Biochemical and Molecular Actions of Nutrients

Salacia reticulata and Its Polyphenolic Constituents with Lipase Inhibitory and Lipolytic Activities Have Mild Antiobesity Effects in Rats

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ABSTRACT *Salacia (S.) reticulata*, a Hippocrateaceae plant distributed in Sri Lankan and Indian forests, has been used as a supplementary food in Japan to prevent obesity and diabetes. We examined the antiobesity effects of the hot water–soluble extract (SRHW) from the roots of *S. reticulata* using obese rat models and an in vitro study. Body weight ($P = 0.07$) and periuterine fat storage ($P = 0.10$) in female Zucker fatty rats (8–9 wk old) tended to be suppressed by oral administration of SRHW (125 mg/kg) for 27 d. Male rats fed a high fat diet were not affected by SRHW. Furthermore, SRHW inhibited porcine pancreatic lipase (PL), rat adipose tissue–derived lipoprotein lipase (LPL) and glycerophosphate dehydrogenase (GPDH) activities with 50% inhibitory concentrations (IC_{50}) of 264 (95% confidence limits: 203–393) mg/L, 15 (12–18) mg/L and 54 (35–85) mg/L, respectively, but did not inhibit hormone-sensitive lipase activity in rat adipose tissue. Next, we examined the effects of polyphenols, di- and triterpenes and salacinol isolated from the roots of *S. reticulata* on lipid metabolizing enzymes and lipolysis. (–)-Epigallocatechin and (–)-epicatechin-(4$\beta\rightarrow$8)-(–)-4′-*O*-methylepigallocatechin inhibited PL activity with IC_{50} of 88 (not calculated) and 68 (26–122) mg/L, respectively. (–)-Epicatechin, 3β,22β-dihydroxyolean-12-en-29-oic acid and the tannin fraction inhibited LPL activity with IC_{50} of 81 (54–214), 89 (62–214) and 35 (24–62) mg/L. Only the tannin fraction inhibited GPDH activity with an IC_{50} of 6.8 (3.4–10.9) mg/L. These constituents may be involved in the lipase and GPDH inhibitory activities of SRHW. On the other hand, SRHW at 100 mg/L tended to enhance lipolysis in rat adipocytes ($P = 0.06$). Significant lipolytic effects were exerted by mangiferin, (–)-4′-*O*-methylepigallocatechin and maytenfolic acid at 100 mg/L ($P < 0.01$). In conclusion, polyphenolic compounds may be involved in the antiobesity effects of SRHW in rats through inhibition of fat metabolizing enzymes (PL, LPL and GPDH) and enhanced lipolysis. J. Nutr. 132: 1819–1824, 2002.

KEY WORDS: • Salacia reticulata • *obesity* • *polyphenol* • *lipase* • *lipolysis* • *rats*

The Hippocrateaceae plant *Salacia* (*S.*) *reticulta* is a woody climber found in Sri Lanka and India. The roots and stems of *S. reticulata* have been used for prevention or remedy of diabetes in these countries. Similarly, the extract from *S. reticulata* is consumed as a food supplement that prevents obesity and diabetes in Japan because it suppresses postprandial hyperglycemia. Recently, we isolated the potent α-glucosidase inhibitors salacinol (1) and kotalanol (2) from this plant. The hot water–soluble extract from the roots of *S. reticulata* (SRHW)[2] was reported to prevent human postprandial hyperglycemia (3) and to decrease the fasting plasma glucose, hemoglobin A_{1C} and body mass index (BMI) in patients with mild type II diabetes (4). Additionally, safety profiles such as acute and subacute toxicity, mutagenicity, antigenicity and phototoxicity (5–7) plus quality control methods (8) of SRHW have been established.

Previously, we investigated the effect of SRHW on body weight gain in standard diet and high sucrose (650 g sucrose/kg) diet–fed rats. Increases in body weight and visceral fat in rats fed either of these diets containing 0.1 g/100 g SRHW were significantly suppressed (9). In the present study of the antiobesity effects of *S. reticulata*, we examined the effects of SRHW in Zucker fatty rats and high fat diet (HFD)-fed rats. To clarify the antiobesity mechanism of SRHW, we also examined the effects of SRHW and constituents of *S. reticulata* on lipid metabolizing enzymes, such as lipases and glycerophosphate dehydrogenase (GPDH). Similarly, we evaluated the lipolytic effects of SRHW and constituents on rat epididymal fat–derived adipocytes.

