

(+)-Catechin in human plasma after ingestion of a single serving of reconstituted red wine¹⁻³

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ABSTRACT

Background: Red wine consumption may decrease the risk of coronary heart disease through the actions of its constituent flavonoids. (+)-Catechin is an abundant flavonoid in red wine.

Objective: The objective was to determine changes in plasma (+)-catechin concentrations after ingestion of a single, moderate serving of dealcoholized red wine reconstituted with either water (DRW) or water and alcohol (ARW).

Design: Nine subjects (5 men, 4 women) ingested, in random order, 120 mL DRW on one day and 120 mL ARW on another day. Both the DRW and ARW contained 35 mg (121 μ mol) free (+)-catechin. Blood samples were collected at 0, 0.5, 1, 2, 3, 4, and 8 h. Plasma was analyzed by gas chromatography–mass spectrometry for (+)-catechin after enzymatic release of sulfate and glucuronide conjugates.

Results: Calcium ions were needed to effectively hydrolyze (+)-catechin conjugates in plasma containing EDTA. Neither the ARW or DRW nor sex affected the area under the curve at 8 h, the maximum concentration (c_{\max}), or the time it took for plasma total (+)-catechin to reach maximum concentration (t_{\max}). Pooled mean (\pm SEM) values for the ARW and DRW were as follows: area under the curve, 306.1 ± 29.5 nmol \cdot h/L; c_{\max} , 76.7 ± 7.5 nmol/L; and t_{\max} , 1.44 ± 0.13 h. The half-life of (+)-catechin in plasma was significantly less ($P = 0.038$) after ingestion of the ARW (3.17 h) than after ingestion of the DRW (4.08 h).

Conclusions: Increases in plasma total (+)-catechin concentrations were not significantly different after single moderate servings of either the ARW or DRW. Alcohol in the ARW hastened the elimination of (+)-catechin from the plasma compartment. (+)-Catechin elimination may represent excretion or conversion to methylated derivatives. *Am J Clin Nutr* 2000;71:103–8.

KEY WORDS (+)-Catechin, antioxidant, flavonoid, red wine, ethanol, pharmacokinetics, humans

INTRODUCTION

The protective effects of vegetable, fruit, and red wine consumption against coronary artery disease and certain types of cancer are partly attributed to the flavonoid content of these foods (1–13). Recognized mechanisms by which flavonoids may contribute to human health include antioxidant action, modulation of immune function, and reduction of platelet adhesion (14).

Flavonoids constitute a broad class of secondary plant metabolites with various activities (15). Thus, plant foods differ in their flavonoid composition and content. It is not clear whether reported flavonoid-derived health benefits are due to specific molecular species or to general flavonoid intakes.

Red wine is believed to constitute a significant dietary flavonoid source in some cultures (16). Red wine contains more flavonoids than does red or purple grape juice because, unlike nonalcoholic grape juice production, the process of winemaking extracts the flavonoids from the seeds and skins of grapes (17). Unlike grape juice, wine contains $\approx 13\%$ ethanol. Ethanol has complex metabolic effects and can act as a fuel source, elevate cardioprotective HDL concentrations, and alter fluid balance and xenobiotic-metabolizing enzyme activities (18, 19). Some investigators have speculated that the presence of alcohol in red wine also improves flavonoid availability by increasing intestinal absorption, either by delaying excretion or perhaps by altering its course through xenobiotic excretion pathways (20). The usual consumption of red wine with a meal or as part of a particular lifestyle may be primarily responsible for its apparent favorable effects (21).

Notably, it remains unknown whether ingestion of flavonoids in the amounts typically encountered in 1 or 2 glasses of red wine increases the concentration of flavonoids subsequently present in human blood. Such information is necessary to test the hypothesis that red wine is a nutritionally important source of flavonoids, to identify relevant flavonoid species, and to establish physiologically relevant concentration ranges for mechanistic investigations.

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Red wine contains substantial amounts of 3 flavonoid classes: flavan-3-ols, flavonols, and anthocyanins (22). This study investigated the changes in plasma concentrations of (+)-catechin, a significant contributor to the flavan-3-ol content of red wine (22). (+)-Catechin was selected because it has demonstrable antioxidant activity *in vitro* (23) and reduces aortic lipid deposition in an atherogenic hamster model (24).

