IOCT 2025 Conference

The 3rd International Online Conference on Toxins

10–12 September 2025 | Online

MDPI

Effects of heterodimeric phospholipases A2 from venom of *Vipera nikolskii* on the rat cardiomyocytes

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INTRODUCTION & AIM

Phospholipases A2 (PLA2) is one of the largest families of snake toxins. Snake venom PLA2s affect various systems in the prey, including the cardiovascular one, however, data on their effect on cardiomyocytes are practically absent.

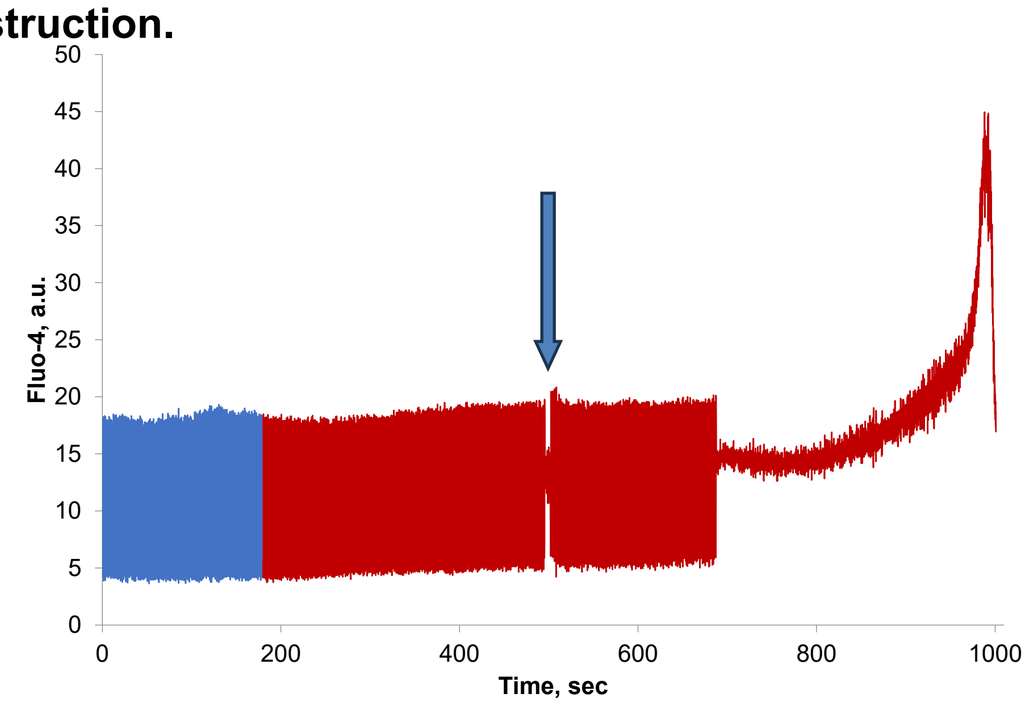
In this work, we investigated the influence of heterodimeric PLA2s HDP-1 and HDP-2 from venom of *Vipera nikolskii* on the isolated rat cardiomyocytes.

