Fd Chem. Toxic. Vol. 31, No. 3, pp. 213–218, 1993
Printed in Great Britain.

0278-6915/93 $6.00 + 0.00

EFFECTS OF *CURCUMA XANTHORRHIZA* ROXB. AND CURCUMINOIDS ON THE LEVEL OF SERUM AND LIVER LIPIDS, SERUM APOLIPOPROTEIN A-I AND LIPOGENIC ENZYMES IN RATS

S. YASNI*, K. IMAIZUMI*†, M. NAKAMURA*, J. AIMOTO* and M. SUGANO‡
*Laboratory of Nutrition Chemistry and ‡Laboratory of Food Science, Department of Food Science and Technology, School of Agriculture (46-09), Kyushu University, Fukuoka 812, Japan

(Accepted 30 October 1992)

Abstract—*Curcuma xanthorrhiza* Roxb., a medicinal plant used in Indonesia, has been shown to exert diverse physiological functions. However, little attention has been paid to its effect on lipid metabolism. We have investigated the effects of *C. xanthorrhiza* on serum and liver lipids, serum high density lipoprotein (HDL)-cholesterol and apolipoprotein (apo) A-I, and liver lipogenic enzymes in rats. In rats given a cholesterol-free diet, *C. xanthorrhiza* decreased the concentrations of serum triglycerides and phospholipids, and liver cholesterol, and increased serum HDL-cholesterol and apo A-I. The activity of liver fatty acid synthase, but not glycerophosphate dehydrogenase, was decreased by the medicinal plant. In rats on a high-cholesterol diet, *C. xanthorrhiza* did not suppress the elevation of serum cholesterol, although it did decrease liver cholesterol. Curcuminoids prepared from *C. xanthorrhiza* had no significant effects on the serum and liver lipids. These studies, therefore, indicate that *C. xanthorrhiza* contains an active principle(s) other than curcuminoids which can modify the metabolism of lipids and lipoproteins.

INTRODUCTION

Curcuma xanthorrhiza Roxb. (Zingiberaceae family, commonly known as temu lawak or Javanese turmeric in Indonesia), which is found both wild and cultivated in Indonesia, has been traditionally used for medicinal purposes (Dharma, 1980). Either the fresh rhizomes or a decoction of dried sliced rhizomes have been used to treat various stomach diseases and liver disorders such as jaundice and gall stones, and promote the flow of bile (Hsu *et al.*, 1985; Perry, 1980). *C. xanthorrhiza* is also used as a tonic in Indonesia (Abdul and Toga, 1985).

The dried rhizomes of *C. xanthorrhiza* have been reported to contain 7–30% essential oils, 30–40% carbohydrate (starch) and 0.02–2.0% aromatic yellow curcuminoids which consist of 58–71% curcumin and 29–42% desmethoxycurcumin (Purseglove *et al.*, 1981; Raharja *et al.*, 1983). Recently, methanol- and ether-soluble fractions from *C. xanthorrhiza* were found to be biologically active, having hypothermic, chologogic and antitumorigenic effects, and prolonging pentobarbital-induced sleeping time (Itokawa *et al.*, 1985; Ozaki and Liang, 1988; Ozaki and Soedigdo, 1988; Yamazaki *et al.*, 1988).

Rhizomes of *Curcuma longa* L. (commonly known as turmeric or kunyit in Indonesia) which is of the same genus as *C. xanthorrhiza*, contain a strong colouring pigment and are used widely in Asian countries as a condiment, particularly as an ingredient of curry powder. Compared with *C. xanthorrhiza*, the effects of *C. longa* on serum lipid concentration have been relatively well investigated. Dixit *et al.* (1988) reported that feeding an ethanolic extract of *C. longa* to Triton-induced hyperlipidaemic rats caused decreased concentrations of serum triglycerides and cholesterol, and an elevated concentration of serum high density lipoprotein (HDL)-cholesterol. In addition, Rao *et al.* (1970) reported a hypocholesterolaemic effect of curcuminoids from *C. longa* in rats fed a high cholesterol diet.

