Thesis Tile Study on Hypocholesterolemic Effect of *Curcuma xanthorrhiza* in Rats and Hamsters

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ABSTRACT

The present study was carried out to investigate the hypocholesterolemic action of the ethyl acetate extract of *C.xanthorrhiza*, an indigenous plant of our country, in rats and hamsters. It was found that a single high dose of *C.xanthorrhiza* (500 mg/kgBW) was required for lowering plasma cholesterol and triglyceride levels in normal rats. However, although the hypolipidemic effect showed a dose dependence, the difference between the doses was not promising. Therefore, hypocholesterolemic rats induced by Triton WR-1339 (250 mg/kgBW) injection was conducted for further study of *C.xanthorrhiza* action. The results demonstrated that the hypocholesterolemic action in the Triton rat model involved with inhibition of both secretion from the liver and/or cholesterol synthesis and

stimulation of cholesterol mobilization from peripheral tissues.

C.xanthorrhiza treatment (0-500 mg/kg/day) for 7 days exhibited the dose-dependent hypolipidemic action in hypercholesterolemic hamsters which maintained with 0.2% BW cholesterol for 3 weeks. C.xanthorrhiza at a dose of 500 mg/kgBW decreased plasma cholesterol level by 18% whereas the plasma triglyceride was reduced by 35%. In accompany to the reduction of plasma cholesterol level, cholesterol content in the liver was increased (15.0±0.9 mg/g liver in cholesterol-fed control to 18.9±0.7 mg/g liver in EtOAc extract-treated group; $P<0.05$) while the triglyceride content was not altered (4.2±0.4 and 5.3±0.5 mg/g liver in control and treated group, respectively). The investigation on liver cholesterol components revealed that the increased cholesterol content was mainly due to the increase in free cholesterol pool. This finding correlated well with the increase in biliary cholesterol and bile salt.

The mechanism responsible for the hypocholesterolemic effect of C.xanthorrhiza was further explored and found to be associated with the increase in excretory cholesterol pool and plasma HDL-cholesterol. The HDL-cholesterol was increased from 38.6±1.2 mg% in cholesterol-fed control to 50.0±2.7 mg% in the C.xanthorrhiza-treated group. Moreover, hepatic VLDL-triglyceride secretion was inhibited by C.xanthorrhiza administration. The triglyceride secretion

rate (TGSR) was 409.5±20.1 µg/min in control while it was 289.8±21.15 µg/min in the C.xanthorrhiza extract-treated group ($P<0.05$). The similar results were obtained when the pure compounds isolated from the extract were administered to hamsters. The potent compounds was suggested to be diarylheptanoid derivatives which is not curcumin.

Therefore, the hypolipidemic action of the EtOAc extract of C.xanthorrhiza associated with inhibition on hepatic VLDL-triglyceride secretion and acceleration of lipid mobilization from extrahepatic tissue to liver and increase excretion of biliary cholesterol. The EtOAc extract of C.xanthorrhiza used here is the crude extract and is not appropriate for clinical used as hypolipidemic drug. Further isolation and purification would be helpful for development of the C.xanthorrhiza as a promising hypocholesterolemic drug in the future.