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Bioprospecting of snake venoms: A mini review

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Abstract
Venom is a source of numerous active natural substances that have specific effects on various biological activities. Snake venom contributed significantly to the treatment of many medical conditions and enhancing the knowledge in pharmacology. Information on the nature and mechanism of action of these toxins has enabled a more scientific approach to the treatment of their intoxications. This paper focuses on knowledge about the biochemical and pharmacological importance of sea shake. In addition, this mini-review discusses the shake venoms, toxicity and therapeutic uses of snake venoms.

Keywords: Snake venoms, toxicology and pharmacology

1. Introduction
The animal Venoms and toxin are now recognized as a major source of novel bioactive molecules that may lead to development of new drugs. Venom is a secretion produced in a specialized gland in one animal delivered to a target animal through the infliction of a wound. This secretion must contain the molecule that disrupts the normal physiological process. Venomous may be used to kill prey and to defend the delivery organisms against attack by predators. Venoms are the complex mixture of pharmacologically highly active substance and can cause a wide range of symptoms. Most of the venoms are complex mixture number of protein, peptides, toxin and non-protein molecules.

The snake venoms are highly modified saliva. It contains zootoxin which facilitates the immobilization and digestion of prey and defends against threats. The venoms are contained in more than 30 different compounds mostly proteins and polypeptides. A complex mixture of proteins, enzymes and other substances with toxic, lethal properties and various other substances are responsible for important but non-lethal biological effects. Some of the bioactive compounds of snake venom have very specific effects on various biological functions including blood coagulation, blood pressure regulation and transmission of the nervous or muscular impulse and have been developed for use as pharmacological or diagnostic tools and even use drugs.

The snake venoms are naturally weak acid and it will become alkaline when it is placed for a long time. Water content 50 to 75% when exposed to air fresh venom is easy to produce foam. The composition of the venom is complex. It differs from species to species. The main ingredient is the toxic protein. Almost all venoms are composed of approximately 90% proteins and peptides. It contains more than 20 kinds of enzymes and toxins and all sorts of smaller molecules. Some toxins have multiple effects. They may vary from presenting neurotoxic (Mion *et al*., 2002; Francischetti *et al*., 1997; Harvey, 2001) [17, 5, 12] cardiotoxic (Tsetlin and Hucho, 2004; Satora *et al*., 2003) [23, 24, 21] or even an inhibitory platelet profile (Russell, 1980; Rucavado *et al*., 1995; Ducancel, 2002; Morris *et al*., 1995) [20, 19, 3, 18]. In addition, it also contains a number of amino acids, carbohydrates, lipids, nucleosides, biological amines and metal ions (Heise *et al*., 1995; Russell, 1980) [13, 20]. The most important components are the substances with a cytotoxic effect, neurotoxins and coagulants.

The snake venoms contain two general types of toxins, neurotoxins and hemotoxins. Neurotoxic venom attacks the central nervous system and usually results in heart failure and breathing difficulties. After the bite, local symptoms were not obvious, less bleeding, swelling and slight fever. However, within a few hours after injury, the rapid systemic symptoms, patients with anxiety excitement, groaning with pain, difficulty swallowing, difficulty breathing, convulsions, respiratory muscle paralysis and the death will appear. In addition, some scientists are now studying this neurotoxin can be used to treat virus such as the rabies virus. Hemotoxic venom attacks the circulatory system and muscle tissue causing excessive scarring, gangrene, permanent disuse of motor skills and sometimes leads to amputation of the

affected area. It can cause rapid swelling of the bite wound, bleeding and pain. The skin will become purplish, black and necrotic. After 6-8 hrs it could be spread to the head, neck, limbs and lower back. If the bite wound has not treated effectively within 4 h at last death will occur due to heart failure or shock. Some of the snake's venoms contain more members of each superfamily show similarity in their primary, secondary and tertiary structures. Among non-enzymatic proteins, superfamilies of three-finger toxins, serine proteinase inhibitors, C-type lectin-related proteins, atrial natriuretic peptides and nerve growth factors have already been well characterized (Zhong *et al*., 2006; Li *et al*., 2005; Ferreira *et al*., 1970) [29, 15, 4]. L-Amino acid oxidase, phospholipase A2, metalloprotease and ribonuclease A are some examples of superfamilies of enzymes in this family (Takasaki *et al*., 1988; Gong *et al*., 1998; Wei *et al*., 2006; Wang *et al*., 2004; Wu *et al*., 2001) [22, 8, 26, 25, 27]. Based on the structure, activity, and components, crude venom is also classified into cardiotoxin, neurotoxin, cytotoxin and myotoxin (Guinea *et al*., 1983; Barbosa *et al*., 2005) [9, 2].