SUBJECTS AND METHODS

Subjects

Five men and women aged 21–49 y were recruited from the University of California Davis campus. Subjects were all healthy, with an average weight of 78.1 ± 4.3 kg (range: 52.3–94.4 kg) and body mass index (BMI; in kg/m^2) of 25.4 ± 1.3 (range: 19.7–33.5). Exclusion criteria were systemic illness (diabetes mellitus, untreated hypothyroidism, and renal or liver disease), smoking, and food allergies. Each subject signed a consent form approved by the Human Subjects Committee at the University of California, Davis, before participation in the study.

Diet

To minimize the confounding effects of dietary flavonoids, subjects were instructed to exclude all fruit, vegetables, wine, tea, chocolate, coffee, and alcoholic beverages from their diets for 3 d before ingestion of the experimental beverages (25). All subjects submitted food records for the testing week to assess dietary compliance.

Wine preparation

Wine is a complex food matrix containing volatile and chemically reactive components and copigments that are sensitive to light, pH, and exposure to air (26). One aim of this study was to determine whether ingestion of red wine flavonoids in conjunction with ethanol results in a pattern for changes in plasma (+)-catechin concentrations different from those after the ingestion of flavonoids without ethanol. However, dealcoholization techniques vary and all invariably change the composition of wine to some degree (27). Therefore, it is not possible to compare outcomes resulting from ingestion of native wine and its dealcoholized counterpart. To hold constant any changes in wine composition introduced by a dealcoholization step, all wine was first dealcoholized and then reconstituted with either water (DRW) to produce an alcohol-free beverage or with water and ethanol (ARW) to produce a beverage with 13% ethanol (by vol).

Alcohol was removed from a 1996 *Cabernet sauvignon* wine (produced at the University of California, Davis) by rotary evaporation under vacuum at 30°C for 1 h. This process reduced the volume by approximately one-half and limited oxygen exposure during the process of alcohol removal. Both reconstituted wine samples contained 35 ± 1 mg (121000 nmol) (+)-catechin and <1 mg (–)-epicatechin (3445 nmol) per 120 mL as determined by HPLC (28). The total amount of low-molecular-weight (<1000) phenolic compounds was 103.5 ± 1 mg per 120 L.

Clinical procedures

On 2 different days, the subjects consumed either the ARW or the DRW after the drinking order was randomly determined. On each study day, a butterfly needle was inserted into a forearm vein of the subjects after they had fasted for 14 h and a baseline blood

sample was collected. After blood collection, the subjects consumed either 120 mL ARW or DRW per their sequence assignment. After 0.5, 1, 2, 3, 4, and 8 h, 20 mL blood was collected into EDTA-containing tubes. The subjects were fed a low-flavonoid lunch after collection of the 3-h blood sample.

Laboratory methods

All solvents and reagents were HPLC or Optima grade; other common reagents were purchased from either Fisher Scientific (Pittsburgh) or Aldrich Chemical Co (Milwaukee) and were the highest grade available.

Sample collection and preparation

Plasma was separated by centrifuging the blood at $1890 \times g$ for 15 min at 4°C and 1-mL aliquots of the plasma were placed into microcentrifuge tubes containing 25 μL ascorbic acid–EDTA solution (0.4 mol NaH_2PO_4 buffer containing 20% ascorbic acid and 0.1% EDTA, pH 3.6) and immediately flushed with nitrogen and stored at -70°C .

(+)-Catechin extraction from plasma

Others had shown that (+)-catechin ingested in very high doses, 8–80 mg/kg body wt, circulates as glucuronide and sulfate conjugates in addition to its free form (29). In the present study, many pilot assays conducted by using plasma from nonstudy volunteers who drank red wine failed to reliably detect (+)-catechin in unhydrolyzed plasma, suggesting that conjugate forms were predominant. Enzymatic treatment of that plasma pool with β -glucuronidase (EC 3.2.1.31) and arylsulfatase (EC 3.1.6.1) increased extractable (+)-catechin 3-fold. However, addition of calcium ions was needed for maximum enzyme activity and conjugate release (7-fold), presumably because of the presence of EDTA (30). Before each extraction, solvents and reagents were degassed; all samples and reagents were kept on ice. Each 1-mL aliquot of plasma was mixed with 100 μL ascorbic acid–EDTA solution and two 500- μL replicates were transferred to separate tubes. To control for losses that might occur during sample processing, a mixture of 2.5 μmol (+)-taxifolin/L, 2.5 μmol ascorbic acid/L, and 2.5 μmol EDTA/L (Apin Chemicals Ltd, Abingdon, United Kingdom) was added to each of the 500- μL portions of plasma, ascorbic acid, and EDTA to achieve a final concentration of 82 nmol (+)-taxifolin/L. Taxifolin was selected as the internal standard because it is a flavonoid and was not present in the test wine. Prepared plasma was then carried through the hydrolysis step.