Recently, Ozaki and Liang (1988) observed the stimulation of bile flow in rats fed essential oils from *C. xanthorrhiza*, in comparison with those fed essential oils from *C. longa*, and identified *d*-camphor as an active principle. In a previous paper, we reported that *C. xanthorrhiza* suppressed elevations of serum glucose and triglycerides in diabetic rats (Sedarnawati *et al.*, 1991). Since little attention has been focused on the role of *C. xanthorrhiza* on lipid metabolism, we have examined the effects of dietary supplementation with this medicinal plant on the concentrations of serum and liver lipids, HDL-cholesterol and apolipoprotein (apo) A-I, and lipogenic enzymes in rats. The effects of curcuminoids prepared from *C. xanthorrhiza* were also investigated. The present results show

†To whom correspondence should be addressed.
Abbreviations: Apo = apolipoprotein; EDTA = ethylenediaminetetraacetic acid; EXHC = exogenous hypocholesterolaemic; HDL = high density lipoprotein; GPDH = glycerophosphate dehydrogenase.

that *C. xanthorrhiza* exerts a marked influence on the metabolism of serum and liver lipids and serum lipoproteins in normal and hypercholesterolaemic rats.

MATERIALS AND METHODS

Preparation of samples. Powdered *C. xanthorrhiza* was purchased from P. T. Mustika Ratu (Jakarta, Indonesia). This medicinal plant is rich in carbohydrates (77%, w/w), and its chemical composition was reported in the previous paper (Sedarnawati *et al.*, 1991).

Curcuminoids were prepared from *C. xanthorrhiza* (Sidik *et al.*, 1986). The residues of *C. xanthorrhiza* extracted with hexane (five-fold excess by weight) were refluxed for 6 hr and refluxing was done three times with 70% methanol at 60°C. The resulting methanol extract was dried using a rotary evaporator. When analysed by thin-layer chromatography (GF 254, E. Merck A.G., Darmstadt, Germany) using CH_3OH—$CHCl_3$ as the developing solvent, the dried extract consisted mainly of two curcuminoids: curcumin (1,7-bis-(4-hydroxy-3 methoxyphenyl)-1,6-heptadiene-3,5-dione) and desmethoxycurcumin (*p*-hydroxycinnamoylferuloylmethane). Each 100 g of *C. xanthorrhiza* yielded approximately 5 g curcuminoids.

Animals and diets. Either male Sprague–Dawley rats (Seiwa Experimental Animals Co., Fukuoka, Japan) or exogenous hypercholesterolaemic (ExHC) rats (Imaizumi *et al.*, 1992) obtained from the Animal Center of Kyushu University School of Medicine (Fukuoka, Japan) were housed individually in stainless-steel cages with wire-meshed bottoms in an air-conditioned room (23 ± 1°C) with a controlled dark–light cycle (lights on 08.00–20.00 hr). The rats were given *ad lib.* a commercial rat chow (Type NMF, Oriental Yeast Co., Tokyo, Japan) and water before starting the experiments.

The standard purified diets contained (% by weight): 20% casein (vitamin-free, Wako Pure Chemicals Co., Osaka, Japan); 15% α-corn starch (Nippon Shokuhin Kakoh Ltd, Aichi, Japan); 10% fat (olive oil from Nacalai Tesque Inc., Kyoto, Japan and safflower oil and lard from the local market); 1% vitamin mixture (AIN mixture, Oriental Yeast Co.); 3.5% mineral mixture (AIN mixture, Oriental Yeast Co); 0.2% choline bitartrate (Katayama Chemicals Co., Osaka, Japan); 0.3% DL-methionine (Nacalai Tesque Inc., Kyoto, Japan); 4–8% cellulose (Type E, Toyo Roshi Kaisha Ltd, Tokyo, Japan); sucrose to make up to 100% (American Institute of Nutrition, 1977). The experimental design is shown in Table 1. In experiment 1, the effects of *C. xanthorrhiza* on the various parameters were examined in rats given a cholesterol-free diet. In experiment 2, the hypocholesterolaemic effect of this medicinal plant was tested, so that rats sensitive to exogenous cholesterol were used, with 10% olive oil provided as a fat source, since 10% olive oil can effectively elevate serum cholesterol levels without the addition of bile salts in this rat strain (Imaizumi *et al.*, 1992). In experiment 3, curcuminoids prepared from *C. xanthorrhiza* were tested with or without the addition of cholesterol to the diet (experiments 3-1 and 3-2, respectively), since a previous experiment had shown that curcuminoids prepared from *C. longa* are effective in suppressing serum cholesterol in hypercholesterolaemic rats (Rao *et al.*, 1970). To prepare the diets for the three experiments, powdered medicinal plants, guar gum (Pfizer Co., Tokyo, Japan), fats and cholesterol (Nacalai Tesque Inc.,) were added to the standard diet at the expense of sucrose as shown in Table 1. Since each experiment had an individual purpose, as described above, we consider that the difference in dietary fat in each experiment will have little influence on the interpretation of the results obtained.

