[1-β-MERCAPTOPROPIONIC ACID, 8-D-NORARGININE]-VASOPRESSIN. A FURTHER ANALOG WITH HIGH AND SPECIFIC ANTIDIURETIC EFFECT

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The shortening of the basic amino acid side chain of [1-β-mercaptopropionic acid, 8-D-arginine]-vasopressine has practically no influence on the magnitude and specificity of the antidiuretic effect.

The elimination of the amino group from the position 1 and the guanylation in position 8 of [8-D-ornithine]-vasopressin yields [1-β-mercaptopropionic acid, 8-D-arginine]-vasopressin[1] (*I*) possessing a remarkable high and specific antidiuretic activity. This compound is very effective in the treatment[2,3] of *diabetes insipidus*. Encouraging results were obtained also when *I* was applied to children suffering from *enuresis nocturna*.

We have prepared recently an analog of *I* containing in the position 8 a lower homolog of arginine because, as we have observed earlier[4], the antidiuretic activity in the "D-series"* seems to be indirectly proportional to the lenghth of the basis amino acid side chain. A vasopressin analog with a high antidiuretic but still relatively strong pressoric effect has recently been prepared also by Bodanszky and coworkers[5] by the insertion of a higher homolog of lysine in position 8.

The coupling of β-benzylthiopropionyl-tyrosyl-phenylalanyl-glutaminyl-asparaginyl-S-benzylcysteine** (m.p. 218–219°C, $[\alpha]_D^{20}$ −30·9° (*c* 0·5, dimethylformamide); for $C_{47}H_{55}N_7O_{10}S_2$ (942·1) calculated: 59·90% C, 5·88% H, 10·41% N, 6·81% S; found: 59·71% C, 5·88% H, 10·18% N, 6·85% S) with prolyl-N^{γ}-benzyloxycarbonyl-D-α,γ-diaminobutyryl-glycine amide (m.p. 154–156°C, $[\alpha]_D^{25}$ +65·8° (*c* 0·1, 1M-CH_3.CO_2H); for $C_{19}H_{27}N_5O_5$ (405·45) calculated: 56·28% C, 6·71% H, 17·27% N; found: 56·30% C, 6·70% H, 17·33% N) yields β-benzylthiopropionyl-tyrosyl-phenylalanyl-glutaminyl-asparaginyl-S-benzylcysteinyl-prolyl-N^{γ}-benzyloxycarbonyl-D-α,γ-diaminobutyryl-glycine amide (m.p. 207–210°C, $[\alpha]_D^{20}$ −27·9° (*c* 0·2, 95% CH_3CO_2H); for $C_{66}H_{80}N_{12}O_{14}S_2$ (1329·4) calculated: 59·62% C, 6·05% H, 12·64% N, 4·83% S; found: 59·76% C, 6·14% H, 12·87% N, 5·09% S). The octapeptide amide derivative

* The term "D-series" denotes vasopressin analogs containing in the position 8 amino acids of the D-configuration.

** Unless stated otherwise, all the optically active amino acids are of L-configuration.

was decarbobenzoxylated (hydrogen bromide in glacial acetic acid) and treated with 1-guanyl-3,5-dimethylpyrazole nitrate. After splitting off the protecting groups from the guanylated product (sodium in liquid ammonia), cyclization ($K_3[Fe(CN)_6]$), desalting (Amberlite IRC 50) and purification (continuous-flow electrophoresis), [1-β-mercaptopropionic acid, 8-D-α-amino-γ-guanidinobutyric acid]-vasopressin was obtained ($[\alpha]_D^{25}$ −53·9° (*c* 0·1, H_2O); amino-acid analysis: Tyr 0·9, Phe 1·0, Glu 1·0, Asp 1·0, Pro 1·0, Narg 0·9, Gly 1·0). Similarly to *I*, the norarginine analog showed a high and very specific antidiuretic effect (of the same order as *I*).

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