Prolonged incubation times (2–3 h) reduced the amount of extractable (+)-catechin. Conjugate hydrolysis was conducted in 13×100 -mm glass screw-capped tubes containing 2500 U β -glucuronidase (G021; Sigma Chemical Co, St Louis), 100 U arylsulfatase (S9754; Sigma Chemical Co) in 120 μL , and 250 μL of 0.6 mol CaCl_2/L per 500- μL replicate at a final pH of 5.0. The samples were flushed with nitrogen, briefly mixed, and incubated with shaking at 37°C for 45 min. Incubation was then stopped and (+)-catechin was immediately extracted by adding 1 mL methylene chloride and 500 μL water, followed by vigorous mixing with a vortex mixer for 1 min before centrifugation at $4500 \times g$ for 10 min at 4°C. Seven hundred microliters of the resulting aqueous supernatant portion was transferred to a clean 15-mL screw-capped plastic tube, and the methylene chloride fraction was reextracted with 750 μL water. The combined aqueous phases, ≈ 1400 μL , were mixed with 2 mL ethyl acetate and centrifuged at $4500 \times g$ for 10 min at 4°C. The supernatant

portion was transferred to a clean 13 × 100-mm glass tube and the aqueous phase was reextracted with 1.5 mL ethyl acetate. The combined extracts, ≈3 mL, were passed through anhydrous sodium sulfate packed in a Pasteur pipette. The eluate was dried under nitrogen and redissolved in 20 μL pyridine before derivatization with 30 μL *N,O*-bis (trimethylsilyl)trifluoroacetamide (Pierce Chemical Co, Rockford, IL) at 65°C for 2 h.

Gas chromatography–mass spectrometry

Trimethylsilyl derivatives of (+)-catechin and (+)-taxifolin in plasma were analyzed by gas chromatography–mass spectrometry (GC–MS) (model 6890 gas chromatograph and model 5973 quadrupole mass spectrometer; Hewlett–Packard, Palo Alto, CA) as described previously (31). Separations were performed by using a DB5 capillary GC column (30 × 0.25 mm internal diameter, 0.25-μm film; J & W Scientific, Folsom, CA). Splitless injections of 2 μL were made and the column temperature was programmed from 150 (held for 3 min) to 230°C at 5°C/min with a final hold at 230°C for 30 min. Helium was used as the carrier gas with a flow rate of 0.7 mL/min and with an average linear velocity of 23 cm/min. Quantitative analysis was performed by using 70-eV electron ionization and select-ion monitoring of fragment ions at a mass-to-charge ratio (*m/z*) of 355 with a dwell time of 100 m/s channel. Notably, this technique would have also detected (–)-epicatechin, a less-abundant red wine flavonoid, if it had been present (31). The wine used in this study contained >1 mg (–)-epicatechin per 120-mL portion, and no (–)-epicatechin was detected in any plasma sample analyzed. These data are not discussed further.

Standard curves

(+)-Catechin in plasma was quantitated by comparison with a series of external standards formulated to contain increasing amounts of (+)-catechin in combination with a fixed amount of the (+)-taxifolin internal standard within a plasma matrix. (+)-Catechin external standard stock solutions were prepared by serial dilution of a concentrated (+)-catechin stock solution (2000 nmol (+)-catechin/L in acetonitrile:water; 30:70, by vol) with the ascorbic acid–EDTA solution. Suitable volumes of the diluted standards were added to achieve final concentrations of 0, 7, 17, 35, 69, 172, and 258 nmol (+)-catechin/L. After extraction and derivatization, a standard curve was constructed by plotting the ratios of the integrated areas of the ion at *m/z* 355 for (+)-catechin and *m/z* 368 for (+)-taxifolin against the ratio of ng (+)-catechin/mL and ng (+)-taxifolin/mL. Ten standard curves were constructed in blank plasma over the 10-d period during which samples were analyzed. Although this method of analysis did not control for potential minor variations arising from day-to-day differences in enzymatic hydrolysis, curves from different days varied by <5% (CV) over this period and therefore the data were pooled to create one standard curve ($y = 0.053x + 0.04$; $R^2 = 0.97$), where *y* is the concentration in ng/mL and *x* is the ratio of (+)-catechin (*m/z* 355) to (+)-taxifolin (*m/z* 368), against which concentrations in unknowns were estimated. Results were expressed as nmol (+)-catechin/L plasma, where the molecular mass of (+)-catechin was 290.1 ng/nmol.