Body weight and food intake were recorded daily. Rats were killed at 11.00 hr without fasting by drawing blood from the abdominal aorta under light diethyl ether anaesthesia. Serum was prepared by centrifugation at 3000 rpm for 15 min at 4°C. The liver and epididymal fat pad were excised immediately, frozen with liquid nitrogen, and kept at −40°C until analysed. All procedures received approval from the University Laboratory Animal Care and Use Committee as conforming to standards for treatment of laboratory animals.

Determination of fatty acid synthase and glycerophosphate dehydrogenase. 2-g portions of each liver were homogenized with a teflon–glass homogenizer (Labo stirrer model LR41C, Yamamoto Scientific Co. Ltd., Tokyo, Japan) in a cold phosphate–carbonate buffer (pH 8.0) containing 70 mM-$NaHCO_3$, 85 mM-K_2HPO_4, 9 mM-KH_2PO_4, 1 mM-ethylenediaminetetraacetic acid (EDTA) and 1 mM-dithiothreitol (Shillabeer *et al.*, 1990). The

Table 1. Experimental design

Experiment no.	Supplements added to the diet*	Strain of rat	No. of days of treatment
1	4% *C. xanthorrhiza* + 8% lard + 2% safflower oil	SD	34
	4% Guar gum + 8% lard + 2% safflower oil	SD	34
	4% Cellulose + 8% lard + 2% safflower oil	SD	34
2	4% *C. xanthorrhiza* + 4% cellulose + 10% olive oil + 1% cholesterol	ExHC	21
	8% Cellulose + 10% olive oil + 1% cholesterol	ExHC	21
3–1	0.2% Curcuminoids + 5% cellulose + 10% olive oil	ExHC	28
	5% cellulose + 10% olive oil	ExHC	28
3–2	0.2% Curcuminoids + 5% cellulose + 10% olive oil + 0.5% cholesterol	ExHC	14
	5% Cellulose + 10% olive oil + 0.5% cholesterol	ExHC	14

*Supplements were added to the standard diet at the expense of sucrose.

Table 2. Effects of *C. xanthorrhiza* and guar gum on growth parameters, concentrations of serum and liver lipids, serum apo A-I and activities of liver FAS and GPDH in Sprague–Dawley rats (experiment 1)*

Parameter	Dietary groups		
	Control	*C. xanthorrhiza*	Guar gum
Body weight (g)			
Initial	324 ± 6	323 ± 6	322 ± 5
Final	438 ± 11	433 ± 11	439 ± 10
Food intake (g/day)	20.6 ± 0.5	19.4 ± 0.6	20.6 ± 0.6
Relative organ weight (g/100 g body weight)			
Liver	4.14 ± 0.17†‡	4.28 ± 0.10†	3.71 ± 0.10‡
Epididymal fat pad	1.82 ± 0.11†	1.44 ± 0.06‡	1.68 ± 0.10†‡
Serum lipids (mg/100 ml)			
Total cholesterol	99.2 ± 7.1	95.6 ± 4.5	80.4 ± 5.4
Esterified	79.2 ± 5.2	77.6 ± 3.5	54.7 ± 6.9
Free	19.4 ± 4.1	22.0 ± 2.3	31.3 ± 6.2
HDL-cholesterol	37.6 ± 2.2†	50.0 ± 3.2‡	41.6 ± 1.8†‡
Triglycerides	432 ± 55†	148 ± 25‡	257 ± 33‡
Phospholipids	217 ± 20†	188 ± 9‡	171 ± 15‡
Apo A-I§	59.8 ± 12†	128 ± 13‡	68.3 ± 11†
Liver lipids (mg/g liver)			
Cholesterol	3.94 ± 0.28†	3.02 ± 0.41‡	2.46 ± 0.08‡
Triglycerides	51.0 ± 6.1†	16.8 ± 3.8‡	26.9 ± 3.2‡
Phospholipids	27.8 ± 0.6†	34.8 ± 1.1‡	32.1 ± 0.7‡
Liver lipogenic enzymes (U/min/mg protein)¶			
FAS	62.3 ± 12†	28.8 ± 2.8‡	60.7 ± 8.4†
GPDH	3587 ± 699	2828 ± 273	3355 ± 591

FAS = fatty acid synthase GPDH = glycerophosphate dehydrogenase

*Rats were fed a cholesterol-free diet for 34 days.