MATERIALS AND METHODS

Animals. Female Zucker fatty rats and male Wistar rats were purchased from Kiwa Laboratory Animals (Wakayama, Japan). Male Crj:CD (SD) IGS rats were obtained from Japan Charles Liver (Yokohama, Japan). The rats were housed in an air-conditioned room at 23 ± 2°C. Rats consumed standard nonpurified diet (MF, Oriental Yeast, Tokyo, Japan) and tap water ad libitum during the prebreeding period. The following experimental protocols were approved by the

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[2] Abbreviations used: BMI, body mass index; FFA, free fatty acids; GPDH, glycerophosphate dehydrogenase; HFD, high fat diet; HSL, hormone-sensitive lipase; IC_{50}, 50% inhibitory concentration; LPL, lipoprotein lipase; PL, pancreatic lipase; SRHW, hot water–soluble extract from the roots of *S. reticulata*.

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Experimental Animal Research Committee at Kyoto Pharmaceutical University.

Preparation of SRHW from S. reticulata. Dried roots of *S. reticulata* (1 kg) obtained from a market in Colombo, Sri Lanka, were crushed and extracted (80°C, 3 h) with 10 L water 3 times. Solvent was evaporated at <40°C followed by spray-drying to obtain SRHW. The yield of SRHW from the roots was 7.5%, and the polyphenol content determined by the colorimetric method using ferrous tartrate (Folin-Denis method) was 24% (10).

Isolation of constituents from the root of S. reticulata. Dried roots of *S. reticulata* (3.1 kg) were crushed and extracted (80°C, 3 h) three times with 10 L methanol (MeOH) to yielded the MeOH extract. The MeOH extract was separated by procedures described previously to give mangiferin (**1**), (–)-epicatechin (**2**), (–)-epigallocatechin (**3**), (–)-4′-*O*-methylepigallocatechin (**4**), (–)-epiafzelechin-(4β→8)-(–)-4′-*O*-methylepigallocatechin (**5**) and (–)-epicathechin-(4β→8)-(–)-4′-*O*-methylepigallocatechin (**6**), hydroxyferruginol (**7**), lambertic acid (**8**), kotalagenin 16-acetate (**9**), 26-hydroxy-1,3-friedelanedione (**10**), maytenfolic acid (**11**) and 3β,22β-dihydroxyolean-12-en-29-oic acid (**12**) and salacinol (**13**) (**Fig. 2**) (8,11). The isolation scheme and yields (%) of compounds **1**–**13** from the dried roots are shown in **Figure 1**. The polyphenol concentration in fraction 3 (tannin fraction) was 63% (10).

Examination of body weight and visceral fat changes in obese rats. Female Zucker fatty rats (8–9 wk old) were fed the nonpurified diet (MF) for 27 d. SRHW (125 mg/kg) suspended in 50 g/L acacia solution was given orally once daily from d 0 to 27. On d 27, rats were deprived of food for 22 h. Visceral fat (mesenteric fat, perirenal fat, and periuterine fat) was removed on d 28 and its weight measured. Male SD rats (5 wk old) were fed HFD (Oriental Yeast) [**Table 1** (12)] or powdered MF for 10 d (d −10 to 0) for acclimation to housing conditions and diets; then they were studied for the next 31 d (d 0–31). SRHW (125 mg/kg) suspended in 50 g/L acacia solution was given orally once daily to half of the rats fed the HFD. On d 32, visceral fat (mesenteric fat, perirenal fat and epididymal fat) was removed and weighed after rats had been deprived of food for 24 h.

