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

Name Linda Chularojanamontri

Degree Master of science(Pharmacy)

Thesis Supervisory Committee

Srichan Phornchiraslip,Ph.D.

Oraphan P. Matangkasombut,Ph.D.

Saichandana Subhanka,Ph.D.

Date of Graduation 14 July B.E.2540(1997)

ABSTRACT

Fluvastatin is a new hypocholesterolemic agent. It is a competitive inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase, the rate limiting step of cholesterol biosynthesis. It has been found to be an effective antihypercholesterolemic. In this experiment, the effect of fluvastatin in comparison to gemfibrozil on plasma lipid parameters, liver mixed function oxidase enzyme and peroxisomal marker enzymes in male Wistar rats had been studied. Rats were administered fluvastatin (5, 10 and 15 mg/kg/day) or gemfibrozil (200 mg/kg twice a day) orally for 6 weeks. Plasma cholesterol was significantly reduced at 2 weeks of treatment in 5, 10 and 15 mg/kg (-41.10%;$P<0.01$). Whereas, 200 mg/kg of gemfibrozil significantly reduced total cholesterol level after 4 weeks (-20.21%;$P<0.01$). Both fluvastatin and gemfibrozil exhibited hypotriglyceridemic effect in rats (triglyceride level was reduced 30.29% and 47.28%;$P<0.01$ after 2 weeks in 5, 10 and 15 mg/kg fluvastatin and gemfibrozil treated rats). Fluvastatin 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 increased liver weight per body weight ratio (increased 1.5 to 2-fold). It also increased liver protein (121.80%;$P<0.01$), microsomal protein (110-123%;$P<0.01$) and cytochrome P-450 content (175-200%;$P<0.01$). 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 fluvastatin treated rats. The result indicated that fluvastatin does not alter rat hepatic microsomal and peroxisomal enzymes activities at the hypolipidemic doses.