§Expressed as an arbitrary unit.

¶FAS: 1 U = 1 nmol NADPH oxidized/min; GPDH: 1 U = 1 nmol NADPH oxidized/min.

Values are means ± SEM for groups of six to eight rats, and different superscripts denote a significant difference at $P < 0.05$ (Student's t-test).

homogenate was then centrifuged at 20,000 *g* (High Speed Refrigerated Centrifuge RS-205, Tomy Seiko Co., Ltd, Tokyo, Japan) for 10 min. The supernatant was centrifuged again at 100,000 *g* (Hitachi 55P–72, Automatic Preparative Ultracentrifuge, Hitachi Koki Co., Ltd, Ibaragi, Japan) for 1 hr at 4°C. The resulting supernatant was frozen immediately with liquid nitrogen and kept at −85°C until used for the assays of fatty acid synthase (FAS; EC 2.3.1.85) and glycerophosphate dehydrogenase (GPDH; EC 1.1.1.8).

The activity of FAS was determined as follows (Nepokroeff *et al.*, 1975). 30 μl 300 nmol NADPH (Oriental Yeast, Co.) and 100 μl of the supernatant were added to 0.5 ml 0.2 mM-potassium phosphate buffer (pH 7.0) containing 0.2 mM-EDTA and 20 μl 50 nmol acetyl CoA (Wako Pure Chemicals Co., Osaka, Japan). After warming for 1–2 min at 30°C, 20 μl 200 nmol malonyl CoA (Sigma Chemical Co., St Louis, MO, USA) was added to the premixture to initiate the reaction, and the change of absorbance was recorded at 340 nm (Hitachi 150-20 Spectrophotometer, Hitachi Ltd., Tokyo, Japan). 1 U FAS activity is defined as 1 nmol NADPH oxidized/min.

GPDH was assayed as follows (Kozak and Jensen, 1974). 10 μl supernatant was added to 0.5 ml 50 mM-triethanolamine–HCl buffer (pH 7.5) containing 5 mM-EDTA and 10 μl NADH (Oriental Yeast Co.). After warming at 30°C for 1–2 min, 10 μl dihydroxyacetonephosphate (Sigma Chemicals Co.) was added to the mixture to initiate the reaction. 1 U GPDH activity corresponds to the oxidation of 1 nmol NADH oxidized/min.

Analytical procedure. Serum and liver lipids were extracted in a chloroform–methanol mixture (2:1, v/v; Folch *et al.*, 1957), and analysed for cholesterol, triglycerides and phospholipids (Imaizumi *et al.*, 1987). HDL-cholesterol was measured by using a commercially available kit (HDL-test, Wako Pure Chemicals Co.). Serum apo A-I was determined by rocket immunoelectrophoresis as described previously (Imaizumi *et al.*, 1982a), and were expressed as an arbitrary unit against a standard serum. Protein content was determined according to the method of Lowry (Lowry *et al.*, 1951).

Statistical method. Data were analysed statistically by Student's t-test.

RESULTS

Since *C. xanthorrhiza* is rich in carbohydrates, 4% cellulose or 4% powdered *C. xanthorrhiza* rhizome was added to the cholesterol-free standard diet at the expense of sucrose (experiment 1). In addition, as a positive control, guar gum which presumably exerts effects different from those of cellulose on the serum and liver lipids (Imaizumi *et al.*, 1982b) was added as a supplement to the standard diet. As shown in Table 2, food intake and body weight gain were similar in all three groups. Relative Liver weight was similar in the rats fed *C. xanthorrhiza* or cellulose, but

