INHIBITORY EFFECTS OF 6-O-PALMITOYL-L-ASCORBIC ACID (ASC16) ON *Bothrops Alternatus* VENOM

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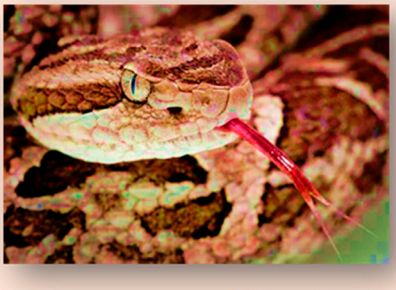
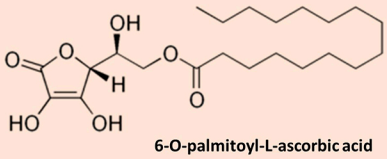
INTRODUCTION



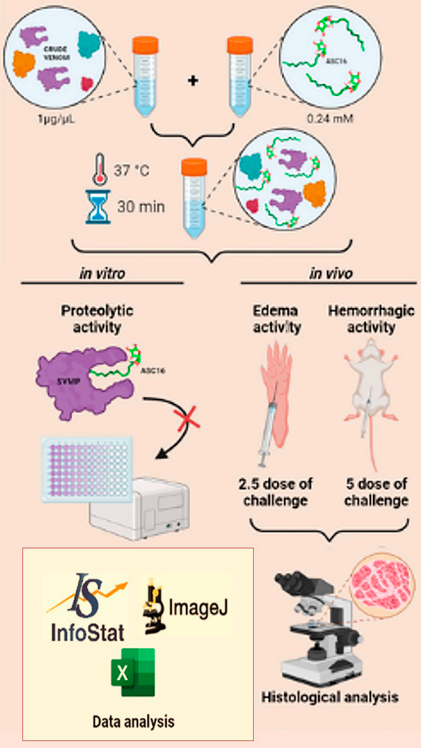
Bothrops alternatus

Snake venoms are a complex mixture of toxins, mostly of enzymatic nature, such as Phospholipases A2 (PLA2), Metalloproteinases (SVMP), Serine proteases (SVSP), others (Ramos and de Araujo 2006). The main damage induced by the venom of Bothrops alternatus are hemorrhage, proteolysis, coagulopathies, edema, other. At present, there is a growing interest in the search for natural or synthetic inhibitors acting on these components and thus allow mitigating their local and systemic effects. For this reason, in the present work we proposed the use of 6-O-palmitoyl-L-ascorbic acid (ASC16) as an inhibitor of the toxic effects induced by *B. alternatus* venom.



6-O-palmitoyl-L-ascorbic acid (ASC16)

MATERIALS AND METHODS



RESULTS

PROTEOLYTIC ACTIVITY

ASC16 inhibited 49.6% of the proteolytic activity "*in vitro*" induced by 25 µg of crude venom (ratio 1:10 w/w).There are significant differences in the presence of the inhibitor ($p<0.05$).

	***B. alternatus* venom**	**Venom + ASC16**
Proteolysis (%)	100	50.4 ± 0.001

EDEMA ACTIVITY

Histological results showed that, as it known, crude venom provoked severe tissue injury, with extensive hemorrhagic areas, abundant inflammatory infiltrate and necrosis. In contrast, the *B. alternatus* venom treated with ASC16 did not cause hemorrhages and it caused mild lesions with little necrosis of muscle fibers and moderate inflammatory infiltrate.

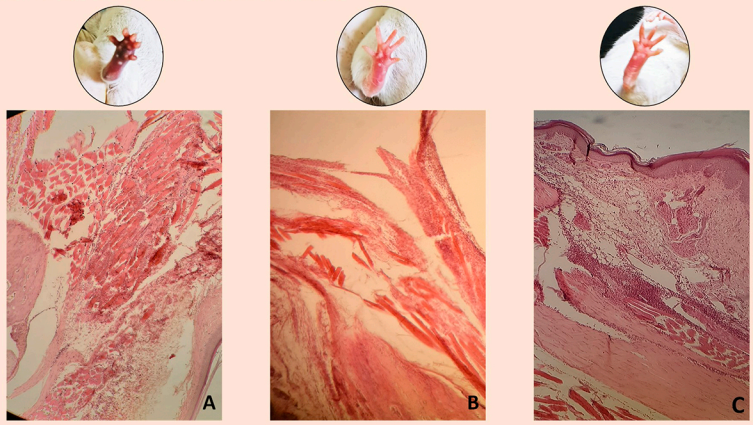


Image 1. *B. alternatus* venom (**A**) caused severe tissue lesions, with extensive hemorrhagic areas, abundant inflammatory infiltrate and necrosis. In contrast, crude venom treated with ASC16 (**B**) did not cause hemorrhage and caused mild lesions with little necrosis of muscle fibers and moderate inflammatory infiltrate. The ASC16 control (**C**) showed some infiltrate. There are significant differences in the presence of the inhibitor ($p<0.05$).

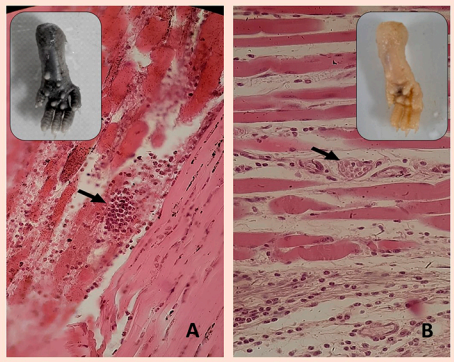


Image 2. A- *B. alternatus* venom generated endothelial membrane damage with red blood cell release. **B-** In the presence of the inhibitor (ASC16) no vessel damage or red blood cell release was observed.

HEMORRHAGIC ACTIVITY

ASC16 inhibited more of 70% hemorrhage activity "*in vivo*". There are significant differences in the presence of the inhibitor ($p<0.05$).

	Released haemoglobin (%)	**Pixels intensity for area (%)**
Crude venom	100	100
Venom + ASC16	21.94	28.2
Healthy control	0	0

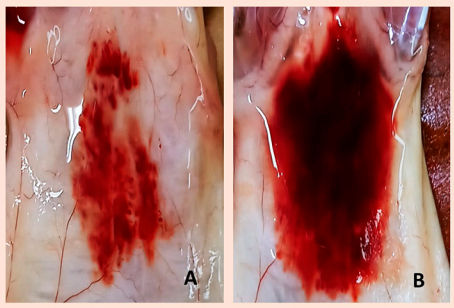


Image 3. A- *B. alternatus* venom generated hemorrhage intense. **B-** In the presence of the inhibitor (ASC16) the hemorrhage reduced considerably in intensity.

CONCLUSION

The results obtained indicate that ASC16 has potential as an inhibitor of SVMP enzymatic activity, suggesting its possible application as a local therapeutic agent. However, to understand in depth the mechanisms of ASC16 inhibition, further studies are required.

REFERENCES

1- Ramos, O. H. P., & Selistre-de-Araujo, H. S. (2006). Snake venom metalloproteases—structure and function of catalytic and disintegrin domains. Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology, 142(3-4), 328-346.

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