Vol. 1: 343 – 352 (2024)

Snake venoms: Valuable therapeutic weapon to combat infectious and non-infectious diseases

*[1]Abdulkadir, A., [1]Ibrahim, Y. O., [1]Abdulrasheed-Adeleke, T., Umar, M. B.

[1]Department of Biochemistry, Federal University of Technology, Minna, Nigeria

ABSTRACT

Snake venoms are a complex mixture of abundant components, containing a variety o biologically active molecules, with peptides and proteins accounting for more than 95 % o venom dry weight. These peptides and proteins have been isolated using differe separation techniques ranging from size exclusion chromatography, ion-exchang chromatography, reversed-phase High-pressure liquid chromatography, affinit chromatography to electrophoretic techniques. Both crude and isolated fractions of venom from different species of snakes have been explored for pharmacological application Catalytic proteins including phospholipase A2, L-amino acid oxidase, hyaluronidases an proteases as well as bradykinin-potentiating peptides are the most widely studied snak venom components. Interestingly, these components of venoms have been shown to b promising drug leads for the production of new therapeutic agents. Although, venoms fro different genera of snakes have been proven to be pharmacologically relevant, thos belonging to genera, *Bothrops, Ophiophagus, Crotalus, Naja,* and *Vipera* tend to be mor relevant and have been explored for same purpose. Snake venom components have bee used in the treatment of numerous diseases including infectious diseases such as bacteria fungal, viral, and protozoan infections, and non-infectious diseases such as cance cardiovascular diseases, and diabetes. Further, there are commercially available drugs mad from snake venoms for the treatment of different diseases. In conclusion, snake venoms ar promising drug leads for development of drugs for a number of diseases. However, stric care must be taken in dosage selection in order to avert morbidities and perhaps mortalit associated with snake venoms at toxic dose.

Keywords: snake venom, phospholipase A2, proteases, amino acid oxidase, infectious diseases

***Corresponding author:** yunusaibrahim1994@gmail.com, +2349067553878

INTRODUCTION

Snake venom is a complex mixture of abundant components, containing a variety of biologically active molecules with peptides and proteins accounting for more than 95 % of snake venom dry weight (the other 5 % contain lipids, carbohydrates, and biogenic amines) (Tasoulis *et al.*, 2022). These proteins perform various functions aiding in capturing and digestion of prey after envenomation. Some proteins function as enzymes catalyzing chemical reaction that disrupt coagulation and induc hemorrhage, while others interfere wit cellular receptors, causing paralysis. Th venom's effects on the body can b hemotoxic, cytotoxic, or neurotoxi leading to blood cell damage, tissu inflammation, or nervous syste disruption, respectively. The specifi physiological impacts depend on the snak species and venom composition (Olivei *et al.*, 2022). Snake venom compositio

n be divided into two groups of proteins
d peptides: enzymatic and non-
zymatic molecules (Akhtar *et al.*, 2021).
zymatic molecules are proteins with
talytic sites and activity, able to speed up
emical reaction rates in the presence of
substrate. The most common and
undant enzymatic molecules are snake
nom phospholipases A2 (PLA2), snake
nom metalloproteinases (SVMP), snake
nom serine proteases (SVSP), and L-
nino acid oxidases (LAAO) (Rodríguez-
argas *et al.*, 2023). The second group is
e non-enzymatic molecules found in
nake venom. These include neurotoxins,
ffecting the nervous system;
ardiotoxins, affecting the heart; and
ytotoxins, damaging cells. The most
ommon non-enzymatic molecules are
hree-finger toxins (3FTx), Kunitz
eptides (KUN), disintegrins (DIS), and
ysteine-rich secretory protein (CRiSP)
Hus *et al.*, 2024).

Many of the components of venom have
been isolated, characterized, and assessed
or their biological actions. Their medical
utility was rapidly discovered (Diniz-
Sousa *et al.*, 2023). Animal venom studies
nitially began with the enthusiasm of
understanding animal envenomation and
associated medical treatments (Diniz-
Sousa *et al.*, 2023). Subsequently,
additional reasons that make animal
venoms attractive to researchers around
the world are the richness, specialization,
and efficiency of their components: most
of these components are peptides that
affect with high selectivity and affinity a
large number of targets such as membrane
receptors, ion channels, enzymes or
various hemostatic pathways (Lodato *et*
al., 2023). From the early 17th century, the
Italian naturalist Felice Fontana illustrated
the influence of snake venoms on blood
coagulation (Suseel *et al.*, 2023).

