Combined effect of sesamin and soybean phospholipid on hepatic fatty acid metabolism in rats

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We studied the combined effect of sesamin (1:1 mixture of sesamin and episesamin) and soybean phospholipid on lipid metabolism in rats. Male rats were fed diets supplemented with 0 or 2 g/kg sesamin, and containing 0 or 50 g/kg soybean phospholipid, for 19 days. Sesamin and soybean phospholipid decreased serum triacylglycerol concentrations and the combination of these compounds further decreased the parameter in an additive fashion. Soybean phospholipid but not sesamin reduced the hepatic concentration of triacylglycerol. The combination failed to cause a strong decrease in hepatic triacylglycerol concentration, presumably due to the up-regulation of Cd36 by sesamin. Combination of sesamin and soybean phospholipid decreased the activity and mRNA levels of hepatic lipogenic enzymes in an additive fashion. Sesamin strongly increased the parameters of hepatic fatty acid oxidation enzymes. Soybean phospholipid increased hepatic activity of 3-hydroxyacyl-CoA dehydrogenase although it failed to affect the activity of other enzymes involved in fatty acid oxidation. Sesamin strongly increased hepatic concentration of carnitine. Sesamin and soybean phospholipid combination further increased this parameter, accompanying a parallel increase in mRNA expression of carnitine transporter. These changes can account for the strong decrease in serum triacylglycerol in rats fed a diet containing both sesamin and soybean phospholipid.

Key Words: sesamin, soybean phospholipid, hepatic lipogenesis, hepatic fatty acid oxidation, carnitine

Sesamin is one of the most abundant lignans in sesame seeds and is epimerized during acid-clay bleaching in the oil-refining process to form episesamin; therefore, sesamin preparations obtained as a byproduct of the oil-refining process contain sesamin and episesamin at about an equivalent ratio. It has been demonstrated that this sesamin preparation exerts a serum lipid-lowering effect on experimental animals and humans. We previously found that the sesamin preparation profoundly and dose-dependently increased the activity and gene expression of fatty acid oxidation enzymes in rat liver. Also, the sesamin preparation decreased hepatic activity and mRNA levels of enzymes involved in fatty acid synthesis. A later study showed that episesamin is more effective than sesamin in increasing the activity and gene expression of fatty acid oxidation enzymes.

Serum and liver lipid-lowering effects of dietary soybean phospholipid have long been recognized in animal and human studies. In relation to this, we previously demonstrated that soybean phospholipid profoundly and dose-dependently increased the activity and mRNA levels of lipogenic enzymes in rat liver. It is apparent that sesamin and soybean phospholipid are dietary factors that profoundly affect hepatic fatty acid metabolism and hence lower the serum lipid level. It is expected that the combination of these compounds in the diet would more profoundly affect hepatic fatty acid metabolism, and hence be effective in reducing lipid levels in serum and tissues and the incidence of atherosclerosis. In these contexts, we here studied the combined effect of sesamin and soybean phospholipid on lipid metabolism in rats.

Materials and Methods

Animals and diets. Male Sprague-Dawley rats obtained from Charles River Japan (Kanagawa, Japan) at 4 weeks of age were housed individually in animal cages in a room with controlled temperature (20–22°C), and lighting (lights on from 07:00 to 19:00), and fed a commercial diet (Type NMF; Oriental Yeast Co., Tokyo, Japan). After 7 days of acclimatization, rats were fed purified experimental diets supplemented in 1 kg with 0 or 2 g sesamin (1:1 mixture of sesamin and episesamin; gift from Takemoto Oil Co., Aichi, Japan), and containing in 1 kg either 31 g soybean oil (Nacalai Tesque, Inc., Kyoto, Japan) or 50 g soybean phospholipid (gift from Taiyo Kagaku Co., Yokkaichi, Japan) for 19 days. These dietary lipids served comparative amounts of fatty acids in diets (30.2 g/kg and 30.3 g/kg, respectively). In addition, all the experimental diets contained 7% coconut oil. The basal composition of the purified experimental diets was (in g/kg): casein, 200; coconut oil, 70; corn starch, 150; cellulose, 20; mineral mixture; vitamin mixture; L-cystine, 3; choline bitartrate, 2.5 and sucrose to 1 kg. Sesamin, soybean oil and soybean phospholipid were added to experimental diets in lieu of sucrose. Phospholipid and fatty acid compositions of soybean phospholipid as well as fatty acid composition of soybean oil are shown in Table 1. Animals had free access to the diets and water during the experimental period. This study was approved by the review board of animal ethics of our university and we followed the university’s guidelines in the care and use of laboratory animals.

