Dietary Sesamin Is Converted to Enterolactone in Humans

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ABSTRACT Sesamin, a major sesame seed lignan, has many biological actions. The specific mechanisms for most of these actions as well as the full metabolic pathway of sesamin in humans are unclear. Two experiments were carried out to determine whether postprandial plasma enterolactone is related to sesamin concentration in sesame seeds and whether enterolactone is the major product of the in vitro fermentation of sesamin. Four subjects (3 women, 1 man) were given a single dose of sesame seeds after they consumed a low-lignan diet for 1 wk. Blood was collected at baseline and at time intervals after intake and plasma was analyzed for plant and mammalian lignan concentrations. Additionally, pure sesamin standard was incubated in vitro with human fecal inoculum to mimic the fermentation process in human gut. We calculated individual pharmacokinetic variables and found high interindividual variation in the plasma plant lignan concentrations. The mammalian lignan appearance rate in plasma shows that sesamin is a major precursor of enterolactone in vivo. In the in vitro experiment, enterolactone was the major metabolite and 3 intermediates were identified, allowing the elucidation of sesamin metabolism in humans. Enterolactone was the major metabolite of sesamin both in vivo and in vitro. The abundance of sesamin in sesame seeds indicates that they are a major food source of enterolactone precursors.

KEY WORDS: enterodiol • enterolactone • lignans • sesame seed • sesamin

Enterolactone is the major end-product of dietary lignan fermentation by mammalian intestinal microflora (1–3). Laboratory and epidemiological data have shown that high plasma and urinary concentrations of enterolactone are inversely correlated with the risk for developing certain chronic diseases, such as cancer and coronary heart disease (4–8). Sesamin, a furanofuran-type lignan, has been identified in several species of Piper genus (9) and from the stem and/or root bark of different tree species (10–13), although the highest concentrations are found in sesame (Sesamum indicum L.) seeds (14,15). Various biochemical actions, mainly related to lipid metabolism, have been attributed to sesamin; they include: specific inhibition of Δ5-desaturation of (n-6) fatty acids (16,17) that interrupt the formation of proinflammatory 2-series prostaglandins (18); hypcholesterolemic activity via inhibition of cholesterol synthesis and absorption (19); antihypertensive effect (20–23); protection against ethanol and carbon tetrachloride-induced liver damage (24); synergy with vitamin E (25); improvement of the bioavailability of vitamin D (26); and a suppressive effect against induced carcinogenesis in animals (27). The mechanisms for some of these effects are unknown, but it has been suggested that sesamin may act as a proacitive substance in the body (28) and that only its metabolites are responsible for the physiological effects observed.

We hypothesized that sesamin could metabolize to enterolactone, and we used 2 different approaches to test this. The in vivo formation of mammalian lignans after intake of a single dose of sesame seeds was studied by examining the plasma levels of lignans in 4 subjects. To compare these levels with the intake, the plant lignan content of the sesame seeds was characterized and quantified. Furthermore, in vitro metabolism of sesamin was studied by fermentating pure standard with human fecal microflora for 24 h.

SUBJECTS, MATERIALS, AND METHODS

Subjects

The human study design (protocol 361/E5/03) was approved by the Ethics Committee for the Department of Medicine, Hospital District of Helsinki and Uusimaa. Four healthy volunteers (3 women and 1 man, S1 to S4) 43.5 ± 16.8 y old with BMI 22.6 ± 2.83 kg/m² were selected among the staff members of the IPMNC (Folkhalsan Research Center). None of the subjects had undergone antibiotic treatment during 1 y preceding the sample collection.

Dietary intervention

Participants were requested to maintain a diet low in lignans for 1 wk prior to the sesame seed supplementation study. An informative sheet with the foods to be avoided (29–31) was provided for each subject. Whole grain products, seeds and nuts, legumes, berries, most vegetables and fruits, tea, beer, and wine were particularly avoided. After this food restriction period, subjects consumed a single dose of sesame seeds and continued the restricted diet for 24 h, after which the samples were collected. Whole, nonroasted sesame (S. indicum L.)
seeds were purchased from a local store in Helsinki. The sample was kept at constant temperature and humidity until use, at which time 50 g of seeds was crushed (A11 Basic Homogenizer, Ika-Werke Gmbh) and given to the participants.

