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Bioavailability and Tissue Distribution of Sesamol in Rat

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Sesamol, generally regarded as the main antioxidative component in sesame oil, can be generated from sesamolin by roasting sesame seed or bleaching sesame oil. This paper reports the bioavailability of sesamol in Sprague−Dawley (SD) rats. Biological fluid was sampled following a dose of sesamol of 50 mg/kg by gastric gavage (po) or by intravenous injection. The pharmacokinetic data of sesamol were calculated by noncompartmental model. The tissue distribution of sesamol (po, 100 mg/kg) in SD rats was also investigated. The concentration changes of sesamol were determined in various tissues and plasma within a 24 h period after oral administration of sesamol. The results showed that the oral bioavailability of sesamol was 35.5 ± 8.5%. Sesamol was found to be able to penetrate the blood−brain barrier and go through hepatobiliary excretion. Sesamol conjugated metabolites were widely distributed in SD rat tissues, with the highest concentrations in the liver and kidneys and the lowest in the brain. It is postulated that sesamol is incorporated into the liver first and then transported to the other tissues (lung, kidneys, and brain). The major metabolites of sesamol distributed in the lung and kidney were glucuronide and sulfate.

KEYWORDS: Sesamol; bioavailability; tissue distribution; glucuronide; sulfate

INTRODUCTION

Sesame (*Sesamum indicum* L.) is rich in nutrients and has long been regarded as one of the functional foods for nutritional supplement and the delay of aging in the Eastern world. Sesame seed and its oil are used for human consumption worldwide in various forms. Sesame seed oil contains sesamolin, sesamin, and sesamol (392, 238, and 11.5−16.1 mg/l00 g of oil, respectively) (*1*). Sesamol is also formed by thermal hydrolysis of sesamolin. Sesamol has been found to be a good antioxidant in lard and hydrogenated vegetable oils (*2*). A recent study reported the anti-photooxidative activity of sesamol due to its ability in scavenging singlet oxygen (*3*). Sesamol has a phenolic and a benzodioxole group in its molecular structure. The phenolic groups of molecules are generally responsible for the antioxidant activity of many natural products (*4–7*). Sesamol has been found to inhibit lipid peroxidation, hydroxyl radical-induced deoxyribose degradation, and DNA cleavage (*8*). In Swiss albino mice, scavenging the free radicals, activating the endogenous antioxidant enzymes (GSH, GST, catalase), protecting the hemopoietic system, and preventing DNA damage are likely to be the mechanisms for the radioprotective activity of sesamol (*9*). On the other hand, benzodioxole derivatives are widely distributed in nature and have been shown to possess antitumor, antioxidant, and many other biological activities (*10–13*). These activities have been attributed to the effect on various enzymes and the scavenging of reactive oxygen species. Sesamol could also attenuate the production of nitric oxide and hydrogen peroxide and reduce monoamine oxidase activity in glial astrocyte cells (*14*). Because a distinct relationship exists between monoamine oxidase activity and the development of neurodegenerative diseases associated with aging, such as Alzheimer's disease and stroke, sesamol might play a role in the prevention of these types of diseases. Fibrinolysis defects play a pivotal role in cardiovascular diseases such as atherosclerosis and atherothrombosis. Furthermore, they are considered to be a risk factor for severe cardiovascular diseases such as myocardium infarction and stroke (*15–17*). Sesamol may enhance an overall vascular fibrinolytic capacity through regulating gene expression of plasminogen activator (*18*). Due to various health beneficial properties of sesamol, it is, therefore, important to understand the bioavailability of sesamol. This paper reports our study on the pharmacokinetics, absorption, and distribution of sesamol in rats.

MATERIALS AND METHODS

Chemicals. Sesamol (purity = 99%), D-saccharic acid-1,4-lactone, hesperetin, 4-hydroxycoumarin, and sulfatase (*Helix pomatia*, S-9626) were obtained from Sigma-Aldrich (St. Louis, MO). All other chemicals

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used were of analytical grade. Liquid chromatographic grade solvents and reagents were obtained from Mallinckrodt Baker (Phillipsburg, NJ). Triply deionized water (Millipore, Bedford, MA) was used for all preparations.

