Pharmacokinetics of Enterolignans in Healthy Men and Women Consuming a Single Dose of Secoisolariciresinol Diglucoside

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ABSTRACT High concentrations of enterolignans in plasma are associated with a lower risk of acute coronary events. However, little is known about the absorption and excretion of enterolignans. The pharmacokinetic parameters and urinary excretion of enterodiol and enterolactone were evaluated after consumption of their purified plant precursor, secoisolariciresinol diglucoside (SDG). Twelve healthy volunteers ingested a single dose of purified SDG (1.31 μmol/kg body wt). Enterolignans appeared in plasma 8–10 h after ingestion of the purified SDG. Enterodiol reached its maximum plasma concentration 14.8 ± 5.1 h (mean ± SD) after ingestion of SDG, whereas enterolactone reached its maximum 19.7 ± 6.2 h after ingestion. The mean elimination half-life of enterodiol (4.4 ± 1.3 h) was shorter than that of enterolactone (12.6 ± 5.6 h). The mean area under the curve of enterodiol (1762 ± 1117 nmol/L·h) was twice as large as that of enterolactone (966 ± 639 nmol/L·h). The mean residence time for enterodiol was 20.6 ± 5.9 h and that for enterolactone was 35.8 ± 10.6 h. Within 3 d, up to 40% of the ingested SDG was excreted as enterolignans via urine, with the majority (58%) as enterolactone. In conclusion, a substantial part of enterolignans becomes available in the blood circulation and is subsequently excreted. The measured mean residence times and elimination half-lives indicate that enterolignans accumulate in plasma when consumed 2–3 times a day and reach steady state. Therefore, plasma enterolignan concentrations are expected to be good biomarkers of dietary lignan exposure and can be used to evaluate the effects of lignans.


KEY WORDS: • enterodiol • enterolactone • lignans • secoisolariciresinol diglucoside • bioavailability

Enterolactone and enterodiol, also called enterolignans, are phytoestrogens with structural similarity to endogenous estrogens. Enterolignans have demonstrated antioxidant and weak (anti-)estrogenic effects (1–4). They are capable of induction of NADPH:quinone reductase (phase II enzymes) (5) and can inhibit enzymes involved in the metabolism of sex hormones [e.g., SHBG, 5α-reductase, and 17β-hydroxysteroid dehydrogenase (6–8)]. Because of these activities, enterolignans may affect the development of chronic diseases. Epidemiological studies suggest that high plasma concentrations of enterolignans are associated with a lower risk of acute coronary events (9,10). Associations between enterolignans and cancer are unclear. Inverse associations were reported only for case-control studies (11–13), whereas no associations between enterolignans and breast or prostate cancer were found in 3 prospective studies (14–16) [reviewed by Arts and Hollman (17)]. Enterolactone and enterodiol are products of bacterial conversion of plant lignans in the human colon (18–20). Plant lignans are naturally occurring compounds that have a polyphenolic structure. Dietary sources of plant lignans are flax, grains, seeds, fruits and vegetables, olive oil, and beverages such as tea, coffee, and wine (21–28).

Secoisolariciresinol, one of the plant lignans, is converted to enterodiol and subsequently to enterolactone by intestinal bacteria (29) (Fig. 1). Matairesinol, another plant lignan, is converted directly to enterolactone. Other precursors of enterolignans are pinosinol, lariciresinol, isolariciresinol, and syringaresinol (30). Enterodiol and enterolactone are absorbed from the large intestine. They are mainly present as glucuronide and sulfate conjugates in body fluids and are excreted via urine (31). Due to different consumption patterns (32), variation in microflora, and use of antibiotics (19,33), among other things, plasma concentrations of enterodiol and enterolactone vary widely among people. We know little about the kinetics of absorption and distribution of enterodiol and enterolactone in the body.

