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Comparative analysis of sesame lignans (sesamin and sesamolin) in affecting hepatic fatty acid metabolism in rats

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Effects of sesamin and sesamolin (sesame lignans) on hepatic fatty acid metabolism were compared in rats. Rats were fed either a lignan-free diet, a diet containing 0·6 or 2 g/kg lignan (sesamin or sesamolin), or a diet containing both sesamin (1·4 g/kg) and sesamolin (0·6 g/kg), for 10 d. Sesamin and sesamolin dose-dependently increased the activity and mRNA abundance of various enzymes involved in hepatic fatty acid oxidation. The increase was much greater with sesamolin than with sesamin. These lignans increased parameters of hepatic fatty acid oxidation in an additive manner when added simultaneously to an experimental diet. In contrast, they decreased the activity and mRNA abundance of hepatic lipogenic enzymes despite dose-dependent effects not being necessarily obvious. Sesamin and sesamolin were equally effective in lowering parameters of lipogenesis. Sesamolin accumulated in serum at 33- and 46-fold the level of sesamin at dietary concentrations of 0·6 and 2 g/kg, respectively. The amount of sesamolin accumulated in liver was 10- and 7-fold that of sesamin at the respective dietary levels. Sesamolin rather than sesamin can account for the potent physiological effect of sesame seeds in increasing hepatic fatty acid oxidation observed previously. Differences in bioavailability may contribute to the divergent effects of sesamin and sesamolin on hepatic fatty acid oxidation. Sesamin compared to sesamolin was more effective in reducing serum and liver lipid levels despite sesamolin more strongly increasing hepatic fatty acid oxidation.

Sesame lignan: Sesamin: Sesamolin: Fatty acid oxidation: Fatty acid synthesis

Sesame seed contains compounds collectively known as lignans. Sesamin and sesamolin are extractable in oil, and sesame seed and the unrefined oil thereof contain these two lignans at a ratio of about 2:1 (Sirato-Yasumoto *et al.* 2001). Another major sesame lignan is sesaminol which can exist as a mono-, di- or tri-glucoside (Katsuzaki *et al.* 1994; Kang *et al.* 1999; Moazzami *et al.* 2006), and is not extractable in oil. During the refining of sesame oil, sesamin is epimerized during acid-clay bleaching to form episesamin, while most of the sesamolin is degraded, with some converted to sesaminol (Fukuda *et al.* 1986). The sesamin preparation obtained as a by-product of the refining of edible sesame oil therefore consists of a 1:1 ratio of sesamin and episesamin, and has been tested extensively for physiological activity in animals. Studies have demonstrated that the sesamin preparation has physiological effects, acting as an antioxidant (Noguchi *et al.* 2001; Ikeda *et al.* 2003) and anti-carcinogen (Hirose *et al.* 1992), lowering blood pressure (Noguchi *et al.* 2001; Nakano *et al.* 2003) and reducing serum lipid (Hirose *et al.* 1991; Ogawa *et al.* 1995) in rats. We previously demonstrated that this sesamin preparation markedly and dose-dependently increased the activity and gene expression of enzymes involved in fatty acid oxidation in rat liver, presumably through the activation of PPARα (Ashakumary *et al.* 1999). We also showed that it lowered the activity and gene expression of hepatic enzymes involved in fatty acid synthesis through the down-regulation of sterol regulatory element binding protein (SREBP)-1 (Ide *et al.* 2001). We therefore concluded that 'sesamin' has strong physiological activity to regulate hepatic fatty acid metabolism. However, we subsequently demonstrated that episesamin is much more effective than sesamin at increasing the activity and gene expression of enzymes involved in fatty acid oxidation. However, the two lignans were equally effective in reducing the parameters for fatty acid synthesis (Kushiro *et al.* 2002). We therefore concluded that the physiological activity of the preparation containing equal amounts of sesamin and episesamin in increasing hepatic fatty acid oxidation is mainly ascribable to the episesamin not sesamin. However, we also observed that sesame seeds greatly increased hepatic fatty acid oxidation when fed to rats despite an absence of episesamin in the seeds (Sirato-Yasumoto *et al.* 2001). As a consequence, we hypothesized that sesame seed contains some unknown compound having strong physiological activity to promote hepatic fatty acid oxidation. A lignan other than sesamin is a candidate for this compound. In spite of sesamolin being one of the major lignans in sesame seed, its physiological activity in affecting hepatic fatty acid metabolism has not been tested. In this context, we examined the effect of sesamolin on hepatic fatty acid oxidation and synthesis in rats and compared it with that of sesamin.

Materials and methods

Materials

Sesamin with a purity exceeding 995 g/kg was kindly donated by Kadoya Sesame Mills Inc. (Kagawa, Japan). Sesamolin was extracted and purified from crude sesame oil (Kadoya Sesame

Abbreviations: DGAT, diacylglycerol acyltransferase; SREBP, sterol regulatory element binding protein.

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Mills Inc.) as follows. Sesame oil (300 g) was vigorously stirred with 600 ml methanol at 70°C for 2 h to extract lignans. After cooling in an ice-bath, the methanol layer was removed, and the oil was re-extracted with 300 ml hot methanol. The methanol extracts were combined, stood at −30°C overnight, and centrifuged at 3000***g*** and −9°C for 10 min. The supernatant was removed and dried *in vacuo* to obtain an oily residue containing approximately 100–120 g lignan/kg. The dried residue obtained from 600 g sesame oil was dissolved in a minimal volume (approximately 25–30 ml) of chloroform and applied to a column prepared with 250 g silicic acid (2·7 × 95 cm). The column was extensively washed with 2 litres of a solvent composed of hexane and ethyl acetate (90:10, v/v) and developed using another mixture of hexane and ethyl acetate (80:20, v/v). Fractions containing sesamolin were combined, dried *in vacuo* and dissolved in hot ethanol, and sesamolin was re-crystallized. These processes were repeated fifteen times to obtain 7 g of the sesamolin preparation. The analysis by HPLC, TLC and GLC of the sesamolin preparation revealed that it contained 126 g TAG/kg, 862 g sesamolin/kg and 12 g sesamin/kg.

