Biochemical, pharmacological and structural characterization of two PLA_2 isoforms Cdr-12 and Cdr-13 from *Crotalus durissus ruruima* snake venom.

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Cdr-12 and Cdr-13 isoforms of PLA_2, a D49 protein, were purified from *C.d. ruruima* venom after one chromatographic step, reverse phase HPLC on μ-Bondapack C-18. The molecular mass by SDS-PAGE of Cdr-12 and Cdr-13 isoforms of PLA_2 was 14333.49 Da and 14296.42 Da and confirmed by MALDI-TOF MS. The amino acid composition showed that both isoforms Cdr-12 and Cdr-13 have a high content of Lys, Tyr, Gly, Arg, and 14 half-Cys residues. The isoforms Cdr-12 and Cdr-13 had a sequence of amino acids of 122 amino acid residues, being Cdr-12: SLLQFNKMIK FETRKNAIPF YAFYGCYCGW GGQGRPKDAT DRCCIVHDCC YGKLAKCNTK WDFYRYSLRS GYFQCGKGTW CEQQICECDR VAAECLRRSL STYRYGYMIY PDSRCREPSE TC and *pI* value 8.37 and Cdr-13: SLVQFEKMIK EETGKNAVPF YAFYGCYCGW GGRGRPKDAT DRCCIVHDCC YEKLVKCNTK WDFYRYSLRS GYFQCGKGTW CEQQICECDR VAAECLRRSL STYRYGKMIY PDSRCREPSE TC with a *pI* value of 8.13. In mice, the PLA_2 isoforms Cdr-12 and Cdr-13 induced myonecrosis and edema, upon intramuscular or subcutaneous injections. *In vitro*, Cdr-12 and Cdr-13 isoforms of PLA_2, caused a potent blockade of neuromuscular transmission in young chicken biventer cervicis preparation and produced cytotoxicity in murine C2C12 skeletal muscle myotubes and lack cytolytic activity upon myoblasts *in vitro*. Thus, the combined structural and functional information obtained identify Cdr-12 and Cdr-13 isoforms as members of the PLA_2 family.

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