Enzyme assays. The activity of lipogenic enzymes was measured spectrophotometrically using 15,000 x g supernatant of the liver homogenate as an enzyme source. Activity levels of various hepatic fatty acid oxidation enzymes were measured spectrophotometrically using the whole liver homogenate as an enzyme source. The peroxisomal palmitoyl-CoA oxidation rate and acyl-CoA oxidase activities were measured using palmitoyl-CoA as a substrate. Carnitine acyltransferase activities were measured using octanoy-CoA and palmitoyl-CoA as substrates. We used crotonoyl-CoA in assaying enoyl-CoA hydratase. The activity of 3-hydroxyacyl-CoA dehydrogenase was assayed in both
Phosphorus content (μmol/g) | Soybean oil | Soybean phospholipid |
--- | --- | --- |
Phospholipid classes (mol%) | — | 877 |
Lyso phosphatidylicholine | — | 10.8 |
Phosphatidylcholine | — | 34.2 |
Phosphatidylinositol | — | 18.1 |
Phosphatidylethanolamine | — | 37.3 |
Fatty acid content (mg/g) | — | 975 |
Fatty acid composition (weight%) | — | 605 |
16:0 | 8.5 | 16.4 |
16:1 | 0.1 | 0.1 |
18:0 | 3.5 | 3.6 |
18:1 | 24.8 | 7.5 |
18:2 | 54.2 | 63.4 |
18:3 | 5.6 | 6.2 |
20:0 | 0.5 | 0.0 |
22:0 | 0.2 | 0.1 |
24:0 | 0.3 | 0.3 |

Table 1. Phospholipid and fatty acid compositions of dietary lipids

Among four groups of rats (17.2–17.9 g/day). Also, sesamin and phospholipid did not affect the growth of animals during the 19 day feeding period and the body weights at the time of killing were 262 ± 4 g and 261 ± 6 g, and 274 ± 5 g and 270 ± 6 g for rats fed a sesamin-free or sesamin-supplemented (2 g/kg) diet containing 0 or 50 g/kg soybean phospholipid, respectively. Sesamin significantly increased the liver weight of animals but soybean phospholipid decreased this parameter. The values were 5.33 ± 0.12 and 4.94 ± 0.09 g/100 g body weight, and 5.95 ± 0.09 and 5.69 ± 0.17 g/100 g body weight for rats fed a sesamin-free or sesamin-supplemented (2 g/kg) diet containing 0 or 50 g/kg soybean phospholipid, respectively.

Effect of sesamin and soybean phospholipid on hepatic fatty acid synthesis. Both sesamin and soybean phospholipid significantly reduced the activities of lipogenic enzymes except for malic enzyme (Fig. 1). The diet containing 2 g/kg sesamin compared to a diet containing 50 g/kg soybean phospholipid was somewhat competent in reducing the activity levels of fatty acid synthase, ATP-citrate lyase, glucose 6-phosphate dehydrogenase, 6-phosphogluconate dehydrogenase, and pyruvate kinase. The combination of sesamin and soybean phospholipid effectively reduced the activity levels of these enzymes in an additive fashion. Meanwhile, soybean phospholipid but not sesamin significantly reduced the activity of malic enzyme.

