrenaline changed little with fava bean consumption (norepinephrine sulfate control $497 \pm 141$ pg/mL compared with $449 \pm 134$ pg/mL after fava bean consumption; adrenaline sulfate control $18.2 \pm 5.2$ pg/mL compared with $54.3 \pm 22.8$ pg/mL after fava bean consumption). In contrast, dopamine sulfate increased substantially, by $200–750$-fold ($1784 \pm 685$ pg/mL after the control diet compared with $617,092 \pm 202,678$ pg/mL after the fava bean diet).

**Urinary catechols**

The treatment $\times$ time interaction was significant for urinary dopa ($P = 0.011$) and dopamine ($P = 0.013$) but not for norepinephrine ($P = 0.909$). Urinary excretion of dopa and dopamine after the control diet did not differ significantly between the three 4-h collection periods (Figure 4; $P = 0.641$ for dopa, $P = 0.905$ for dopamine, in a comparison of $\mu$g excreted/4 h during the 0–4-h, 4–8-h, and 8–12-h postbreakfast samples by the Friedman test). Fava bean consumption increased urinary dopa excretion during the first 2 periods of urine collection, compared with the urinary dopa excretion after the fixed-sodium diet without fava beans. Maximum dopa excretion occurred 4–8 h after breakfast ($21.2 \pm 8.7$ compared with $4.4 \pm 3.0$ $\mu$g/4 h; $P = 0.002$). Urinary dopamine concentrations similarly increased after fava bean consumption ($P = 0.005$ for each of 3 collections), reaching its peak with a 6.5-fold elevation during the 4–8-h collection ($360 \pm 235$ compared with $54.0 \pm 29.5$ $\mu$g/4 h; $P = 0.001$). The peaks at 4–8 h after breakfast (between 1200 and 1600 h) reflect the added effect of the fava beans eaten at 1200 h, when concentrations remained elevated from breakfast. Excretion of dopa and dopamine dropped markedly after 1600 h on the fava diet day. Urinary norepinephrine excretion showed a significant treatment main effect (control diet: $5.5 \pm 2.4$ $\mu$g/4 h; fava bean diet: $12.6 \pm 5.4$ $\mu$g/4 h; $P < 0.001$) by Wilcoxon’s matched-pairs signed-rank test, but a nonsignificant main effect of time ($P = 0.951$, by Friedman test).

**Urinary sodium**

Although the treatment $\times$ time interaction for urinary sodium excretion was not significant ($P = 0.194$), diet had a significant effect on sodium excretion ($P < 0.001$ for treatment main effect, $P = 0.616$ for time main effect). Despite the substantial increases in sodium excretion...
in plasma and urinary dopa and dopamine after fava bean consumption, urinary sodium excretion was lower (21 ± 7.8 compared with 33 ± 15 mEq/4 h) after the fava bean breakfast.

The treatment × time interaction for urinary volume was significant (P = 0.020). Volumes of urine collected 0–4 and 4–8 h after breakfast did not differ between the control and fava bean diets (Figure 5; 512 ± 251 and 544 ± 323 mL/4 h after the control diet and 663 ± 367 and 555 ± 246 mL/4 h after the fava bean diet). The volume of the 8–12-h urine collection decreased after the fava bean diet (374 ± 309 compared with 692 ± 499 mL/4 h; P = 0.011). Urinary creatinine excretion ranged from 208 ± 79 mg/4 h (4–8 h after the fava bean diet) to 324 ± 99 mg/4 h (0–4 h after the fava bean diet). Normalization of urinary sodium data to creatinine excretion, to correct for variation in the urine flow rate, eliminated the difference at 4–8 h after breakfast (114 ± 46 mEq/g after the control diet compared with 112 ± 42 mEq/g after the fava bean diet; P = 0.861), but enhanced the difference at 0–4 h after breakfast (112 ± 51 mEq/g after the control diet compared with 76 ± 21 mEq/g after the fava bean diet; P = 0.028).

Hemodynamic measurements

We analyzed the effect of fava bean ingestion on supine blood pressure, heart rate, and orthostatic changes. Values before breakfast were similar on the 2 study days (systolic blood pressure: 101 ± 12 compared with 102 ± 12 mm Hg, P = 0.861; diastolic blood pressure: 59 ± 6 compared with 60 ± 8 mm Hg, P = 0.154; heart rate: 58 ± 12 compared with 60 ± 13 beats/min, P = 0.574). Supine measurements did not differ as a result of fava bean consumption at any time (P > 0.05 by Wilcoxon's and repeated-measures ANOVA; data not shown). Although standing systolic and diastolic blood pressures were significantly higher after the fava diet than after the control study diet, the orthostatic changes in blood pressure did not differ between diets (Table 1).