Animals and Diets. The experimental protocol was approved by the National Laboratory Animal Center (Taipei, Taiwan.) Inbred male Sprague−Dawley (SD) rats [body wt = 275 ± 25 g, mean ± SD] were housed in pairs in cages in a room with controlled temperature (20−22 °C), controlled relative humidity (50−70%), and a 12 h light/dark cycle (lights on at 7:00 a.m.). The rat diet was AIN 93 M diet (St. Louis, MO). Rats consumed their food ad libitum and had unlimited access to water; their weight and food consumption were determined weekly.

Pharmacokinetics Experiments. *Blood Sampling and Sample Preparation.* Two groups of rats were used for the experiments. One group of rats was given orally sesamol (50 mg/kg), and the other group was intravenously injected sesamol (5 mg/kg) through the femoral vein. Sesamol was dissolved in normal saline at doses of 5 and 50 mg/kg for intravenous (iv) injection and oral administration (po), respectively. The whole blood samples were directly obtained by heart puncture and collected from the same animal at 0, 2, 5, 15, 30, 60, 90, 120, 240, 360, 480, 720, and 1440 min after oral administration. Each sample (100 μL) was either hydrolyzed with 50 μL of enzyme [1000 units of sulfatase activity with β-glucuronidase inhibitor (D-saccharic acid-1,4-lactone, 7.5 mg/mL) in 0.1 N NaOAc buffer (pH 5.0, with 200 mg/mL ascorbic acid)/g of tissue for incubator at 37 °C] or not hydrolyzed but processed immediately with the addition of the same volume of sodium acetate buffer without enzyme mix (*22–24*). Each blood sample was centrifuged at 2900*g* for 10 min. The resulting plasma sample (100 μL) was vortex-mixed with 200 μL of internal standard (hesperetin, 5 μg/mL) solution. The denatured protein precipitate was separated by centrifugation at 8000*g* for 10 min. An aliquot (20 μL) of the supernatant was directly injected onto the HPLC for analysis (*19–21*). Data from these samples were used to construct pharmacokinetic curves of sesamol concentration in plasma versus time. The same sample handling process was used for the determination of precision and accuracy.

Determination of Sesamol in Plasma. Separation of the unbound sesamol from various biological fluids was performed by a Luna C18 column (250 × 4.6 mm, 5 μm, Phenomenex, Torrance, CA), protected by an RP18 guard column (15.0 mm × 3.2 mm, 5 μm, Phenomenex). Columns were housed in a column heater set at 30 °C. The solvents for elution were methanol (solvent A) and 1% acetic acid buffer, pH 6.0 (solvent B). The elution program at a flow rate of 1 mL/min was as follows: 0−5 min, linear gradient from 50 to 30% B; 5−10 min, linear gradient from 30 to 0% B; 10−15 min, isocratic at 0% B; 15−25 min, linear return to 50% B. Total run time was 25 min. The UV detector was set at the wavelength of 290 nm.

Pharmacokinetic Application. Pharmacokinetic calculations were performed on each individual set of data using the pharmacokinetic software WinNonlin Standard Edition Version 1.1 (Pharsight Corp., Mountain View, CA) by noncompartmental method. The area under the curve (AUC) is used as a measure of the total amount of unaltered drug that reaches the systemic circulation. The oral bioavailability (*F*) is defined as the fraction of unchanged drug reaching the systemic circulation following administration through the oral route.

The concentrations of sesamol sulfate and sesamol glucuronide were calculated from the following equation:

$$\text{concn}_{\text{sulfate}} = \text{concn}_{\text{parent form + conjugates (sulfatase)}} - \text{concn}_{\text{parent form}}$$

$$\text{concn}_{\text{glucuronide}} = \text{concn}_{\text{conjugates (sulfatase)}} - \text{concn}_{\text{sulfate form (sulfatase with inhibitor)}}$$

The absolute oral bioavailability of a drug is generally measured by comparing the respective AUCs after oral and intravenous administration according to the following equation:

$$F = \frac{\text{AUC}_{\text{po}}/\text{dose}_{\text{po}}}{\text{AUC}_{\text{iv}}/\text{dose}_{\text{iv}}}$$

Distribution Experiment. Five groups (1, 3, 6, 9, and 24 h) of animals ($n = 6$) were administered via gastric gavage 100 mg/kg of body weight sesamol dissolved in normal saline for 4 days in three daily doses (300 mg/kg/day). After consuming the sesamol diet for 4 days, rats were anesthetized in the morning of the fourth day (100 mg/kg), without overnight fasting, using CO_2 as a carrier. The liver, lung, brain, plasma, and intestine were collected at 1, 3, 6, 9, and 24 h after the administration. Rats were fully bled via the abdominal aorta. Blood (8−12 mL) was collected in heparin tubes, and plasma was subsequently prepared in centrifuge tubes by centrifuging for 20 min at 1000*g* and 4 °C. After blood collection, the tissues were dissected, weighed, and immediately frozen in liquid nitrogen.

