Avenanthramides Are Bioavailable and Have Antioxidant Activity in Humans after Acute Consumption of an Enriched Mixture from Oats\textsuperscript{1,2}

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Abstract

The consumption of polyphenols is associated with a decreased risk of cardiovascular disease. Avenanthramides (AV), alkaloids occurring only in oats, may have anti-atherosclerotic activity, but there is no information concerning their bioavailability and bioactivity in humans. We characterized the pharmacokinetics and antioxidant action of avenanthamide A, B, and C in healthy older adults in a randomized, placebo-controlled, 3-way crossover trial with 1-wk washout periods. Six free-living subjects (3 mol/L, 3 F; 60.8 ± 3.6 y) consumed 360 mL skim milk alone (placebo) or containing 0.5 or 1 g avenanthamide-enriched mixture (AEM) extracted from oats. Plasma samples were collected over a 10-h period. Concentrations of AV-A, AV-B, and AV-C in the AEM were 154, 109, and 111 nmol/g, respectively. Maximum plasma concentrations of AV (free + conjugated) after consumption of 0.5 and 1 g AEM were 112.9 and 374.6 nmol/L for AV-A, 13.2 and 96.0 nmol/L for AV-B, and 41.4 and 89.0 nmol/L for AV-C, respectively. Times to reach the C\textsubscript{max} for both doses were 2.30, 1.75, and 2.15 h for AV-A, AV-B, and AV-C and half times for elimination were 1.75, 3.75, and 3.00 h, respectively. The elimination kinetics of plasma AV appeared to follow first-order kinetics. The bioavailability of AV-A was 4-fold larger than that of AV-B at the 0.5 g AEM dose. After consumption of 1 g AEM, plasma reduced glutathione was elevated by 21\% at 15 min (\textit{P} ≤ 0.005) and by 14\% at 10 h (\textit{P} ≤ 0.05). Thus, oat AV are bioavailable and increase antioxidant capacity in healthy older adults. J. Nutr. 137: 1375–1382, 2007.

Introduction

Consumption of whole-grain foods is associated with a decreased risk of several chronic diseases, including cancer, type 2 diabetes, and cardiovascular disease (1–9), with benefits attributed to their content of vitamins, minerals, essential fatty acids, fiber, and phytochemicals, including several phenolic compounds (10,11). Although they are not essential nutrients, phenolic acids and polyphenols have been found to possess an array of bioactivity, including antioxidation, antiproliferation, anti-inflammation, and detoxification, which may contribute to the promotion of good health (12). Oats (\textit{Avena sativa} L.), which are normally consumed as whole-grain cereal, contain small amounts of free phenolic acids, including caffeic, \textit{p}-coumaric, ferulic, \textit{p}-hydroxybenzoic, \textit{p}-hydroxyphenylacetic, protocatechuic, sinapic, syringic, and vanillic acids, and flavonoids such as apigenin, kaempferol, luteolin, quercetin, and tricin (13–15). However, larger amounts of these compounds are present in both soluble and insoluble conjugated forms as various esters, ethers, glycosides, and amides (14–16).

Collins et al. (17–19) isolated and characterized a group of hydroxycinnamoylanthranilate alkaloids, called avenanthramides (AV)\textsuperscript{5} (Fig. 1), that are unique to oats and represent the major alcohol-soluble phenolic antioxidants found in the oat kernel (13,20). AV consist of the amide conjugates of anthranilic acid or its hydroxylated derivatives and hydroxycinnamic or avenalumic acids (17–19). These compounds are regarded as key phytoalexins in the defense mechanisms of oats against certain pathogens (21). They are constitutively expressed in the kernels, appearing in almost all milling fractions, but occur in the highest concentration in the bran and outer layers of the...
Mixture (AEM) extracted from oats. Constituents in subjects after they consumed an AV-enriched preparation have not been assessed in humans, so we characterized the antioxidant activity of AV-C, their consumptions largely dependent on their bioavailability. Although the results of Ji et al. (27) implicate the bioavailability of AV-C, their in vivo efficacy of phytochemicals, including AV, is dependent on their bioavailability. The results from Ji et al. (27) implicate the bioavailability of AV-C, their consumptions primarily dependent on their bioavailability. Although the results of Ji et al. (27) implicate the bioavailability of AV-C, their in vivo efficacy of phytochemicals, including AV, is dependent on their bioavailability. Although the results from Ji et al. (27) implicate the bioavailability of AV-C, their consumptions in vivo efficacy of phytochemicals, including AV, is largely dependent on their bioavailability. Although the results from Ji et al. (27) implicate the bioavailability of AV-C, their consumptions in vivo efficacy of phytochemicals, including AV, is dependent on their bioavailability.

