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PORNPIKUL SRIVORAPHAN: STUDY OF THE EFFECT OF
PHLORACETOPHENONE ON LIPID METABOLISM IN
HYPERCHOLESTEROLEMIC HAMSTERS. THESIS ADVISORS: PAWINEE
PIYACHATURAWAT, Ph.D., PRAYAD KOMARATAT, Ph.D., APICHART
SUKSAMRARN, Ph.D. WISUDA SUVITAYAVAT, Ph.D. 121 p. ISBN 974-663-
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Phloracetophenone or 2,4,6-trihydroxyacetophenone (THA) is the aglycone part of 4,6-dihydroxy-2-O-(β -D-glucopyranosyl) acetophenone, a naturally occurring compound from *Curcuma comosa* Roxb. (family Zingiberaceae). This compound has been reported to effectively stimulate bile secretion by enhancing bile acid excretion which subsequently decreases plasma cholesterol. A hypocholesterolemic effect of this compound is of interest as it may have potential for development as a hypolipidemic drug. In the present study, the aim is to investigate the *in vivo* hypolipidemic activity and mechanism of THA by using hypercholesterolemic male hamsters. Hypercholesterolemia hamsters was induced by daily supplementary feeding with cholesterol at a dose of 0.2% body weight. By 3 weeks, plasma cholesterol was elevated to approximately 250-350 mg% at which time animals were randomly assigned for experimentation. Intragastric administration of THA (300-800 μ mol/kg twice a day for 7 days) to the hypercholesterolemic animals decreased both plasma cholesterol and triglyceride levels in a dose-dependent manner. THA at dose of 400 μ mol/kg effectively lowered plasma cholesterol by 48.1% and plasma triglyceride by 74.7%. Maximum hypolipidemic effect of THA treatment was attained after 10 days of treatment. From analysis of all major plasma lipoprotein fractions, it is indicated that THA significantly decreased concentration of plasma VLDL and LDL-cholesterol but not HDL-cholesterol. Moreover, hepatic triglyceride and cholesterol contents of both free and bound pools were not significantly altered by THA treatment, suggesting that hypolipidemic action of THA was associated with neither a decreased synthesis of secretory lipid nor an increased uptake for accumulation in liver. However, THA markedly stimulated activity of cholesterol 7 α -hydroxylase activity (7-fold) which enhanced conversion of cholesterol into bile acid. Corresponding to the increase of this enzyme activity, THA increased fecal excretion of both bile acid and cholesterol. These results suggest that THA exerts its hypolipidemic effect by stimulating hepatic conversion of cholesterol to bile acid for disposal via biliary secretion. This compound may have potential for development as a therapeutic agent for lowering lipids in patients.