Biochemical composition of Snake Venoms

Snake venoms are complex mixture contain protein and enzymes. Protein and peptides make 80-90% of the dry weight of venom. In addition to that snake venoms contain inorganic compounds such as sodium, calcium, potassium, magnesium and small amounts of zinc, nickel, cobalt, iron and manganese. Zinc has necessary pharmacological Properties of anticholinesterase activity; calcium is required for activation of enzyme-like phospholipase. Some snake venoms also contain carbohydrate, lipid, biogenic amines and free amino acids (Vivek *et al*., 2013) [33].

Pharmacological Properties of Snake Venoms

Many toxins from snake venom are investigated and formulated into drugs for the treatment of several diseases such as cancer, hypertension, and thrombosis. In general, the venoms of rattlesnakes and other new world crotalids produce alterations in resistance of blood vessels, changes in blood cells and coagulation mechanism, direct or indirect changes in cardiac and pulmonary dynamics. There may be alterations in nervous system and respiratory system (Gallacci and Cavalcante, 2010; Marcussi *et al.*, 2007; Gutierrez, 2005) [7, 16, 10]. The effectiveness of venom and its outcome on human depend on the type and amount of venom injected and the site where it is deposited. Clinical experiments and history show that the death may occur within less than 1 h to several days while the most deaths occurred between 18 to 32 hrs. Snake venoms significantly lower the blood pressure in human victims and experimental animals. Hypotension and shock are associated with snake venom poisoning (Aguilar *et al.*, 2007) [1].

Experimentally, it has been found that an intravenous bolus injection of *Crotalus* sp. venom causes an immediate fall in blood pressure and varying degree of shock, associated with initial heme concentration followed by a decrease in heamatocrit values (Gutierrez *et al.*, 2003) [11]. Captopril was isolated from *Bothrops jararaca* venom is an example of a therapeutic derived from the snake venoms (Yamazaki *et al*., 2003) [28]. Increased blood volume in the lung and pulmonary artery pressure with a concomitant decrease in pulmonary artery flow and a relatively stable heart stroke volume are noticed. When *Crotalus* venom is given IV slowly for over a period of 30 min, there is hypovolume secondary to an increase in capillary permeability to proteins and RBCs. According to Koh and Kini discovered the experimental results showed initial haemoconcernatration, lactacidamiea and lipoprotienamia, respiration becomes labored and if period prolongs animal becomes oliguric, rales develop and the animal dies.

Therapeutics Application of Snake Venom

Therapeutic application of venom proteins Snake venom is known to be highly toxic and lethal, which makes snakes to be among the most feared creatures. The properties that make venom fatal are also what make it so valued for medicine (McCleary and Kini, 2013) [30]. Many diseases can be treated and controlled using venom toxins because most of these toxins target the same molecules that need to be controlled to treat diseases. Venom proteins are highly specific which makes them appreciated for drug use because of the decrease in prospective side effects (Holland, 2013) [31].

The dynamic components of snake venom are the peptides and proteins, functioning as toxins and enzymes that target precise molecules (Zahida *et al.*, 2015) [32]. Numerous compounds found in snake venoms have been utilized as a protein source for drug production and developed for the treatment of conditions such as cancer, hypertension, thrombosis and microbial invasion in cases where there is resistance to antibiotics. The snake venom contains at least 25 enzymes but no single venom contains all of them. These enzymes are protein in nature but few depend on certain non-protein prosthetic groups or cofactors (Vivek *et al.*, 2013) [33].