DISCUSSION

This study showed that ingestion of fava beans raised plasma dopa concentrations and urinary dopa and dopamine excretion, but it did not stimulate urinary sodium excretion, in contrast with our hypothesis. Fava beans may therefore be effectively used to increase plasma dopa, as was shown previously in patients with Parkinson disease (3, 6, 7) but are unlikely to worsen orthostatic hypotension in these patients. Absence of a natriuretic effect is consistent with a variable role for renal dopamine in regulating sodium excretion. Possible explanations include an inadequate increase in plasma dopa or renal dopamine, other fava bean–induced changes that offset the natriuretic effect, and an inappropriate dietary sodium load consumed by our participants.

The renal dopamine system is a major regulator of renal sodium excretion (8). A sodium load, either dietary or by infusion, often increases not only urinary sodium but also dopamine excretion in humans (23) and in rats (24). Dopamine inhibits Na⁺, K⁺-ATPase activity (25, 26), and the Na+/H+ exchanger (27) in the renal tubule, and dopamine produced locally in response to a high-salt diet can thereby control renal sodium transport and excretion (25). Accordingly, dopamine receptor blockade attenuates sodium excretion associated with a saline infusion in rats (28) and a moderate sodium load in dogs (29, 30). Moreover, inhibition of aromatic l-amino acid decarboxylase, the enzyme converting dopa to dopamine, transiently decreases both urinary dopamine and sodium in healthy volunteers consuming their normal diet (31).

Conflicting data, nevertheless, indicate that renal dopamine is not consistently linked to sodium excretion even in high-sodium situations. Sodium loads can increase urinary sodium excretion without influencing urinary dopamine (12), and changes in urinary dopamine occur without effects on urinary sodium (10).

FIGURE 5. Mean (±SEM) urinary excretion of sodium and 4-h urine volumes. After breakfast consisting of a fixed-sodium diet (black bars) or the fixed-sodium diet plus fava beans (gray bars), 4-h urine samples were collected at 0–4 (n = 10), 4–8 (n = 13), and 8–12 (n = 13) h. The treatment × time interaction was significant for volume (P = 0.020) but not for sodium (P = 0.194) by general linear model analysis. A Wilcoxon’s matched-pairs signed-rank test was used to test for significant differences between data obtained with and without fava beans during each collection period. P values are included for NE because the main effect of treatment was significant (P < 0.001).

FIGURE 4. Mean (±SEM) urinary excretion of dopa, DA, and NE. After breakfast consisting of a fixed-sodium diet (black bars) or the fixed-sodium diet plus fava beans (gray bars), 4-h urine samples were collected at 0–4 (n = 10), 4–8 (n = 13), and 8–12 (n = 13) h. The treatment × time interaction was significant for dopa (P = 0.011) and DA (P = 0.013) but not for NE (P = 0.909) by general linear model analysis. A Wilcoxon’s matched-pairs signed-rank test was used to test for significant differences between data obtained with and without fava beans during each collection period. P values are included for NE because the main effect of treatment was significant (P < 0.001). DA, dopamine; dopa, dihydroxyphenylalanine; NE, norepinephrine.
et al (11) showed a dose-dependent effect of oral L-dopa on plasma dopa, dopamine, and sodium in patients with congestive heart failure. A 0.1-g dose of L-dopa resulted in plasma dopa and urinary dopamine concentrations similar to those in our study with a variable natriuretic response, in contrast with a >50-fold increase in urinary dopamine and a doubling of sodium excretion after a 0.25-g dose. Others (12–14) proposed that urinary sodium excretion can only be stimulated by renal dopamine after an oral dose of L-dopa (36, 37), dopa infusion (21), or gludopa was similar to the doubling of plasma norepinephrine elicited by the 150-mEq Na/d diet used in our study (8), D2-like receptors are able to interact with D1-like receptors to increase renal sodium excretion (33, 34). It is, therefore, unlikely that the antinatriuretic response observed in this study was related to preferential or concomitant stimulation of different dopamine receptor subtypes.