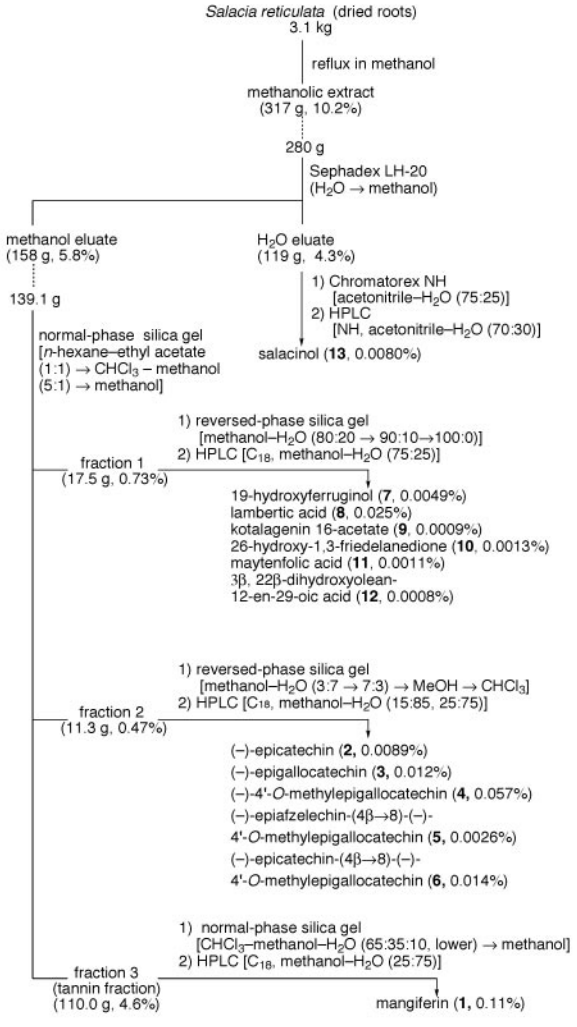

FIGURE 1 Isolation of components from the roots of *Salacia reticulata*.

TABLE 1

Composition of the high fat diet (HFD)

	g/kg dry diet
Lard[1]	580
Fish meal	300
Skimmed soybean meal	100
Vitamin mix[2]	19
Mineral mix[3]	0.6
DL-Methionine	0.4

[1] Lard provided the following (g/100 g lard): 14:0, 2.0; 14:1, 0.3; 15:1, 0.1; 16:0, 26.5; 16:1, 3.7; 17:0, 0.5; 17:1, 0.4; 18:0, 12.1; 18:1, 42.5; 18:2(n-6), 9.8; 18:3(n-3), 0.7; 20:0, 0.2; 20:1, 0.6; 20:4(n-6), 0.3.

[2] Vitamin mix provided the following (mg/kg dry diet): retinol acetate, 2.28; cholecalciferol, 0.038; *dl*-α-tocopherol acetate, 76; menadione, 1.25; thiamine acetate, 19; riboflavin, 14.59; pyridoxine, 3.01; cyanocobalamin, 0.72; nicotinic acid, 22.8; pantothenic acid Ca, 19; inositol, 22.8; folic acid, 0.68; choline chloride 957.6.

[3] Minral mix provided the following (mg/kg dry diet): Ca, 168; Mn, 12; Fe, 20.4; Zn, 18; Cu, 1.32; Co, 0.36; I, 0.204; Mg, 0.0072.

Lipase inhibition. An inhibitory test for pancreatic lipase (PL) activity was performed with a commercial kit (Lipase Kit S; Dainippon Pharmaceutical, Osaka, Japan) and porcine PL (Sigma-Aldrich, St. Louis, MO). The reaction mixture containing test sample was incubated for 30 min. A hormone-sensitive lipase (HSL) activity inhibitory test was performed according to a slightly modified method of Berger and Barnard (13). Rat fat pads from Wistar rats were treated with test sample for 30 min and stimulated with 10 μmol norepinephrine/L for 3 h. Glycerol released into the medium was determined (F-kit glycerol; Boehringer Mannheim, Mannheim, Germany). Rat (Wistar) fat pad-derived lipoprotein lipase (LPL) activity was determined by the method of Motoyashiki et al. (14). Test samples were treated for 2 h and the released free fatty acids (FFA) were measured (NEFA C-test Wako; Wako Pure Chemical, Osaka, Japan).

GPDH inhibition. Rat epididymal fat (1 g) from Wistar rats was homogenized in 0.25 mol sucrose/L (4 mL) and centrifuged (700 × *g*, 4°C, 10 min). The infranatant was further centrifuged (54000 × *g*, 4°C, 30 min) and the resulting infranatant was used as the GPDH source. The GPDH activity inhibitory test was performed with a commercial kit (GPDH activity test; Hokudo, Sapporo, Japan).