Collection and storage of plasma samples

Blood samples were collected from each participant at the beginning of the low-lignan diet period (initial) and before supplementation (0 h) to test the efficacy of the restricted diet. Following supplementation with sesame seeds, samples were collected at 0.5, 1, 2, 4, 8, 10, and 24 h via catheter from the brachial vein into evacuated tubes with heparin. Blood samples were cooled to room temperature and centrifuged (10 min, 2000 \(g\)) to separate the plasma (15–20 mL), which was stored at \(-20^\circ\)C until analysis.

Fecal fermentation

The incubation method of Aura et al. (32) was modified as follows: a carbonate-phosphate buffer solution with trace elements was maintained in an anaerobic chamber for 2 d prior to fermentation. A quantity of 1.89 mg of sesamin was dissolved in 1 mL of methanol, from which 100 \(\mu L\) (corresponding to 0.5 \(\mu mol\)) was placed into 50-mL glass vials. After evaporation of the methanol, bottles were transferred to the anaerobic chamber where 5 mL of fecal suspension was added. Feces were collected from 3 healthy human volunteers, who consumed a Western diet, presented no digestive diseases, and had not received antibiotics for at least 3 mo prior to the study. Freshly passed feces were immediately taken in an anaerobic chamber, pooled, and homogenized at the same time with an equal weight of culture medium using a Waring blender. The slurry was diluted to 5.0% (w:w) with culture medium, filtered through a 1-mm sieve, and used immediately as inoculum. Bottles were closed tightly to ensure anaerobic conditions. Duplicate samples and blanks (only fecal suspension) were incubated with magnetic stirring for 24 h at 37°C. The fermentation was terminated by immersion of the vials in liquid nitrogen, and subsequently samples were freeze-dried and stored at constant temperature and humidity.

Analytical methods

**Reference compounds.** Plant-isolated standards of sesamin (Ses),\(^3\) and lariciresinol (Lar) were provided by Prof. Nishibe (Department of Pharmacognosy, University of Hokkaido) and Dr. Deyama (Yomeishu Seizo). Pinoresinol (Pin) and syringaresinol (Syr) were synthesized by Dr. Botting's group (School of Chemistry, University of St. Andrews). Synthetic standards of isolariciresinol (IsoL, or cyclolariciresinol), matairesinol (Mat), secoisolariciresinol (Seco), anhydrosecoisolariciresinol (Anse, or shonanin), enterolactone (Enl), and enterodiol (End) as well as the deuterated standards \(^2H_6\)-matairesinol, \(^2H_6\)-secoisolariciresinol, and \(^2H_6\)-anhydrosecoisolariciresinol were provided by Prof. Wåhlin (Laboratory of Organic Chemistry, University of Helsinki). \(^7\)-hydroxymatairesinol (Hmr) was a gift from Hormos Medical (Fig. 1). All standards for quantitative analysis were dissolved in methanol.

**Lignans in sesame seed.** The lignan content of the sesame seeds was determined using a modified gas chromatography-mass spectrometry (ID-GC-MS) method described earlier (33). Approximately 50 mg of sample was first extracted twice with a mixture of acetone/water in order to release the nonconjugated fraction of lignans as well as those conjugated forms that are easily extractable, i.e., not strongly bound to the matrix (34). One aliquot of the supernatant was added with deuterated internal standards and directly transferred to the GC-MS system for analysis. A second aliquot from the supernatant and 1 aliquot of the residue underwent further treatment as described (35) after addition of the internal standards. After the sample pretreatment, the extracts were derivatized with quick silylation mixture (QSM) (pyridine/hexamethyldisilazane/trimethylchlorosilane, 9:3:1) and aliquots of 1 \(\mu L\) were injected into the GC-MS system (Fisons Instrumentation) as reported (35).

\(^3\)Abbreviations used: Anse, anhydrosecoisolariciresinol; End, enterodiol; Enl, enterolactone; Hmr, \(^7\)-hydroxymatairesinol; IsoL, isolariciresinol; Lar, lariciresinol; Mat, matairesinol; Pin, pinoresinol; QSM, quick silylation mixture; Seco, secoisolariciresinol; Ses, sesamin; Syr, syringaresinol.

