THE EFFECT OF LOSARTAN ON ANG II AND ANG IV-INDUCED CHANGES IN TYROSINE PROTEIN KINASE/activity IN RAT PITUITARY IN VITRO

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Angiotensin II is an octapeptide hormone of the renin-angiotensin family. AngII is released from the brain, and a number of Ang II receptors were found in the pituitary in the vicinity of the pituitary gland. This multifunctional peptide can act within the target cells through the AT1 receptor via the activation of several membrane and cytosolic enzymes like phospholipases C, D, and A2, protein kinase C or tyrosine protein kinases (PTK). Angiotensin IV (AngIV) is the biologically active fragment of AngII. It is suggested that AngIV acts via specific membrane receptor, which is believed to have intrinsic PTK activity, which is distinct from AT1.

The aim of our study was to compare the changes in AngII and AngIV effects on PTK-induced phosphorylation and to investigate if the losartan, the specific antagonist of the AT1 receptor, can modify AngII- and AngIV-induced changes in PTK activity. The homogenate of the male rat pituitary was a source of endogenous tyrosine protein kinase. The determination of TK activity was performed as per the method of Hirano et al., using the synthetic polymer poly-[L-Glu80,L-Tyr20] (4:1) as a substrate and 32P γATP as a donor of radioactive phosphorus. PTK activity was defined as pmoles of 32P incorporated into 1 mg of protein per minute. The results were compared to those for a control group containing none of the tested substances. The degree of substrate phosphorylation in this control group was assumed to be 100%.

The results show that AngII alone has no effect on protein phosphorylation by PTK, whereas AngIV increased PTK activity (130% of the control value). When AngII or AngIV were incubated together with losartan, PTK activity was diminished to 70% of the control value, although losartan alone weakly increased 32P incorporation into polyGluTyr. The above results suggest that AngIV affects PTK activity more strongly than AngII, and that losartan can modify basal and Ang-induced PTK phosphorylation.

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