Lipolysis from rat epididymal fat-derived adipocytes. A commercial culture kit (Rat Preadipocyte Total Kit, Toyobo, Osaka, Japan) was used for the lipolysis experiment. Briefly, rat (Wistar) epididymal fat-derived preadipocytes (6.5×10^3 cells/well) in 200 μL of medium were plated onto 48-well collagen-coated plates (Sumilon; Sumitomo Bakelite, Tokyo, Japan) and were cultured for 2 d. The medium was changed to differentiation medium containing dexamethasone and insulin, and the cells were cultured for 9 d. During culture, the medium was changed once every 3 d. After culture, the medium was changed to one containing sample, and the cells were cultured for another 18 h. The supernatant was removed and the cells were sonicated in 200 μL of PBS. The triglyceride content of the cells was measured (Triglyceride G-test Wako; Wako Pure Chemical).

Statistics. Results were expressed as means and SEM. IC_{50} are presented with 95% confidence limits. Significance of the differences between two independent groups was examined by Student's *t* test. For three or more independent groups, one-way ANOVA followed by Dunnett's or Fisher's protected least significant difference test was used. Differences with $P < 0.05$ were considered significant.

RESULTS

Body weight and fat accumulation in obese rats. SRHW did not affect food consumption in Zucker fatty or HFD-fed rats (data not shown). Oral administration of SRHW (125 mg/kg) tended to suppress body weight of Zucker fatty rats on d 25 and 27 ($P = 0.07$) (**Fig. 3**). SRHW also slightly suppressed ($P = 0.10$) periuterine fat accumulation in Zucker fatty rats (**Table 2**). SRHW suppressed neither body weight nor visceral fat (perirenal, mesenteric and epididymal fat) accumulation in male HFD-fed rats.

Lipase inhibition. SRHW inhibited porcine PL and LPL in rat adipocytes in a concentration-dependent manner but it did not inhibit HSL activity (**Fig. 4**). The IC_{50} of constituents isolated from *S. reticulata* (Fig. 2) on PL and LPL activities are shown in **Table 3**. (–)-Epigallocatechin (**3**) and (–)-epicatechin-(4β→8)-(–)-4′-*O*-methylepigallocatechin (**6**) inhibited PL activity. (–)-Epiafzelechin-(4β→8)-(–)-4′-*O*-methylepigallocatechin (**5**), lambertic acid (**8**) and the tannin fraction had weak inhibitory effects on PL activity. On the other hand, the tannin fraction showed the most potent inhibition of LPL activity. (–)-Epicatechin (**2**) and **12** weakly inhibited the activity.

GPDH inhibition. SRHW inhibited the activity of GPDH prepared from rat epididymal fat in a concentration-dependent manner (**Fig. 5**, *upper panel*). Among the constituents of *S. reticulata*, only the tannin fraction showed potent inhibitory activity (Fig. 5, *lower panel*). The inhibitory activities of the other compounds were < 15% at 100 mg/L (data not shown).

Lipolytic activity. An 18-h treatment with SRHW tended to decrease the remaining triglycerides that reflect lipolysis in adipocytes ($P = 0.06$) at 100 mg/L (**Table 4**). Among the constituents of *S. reticulata*, mangiferin (**1**), (–)-4′-methylepigallocatechin (**4**) and maytenfolic acid (**11**) had lipolytic activity at 100 mg/L ($P < 0.01$).

DISCUSSION

We demonstrated that daily consumption of SRHW (125 mg/kg) tended to suppress body weight 14% in Zucker fatty rats with distinct obesity and hypertriglyceridemia. Recently, epigallocatechin gallate from green tea was reported to reduce body weight as well as food consumption (15). Changes in hormonal secretions including leptin and insulin are thought to be involved in suppression of appetite. Although the effect of SRHW was moderate and not significant, it is interesting

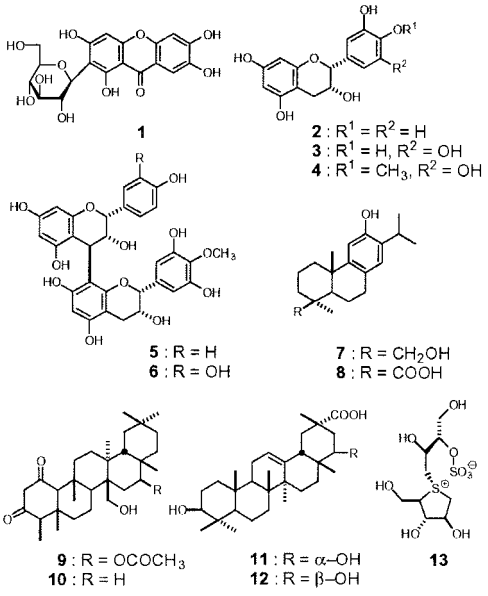

FIGURE 2 Compounds isolated from *Salacia reticulata*.