Chronic diseases, including CVDs, cancer, diabetes, and chronic pain, are the leading causes of death and disability worldwide. These conditions have been treated using drugs derived from Viperidae and Elapidae venoms. For example, Captopril, used for hypertension and diabetic nephropathy, was developed from the bradykinin-potentiating peptide (BPP) in snake venom (Bedraoudi *et al.*, 2023). Disintegrins (DIS), peptides isolated from snake venoms and act as anti-coagulant agents, inhibiting platelet aggregation and promoting hemorrhage, resulted in the development of Eptifibatide and Tirofiban, two FDA-approved drugs for the treatment of acute coronary syndrome. Among approved venom-derived molecules for the treatment of chronic diseases and pain, we find Captopril, Enalapril, Eptifibatide, Tirofiban, Defibrase, Reptilase, and Cobratide that have either been approved by the FDA (USA), the EMA (Europe), or the National Medical Products Administration (NMPA) (China) (Ladato *et al.*, 2023; Messadi, 2023; de Oliveira *et al.*, 2023).

Pharmacological Potentials of Snake Venoms

Snake venoms have been presented to be an essential tool in medicine owing to the presence of wide range of bioactive principles in them. These bioactive principles; enzymatic and non-enzymatic, have been implicated in the treatment of various diseases including infectious and infectious diseases.

Treatment of Infectious Disease

A number of diseases caused by microorganisms including bacteria, fungi, protozoans, and virus have been treated or managed using venoms from different species of snakes. Below are infectious

diseases that have been treated/or managed using snake venoms.

Antiprotozoal effects of snake venoms

Protozoans have been reported to cause diseases that are life-threatening in both human and animals. However, snake venoms have been shown to possess the potentials of inhibiting their growth, targeting different stages of their life-cycle. Crude venom of *Bothrops moojeni* has been found to inhibit the growth of W2 strain of *Plasmodium falciparum in vitro*. The basic phospholipase A2 isolated from *Paraguayan Bothrops diporus* has also been linked with the same inhibitory effect, also targeting the W2 strain of *P. falciparum* (Vitorino *et al.*, 2020). Vitorino *et al.* (2020) also reported PLA2s, BdTX-I, BdTX-II, and BdTX-III venom fraction of *Bothrops diporus* to inhibit the growth of W2 strain of *P. falciparum*. A study by Abdullahi *et al.* (2021) revealed that venom fraction of *Naja naja oxiana* inhibited the growth of *P. falciparum* by inhibiting intraerythrocytic development of the parasite. According to Abdullahi *et al.* (2021), p-Acl and p-AclR7 fractions of *Agkistrodon contortrix* exerted cytotoxic actions against *Leishmania. amazonensis* and *Leishmania. infantum*, respectively. Also, venom fraction NNOV-FK from *Naja naja oxiana* inhibited the growth of *Leishmania tropica* by significantly increasing the levels of TNF-α, interleukins-12 and iNOS gene while drastically reducing the level of IL-10 (T helper 2 markers) (Abdullahi *et al.*, 2021). Also, Almeida *et al.* (2023) reported BatxC fraction of venom of *Bothrops atrox* to inhibit all the developmental stages of *Trypanosoma cruzi* with high selective index of 315, and also caused necrosis. In addition, acidic PLA2s, BasPAC-I, BASPAC-II, BASPAC-III, and BASPAC-IV from venom of *Bothrops asper* exerted substantial inhibition against *L. infantum* promastigotes and *T. cruzi* epimastigotes with 30% anti-parasitic activity. The basic PLA2s BASPB-II, and BASP-IV s inhbited the growth of *P. falciparum* with 30% anti-parasitic activity, whereas the crude venom substantially inhibit the parasites with IC_{50} of 8.60 and 34.70 µg/mL against *L. infantum* promastigotes and *T. cruzi* epimastigotes. Soares *et al.* (2020) reported ML-LAAO venom fraction of *Micrurus lemniscatus* to inhibit the growth of *L. amazonensis* and *L. chagasi in vitro* in a concentration-dependent fashion. The crude venom of *Naja nigricollis* and *Bitis arietans* have been respectively shown to exhibit trichomonicidal potency against *Trichomonas vaginalis*. BJussuLAAO-II venom fraction of *Bothrops jararacuccu* and BmooLAAO-II venom fraction of *Bothrops moojeni* to be cytotoxic to *L. amazonensis* and *L. braziliensis* respectively (Abdullahi *et al.*, 2021). Furthermore, crude venom and BmatTX-IV of *Bothrops mattogrossensis* was found to inhibit the cellular viability of *L. infantum* promastigotes *in vitro* and *T. cruzi* epimastigotes respectively (Alfonso *et al.*, 2019).