Animals and diets

Male Sprague-Dawley rats obtained from Charles River Japan (Kanagawa, Japan), were housed individually in animal cages in a room with controlled temperature (20–22°C), humidity (55–65 %) and lighting (lights on from 7.00 to 19.00 hours), and fed a commercial non-purified diet (Type NMF, Oriental Yeast Co., Tokyo, Japan) for 5 d. Then they were fed a purified diet free of lignan for 4 d to acclimatize them to the purified experimental diet and to deplete any possible sesame lignan in the body. After this period of acclimation, the animals were divided into six groups with equal mean body weights consisting of seven or eight rats each and continued to be assigned a diet free of lignan or fed the purified diets containing 0·6 and 2 g lignan (sesamin or sesamolin)/kg, and a diet simultaneously containing 1·4 g sesamin/kg and 0·6 g sesamolin/kg. The last diet was included in this experiment because in sesame seed, the ratio of sesamin to sesamolin is about 2:1. As the sesamolin preparation employed in the present study contained small amounts of sesamin, the 0·6 g/kg sesamolin diet actually contained 0·008 g sesamin/kg and 0·592 g sesamolin/kg, and the 2 g/kg sesamolin diet contained 0·027 g sesamin/kg and 1·973 g sesamolin/kg. The compositions of the experimental diets are shown in Table 1. The lignan preparation was added to the experimental diets instead of saccharose. As the sesamolin preparation contained 126 g TAG/kg, we added maize oil, which is similar in fatty acid composition to sesame seed oil, appropriately in amounts of 0·20–0·29 g/kg to the various experimental diets except the 2 g/kg sesamolin diet. This made the experimental diets indistinguishable in fat content and fatty acid composition. The lignan concentrations in diets employed in the present study may correspond to the consumption of considerable amounts of sesame seeds when they are extrapolated to human diets; 1 kg sesame seeds usually contains 5–7 g lignan as sesamin and sesamolin (Yamashita *et al.* 1995; Sirato-Yasumoto *et al.* 2001; Yasumoto *et al.* 2003). Therefore, to attain the lignan concentrations of 0·6 and 2 g/kg, approximately 86–120 and 280–400 g, respectively, sesame seeds need to be present in 1 kg diet. A nutritional survey in Japan carried out in 2002 (http://www.mhlw.go.jp/houdou/2003/12/h1224-4.html) indicated that the daily food intake of adults is approximately 430 g. This means that the consumption of 0·6 and 2 g lignan/kg corresponds to the daily consumption of 37–52 and 123–172 g, respectively, sesame seeds in adult man.

Enzyme assays

At the end of the experiments, rats were anaesthetized using diethyl ether and killed by bleeding from the abdominal aorta, after which the livers were quickly excised. Approximately 1·5 g of each liver were homogenized in 10 ml 0·25 M-sucrose containing 1 mM-EDTA and 3 mM-Tris–HCl (pH 7·2), and centrifuged at 200 000 ***g*** for 30 min. Potassium cyanide-insensitive palmitoyl-CoA-dependent NAD reduction (peroxisomal fatty acid oxidation) and the activity of enzymes involved in fatty acid oxidation including acyl-CoA oxidase, carnitine palmitoyltransferase, enoyl-CoA hydratase, 3-hydroxyacyl-CoA dehydrogenase and 3-ketoacyl-CoA thiolase were measured spectrophotometrically in the whole liver homogenates as an

Table 1. Composition of experimental diets (g/kg)*

	Dietary lignans					
Ingredients	Lignan-free	Sesamin (0·6 g/kg)	Sesamin (2 g/kg)	Sesamolin (0·6 g/kg)	Sesamolin (2 g/kg)	Sesamin (1·4 g/kg) + Sesamolin (0·6 g/kg)
Casein	200	200	200	200	200	200
Palm oil	100	100	100	100	100	100
Maize oil	0·29	0·29	0·29	0·20	0	0·20
Maize starch	150	150	150	150	150	150
Cellulose	20	20	20	20	20	20
Vitamin mixture†	10	10	10	10	10	10
Mineral mixture†	35	35	35	35	35	35
L-Cystine	3	3	3	3	3	3
Choline bitartrate	2·5	2·5	2·5	2·5	2·5	2·5
Sesamin	0	0·6	2	0	0	1·4
Sesamolin	0	0	0	0·69	2·29	0·69
Saccharose	479·2	478·6	477·2	478·6	477·2	477·2

* Purity of sesamin preparation exceeds 995 g/kg. Sesamolin preparation contained 862 g sesamolin/kg, 12 g sesamin/kg and 126 g TAG/kg.
† Compositions of vitamin and mineral mixtures were the same as described by Reeves *et al.* (1993).

enzyme source as detailed previously (Ashakumary *et al.* 1999). Acyl-CoA oxidase and carnitine palmitoyltransferase activities were measured using palmitoyl-CoA as a substrate. *t*-2-Oct-enoyl-CoA, acetoacetyl-CoA, 3-ketooctanoyl-CoA and sorboyl-CoA were employed as substrates to assay the activities of enoyl-CoA hydratase, 3-hydroxyacyl-CoA dehydrogenase, 3-keotacyl-CoA thiolase and 2,4-dienoyl-CoA reductase, respectively. The activity of enzymes involved in fatty acid synthesis was measured using the 200 000 ***g*** supernatant of the liver homogenate (Ide *et al.* 2001).

RNA analyses

RNA in liver was extracted (Chomczynski & Sacchi, 1987), and mRNA abundance was analysed by a quantitative real-time PCR using an Applied Biosystems Prism 7000 sequence detection system (Applied Biosystems, Foster City, CA, USA) as detailed elsewhere (Ide, 2005). The nucleotide sequences of primers and probes designed using Primer Express Software (Applied Biosystems) are listed in Table 2. mRNA abundance was calculated as a ratio to the β-actin level in each cDNA sample and expressed as a percentage, assigning the value in rats fed a lignan-free diet as 100.

Analyses of lipids and lignans

Liver lipids were extracted and purified (Folch *et al.* 1957). Liver TAG, phospholipid and cholesterol concentrations in the lipid extract were determined as described before (Ide *et al.* 1978). Serum TAG, cholesterol, phospholipid and NEFA concentrations were measured using commercial enzyme kits (Wako Pure Chemical, Osaka, Japan). Concentrations of sesamin and sesamolin in liver and serum were analysed by HPLC as detailed previously (Ide *et al.* 2004; Kushiro *et al.* 2004).

