INTERACTIONS BETWEEN ANGIOTENSIN II, CAPTOPRIL AND ENALAPRIL ON THE GUINEA-PIG ISOLATED GALLBLADDER

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Although the pharmacology of angiotensin II, captopril and enalapril has already been extensively studied, reports on the interactions of angiotensin II and the angiotensin converting enzyme (ACE) inhibitors, captopril and enalapril on the gallbladder are still scarce. Therefore, the aim of the present experiments was to investigate the effect of angiotensin II as well as the interactions of angiotensin II and the ACE inhibitors, captopril and enalapril on the guinea-pig isolated gallbladder.

Guinea-pigs of both sexes (400-500 g) were killed by cervical dislocation and the gallbladder was removed. Strips of the gallbladder body of whole wall thickness, perpendicular on the longitudinal axis of the gallbladder were cut. The strips were set up in an isolated organ bath of 15 ml in Tyrode solution gassed with 95% O_2 and 5% CO_2 at 37°C and placed under a load of 0.5 g. Recordings were made on a smoked drum with a frontal writing isotonic lever. Angiotensin II was cummulatively applied to the organ bath. Each strip was used for evaluation of the effect of only one dose of captopril or enalapril.

Concentration-response curves were constructed using linear regression according to the method of least squares. A coefficient of correlation (r) of linear regression was used to determine the existence and significance of concentration-response correlation. The results were considered statistically significant when $p<0.05$. The concentrations of angiotensin, captopril and enalapril refer to the peptide or to the drugs.

In the first series of experiments the effect of angiotensin II on the gallbladder isolated preparation was investigated. Angiotensin II in concentrations from 3×10^{-7} to 2×10^{-5} M contracted the gallbladder isolated preparations. The contractile effect of angiotensin II was concentration-dependent ($r=0.99$, $p< 0.01$).

In the second series of experiments the effect of the ACE inhibitors, captopril and enalapril on the gallbladder isolated preparations was tested. Both captorpil (4×10^{-9} x 4×10^{-7} M) and enalapril (2×10^{-9} - 2×10^{-7} M) virtually had no effect on the motility of the isolated gallbladder preparations.

Finally, in the third series of experiments interactions between angiotensin II and the ACE inhibitors, captopril and enalapril on the gallbladder isolated preparations was investigated. Captorpil (4×10^{-9} - 4×10^{-7} M) and enalapril (2×10^{-9} - 2×10^{-7} M) exerted no observable effects on the concentration-response curve for angiotensin II.

Previous experiments on the guinea-pig sphincter of Oddi in vitro revealed that angiotensin II contracted this tissue (Harada at al., 1986). In the present experiments, angiotensin II contracted also in vitro the gallbladder of the guinea-pig. The contractile effect of the peptide was concentration-dependent. Similarly, angiotensin II contracts the guinea pig isolated ileum and at the same time removes the peristaltic block previously abolished by ganglionic blocking agents, morphine, adrenaline and atropine (Robertson and Rubin, 1962, Beleslin, 1968). It follows then that the characteristic effect of angiotensin II in the gastrointestinal tract is the contractions of this system.