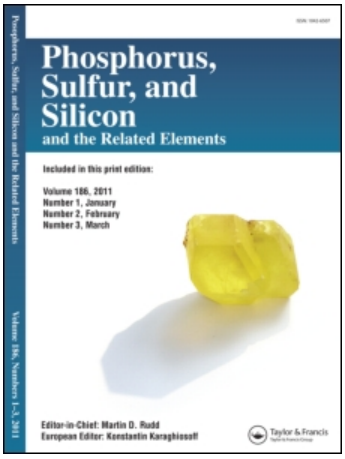

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NEW TYPES OF COMMON FRAGMENTS IN THE PERTIDE-PROTEIN BIOREGULATORS CONTAINING CYSTINE

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NEW TYPES OF COMMON FRAGMENTS IN THE PEPTIDE-PROTEIN BIOREGULATORS CONTAINING CYSTINE

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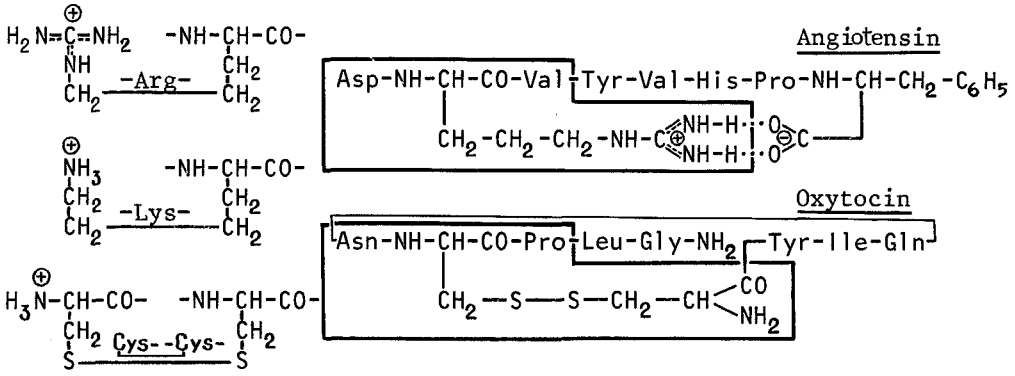
Our attempts to investigate the basic principles underlying the structural and functional organization of peptide-protein bioregulators had revealed the presence in their amino acid sequences of two types of "common" fragments. Type I was Gly/X-COOH-B-Pro/Val-Pro/Val, X being an amino acid with a free carboxylic group and B - a basic amino acid (arginine, lysine) or a dicarboxylic acid amide; as exemplified by the sequences of α-MSH 10→13, wasp kinin 9→12, ACTH 18→20, α-MSH 22←19, angiotensin 1→3, bradykinin 1→3, insulin B 30←28, ranatensin 4←2, etc. Type II was B-Pro/Val-B-Pro/Val, e.g. sequences of the substance P 1→4, fibrinopeptide B 13→16, bradykinin-potentiating peptide B 6→9, snake venom toxins of Naja Nivea 49←46 and Naja Naja oxiana 46←43, etc. The common fragments were found (1) to contain equifunctional amino acid residues (Lys and Arg, Pro and Val, and others); (2) to occur in the structures of biologically active peptides of widely diverse origins and functions; (3) to be situated in the vicinity of specifically active centres of the molecules and lastly; (4) to affect the activity of the "specific" part of the molecule increasing it, on an average, by three orders of magnitude. The foregoing facts indicate the great importance of these fragments in determining the biological activity of the compounds as well as the universal occurence of the phenomenon.

Presently, we identified cystine-containing analoques of both types of common fragments in which one or two basic amino acid residues were substituted by cystine, e.g. X-COOH/X-$CONH_2$-Cys_2-Pro/Val (sequences of urogastrone 5→7, fish insulin A 12←10, α-lutropin 10→12, nerve growth factor 16←14, oxytocin and vasopressin 5→7, etc.), or B-Pro/Val-Cys_2-Pro/Val and Cys_2-Pro/Val-Cys_2-Pro/Val (sequences characteristic of a large group of snake venom toxins, e.g. of Naja Naja oxiana 44←41, murine nerve growth factor 108→111, sheep prolactin 6←3, pig α-lutropin 3→6, etc.). Comparing the

structure of the common fragments with that of their cystine-containing analogues lends support to our view that they are centrally involved in determining and stabilizing the three-dimensional structure of the bioregulator molecule. This is effected either by closing the disulphide bond between the cysteine residues or by ionic bonding between the basic amino acid and a negatively charged group of another amino acid (see Fig.).



Disulphide and ionic type bonds appear to be equifunctional as evidenced by comparing the structures of homologous proteins: it was demonstrated that the similar structural architecture of the protein globule and that of its active centre is stabilized either by disulphide bonds, or by electrostatic interactions of ionic pairs (Arg-Asp, Arg-Glu, Lys-Asp, etc.) situated in strictly specific positions of the polypeptide chain (serine proteases, lyzocymes). The above assumption is further substantiated by the results of the semi-empirical conformational analysis of hormones and kinins, which are indicative of a quasicyclic structure for linear oligopeptides (quasicycles occur in angiotensin 2→8, bradykinin 1→9, xenopsin 3/4→8, etc.).