Plant Foods and Herbal Sources of Resveratrol

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INTRODUCTION

Resveratrol (3,5,4′-trihydroxystilbene) is a phytoalexin, produced by plants in response to damage, particularly in grapevines (I), pines, and legumes (2). It is a member of the stilbene family and can be found in the cis or trans configurations, either glucosylated (see structures I–IV in Scheme 1) or in lower concentrations as the parent molecule of a family of polymers named viniferins. Stilbenes are reported to be potentially important cancer chemoprotective agents, being able to inhibit cellular events associated with carcinogenesis, including tumor initiation, promotion, and progression (3). trans-Resveratrol (I) and its glucoside (III) have also been proposed as contributors to the cardioprotective properties of red wine (2) as it has been shown that trans-resveratrol can inhibit LDL oxidation, the initial stage of the pathogenesis of atherosclerosis (2).

In countries with high intakes of soya-derived phytoestrogenic isoflavones, the development of osteoporosis, menopausal symptoms, and breast and prostate cancer are relatively rare (5). Resveratrol has also been reported to have estrogenic activity due to its structural similarity to the estrogenic agent diethylstilbestrol. Using estrogen-positive MCF-7 human breast cancer cells, trans-resveratrol was found to competitively inhibit binding of [3H]estradiol to type 1 estrogen receptors as well as activating the receptors. This ability to antagonize estrogen binding provides a rationale for the possible use of trans-resveratrol in the prevention or treatment of breast cancer (6).

Despite the varied, yet potent, biological activities of stilbenes, little attention has focused on their presence and concentration in the diet. The major dietary sources of stilbenes include grapes, wine, soy, peanuts, and peanut products (5) although they may also be ingested from herbal remedies. The current study was undertaken to determine levels of trans- and cis-resveratrol (I and II) and their glucosides (III and IV) in peanuts, black grapes, red wines, and the Itadori plant (Polygonum cuspidatum Sieb et Zucc), which is known in the U.K. as Japanese knotweed. It is an extremely noxious weed that has invaded many areas of Europe and North America. In its native Asia, Itadori root is dried and infused to produce a tea. Itadori means “well-being” in Japanese, and Itadori tea has been used for centuries in Japan and China as a traditional herbal remedy for many diseases including heart disease and stroke (7). The active agent is believed to be trans-resveratrol and its glucoside (2).

KEYWORDS: Stilbene; resveratrol; wine; grape; peanut; peanut butter; Itadori root

MATERIALS AND METHODS

Chemicals. trans-Resveratrol (I) was obtained from Sigma (Poole, Dorset, U.K.) and trans-resveratrol-O-β-D-glucoside (III) was supplied by Apin (Abingdon, Oxford, U.K.). Compound III was also isolated and crystallized from the root of P. cuspidatum supplied by the Weed

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Research Institute, Utsunomiya, Japan. The fresh root (ca. 1 kg) was chopped into small pieces and extracted first with methanol and then 80% aqueous methanol. The extracts were combined and reduced to an aqueous solution in vacuo. After the precipitated material was removed filtration, the filtrate was partitioned against diethyl ether after which the aqueous phase was kept in darkness at 4 °C for 4 days, allowing light brown crystals to form. The crude crystals were repeatedly recrystallized from aqueous methanol to give 1 H nuclear magnetic resonance (NMR) and 13 C NMR. 

Itadori Root

Table 1. Content of trans-Resveratrol and trans-Resveratrol Glucoside in Selected Tissues