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**Materials and Methods**

**Chemicals and solvents.** The following reagents were obtained from Sigma: BHT, Folin-Ciocalteu phenol reagent, copper sulfate, EDTA, β-glucuronidase type H-2 (containing sulfatase from Helix pomatia), glutathione reductase (type III), NADP, sodium 1-octanesulfonate monohydrate, reduced glutathione, sodium azide, sodium chloride, sodium phosphate monobasic, sodium phosphate dibasic, 2',3',4'-trihydroxyacetophenone, Tris buffer, and vitamin E (α-tocopherol). All organic solvents, glacial acetic acid, and potassium bromide were purchased from Fisher. Pure synthetic AV-A, AV-B, and AV-C were produced according to the method of Baird and Smalley (31).

**AEM preparation.** The AEM was prepared from hulled oats developed to contain high concentrations of antioxidants at Agriculture and Agri-Food Canada, ECORC, and it was grown in seed plots in Plessisville, Quebec, during the 2000 crop year. The details of AEM preparation have been described previously (29) and the same AEM was used in our study. Briefly, dry, cleaned oats were processed in a Satake pearling mill (type RMB, 36 abrasive roller, 1 mm slit screen) to obtain a 0–21% (by weight) oat bran fraction containing ~520 mg/kg AV-A equivalents. The AEM was produced from this oat bran through procedures consisting of acidified aqueous-ethanol extraction, 2 types of preparative batch chromatography, evaporation, and freeze drying. This semipurified powdered mixture was stored at −20°C until use in the study. In all, 20.0 g of AEM was produced. One gram AEM contained 400 mg GAE. Concentrations of the 3 major components, AV-A, AV-B, and AV-C in the AEM were 154, 109, and 117 μmol/g, respectively (29). The structures of the 3 major AV and their HPLC-electrochemical detection (ECD) chromatogram in AEM are shown in Figure 1 and Figure 2A, respectively.

**Subjects.** Six healthy older adults (3 males and 3 females) were recruited with the following baseline characteristics: 60.8 ± 3.6 y of age; body weight of 70.9 ± 5.8 kg; systolic and diastolic blood pressure of 127.8 ± 7.7 and 73.5 ± 5.5 mm Hg, respectively, and a BMI of 25.4 ± 1.3. All participants were in good health as determined from a medical history questionnaire, a physical examination, an electrocardiogram test, and normal results of standard clinical laboratory tests. Subjects also fulfilled the following eligibility criteria: 1) no history of cardiovascular, hepatic, gastrointestinal, or renal disease; 2) no alcoholism; 3) no antibiotic or supplemental multivitamin or mineral use for ≥4 wk (and 3 mo for 60 mg vitamin C, 30 IU vitamin E, and/or 70 μg selenium) before the start of the study; and 4) no recent history of smoking. They were asked to consume a low-flavonoid diet for 1 wk before visits, according to the low-flavonoid diet guideline designed by the study dietitian, in which all berries, apples, pears, citrus fruits, fruit juices, onions, chocolate, wine, coffee, any kind of tea, beans, nuts, soy products, and most spices were excluded from the daily diet. During their visits, the participants were provided with a low-flavonoid lunch and dinner prepared in the Metabolic Research Unit at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University. The results of three 3-d dietary records before each visit indicated subject compliance to the low-flavonoid dietary guideline. The study protocol was approved by the Institutional Review Board of Tufts University Health Sciences/Tufts-New England Medical Center and written consent was obtained from each participant.

**Study Design.** In a placebo-controlled, 3-way crossover design with a 1-wk washout period between treatments, the subjects were randomly assigned to consume 360 mL skim milk alone (placebo) or containing 0.5 or 1 g AEM at 30 min after ingestion of the meal. AEM was not completely soluble in skim milk, residual AEM in the glass was rinsed with water and completely consumed by each subject. Each subject was admitted to the Metabolic Research Unit in the morning after a 12-h overnight fast. Following a check of vital signs, an intravenous catheter was inserted into one forearm and a baseline blood sample was obtained. After drinking the test beverage in ~5 min, 8 blood samples were collected at 15, 30, and 45 min and at 1, 2, 3, 5, and 10 h. Lunch and dinner meals, designed to contain low flavonoids and meet the recommended dietary allowances for protein and energy (32), were provided under the supervision of a dietitian. Foods included for lunch were cream of mushroom soup, canned tuna, corn oil, fat-free mayonnaise, white bread, saltine crackers, ginger ale, and angel food cake. Foods included for dinner were turkey breast, cauliflower, corn oil, cooked white rice, baked potato, and butter. The same meals were served during each visit. These meals were provided at 4 and 9 h after consumption of the AEM. The consumption of water, salt, sugar, and ginger ale was unlimited, but food and other beverages were not allowed during the test period.