Statistical analysis and calculation of kinetic indexes

Statistical analysis was performed by using the SAS software package for general linear models (version 6.12; SAS Institute Inc, Cary, NC). Values are reported as means ± SEMs unless noted otherwise, and the significance level was set at $\alpha = 0.05$.

The area under the curve (AUC) from 0 to 8 h was calculated by using the trapezoidal rule and plasma (+)-catechin concentrations measured at 0, 0.5, 1, 2, 3, 4, and 8 h after a single oral dose administered at time 0 (32). Maximum plasma concentrations of (+)-catechin from 0 to 8 h postdose were defined as c_{\max} . The time to maximum plasma concentration (t_{\max}) was defined as the time in hours at which c_{\max} was reached. The elimination half-life for (+)-catechin was computed by using the following formula:

$$t_{1/2} = -\ln(2)/\beta \quad (1)$$

where β is the slope of the linear regression of the ln of plasma (+)-catechin concentrations 3, 4, and 8 h after beverage consumption.

The study had an open-label, randomized, 2-period crossover design with repeated measurements over time. A multivariate test was used to determine the significance of any differences in (+)-catechin concentrations between the ARW and DRW regimens over time (33). Comparisons between the 2 regimens for c_{\max} , 8-h AUC, and $t_{1/2}$ were based on crossover models that included terms for sequence, subject, subject within sequence (considered as a random effect), period, and regimen in the analysis of variance model. Tests for potential differences between sexes in 8-h AUC, c_{\max} , and $t_{1/2}$ were done by using Student's *t* tests. For t_{\max} , a Wilcoxon signed-rank test was used to test for differences between regimens. Fisher's exact tests were used to test for differences between sexes.

RESULTS

Subjects adhered to the low-flavonoid diet, as judged by diet records. This impression was corroborated by the low 0-h plasma total (+)-catechin concentration (≤ 2.0 nmol/L) before ingestion of either the ARW or DRW. This value is at the limit of detection for the method used (31). These values also indicate that the interval between beverage testing, 2 d, was sufficient to regain baseline concentrations before ingestion of the second beverage.

Plasma total (+)-catechin concentrations, measured after conjugate hydrolysis, increased in response to dietary (+)-catechin ingestion. Consumption of 121 000 nmol (+)-catechin as either the ARW or DRW rapidly increased plasma total (+)-catechin concentrations (**Figure 1**). Changes in plasma total (+)-catechin concentrations during the 8 h after ingestion of the ARW or DRW varied substantially among the individuals studied. Peak plasma total (+)-catechin concentrations varied from 40 to 130 nmol/L after ARW ingestion and from 30 to 110 nmol/L after DRW ingestion. Thus, plasma total (+)-catechin increased 15- to 65-fold depending on the individual studied. However, within a given individual, results observed after consumption of either the ARW or DRW were not significantly different. The lack of difference in the overall response was apparent after mean changes in plasma total (+)-catechin over time were calculated for each beverage and plotted, as shown in **Figure 2**.