Preparation of Samples. All tissues were lyophilized before further processing. Rat tissues were pooled per intake group (6 rats/group) and ground and homogenized (Polytron). Liver, kidney, lung, brain, and intestine tissues required additional homogenization in the mill. Samples were stored in airtight containers at −20 °C.

Extraction. For extraction, whole rat tissues were weighed in 50 mL tubes. The samples were homogenized (Polytron) in 10 mL of 0.5 mol/L sodium acetate buffer (NaOAc, pH 5.0, with 200 mg/mL ascorbic acid)/g of tissue with a vortex. The samples were deproteinized with acetonitrile. The extract was transferred to a 25 mL tube and centrifuged for 10 min at 10000*g* and 4 °C. The supernatant was transferred to a clean tube, and the residue was extracted two more times. The organic solvent from the supernatant was evaporated at 50 °C. Tubes were weighed before and after evaporation of extraction solvent. Subsequently, the residues were dissolved with 1 mL of 0.1 N NaOAc (pH 5.0, with 200 mg/mL ascorbic acid) buffer. Each sample (100 μL) was either hydrolyzed with 50 μL of enzyme (1000 units of sulfatase activity or 1000 units of sulfatase with β-glucuronidase inhibitor (D-saccharic acid-1,4-lactone, 7.5 mg/mL) in 0.1 N NaOAc buffer (pH 5.0, with 200 mg/mL ascorbic acid)/g of tissue for incubator at 37 °C or not hydrolyzed but processed immediately with the addition of the same volume of NaOAc buffer without enzyme mix (*22–24*). Subsequently, all samples were deproteinized with 250 μL of internal standard (hesperetin, 5 μg/mL in acetonitrile) solution and centrifuged for 10 min at 10000*g* and 4 °C. After centrifugation, 1 mL of supernatant was injected into the HPLC system. Plasma and tissue samples were analyzed according to a similar method as described previously.

Determination of Sesamol Distributed in Tissues. The HPLC system consisted of Hitachi L7100 pumps (Hitachi, Tokyo, Japan) and a Hitachi L7420 UV−vis detector (Hitachi). Separation was achieved by injecting 20 μL of sample onto a Luna C18 column (250 × 4.6 mm, 5 μm, Phenomenex), protected by an RP18 guard column (15.0 mm × 3.2 mm, 5 μm, Phenomenex). Columns were housed in a column heater set at 30 °C. The solvents for elution were 100% methanol (solvent A) and 1% acetic acid, pH 6 (solvent B). The elution program at a flow rate of 1 mL/min for rat tissue samples was as follows: 0−5 min, linear gradient from 50 to 80% A; 5−10 min, linear gradient from 80 to 100% A. Peaks were detected with a UV−vis detector at 290 nm. The elution program for rat plasma extract at a flow rate of 1 mL/min was as follows: 0−15 min, linear gradient from 40 to 70% A; 15−16 min, linear gradient from 70 to 100% A. Peaks were detected with a UV−vis detector at 290 nm.

Identification of sesamol and sesamol metabolites was carried out by LC-MS/MS analysis. These analyses were performed on a Hitachi HPLC system equipped with an electrospray ionization ion trap mass spectrometer (ThermoFinnigan LCQ Advantage, San Jose, CA). The separation was achieved using a Luna C18 column (250 × 4.6 mm i.d.; 5 μm, Phenomenex). For the operation in MS/MS mode, a mass spectrometer with an electrospray ionization (ESI) was used. During the analyses, the ESI parameters were set as follows: capillary voltage, −9.52 kV for negative mode; source voltage, 3.94 kV; source current, 6.15 uA; sheath gas flow rate, 34.57 au; capillary temp, 200 °C; tube lens voltage, −30 V. Selected reaction monitoring (SRM) was used to monitor the transition of the deprotonated molecule *m/z* 137 $[M - H]^-$ to the product ion 109 for sesamol analysis. All LC-MS/MS data were processed by the Xcalibur version 2.0 data acquisition software.