**FIGURE 1** Chemical structures of the plant lignans identified in sesame seeds and the mammalian lignans enterodiol and enterolactone.
**TABLE 1**

Lignan concentration of nonroasted, whole sesame seeds

<table>
<thead>
<tr>
<th>Lignan</th>
<th>Seco$^1$</th>
<th>Syr</th>
<th>Mat</th>
<th>Hmr</th>
<th>Lar$^2$</th>
<th>Pin</th>
<th>Ses</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free fraction</td>
<td>0.02</td>
<td>—</td>
<td>3.77</td>
<td>33.9</td>
<td>90.8</td>
<td>191</td>
<td>9590</td>
<td>9880</td>
</tr>
<tr>
<td>Total lignans</td>
<td>0.41</td>
<td>0.89</td>
<td>20.5</td>
<td>33.9</td>
<td>150</td>
<td>723</td>
<td>9590</td>
<td>10870</td>
</tr>
</tbody>
</table>

$^1$ Sum of Seco and Anse.
$^2$ Sum of Lar and IsoL.

**Lignans in plasma and fecal fermentation samples.** Determination of plant and mammalian lignans in human plasma was carried out by HPLC with coulometric electrode array detector following a previously published method (36). For the quantification of Ses in plasma, 500 μL of sample was extracted twice with 3 mL of diethyl ether in Vortex. Organic phases were pooled, evaporated under N$_2$ flow, and redissolved in 100 μL methanol. Extracts were purified in C$_{18}$-cartridges (Waters) with 6 mL methanol elution, evaporated to dryness, and redissolved in 100 μL QSM to be injected into the GC-MS under the same conditions described above except for the oven temperature program, which was 170°C (for 1 min), increased 50°C/min to 230°C, increased 1°C/min to 247°C, and finally increased 20°C/min to 280°C and kept for 5 min. Injection volume was 2 μL. Identification of the metabolites formed during the in vitro fecal fermentation of sesamin was performed by GC-MS as described earlier (2).

**Data analysis**

Noncompartmental pharmacokinetic analysis of the data was conducted with PK Solutions 2.0 (Summit Research Services). A best-fit line was calculated after assessment of the residuals and visual inspection of the line. Values are means ± SEM, n = 3. Comparison of the means was carried out using ANOVA and Tukey’s HSD test at $\alpha = 0.05$ with SPSS for Windows 11.0.

**RESULTS**

The total concentration of lignans in the sesame seed sample was ~373 mg/100 g (10.8 nmol/g) and was characterized by a high content of nonconjugated lignans. In addition to sesamin, whose chemical structure does not permit conjugation, almost 35% of the lignans appeared in a free form, being liberated from the matrix after the first organic (acetone/water) extraction. Ses and Hmr were found only in free form, Lar was mainly found in free form, and Pin, Mat, and Syr appeared mostly after the hydrolysis of the residue and therefore they probably were conjugated in sesame seeds (Table 1). During the sample pretreatment Seco was converted to Anse (33), and Lar was converted to IsoL due to the acidic conditions during the process. The extent of these conversions cannot be defined because it varied depending on the matrix and therefore the results were expressed as the sum of the correspondent plant lignan forms (Table 1). Two isomers of sesaminol (Fig. 1), appearing in considerable amounts in the hydrolyzed residue, were tentatively identified (M$^+$ 442, base peak m/z 149, retention times 19.8 and 20.4 min), although their quantification was not possible due to the lack of a standard.

Only the mammalian lignans End and Enl were found in the prechallenge samples (initial diet) of all participants. Concentrations of End and Enl were 4.10 ± 4.50 and 45.9 ± 58.5 nmol/L. S1 had low plasma concentrations of Seco (3.70 nmol/L) and Mat (3.30 nmol/L), and S2 had Seco (5.30 nmol/L) and Pin (2.20 nmol/L) in plasma. After the food restriction period (0 h time point), enterolactone levels were reduced 77%, with concentrations varying from 0.60 to 9.90 nmol/L (S1 and S4, respectively). No other lignans were detected in plasma after the food restriction period. Values of 0 h time point were subtracted from the values at the different time points. Ten different lignans were quantified in the subsequent plasma samples (Fig. 2) and mean pharmacokinetic parameters were calculated from the individual values (Table 2). Values for Anse were added to those of Seco and similarly IsoL values were added to Lar. Most of the plant lignans quantified reached their maximum concentration in plasma before 2 h and Pin, Mat, Hmr, and Ses were more...
Syr, which are common plant lignans in other grains. Concentrations of Seco and Anse are low. Hmr, a compound thought to be mainly present in knot heartwood (3) and for which chemopreventive properties have been described (41,42), was present in considerable amounts.