Fig. 2 shows mRNA levels of proteins related to lipogenesis. There are two types of acetyl-CoA carboxylase, i.e., alpha and beta. The alpha but not beta form appears to be involved in fatty acid synthesis in cytosol. Mammalian tissues contain 3 distinct isoforms of malic enzyme (malic enzyme 1, 2 and 3). Malic enzyme 1 appears to be involved in the regulation of lipogenesis. There are four isoforms of pyruvate kinase in mammals. L-pyruvate kinase is an enzyme expressed in the liver. Adiponutrin is a protein presumed to be involved in the regulation of lipogenesis. We also analyzed mRNA expressions of enzymes involved in the desaturation of fatty acids, i.e., stearoyl-CoA desaturase 1, and Δ^5- and Δ^6-desaturases.

Consistent with the observations made on enzyme activity, both sesamin and soybean phospholipid significantly reduced mRNA levels of acetyl-CoA carboxylase α, fatty acid synthase, ATP-citrate lyase, glucose 6-phosphate dehydrogenase, 6-phosphogluconate dehydrogenase and L-pyruvate kinase. Combination of sesamin and soybean phospholipid further decreased the mRNA levels of these enzymes. The values in rats fed a diet simultaneously containing sesamin and soybean phospholipid were 11–32% of those observed with a diet free of these compounds. Both sesamin and soybean phospholipid also significantly lowered mRNA expression of adiponutrin, spot14 and stearoyl-CoA desaturase 1. Marked changes in mRNA expression of adiponutrin due to feeding with sesamin and soybean phospholipid were observed. The levels in rats fed a diet solely containing either sesamin or soybean phospholipid were 7% and 29%, respectively, of the value observed on the control diet. The value was extremely low with the diet containing both sesamin and soybean phospholipid (0.4% of the value observed on a control diet). Consistent with the observations made on enzyme activity, soybean phospholipid but not sesamin lowered the mRNA expression of malic enzyme 1. The level observed with a diet containing sesamin and soybean phospholipid in combination was the same as the value observed with a diet solely containing soybean phospholipid. The responses to sesamin and soybean phospholipid of mRNA expression of Δ^5- and Δ^6-desaturases resembled that observed with malic enzyme 1. Sterol regulatory element binding protein-1c (SREBP-1c) is a transcription factor involved in the regulation of the gene expression of many lipogenic enzymes. In spite of the fact that both sesamin and soybean phospholipid were effective in reducing the activity and mRNA levels of many lipogenic enzymes, soybean phospholipid but not sesamin significantly lowered mRNA levels of this transcription factor.
Effect of sesamin and soybean phospholipid on hepatic fatty acid oxidation. Consistent with the observations made in previous studies, sesamin significantly increased the activities of many enzymes involved in hepatic fatty acid oxidation (Table 2). Soybean phospholipid did not affect the activity of various enzymes involved in hepatic fatty acid oxidation except 3-hydroxyacyl-CoA dehydrogenase. Both sesamin and soybean phospholipid increased the activity of this enzyme in an additive fashion. This was confirmed in the enzyme activity measured in both reverse and forward reactions using acetoacetyl-CoA substrate for the former and 3-hydroxybutyryl-CoA and 3-hydroxydecanoyl-CoA substrates for the latter, respectively.

Consistent with the observations made on enzyme activities, sesamin increased mRNA levels of many enzymes involved in fatty acid oxidation. In spite of the fact that soybean phospholipid increased the activity of 3-hydroxyacyl-CoA dehydrogenase, this dietary factor was totally irrelevant in affecting mRNA levels of proteins which exhibit 3-hydroxyacyl-CoA dehydrogenase activity (peroxisomal bifunctional enzyme having enoyl-CoA hydratase/3-hydroxyacyl-CoA dehydrogenase activities, subunits of mitochondrial trifunctional enzyme having 3-hydroxyacyl-CoA dehydrogenase/3-ketoacyl-CoA thiolase/enoyl-CoA hydratase activities and mitochondrial 3-hydroxyacyl-CoA dehydrogenase. Sesamin caused about 1.5-fold increase in mRNA level of peroxisome proliferator activated receptor α (PPARα), a transcription factor involved in the regulation of gene expression of many fatty acid oxidation enzymes. However, soybean phospholipid was totally irrelevant in modulating this parameter. In addition to the mRNA levels of various fatty acid oxidation enzymes and PPARα, we also measured the mRNA level of Cd36 which, mediates the transport of fatty acids from the blood stream into hepatocytes and hence is involved in the regulation of fatty acid metabolism in the liver. Consistent with a previous observation, sesamin significantly increased the mRNA level of this protein but soybean phospholipid did not affect this parameter.