**Sample collection and storage.** The blood samples were collected using EDTA vacutainers via the forearm catheter and immediately processed. Whole blood samples were centrifuged at 1000 X g at 4°C for 15 min using a Sorvall RT6000 (Du Pont). Plasma aliquots of 1.5 mL were flushed with N2, stored at 4°C, and used for LDL oxidation assay within 3 d. An aliquot of plasma was treated with an equivalent volume of 3% hydrogen peroxide and 0.1 mL of 10% trichloroacetic acid, and centrifuged at 14,000 X g for 10 min at
After enzyme digestion, AV in plasma were extracted with acetonitrile; 500 μL was used to free AV from glucuronide and sulfate conjugates (34). Free AV were incubated at 37°C for 30 min before initiation of oxidation. Formation of conjugated dienes was monitored by absorbance at 234 nm at 37°C over 6 h using a UV1601 spectrophotometer (Shimadzu) equipped with a 6-position automated sample changer. The results of the LDL oxidation are expressed as lag time (defined as the intercept at the abscissa in the diene-time plot) (41).

**Pharmacokinetics and statistics.** All results are reported as means ± SEM. The maximum plasma concentration (Cmax) and the time to reach Cmax (Tmax) were determined. The area under the curve (AUC) of plasma AV concentration vs. time curve (0–10 h) was calculated using the linear trapezoidal integration (42). The elimination half-life (T1/2) was calculated as log10 conversion before statistical analysis. The differences in AUC, Tmax, and the log plasma AV concentration vs. time curve (43). The bioavailability of AV was estimated as the ratio of the AUC of plasma AV concentration to dose. The influence of AEM consumption on measured biomarkers was expressed as the percentage of change from the respective 0-h value (baseline) at each visit. The AUC for the percentage of change for each biomarker vs. time curve (0–10 h) was estimated using the same rule for plasma AV. All percentages of change and AUC data were normalized by a log10 conversion before statistical analysis. The differences in AUC, Tmax, Cmax, and bioavailability of AV between the 2 AEM doses were analyzed by 1-way ANOVA and the post hoc Tukey-Kramer honestly significant difference (HSD) test. Differences with P ≤ 0.05 were considered significant. The JMP IN 4 statistical software package (SAS Institute) was used to perform all statistical analyses.