Statistical Analysis. All samples were extracted in triplicate. Sesamol, sesamol glucuronide, and sesamol sulfate concentrations were expressed in micrograms per gram of tissue or micrograms per milliliter of plasma. Tissues of six rats were pooled before analysis. Data were analyzed

Table 1. Pharmacokinetic Parameters of Sesamol, Sesamol Sulfate, and Sesamol Glucuronide in Rat following Sesamol Administration[a]

	sesamol		sesamol sulfate		sesamol glucuronide	
	po (50 mg/kg)	iv (5 mg/kg)	po	iv	po	po
T_{max} (min)	2.5 ± 1.2		7.3 ± 3.4	4.3 ± 1.5	17.5 ± 6.1	11.7 ± 5.8
C_{max} (μg/mL)	1.4 ± 0.7	2.3 ± 0.6	17.5 ± 6.8	15.8 ± 9.1	34.0 ± 13.0	8.9 ± 4.0
$t_{1/2}$ (min)	563.7 ± 36.9	29.2 ± 6.1	257.3 ± 72.6	251.0 ± 72.6	122.9 ± 15.5	1601.5 ± 399.2
AUC (min · μg/mL)	501.3 ± 200.8	141.4 ± 9.0	2034.4 ± 717.7	646.2 ± 129.7	1266.7 ± 438.9	744.6 ± 157.3
AUC/dose (min/L)	10.0 ± 4.0	28.3 ± 1.8	40.7 ± 14.4	129 ± 25.9	25.3 ± 8.3	148.9 ± 94.4
bioavailability(%)	35.5 ± 8.5		31.5 ± 3.7		17.0 ± 7.7	

[a] Data are expressed as mean ± SD (n = 6).

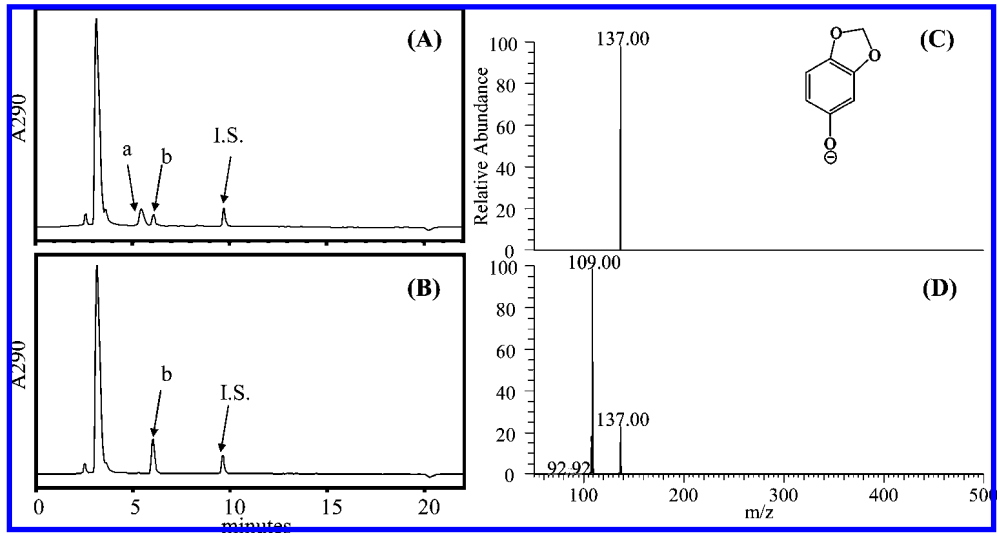

Figure 1. HPLC chromatograms and mass spectra of sesamol in the plasma extracts: (**A**) rat plasma after 5 min of oral administration; (**B**) rat plasma after 5 min of oral administration with sulfatase treatment; (**C**) full-scan mass spectrum of sesamol (molecular weight = 137 $[M - H]^-$) and (**D**) its product ions (MS/MS chromatograms; m/z 137→m/z 109) in LC-MS/MS with electrospray negative-ion mode. Peaks: a, sesamol sulfate/glucuronide; b, sesamol; I.S., internal standard.

by t-test analysis of variance, and differences were considered to be statistically significant at $P < 0.05$.