To evaluate the exposure to enterolignans, data on the absorption, distribution, and excretion of enterolignans are needed. So far, no studies have been carried out with isolated lignans in humans, but several studies used lignan-rich foods. Plasma and urinary concentrations of enterolignans increased after eating flax or flax-containing products for several weeks (34–39). Two studies investigated the absorption and excretion of enterolignans after a single dose of lignan-rich foods. Nesbitt et al. (40) found a dose-dependent urinary excretion of enterodiol and enterolactone after consumption of 5, 15, or...
25 g ground flax. Plasma concentrations of enterolignans started to increase 9 h after intake and were still higher than baseline values after 12 and 24 h. In a study carried out by Mazur et al. (24), enterolactone plasma concentrations started to increase 8 h after consumption of 500 g of strawberries. Urinary excretion of enterolactone increased also, with the highest excretion between 25 and 36 h. In both studies no plasma samples were taken after 24 h, when enterolignan concentrations are probably still high. Furthermore, the investigators used foods that contain various precursors of enterolignans. They were not able to calculate pharmacokinetic parameters, such as the maximum concentration and mean residence time.

In the present study, we investigated the absorption and excretion of enterodiol and enterolactone in healthy men and women consuming a single dose of secoisolariciresinol diglucoside (SDG), which is the major lignan in flax. Based on a pilot study we designed an optimal sampling schedule, which covered the increase in plasma and urine concentrations of enterolignans and their return to baseline. This is the first report describing the pharmacokinetics of enterodiol and enterolactone.

FIGURE 1 Conversion of secoisolariciresinol diglucoside by bacteria in the colon.

### MATERIALS AND METHODS

#### Subjects.

The Medical Ethical Committee of the Department of Human Nutrition at Wageningen University approved the study, and all subjects gave their informed consent. Six men and 6 women participated in this study. The participants ranged from 18 to 25 y old. None of the subjects had diarrhea or had used antibiotics or other medication in the past 3 months, except for oral contraceptives or painkillers. All subjects were generally healthy (self-reported). The weight of the men was 73.0 ± 6.8 kg (mean ± SD), and the weight of the women was 67.6 ± 4.5 kg. Subjects in men was 21.5 ± 1.3 kg/m² and 23.5 ± 1.6 kg/m² in women. Subjects were excluded if their hemoglobin concentration was low (<7.5 mmol/L for women and <8.5 mmol/L for men) or if their urine contained traces of glucose or protein (test strip for rapid determination of protein and glucose in urine, Macherey-Nagel). Vegans, vegetarians (defined as persons who consume fish or meat less than once a week), and people consuming flax-containing supplements were excluded, as were pregnant or lactating women.

#### Diet.

To avoid interference from other dietary sources of lignans, the participants started a diet poor in lignans 7 d prior to the study and followed it throughout the experiment. The participants were given a list of lignan-containing foods and beverages and were asked to avoid them. They avoided dried fruits, berries, several vegetables (e.g., asparagus, broccoli, and zucchini), legumes, seeds and nuts (e.g., flax, sesame, and peanut), breakfast cereals, cereal and muesli bars, whole-grain products (e.g., rye bread, whole grain bread, and brown rice), olives, virgin olive oil, herbal tea, grape juice, and orange juice. Furthermore, they limited their consumption of black tea and coffee to a maximum of 2 cups (500 mL) a day. Consumption of selected wheat products (white bread, pasta), white rice, milk products (milk, yogurt, cheese), meat and fish, several fruits (e.g., apple, pear), and vegetables (e.g., cucumber, tomato, paprika, cabbage) was allowed so that, in principle, the intake of micro- and macronutrients was adequate. To ensure an adequate fiber intake, wheat bread with a low lignan content (37 g lignans/100 g bread) was supplied daily. Bread is an important source of fiber in the Netherlands. Every day a standard breakfast (low lignans) was provided at the Division of Human Nutrition. Lunch and dinner were also provided on the first 2 d of the study.

#### Lignan supplement.

On d 1 of the study after a 12-h overnight fast, the subjects consumed 1.31 μmol SDG/kg body wt (0.9 mg SDG/kg body wt) in water, just before having their breakfast at around 0800 h. SDG was obtained from the Institute of Food Chemistry, Technical University of Braunschweig. SDG was isolated from a natural source, i.e., flax (Linum usitatissimum L.) (41). For isolation, extraction, and purification of SDG only p.a. quality solvents (food grade) were used. In order to remove remaining traces of solvents the SDG extract was freeze-dried. The purity was above 93%. One day before consumption, the supplement was weighed, dissolved in 50 mL water, and then kept at −20°C. The supplement was thawed 1 h before consumption.

#### Collection of samples.

Venous blood samples were taken into vacuum tubes containing EDTA immediately before the intake of SDG (0 h), every 3 h over the next 36 h, and at time points 48, 72, and 96 h. Samples were centrifuged within 30 min at 1187 × g for 10 min at 4°C, and plasma was stored at −80°C until analysis.