Statistical analysis

Data were expressed as means and their standard errors. StatView for Macintosh (SAS Institute Inc., Cary, NC, USA) was used for statistical analyses. D'Agostino–Pearson's test was used to inspect the constancy of the variance of the observations. If variances were heterogeneous, they were transformed logarithmically. The transformations were successful in rendering the variance of the observations constant, and hence the transformed values were used for subsequent statistical evaluations. The data were analysed with a one-way ANOVA, followed by a Tukey–Kramer *post hoc* analysis to detect significant differences in the means at the level of $P < 0{\cdot}05$.

Results

Activities and mRNA levels of enzymes involved in hepatic fatty acid oxidation

No significant differences in the mean values for food intake (18·8–20·7 g/d) were seen among the groups. Growth was significantly higher in rats fed the 0·6 g sesamolin/kg diet (96·4 (SEM 2·9) g/10 d) than in rats fed the 2 g sesamin/kg diet (80·2 (SEM 4·1) g/10 d). However, no other significant differences were seen in this parameter. Liver weight was significantly higher in rats fed the 2 g sesamolin/kg diet (6·36 (SEM 0·09) g/100 g body weight) than in the other groups (5·40–5·81 g/100 g body weight). Also, it was significantly higher in rats fed the 0·6 g sesamolin/kg diet (5·81 (SEM 0·09) g/100 g body weight) than in those fed the 2 g sesamin/kg diet (5·40 (SEM 0·15) g/100 g body weight). No other significant differences were seen in this parameter.

Sesamin and sesamolin, compared to a lignan-free diet, dose-dependently increased activities of various enzymes involved in fatty acid oxidation (Table 3). The increases were, however, much greater with sesamolin than with sesamin. Activities of enzymes involved in hepatic fatty acid oxidation in rats fed sesamolin at dietary levels of 0·6 and 2 g/kg were 1·2–1·7-fold and 2·0–4·2-fold, respectively, those in the animals fed a lignan-free diet. The increases observed with the 2 g sesamin/kg diet (1·3–1·9-fold levels observed in rats fed a lignan-free diet) were much lower than the increases obtained with the 2 g sesamolin/kg diet. The levels in this group were comparable to those observed with the 0·6 g sesamolin/kg diet. A diet containing 0·6 g sesamin/kg compared to a lignan-free diet slightly but significantly increased the activities of carnitine palmitoyltransferase, 3-hydroxyacyl-CoA dehydrogenase and 2,4-dienoyl-CoA reductase, but did not affect other parameters. The impact of sesamin and sesamolin on hepatic fatty acid oxidation appeared additive. The activity levels of enzymes in rats fed a diet containing 1·4 g sesamin/kg as well as 0·6 g sesamolin/kg were 1·8–2·6-fold those in rats fed a lignan-free diet.

Divergent effects of sesamin and sesamolin on the mRNA abundance of enzymes involved in hepatic fatty acid oxidation were also confirmed (Table 4). The mRNA abundance of peroxisomal enzymes in rats fed sesamolin at dietary levels of 0·6 and 2 g/kg were 1·6–3·7-fold and 2·5–6·4-fold, respectively, levels in rats fed a lignan-free diet. Also, the mRNA abundance of peroxin 11α (a peroxisomal membrane protein; Schrader *et al.* 1998) in rats fed the 0·6 and 2 g sesamolin/kg diets was 3·2- and 6·4-fold, respectively, that in rats fed a lignan-free diet. Again, sesamin was less effective in increasing these parameters. The values in rats given sesamin at a dietary level of 2 g/kg were comparable to those in rats given sesamolin at 0·6 g/kg. The impact of the combination of sesamin and sesamolin at dietary levels of 1·4 and 0·6 g/kg, respectively, in affecting the mRNA abundance of peroxisomal proteins appeared additive. Lignans also increased the mRNA abundance of mitochondrial enzymes involved in the β-oxidation of fatty acids and microsomal cytochrome P450 IV A1 involved in the ω-oxidation of fatty acids (Simpson, 1997). Lignan-dependent increases in mRNA levels of mitochondrial enzymes were generally weaker than those observed for peroxisomal proteins. Sesamolin compared to sesamin was also more competent in increasing mRNA abundance of enzymes involved in mitochondrial fatty acid oxidation and cytochrome P450 IV A1. Sesamin and sesamolin together at dietary levels of 1·4 and 0·6 g/kg, respectively, appeared to increase these parameters in an additive manner.

Activities and mRNA abundance of enzymes involved in hepatic lipogenesis

Sesamin at 0·6 and 2 g/kg decreased the activity of hepatic lipogenic enzymes except on one occasion (pyruvate kinase activity in rats fed 0·6 g sesamin/kg diet) (Table 5). A dose-dependent effect of this compound on activity levels was not necessarily clear. Activity levels of ATP-citrate lyase

