Reversible thrombocytopenia of functional platelets after the nose-horned viper venom envenomation is induced by a snaclec

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Profound and transient thrombocytopenia of functional platelets without bleeding was observed in patients envenomed by *Vipera a. ammodytes* (*Vaa*). Such condition was rapidly reversed by Fab fragments of antibodies raised against the whole *Vaa* venom, leaving platelets fully functional. It was proposed that snake venom C-type lectin-like proteins (snaclecs) were responsible for the action. To test this hypothesis, we purified snaclecs from the crude venom, biochemically characterized them and studied their interaction with platelets. Six *Vaa*-snaclecs were isolated from the venom using combination of five consecutive liquid chromatography steps. They were structurally characterized by Edman sequencing and mass spectrometry. Platelet count, agglutination and aggregation assays, and standard blood coagulation tests revealed that the most potent antiplatelet substance among them was *Vaa*-snaclec-3/2, a covalent heterodimer of *Vaa*-snaclec-3 (α-subunit) and *Vaa*-snaclec-2 (β-subunit). Using flow cytometry, we demonstrated that *Vaa*-snaclec-3/2 causes thrombocytopenia by inducing platelet agglutination after binding to the platelet receptor GPIb. Importantly, this effect was reversible leaving platelets competent. *In vivo*, *Vaa*-snaclec-3/2 was able to protect the mice from ferric chloride-induced carotid artery thrombosis raising a promise of its application as an antiplatelet drug in interventional angiology and cardiology.

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