Some of the components isolated from various snake venoms are Phospholipase A2, ancrod cobra venom factor, peptides, cytotoxins, crotoxin, Lamino acid oxidases (LAAOs), lectins, metalloproteinases, disintegrins, serinoproteases, hyaluronidase, cholinesterases, salmosin, cathelicidin-BF, aggretin, obtustatin, rhodostomin, albolabrin, colombistatin, saxatilin and lebecetin which show hopeful applications in management of various human diseases (Liu *et al.*, 2014) [34]. According to Leonardo *et al.*, the toxicological effects of several isolated snake venom, proteins and peptides have practical presentations as pharmaceutical agents. For example, thrombolytic agents have been used in several cases of vascular disorder, antimicrobial activity against gram positive and gram negative bacteria and anti-viral activity and also cancer treatment.

Conclusion

Snake venoms are the complex mixtures of several biologically active proteins, peptides, enzymes, organic and inorganic compounds. It also has potential and developing drugs for use as several diseases. It offers promise for identifying new prospective drugs.

Reference

1. Aguilar I, Guerrero B, Salazar AM, Giron ME, Perez JC, Sanchez EE, *et al*. Individual venom variability in the South American rattlesnake *Crotalus durissus cumanensis*. Toxicon. 2007; 50: 214-224.
2. Barbosa PS, Martins AM, Havt A, Toyama DO, Evangelista JS, *et al*., Renal and antibacterial effects induced by myotoxin I and II isolated from *Bothrops jararacussu* venom. Toxicon, 2005; 46:376-386.
3. Ducancel F. The sarafotoxins. Toxicon. 2002; 40:1541-1545.
4. Ferreira SH, Bartelt DC, Greene LJ. Isolation of