RESULTS

Pharmacokinetic Study in Rats. We studied the pharmacokinetics of sesamol with gastric gavage (po) or intravenous (iv) injection to rats. Biological fluid was sampled following dosesof sesamol of 50 mg/kg po and 5 mg/kg iv injection. The pharmacokinetic data were calculated by noncompartmental model (**Table 1**). The oral bioavailability is defined as the fraction of the dose that reaches the systemic circulation as intact drug. Blood samples were collected at various time intervals after sesamol administration and then assayed by a validated HPLC system. After sesamol administration (po and iv), the maximum concentrations of sesamol were 1.4 ± 0.7 and 2.3 ± 0.6 μg/mL; the half-lives were 563.7 ± 36.9 and 29.2 ± 6.1 min; and AUCs were 501.3 ± 200.8 and 141.4 ± 9.0 min·μg/mL, respectively. The results showed that the concentrations of sesamol declined rapidly and that the elimination half-lives did not relate to the dosage ranges. The oral bioavailability of sesamol was 35.5 ± 8.5% in rats. After sesamol administration (po), the maximum concentrations of sesamol sulfate and glucuronide were 17.5 ± 6.8 and 34.0 ± 13.0 μg/mL; the half-lives were 257.3 ± 72.6 and 122.9 ± 15.5 min; and AUCs were 2034.4 ± 717.7 and 1266.7 ± 438.9 min μg/mL, respectively.

The full scan in a negative ion mode (scan range from m/z 50−500) was used to identify the analyte. With full-scan mass spectra for the determination of sesamol (precursor ion is 137 $[M - H]^-$) a tube lens offset voltage of −40 eV was applied. Then, collision energies for collision-induced dissociation (CID) adjusted to 25% were optimized to produce the main product ion at m/z 109, as shown in **Figure 1**. Panels **A** and **B** of **Figure 2** show the MS/MS spectra of the extract for collected rat plasma sample after sesamol administration (50 mg/kg, po), with mass transitions of m/z 217 $[M - H]^-$→137 $[M - H - SO_3]^-$→109 $[M - H - SO_3 - CO]^-$ for sesamol sulfate and m/z 313 $[M - H - C_6H_8O_6]^-$→137 $[M - H - C_6H_8O_6]^-$→109 $[M - H - C_6H_8O_6 - CO]^-$ for sesamol glucuronide, respectively.

Distribution Study. To investigate the distribution of sesamol in rats, the concentrations of sesamol were determined in tissues and plasma within 9 h after administration to rats. Tissue concentrations of sesamol and sesamol metabolites were analyzed by HPLC. Sesamol metabolites (glucuronide/sulfate) were widely distributed in rat tissues, with the highest concentrations in plasma and lung and the lowest in brain. Sesamol may be, at first, incorporated into the liver and then transported to the other tissues (lung, kidney, and brain) (**Figure 3**).

To investigate the distribution of sesamol and conjugated metabolites in rats, we administered sesamol to rats and determined their concentrations in tissues within 24 h after administration. In the whole tissues (**Figure 3**), the concentrations of sesamol and conjugated metabolites had reached a maximum at 60 min after administration and were rarely found after 9 h. However, sesamol concentration was significantly greater than that of conjugated metabolites in the brain. In the plasma, sesamol metabolites (glucuronide/sulfate) concentrations were also significantly greater than that of sesamol. The highest sesamol and conjugated metabolites concentration were found