**Results**

**Pharmacokinetics of oat AV.** After consumption of skim milk (control) or 0.5 or 1.0 g of AEM in milk, the total content of free plus conjugated AV concentration vs. time curve (0–10 h) was examined using a paired t test; the same approach was used to test differences in MDA, GSH, GSSG, and GSH/GSSG between the vehicle and 1-g AEM dose. These analytes were not measured in the 0.5-g AEM portion of the experiment because there were no effects when subjects consumed the 1.0-g AEM dose. Pharmacokinetic parameters, GPx, and LDL lag time were analyzed by 1-way ANOVA and the post hoc Tukey-Kramer honestly significant difference (HSD) test. Differences with P ≤ 0.05 were considered significant. The JMP IN 4 statistical software package (SAS Institute) was used to perform all statistical analyses.
plus conjugated AV-A, AV-B, and AV-C after glucuronidase/sulfatase hydrolysis were determined by HPLC-ECD. Three major AV present in the AEM were detected in plasma after administration, with no AV apparent at baseline (Fig. 2B). Although earlier time points were not assessed to determine the first appearance of AV in plasma, AV-A, AV-B, and AV-C were detected 15 min after AEM consumption at both doses (Fig. 3). Key pharmacokinetic parameters are summarized in Table 1. At 1.0 g AEM, the ranges of C\text{max} for AV-A, AV-B, and AV-C were 166.7 to 1002.2, 49.3 to 153.5, and 29.6 to 328.1 nmol/L, and at 0.5 g AEM the ranges were 50.2 to 226.3, 5.0 to 31.4, and 10.5 to 112.5 nmol/L, respectively. The C\text{max} of the AV-A, AV-B, and AV-C among the participants after consuming 1.0 g AEM were 231, 627, and 115% larger than after they consumed the 0.5 g AEM dose, respectively (P < 0.001). Although earlier time points were not assessed to determine the first appearance of AV in plasma, AV-A, AV-B, and AV-C were detected 15 min after AEM consumption at both doses (Fig. 3). Consistent with AV-A having the highest C\text{max}, its AUC was 2-fold larger than that of AV-C following the 1.0 g dose and 7-fold larger than that of AV-B following the 0.5 g dose (P < 0.05). The bioavailabilities of the AV were compared using the ratio of AUC to the amount of AV consumed. The AV-A bioavailability was 4-fold greater than that of AV-B following intake of 0.5 g AEM (P < 0.05), but did not differ significantly after the 1.0 g dose. The bioavailabilities of AV-A and AV-B were 0.9-fold and 3.4-fold larger, respectively, after the 1.0 g than after the 0.5 g AEM dose (P < 0.05). Based on a plasma volume of 40 mL/kg body weight in humans (44), plasma total AV contents at T\text{max} were 30.0 ± 0.07, 0.03 ± 0.01, 0.11 ± 0.01 μmol for AV-A, AV-B, and AV-C after the 0.5 g doses, and 1.01 ± 0.34, 0.27 ± 0.05, and 0.24 ± 0.13 μmol after the 1.0 g dose, respectively. The ratios of the total plasma content at T\text{max} to the respective oral doses were 0.39 ± 0.08, 0.06 ± 0.01, and 0.20 ± 0.07% for AV-A, AV-B, and AV-C after the 0.5 g dose; and 0.65 ± 0.20, 0.24 ± 0.04, and 0.21 ± 0.11% after the 1.0 g dose, respectively.

**Biomarkers of antioxidant capacity and lipid peroxidation.** Baseline plasma GSH and GSSG concentrations and the GSH/GSSG ratio were 1.02 ± 0.10 and 0.06 ± 0.01 μmol/L and 18.1 ± 2.7, respectively. After consumption of 1.0 g AEM, plasma GSH increased 21% from baseline at 15 min (P < 0.005) and then decreased toward the original concentration (Fig. 4). The AUC of the GSH time course was increased by the 1.0 g AEM dose (P < 0.05) (Table 3). Plasma GSSG and GSH/GSSG were not affected 10 h after AEM intake (data not shown), consistent with the AUC results. Plasma GPx activity was 138.8 ± 8.4 U/L at 0 h and increased 30–35% after each of the 3 treatments, suggesting a postprandial response of this antioxidant enzyme. The GPx AUC after the 3 treatments did not differ. Plasma MDA was 1.50 ± 0.14 μmol/L before AEM consumption and neither its concentration nor AUC were affected by the treatments. At 0 h, the lag time of LDL oxidation was 50.1 ± 6.98 min and was not extended by AEM intake. Similarly, the AUC of LDL oxidation lag time was not affected by the treatments. After the in vitro addition of 6 μmol/L α-tocopherol prior to Cu\textsuperscript{2+}-induced oxidation, the lag time of LDL oxidation at 0 h was extended from 50.1 ± 1.6 to 112.9 ± 4.4 min. Consistent with a T\text{max} at 3 h after AEM consumption, the lag times with added α-tocopherol after intake of 0.5 and 1.0 g AEM were 125.4 ± 13 and 116.8 ± 9.5% of that at 0 h, respectively, with 98.1 ± 3.8% after the skim milk vehicle (P < 0.1); there was no difference in the LDL lag time between the 2 AEM doses (Fig. 5). To reduce the influence of the variation in the baseline values, the percentage of change from 0 h was used to determine the change obtained with in vitro addition of α-tocopherol.