Urinary samples were collected beginning 24 h prior to the intake of SDG until 72 h after the intake of SDG. The participants stored each bottle on dry ice immediately after voiding. Each day, urine samples were collected from the participants’ homes to the laboratory, where they were kept at −20°C. At the laboratory, urine samples were thawed and homogenized. To obtain 24-h urine samples, the samples of 1 d were pooled per subject.

#### Logistics.

During the study, blood samples t = 0–12 h and t = 24–96 h were taken at the Division of Human Nutrition at Wageningen University. Samples t = 15–21 h, which were collected during the night, were drawn at the hospital Gelderse Vallei in Ede, where the subjects stayed overnight. Volunteers were transported between the 2 sites under supervision of a research nurse.

#### Analytical methods.

Total enterodiol and enterolactone concentrations were measured in plasma and urine after hydrolysis of conjugates using a freshly prepared enzyme mixture of β-glucuronidase and β-glucuronidase (25). The plasma and urine concentrations of enterodiol and enterolactone were measured using high-performance liquid chromatography (HPLC). The HPLC method has been described in detail elsewhere (25). Briefly, the plasma and urine samples were hydrolyzed for 4 d at 2°C. The conjugated lignans were subsequently converted to their respective glucuronide and sulfate derivatives using a freshly prepared enzyme mixture of β-glucuronidase and β-glucuronidase. The enzymatic reaction was stopped after 12 d. After purification, the samples were reconstituted and diluted for analysis. The HPLC system consisted of a Waters 2695 system (Millipore, Billerica, MA) equipped with a Waters 474 system (Millipore). The samples were analyzed using a reverse-phase C-18 column (250 × 4.6 mm; particle size, 3 μm; Waters, Milford, MA) and the following mobile phase: 0.1 M potassium dihydrogenphosphate (pH 3.6) and acetonitrile (1:9, v/v). The flow rate was 1 mL/min, and the column temperature was 40°C. Absorbance was monitored at 280nm, and lignan concentrations were determined by using a calibration curve. Arachis hydrolysates were used as standards.

#### Abbreviations used:

- AUC, area under the curve
- SDG, secoisolariciresinol diglucoside
- SDG, secoisolariciresinol diglucoside
- RI, retention index

2 Abbreviations used: AUC, area under the curve; SDG, secoisolariciresinol diglucoside; t_{onset}, onset of the plasma curve.
dase sulfatase from Helix Pomatia (G1512, Sigma) in sodium acetate buffer (0.5 mol/L, pH 5.0).

**Urine analyses.** Quantification of enterodiol and enterolactone in urine was performed by HPLC with electrochemical detection as described previously (42). The original method was slightly modified. Briefly, 200 μL of urine was mixed with an equal amount of buffer and 40 μL of enzymes (50 μL/L). Subsequently, samples were incubated at 37°C for 2 h and extracted twice with diethyl ether. Prior to the analysis, extracts were filtered, transferred into vials, and injected into the HPLC system. To separate the enterolignans from other compounds, we used a binary gradient. Mobile phase A consisted of 15% acetonitrile in 50 mmol/L sodium acetate buffer (pH 5.0). Mobile phase B consisted of 60% acetonitrile in 50 mmol/L sodium acetate buffer (pH 5.0). A total of 100 μL extract was injected onto 2 Chromolith columns (100 × 4.6 mm each; Merck) in series. The gradient at a flow rate of 2.5 mL/min was as follows: 0–8.5 min, linear from 0 to 15% mobile phase B; 8.5–14.5 min, linear from 15 to 38% B; 14.5–14.7 min linear from 38% to 100% B; 14.7–16.7 min, isocratic at a flow rate of 2.5 mL/min was as follows: 0–1.0 min, isocratic at 10% B; 1.0–7.0 min, linear return from 10% to 100% B; 7.0–10.0 min, isocratic at 100% B to equilibrate. For detection and quantification of enterolignans, we used a 4-channel Coularray HPLC detection system. Enterodiol and enterolactone were quantified at 650 mV. Determinations in urine were carried out in duplicate. The limit of detection, i.e., the concentration producing a peak height 3 times the SD of the baseline noise, was 0.2 nmol/L for enterodiol and 0.6 nmol/L for enterolactone. The recovery of 10 nmol/L enterodiol and enterolactone aglycone was 98 ± 16% (mean ± SD, n = 6). The within-run CV was 6% for enterodiol and 3% for enterolactone (n = 6), and the between-run CV was 16–18% for both enterolignans (n = 12).