Table 2. Primers and probes for real-time PCR of mRNA

Genes	Sense primer	Antisense primer	Probe	Length of PCR products (bp)	GenBank accession no.
Acetyl-CoA carboxylase	5′-CATCGTCTATTGTGGCTCAAACTG-3′	5′-TCTTGCCAATCCACTCGAAGA-3′	5′-ATCCCCACTCTTCCCTGGAGTGGC-3′	79	NM_022193
Acyl-CoA oxidase	5′-CCTGGAGGGCCTGACAGA-3′	5′-AAGGTTTTTTGCAGCGATTTCT-3′	5′-CCTACAAGCTTCGTGCAGCCAGATTGG-3′	70	NM_017340
Adiponutrin	5′-CAGACAACGTCCACCAGATCAT-3′	5′-TTCTCCCCATCGGACACTCT-3′	5′-TCTGGCAAGGTTTACATCTCACTCA-3′	70	XM_217006
ATP-citrate lyase	5′-CGTGTGCTCCCGAGATGAG-3′	5′-CCCCAGTAAAACTTCTGCTTATGATC-3′	5′-TGGCTGCTATGGTCTACCCGTTCACG-3′	81	NM_016987
β-Actin	5′-TTCAACACCCCAGCCATGT-3′	5′-GTGGTACGACCAGAGGCATACA-3′	5′-CGTAGCCATCCAGGCTGTGTTGTCC-3′	68	NM_031144
Bifunctional enzyme	5′-CGCCCTCAGCTGGTGATT-3′	5′-GCTAGGAATGACCTCTAGCAACCT-3′	5′-ACCCACTTCTTCTCACCAGCCCA-3′	75	NM_133606
Carnitine octanoyltransferase	5′-TGGAAAATCAATTGGCTAAGTCAA-3′	5′-GGGCAAGGGCGGAAGA-3′	5′-TGAAGAACGAACATTCCAGTACCAGGAC-3′	71	NM_031987
Carnitine palmitoyltransferase II	5′-ACCAGCAGATGAACCACAACAT-3′	5′-AAGCCCCCAAGGCTCACT-3′	5′-CCACCAGCACTCTGAACAGCCCA-3′	70	J05470
DGAT 1	5′-CACGAATCATTGAGCGTC TCTTA-3′	5′-GCCAATAGAAGAAGATGAGCCATATC-3′	5′-AGCTGGCGGTCCCCAACCATC-3′	72	NM_053437
DGAT 2	5′-GGCTGATAGCTGCTCTCTACTTCA-3′	5′-TGTGATCTCCTGCCACCTTTC-3′	5′-CTGGCATTTGACTGGAACACGCCC-3′	76	NM_001012345
Cytochrome P450 IV A1	5′-CGGGCGATCAGATCCAAA-3′	5′-GAGCAAACCATATCCGATCCA-3′	5′-ATGGCGTCTACAGATTGCTAGCTCC-3′	70	NM_175837
Δ^3,Δ^2-Enoyl-CoA isomerase	5′-GCCTGGACTTGATGGAGATGTAT-3′	5′-TCCTGCACAGCCTTCCAGTA-3′	5′-CGGAACCCAGCCCACTATGCTG-3′	70	NM_017306
2,4-Dienoyl-CoA reductase	5′-CTTGGCAAGGCAATGACAACT-3′	5′-CAATATTCCTGCTCGCGATCA-3′	5′-CCGCTCCAGCCTGGGTGC-3′	70	NM_057197
Fatty acid synthase	5′-GCGGGCGTGGTAATGCT-3′	5′-CTGTTCGCAAATACGCTCCAT-3′	5′-CCAATCCAACTATGGCTTCGCCAACTC-3′	71	NM_017332
Glucose 6-phosphate dehydrogenase	5′-CAGGCCAACCGTCTGTTCTAC-3′	5′-CTTGAATGTTCTTGGTGACTGCTT-3′	5′-TGGCCTTGCCCCCCACTGTC-3′	70	NM_017006
Mitochondrial glycerol 3-phosphate acyltransferase	5′-CAGCAAGTCCTGCGCTATCA-3′	5′-TTCCCTGCCTGTGTCTGTAGAG-3′	5′-CCCACATTGTGGCCTGCCTGCT-3′	71	NM_017274
Mitochondrial 3-ketoacyl-CoA thiolase	5′-AACGTGAGTGGAGGTGCCATA-3′	5′-GGTGTGCGGTGATTCTGGAT-3′	5′-CCCTGGGTCACCCGCTGGG-3′	70	NM_130433
Peroxin 11α	5′-GTGTGAGCACTGGCCGTAAA-3′	5′-CTCTGCTCAGTGGCCTGGAT-3′	5′-TTCAGACTAGGCAACGTGCTCCATGC-3′	70	NM_053487
Peroxisomal 3-ketoacyl-CoA thiolase	5′-GGGTCCCTCCTGACATCATG-3′	5′-TCACAGTCAGCCCTGCTTTCT-3′	5′-CCTATGCCATCCCTGCGGC-3′	78	J02749
Pyruvate kinase	5′-CAAAGCAGGGATGAACATTGC-3′	5′-GATGGATTCTGCATGGTACTCATG-3′	5′-CGACTCAACTTCTCCCATGGCTC-3′	70	M17685
Spot 14	5′-TCGGAGGAGCTGGACCTAGA-3′	5′-GGTGGGTAAGGATGTGATGGA-3′	5′-AGTTCCACCTGCACTTCTCCAGC-3′	70	NM_012703
SREBP-1a	5′-GAGGCGGCTCTGGAACAG-3′	5′-ACGCGGCGCTCTTGACCGA-3′	5′-TGAGCTGAAGCATGTCTTCGA-3′	85	XM_213329
SREBP-1c	5′-GCGCGGACGACGGA-3′	5′-AGTCACTGTCTTGGTTGTTGATGAG-3′	5′-CCATGGATTGCACATTTGAAGACATGCT-3′	72	L16995
Trifunctional enzyme subunit α	5′-GAAGGCTGACATGGTGATTGAG-3′	5′-CCACTTCCTTTAACACTTTGTGCTT-3′	5′-CTGTCTTCGAGGACCTCGCTGT-3′	71	NM_130826
Trifunctional enzyme subunit β	5′-TGGTGGAAGGTGTCCGAATT-3′	5′-CAAATCATGTGGCATTAGGTCTTT-3′	5′-TTTCTGCTGTCAGGCACTTCG-3′	71	NM_133618

DGAT, diacylglycerol acyltransferase; SREBP, sterol regulatory element binding protein.

Table 3. Effect of dietary lignans on the activity of hepatic enzymes (μmol/min per 100 g body weight) involved in fatty acid oxidation in rats*
(Mean values with their standard errors, *n* 7–8)

	Dietary lignans											
	Lignan-free		Sesamin (0·6 g/kg)		Sesamin (2 g/kg)		Sesamolin (0·6 g/kg)		Sesamolin (2 g/kg)		Sesamin (1·4 g/kg) + Sesamolin (0·6 g/kg)	
Enzymes	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Peroxisomal palmitoyl-CoA oxidation	1·70^{a}	0·06	1·83^{a}	0·14	2·48^{b}	0·13	2·56^{b}	0·10	7·15^{d}	0·29	4·22^{c}	0·19
Acyl-CoA oxidase	1·56^{a}	0·07	1·68^{a}	0·05	2·04^{b}	0·07	2·48^{c}	0·08	4·99^{e}	0·27	3·10^{d}	0·12
Carnitine palmitoyltransferase	3·41^{a}	0·16	4·48^{b}	0·34	6·42^{c}	0·27	5·60^{c}	0·36	9·51^{e}	0·54	7·85^{d}	0·41
Enoyl-CoA hydratase	6272^{a}	156	6070^{a}	413	8299^{b}	339	7766^{b}	467	12 557^{d}	632	11 047^{c}	581
3-Hydroxyacyl-CoA dehydrogenase	241^{a}	10	309^{b}	19	455^{c}	16	404^{c}	26	791^{e}	25	616^{d}	29
3-Ketoacyl-CoA thiolase	244^{a}	10	273^{a}	16	392^{b}	28	400^{b}	23	852^{d}	67	582^{c}	43
2,4-Dienoyl-CoA reductase	3·54^{a}	0·17	4·84^{b}	0·28	5·83^{c}	0·25	5·57^{bc}	0·29	9·10^{e}	0·41	7·13^{d}	0·49