Antibacterial effects of snake venoms

Venoms from different snake species have potency to significantly inhibit the growth both Gram positive and Gram-negative bacteria. Crude venom of Ophiophagus hannah was reported to inhibit the growth of *S. aureus*, *E. coli*, *S. epidermis*, *S. saprophyticus*, *S. lugdunensis*, and *E. faecalis* with MIC of 8.00, 8.00, 4.00, 4.00 and 8.00 µg/mL, respectively. LAAO fro different snake species including (Kurfi *al.*, 2022) reported bactericidal activit of LAAO from venom of *Bothrop alterna*

against E. coli and S. aureus respectively in a concentration-dependent manner with maximum activity being observed at 48 µg/mL. Similarly, Alves *et al.* (2020) reported LAAO from *Bothrops marajoensis* to significantly inhibit the growth of *S. cholesraesuis*, *S. aureus*, E. coli, and *P. aeruginosa*. In addition, L-amino acid oxidase (LAAO) from venom of *Bothrop leucurus* was found to inhibit the growth of S. aureus in a concentration-dependent manner with maximum inhibition being observed at 100 µg/mL (Alves *et al.*, 2020). LAAO isolated from venom *Crotalus durissus* has been reported to inhibit the growth of *Xanthomonas axonopodis* and *Staphylococcus mutans* with IC_{50} values of 35 and 12.3 µg/mL respectively. (Bocian & Hus, 2020) The antibacterial activities of LAAO have been strongly linked to the production of H_2O_2 by the enzyme which triggers apoptosis in the bacteria (Bocian & Hus, 2020). Similarly, PLA2s from different snake species have been reported to possess antibacterial potential. For example, *Bothrops marajoensis* was reported to exert bactericidal action against the growth of different bacterial species including *S. cholesraesuis*, *S. aureus*, E. coli, and *P. aeruginosa* in a concentration-dependent fashion with an IC_{50} of 32.25 µg/mL (Alves *et al.*, 2020). In addition, PLA2s isolated from venom of *Porthidium nasutum* inhibited the growth of *S. aureus* with an MBC and MIC of 32 and 16 µg/mL respectively. However, this PLA2 was not active against *E. coli* (Teodoro *et al.*, 2022).

Antifungal effects of snake venoms

Fungal diseases kill more than 1.5 million and affect over a billion people globally (Bongomin *et al.*, 2022). However, they are still regarded as neglected tropical disease by public health authorities even though most deaths from fungal diseases are avoidable. Serious fungal infections occurs as a consequence of other health problems including asthma, AIDS, cancer, organ transplantation, and corticosteroid therapies (Bongomin *et al.*, 2022).

Antifungal potential of metalloproteinases and PLA2s from venom of *Crotalus durissus cumanensis* against *Candida parapsilosis* and *Sporothrix schenckii* have been reported (Cañas, 2022). Also, crotamine from the venom of *Crotalus durissus terrificus* exerted inhibitory effects against similar fungi (Hayashi *et al.*, 2022). Furthermore, LAAO from *Bothrops marajoensis* has also been reported to possess antifungal effect against *Candida albicans* (Alves *et al.*, 2020).