Eight hours after ingestion of the ARW or DRW, mean plasma (+)-catechin concentrations had dropped to ≈20 nmol/L. AUC, c_{\max} , t_{\max} , and $t_{1/2}$ values were calculated to better describe and statistically compare changes in plasma total (+)-catechin after ingestion of the ARW and DRW (**Table 1**). The 8-h AUCs after ingestion of either the ARW or DRW were not significantly different and averaged 306.1 ± 29.5 nmol·h/L. The BMIs of the subjects correlated inversely with 8-h AUCs: $r = -0.694$ ($P < 0.038$) for the ARW and $r = -0.661$ ($P < 0.052$) for the DRW. Ingestion of either the ARW or DRW resulted in t_{\max} and c_{\max} values that



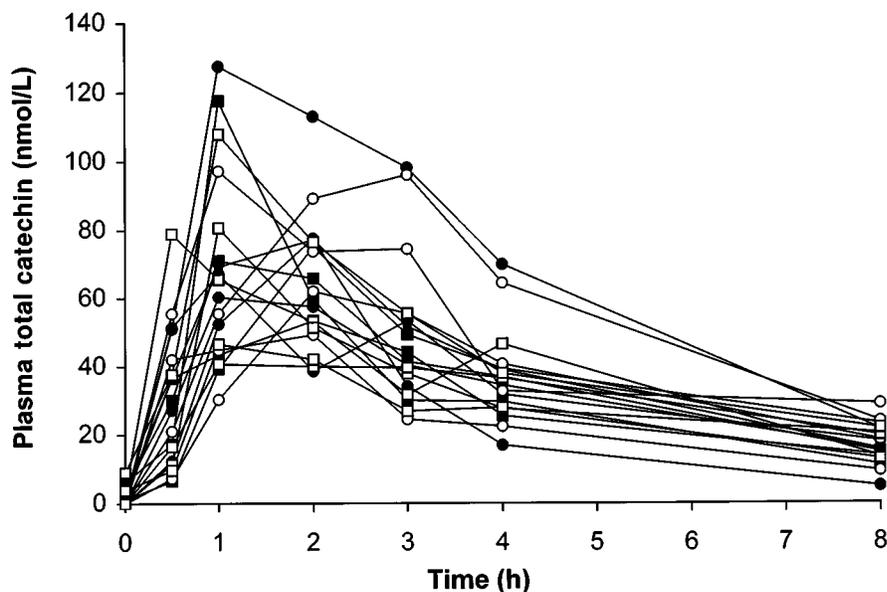


FIGURE 1. Individual changes in plasma total (+)-catechin concentrations after ingestion of 120 mL dealcoholized red wine reconstituted to its original volume with either water and ethanol to contain 13% ethanol (filled symbols) or water (open symbols) by 5 men (squares) and 4 women (circles). Concentrations were measured by gas chromatography–mass spectrometry after enzymatic hydrolysis of glucuronide and sulfate conjugates and formation of trimethylsilylated derivatives.

were not significantly different and that averaged 1.44 ± 0.13 h and 76.7 ± 7.5 nmol/L, respectively. In contrast, the $t_{1/2}$ value for plasma (+)-catechin was 0.91 h less (22%) after ingestion of the ARW (3.17 h) than after the DRW (4.08 h). As shown in **Table 2**, calculated average values of plasma c_{\max} were not significantly different in men and women. The 13% higher 8-h AUC and the 20% lower $t_{1/2}$ values in women than in men were not significantly different.

DISCUSSION

The results of the present study showed clearly that plasma total (+)-catechin concentrations are responsive to dietary (+)-catechin intakes as might be provided by moderate red wine intakes. The extent to which plasma total (+)-catechin concentrations increased was not affected by coingestion of ethanol. In this small study, the subjects' sex was not related to observed changes in plasma total (+)-catechin concentrations.