^{a,b,c,d,e} Mean values within a row with unlike superscript letters were significantly different ($P<0·05$).
*For details of procedures, see pp. 86–87.

and pyruvate kinase were significantly lower in rats fed the 2 g sesamin/kg diet than in those fed the 0·6 g sesamin/kg diet. Fatty acid synthase and glucose 6-phosphate dehydrogenase activities tended to be lower in rats fed the 2 g sesamin/kg diet than in rats fed the 0·6 g sesamin/ kg diet, but significant differences were not observed. Sesamolin also reduced the activity of lipogenic enzymes. Dose-dependent effects of this compound on activity levels were observed. The activity levels of fatty acid synthase, ATP-citrate lyase, glucose 6-phosphate dehydrogenase and pyruvate kinase were all lower in rats fed the 2 g sesamolin/kg diet than in rats fed the 0·6 g sesamolin/kg diet. In contrast to the situation observed for fatty acid oxidation enzymes, the activity levels of lipogenic enzymes at the respective dietary levels were comparable between rats fed sesamin and sesamolin. The values in rats fed a diet containing 1·4 g sesamin/kg and 0·6 g sesamolin/kg were the same as those observed with the 2 g sesamin/kg or 2 g sesamolin/kg diet.

Lignan-containing diets irrespective of the dietary levels, compared to a lignan-free diet, significantly decreased the mRNA abundance of enzymes involved in fatty acid synthesis (acetyl-CoA carboxylase, fatty acid synthase, ATP-citrate lyase, glucose 6-phosphate dehydrogenase and pyruvate kinase; Table 6). In addition to the mRNA abundance of these enzymes, we measured the mRNA levels of enzymes involved in glycerolipid biosynthesis (mitochondrial glycerol 3-phosphate acyltransferase and diacylglycerol acyltransferase (DGAT) 1 and 2) and of proteins presumed to be involved in the regulation of lipogenesis (spot 14 and adiponutrin) (Kinlaw *et al.* 1995; Baulande *et al.* 2001; Jenkins *et al.* 2004; Ide, 2005; Johansson *et al.* 2006). Sesamin and sesamolin at a dietary level of 0·6 or 2 g/kg each significantly decreased the mRNA abundance of mitochondrial glycerol 3-phosphate acyltransferase, spot 14 and adiponutrin, and diets containing 2 g/kg but not 0·6 g/kg of these lignans significantly reduced the mRNA abundance of DGAT 2. However, sesamin and sesamolin did not affect the mRNA abundance of DGAT 1. Dose-dependent effects of lignans on the mRNA abundance of enzymes involved in fatty acid and glycerolipid biosynthesis, and spot 14 and adiponutrin, were not necessarily obvious. The abundance of mRNA for ATP-citrate lyase, adiponutrin and DGAT 2 was significantly lower in rats fed the 2 g sesamin/kg diet than in rats fed the 0·6 g sesamin/ kg diet. However, significant differences between the two groups were not found for other parameters. Also, the abundance of mRNA for acetyl-CoA carboxylase, ATP-citrate lyase, pyruvate kinase and mitochondrial glycerol 3-phosphate acyltransferase, but not for other enzymes, was significantly lower in rats fed the 2 g sesamolin/kg diet than in those fed the 0·6 g sesamolin/kg diet. Again, mRNA abundances for these enzymes at the respective dietary levels were comparable between rats fed sesamin and sesamolin. Also, the values in rats fed a diet containing 1·4 g sesamin/kg and 0·6 g sesamolin/kg in combination were indistinguishable from those observed with the 2 g sesamin/kg and 2 g sesamolin/kg diets. We measured mRNA levels of SREBP-1a and -1c involved in regulating the gene expression of lipogenic enzymes (Kim *et al.* 1999; Shimomura *et al.* 1999; Horton *et al.* 2002). There were no significant differences in SREBP-1a mRNA abundance among the groups. SREBP-1c mRNA abundance was significantly lower in rats fed diets

Table 4. Effect of dietary lignans on mRNA abundance (%) of hepatic enzymes involved in fatty acid oxidation in rats*
(Mean values with their standard errors, *n* 7–8)

	Dietary lignans											
	Lignan-free		Sesamin (0·6 g/kg)		Sesamin (2 g/kg)		Sesamolin (0·6 g/kg)		Sesamolin (2 g/kg)		Sesamin 1·4 (g/kg) + sesamolin (0·6 g/kg)	
Enzymes	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Peroxisomal proteins												
Carnitine octanoyltransferase	100[a]	8	196[b]	12	359[c]	43	370[c]	38	644[d]	48	428[c]	17
Acyl-CoA oxidase	100[a]	2	124[a]	8	164[b]	12	159[b]	6	249[d]	16	208[c]	8
Bifunctional enzyme	100[a]	5	143[b]	8	222[c]	30	222[c]	22	612[d]	49	511[d]	75
3-Ketoacyl-CoA thiolase	100[a]	9	122[a]	8	212[b]	25	241[b]	18	630[d]	56	408[c]	22
Peroxin 11α	100[a]	10	135[a]	13	293[b]	45	318[b]	32	643[d]	53	424[c]	25
Mitochondrial proteins												
Carnitine palmitoyltransferase II	100[a]	6	116[a]	7	128[b]	10	136[b]	8	177[c]	13	141[b]	9
Trifunctional enzyme subunit α	100[a]	5	121[b]	5	135[bc]	9	143[c]	7	184[e]	3	157[d]	7
Trifunctional enzyme subunit β	100[a]	5	110[a]	3	139[b]	8	156[b]	9	214[c]	14	149[b]	11
3-Ketoacyl-CoA thiolase	100[a]	5	122[a]	9	164[b]	14	160[b]	7	232[d]	6	197[c]	5
Δ^3,Δ^2-Enoyl-CoA isomerase	100[a]	5	147[a]	10	278[b]	27	272[b]	28	512[d]	22	405[c]	14
2,4-Dienoyl-CoA reductase	100[a]	6	119[a]	6	142[b]	9	148[b]	12	212[c]	17	179[c]	8
Cytochrome P450 IV A1	100[a]	5	139[a]	8	286[b]	28	290[b]	29	562[d]	24	427[c]	11

[a,b,c,d,e] Mean values within a row with unlike superscript letters were significantly different ($P<0·05$).
* For details of procedures, see p. 87.

containing lignans than in those fed a lignan-free diet. However, neither the type nor dietary level of lignan affected this parameter.