Effect of sesamin and soybean phospholipid on mRNA levels of proteins involved in the regulation of carnitine metabolism in the liver. Consistent with previous observations, sesamin greatly increased the carnitine concentration and mRNA level of carnitine transporter in the liver (Fig. 3). Soybean phospholipid did not affect these values when the diet was free of sesamin. Interestingly, however, hepatic carnitine
concentration was much higher in rats fed a diet containing sesamin and soybean phospholipid in combination than in the animals fed a diet solely containing sesamin. This was accompanied by a parallel increase in the mRNA level of carnitine transporter. Changes in the rate of hepatic carnitine synthesis appear to be one factor altering the concentration of carnitine in this tissue.\(^{(27,28)}\)

We therefore analyzed mRNA levels of hepatic enzymes involved in carnitine biosynthesis (ε-trimethyllysine hydroxylase, γ-trimethylaminobutyraldehyde dehydrogenase and γ-butyrobetaine hydroxylase 1) in the present study. However, sesamin and soybean phospholipid were totally ineffective in altering these values.

**Effect of sesamin and soybean phospholipid on serum and liver lipids.** Sesamin and soybean phospholipid significantly lowered serum concentrations of triacylglycerol in an additive fashion, and the level observed with a diet containing both of these dietary factors was the lowest among the groups (Table 3). Sesamin and soybean phospholipid solely added to experimental diets at the levels of 2 g/kg and 50 g/kg, respectively, were equally effective in reducing serum lipid concentrations of cholesterol and phospholipid; however, these dietary factors when added in combination did not cause additive decreases in these parameters. As expected, sesamin significantly increased serum concentrations of β-hydroxybutyrate. Soybean phospholipid when added solely to the diet was in no way effective in increasing this parameter. Interestingly, however, the value became significantly higher in rats given sesamin and soybean phospholipid in combination than in the animals fed a diet containing sesamin alone.

Soybean phospholipid solely added to the diet strongly reduced the hepatic triacylglycerol concentration; however, sesamin did not affect this parameter. The value was significantly lower in the animals fed both soybean phospholipid and sesamin than in those fed a diet solely containing sesamin and a diet free of these...
Compared to the former (soybean phospholipid), the value was significantly lower in rats fed both of these components than in the animals fed only containing sesame, but was comparable to the value in those fed solely containing soybean phospholipid. Both soybean phospholipid and sesamin significantly increased the hepatic concentration of cholesterol, the former being more competent than the latter in this respect. The value was significantly lower in rats fed both of these compounds than in the animals fed a diet only containing sesamin, but was comparable to the value in those fed only containing soybean phospholipid. Both soybean phospholipid and sesamin significantly increased the hepatic concentration of phospholipid, the latter being more competent in this respect.

Sesame lignans were detected in both the serum and liver in rats fed sesamin-containing diets but not in the animals fed sesamin-free diets. Although the sesamin preparation used in this study contained both sesamin and epi-sesamin in equal amounts, epi-sesamin predominated in both the serum and liver. Total lignan and epi-sesamin but not sesamin concentrations in serum were significantly lower in rats fed soybean phospholipid-containing diets than in the animals fed diets free of this compound. Epi-sesamin but not sesamin and total lignin concentrations in liver were significantly lower in the former than in the latter.

