BRADYKININ ANTAGONISM

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Previously we have shown that the C-phenylglycine-n-heptyl ester / CPHE /* is a very potent inhibitor of bradykinin both in vitro and in vivo.
Amino acid containing aromatic / Phe / and basic amino acids / Arg, Lys / are very important in the receptor-bradykinin interaction. Therefore we decided to synthetize heptyl esters both of basic and aromatic amino acids to find a more potent and a more specific inhibitor of bradykinin.
Arginine-heptyl ester / AHE / inhibits the bradykinin and 5-HT induced smooth muscle contraction more than the CPHE does while the phenylalanine-heptyl ester / PHE / is not so effective. Increased vascular permeability was induced by intracutaneous injection of bradykinin, various vasoactive substances and their releasers into rats. Vascular permeability was inhibited greatly with PHE and AHE, even if the agonists and antagonists were injected at the same time. CPHE was more effective against 5-HT induced permeability than the PHE or AHE.
Bronchus contraction induced by aerosol of different vasoactive substances in guinea-pigs was abolished applying PHE, AHE, CPHE in aerosol. PHE was the most potent inhibitor.
Skin Reactive Factor / SRF / was isolated from the lymphocytes of tuberculine hypersensitive patients. The SRF vascular permeability inducing effect was inhibited about 40%.
* Kindly supplied by SOLCO Basle LTD.

URINARY KALLIKREIN EXCRETION IN HYPERTENSION: FURESEMIDE AND THEOPHYLLINE EFFECTS AND EMATIC DOPAMINE-BETA HYDROXILASE CORRELATION

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1) Furesemide "in vivo" and "in vitro" reduces human esterasic urinary kallikrein activity. This enzimatic inhibition was observed in patients with secondary hypertension, while no significant variations were found in patients with essential hypertension. In the latter subjects, with impaired glucose tollerance test, significant increments of urinary kallikrein excretion were observed.
2) Theophylline which inhibits cyclic nucleotide phosphodiesterase and increases the intracellular steady state level of cyclic 3', 5'-AMP, did not determinate any variation of human urinary kallikrein excretion.