Dear Editor,

Accidents with venomous animals are a significant cause of global morbidity and mortality. Through the evolution, these animals have used their venomous apparatus for defence and prey capture. During the adaptation process in environment, several changes have occurred in snake venoms constitution. Nowadays, it is currently known that these animals are able to accumulate a mixture of different compounds that can produce from local damage (through) irreversible systemic alterations. Researches involving snake venom generally focus the discovery of a better understanding of: 1) the clinical aspects of human poisoning; 2) the mechanisms of action of venom toxins; 3) the prospection of toxins with therapeutic potential; 4) the development of biological tools for the diagnosis of several diseases; 5) and development of complementary alternatives to traditional anti-venom therapies.

Development of new drugs represents one of the most promising sectors of the pharmaceutical industry. Since the middle of 20th century, an increasing number of medicines have being developed. Most of them resulted from extraction and isolation of plant, animal and microorganism toxins. As an example of one of these cases, snake venoms were also assayed in order to investigate their antimicrobial and antitumoral activities with promising results.

The ability of some snake venom toxins to cause toxicity is associated with the high specificity and affinity for functional organized cell and tissues. In spite of their toxicological effects, several isolated snake venom proteins (such as, phospholipases A₂, metalloproteinases, serineproteases, L-amino acid oxidases, lectins and others) and peptides (bradykinin potentiators, natriuretic, analgesic peptides and others) have found practical application as pharmaceutical agents.
The best example is the inhibition of the angiotensin-converting enzyme (ACE) by
the bradykinin potentiating peptide (BPP9) isolated from the Bothrops jararaca
snake venom, which was used for the development of Captopril, a potent anti-
hypertensive, by Squibb Corporation. Additionally, thrombolytic agents have been
used in several cases of vascular disorder, for example, the batroxobin, a
serineprotease isolated from Bothrops atrox and B. moojeni snake venoms, was
used to treat vascular thrombosis. Concerning the treatment of another critical
disease such as cancer, there is a great interest in drug design, in which venom
toxins could provide structural templates for the study of new molecules or cellular
mechanisms.

In the past, snake venom was used to understand the molecular mechanism
of some receptors, such as acetylcholine (ACh) and their involvements with some
diseases. Two groups of toxins (α-BuTX and erabutoxin) isolated from Bungarus
multicinctus and Laticauda semifasciata, respectively, showed high affinity toward
normal and tumoral cells, displaying both cytotoxic effect. The interactions of toxins
with ACh receptor, have lead the application of these compounds as probes to
elucidate not only the neurophysiology but also to study some tumoral cells.
Although α-BuTX inhibited neuroblastoma, it failed during in vivo assays due to its
high toxicity. Thus, these finds gave new directions and possible application of
snake venom toxins in cancer treatment.

Snake venom LAAOs are enzymes with antitumoral and antimicrobial
properties. For example, LAAO from Trimeresurus stejnegeri showed antiviral
activity, as well as cytotoxic effect on lymphocitic leukemia C8166 cells, emerging
the discussing of H$_2$O$_2$ role upon cytotoxic activity. Recently, a novel Bothropoides
mattogrossensis LAAO and synthetic peptides (BmLAO-f1, BmLAO-f2 and BmLAO-
f3) showed antibacterial activity against Gram-positive and Gram-negative bacteria.

Phospholipases A$_2$ (PLA$_2$s; EC 3.1.1.4) are enzymes of high medical-scientific
interest due to their involvement in several inflammatory human diseases and in
envenomation by snake and bee venoms. VRCTC-310-Onco is a new
pharmaceutical product under development as an anti-neoplastic agent composed
of crotoxin (a PLA$_2$ from Crotalus durissus terrificus) and cardiotoxin (from Naja
naja atra) at equimolar ratio. C-terminal peptides derived from Lys49 PLA$_2$
homologues are able to induce antitumoral, antifungal, antibacterial, antiparasite
and antiendotoxic effects. Clearly, these peptides have a high potential for
therapeutic use in several medical and biological areas.

Metalloproteases and disintegrins are important components of most viperid
and crotalid venoms that can triggers haemorrhage by causing changes in blood
coaulation or interacting with the main components of extracellular matrix such as
collagen, laminin and fibronectin. The structural similarity between mammalian
MMPs (ADAM) and SVMPs (low and high MMPs) including disintegrins, reinforce the
idea that snake venom components can exhibit medical interest as potential
molecules for the treatment of animal tumours. Similarly, snake venom thrombin-
like enzymes (SVTLEs) are very useful for blood measurements of several
parameters and the treatment of vascular thrombosis. Other important medical
application is a new fibrin sealant composed of animal fibrinogen and Crotalus
durissus terrificus thrombin-like enzyme, which was tested in animals and humans.

Concluding, use of snake venom for medicinal purposes dates back to
ancient times, the past few decades have seen several new drugs derived from
natural bioactive compounds. Recent advances in several biotechnological areas
indicate new possibilities for contributions to clinical medicine and biomedical
research from snake venom.
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References