**Discussion**

**Combined effect of sesamin and soybean phospholipid on hepatic lipogenesis.** Many lipogenic enzymes are under the control of SREBP-1. This transcription factor also regulates the gene expression of enzymes involved in the desaturation of fatty acid (stearoyl-CoA desaturase 1, and Δ6- and Δ5-desaturases). (29,30) It has been reported that the expressions of the genes of malic enzyme (29,30) as well as fatty acid desaturases (29,30) are dually regulated by SREBP-1 and PPARα. Our previous studies showed that both sesamin (1,29) and soybean phospholipid (29,30) decreased the activity and mRNA levels of many enzymes involved in hepatic lipogenesis. These previous findings were also confirmed in the present study (Fig. 1 and 2). Also, the experimental diet containing both of these compounds effectively decreased many of these parameters in an additive fashion. However, the responses to sesamin and soybean phospholipid of mRNA levels of malic enzyme 1, and of Δ6- and Δ5-desaturases were considerably different from those of other enzymes (Fig. 2). Sesamin appears to be an agonist of PPARα, (29,30) and hence is expected to stimulate gene expressions of these enzymes, and at the same time, the lignan should conversely down-regulate their mRNA expression through a SREBP-1-dependent mechanism. (29,30) These effects will cause only a moderate change in the mRNA expression of these genes, as actually observed in rats fed sesamin in the current study. In spite of the fact that the gene of stearoyl-CoA desaturase 1 is also under the control of both SREBP-1 and PPARα, sesamin and soybean phospholipid are almost comparable in their abilities to reduce mRNA expression of this gene, and a combination of these compounds reduced the parameter in an additive fashion (Fig. 2). Therefore, the sensitivities to SREBP-1 and PPARα of these fatty acid desaturase genes may be mutually different. As expected, soybean phospholipid, unlike sesamin,
decreased mRNA expressions not only of the various lipogenic enzymes, including malic enzyme 1, but also various fatty acid desaturases. The combination of this compound with sesamin results in the lowering of the expression of malic enzyme 1 and Δ⁵- and Δ⁶-desaturases to the levels observable in rats fed a diet solely containing soybean phospholipid. It was suggested that the combination of sesamin and soybean phospholipid potentiated the down-regulation of the SREBP-1 signaling pathway and overcame the sesamin-mediated stimulation of PPAR action on Δ⁵- and Δ⁶-fatty acid desaturase genes and the malic enzyme 1 gene.

It has been well demonstrated that many enzymes involved in lipogenesis are under the control of SREBP-1. It is reasonable to consider that both sesamin and soybean phospholipid decreased hepatic lipogenesis through a SREBP-1-dependent mechanism. However, the mRNA level of SREBP-1c did not parallel those of lipogenic genes (Fig. 2). This is not surprising because the protein levels of the mature active form of SREBP-1 do not necessarily parallel the mRNA levels of this transcription factor. Determination of the protein levels of mature form of SREBP-1 is required to clarify this point.

Combined effect of sesamin and soybean phospholipid on hepatic fatty acid oxidation. In the present study, we confirmed previous findings that sesamin increased the hepatic activity and mRNA levels of various fatty acid oxidation enzymes. It is reasonable that sesamin is a ligand and activator of PPARα and hence increases hepatic fatty acid oxidation. We observed in the present study that sesamin increased mRNA levels of PPARα (Table 2). Therefore, an increase in gene expression of this transcription factor may also be involved in the sesamin-dependent increase in hepatic fatty acid oxidation.

