

Possible pharmacological applications of some snake venom metalloproteinases (SVMPs)

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Abstract

We report the effects of two snake venom metalloproteinases (SVMPs), P-III from *Crotalus simus* and BaP1 from *Bothrops asper*, over the nanovesicles release and on the angiogenesis process. The nanovesicles are usually released as a biological answer of some cells, for instance, platelets, when an environment alteration occurs. Also, these enzymes show degradation effects over the extracellular matrix and may show relevance in angiogenesis. The angiogenic inhibition caused by these enzymes might be used as starting point for solid tumors treatments related research. When BaP1 and P-III enzymes have been applied on human blood plasma samples, the release of nanovesicles with exosome comparable sizes have been observed. Indications of inhibitory effects in angiogenesis when these two enzymes applied in 11 days-old chicken embryonated eggs were also evidenced.

Key words: Metalloproteinases, angiogenesis, exosomes

Introduction

Snake venoms are powerful mixtures of many toxins and enzymes among other chemical species whose applicability has shown to be very ample, such as in drug development. Metalloproteinases (SVMPs) are one of the main classes of enzymes in these mixtures. SVMPs are responsible for cleavage of extracellular matrix causing local hemorrhages. These enzymes are also fibrinolytic, pro-coagulant, mionecrotic, inflammatory and have an important role in TNF- α formation¹. When the environment alters, the affected cell releases signaling vesicles. One of the released products is exosome, which is a nanovesicular particle, with size from 60 to 130 nm. Derivated from the cells and present in body fluids, such as blood, exosomes participate in coagulation, inflammation, survival, cellular homeostasis, intercellular communication and transport². Snake Venom enzymes also have degradation effects over the extracellular matrix, in collagen IV cleavage and might show relevance in angiogenesis.

Results and Discussion

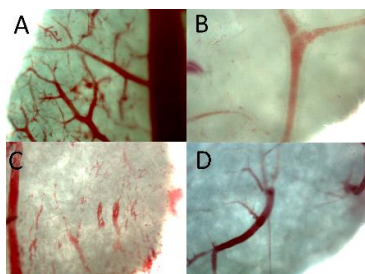


Image 1. Chorioallantoic membrane (CAM) test results in 11 days-old chicken embryonated eggs. A– Positive Control; B– Negative control; C – 10 μ L BaP1 (0,5 μ M); D – 10 μ L PIII (0,5 μ M).

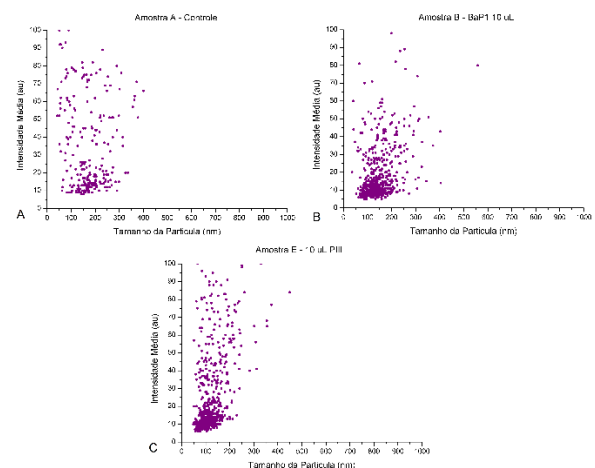


Image 2. Nanosight size analysis results: A- Human blood plasma control sample with PBS-1X; B- Human blood plasma sample with 10 μ L BaP1 (0,5 μ M); C- Human blood plasma sample with 10 μ L P-III (0,5 μ M).

Conclusions

A great release of nanoparticles with sizes indicative for exosomes has been observed upon administration of the two SVMPs in human blood plasma samples. The angiogenic process has been affected, showing inhibition comparable to the inhibitory effect of the negative control in embryonated eggs.

Acknowledgements



¹ Gutiérrez, J. M.; Recuvado, A. *Biochimie* **2000**, *82*, 841-850.

² Keller, S. *et al. Immunology Letters* **2006**, *107*, 102-108.