Enzymatic Activity and Inhibition of the Neurotoxic Complex Vipoxin from the Venom of *Vipera ammodytes meridionalis*

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Z. Naturforsch **57c**, 1078–1083 (2002); received March 26/July 16, 2002

Neurotoxin, Phospholipase A2, Snake Venom

Vipoxin from the venom of *Vipera ammodytes meridionalis* is an unique neurotoxic complex between a toxic phospholipase A2 and a highly homologous non-toxic protein inhibitor. It is an example of evolution of a catalytic and toxic function into inhibitory and non-toxic one. The activity of the *V. ammodytes meridionalis* toxin is 1.7 times higher than that of the closely related (92% sequence identity) neurotoxic complex RV4/RV7 from the venom of *Vipera russelli formosensis*. The enhanced enzymatic activity of vipoxin is attributed to limited structural changes, in particular to the substitutions G54R and Q78K in the PLA2 subunit of the complex and to the T54R substitution in the inhibitor.
Oleyloxyethylphosphocholine, aristolochic acid and vitamin E suppressed the enzymatic activity of vipoxin and its isolated PLA2 subunit. These compounds influence inflammatory processes in which PLA2 is implicated. The peptide Lys-Ala-Ile-Tyr-Ser, which is an integral part of the PLA2 components of the two neurotoxic complexes from *V. ammodytes meridionalis* and *V. russelli formosensis* (sequence 70–74) activated vipoxin increasing its PLA2 activity by 23%. This is in contrast to the inhibitory effect of the respective pentapeptides with 70–74 sequences on other group II PLA2s. Surprisingly, the same peptide inhibited 46% of the *V. russelli formosensis* PLA2 activity. The limited changes in the structure of the two highly homologous neurotoxins lead to considerable differences in their interaction with native peptides.