it was significantly lower in rats fed guar gum than in those fed *C. xanthorrhiza*. The relative weight of the epididymal adipose tissue was significantly lower in rats fed the medicinal plant than in those fed cellulose. Concentrations of serum triglycerides and phospholipids, and those of liver triglycerides, were significantly lower in rats fed *C. xanthorrhiza* than in those fed cellulose. In comparison with the controls, the medicinal plant decreased liver cholesterol and increased liver phospholipids, but did not affect serum levels of free and esterified cholesterols. In addition to these changes, the medicinal plant, in comparison with cellulose, caused elevations in serum HDL-cholesterol and apo A-I, and a reduction in liver FAS activity. Liver GPDH activity was similar in rats fed cellulose and those fed *C. xanthorrhiza*. In general, the response of these lipid parameters in rats fed guar gum was similar to that in rats fed *C. xanthorrhiza*, but there were clear differences in the concentrations of serum apo A-I and the activity of liver FAS. Thus, *C. xanthorrhiza* contains some specific principles which influence serum and liver lipid metabolism and which are different from those in guar gum.

To assess a preventive effect of *C. xanthorrhiza* on the elevation of serum and liver cholesterols, ExHC rats that are genetically susceptible to exogenous cholesterol (Imaizumi *et al.*, 1992) were used in experiment 2. To facilitate the elevations of serum and liver cholesterols in ExHC rats, 1% (w/w) cholesterol and 10% (w/w) olive oil were added to the standard diet. As shown in Table 3, food intake and body weight gain were significantly lower in rats fed the medicinal plant than in those fed control diet. The medicinal plant increased the relative liver weight and decreased the relative weight of the epididymal fat pad. Although *C. xanthorrhiza* decreased the concentrations of liver cholesterol, it was not effective in preventing an elevation of serum cholesterol. In addition, the medicinal plant, in comparison with cellulose, decreased the concentrations of liver triglycerides, but elevated serum triglycerides. The concentration of serum and liver phospholipids, and serum HDL-cholesterol and apo A-I were higher in rats fed *C. xanthorrhiza* than in those fed the control diet.

Table 3. Effects of *C. xanthorrhiza* on growth parameters and concentrations of serum and liver lipids and serum apo A-I in ExHC rats (experiment 2)*

Parameter	Diet	
	Control	*C. xanthorrhiza*
Body weight (g)		
Initial	151 ± 2	152 ± 1
Final	315 ± 2	292 ± 4†
Food intake (g/day)	19.7 ± 0.2	16.2 ± 0.4†
Relative Organ weight (g/100 g body weight)		
Liver	5.29 ± 0.06	6.72 ± 0.14†
Epididymal fat pad	1.52 ± 0.08	1.12 ± 0.04†
Serum lipids (mg/100 ml)		
Cholesterol	330 ± 15	461 ± 32†
HDL-cholesterol	13.9 ± 0.4	21.9 ± 0.8†
Triglycerides	131 ± 12	253 ± 22†
Phospholipids	274 ± 7	399 ± 17†
Apo A-I§	27.9 ± 0.5	68.6 ± 7.7†
Liver lipids (mg/g liver)		
Cholesterol	69.7 ± 4.5	41.2 ± 3.3†
Triglycerides	47.6 ± 2.4	21.3 ± 1.1†
Phospholipids	24.0 ± 0.4	28.5 ± 0.7†

*Rats were fed on a high cholesterol diet for 21 days.
§Expressed as an arbitrary unit.
Values are means ± SEM for groups of five to eight rats and those marked with a dagger differ significantly (Student's *t*-test) from the control group value (†$P < 0.05$).

Since it has been reported that curcuminoids prepared from *C. longa* prevent hypercholesterolaemia in rats fed a high cholesterol diet (Rao *et al.*, 1970), curcuminoids prepared from *C. xanthorrhiza* were added to cholesterol-free and cholesterol-enriched diets at a level of 0.2%, which is equivalent to 4% *C. xanthorrhiza*. As shown in Table 4, curcuminoids did not significantly influence lipid parameters, growth parameters or organ weights, except for a reduction of food intake and body weight gain and an elevation of relative liver weight when fed with a high cholesterol diet.

DISCUSSION

The present study showed that *C. xanthorrhiza* decreases concentrations of serum and liver triglycerides, and increases serum HDL-cholesterol and apo A-I in rats fed a cholesterol-free diet. In the present study, guar gum also decreased the concentrations of serum and liver triglycerides, but it had no significant effect on the levels of serum HDL-cholesterol and apo A-I, or on liver FAS activity. Curcuminoids appear not to be responsible for these alterations induced by *C. xanthorrhiza*, since this material had no significant influence on the serum and liver lipid parameters. These alterations can be attributed to specific principles of *C. xanthorrhiza*, since administration of this medicinal plant suppressed the activity of liver FAS which catalyses conversion of malonyl CoA to palmitate, but had no effects on the activities of liver GPDH which works at the branching point between triglyceride synthesis and the glycolytic pathway.