**Pharmacokinetic analysis.** A 1-compartmental pharmacokinetic model was used to describe the absorption and disposition of lignans (MW/Pharm, Mediware) (43). The area under the curve (AUC) for plasma was calculated using the trapezoidal rule. When participants followed a diet low in lignans for 7 d, total enterolignan concentrations in plasma were reduced by half (data not shown). However, due to the abundance of lignans in foods, plasma concentrations of enterodiol were not zero at the start of the study. Baseline plasma concentrations of enterodiol fluctuated between 0.3 and 12 nmol/L (mean 3.4 nmol/L), and concentrations of enterolactone fluctuated between 3.3 and 15 nmol/L (mean 7.2 nmol/L). To calculate the AUC and maximum concentration, baseline values for each person were subtracted from the crude pharmacokinetic parameters.

**Statistical analysis.** An independent t-test was used to study sex differences. Two-sided Pearson correlation coefficients were calculated. In all tests, differences were considered significant at P ≤ 0.05. Differences between enterodiol and enterolactone were not tested because the pharmacokinetic parameters are not independent. All statistical analyses were performed using the SPSS statistical software package (version 10.0). Data are means ± SD, unless stated differently.

**RESULTS**

Pharmacokinetic analysis of the plasma curves showed that it took ~8–10 h (Table 1) before both enterolignans appeared in plasma. Although the maximum plasma concentration of enterodiol (73 ± 40 nmol/L) was exceeded, the maximum plasma concentration of enterolactone (56 ± 30 nmol/L), the AUC of enterolactone (1762 nmol/L·h) was approximately twice that of enterodiol (966 nmol/L·h). As expected, we found clear differences in the plasma concentration-time course for enterodiol and enterolactone. The maximum concentration of enterodiol was reached 14.8 ± 5.1 h after consumption of SDG, while the maximum concentration of enterolactone was reached 19.7 ± 6.2 h postdose. In addition, the elimination half-life of enterodiol (4.4 ± 1.3 h) was much shorter than that of enterolactone (12.6 ± 5.6 h). The residence time of enterodiol was ~21 h and that of enterolactone was ~56 h.

Most of the enterolignans were excreted in urine within the first 2 d (Fig. 2). Within 3 d, up to 40% of the ingested SDG was excreted via urine, with the majority excreted (58%) as enterolactone (Fig. 3). The urinary excretion of enterolactone correlated very well with the amount of enterolactone in plasma, based on the AUCs (r = 0.673, P = 0.016). The correlation between the urinary excretion of enterodiol and the amount of enterolactone in plasma was not significant, but tended to be positive (r = 0.432, P = 0.16).

Although all subjects ingested the same dose of SDG per kilogram of body weight, there was a substantial variation among subjects in plasma concentration and urinary excretion of enterodiol and enterolactone (Figs. 2 and 4). In 5 subjects the AUC of enterolactone was more than twice that of enterodiol (Fig. 4A and B). In 5 other subjects the AUC of enterolactone was only ~1–2 times the AUC of enterodiol (Fig. 4C). In 2 subjects the AUC of enterodiol exceeded the AUC of enterolactone. In 1 of those subjects enterolignan concentrations hardly increased at all (Fig. 4D).

When data for men and women were analyzed separately, some pharmacokinetic parameters differed (Table 1). The onset of the plasma curve (t_{onset}) of both enterolignans tended to
be earlier in women than in men (enterodiol, $P = 0.06$; enterolactone, $P = 0.42$). This was in agreement with the time to reach the maximum concentration, which was earlier in women. Furthermore, the maximum concentrations of both enterolignans tended to be higher in women than in men (enterodiol, $P = 0.52$; enterolactone, $P = 0.11$). Additionally, the residence time of enterodiol and enterolactone was shorter in women than in men. The AUC and elimination half-life of both enterolignans did not differ between men and women.