We found that not only sesamin but also soybean phospholipid caused a considerable increase in the activities of 3-hydroxyacyl-CoA dehydrogenase (Table 2). This unexpected finding was confirmed using various substrates. However, the phospholipid was not effective in altering the activities of other enzymes, except for a slight increase in the peroxisomal palmitoyl-CoA dehydrogenation.
rate. Three enzyme molecules have so far been identified to possess 3-hydroxacyl-CoA dehydrogenase activities, i.e., peroxisomal bifunctional enzyme having enoyl-CoA hydratase/3-hydroxacyl-CoA dehydrogenase activities (Ehhadh), mitochondrial trifunctional enzyme having 3-hydroxacyl-CoA dehydrogenase/3-ketoacyl-CoA thiolase/enoyl-CoA hydratase activities (this enzyme is composed of two subunits, Hadha and Hadhb) and mitochondrial monofunctional 3-hydroxacyl-CoA dehydrogenase (Hadh). Soybean phospholipid, however, did not affect mRNA levels of all these enzymes (Table 2). It is therefore uncertain which enzyme molecule is responsible for the soybean phospholipid-dependent change in 3-hydroxacyl-CoA dehydrogenase activity. There is a possibility that up-regulation of enzyme molecules that have not hitherto been identified is responsible. Alternatively, soybean phospholipid may stimulate the gene expression of known enzymes at the level of translation without affecting mRNA levels of the enzymes.

In relation to the physiological activity of sesamin and soybean phospholipid affecting hepatic fatty acid oxidation, we confirmed a previous finding that sesamin strongly increased the hepatic concentration of carnitine (Fig. 3). Moreover, we found that soybean phospholipid increased hepatic carnitine concentration when it was added to a sesamin-containing diet. As the changes in hepatic carnitine concentration well paralleled those in mRNA levels of carnitine transporter (Fig. 3), the alteration in the gene expression of this transporter may be primarily responsible for the changes in hepatic carnitine concentration. mRNA expression of carnitine transporter is under the control of PPARα. Therefore, it is likely that sesamin activated PPARα and hence up-regulated mRNA expression of the transporter. However, soybean phospholipid-dependent changes in carnitine transporter mRNA levels can not be accounted for by a PPARα-mediated mechanism because soybean phospholipid failed to increase mRNA expressions of various fatty acid oxidation enzymes many of which are targeted by PPARα. The mechanism underlying the up-regulation of mRNA expression of carnitine transporter in rats given a diet containing both sesamin and soybean phospholipid is currently unknown. A diet containing both sesamin and soybean phospholipid compared to a diet solely containing sesamin significantly increased hepatic activity of 3-hydroxacyl-CoA dehydrogenase and carnitine concentration. Therefore, it is plausible that the former increased β-oxidation in the liver more than the latter. In fact, serum concentration of β-hydroxybutyrate was significantly higher in rats given a diet containing both sesamin and soybean phospholipid than in the animals given a diet solely containing sesamin.

### Table 3. Effect of sesamin and soybean phospholipid on the concentrations of serum and liver lipids and lignans, and serum β-hydroxybutyrate