The main metabolite after 24 h fermentation of the pure sesamin standard with human intestinal microflora was Enl, but some other intermediates were also identified (Table 3). Metabolites eluting at retention times 6.9 and 7.6 min were identified using authentic reference compounds as End and Enl, respectively. Three other metabolites named M1, M2, and M3 at retention times 14.0, 16.0, and 19.7 min were tentatively identified by interpretation of their trimethylsilylated mass spectra (Fig. 3).

DISCUSSION

Sesame seeds are a rich source of lignans. In addition to sesamin, other lignans such as sesamolin, sesaminol, sesamolinol, and Pin have been isolated from sesame seed or sesame seed oil (37), although a more complete characterization of the sesame seed lignan fraction has not been published before. In our study, Pin, Lar, Hmr, Mat, Syr, and Seco were quantified. Flaxseed is the richest known source of mammalian lignan precursors (31), but our study shows that sesame seeds may contain comparable or even higher amounts of plant lignans, mainly Ses, but also Pin, Lar, and Hmr, which are converted to enterolactone. This can be important when the worldwide use of sesame seeds as a food and as an oilseed is considered. Ses is a lipophilic lignan and it is extracted together with the oil in the unsaponifiable fraction (44), resulting in sesame oil very rich in lignans. Seco appears in flaxseed as a diglucoside, being part of the complex phenolic polymers that are insoluble in oil matrices, and therefore flaxseed oil may contain negligible amounts of lignans compared to sesame oil.

Plant lignans undergo extensive metabolism in the intestine that depends on the individual characteristics of the intestinal microflora. Although some pathways of lignan metabolism in the gut have been elucidated (2,3), the extent and rate of in vivo conversion have not yet been defined and very little is know of the absorption process. Individual characteristics of the intestinal microflora can explain the high inter-

<table>
<thead>
<tr>
<th>Lignan</th>
<th>( t_{1/2a}^2 )</th>
<th>( t_{max}^3 )</th>
<th>( C_{max}^4 )</th>
<th>( t_{1/2e}^5 )</th>
<th>AUC ( ^6 )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>h</td>
<td>nmol/L</td>
<td>h</td>
<td>nmol \cdot h/L</td>
<td></td>
</tr>
<tr>
<td>Ses</td>
<td>0.24 ± 0.01</td>
<td>1.00 ± 0.00</td>
<td>105 ± 11.7</td>
<td>2.08 ± 0.58</td>
<td>362 ± 92.0</td>
</tr>
<tr>
<td>Pin</td>
<td>0.26 ± 0.11</td>
<td>1.13 ± 0.63</td>
<td>209 ± 93.3</td>
<td>4.30 ± 1.27</td>
<td>689 ± 90.5</td>
</tr>
<tr>
<td>Lar ( ^7 )</td>
<td>0.72 ± 0.28</td>
<td>5.50 ± 1.50</td>
<td>54.3 ± 3.18</td>
<td>4.32 ± 1.39</td>
<td>438 ± 54.1</td>
</tr>
<tr>
<td>Hmr</td>
<td>0.46 ± 0.07</td>
<td>1.25 ± 0.50</td>
<td>103 ± 34.0</td>
<td>5.94 ± 3.15</td>
<td>451 ± 134</td>
</tr>
<tr>
<td>Mat</td>
<td>0.56 ± 0.55</td>
<td>1.75 ± 1.50</td>
<td>156 ± 119</td>
<td>3.22 ± 0.40</td>
<td>868 ± 308</td>
</tr>
<tr>
<td>Seco ( ^8 )</td>
<td>1.45 ± 0.59</td>
<td>6.25 ± 2.25</td>
<td>40.2 ± 23.8</td>
<td>nc ( ^9 )</td>
<td>nc</td>
</tr>
</tbody>
</table>

1 Values are means ± SEM, \( n = 4 \).
2 Absorption half-life.
3 Time needed to maximum plasma concentration.
4 Maximum plasma concentration.
5 Elimination half-life.
6 Area under the curve (observed area).
7 Sum of Lar and IsoL.
8 Sum of Seco and Anse.
9 Noncalculated values. Seco presented a plateau or a secondary absorption phase in all subjects.