**DISCUSSION**

Our study is the first pharmacokinetic study on enterodiol and enterolactone in humans consuming a single dose of purified SDG. A substantial part (at least 40%) of the metabolites of SDG, enterodiol and enterolactone, becomes available in the blood circulation and is subsequently excreted. Enterodiol and enterolactone are absorbed 8–10 h after consumption of SDG and eliminated slowly. The systemic exposure to enterolactone, as computed from the mean AUC, was approximately 2 times the exposure to enterodiol. This difference in systemic exposure might be explained by enterohepatic circulation. This causes enterodiol to reach the colon for a second time, where it is available for oxidation into enterolactone. As a result, predominantly enterolactone is absorbed. This is evidenced by the second peak of enterolactone, which was seen in 5 out of 12 subjects in this study. We did not observe a clear second peak of enterodiol in plasma in any of the subjects. Evidence for enterohepatic circulation of enterolignans has been demonstrated in rats (44) and pigs (45). Alternatively, the difference in systemic exposure between enterodiol and enterolactone might be explained by an efficient enterolactone production from enterodiol immediately after it is formed from SDG. A third option could be that enterolactone is more efficiently absorbed. However, the absorption half-life of enterolactone is longer than that of enterodiol, thus suggesting the opposite.

**TABLE 1**

Pharmacokinetic parameters of enterodiol and enterolactone in healthy men and women consuming a single dose of SDG1,2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Enterodiol</th>
<th></th>
<th>Enterolactone</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Males</td>
<td>Females</td>
<td>Total</td>
</tr>
<tr>
<td>$n$</td>
<td>12</td>
<td>6</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>$t_{lag}$, h</td>
<td>10.1 ± 4.3</td>
<td>12.5 ± 4.4</td>
<td>7.8 ± 2.9</td>
<td>8.3 ± 4.0</td>
</tr>
<tr>
<td>Absorption</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Half-life, $t_{1/2}$ (abs), h</td>
<td>2.8 ± 1.7</td>
<td>3.4 ± 1.8</td>
<td>2.2 ± 1.5</td>
<td>6.4 ± 4.3</td>
</tr>
<tr>
<td>$C_{max}$, nmol/L</td>
<td>73 ± 40</td>
<td>65 ± 33</td>
<td>81 ± 47</td>
<td>56 ± 30</td>
</tr>
<tr>
<td>$t_{max}$, h</td>
<td>14.8 ± 5.1</td>
<td>17.8 ± 4.1</td>
<td>11.7 ± 4.2*</td>
<td>19.7 ± 6.2</td>
</tr>
<tr>
<td>Elimination</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Half-life, $t_{1/2}$, h</td>
<td>4.4 ± 1.3</td>
<td>4.6 ± 1.1</td>
<td>4.1 ± 1.5</td>
<td>12.6 ± 5.6</td>
</tr>
<tr>
<td>AUC, nmol/L · h</td>
<td>966 ± 639</td>
<td>1019 ± 794</td>
<td>914 ± 511</td>
<td>1762 ± 1117</td>
</tr>
<tr>
<td>Mean residence time, h</td>
<td>20.6 ± 5.9</td>
<td>23.9 ± 4.7</td>
<td>17.3 ± 5.4*</td>
<td>35.8 ± 10.6</td>
</tr>
</tbody>
</table>

1 All values are means ± SD. * Different from males, $P ≤ 0.05$.
2 AUC and $C_{max}$ are corrected for baseline values. $t_{lag}$ is time to reach first appearance in plasma; $t_{1/2}$ abs is absorption half-life; $C_{max}$ is maximum plasma concentration; $t_{max}$ is time to reach $C_{max}$; $t_{1/2}$ is elimination half-life.

**FIGURE 2** 24-h urinary excretion of enterodiol and enterolactone from 12 healthy subjects consuming a single dose of SDG around 0800 h on d 1. Values are means ± SD, $n = 12$.

**FIGURE 3** Cumulative urinary excretion of enterodiol and enterolactone from healthy men and women consuming a single dose of SDG. Values are corrected for baseline concentrations and expressed as percentages of the ingested dose. Values are means ± SD, $n = 12$. 
The delayed appearance of enterodiol and enterolactone in plasma indicates that absorption of lignans occurs in the colon. Other studies observed the same delayed appearance of 8–9 h with lignan-rich products (24,40), suggesting that the food matrix did not play an important role in the release of enterolignans.