<table>
<thead>
<tr>
<th>Soybean PL (g/kg)</th>
<th>0</th>
<th>50</th>
<th>0</th>
<th>50</th>
<th>Two-way ANOVA (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>50</td>
<td>0</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td><strong>Sesamin</strong></td>
<td></td>
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<tr>
<td><strong>Soybean PL</strong></td>
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<tr>
<td><strong>Sesamin × Soybean PL</strong></td>
<td></td>
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<td></td>
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<tr>
<td><strong>Serum components</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Triacylglycerol (mmol/L)</strong></td>
<td>3.47 ± 0.38</td>
<td>2.48 ± 0.30</td>
<td>1.91 ± 0.21</td>
<td>0.99 ± 0.09</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Cholesterol (mmol/L)</strong></td>
<td>2.58 ± 0.09b</td>
<td>1.96 ± 0.07a</td>
<td>1.94 ± 0.08a</td>
<td>1.79 ± 0.09a</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Phospholipid (mmol/L)</strong></td>
<td>2.94 ± 0.11b</td>
<td>2.23 ± 0.13a</td>
<td>2.35 ± 0.12a</td>
<td>2.24 ± 0.15a</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td><strong>β-Hydroxybutyrate (mmol/L)</strong></td>
<td>0.108 ± 0.008b</td>
<td>0.104 ± 0.005a</td>
<td>0.149 ± 0.007b</td>
<td>0.186 ± 0.008b</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Liver components</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sesamin (mmol/L)</strong></td>
<td>—</td>
<td>—</td>
<td>0.089 ± 0.011</td>
<td>0.086 ± 0.005</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Sesamin (mmol/g)</strong></td>
<td>—</td>
<td>—</td>
<td>0.716 ± 0.061b</td>
<td>0.434 ± 0.064a</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Sesamin (nmol/g)</strong></td>
<td>—</td>
<td>—</td>
<td>0.805 ± 0.072b</td>
<td>0.521 ± 0.068a</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Epsilasmin (nmol/L)</strong></td>
<td>—</td>
<td>—</td>
<td>4.40 ± 0.53</td>
<td>3.15 ± 0.40</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Epsilasmin (nmol/L)</strong></td>
<td>—</td>
<td>—</td>
<td>12.9 ± 1.1b</td>
<td>8.91 ± 0.90a</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Total (nmol/L)</strong></td>
<td>—</td>
<td>—</td>
<td>26.2 ± 3.1</td>
<td>18.0 ± 2.4</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Values are means ± SEM, n = 7. Means in a row with superscripts without a common letter differ (p<0.05). PL, phospholipid; ns, not significant.
A diet solely containing soybean phospholipid profoundly decreased the hepatic concentration of triacylglycerol; however, a diet solely containing sesamin failed to do so (Table 3). The value was lower in animals fed both of these compounds than in animals fed a diet solely containing sesamin and a diet free of sesamin and phospholipid, but was higher than the value in animals fed a diet solely containing soybean phospholipid. In relation to this, sesamin profoundly increased hepatic mRNA expression of Cd36 (Table 2). It has been indicated that Cd36 gene is targeted by both PPARα and PPARγ(26,36) Therefore, both PPARα and PPARγ agonists increase mRNA expression of Cd36 in tissues(36) Sesamin appears to be an agonist to activate PPARα.(2) Therefore, it is reasonable that this lignan increases mRNA expression of Cd36 in the liver. Moreover, our recent study(26) raised the possibility that sesamin increases mRNA expression of hepatic Cd36 through up-regulation of gene expression of PPARγ. Recent studies in mice(14,38,39) indicated that Cd36 plays a crucial role in the transport of fatty acid in hepatocytes and hence regulates hepatic triacylglycerol concentration. Therefore, up-regulation of Cd36 can account for the failure of sesamin to decrease hepatic triacylglycerol, although this compound reduced hepatic lipogenesis and increased fatty acid oxidation.

Phospholipids are crucial in the emulsification of lipophilic compounds. There is the possibility that dietary soybean phospholipid helps emulsification and in turn stimulates intestinal absorption of sesamin, a lipophilic compound. This may contribute to the physiological effects of a diet containing both sesamin and soybean phospholipid on hepatic fatty acid metabolism observed in the present study. The observation that dietary phospholipid rather decreased serum and liver levels of the sesame lignan (Table 3) does not support this consideration.

In conclusion, sesamin and soybean phospholipid effectively decreased the serum triacylglycerol concentration and the combination of these compounds further decreased this parameter in an additive fashion. Strong additive reduction of hepatic lipogenesis may be primarily responsible. In addition, there is the possibility that not only sesamin but also soybean phospholipid increased hepatic fatty acid oxidation. Therefore, the additive increase in hepatic fatty acid oxidation by these dietary factors may also account for the observed change in serum triacylglycerol levels. The situation is considerably different in the liver. Soybean phospholipid but not sesamin strongly decreased hepatic triacylglycerol concentration. The addition of sesamin to a diet containing soybean phospholipid rather increased this parameter. Up-regulation by sesamin of Cd36 may account for this consequence.

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Conflict of Interest

No potential conflicts of interest were disclosed.

References