In the present study, *C. xanthorrhiza* increased serum HDL-cholesterol and apo A-I, irrespective of the presence or absence of dietary cholesterol. The effect of the medicinal plant on the distribution of serum lipoprotein–cholesterols and metabolism of HDL remains to be determined, as elevated concentrations of HDL has been postulated to be beneficial for preventing atherogenesis (Miller and Miller, 1975).

As shown in the present study, *C. xanthorrhiza* exhibited no cholesterol-lowering activity in blood plasma in rats fed a high cholesterol diet. It has been reported that curcuminoids prepared from *C. longa* suppress an elevation of serum cholesterol in rats fed a high cholesterol diet (Rao *et al.*, 1970), and decrease elevations of serum cholesterol and triglycerides in Triton-treated hyperlipidaemic rats (Dixit *et al.*,

Table 4. Effects of curcuminoids on growth parameters, and the concentrations of serum and liver lipids in ExHC rats (experiment 3)*

	Diet			
	Cholesterol-free		High cholesterol	
Parameter	Control	Curcuminoids	Control	Curcuminoids
Body weight (g)				
Initial	116 ± 7	118 ± 9	253 ± 8	243 ± 6
Final	313 ± 7	326 ± 8	329 ± 6	313 ± 6†
Food intake (g/day)	16.8 ± 0.4	17.4 ± 0.4	21.1 ± 0.2	19.5 ± 0.2†
Relative Organ weight (g/100 g body weight)				
Liver	4.30 ± 0.12	4.44 ± 0.13	4.64 ± 0.05	4.83 ± 0.06†
Epididymal fat pad	1.65 ± 0.05	1.95 ± 0.12	1.68 ± 0.03	1.59 ± 0.04
Serum (mg/100 ml)				
Cholesterol	75.5 ± 3.1	86.3 ± 3.8	367 ± 26	311 ± 32
HDL-cholesterol	31.9 ± 0.6	31.7 ± 1.1	15.6 ± 0.5	16.2 ± 0.6
Triglycerides	252 ± 45	252 ± 52	127 ± 10	130 ± 6
Phospholipids	162 ± 4	171 ± 9	187 ± 15	196 ± 6
Liver (mg/g liver)				
Cholesterol	3.59 ± 0.13	3.22 ± 0.24	44.1 ± 1.4	44.1 ± 1.8
Triglycerides	13.6 ± 0.9	13.4 ± 0.3	20.5 ± 1.3	20.1 ± 1.6
Phospholipids	25.6 ± 1.4	26.5 ± 1.4	24.7 ± 0.5	24.3 ± 0.4

*Rats were fed a cholesterol-free diet for 28 days (experiment 3-1) or a high cholesterol diet for 14 days (experiment 3-2).
Values are means ± SEM for groups of six to eight rats, and those marked with a dagger differ significantly (Student's *t*-test) from the control group value (†$P < 0.05$).

1988). Such hypolipidaemic effects were not observed in the present experiment, when curcuminoids prepared from *C. xanthorrhiza* were added to a high cholesterol diet. The discrepancy between the present and the previous studies (Dixit *et al.*, 1988; Rao *et al.*, 1970) may be due to the composition of curcuminoid preparations, since those from *C. longa* are composed of curcumin, desmethoxycurcumin and bis-desmethoxycurcumin (Setijadi, 1985; Tonnesen and Karlsen, 1983), whereas *C. xanthorrhiza* has no bis-desmethoxycurcumin (Tonnesen and Karlsen, 1983).