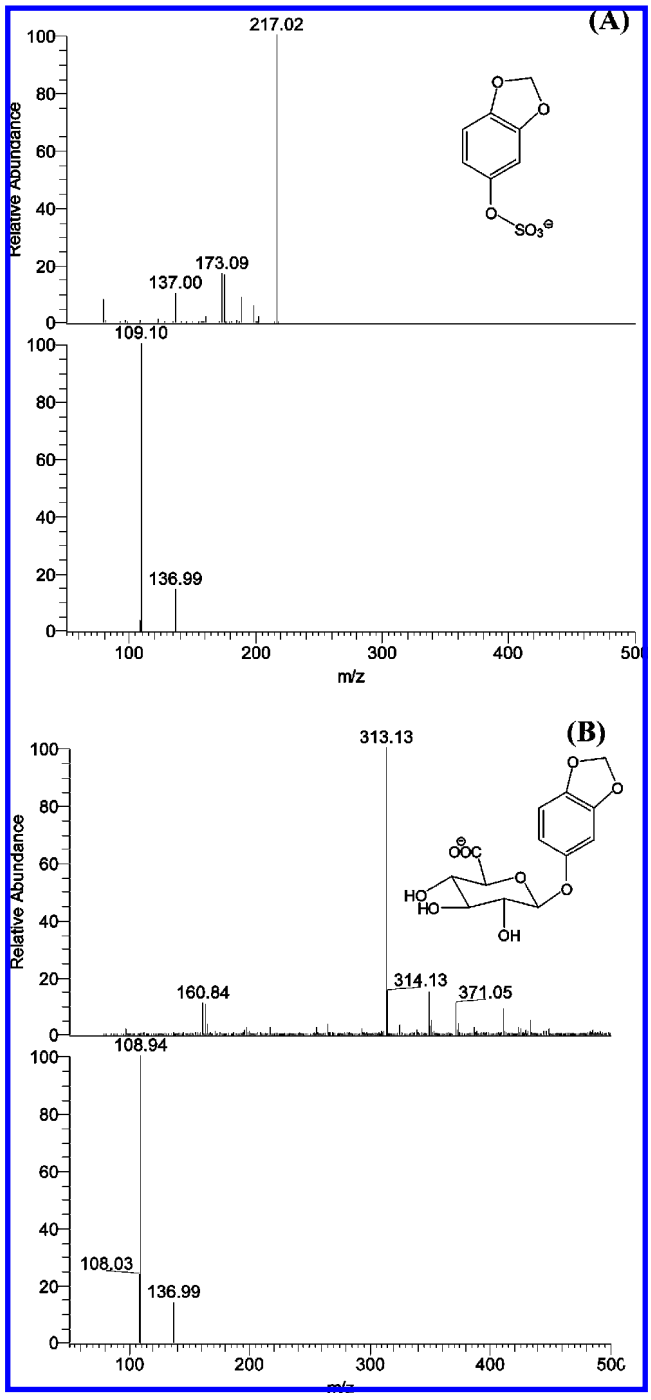

Figure 2. LC-MS/MS spectra of plasma extracts acquired by monitoring the fragmentation transition of (**A**) sesamol sulfate (MS/MS spectra; *m*/*z* 217→*m*/*z* 137, 109) and (**B**) sesamol glucuronide (MS/MS spectra; *m*/*z* 313→*m*/*z* 137, 109).

60 min after administration. In the lung, liver, and kidney, sesamol metabolite (glucuronide/sulfate) concentrations were significantly greater than that of sesamol. In the plasma, sesamol and sesamol sulfate were first detected at 60 min after administration, comparatively later than the other tissues.

An important parameter for pharmacokinetic analyses of a drug is the AUC, which represents the total drug exposure integrated over time (**Table 2**). The AUC is traditionally the relationship between time and plasma concentration, but it can also be applicable to the concentration of drug in tissues. It is the best estimate of drug delivery and an indicator of response. AUCs after the administration of sesamol were in the following order: intestines > lung > plasma > brain > kidney > liver. It wis important to note that the AUCs of sesamol metabolites (glucuronide/sulfate) in kidney, lung, and plasma were increased remarkably. The AUCs of sesamol metabolites were in the order plasma > intestine > kidney (**Table 2**). On the other hand, the maximum concentrations of sesamol metabolites in various tisuues were in the order plasma > lung ∼ kidney ∼ liver (**Figure 3**). It is suggested that one of the reasons that sesamol was able to cross the blood−brain barrier (BBB) may be due to its higher lipophilicity compared to sesamol metabolites. In addition, the results indicated that sesamol penetrates the BBB and goes through hepatobiliary excretion. In the intestines, sesamol metabolite (glucuronide/sulfate) concentrations were also significantly higher than in other tissues.

DISCUSSION

In this study, we measured the concentrations of sesamol and conjugated metabolites in rats to investigate (1) the accumulation of sesamol and conjugated metabolites in the lung and kidney of rats after short-term administration of sesamol, (2) the stomachic absorption of sesamol and its conjugated metabolites, and (3) the distribution of sesamol and its conjugated metabolites (sulfate/glucuronide) in rat tissues and plasma within 24 h after sesamol administration.