Serum and liver lipid and lignan levels

All the diets containing lignan compared to a lignan-free diet significantly decreased serum TAG, cholesterol, phospholipid and NEFA levels with one exception (the cholesterol concentration in rats fed the 0·6 g sesamolin/kg diet; Table 7). Also, serum TAG, cholesterol and phospholipid but not NEFA concentrations were significantly lower in rats fed the 2 g sesamin/kg diet than in those fed the 0·6 g sesamin/ kg diet. However, no dose-dependent decreases were observed with sesamolin. Sesamin and sesamolin at both 0·6 and 2 g/kg significantly reduced hepatic TAG levels. Decreases were greater in rats fed sesamin than in rats fed sesamolin. Hepatic TAG levels in rats fed a diet containing both 1·4 g sesamin/kg and 0·6 g sesamolin/kg were approximately the same as those obtained with the 2 g sesamolin/kg diet. Also, diets containing lignans compared to a lignan-free diet significantly lowered hepatic cholesterol levels. Among the rats fed various lignan-containing diets, values were significantly higher in the animals given the 0·6 g sesamolin/kg diet than in those fed the 2 g sesamolin/kg diet. However, no other differences were detected among rats fed lignan-containing diets. Hepatic phospholipid levels were significantly higher in rats fed the 2 g sesamolin/kg diet and a diet containing both sesamin and sesamolin than in the other groups.

Lignan was detected neither in serum nor in liver of rats fed a lignan-free diet. Sesamin and sesamolin dose-dependently increased lignan levels in serum and liver. As the sesamolin preparation employed in the present study contained small amounts of sesamin, both sesamin and sesamolin were detected in serum and liver of rats fed the 0·6 and 2 g sesamolin/kg diets. However, sesamin comprised less than 1 % of the total amount of lignan in all cases. The amounts accumulated were much greater for sesamolin than for sesamin. In rats fed the 0·6 g lignan/kg diet, amounts of sesamolin accumulated were 46- and 11-fold those for sesamin in serum and liver, respectively. Also, at a dietary level of 2 g/kg, amounts of sesamolin accumulated were 33- and 7-fold those of sesamin in serum and liver, respectively. The ratio of sesamin to sesamolin was 2·3 in the diet containing both these compounds. However, the ratio of sesamin to sesamolin in the serum and liver of rats fed this diet was merely 0·08 and 0·44, respectively.

Discussion

Sesamin is the most abundant lignan in sesame seeds, and has weak physiological activity to promote hepatic fatty acid oxidation (Kushiro *et al.* 2002). We found that the feeding of sesame seeds increased hepatic fatty acid oxidation to an extent greater than is to be expected given the sesamin content of the seeds (Sirato-Yasumoto *et al.* 2001). This indicated that sesame seed contains some unknown compound having strong physiological activity to increase hepatic fatty acid oxidation. We found in the present study that sesamolin is much more effective than sesamin in increasing hepatic fatty acid oxidation. Therefore, it is possible that sesamolin rather than sesamin accounts for the potent physiological effect of sesame seeds on hepatic fatty acid oxidation. We previously demonstrated that episesamin compared with sesamin is much more competent in increasing hepatic fatty acid oxidation (Kushiro *et al.* 2002). Our preliminary experiment indicated that the physiological activity of sesamolin in increasing hepatic fatty acid oxidation was comparable to that of episesamin (T Ide *et al.* unpublished observation).

We have demonstrated that not only sesamin but also sesamolin has physiological activity to reduce the activity and mRNA abundance of hepatic enzymes involved in fatty acid

Table 5. Effect of dietary lignans on the activity of hepatic lipogenic enzymes (μmol/min per 100 g body weight) in rats*
(Mean values with their standard errors, *n* 7–8)

	Dietary lignans											
	Lignan-free		Sesamin (0·6 g/kg)		Sesamin (2 g/kg)		Sesamolin (0·6 g/kg)		Sesamolin (2 g/kg)		Sesamin (1·4 g/kg) + sesamolin (0·6 g/kg)	
Enzyme	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Fatty acid synthase	19·3^{c}	0·5	11·3^{ab}	2·4	7·71^{a}	1·27	12·7^{b}	1·2	8·63^{a}	0·90	8·51^{a}	0·64
ATP-citrate lyase	53·6^{c}	2·8	33·5^{b}	5·1	22·8^{a}	3·2	34·9^{b}	2·6	17·9^{a}	1·7	23·5^{a}	1·9
Glucose 6-phosphate dehydrogenase	99·1^{c}	5·7	50·7^{b}	8·7	35·4^{ab}	5·3	48·9^{b}	7·0	31·8^{a}	4·0	32·7^{ab}	3·4
Pyruvate kinase	238^{c}	18	202^{bc}	17	146^{a}	14	190^{b}	10	117^{a}	5	131^{a}	6

^{a,b,c} Mean values within a row with unlike superscript letters were significantly different ($P<0·05$).
* For details of procedures, see p. 87.

Table 6. Effect of dietary lignans on mRNA abundance (%) of hepatic proteins involved in lipogenesis in rats*
(Mean values with their standard errors, *n* 7–8)