Antiviral effects of snake venoms

Like other microorganisms, viruses have also been inhibited by snake venoms from different species of snakes. El-Bitar *et al.* (2018) reported venom of *Cerastes vipera* to exert antiviral activity against Hepatitis C virus with an IC_{50} of 1 ng/ml and CC_{50} of 1000 ng/ml. The selective index of the snake venom was found to be 1000-fold than the IC_{50}. In an *in vitro* study, Yonys *et al.* (2019) evaluated the virucidal activity of venom of *Naja Nubiae* against Rift Valley Fever virus (RVFV) and Herpes Simplex Virus Type -1 (HSV-1) using cell lines and reported that the venom possessed virucidal activity against the two viruses. However, RVFV was found to be more susceptible to the venom than HSV-1. In another study, PLA2s from isolated from venoms of *Bungarus fasciatus*, *Vipera ursinii renardi*, and *Viper v. nikolskii* respectively were shown to exhibit virucidal activities against HIV-1 [illegible]. It was revealed that dimeric PLA2s HDP and HDP-2 were only the phospholip

2 found to inhibit HIV-1 IIIB replication with the IC_{50} values of 0.67 and 0.28 µg/ml, respectively. Furthermore, PLA2s (Vur-PLA2, HDP-1, HDP-2, HDP-II, HDP-2P, and HDP-2P mac1) isolated from the venoms of *V. nikolskii* and *V. ursinii renardi* vipers have been reported to exhibit strong virucidal activity against SARS-CoV-2 and inhibit the viral spike glycoprotein interaction with ACE2 with IC_{50} values of 1.88, 0.08, 0.17, 7.71, 0.06, and 4.17 µg/mL, respectively (Shulavin *et al.*, 2022).

Treatment of non-infectious diseases

Snake venoms have been employed not only in the treatment and/or management of infectious diseases, but they have also been integral part of modern medicine in the treatment of non-infectious diseases affecting humans and animals.

Cancers

Cancers are a large group of non-communicable diseases that causes morbidity and mortality globally. Cancer results from genetic or epigenetic factors, which alter genetic makeup leading to uncontrolled cell growth in tissues or organs of the body (Kalita *et al.*, 2024). The leading cause of cancer-associated deaths is as a result of metastasis, whereby the abnormally dividing cells grow uncontrollably and invade other parts of the body (Kalita *et al.*, 2024). The current treatments for cancers include chemotherapy, radiotherapy, immunotherapy, and surgery. The cytotoxic effects of snake venom and its toxins lead to damage to cells and tissues. These venom-based toxins with cytotoxic effects can be harnessed and used as potential anticancer agents (Ma & Kwok, 2022). Crude venoms of different snake species have been explored in search for potent anticancer bioactive principles. Crude venoms of *Naja haje*, *Naja nigricollis*, *Cerastes cerastes*, *Lelurus pure* have been tested on different cancer cell lines (vero, MDCK, MEC-7, and CACO-2). These venoms showed appreciable anticancer activities against all the cell lines. However, venom of *Cerastes cerastes* showed the highest anticancer activity. It was found that the cytotoxicity to normal cells (MDCK) was much lower than those of cancer cells (CACO-2 and MCF-7) (Alyan *et al.*, 2014). Also, in an *in vivo* study by administration of venoms of *C. cerastes* and N. Haje led to significant up regulation of pro-apoptotic genes (P53 and BAX) with concomitant down regulation of anti-apoptotic gene (Bcl-2) which favour apoptosis of cancer cells (Alyan *et al.*, 2014). Furthermore, Offor & Plater, (2024) reported cytotoxins 1N, 2N, 3N, and 4N isolated from venom of Naja nigricollis to exert tozic effects on non-small cell lung adenocarcinoma A549 cells, breast adenocarcinoma MDA-MB-231 cells, and colorectal adenocarcinoma HT-29 cells, with attractive LC_{50} values. However, these toxins also induced hemolysis of normal cells, human umbilical vein endothelial HUVEC cells and mouse red blood cells (RBC) which they were also tested against. As result, the development of anti-cancer drug using venom has been limited.