Plasma dopamine and norepinephrine also increased after fava bean consumption. Dopamine could have been released into the bloodstream after its formation from dopa in the gut and from dopa taken up by nonneuronal cells and by sympathetic noradrenergic nerves (35) (Figure 6). Increases in plasma norepinephrine presumably are related to the uptake of circulating precursors into neurons (13); we found no evidence that the fava bean norepinephrine content was contributory, and the change was similar to the doubling of plasma norepinephrine elicited by standing. Plasma dopamine and norepinephrine have not been measured in previously published studies of fava beans (3, 7, 15). However, others have shown increases in plasma dopamine after an oral dose of L-dopa (36, 37), dopa infusion (21), or gludopa administration (38) with a much smaller increase (11) or no increase (37) in plasma norepinephrine. Data collected after norepinephrine or dopamine infusion indicate that plasma concentrations of these transmitters must be much higher than those found in the current study to elicit hemodynamic responses, including changes in blood pressure or renal blood flow (13, 39).

Grossman et al (11) found no changes in urinary norepinephrine as a result of L-dopa, in contrast with the increase after fava bean consumption. Because medullary interstitial norepinephrine modulates the natriuretic response (40), norepinephrine increases after fava bean consumption may have worked against any renal dopamine-mediated natriuresis. Unknown components of the fava beans might also have contributed to an antinatriuretic effect.

Because renal dopamine is produced after uptake of circulating dopa in the renal proximal tubule cells (32) (Figure 6), the increase in plasma dopa after fava bean consumption may stimulate urinary dopamine synthesis and potentially sodium excretion. In patients with Parkinson disease, fava bean pods containing 250–500 mg dopa increase plasma dopa to peak concentrations up to 50-fold higher than in our study and produce a motor response similar to that of L-dopa medication (7). Although the lower dopa content of our beans likely contributed to the much smaller elevation of plasma dopa concentrations in our healthy population, another contributor might be variability in absorption of dopa from the fava beans (7). Another factor is the carbidopa given with the fava bean pods in the Kempster study, which almost certainly enhanced the increase in plasma dopa. Accordingly, in a separate study, persistent effects of carbidopa were proposed to account for the higher plasma dopa concentrations in patients with Parkinson disease than in healthy subjects after fava bean consumption (3). It is therefore possible that different responses to fava beans between healthy volunteers and patients with Parkinson disease are related to the pathophysiology of this disease and/or to the medications taken by the patients.

Unfortunately, urinary sodium excretion was not assessed in the studies in patients with Parkinson disease (3, 7). In a report of increased plasma dopa and stimulated natriuresis in healthy individuals fed fava seedlings (15), plasma and urinary data vary considerably from our values and other studies, which makes it difficult to compare the natriuretic effect. Plasma dopa and urinary dopamine concentrations for our participants might have been inadequate to stimulate urinary sodium excretion. Grossman et al (11) showed a dose-dependent effect of oral L-dopa on plasma and urinary dopa, dopamine, and sodium in patients with congestive heart failure. A 0.1-g dose of L-dopa resulted in plasma dopa and urinary dopamine concentrations similar to those in our study with a variable natriuretic response, in contrast with a >50-fold increase in urinary dopamine and a doubling of sodium excretion after a 0.25-g dose. Others (12–14) proposed that urinary sodium excretion can only be stimulated when the urinary dopamine concentration far surpasses that produced by fava bean consumption in the current study. Importantly, the fava beans used in our study were obtained from a grower whose farm provides a large component of the fava beans used for medicinal purposes in patients with Parkinson disease in California.

To the extent that the natriuretic effect of renal dopamine is modulated by sodium load, the 150-mEq Na/d diet used in our study may not have been optimal for detecting natriuresis induced by fava beans. Our dietary sodium level is believed to reflect the American average. However, we cannot rule out the possibility of a fava bean–induced natriuresis with lower or higher dietary sodium.

Although dopamine’s natriuretic effect is primarily mediated by the D1 dopamine receptor, especially during a sodium-replete state (8), D2-like receptors are able to interact with D1-like receptors to increase renal sodium excretion (33, 34).