The absorption and metabolism of other simple phenols have been reported. With a single oral administration of 160 mg/kg phloroglucinol (benzene-1,3,5-triol) to humans, it was found that the absorption of phloroglucinol into blood was rapid, and the maximum concentration of parent compound was attained within 0.33 h after dosing (*25*). Kim and Matthews (*26*) reported the metabolism and excretion of resorcinol in F344 rats. An analysis of bile indicated that at least 50% of the dose excreted in bile undergoes enterohepatic circulation to be eventually excreted in urine. Diniz et al. (*27*) reported that a simple phenol (phloroglucinol) showed the highest brain−blood distribution coefficient and permeability coefficient in the biopartitioning micellar chromatography (BMC) system. These studies suggested that phenols can be effectively absorbed, and the parent compounds and their metabolites may act as antioxidants in the blood circulation. In the current study, we also found that sesamol can be absorbed and distributed to the blood as the intact form when sesamol was orally administered to rats. Comparison of the time course of changes in plasma concentrations of phloroglucinol and resorcinol suggested that sesamol was directly absorbed and distributed to the blood and that the plasma concentrations increased in the period up to 2.5 min postadministration and then gradually decreased.

Several studies have shown that phenolic compounds are able to induce phase II enzymes (*28*). Miksits et al. (*29*) reported the sulfation of resveratrol in human liver cytosol. When resveratrol was incubated with human recombinant sulfotransferases (SULTs), it was demonstrated that *trans*-resveratrol-3-*O*-sulfate was exclusively formed by SULT1A1, whereas *trans*-resveratrol-4′-*O*-sulfate was selectively formed by SULT1A2. Phase II conjugates formed inside hepatocyte are typically too hydrophilic to passively diffuse across the canalicular membrane into bile or across the hepatic basolateral membrane into sinusoidal blood (*30*). Most polyphenols excreted into urine are conjugated to glucuronide, sulfate, and methyl groups (*31*). Enzymes in the intestinal mucosa and in the liver perform the conjugation reactions (*32*).

Our results demonstrated that sesamol was absorbed from the gastrointestinal tract and appeared in the plasma mainly as sulfate and glucuronide conjugates. After administration of