The present study showed that *C. xanthorrhiza* decreases the liver cholesterol in rats fed a cholesterol-free diet, and suppresses the accumulation in rats fed a high cholesterol diet. Ozaki and Liang (1988) reported that feeding essential oils prepared from *C. xanthorrhiza* increases bile flow in rats. Increased bile flow, therefore, may partly be attributed to the reduction of liver cholesterol in rats fed the medicinal plant. In the previous experiment we have shown that feeding *C. xanthorrhiza* to streptozotocin-induced diabetic rats increases faecal cholesterol, whereas faecal bile acid excretion was rather lower (Sedarnawati *et al.*, 1991). Beynen (1987) also reported that feeding Temoe Lawak Singer, a mixture of *Curcuma aromatica rhizoma*, *Curcuma amara rhizoma* and *Rhamni purshianae cortex*, somewhat decreases faecal bile-acid excretion in rats fed a high cholesterol diet, although serum and liver cholesterol are lowered. Thus, *C. xanthorrhiza* may selectively increase biliary cholesterol, but not bile acids. The influence of *C. xanthorrhiza* in absorptive processes of dietary cholesterol remains to be determined.

The activity of liver FAS has been reported to be regulated nutritionally. In comparison with saturated fatty acids, polyunsaturated fatty acids decrease the activity and consequently the concentrations of liver and serum triglycerides (Clarke *et al.*, 1977). Shillabeer *et al.*, (1990) showed that in rats a diet rich in polyunsaturated fatty acids, in comparison with one high in saturated fatty acids, decreases both liver FAS activity and adipose tissue weight. The present study showed that *C. xanthorrhiza* decreases the activity of liver FAS and the weight of the epididymal fat pad, while liver GPDH is not influenced in rats fed cholesterol-free diet. Thus, decreased circulatory triglycerides may partly lead to a reduction of fat deposition in the adipocytes. However, this was not so in rats fed a high cholesterol diet. It remains a possibility that *C. xanthorrhiza* directly affects lipid metabolism in adipose tissues.

In summary, the present experiments indicated that the rhizome of *C. xanthorrhiza* exerts a marked influence on serum and liver lipids, and serum lipoprotein metabolism. Since *C. xanthorrhiza* has been used traditionally, and its safety as a food ingredient has been proven for a long time, the application of this traditional medicinal plant to the food and pharmaceutical industries is of great interest.

Acknowledgements—We are sincerely grateful to Dr Sidik and his technical staff of Padjadjaran University, Bandung, Indonesia, for providing us with literature on the Curcuma species and supplying us with curcuminoids. This research was partly supported by the Yamasaki Spice Foundation.

REFERENCES

Abdul H. L and Toga S. (1985) Temu Lawak, kinds of uses and beneficial effect (in Indonesian). In *Proceedings of The National Symposium on Temu Lawak, Bandung, Indonesia, 17 September 1985.* Edited by M. W. Moelyono. pp. 220–224. Research Institute of Padjadjaran University, Bandung, Indonesia.

Beynen A. C. (1987) Lowering of serum cholesterol by Temoe Lawak Singer, a *Curcuma* mixture. *Artery* **14,** 190–197.

Clarke S. D., Romsos D. R. and Leveille G. A. (1977) Influence of dietary fatty acids on liver and adipose lipogenesis and on liver metabolites in meal-fed rats. *Journal of Nutrition* **107,** 1277–1287.

Dharma A. P. (1980) *The Indonesian Traditional Medicinal Plants* (in Indonesian). p. 291. PN Balai Pustaka, Jakarta, Indonesia.

Dixit V. P., Jain P. and Joshi S. C. (1988) Hypolipidaemic effects of *Curcuma longa* L. and *Nardostachys jatamansi* DC. In triton-induced hyperlipidaemic rats. *Indian Journal of Physiological Pharmacology* **32,** 299–304.

Folch J., Lees M. and Sloane-Stanley G. H. (1957) A simple method for the isolation and purification of total lipids from animal tissues. *Journal of Biological Chemistry* **226,** 497–506.

Hsu H.-S, Chen Y.-P, Shen S.-J, Hsu C.-S, Chen C.-C and Chang H.-C (1986) *Oriental Materi Medica; A Concise Guide*. p. 932. Oriental Healing Arts Institute, USA.

Imaizumi K., Lu Y.-F. and Sugano M. (1987) Characterization of serum polipoprotein patterns in rats during suckling and post-weaning periods. *Biochimica et Biophysica Acta* **917,** 269–278.

Imaizumi K., Murata M. and Sugano M. (1982a) Effects of dietary polyunsaturated phospholipid on the chemical compositions of serum lipoproteins in rats. *Journal of Nutritional Science and Vitaminology* **28,** 281–294.

Imaizumi K., Nagatomi A., Sato M., Tominaga A. and Sugano M. (1992) Cholesterol metabolism in ExHC (exogenous hypercholesterolemic) rats. *Biochimica et Biophysica Acta* **1123,** 101–109.

