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Preliminary data on the inhibition of pentagastrin stimulated gastric secretion induced by some natural and synthetic peptides

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In previous papers cholecystokinin (CCK) and caerulein were found to inhibit gastric secretion induced by pentagastrin in man and dogs (Stening, Johnson & Grossman, 1969; Brooks, Agosti, Bertaccini & Grossman, 1970). This probably depended on a competitive antagonism between gastrin and these two peptides which, as partial agonists, competed with gastrin for an active site in the secretory process. On the basis of these results we synthesized and submitted to thorough pharmacological examination a series of caerulein-like peptides (Bertaccini, 1969) in the hope of finding some compounds endowed with the same inhibitory activity but devoid of the stimulant effect of the natural peptides. Among 25 compounds examined on Heidenhain pouch dogs two substances were found of considerable interest: an heptapeptide similar to the C-terminal heptapeptide of caerulein but with a nor-leucine instead of the methionine residue (Boc-Tyr(SO_3H)-Thr-Gly-Trp-Nle-Asp-Phe . NH_2) and a pentapeptide with the following structure: (H-Tyr(SO_3H)-Trp-Met-Asp-Phe . NH_2). The first compound is endowed with a striking inhibitory activity but retains a certain stimulant cholecystokinetic effect. The second is less active as an inhibitor but it is almost completely devoid of stimulant activities. The heptapeptide showed a remarkable effect also in a few human volunteers. In another series of experiments also the natural peptide Bombesin (Pyr-Gln-Arg-Leu-Gly-Asn-Gln-Trp-Ala-Val - Gly - His-Leu-Met . NH_2) which is completely different from gastrin and CCK both from a chemical and a pharmacological point of view was shown to inhibit significantly the hypersecretion induced by pentagastrin. The mechanism of action is probably connected with a release of gastrin and/or of cholecystokinin provoked by bombesin as shown by Erspamer, Melchiorri, Sopranzi, Torsoli, Corazziari & Improta (1973); Torsoli, Corazziari, Habib, Melchiorri, Delle Fave & Improta (1973). Of course a direct effect of bombesin cannot be excluded.

The present data were discussed and the possibility that an antisecretory effect may be present also in a caerulein-like compound lacking the tyrosyl-sulphate group in position seven is pointed out.

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