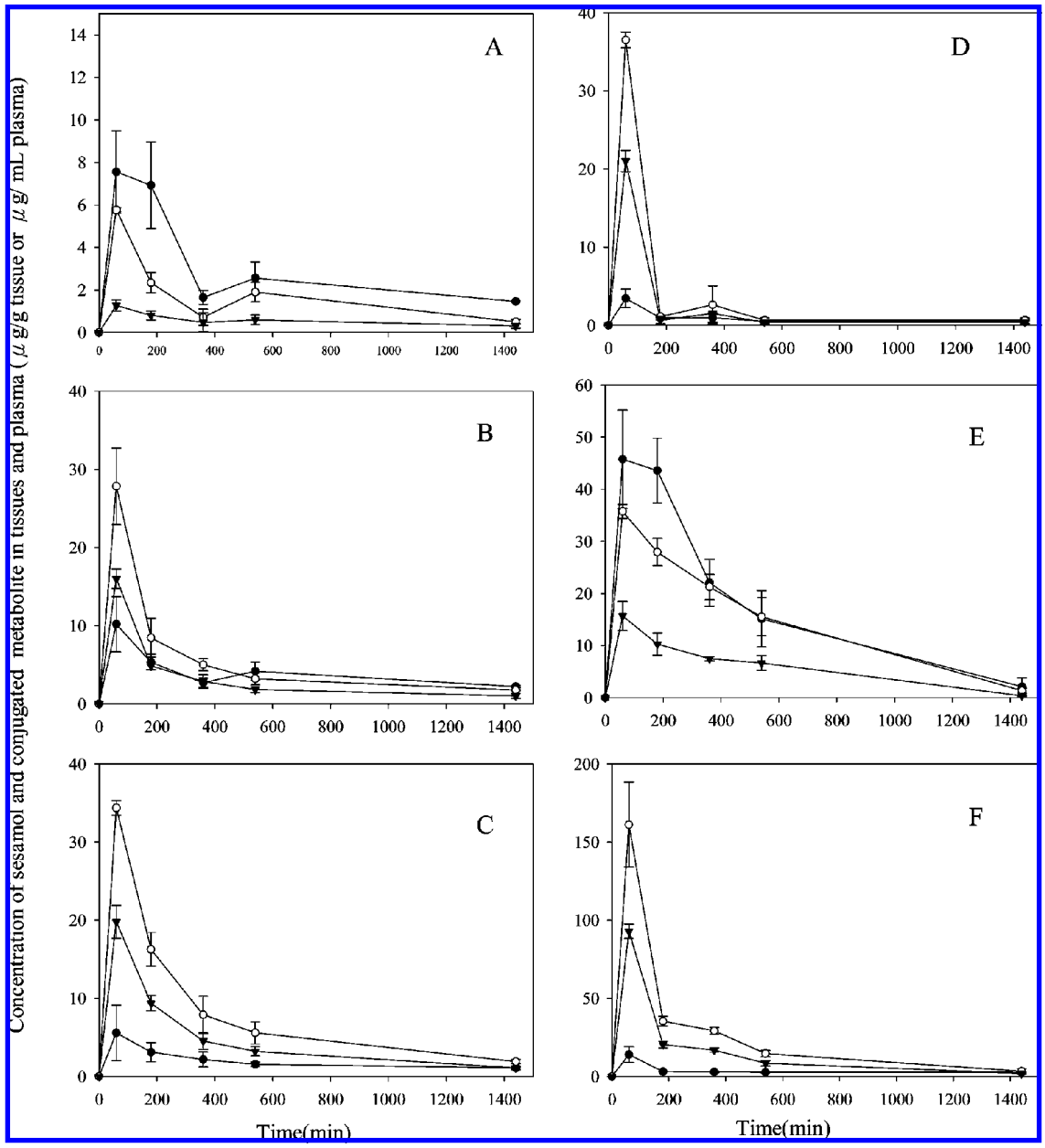

Figure 3. Time-dependent changes of sesamol (●), sesamol glucuronide (○), and sesamol sulfate (▼) concentration in rat tissues after oral administration: (**A**) brain; (**B**) lung; (**C**) kidney; (**D**) liver; (**E**) intestines; (**F**) plasma. Sesamol metabolites (glucuronides and sulfates) were extracted from the tissues collected at 60, 80, 360, 540, and 1440 min after their administration and analyzed by HPLC.

Table 2. Area under the Curve (AUC) of Free Form and Conjugated Sesamol in Rat Tissue[a]

AUC	liver (min · μg/g)	lung (min · μg/g)	kidney (min · μg/g)	intestines (min · μg/g)	plasma (min · μg/mL)	brain (min · μg/g)
sesamol	1787 ± 599	8826 ± 1360	4059 ± 673	33743 ± 9080	6855 ± 1569	6181 ± 490
sesamol glucuronide	4187 ± 2474	9772 ± 969	12556 ± 1788 *	18995 ± 6040 *	49233 ± 5476 *	2113 ± 1619 *
sesamol sulfate	2412 ± 1425	5629 ± 558 #	7233 ± 1030 *#	10942 ± 3479 *	28361 ± 3154 *#	1217 ± 932 *#

[a] Data are expressed as mean ± SD ($n = 6$): *, $p < 0.05$ compared with group sesamol; *, $p < 0.05$ compared with group Sesamol glucuronide.

sesamol to rats, sesamol metabolites (glucuronide/sulfate) were widely distributed in rat tissues, with the highest concentrations in plasma and intestines and the lowest in brain. Glucuronide was the major metabolite in tissues, followed by the sulfate conjugate. Sesamol may be incorporated first into the liver and then transported to the other tissues (lung, kidney, and brain). The concentration of sesamol was significantly lower than those of its conjugated metabolites in rat tissues and plasma. Our distribution study also showed that sesamol and its conjugated metabolites are lost from the body within 24 h and are not accumulated.

These findings imply that sesamol absorption starts before it reaches the intestines, and the stomach and the jejunum are sites of sesamol absorption in rats. The major plasma metabolites of sesamol in rats were identified as sesamol sulfate/glucuronide. According to LC-MS/MS analysis of pooled plasma samples, sesamol appeared to be efficiently metabolized in SD rats. However, sesamol and its metabolites were still present in the

intestines, and as enterohepatic cycling is highly probable in rats, this could partly explain the apparent slower elimination of sesamol sulfate as compared to sesamol. Thus, organs of the digestive area are suggested to be the metabolic pathway with enzymatic conversions (sulfation and/or glucuronoconjugation) for sesamol. The results of this study have provided detailed quantitative measurments of conjugated metabolites of sesamol in the tissues after administration. The pharmacokinetics presented should allow better and more relevant understanding of the bioactivity and role of dietary sesamol in the prevention of diseases related to oxidative stress.

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