	Dietary lignans											
	Lignan-free		Sesamin (0·6 g/kg)		Sesamin (2 g/kg)		Sesamolin (0·6 g/kg)		Sesamolin (2 g/kg)		Sesamin (1·4 g/kg) + sesamolin (0·6 g/kg)	
Proteins	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Acetyl-CoA carboxylase	100^{d}	13	71·2^{c}	10·0	56·2^{bc}	4·5	57·2^{bc}	2·4	40·6^{a}	2·3	46·4^{ab}	3·1
Fatty acid synthase	100^{c}	17	67·5^{b}	9·3	50·0^{ab}	5·8	57·7^{ab}	4·8	50·4^{ab}	5·0	42·8^{a}	4·0
ATP-citrate lyase	100^{d}	7	79·8^{c}	8·0	63·3^{ab}	4·0	68·0^{bc}	3·5	57·8^{a}	3·9	54·9^{a}	1·7
Glucose 6-phosphate dehydrogenase	100^{c}	8	55·4^{b}	8·4	44·8^{ab}	3·9	48·3^{ab}	3·3	36·5^{a}	4·8	35·8^{a}	2·8
Pyruvate kinase	100^{c}	7	65·0^{b}	7·1	51·3^{b}	3·3	59·6^{b}	3·8	31·1^{a}	2·0	38·0^{a}	4·1
Mitochondrial glycerol 3-phosphate acyltransferase	100^{d}	5	62·2^{bc}	6·0	52·9^{ab}	6·2	69·3^{c}	4·5	47·6^{ab}	5·5	42·2^{a}	4·8
DGAT 1	100^{a}	9	101^{a}	5	112^{a}	11	106^{a}	8	112^{a}	8	108^{a}	13
DGAT 2	100^{c}	8	92·4^{bc}	8·9	67·3^{a}	7·7	83·3^{abc}	12·3	64·8^{a}	6·1	74·0^{ab}	5·6
Spot 14	100^{b}	10	61·2^{a}	3·7	52·3^{a}	3·9	61·9^{a}	5·6	58·6^{a}	6·5	54·9^{a}	5·5
Adiponutrin	100^{c}	9	69·0^{b}	11·7	45·5^{a}	6·9	56·6^{ab}	4·7	40·3^{a}	4·7	36·9^{a}	3·5
SREBP-1a	100^{a}	6	107^{a}	9	95·3^{a}	4·7	101^{a}	8	91·5^{a}	4·2	100^{a}	6
SREBP-1c	100^{b}	7	79·7^{a}	7·2	62·8^{a}	8·0	79·2^{a}	3·8	75·1^{a}	6·7	63·3^{a}	6·2

DGAT, diacylglycerol acyltransferase; SREBP, sterol regulatory element binding protein.
^{a,b,c} Mean values within a row with unlike superscript letters were significantly different ($P<0·05$).
* For details of procedures, see p. 87.

synthesis. However, the extent of the reduction was comparable between sesamin and sesamolin. In relation to this, we previously observed that episesamin and sesamin decreased the activity and mRNA abundance of enzymes involved in fatty acid synthesis to similar levels (Kushiro *et al.* 2002). Therefore, sesamin, sesamolin and episesamin appear to be equally effective in decreasing hepatic fatty acid synthesis despite the considerable differences in their propensities to affect fatty acid oxidation.

We found that sesamin and sesamolin reduced the mRNA abundance not only of the enzymes involved in hepatic fatty acid synthesis, but also of the enzymes involved in glycerolipid biosynthesis including mitochondrial glycerol 3-phosphate acyltransferase and DGAT 2 though not DGAT 1. Therefore, it is plausible that these changes also can account for the lipid-lowering effect of dietary lignans. Measurements of the activities of these enzymes are required to confirm this notion. We also have confirmed previous findings that changes in mRNA expression of spot 14 and adiponutrin paralleled those of enzymes involved in fatty acid synthesis (Kinlaw *et al.* 1995; Ide, 2005). Both sesamin and sesamolin dose-dependently promoted hepatic fatty acid oxidation. However, the dose-dependency of their effects on the activity and mRNA abundance of enzymes involved in fatty acid synthesis is not as clear. The situation was the same for the mRNA abundance of enzymes involved in glycerolipid biosynthesis as well as of spot 14 and adiponutrin. With regard to the dose-dependent effect of the lignan preparation containing equal amounts of sesamin and episesamin, we previously observed that this preparation, at dietary levels of up to 2 g/kg, dose-dependently decreased the activity and mRNA abundance of lipogenic enzymes to levels 37–56 % of those observed with a lignan-free diet (Ide *et al.* 2001). However, no further decreases were observed with a diet containing 4 g/kg of this preparation. This indicates that the effect of lignans on hepatic lipogenesis is saturable at a relatively low dietary level which makes observation of the dose-dependent effect of lignans difficult. Many studies have indicated that SREBP-1 is involved in the regulation of the gene expression of enzymes involved in fatty acid synthesis (Kim *et al.* 1999; Shimomura *et al.* 1999; Horton *et al.* 2002). There are two types of SREBP-1, termed SREBP-1a and -1c. In the present study, we found that both sesamin and sesamolin reduced the mRNA abundance of SREBP-1c despite the absence of any clear-cut dose-dependent effects of these lignans on this parameter. However, these lignans did not affect the mRNA abundance of SREBP-1a. This supports the notion (Kim *et al.* 1999; Shimomura *et al.* 1999; Horton *et al.* 2002) that SREBP-1c, not -1a, is mainly involved in the regulation of hepatic fatty acid synthesis.

We found that sesamolin is more effective than sesamin in increasing hepatic fatty acid oxidation. But these compounds are equally effective in decreasing hepatic lipogenesis. This is not surprising, because these pathways are controlled by different signalling systems. There is a general consensus that PPARα is involved in the regulation of hepatic fatty acid oxidation (Schoonjans *et al.* 1996; Reddy & Hashimoto, 2001). It is likely that sesame lignans are the ligands and activators of PPARα (Ashakumary *et al.* 1999). It is possible that the binding affinity for and hence the ability to activate PPARα is greater for sesamolin than for sesamin, and therefore sesamolin increases hepatic fatty acid oxidation more than does sesamin. However, the levels of lignans accumulated in liver and serum are much higher for sesamolin than for sesamin. The present observation indicates that the difference in bio-availability is primarily responsible for the divergent effects of sesamin and sesamolin on hepatic fatty acid oxidation. In relation to this, episesamin is much more competent than sesamin in increasing hepatic fatty acid oxidation (Kushiro *et al.* 2002). Also, we proved that tissue and serum levels of episesamin well exceeded those of sesamin in rats fed the preparation containing equivalent amounts of sesamin and episesamin (Umeda-Sawada *et al.* 1999; Ide *et al.* 2004; Kushiro *et al.* 2004). In the present study, there were strong positive correlations between the total amount of hepatic lignan and activity (r 0·69–0·83) and the mRNA abundance of hepatic fatty acid oxidation enzymes (r 0·62–0·80). However, the present observation does not necessarily support the notion that the physiological activity of lignan in affecting hepatic fatty acid oxidation is solely dependent on its bio-availability. For instance, the total amount of hepatic lignan in rats fed the 0·6 g sesamolin/kg diet was more than 2-fold the value in rats fed the 2 g sesamin/kg diet. However, in this situation, we observed that the levels of activity and mRNA abundance of the enzymes involved in hepatic fatty acid oxidation were approximately the same in rats fed the 0·6 g sesamolin/kg diet as in rats fed the 2 g sesamin/kg diet. Therefore, it is reasonable that sesamin compared to sesamolin is more competent in activating PPARα and hence in activating hepatic fatty acid oxidation. In spite of this, the poor bio-availability of sesamin may cause the activity levels and mRNA abundance of hepatic enzymes involved in fatty acid oxidation to be much lower with sesamin than with sesamolin when the two lignans are given to rats at the same dietary level. It is currently unknown if the difference in the rate of intestinal absorption or of the catabolism is involved in the great diversity in the accumulation of sesamin and sesamolin in serum and liver.