### TABLE 1

<table>
<thead>
<tr>
<th></th>
<th>Control diet</th>
<th>Fava bean diet</th>
<th>( P^1 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>65 ± 5(^2)</td>
<td>66 ± 13</td>
<td>0.724</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>102 ± 8</td>
<td>104 ± 7</td>
<td>0.326</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>60 ± 6</td>
<td>59 ± 6</td>
<td>0.838</td>
</tr>
<tr>
<td>Standing 30 min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>90 ± 20</td>
<td>87 ± 18</td>
<td>0.109</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>104 ± 14</td>
<td>108 ± 14</td>
<td>0.007</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>70 ± 10</td>
<td>74 ± 9</td>
<td>0.050</td>
</tr>
<tr>
<td>Change from supine to upright</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>26 ± 9</td>
<td>22 ± 8</td>
<td>0.091</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>1 ± 10</td>
<td>5 ± 12</td>
<td>0.122</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>10 ± 7</td>
<td>14 ± 11</td>
<td>0.476</td>
</tr>
</tbody>
</table>

\(^1\)Derived by using a Wilcoxon’s matched-pairs signed-rank test.  
\(^2\)Mean ± SD (all such values).

FIGURE 6. Effect of dietary dopa on plasma and urinary catechols and urinary sodium excretion. DA, dopamine; DA-S, dopamine sulfate; DHPG, dihydroxyphenylglycol; dopa, dihydroxyphenylalanine; DOPAC, 3,4-dihydroxyphenylacetic acid; DOPA-S, dopa sulfate; MAO, monoamine oxidase; NE, norepinephrine.
Even more impressive than our 15-fold increase in plasma dopamine was the >250-fold increase in dopamine sulfate. Both dopa and dopamine are substrates for gut sulfotransferase, and ~95% of circulating dopamine is in the sulfoconjugated form (41). Plasma dopamine sulfate concentrations increase after meals more so than plasma dopa or dopamine (21); therefore, it is not surprising that a meal enriched with dopa substantially increased dopamine sulfate. Dopamine sulfate has not previously been measured after fava bean consumption, but its presence no doubt modulates the effects of fava bean ingestion on circulating dopa and free dopamine. Although it has been proposed that dopamine sulfate could be deconjugated to free dopamine (35, 42), it is not known to what extent, if any, this actually occurs.

Potential renotoxic effects of such high dopamine concentrations in the kidney must be considered. Patients with a dopamine β-hydroxylase deficiency have elevated plasma dopa and urinary dopamine as a result of a congenital absence of the enzyme that converts dopamine to norepinephrine. Elevations in blood urea nitrogen and serum creatinine have been reported in these patients (43–46), and it has been proposed that excessive renal dopamine impairs their kidney function (47).

Limitations of this study include the inability to test whether further increases in plasma dopa or dietary sodium would have produced a different effect on urinary sodium excretion. We also did not assay other hormones important for the regulation of natriuresis: arginine vasopressin, antidiuretic hormone, endothelin, aldosterone, natriuretic peptides, etc. The period of study was limited by the stability of dopa in our batch of fava beans. Despite being stored at −40°C, dopa concentrations began to decline after 1 y. Obtaining the beans from a source used by patients with Parkinson disease and using a diet with an amount of sodium representative of the American diet allowed us to assess the natriuretic effect of fava beans under physiologically relevant conditions. We are however unable to generalize these findings in healthy volunteers to patients with Parkinson disease.

This was the first study to describe the effects of fava beans in healthy volunteers in balance on a fixed-sodium, low-monosodium diet. The fava beans serve as a source of dopa for renal dopamine synthesis. Fava beans significantly increased plasma and urinary dopa and dopamine. However, fava bean consumption failed to induce a dopamine-associated natriuretic effect, which highlights the potential for many factors to influence this relation.

We thank Kisha Batey and Angie Sneed for their assistance with the catechol analysis; Maciej Buchowski, Cynthia Dossett, and Damaris Santana for dietary support; and the nursing staff of the Vanderbilt Clinical Research Center. The authors’ responsibilities were as follows—EMG, DR, and TSC: conceived of and designed the research; TSC: performed the study and prepared the first draft of the manuscript; SL: performed the catechol analyses; EMG: analyzed the data and prepared the figures; EMG, DR, TSC, and MCF: interpreted the results of the experiments; EMG, DR, and MCF: edited and revised the manuscript; and EMG, TSC, DR, MCF, and SL: approved the final version of the manuscript. None of the authors had a personal or financial conflict of interest.

REFERENCES