bradykinin-potentiating peptides from *Bothrops jararaca* venom. Biochemistry. 1970; 9:2583-2593.
5. Francischetti IM, Saliou B, Leduc M, Carlini CR, Hatmi M, *et al*., Convulxin, a potent platelet-aggregating protein from *Crotalus durissus terrificus* venom, specifically binds to platelets. Toxicon. 1997; 35:1217-1228.
6. Fry BG. From genome to venome: Molecular origin and evolution of the snake venom proteome inferred from phylogenetic analysis of toxin sequences and related body proteins. Genome Res. 2005; 15:403-420.
7. Gallacci M, Cavalcante WLG. Understanding the in vitro neuromuscular activity of snake venom Lys49 phospholipase A2 homologues. Toxicon. 2010; 55:1-11.
8. Gong W, Zhu X, Liu S, Teng M, Niu L. Crystal structures of acutolysin A, a three-disulfide hemorrhagic zinc metalloproteinase from the snake venom of *Agkistrodon acutus*. J Mol. Biol., 1998; 283:657-668.
9. Guinea ML, Tamiya N, Cogger HG. The neurotoxins of the sea snake *Laticauda schistorhynchus*. Biochem. J 1983; 213:39-41.
10. Gutierrez JM, Alexandra R, Escalante T, Díaz C. Hemorrhage induced by snake venom metalloproteinases: biochemical and biophysical mechanisms involved in microvessel damage. Toxicon. 2005; 45:997-1011.
11. Gutierrez JM, Ownby CL. Skeletal muscle degeneration induced by venom phospholipases A2: insights into the mechanisms of local and systemic myotoxicity. Toxicon. 2003; 42:915-931.
12. Harvey AL. Twenty years of dendrotoxins. Toxicon. 2001; 39:15-26.
13. Heise PJ, Maxson LR, Dowling HG, Hedges SB. Higher-level snake phylogeny inferred from mitochondrial DNA sequences of 12S rRNA genes. Mol. Biol. Evol. 1995; 12:259-265.
14. Koh CY, Kini RM. From snake venom toxins to therapeutics - Cardiovascular examples. Toxicon. 2012; 59:497-506.
15. Li WF, Chen L, Li XM, Liu J. A C-type lectin-like protein from *Agkistrodon acutus* venom binds to both platelet glycoprotein Ib and coagulation factor IX/factor X. Biochem. Biophys. Res. Commun. 2005; 332:904-912.
16. Marcussi S, Sant'Ana CD, Oliveira CZ, Rueda AQ, Menaldo DL, Beleboni RO, *et al*. Snake venom phospholipase A2 inhibitors: medicinal chemistry and therapeutic potential. Cur Topics Med Chem. 2007; 7:743-756.
17. Mion G, Olive F, Hernandez E, Martin YN, Vieillefosse AS, Goyffon M. Action of venoms on blood coagulation: Diagnosis of hemorrhagic syndromes. Bull. Soc. Pathol. Exot. 2002; 95:132-138.
18. Morris VL, Schmidt EE, Koop S, MacDonald IC, Grattan M, *et al*., Effects of the disintegrin eristostatin on individual steps of hematogenous metastasis. Exp. Cell Res. 1995; 219:571-578.
19. Rucavado A, Borkow G, Ovadia M, Gutierrez JM, Immunological studies on BaH1 and BaP1, two hemorrhagic metalloproteinases from the venom of the snake *Bothrops asper*. Toxicon. 1995; 33:1103-1106.
20. Russell FE. Venoms. In: Snake Venom Poisoning, Lippincott, J.B. and G.M. Persol (Eds.). Lippincott, Philadelphia, 1980, 139-234.
21. Satora L, Morawska J, Targosz D. Cardiotoxicity of vertebrates venoms. Przegl. Lek. 2003; 60:199-201.
22. Takasaki C, Kimura S, Kokubun Y, Tamiya N. Isolation, properties and amino acid sequences of a phospholipase A2 and its homologue without activity from the venom of a sea snake, *Laticauda colubrine*, from the Solomon Islands. Biochem. J. 1988; 253:869-875.
23. Tsetlin VI, Hucho F. Snake and snail toxins acting on nicotinic acetylcholine receptors: Fundamental aspects and medical applications. FEBS Lett. 2004; 557:9-13.
24. Tsetlin VI, Hucho F. Snake and snail toxins acting on nicotinic acetylcholine receptors: Fundamental aspects and medical applications. FEBS Lett. 2004; 557:9-13.
25. Wang WJ, Shih CH, Huang TF. A novel P-I class metalloproteinase with broad substrate-cleaving activity, agkislysin, from *Agkistrodon acutus* venom. Biochem. Biophys. Res. Commun. 2004; 324:224-230.
26. Wei JF, Wei XL, Chen QY, Huang T, Qiao LY, *et al*., 2006. N49 phospholipase A2, a unique subgroup of snake venom group II phospholipase A2. Biochim. Biophys. Acta, 1760, 462-471.
27. Wu WB, Peng HC, Huang TF. Crotalin, a vWF and GP Ib cleaving metalloproteinase from venom of *Crotalus atrox*. Thromb. Haemost. 2001; 86:1501-1511.
28. Yamazaki Y, Takani K, Atoda H, Morita T. Snake venom vascular endothelial growth factors (VEGFs) exhibit potent activity through their specific recognition of KDR (VEGF receptor 2). J Biol Chem. 2003; 278:51985-51988.
29. Zhong SR, Jin Y, Wu JB, Chen RQ, Jia YH, *et al*., Characterization and molecular cloning of dabocetin, a potent antiplatelet C-type lectin-like protein from *Daboia russellii siamensis* venom. Toxicon. 2006; 47:104-112.
30. McCleary JR, Kini RM. Non-enzymatic proteins from snake venoms: A gold mine of pharmacological tools and drug leads. Toxicon. 2013; 62:56-74.
31. Holland SJ. The bite that Heals. National Geographic website, 2013.
32. Zahida YR, Mirza R, Rafsan ZT, Foyasal MK, Bapari MR, Dipu R, *et al*. Functional characterization of elapid venom toxin proteins and related non-toxin proteins of human through comparative analysis. Trends in Bioinformatics. 2015; 8:86-92.
33. Vivek KV, Keyur B, Hardik B, Utsav P. Therapeutic potential of snake venom in ancer therapy: current perspectives. Pacific J Trop. Biomed. 2013; (2):156-162.
34. Liu C, Yang, H, Zhang L, Wang Y. Biotoxins for cancer therapy. Asian Pacific J Cancer Prev. 2014; 15(12):4753-4758.
35. Leonardo AC, Juliana CS, Kayena DZ, Andrea AD, Amy NG, Maurício VM, *et al*. Antitumoral activity of snake venom proteins: New Trends in Cancer Therapy. Biomed. Res. 2014; 1:31-40.