**Discussion** Among the monocot cereal grains, avenanthramides are unique to oats. Our results demonstrate the bioavailability and antioxidant actions of these naturally occurring phytochemicals in humans. At doses of 0.5 and 1.0 g AEM containing 187.5 and 374 μmol total AV, respectively, we found that these compounds...
TABLE 1 Pharmacokinetics of avenanthramides in older adults after acute intake of AV-enriched mixture

<table>
<thead>
<tr>
<th>AV-enriched mixture1</th>
<th>C&lt;sub&gt;max&lt;/sub&gt; (nmol/L)</th>
<th>T&lt;sub&gt;max&lt;/sub&gt; (h)</th>
<th>T&lt;sub&gt;1/2&lt;/sub&gt; (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.5 g</td>
<td>1.0 g</td>
<td>0.5 g</td>
</tr>
<tr>
<td>AV-A</td>
<td>112.9 ± 28.2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>374.6 ± 131.3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.3 ± 0.2</td>
</tr>
<tr>
<td>AV-B</td>
<td>132.3 ± 39.3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>96.0 ± 16.8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.0 ± 0.0</td>
</tr>
<tr>
<td>AV-C</td>
<td>414.0 ± 15.8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>89.0 ± 48.3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.3 ± 0.2</td>
</tr>
</tbody>
</table>

1 Values are mean ± SEM, n = 6. Means in column with superscripts without a common letter differ, P ≤ 0.05 (Tukey’s HSD test; C<sub>max</sub> data were log<sub>10</sub> transformed).<sup>a</sup>Different from the 10-g dose, P ≤ 0.001 (paired t test after C<sub>max</sub> data were log<sub>10</sub> transformed).

Despite their structural similarity, the T<sub>max</sub> of phenols can vary markedly. We have previously shown that p-coumaric and sinapic acids containing a hydroxycinnamoyl functional group had a different plasma concentration time profile in hamsters fed an oat extract; we also found different T<sub>max</sub> of catechin and epicatechin in hamsters fed an almond skin extract (30,33). The AV investigated in this study have the same basic structure with differences only in the hydroxycinnamic acid moiety with R<sub>3</sub> substitutions in AV-A, AV-B, and AV-C of H, OCH<sub>3</sub>, and OH, respectively (see Fig. 1). AV plasma C<sub>max</sub> were simply dependent upon the administered dose. In contrast, T<sub>max</sub> and T<sub>1/2</sub> were dependent on AV structure, with the OCH<sub>3</sub> group in the hydroxycinnamoyl moiety of AV possessing a shorter T<sub>max</sub> and longer T<sub>1/2</sub> than that of AV-A, which lacks this substitution and is thus more hydrophilic. The elimination AV from plasma followed first-order kinetics, further suggesting the dependence of T<sub>max</sub> and T<sub>1/2</sub> on the specific AV structure. Although plasma AV were higher after the 1.0 g than the 0.5 g dose, adjusting for dose with the use of the AUC to oral dose ratio revealed that the larger dose had a disproportionately greater bioavailability. This might be due to an insufficient capacity of the phase II metabolism toward AV; e.g., less AV-A and AV-B may be conjugated through glucuronidation and sulfation for urinary and/or biliary excretion. However, it is not clear why AV-C did not show a similar differentiation between doses. The smaller ratio of AUC to oral dose of AV-B than AV-A at the 0.5 g dose also suggests a dependence of bioavailability on AV structure, especially when the ortho position of the hydroxycinnamoyl moiety is substituted with an OCH<sub>3</sub> group. The mechanism by which this disparity occurs requires further research.

![FIGURE 4 Percentage of change from baseline in plasma GSH concentrations in older adults for 10 h after consumption of vehicle (0.0 g) or 1.0 g AEM. Values are mean ± SEM, n = 6. **Different from vehicle, P = 0.005 (paired t test; data were log<sub>10</sub> transformed).](image)

Bioavailability of oat avenanthramides

**TABLE 2** Bioavailability of AV in older adults after acute intake of AV-enriched mixture

<table>
<thead>
<tr>
<th>AV oral dose</th>
<th>AUC (nmol·h·L&lt;sup&gt;-1&lt;/sup&gt;)</th>
<th>Bioavailability by 10 h (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 g</td>
<td>1.0 g</td>
<td>0.5 g</td>
</tr>
<tr>
<td>AV-A</td>
<td>77.0</td>
<td>154.0</td>
</tr>
<tr>
<td>AV-B</td>
<td>55.0</td>
<td>109.0</td>
</tr>
<tr>
<td>AV-C</td>
<td>55.5</td>
<td>111.0</td>
</tr>
</tbody>
</table>