that SRHW suppressed body weight without affecting food consumption. On the other hand, SRHW suppressed neither body weight nor visceral fat accumulation in HFD-fed SD rats. Han et al. (16) reported that oolong tea (50 g/kg included in diet) moderately suppressed body weight in HFD-fed mice. Caffeine and phenolic compounds have been suggested to be involved in the antiobesity effects of oolong tea. Moreover, among phenolic compound-rich foods, green tea (17) and black tea (18) extracts prevent diet-induced hypertriglyceridemia and hypercholesterolemia in rats. Yugaratani et al. (19) reported that orally administered tannic acid (100 mg/rat, 10

TABLE 2

Effects of the hot water–soluble extract from the roots of Salacia reticulata (SRHW) on visceral fat accumulation in female Zucker fatty rats and male SD rats fed a high fat diet (HFD)[1]

	Zucker fatty rats		SD rats	
Treatment	Vehicle	SRHW	Vehicle	SRHW
		g		
Periuterine fat	28.0 ± 2.2	23.6 ± 0.3	—	—
Perirenal fat	12.4 ± 1.4	13.3 ± 0.9	14.4 ± 2.2	12.9 ± 1.6
Mesenteric fat	11.9 ± 0.8	11.3 ± 0.7	8.0 ± 1.0	7.6 ± 0.5
Epididymal fat	—	—	10.9 ± 1.4	10.6 ± 1.1

[1] Values are means ± SEM, $n = 6$ or 7.

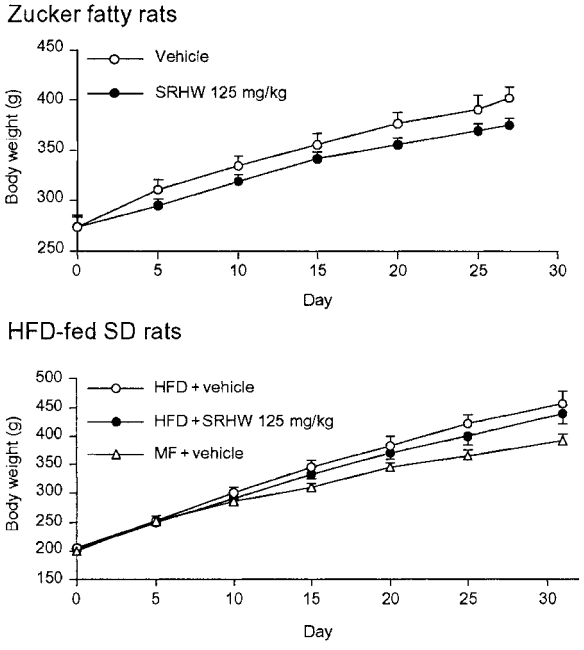

FIGURE 3 Effects of the hot water–soluble extract from the roots of *Salacia reticulata* (SRHW) on body weights of female Zucker fatty rats and high fat diet (HFD)- or standard diet (MF)-fed male SD rats. Each point represents the mean ± SEM, $n = 6$ or 7.