<table>
<thead>
<tr>
<th>Sample</th>
<th>trans-resveratrol</th>
<th>cis-resveratrol</th>
<th>trans-resveratrol glucoside</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black Grapes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Merlot</td>
<td>0.5 ± 0.0</td>
<td>ND</td>
<td>7.3 ± 0.4</td>
<td>7.8 ± 0.4</td>
</tr>
<tr>
<td>Merlot</td>
<td>ND</td>
<td>ND</td>
<td>5.5 ± 0.3</td>
<td>5.5 ± 0.3</td>
</tr>
<tr>
<td>Cabernet Sauvignon</td>
<td>0.5 ± 0.0</td>
<td>ND</td>
<td>2.2 ± 0.4</td>
<td>2.7 ± 0.4</td>
</tr>
<tr>
<td>Cabernet Sauvignon</td>
<td>ND</td>
<td>ND</td>
<td>1.5 ± 0.1</td>
<td>1.5 ± 0.1</td>
</tr>
<tr>
<td>commercial root</td>
<td>523 ± 1</td>
<td>ND</td>
<td>1653 ± 2</td>
<td>2170 ± 9</td>
</tr>
<tr>
<td>young leaf</td>
<td>ND</td>
<td>ND</td>
<td>867 ± 17</td>
<td>867 ± 17</td>
</tr>
<tr>
<td>young stem</td>
<td>ND</td>
<td>ND</td>
<td>497 ± 4</td>
<td>497 ± 4</td>
</tr>
<tr>
<td>old leaf</td>
<td>ND</td>
<td>ND</td>
<td>370 ± 9</td>
<td>370 ± 9</td>
</tr>
<tr>
<td>old stem</td>
<td>ND</td>
<td>ND</td>
<td>83 ± 3</td>
<td>83 ± 3</td>
</tr>
<tr>
<td>Itadori Root</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>peanuts (boiled)</td>
<td>5.1 ± 2.8</td>
<td>ND</td>
<td></td>
<td>5.1 ± 2.8</td>
</tr>
<tr>
<td>peanut butter</td>
<td>0.3 ± 0.1</td>
<td>ND</td>
<td></td>
<td>0.3 ± 0.1</td>
</tr>
<tr>
<td>Peanut Productsb</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Data expressed as μg/g fresh weight ± SE (n = 3). cis-Resveratrol was quantified as trans-resveratrol equivalents; ND, not detected. From Sobolev et al. (15).*

HPLC Analysis of Samples. trans- and cis-Resveratrol in samples were analyzed on a 250 mm × 4.6 mm i.d., 5 μm ODS Hypersil (Shandon, Astmoor, U.K.) column, eluted at a flow rate of 1 mL/min with 25% acetonitrile in 0.5% aqueous formic acid using a photodiode array detector at 307 nm and a fluorimeter operating at excitation 298 nm and emission 385 nm. trans-Resveratrol-O-β-glucoside and its cis isomer were separated using a mobile phase of 17% acetonitrile in 0.5% aqueous formic acid (10) although subsequently only the trans isomer was detected in extracts that were analyzed.

RESULTS AND DISCUSSION

Levels of Stilbenes in Wines and Grapes. Grapes were found to contain mainly trans-resveratrol glucoside in concentrations ranging from 1.5 to 7.3 μg/g (Table 1). The aglycone trans-resveratrol was also present in two of the four grape samples at a concentration of 0.5 μg/g, while cis-resveratrol was not present in detectable amounts in any of samples that were analyzed. The stilbene content of grapes is dictated by three factors: cultivar, disease pressure, and time. The trans-resveratrol content of Californian table grapes, for instance, exhibits a ca. 20-fold variation between different clones. Levels of 0.16 μg/g have been reported in Crimson seedless grapes, as compared with 3.0 μg/g in Fantasia seedless grapes (11).
The present study found that trace levels of trans-resveratrol and related stilbenes were detected in red wines and peanut butter by other investigators. Table 2. Content of trans-Resveratrol and trans-Resveratrol Glucoside in Selected Beverages.

<table>
<thead>
<tr>
<th>Sample</th>
<th>trans-resveratrol</th>
<th>cis-resveratrol</th>
<th>trans-resveratrol glucoside</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>red wines</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pinot Noir, 1994 (California)</td>
<td>1057 ± 60</td>
<td>746 ± 9</td>
<td>ND</td>
<td>1803 ± 71</td>
</tr>
<tr>
<td>Cabernet Sauvignon, 1996 (Bulgaria)</td>
<td>672 ± 10</td>
<td>520 ± 16</td>
<td>189 ± 5</td>
<td>1380 ± 25</td>
</tr>
<tr>
<td>Merlot, 1994 (Chile)</td>
<td>48 ± 1</td>
<td>152 ± 5.3</td>
<td>ND</td>
<td>200 ± 3</td>
</tr>
<tr>
<td>Cabernet Sauvignon, 1995 (California)</td>
<td>53 ± 1</td>
<td>45 ± 1</td>
<td>ND</td>
<td>98 ± 3</td>
</tr>
<tr>
<td>Itadori tea</td>
<td>68 ± 1</td>
<td>ND</td>
<td>906 ± 3</td>
<td>974 ± 2</td>
</tr>
</tbody>
</table>