Mass spectra of metabolites of sesamin identified in 24-h fecal fermentation extracts

<table>
<thead>
<tr>
<th>Lignan</th>
<th>RT</th>
<th>( M^+ )</th>
<th>Ion, abundance</th>
</tr>
</thead>
<tbody>
<tr>
<td>End</td>
<td>6.9</td>
<td>590</td>
<td>147(14), 165(7), 180(100), 217(25), 231(33), 410(18)</td>
</tr>
<tr>
<td>Enl</td>
<td>7.6</td>
<td>442</td>
<td>149(9), 165(12), 180(100), 193(3), 205(7), 263(5), 442(6)</td>
</tr>
<tr>
<td>M1</td>
<td>14.0</td>
<td>560</td>
<td>135(25), 149(31), 179(34), 203(16), 267(21), 310(100), 470(5), 560(4)</td>
</tr>
<tr>
<td>M2</td>
<td>16.0</td>
<td>486</td>
<td>128(1), 149(77), 161(47), 193(60), 271(16), 281(20), 293(22), 468(49)</td>
</tr>
<tr>
<td>M3</td>
<td>19.7</td>
<td>618</td>
<td>179(46), 193(20), 267(50), 281(100), 293(42), 310(18), 335(10), 618(21)</td>
</tr>
</tbody>
</table>
subject variation in plasma plant lignans. We found high plasma concentrations of Pin, in agreement with its predominance in sesame seeds. It seems that no Pin precursor exists in sesame seeds because the intersubject variability is much lower compared to that of the other lignans (Table 2). For other lignans it is not possible to deduce whether their plasma concentrations are attributable to their presence in sesame seeds or to metabolic conversions in the gut. Plasma Seco concentrations vary greatly because its amount in plasma depends on the rate of precursor conversion by individual intestinal microflora. It was not possible to calculate the elimination rate and AUC for Seco due to the appearance of a second absorption phase in most of the subjects. No conversions of Seco to Anse or Lar to Isol during the plasma sample pretreatment were reported (36) and the quantified levels should reflect the actual plasma concentrations. However, we decided to express the values of Seco and Lar as the sum of the correspondent forms in order to simplify the data treatment. Anse and Isol could have been formed by the action of intestinal microflora and subsequently absorbed. This should be taken into consideration when studying samples containing larger concentrations of Seco and Lar. Considerable amounts of plant lignans exist in plasma after sesame seed intake, suggesting a possible physiological role of these compounds in vivo.

This study aimed to determine how a challenge with sesame seeds modifies the levels of lignans in humans consuming their normal diets. The time points selected in this trial were appropriate for the rapidly absorbed plant lignans but not sufficient for the mammalian lignans. During the interval from 10 to 24 h, mammalian lignan concentrations could have reached their maximum, and our 24-h data could represent the plateau or even the elimination phase. Further studies are required to cover this interval, as well as to show continued elimination. Nevertheless, it can be seen that mammalian lignans did not appear in plasma before 8 h after the intake of sesame seeds. When mean levels of Enl and End are compared, the high interindividual variation is evident (Table 4). However, this variation is much smaller considering total mammalian lignan concentration (1073–1547 nmol/L; median 1223 nmol/L). The production of enterolactone in humans intrinsically depends on intestinal microflora characteristics, but the extent of conversion at 24 h seems to be the same when both mammalian lignans are considered.

Increased amounts of mammalian lignans in plasma after several days of food (flaxseed) supplementation have been published before (45–48), but very few studies have investigated the appearance of mammalian lignans in plasma immediately after supplementation. Nesbitt and co-workers (49) provided 25 g raw flaxseed to 9 volunteers, and there was an increase in mammalian lignans in plasma at 9 h, reaching a plateau until 24 h (last sample collection) when the mammalian lignan concentration was approximately 2-fold higher than at baseline. In our experiment, when the concentrations of the initial diet (9.90–143 nmol/L, median 25.3 nmol/L) were compared with the concentrations at 24 h, the mean increment in plasma mammalian lignans was 50-fold. These results suggest that sesame seeds contain a major source of Enl, apparently Ses, which is very efficiently converted to enterolactone.