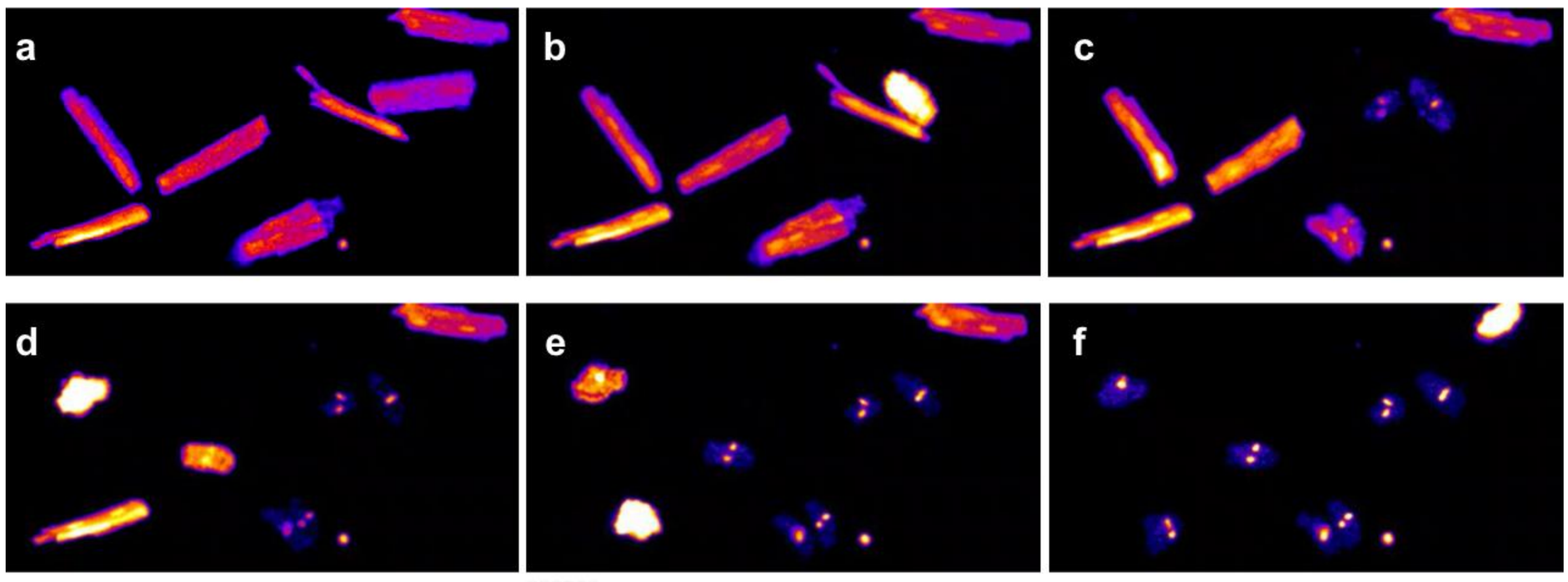
METHOD

Cardiomyocyte were prepared from hearts of anesthetized animals. Only rod-shaped cardiomyocytes with clear striations were used. They were stained with a fluorescent probes Fura-2 or Fura-4. The fluorescence in cardiomyocytes was measured using Cell Observer fluorescent station based on an AxioVert 200M motorized inverted microscope equipped with 10x PlanApochromat objective and Orca-Flash R2 monochrome camera.

RESULTS

In the experiments under conditions of electrical stimulation, after recording control values of the fluorescent response (blue trace), HDP-2 was added and changes in the fluorescence were recorded until cell death (red trace). In all cases, a "pause" in contractions was observed (arrow), characterized by increase in intracellular calcium and decrease in the amplitude of the fluorescent response. Then, the rhythm recovered, and later hypercontracture was observed followed by cell destruction.





Changes over time of [Ca2+]i and shape of cardiomyocytes under treatment with 10 μM HDP-2. a) Before HDP-2 application; b-e) different time intervals after HDP-2 application; f) 45 min after HDP-2 application. Yellow color indicates high Ca2+ concentration.

After HDP-2 (10 μM) application, there is prolonged lag phase with no changes in cell morphology and probe signal. Then, fluctuations in the cytosolic calcium level ([Ca2+]i) are observed, followed by a sharp increase in [Ca2+]i and the onset of hypercontracture, with subsequent disruption of the plasma membrane.

CONCLUSION

In isolated rat cardiomyocytes, PLA2 HDP-2 from *Vipera nikolskii* venom induced elevation of cytosolic calcium level followed by hypercontracture and cell destruction. This is the first indication for direct effect of snake venom D49 PLA2 on cardiomyocytes.

FUTURE WORK

In the future, we plan to study the role of HDP-2 subunits in the observed effects, as well as the molecular mechanisms underlying the effects of HDP-2 on cardiomyocytes.