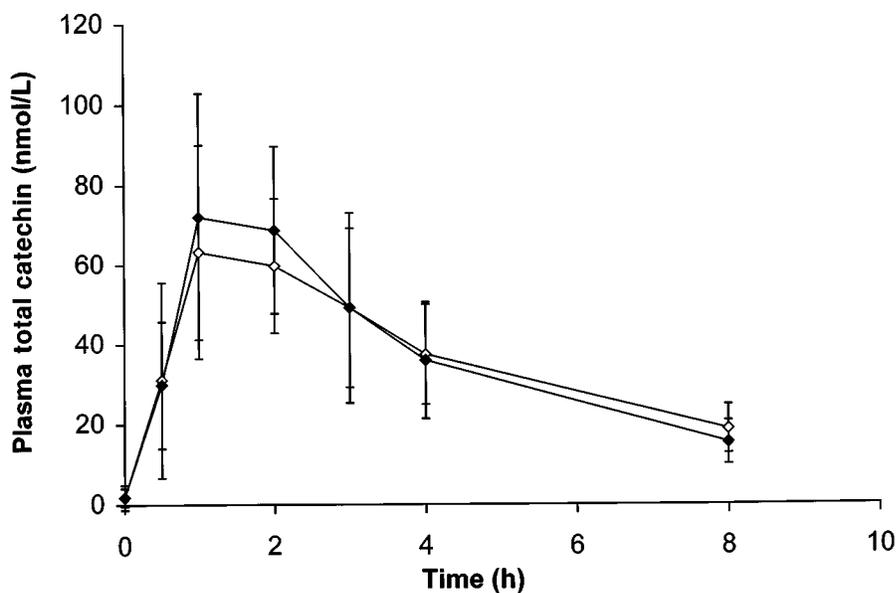


FIGURE 2. Mean (\pm SEM) changes in plasma total (+)-catechin concentrations after ingestion of 120 mL dealcoholized red wine reconstituted to its original volume with either water and ethanol to contain 13% ethanol (\blacklozenge) or water (\diamond) by 5 men and 4 women. Concentrations were measured by gas chromatography–mass spectrometry after enzymatic hydrolysis of glucuronide and sulfate conjugates and formation of trimethylsilylated derivatives.

TABLE 1Pharmacokinetic indexes calculated from changes in plasma total (+)-catechin concentrations (nmol/L)¹

	ARW	DRW
8-h AUC (nmol·h/L)	306 ± 34	306 ± 29
<i>t</i> _{max} (h)	1.44 ± 0.24	1.44 ± 0.18
<i>c</i> _{max} (nmol/L)	78.3 ± 8.9	75.1 ± 8.5
<i>t</i> _{1/2} (h)	3.17 ± 0.27 ²	4.08 ± 0.38

¹ $\bar{x} \pm \text{SEM}$; *n* = 5 M and 4 F. Plasma (+)-catechin concentrations were measured 0, 0.5, 1, 2, 3, 4, and 8 h after ingestion of 121 000 nmol (+)-catechin as dealcoholized red wine reconstituted to its original volume with either water (DRW) or water and ethanol to contain 13% ethanol (by vol) (ARW). 8-h AUC, area under the curve at 8 h; *t*_{max}, time to maximum plasma concentration; *c*_{max}, maximum plasma concentration; *t*_{1/2} elimination half-life.

²Significantly different from DRW, *P* = 0.038.

The fixed amount of (+)-catechin consumed in this study was selected to represent an amount that might be encountered in a normal diet as part of a single meal (22). Individual doses ranged from 1300 to 2300 nmol/kg (0.37 to 0.67 mg/kg). The red wine matrix used in this study provided flavonoids other than (+)-catechin, and the total flavonoid intake (104 mg) in the present study was ≈360 000 nmol, or ≈4600 nmol/kg body wt. Current understanding of (+)-catechin absorption and metabolism is based on earlier studies by others who tested aqueous suspensions of purified (+)-catechin in oral doses of 27 600–276 000 nmol/kg (8–80 mg/kg) (see reference 34 for a concise review). These high doses were intended to assess the compound's toxic potential and to accommodate the relatively insensitive methods available at the time. In a human study that used higher doses (≈92 000 nmol/kg) than used in the present study, appreciable amounts of free (+)-catechin were detected in plasma (29). The extent of (–)-epicatechin conjugation also appears to be dose dependent (35). Notably, a dose of 172 000 nmol (–)-epicatechin/kg body wt in rats produced peak plasma concentrations of 1000 nmol free (–)-epicatechin/L and 11 000 nmol (–)-epicatechin glucuronides/L, whereas 860 000 nmol (–)-epicatechin/kg body wt increased peak free (–)-epicatechin concentrations 8-fold and (–)-epicatechin glucuronides 2.5-fold. Hackett et al (29) concluded that the body's ability to conjugate flavonoids could be overwhelmed. A dose of 860 000 nmol (–)-epicatechin/kg body wt would provide ≈15 g

TABLE 2Effect of sex on pharmacokinetic indexes calculated from changes in plasma total (+)-catechin concentrations (nmol/L)¹

	Women ² (<i>n</i> = 4)	Men (<i>n</i> = 5)
8-h AUC (nmol·h/L)	327 ± 64	289 ± 22
<i>t</i> _{max} (h)	1.6 ± 0.2	1.3 ± 0.1
<i>c</i> _{max} (nmol/L)	76.5 ± 9.6	76.8 ± 13.4
<i>t</i> _{1/2} (h)	3.2 ± 0.4	4.0 ± 0.3