*Data expressed as μg/100 mL ± SE (n = 3); ND, not detected. cis-Resveratrol was quantified as trans-resveratrol equivalents.*

In addition to trans-resveratrol and its glucoside, cis-resveratrol was detected in red wines (Table 2). The total stilbene content of red wines ranged from as little as 98 μg/100 mL to over 1803 μg/100 mL, with cis- and trans-resveratrol each contributing a similar proportion. trans-Resveratrol glucoside was detected in only one sample (Cabernet Sauvignon, Bulgaria). Levels of stilbenes in red wine can vary depending on grape variety, vinification approach, and climate. In red wines, the majority of the stilbenes are present as aglycones rather than glucosides due to sugar cleavage presumably occurring during vinification. However, while many studies have confirmed the presence of cis-resveratrol, trans-resveratrol, trans-resveratrol glucoside, and other related stilbenes in red wine, they are generally found in lower levels than many other phenolics. For instance, total flavonoids in red wine can range from 550 to 6020 μg/100 mL, with total catechins and 9210–18 800 μg/100 mL for total hydroxycinnamates.

Levels of Stilbenes in Peanuts and Peanut Butter. Analysis of one sample of peanuts and another of peanut butter in the present study found that trans-resveratrol and its glucoside were present but in very small amounts below the 200 ng/g limit of quantification. Trace levels of trans-resveratrol and related stilbenes have, however, been quantified in peanuts and in peanut butter by other investigators, and these data are presented in Table 1.

Levels of Stilbenes in Itadori Plants and Tea. Leaf and stem tissue from both young and old Itadori plants collected in Glasgow were analyzed (Table 1). Only trans-resveratrol glucoside was detected, with higher concentrations found in young stem (497 μg/g) as compared to old stem tissue (83 μg/g). A similar pattern was noted with young and old leaf tissues. It is noteworthy that while Itadori tea contains predominately trans-resveratrol glucoside, the cis and trans aglycones predominate in red wines (Table 2). This discrepancy is perhaps surprising considering that Merlot and Cabernet Sauvignon grapes that were analyzed had a stilbene content of 1.5–55 μg/g as compared to 2170 μg/g for the Itadori root used to produce the tea. This apparent discrepancy is because ca. 100 g of grapes are used to produce 100 mL of wine while 100 mL of tea is made from only 1 g of Itadori root powder.

Absorption of Stilbenes. It is noteworthy that while Itadori tea contains predominately trans-resveratrol glucoside, the cis and trans aglycones predominate in red wines (Table 2). This difference may be important when the absorption and potential bioavailability of the stilbenes is considered. Despite the increasing interest surrounding trans-resveratrol and the other stilbenes, few studies have been carried out with animals or humans to investigate their absorption.
the glucuronide conjugate passes into the blood stream (20). This hypothesis is not in keeping with other reports on the presence of trans-resveratrol in kidneys, liver, and plasma of rats (18, 19). Further work is required on the absorption and metabolism of trans-resveratrol and its glucoside to clarify matters.

Speculation that trans-resveratrol is a biomedically active agent in red wine has led to the production of red wine extracts and stilbene capsules (www.newu.com, www.myvitanet.com). These have been marketed as a safe, alcohol-free source of resveratrol. Like red wine, Itadori tea contains high concentrations of stilbenes in the form of trans-resveratrol glucoside and for those who do not consume alcoholic beverages, it too may be a suitable source of resveratrol. However, before widespread use of the tea in the Western world can be recommended, the biological effects of other components present in the brew requires investigation. While there are many reports on the anticancer effects of resveratrol derivatives in in vitro test systems (3), little is known about their absorption, metabolism, bioavailability, and, more important, biological effects in vivo.

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