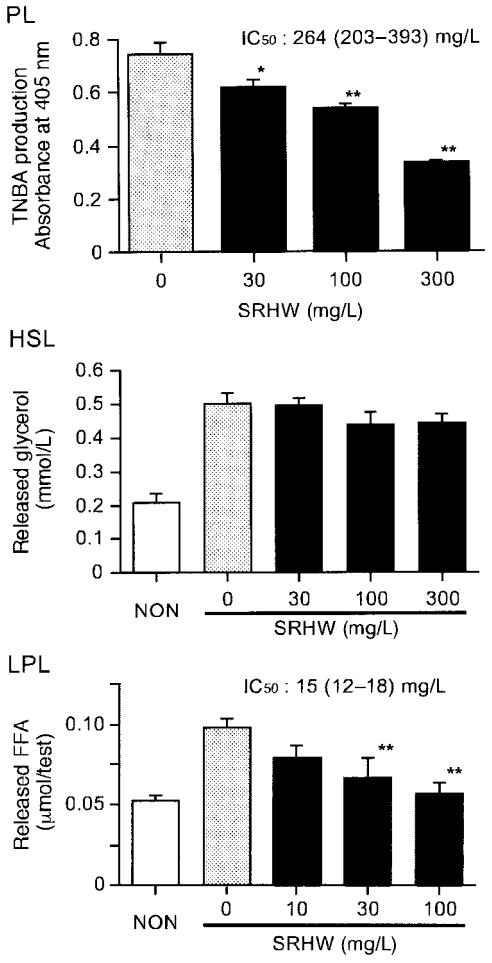

FIGURE 4 Inhibitory effects of the hot water–soluble extract from the roots of *Salacia reticulata* (SRHW) on porcine pancreatic lipase (PL), hormone sensitive lipase (HSL) and lipoprotein lipase (LPL) activities in rats. The 50% inhibitory concentrations (IC_{50}) are means with 95% confidence limits. Each column represents the mean ± SEM, $n = 4$. *,**Different ($P < 0.05$, $P < 0.01$) from the untreated group (0 mg/L) by Dunnett's test. TNBA, 5-thio-2-nitrobenzoic acid; FFA, free fatty acids; NON, nonstimulation (native release).

wk) reduced serum triglycerides and fat deposition, and lowered hepatic lipase activity in HFD-fed rats. On the other hand, green tea facilitated bile acid and cholesterol excretion into fecal matter, and lowered serum cholesterol levels (20). Also, catechin was reported to increase fat excretion (21). Because SRHW contains a high concentration of polyphenols (24%) including mangiferin (**1**), catechins and condensed tannins, the polyphenols in SRHW may reduce body weight by higher dose administration or feeding with diet. We previously reported that SRHW reduced body weight in rats fed standard and high sucrose diets (9). A reduction in absorbed carbohydrates from the gut was involved with this effect. α-Glucosidase inhibitors that have been suggested to affect carbohydrate absorption include salacinol (**13**) (1) and mangiferin (**1**) (8). Although **13** has potent α-glucosidase inhibitory activity, comparable to acarbose, its SRHW content is low. Moreover, the activity of mangiferin (**1**), highly concentrated in SRHW, is weak. Thus, it is not likely that the suppressive effect of SRHW on body weight is completely dependent on a reduction in carbohydrate absorption. These and previous observations illustrate the need to clarify the other mechanisms involved in the antiobesity effects and the active constituents, particularly polyphenols.

Reducing fat absorption is an effective way to suppress body weight gain, as seen in the clinical use of orlistat, a specific PL inhibitor, in obese patients (22). On the other hand, naturally occurring substances that interrupt PL action, such as chitin-chitosan (23) and chondroitin sulfate, are prescribed in alternative formulas. Here, we examined the effects of SRHW on PL activity, and found that it inhibited PL activity in a concentration-dependent manner with an IC_{50} of 264 mg/L. Among the constituents isolated from *S. reticulata*, catechins (**3** and **6**) showed potent inhibitory activity. The tannin fraction (63% polyphenols determined by the Folin-Denis method) also inhibited PL activity. These findings suggest that phenolic compounds in SRHW are involved mainly in PL inhibitory activity. In general, highly polymerized polyphenols (condensed tannins) form complexes with protein and diminish gastrointestinal enzyme activities such as trypsin, α-amylase and PL (24). Although this potency increases with the degree of polymerization, Horigome et al. (25) suggested that the affinity of condensed tannins for lipase was lower than that of trypsin or α-amylase. In our study, no clear relationship between the potency of PL inhibition and degree of polymerization of epicatechin, or structural relationship could be established.

The other lipases found in adipose tissue or in the blood vessels around them participate in fat storage in adipocytes. HSL, which is activated by norepinephrine, causes lipolysis of deposited triglycerides and release of glycerol and fatty acids into the blood stream. On the other hand, LPL hydrolyzes triglycerides carried in chylomicrons and LDL, and it acts on fat stored in adipocytes. Interestingly, SRHW strongly inhibited adipose tissue–derived LPL activity with an IC_{50} of 15 mg/L, but not HSL activity at a high concentration (300 mg/L). This finding indicates that SRHW may inhibit fat accumulation in adipose tissue from lipid in the blood stream. As a result of examining the effects of constituents from *S. reticulata* on LPL activity, (–)-epicatechin (**2**), 3β,22β-dihydroxyolean-12-en-29-oic acid (**12**) and the tannin fraction showed inhibitory activity. However, **12** is a hydrophobic compound. Because it is not water extractable and is barely present in SRHW (data not shown), the phenolic constituents are suggested to act on fat storage.

