The 1.4 Å Structure of Dianthin 30 Indicates a Role of Surface Potential at the Active Site of Type 1 Ribosome Inactivating Proteins

Simona Fermani[a], Giuseppe Falini[a], Letizia Polito[b], Andrea Bolognesi[b], [a]*Departimento di Chimica,* [b]*Dipartimento di Patologia Sperimentale, University of Bologna, Italy.* E-mail: simona.fermani@unibo.it

Ribosome inactivating proteins inhibit protein synthesis through a unique RNA *N*-glycosidase activity that depurinates major RNA. The cleaved *N*-glycosidic bond corresponds to adenine$_{4324}$ residue of 28S eukaryotic mammalian rRNA or adenine$_{2660}$ of 23S *Escherichia coli* rRNA, both located in a loop containing a GAGA sequence, highly conserved in rRNAs from bacteria, plants, and animals. This suggests that RIPs recognize this specific structure. Ribosomes invariably damaged by RIPs, cannot interact properly with elongation factors 2 with subsequent cell death (apoptosis). Although RIPs show similar chemical–physical properties and identical enzymatic activity, they act differently on ribosomes from various plants, protozoa, and animals. The three-dimensional structure of dianthin 30, a type 1 (single-chain) RIP of *Dianthus caryophyllus* (leaves), is here presented at 1.4 Å, a resolution never achieved before for any RIP. The fold typical of RIPs is conserved, despite some differences in the loop regions. The general structure comparison by superimposed α-carbon (249 atoms) and the sequence alignment by structure for dianthin 30 and saporin-S6 give a root mean square deviation of 0.625 Å. Despite the differences reported for the biological activities of the two RIPs, their structures fit quite well and both show a protein segment containing strands β7, β8, and β9 shorter than other RIPs. However, the surface electrostatic potential in the active site region neatly distinguishes dianthin 30 from saporin-S6. The possible relationship between the charge distribution and the behavior of the proteins toward different substrates is discussed. [1]

[1] Fermani S., Falini G., Ripamonti A., Polito L., Stirpe F., Bolognesi A., *Journal of Structural Biology*, 2005, **149(2)**, 204.

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