Imaizumi K., Tominaga A., Mawatari K. and Sugano M. (1982b) Effect of cellulose and guar gum on the secretion of mesentric lymph, chylomicrons in meal-fed rats. *Nutrition Reports International* **26,** 263–269.

Itokawa H., Hirayama F., Funakoshi K. and Takeya K. (1985) Studies on the antitumor bisabolane sesquiterpenoids isolated from *Curcuma xanthorrhiza*. *Chemical Pharmacology Bulletin* **33,** 3488–3492.

Kozak L. P. and Jensen J. T. (1974) Genetic and developmental control of multiple forms of L-glycerol 3-phosphate dehydrogenase. *Journal of Lipid Research* **31,** 7775–7781.

Lowry O. H., Rosebrough N. J., Farr A. L. and Randall R. J. (1951) Protein measurement with the Folin phenol reagent. *Journal of Biological Chemistry* **193,** 265–275.

Miller G. J. and Miller N. E. (1975) Plasma-high-density-lipoprotein concentration and development of ischemic heart-disease. *Lancet* **i,** 16–19.

Nepokroeff C. M., Lakshmanan M. R. and Porter J. W. (1975) Fatty acid synthase from rat liver. *Methods in Enzymology* **37,** 37–44.

Ozaki Y. and Liang O. B. (1988) Cholagogic action of the essential oil obtained from *Curcuma xanthorrhiza* Roxb. *Shoyakugaku zasshi* **42,** 257–263.

Ozaki Y. and Soedigdo S. (1988) Cholagogic effect of Zingiber plants obtained from Indonesia. *Shoyakugaku zasshi* **42,** 333–336.

Perry M. L. (1980) *Medicinal Plants of East and South East Asia, Attributed Properties and Uses*. p. 620. MIT Press, Cambridge, USA

Purseglove J. W., Brown E. G., Green C. L. and Robins S. R. J. (1981) *Spices*. Vol. II. Longman, London.

Raharja P., Lapua P., Laban S., Jolanda C. R. and Abdul R. (1983) *Research in Various Kinds of Temu Lawak Drink* (in Indonesian). Industrial Research and Development Institute, Ujung Pandang, Indonesia.

Rao D. S., Sekhara N. C., Satyanarayama M. N. and Srinivisan M. (1970) Effect of curcumin on serum and liver cholesterol level in the rat. *Journal of Nutrition* **100,** 1307–1317.

American Institute of Nutrition (1977) Report of the Ad Hoc Committee on standards for nutritional studies. *Journal of Nutrition* **107,** 1340–1348.

Sedarnawati Y., Imaizumi K. and Sugano M. (1991) Effects of an Indonesian medicinal plant, *Curcuma xanthorrhiza* Roxb., on the levels of serum glucose and triglyceride, fatty acid desaturation, and bile acid excretion in streptozotocin-induced diabetic rats. *Agricultural and Biological Chemistry* **55,** 3005–3010.

Setijadi T. (1985) The Identification of the Active Ingredients of Curcuma xanthorrhiza Roxb. and *Curcuma domestica* Val. after Extraction with Supercritical Carbon Dioxide. Report by the P. T. Darya-Varia Laboratoria, Cicadas-Gunung Putri, Bogor, Indonesia.

Shillabeer G., Hornford J., Forden J. M., Wong N. C. W. and Lau D. C. W. (1990) Hepatic and adipose tissue lipogenic enzyme mRNA levels are suppressed by high fat diets in the rat. *Journal of Lipid Research* **31,** 623–631.

Sidik (1986) Isolation Technical Development of Essential Oil, Curcuminoid and Starch from Temu Lawak and Turmeric for Industry (in Indonesian). Research project carried out at the Pharmacology Laboratory, Padjadjaran University, Bandung, Indonesia.

Tonnesen H. H. and Karlsen J. (1983) High-performance liquid chromatography of curcumin and related compounds. *Journal of Chromatography* **259,** 367–371.

Yamazaki M., Maebayashi T., Iwase N. and Kaneko T. (1988) Studies on pharmacologically active principles from Indonesian crude drugs. I. Principles prolonging pentobarbital-induced sleeping time from *Curcuma xanthorrhiza* Roxb. *Chemical Pharmacology Bulletin* **36,** 2070–2074.