

Cardiotoxicity of Kenyan green mamba (*Dendroaspis angusticeps*) venom and its fractionated components in primary cultures of rat myocardial cells.

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Abstract:

The cardiotoxic actions of Kenyan green mamba (*Dendroaspis angusticeps*) venom have been investigated using primary myocardial cell cultures isolated from neonatal rat hearts. The cardiotoxic actions of the whole venom and its fractionated components were evaluated on the basis of leakage of lactate dehydrogenase (LDH), changes in morphology, cell membrane lysis, decreases in viability and inhibition of spontaneous beating activity. The whole venom caused time- and concentration-dependent arrest of myocardial contraction, leakage of LDH, extensive disruption of cell monolayer, and decreases in viability. The venom was separated into 6 (DaI to DaVI) fractions by gel permeation chromatography on Sephadex G-50. Spontaneous beating activity was abolished by DaI to DaVI at high concentrations, while at lower doses they induced progressive depression of beating frequency after a 3-h treatment period. DaI to DaIV caused significant leakage of LDH, morphological damage, and decreases in viability after a 6-h incubation period. The most cardiotoxic fraction (DaIV), which also contains about 54% of the total protein of the whole venom, was fractionated into 18 polypeptides (Da1 to Da18) by ion exchange chromatography on Bio-Rex 70. On the basis of their ability to abolish myocardial contractility, release LDH, alter cellular structure, lyse cell membranes and reduce viability, the 18 fractions have been divided into 4 arbitrary subgroups of cytotoxins: cardiotoxins, Da1 to Da3; cardiotoxin-like polypeptides, Da4 to Da12, Da14; less active membrane lytic polypeptides, Da13, Da15 to Da17; and membrane lytic polypeptide, Da18. Marked synergistic cell membrane lysis occurred in myocardial cell cultures treated simultaneously with 2 cardiotoxin-like polypeptides, Da7 and Da11. It is suggested that the additive and synergistic cardiotoxic effects of high molecular weight cytotoxic proteins (DaI to DaIII), very low molecular weight cholinomimetic substances (DaV to DaVI) and the 4 subgroups of cardiotoxins may directly contribute to the pronounced cardiovascular problems observed in victims of green mamba bites.