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Crystal Structures of Free Textilinin-1 and its Complex with the Catalytic Domain of Human Plasmin.

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Textilinin-1 (TxIn-1) is a small multiply disulfide bonded protein isolated from the venom of the Australian common brown snake, *Pseudonaja textilis textilis*. It is a Kunitz type serine protease inhibitor that works as an anti-fibrinolytic agent by blocking the activity of plasmin and/or other proteases involved in fibrinolysis. The crystal structures of free recombinant TxIn-1 and its complex with human recombinant microplasmin, the catalytic domain of plasmin; residues 542-791, have been determined to 1.63 Å and 2.8 Å resolution respectively. The primary binding loop of TxIn-1 to microplasmin adopts multiple conformations in the free structure. However, when bound in the complex this loop is ordered, forming a stable Michaelis complex with microplasmin. Arginine 17 from TxIn-1 (ArgT17) protrudes into the specificity pocket (P1 site) of microplasmin making ionic contact with aspartate 735 (AspP735). The carbonyl carbon of ArgT17 makes a shorter than van der Waals contact with the hydroxyl of SerP741, a residue in the catalytic triad. The side chain of HisP603, which is also part of the catalytic triad, has an orientation not observed in any other plasmin structure. The structure of the complex between TxIn-1 and microplasmin will assist in the development of antifibrinolytic therapeutic agents.

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