Thesis Title The Effect of Pravastatin on Rat Hepatic Microsomal and Peroxisomal Enzymes Activity

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ABSTRACT

Pravastatin (Mevalotin®; Sankyo Co., Tokyo) is a new hypocholesterolemic agent. It is a competitive inhibitor of 3-hydroxy-3-methyl glutaryl coenzyme A reductase, the rate limiting step of cholesterol biosynthesis. It has been found to be an effective anti-hypercholesterolemia. In this experiment, the effect of pravastatin on plasma lipid parameters, liver mixed function oxidase enzyme and peroxisomal marker enzymes in male Wistar rats had been studied; in comparison to gemfibrozil. Rats were administered pravastatin (15 or 30 mg/kg/day) or gemfibrozil (200 mg/kg twice a day) orally for 6 weeks. Plasma cholesterol was significantly reduced after 6-week of treatment with pravastatin 30 mg/kg (-21.10%; $P<0.05$) but not with pravastatin 15 mg/kg and gemfibrozil. Both pravastatin and gemfibrozil exhibited hypotriglyceridemic effect in rats (triglyceride level was reduced -35.21% and -47.28%, $P<0.01$ after 2 weeks in 30 mg/kg pravastatin- and gemfibrozil-treated rats ,and -13.31%, $P<0.05$ after 4 weeks in 15 mg/kg pravastatin-treated rats). Pravastatin had no effect on percent liver weight per body weight ratio, protein content, microsomal cytochrome P-450

and peroxisomal enzymes (catalase and fatty acyl CoA oxidase, FACO) activity. On the contrary, gemfibrozil markedly induced liver weight per body weight ratio increased 1.5- to 2-fold). It also increased liver protein (112.8%, $P<0.01$), microsomal protein (111-120%, $P<0.05$) and cytochrome P-450 content (180-200%, $P<0.01$). In addition, gemfibrozil also possesses peroxisomal proliferating effects (catalase activity increased about 2-fold and FACO activity increased 8- to 10-fold). These hepatic effects of gemfibrozil were not observed in pravastatin-treated rats. The result indicated that pravastatin does not alter rat hepatic microsomal and peroxisomal enzymes activity at its antihyperlipidemic doses.