GPDH contained in adipocytes is a key enzyme in the metabolic conversion of glucose to triglyceride (26). This enzyme is involved in storage of fat originating from absorbed carbohydrates. SRHW inhibited GPDH activity in a dose-dependent manner, and its IC_{50} was 54 mg/L. Among the constituents in *S. reticulata*, only the tannin fraction strongly inhibited GPDH activity (IC_{50}, 6.8 mg/L). Condensed tannins seemed to reduce sugar-derived fat accumulation. Ardevol et al. (27) reported that grape-derived highly condensed procyanidin decreased GPDH activity. On the other hand, catechin and epicatechin reduced these activities. This finding supports ours.

Finally, we examined the induction of lipolysis by SRHW in rat epididymal fat-derived adipocytes. SRHW weakly decreased the remaining triglycerides in adipocytes due to lipolysis at 100 mg/L. Among the constituents of *S. reticulata*, mangiferin (**1**), (–)-4′-*O*-methylepigallocatechin (**4**) and maytenfolic acid (**11**) induced lipolysis. Because **1** was highly concentrated (0.9–2.3%) in SRHW (8), this compound is thought to be involved in the lipolysis induction by SRHW. Ardevol et al. (27) reported that grape-derived highly condensed procyanidin had lipolytic activity in 3T3-L1 adipocytes. On the other hand, catechins, major constituents of

TABLE 3

Effects of constituents from the roots of Salacia reticulata on porcine pancreatic lipase (PL) and rat lipoprotein lipase (LPL) activities

	PL	LPL
	IC_{50}[1] (95% confidence limits) [Inhibition[2]]	
	mg/L [%]	
Vehicle	—[3]	— [0.0 ± 7.4]
Mangiferin (**1**)	— [−1.0]	— [24.8 ± 1.2]
(−)-Epicatechin (**2**)	— [9.3]	81 (54–214) [56.1 ± 2.8**]
(−)-Epigallocatechin (**3**)	88 (—) [91.2 ± 5.3**]	— [44.9 ± 3.4**]
(−)-4′-*O*-Methylepigallocatechin (**4**)	— [16.8 ± 0.3**]	— [18.9 ± 0.1**]
(−)-Epiafzelechin-(4β → 8)-(−)-4′-*O*-methylepigallocatechin (**5**)	270 (—) [58.8 ± 1.4**]	— [13.0 ± 0.1]
(−)-Epicatechin-(4β → 8)-(−)-4′-*O*-methylepigallocatechin (**6**)	68 (26–122) [51.8 ± 1.5**]	— [28.8 ± 0.9*]
19-Hydroxyferruginol (**7**)	— [86.3 ± 2.1**]	— [7.4 ± 0.3]
Lambertic acid (**8**)	225 (149–474) [52.5 ± 0.5**]	— [34.0 ± 3.6**]
Kotalagenin 16-acetate (**9**)	— [50.6 ± 0.9**]	— [19.1 ± 1.9]
26-Hydroxy-1,3-friedelanedione (**10**)	— [35.2 ± 1.0**]	— [−1.8 ± 0.0]
Maytenfolic acid (**11**)	— [−27.9]	— [−3.8 ± 0.0]
3β,22β-Dihydroxyolean-12-en-29-oic acid (**12**)	— [−20.9]	89 (62–214) [52.0 ± 1.6**]
Salacinol (**13**)	— [12.6 ± 0.1**]	— [13.6 ± 0.4]
Tannin fraction	188 (138–294) [65.5 ± 2.4**]	35 (24–62) [107.8 ± 4.8**]

[1] Values are means and 95% confidence limits. *,** Significant difference ($P < 0.05$, $P < 0.01$) between each test sample and the vehicle by Dunnett's test; IC_{50}, 50% inhibitory concentration.
[2] Inhibition at 300 mg/L (PL) or 100 mg/L (LPL). Values represent mean or mean ± SEM, $n = 4$.
[3] —, not calculated.