1 Values are mean ± SEM, n = 6. Means in column with superscripts without a common letter differ, P ≤ 0.05 (Tukey’s HSD test; C<sub>max</sub> data were log<sub>10</sub> transformed). Means in the same category and row differ, <sup>1</sup>P ≤ 0.05 and <sup>2</sup>P ≤ 0.001 (paired t test after AUC were log<sub>10</sub> transformed).
TABLE 3  Percent change from baseline in the AUC of plasma glutathione, malondialdehyde, and lag time of LDL oxidation in older adults after acute intake of AV-enriched mixture

<table>
<thead>
<tr>
<th>AEM, g</th>
<th>GSH</th>
<th>GSSG</th>
<th>GSH/GSSG</th>
<th>GPx</th>
<th>Lag time of LDL oxidation with vitamin E²</th>
<th>MDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>130 ± 37</td>
<td>934 ± 67</td>
<td>1070 ± 95</td>
<td>1340 ± 128</td>
<td>988 ± 13</td>
<td>997 ± 28</td>
</tr>
<tr>
<td>0.5</td>
<td>130 ± 37</td>
<td>934 ± 67</td>
<td>1070 ± 95</td>
<td>1340 ± 128</td>
<td>988 ± 13</td>
<td>997 ± 28</td>
</tr>
<tr>
<td>1.0</td>
<td>130 ± 37</td>
<td>934 ± 67</td>
<td>1070 ± 95</td>
<td>1340 ± 128</td>
<td>988 ± 13</td>
<td>997 ± 28</td>
</tr>
</tbody>
</table>

1 Values are mean ± SEM, n = 6. *Different from the 0 g dose, P ≤ 0.05, (paired t test; AUC data were log_{10} transformed).

2 α-tocopherol was added in vitro at a final concentration of 6 μmol/L.

3 Not determined.

The bioactivity of AV has been shown in vitro and in animal models. For example, AV modulates antioxidant defense enzymes in rats (27) and may contribute to the increased resistance of LDL to oxidation in hamsters (30). The antioxidant activity of AV is dependent upon their structure, with AV-C being more potent than AV-A and AV-B in AEM (25). We found AV and other constituents in AEM can affect antioxidant status in humans by increasing plasma GSH, although we did not determine whether this change resulted from an increase in hepatic release or synthesis, enhanced recycling, or some other mechanism. Interestingly, many flavonoids also increase plasma GSH concentration (52,53). However, the effect of AV and other constituents in AEM on other thiol/disulfide systems, e.g., thioredoxin and cysteine, remains to be tested. In this study, AV and other AEM constituents did not affect other measures of antioxidant capacity or lipid peroxidation, i.e., GPx, MDA, and LDL resistance to oxidation. However, providing α-tocopherol in vitro during the ex vivo assessment of LDL oxidizability, we found that vitamin E unmasked an AEM effect on LDL, particularly about the T_max. Thus, AV and other AEM constituents had an impact on the resistance of LDL to oxidation that was apparent in this situation probably only when interaction between in vitro added vitamin E and endogenous antioxidants in LDL occurred during the assay. Using the same approach in vitro, we showed a similar synergy between oat bran phenols and vitamin C and between almond skin phenols and vitamin E (30,33). The mechanism underlying this synergistic relation is still under investigation.

In considering the potential mechanisms of AV action, it is worthwhile noting that both AV and Tranilast have been reported to block the expression of vascular endothelial cell adhesion molecules and cytokines via inhibition of nuclear factor-κB (NF-κB) and its transcriptional coactivator (29,54), suggesting potential antiatherogenic activity. Interestingly, Tranilast has been tested in clinical trials for the prevention of restenosis and found to block the proliferation and deposition of vascular matrix fibroids and the migration of aortic smooth muscle cells into the vessel intima following arterial injury (48,55,56).

In summary, this randomized, crossover clinical trial showed that three AV, derived from oats, were bioavailable in humans with AV-A being the most bioavailable. The T_1/2 and T_max of AV were comparable, albeit with slight differences that depended upon dose and structure. AV and other AEM constituents after a single oral administration enhance some antioxidant defenses in vivo via increasing GSH status and acting in synergy with other antioxidants such as vitamin E. However, the antioxidant effect of chronic AV consumption in amounts relevant to current dietary intakes remains to be explored. As bioavailable and bioactive phytochemicals, AV and other AEM constituents may contribute to the health benefits associated with the consumption of oats. Further research on the metabolism of AV and on the bioavailability of related phenols from oats and other whole grains is warranted.

Acknowledgment

We thank Helen Rasmussen, RD, for her assistance in constructing the guidelines for the low flavonoid diet and counseling the subject volunteers.

Literature Cited