¹ $\bar{x} \pm \text{SEM}$. Plasma catechin concentrations were measured 0, 0.5, 1, 2, 3, 4, and 8 h after ingestion of 121 000 nmol (+)-catechin as dealcoholized red wine reconstituted to its original volume with either water (DRW) or water and ethanol to contain 13% ethanol (by vol) (ARW). 8-h AUC, area under the curve at 8 h; *t*_{max}, time to maximum plasma concentration; *c*_{max}, maximum plasma concentration; *t*_{1/2} elimination half-life.

²Individual values were pooled by averaging individual plasma total (+)-catechin concentrations observed after DRW and ARW ingestion. The resultant average values for each time point were used in subsequent calculations.

(–)-epicatechin/d to a 60-kg individual, or a dietary concentration of ≈3 g/100 g dry matter. Such intakes exceed generous estimates of dietary flavonoid intake (25). In pilot experiments conducted in the course of the present studies, little free (+)-catechin was detected in casual plasma specimens from nonstudy, wine-drinking volunteers, necessitating an enzymatic hydrolysis step before the sample analysis. The technique used liberated both glucuronide and sulfate conjugates; thus, it was not possible to determine whether the composition of conjugates differed with ARW and DRW consumption.

Changes in plasma total (+)-catechin concentrations are assumed to reflect the summated effects of intestinal absorption, tissue and gut flora metabolism, and excretion of ingested (+)-catechin. Thus, the 3- to 4-fold differences observed in plasma total (+)-catechin concentrations among individuals over time could reflect many factors. Others reported that urinary (+)-catechin varied 2-fold in 3 subjects drinking 2 g purified (+)-catechin dissolved in water (36). Genetic and sex-linked variation is well known to occur in xenobiotic metabolism, including variations in conjugate formation (37). (+)-Catechin is readily metabolized by catechol *O*-methyltransferase (EC 2.1.1.6), becoming a 3'-methyl-*O*-(+)-catechin conjugate (38). Catechol *O*-methyltransferase methylates a wide range of catechols, including estrogen. Although the methods used in the present study did not detect 3'-methyl-*O*-(+)-catechin directly, nor cleave the methyl moiety, it is possible that individual differences in plasma total (+)-catechin concentrations over time reflected the extent of 3'-methyl-(+)-catechin formation.

Speculation exists that ethanol may alter flavonoid absorption or metabolism (20). Overall, in the present study, the presence or absence of ethanol had no significant effect on calculated 8-h AUCs, *c*_{max}, or *t*_{max} for (+)-catechin, nor were there any significant differences in these indexes between men and women. However, women are known to differ in their metabolism of ethanol (39). The *t*_{max} value of 1.44 h reported herein is similar to several values obtained with doses of (+)-catechin not attainable through the diet (34). These observations suggest that ethanol, at the intakes used in this study, does not acutely affect changes in plasma (+)-catechin concentrations caused by physiologically relevant amounts of dietary (+)-catechin. However, the calculated *t*_{1/2} value of plasma (+)-catechin was 22% shorter with the ARW than with the DRW. From the available data it is not possible to determine whether the more rapid decline in plasma total (+)-catechin was the result of increased excretion or conversion to methylated forms or to influenced conjugation pathways. Studies are underway to address these points directly. In the future it will also be necessary to determine whether food intake influences (+)-catechin utilization within the body because wine is typically consumed as part of a meal.

The results presented herein suggest that red wine provides 2 independent factors capable of contributing to vascular health when consumed in moderation. First, moderate ethanol intakes can act independently to increase plasma HDL concentrations and reduce platelet adhesiveness (18, 19). Second, the data showed that plasma (+)-catechin concentrations do increase after consumption of amounts of flavonoids present in a single serving of wine. Notably, inclusion of (+)-catechin as the sole dietary flavonoid at a dose comparable with the total flavonoid intake used in the present study, ie, 200 mg/kg dry matter, reduced aortic lipid deposits in an atherogenic hamster model (24). Whether the plasma (+)-catechin concentrations observed in this study afford effective cardiovascular protection in humans remains to be determined.

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