green tea, have been reported to enhance thermogenesis in rat brown adipose tissue (28). This effect is considered to be due to norepinephrine accumulation caused by inhibition of catechol O-methyl transferase and transcellular phosphodiesterase. Ong et al. (29) showed that tannic acid (hydrolyzable tannin), excluding the catechin monomer and gallic acid, inhibited insulin-stimulated lipogenesis in rat adipose tissue with an IC_{50} of 350 mmol/L. This inhibitory effect may result from inhibition of the insulin receptor phosphorylation and

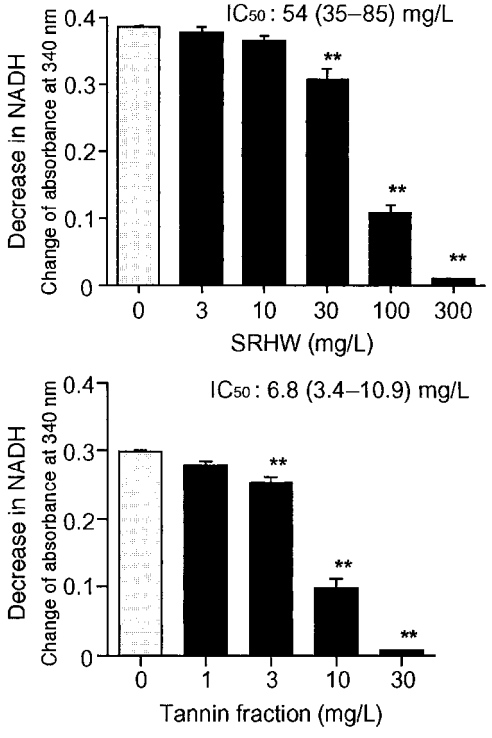

FIGURE 5 Inhibitory effects of the hot water–soluble extract from the roots of *Salacia reticulata* (SRHW) and the tannin faction on glycerophosphate dehydrogenase (GPDH) activity in rats. Each column represents the mean ± SEM, $n = 4$. **Different ($P < 0.01$) from the untreated group (0 mg/L) by Dunnett's test.

TABLE 4

Lipolytic effects of the hot water–soluble extract from the roots of Salacia reticulata (SRHW) and its constituents on rat epididymal fat-derived cultured adipocytes[1]

	Remaining triglyceride in adipocyte[2]
	% of vehicle
Vehicle	100.0 ± 5.4
SRHW	90.0 ± 5.1
Mangiferin (**1**)	64.7 ± 3.7**
(−)-Epicatechin (**2**)	65.8 ± 10.4
(−)-Epigallocatechin (**3**)	88.1 ± 10.5
(−)-4′-*O*-Methylepigallocatechin (**4**)	61.3 ± 6.0**
(−)-Epiafzelechin-(4β → 8)-(−)-4′-*O*-methylepigallocatechin (**5**)	78.8 ± 5.6
(−)-Epicatechin-(4β → 8)-(−)-4′-*O*-methylepigallocatechin (**6**)	76.1 ± 11.4
19-Hydroxyferruginol (**7**)	92.8 ± 3.7
Lambertic acid (**8**)	98.0 ± 8.8
Kotalagenin 16-acetate (**9**)	111.9 ± 5.1
26-Hydroxy-1,3-friedelanedione (**10**)	99.4 ± 5.4
Maytenfolic acid (**11**)	62.8 ± 2.5**
3β,22β-Dihydroxyolean-12-en-29-oic acid (**12**)	92.1 ± 8.0
Salacinol (**13**)	75.3 ± 6.6
Tannin fraction	86.2 ± 0.7

[1] Values are means ± SEM, $n = 4$. ** Different ($P < 0.01$) from the vehicle Fisher's protected least significant difference test.
[2] Each sample was treated at 100 mg/L.

receptor-associated tyrosine kinase phosphorylation. Mangiferin (**1**) and **4**, phenolic constituents of SRHW, may enhance lipolysis via these mechanisms.

In conclusion, we showed that oral administration of SRHW weakly reduced body weight in female Zucker fatty rats. Various polyphenols that are highly concentrated in SRHW, including mangiferin (**1**), catechins, and condensed tannins, may be involved in the antiobesity effects of SRHW through inhibition of lipid-metabolizing enzymes and stimulation of lipolysis.

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