Plant synthesis of sesame seed lignans was recently studied (50), and Pin was identified as a precursor of Ses. Pin could be an intermediate of Ses breakdown in humans, but the maximum plasma concentrations of the plant lignans, including

![FIGURE 3](https://academic.oup.com/jn/article-abstract/135/5/1056/4663897)

**FIGURE 3** Total ion current chromatograms of 24-h fermentation extracts of (A) fecal blank and (B) pure sesamin standard and chemical structures of the main metabolites (in addition to Enl and End) of Ses tentatively identified as (M1) 3',4'-methylendioxy-7,9'-epoxy lignane-3,4,9-triol or 3,4'-methylendioxy-7,9'-epoxy lignane-9,3',4'-tetraol, (M2) 3,4'-methylendioxy-7,9'-7,9'-9-diepoxy lignane-3,4-diol, and (M3) 7,9'-7,9'-diepoxy lignane-3,4,3',4'-tetraol.

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### TABLE 4

Plasma lignan concentrations at 3 time points in 4 subjects who consumed a single portion of sesame seeds

<table>
<thead>
<tr>
<th>Time point</th>
<th>Enl</th>
<th>End</th>
<th>Enl + End</th>
<th>Ses</th>
<th>Plant lignans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial(^4)</td>
<td>45.9 ± 29.6(^a)</td>
<td>4.06 ± 2.24(^a)</td>
<td>49.9 ± 28.6(^a)</td>
<td>—</td>
<td>6.50 ± 3.03(^a)</td>
</tr>
<tr>
<td>0 h</td>
<td>4.25 ± 2.52(^a)</td>
<td>0.43 ± 0.43(^a)</td>
<td>4.67 ± 2.85(^a)</td>
<td>—</td>
<td>0.90 ± 0.52(^a)</td>
</tr>
<tr>
<td>(t_{max})(^5)</td>
<td>567 ± 324(^b)</td>
<td>699 ± 238(^b)</td>
<td>1286 ± 100(^b)</td>
<td>105 ± 11.7</td>
<td>605 ± 104(^b)</td>
</tr>
</tbody>
</table>

1 Values are means ± SEM, \(n = 4\).
2 Means in a column without a common letter differ, \(P < 0.05\). Values in rows were compared by Tukey’s test (multiple comparison of means).
3 Sum of the plant lignans present in plasma at each time point.
4 Normal diet values, prior to the low-lignan diet period.
5 Time of peak plasma concentration.
Pin, in the present study do not support this idea. Ses seems to be metabolized by an alternative pathway that does not involve the plant lignans studied in this trial. In vitro metabolites M1, M2, and M3 found together with End and Enl support the idea of a different pathway; the structures of the metabolites M2 and M3 are identical to the metabolites identified in vitro by Nakai and co-workers (28), who postulated that Ses is absorbed in the intestine and selectively captured in the liver due to its hydrophobicity and metabolized to M2 and M3. In our study the same metabolites were found after fermentation with human microflora, suggesting that oxidative demethylation to afford catechol groups is not an exclusive process of the dependent mixed function oxidases. Additionally, Ses bioavailability was limited, with only moderate concentrations found in plasma after sesame seed intake. These findings suggest that Ses is not completely absorbed as such but is metabolized by the intestinal microflora to a series of demethylated intermediates (M2 and M3) that might be absorbed as such or transformed in situ to mammalian lignans, which will be subsequently absorbed. The Ses fraction absorbed might undergo metabolism in the liver, explaining previous results (28). These findings are in contrast with previously reported studies in which Ses was present in high amounts in plasma of rats fed pure compounds (51) and recently in serums of mice and rats (52). In the report of Hirose and co-workers (53), Ses was not found in the serum of male rats after the intake of sesame-supplemented diets and a very limited absorption of Ses to the lymph and fecal excretion of 15–34% has been reported, supporting our idea of the transformation of Ses by the intestinal microflora. A selective absorption of sesamin through the portal vein and metabolism in the liver to compounds M2 and M3 (28) that could go under enterohepatic circulation and be deconjugated, demethylated, and transformed to mammalian lignans is also possible, and human metabolism of Ses might be a combination of the 2 mechanisms described. Further experiments should be carried out in order to completely understand the pathway. However, Enl, independent of the intermediates, is the final product of this process and this should be taken into account when physiological actions of Ses are considered.

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LITERATURE CITED