The difference in time to reach the maximum plasma concentration between enterodiol and enterolactone might be overestimated. Data points from the enterohepatic circulation (second peak) were used in the 1-compartmental model, and thus the time to reach the maximum plasma concentration might be overestimated, especially for enterolactone. A similar problem may have influenced the absorption and elimination half-lives. A specific kinetic model, which takes into account enterohepatic circulation, may lead to more precise kinetic parameters. However, this is only feasible when there are enough data points to calculate the enterohepatic contribution. This kind of experiment would impose a considerable burden to the volunteers involved. The order in which SDG is converted, SDG ➞ enterodiol ➞ enterolactone, is consistent with the difference in absorption half-life between enterodiol and enterolactone. In a number of subjects the absorption and elimination half-lives were identical for both compounds. This means that the absorption governs the elimination, that the intrinsic elimination of the compound is faster than measured here, and that the observed elimination half-life is apparent.

The difference between men and women in the time to reach the maximum plasma concentration might be explained by the smaller blood volume in women, even when adjusted for body weight (46), because the enterolignans are confined to the blood compartment. When this volume is smaller, enterolignans will reach maximum concentrations earlier, and maximum plasma concentrations will be higher.

We did not measure metabolites of SDG other than enterodiol and enterolactone or the plant lignan itself. Jacobs et al. (48) detected 9 hydroxylated metabolites of enterodiol and enterolactone in the urine of 4 humans ingesting flax for 5 d. These metabolites accounted for <3% of the total urinary lignan excretion. Additionally, enterodiol and enterolactone accounted for 82% of the total amount of lignans excreted in the urine of humans consuming their habitual diet (unpublished results, Tarja Nurmi, University of Kuopio, Finland). Thus, we expect enterodiol and enterolactone to be the main metabolites.

In 1 subject plasma concentrations of enterolactone did not increase after consumption of SDG, while plasma enterodiol concentrations did increase. The habitual concentrations of enterolactone, measured before the lignan-poor diet was begun, were also exceptionally low in this subject (3 nmol/L) compared to others (29 ± 7 nmol/L). The urinary enterolactone excretion after consumption of SDG was also low, only 4% of the ingested dose, whereas the total amount of enterolignans excreted was approximately the same as in other subjects. This suggests that this subject was not able to convert enterodiol to enterolactone, likely due to the absence of specific bacteria in the colon that are responsible for the oxidation of enterodiol. The enterolactone present was likely formed from other lignan precursors in the diet, such as matairesinol, which can be directly converted to enterolactone. A similar observation was made by Nesbitt et al. (40), who...
found that 2 of 9 subjects produced little or no entero-lactone during flaxseed supplementation for 7 d.

As demonstrated in other studies (37,40,49), we observed a wide variation in both urinary excretion and plasma concentrations of enterolignans among subjects. The variation is most likely due to differences in microflora between subjects. Other factors that could explain variation, such as background diet and age, were controlled for in our study. SDG was consumed purified; therefore, the food matrix could not have contributed to the variation either.

The health implications of the higher systemic exposure to entero-lactone than to entero-diol are not clear. Thus far, most studies investigated only the effect of entero-lactone. A few studies compared the effects of entero-lactone and entero-diol and showed that they have similar antioxidant activities (1,2). However, entero-lactone had a greater ability than entero-diol to inhibit the binding of estradiol and testosterone to sex steroid binding protein (50) or to inhibit human aromatase in vitro (51). Further studies are necessary to determine whether the physiological effects of entero-diol and entero-lactone are different. Therefore, investigators must quantify concentrations of entero-diol and entero-lactone in experimental and epidemiological studies in order to understand the metabolism and effect of both compounds. Furthermore, bioavailability studies for other important dietary enterolignan precursors, such as pinoresinol and lariciresinol, are needed. Whether the absorption, distribution, and elimination are influenced by other factors, such as food matrix, is also of interest.

Our data show that at least 40% of the ingested SDG is available for the body. The measured residence time and elimination half-life indicate that enterolignans will accumulate in plasma when consumed 2–3 times a day. Thus steady-state plasma concentrations of entero-diol and entero-lactone are likely to be achieved because plant lignans are present in many foods and beverages (21–26). As a result, plasma enterolignan concentrations are expected to be suitable biomarkers of lignan exposure and may be used to evaluate the effects of lignans.

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