It has been indicated that alterations in hepatic fatty acid synthesis (Windmueller & Spaeth, 1967; Rustan *et al.* 1992) and oxidation (Ide & Ontko, 1981; Ide *et al.* 1982; Rustan *et al.* 1992) are crucial in regulating liver and serum lipid levels. In the present study, diets containing lignan compared to a lignan-free diet reduced serum concentrations of TAG, cholesterol, phospholipids and NEFA. Also, hepatic levels of TAG and cholesterol were significantly lower in rats fed the former than those given the latter. Sesamolin and sesamin were equally effective in reducing lipogenesis. However, the former compared to the latter strongly increased hepatic fatty acid oxidation. This should cause the hepatic availability of fatty acids for the synthesis of TAG and hence subsequent secretion of this lipid molecule as a TAG-rich lipoprotein to be lower in rats fed sesamolin than in those fed sesamin. However, we found that sesamolin compared to sesamin is not more effective in reducing serum lipid concentrations. At a dietary level of 2 g/kg, we observed that serum cholesterol and phospholipid levels were even higher in rats fed sesamolin than in those fed sesamin. Also, the hepatic TAG-lowering effect was stronger with sesamin than with sesamolin. It is apparent that changes in hepatic fatty acid oxidation and synthesis alone cannot account for the alteration of serum and liver lipid levels caused by dietary sesamin and sesamolin. Changes in the mRNA abundance of enzymes involved in glycerolipid biosynthesis cannot account for this either. It is

Table 7. Effect of dietary lignans on serum and liver lipid and lignan levels in rats*
(Mean values with their standard errors, *n* 7–8)

	Dietary lignans											
	Lignan-free		Sesamin (0·6 g/kg)		Sesamin (2 g/kg)		Sesamolin (0·6 g/kg)		Sesamolin (2 g/kg)		Sesamin (1·4 g/kg) + sesamolin (0·6 g/kg)	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Serum lipids (μmol/l)												
TAG	2820^{d}	150	2090^{c}	240	1530^{ab}	140	1760^{bc}	160	1780^{bc}	80	1260^{a}	80
Cholesterol	2410^{c}	110	2050^{b}	110	1730^{a}	50	2230^{bc}	100	2080^{b}	150	2070^{b}	80
Phospholipid	2960^{d}	80	2400^{bc}	170	2100^{a}	80	2640^{c}	20	2510^{bc}	90	2310^{ab}	60
NEFA	1170^{b}	120	796^{a}	143	677^{a}	41	791^{a}	52	865^{a}	46	698^{a}	36
Serum glucose (μmol/l)	9180^{b}	230	8630^{ab}	230	8000^{a}	320	9070^{b}	390	8980^{b}	300	9100^{b}	280
Serum lignans (μg/l)												
Sesamin	0·0^{a}	0·0	8·8^{b}	0·8	31·4^{c}	4·6	1·1^{a}	0·2	1·2^{a}	0·9	31·5^{c}	3·6
Sesamolin	0·0^{a}	0·0	0·0^{a}	0·0	0·0^{a}	0·0	401·0^{b}	50·0	1030·0^{c}	80·0	392·0^{b}	38·0
Total	0·0^{a}	0·0	8·8^{b}	0·8	31·4^{c}	4·6	402·1^{d}	50·0	1031·2^{e}	80·0	423·5^{d}	39·0
Liver lipids (μmol/100 g body wt)												
TAG	373^{c}	34	153^{a}	16	133^{a}	13	306^{b}	19	260^{b}	22	245^{b}	14
Cholesterol	31·6^{c}	0·8	23·8^{ab}	1·2	23·6^{ab}	1·0	26·1^{b}	1·1	22·2^{a}	0·6	24·3^{ab}	0·8
Phospholipid	223^{a}	9	223^{a}	18	237^{a}	10	236^{a}	13	305^{b}	14	316^{b}	20
Liver lignans (μg/100 g body wt)												
Sesamin	0·00^{a}	0·00	1·83^{b}	0·28	7·12^{c}	1·08	0·19^{a}	0·02	0·08^{a}	0·02	7·33^{c}	0·81
Sesamolin	0·00^{a}	0·00	0·00^{a}	0·00	0·00^{a}	0·00	19·6^{b}	2·9	51·0^{c}	8·6	16·6^{b}	1·2
Total	0·00^{a}	0·00	1·83^{b}	0·28	7·12^{c}	1·08	19·8^{d}	2·9	51·1^{e}	8·7	23·9^{d}	1·9

^{a,b,c,d,e} Mean values within a row with unlike superscript letters were significantly different ($P<0·05$).
* For details of procedures, see p. 87.

difficult to explain why sesamin had a stronger lipid-lowering effect than sesamolin. It has been observed that compounds that induce hepatic fatty acid oxidation cause liver hypertrophy accompanying an increase in the hepatic phospholipid level (Yanagita *et al.* 1987; Pennacchiotti *et al.* 2001). Consistent with these observations, the 2 g sesamolin/kg diet and diet containing both sesamin and sesamolin increased liver weights and hepatic phospholipid levels in the present study. This may be a consequence of the proliferation of mitochondria and peroxisomes (Yanagita *et al.* 1987; Ashakumary *et al.* 1999; Pennacchiotti *et al.* 2001).

In conclusion, sesamin and sesamolin stimulated hepatic fatty acid oxidation. Sesamolin was much more effective than sesamin in increasing the parameters of hepatic fatty acid oxidation, while these compounds were equally effective in decreasing lipogenesis. Sesamolin compared to sesamin accumulated more in serum and liver. Differences in bioavailability may account for the divergent effects of dietary sesamin and sesamolin on hepatic fatty acid oxidation.

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