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NARONGCHAI CHAKSUPA : EFFECTS OF LOSARTAN AND ENALAPRIL ON BLOOD GLUCOSE LEVEL IN ALLOXAN-INDUCED DIABETIC RATS AND ON TRIGLYCERIDE AND TOTAL CHOLESTEROL LEVELS IN CHOLESTEROL-INDUCED HYPERLIPIDEMIC RATS. THESIS ADVISORS : NONGLUCK SOOKVANICHASILP, Dr.Ph.m.Sc., SRICHAN PHORNCHIRASILP, Ph.D. 100 p. ISBN 974-664-188-3

Dyslipidemia and diabetes mellitus co-exist with hypertension. Antihypertensives with serum lipid- and/or blood sugar-lowering effects will provide beneficial effects for hypertensive patients with these disorders. The effects of enalapril, an angiotensin-converting enzyme (ACE) inhibitor, and losartan, an angiotensin II receptor antagonist, on serum lipids and serum glucose were therefore investigated in rats fed a high cholesterol diet and in alloxan-induced diabetic rats, respectively. Male Sprague-Dawley rats (weighing 180-220 g) were used. In the study of serum lipids, cholesterol-mixed food was given throughout the study period to all animals except those of the normal control group. Rats with serum total cholesterol > 120 mg/dl were divided into 5 groups, consisting of 8 animals per group. Losartan at doses of 20 and 40 mg/kg/day as well as enalapril at doses of 10 and 20 mg/kg/day were orally administered to 4 individual groups for 4 weeks. The fifth group served as the high cholesterol control group. In the study of serum glucose, rats were given alloxan monohydrate by intraperitoneal injections at a single dose of 100-160 mg/kg in 0.9% NaCl solution. Those with serum glucose concentrations > 200 mg/dl were divided into 5 groups and the drugs were given in the same manner as mentioned in the previous study.

The present study demonstrated that both doses of enalapril (10 and 20 mg/kg) could significantly reduce serum cholesterol throughout the study period, whereas a lower dose (20 mg/kg) of losartan revealed a significant reduction in serum cholesterol only at week 1 and a higher dose (40 mg/kg) of losartan at week 4. The maximum values of % mean changes in serum cholesterol compared with week 0 in rats treated with 20 mg losartan, 40 mg losartan, 10 mg enalapril and 20 mg enalapril were -25.34 ± 2.15 , -37.96 ± 3.18 , -31.62 ± 5.22 and -47.66 ± 4.00 %, respectively. In case of serum triglyceride, both drugs demonstrated no serum triglyceride-lowering effect. On the other hand, both doses of enalapril and the higher dose of losartan seemed to produce elevated triglyceride levels. In alloxan-induced diabetic rats, only a trend of decrease in serum glucose levels was detected in all groups throughout the study period, however, there were no significant differences in those serum glucose levels when compared with the levels at week 0 of individual groups. Mean concentrations of serum glucose before and after any treatments in all diabetic rats ranged from 391.12 ± 50.39 to 475.98 ± 38.50 mg/dl, and from 323.84 ± 62.93 to 378.53 ± 37.25 mg/dl, respectively. This finding may provide some evidence of the beneficial effect of enalapril and probably losartan as well on hypertensive patients associated with hypercholesterolemia.