Cardiovascular diseases

Cardiovascular diseases (CVDs) are a vast group of heart and blood vessels diseases of various etiologies. They lead to impairment of the normal functions of various organs and, in severe cases, death (Osipov *et al.*, 2023). They put a huge burden on health care systems and the economy around the world. According to WHO, more than 17 million people die

from heart diseases every year. By 2030, this number is estimated to exceed 23 million. Currently, a large number of drugs with various mechanisms of actions exist, and they are used for the treatment of CVDs. These drugs are however associated with adverse side effects (Osipov *et al.*, 2023). A number of snake venom components, most especially the non-enzymatic components, have been found to profoundly possess cardioprotective effects. Bradykinin-potentiating peptides have been reported to inhibit the conversion of angiotensin I to angiotensin II by the enzyme angiotensin-converting enzyme (ACE) thus lowering the blood pressure through decrease in the concentration of angiotensin II and increase in the concentration of bradykinin (Guo *et al.*, 2021). Natriuretic peptides have also been reported to reduce calcium influx into the muscle cells by interacting with natriuretic peptide receptors A, B, and C thus lowering blood pressure through reduction in vascular resistance and decrease in the volume of circulating blood (da Silva *et al.*, 2021 and Ichiki *et al.*, 2022). Sarafotoxins Increased vasoconstriction followed by narrowing of the bronchi and increased airway resistance as well as an increase in hydrostatic pressure of microvessels in the lungs, which leads to their edema. Failure of various parts of the heart, mainly the left ventricle (Galli *et al.*, 2020 and Van Baelen *et al.*, 2022). These toxins elicit its effects by interacting with Endothelin type A (ETA) and B (ETB) receptors. Furthermore, three-finger toxins interact with cell membranes, adrenergic receptors, and cholinergic receptors resulting in the suppression of contractility and irreversible contracture of the myocardium; lowering blood pressure; cardioprotection (Averin *et al.*, 2022). Cysteine-rich secretory proteins (CRISPs) also cause inhibition or activation of aortic smooth muscle contraction by exerting actions on Voltage-gated ion channels (Tadokoro *et al.*, 2020). Alternagin-C stimulates Enhancement of cardiac activity, protection against hypoxia/reoxygenation-induced cardiomyocyte negative inotropism by binding to Integrin α2β1 and VEGFR-2 (Monteiro *et al.*, 2022). Endothelial vascular growth factors have been reported to possess cardioprotective effect by causing reduction in reperfusion injury to the heart and infarct size. This effect is instigated by their interaction with Receptor tyrosine kinases VEGFR-1, VEGFR-2, and VEGFR-3 (Ferreira *et al.*, 2021 and Messadi, 2023).

Antidiabetic effects of snake venom

Diabetes is a chronic disease resulting from impaired insulin secretion and function, leading to persistent hyperglycemia and its severe complications. The treatment for type I diabetes involves insulin injections while type II diabetes treatments include metformin and sulfonylureas, along with lifestyle changes. This medicine can be expensive and associated with adverse side effects (Shahdadi *et al.*, 2024). Therefore, the search for new therapeuti agents continues. Snake venoms being reservoir of diverse proteins and peptide have proven to find its application in t treatment of diabetes. Da Silva *et* (2023) reported that peptides isolat from the venom of *Crotalus duris terrificus* lowered blood glucose leve to 37% at a dose of 0.2 mg/mice in rat with high-fat diet. Similarly, antidiabetic potency of venom of *Naj oxiana* was evaluated in diabetic rat models induced with strepto and nicotinamide. In either of the

of induction, the venom caused significant decrease in fasting blood glucose of the diabetic rats at dose of 0.2 mg/kg body weight (Shahdadi *et al.*, 2024). In a study by PLA2s isolated from the venom of *N. nigricollis* stimulated insulin release from rat clonal β-cells with about 6-fold increase in the rate at a concentration of 1 µM.

CONCLUSION

Despite the fearfulness and danger of snakes in them of morbidities and mortalities associated with their bites, snake venoms remain an important depot of vast number of bioactive compounds mainly proteins and peptides which are either enzymatic or non-enzymatic. These bioactive proteins/peptides have potential to be employed as leads in the design of drugs for the treatment of different diseases including infectious and non-infectious ones. In addition to available FDA-approved drugs from snake venoms which are majorly cardio-protective drugs, there are numerous drugs that can be designed using snake venoms as leads to help human combat life-threatening diseases such as cancers, diabetes, among others.

REFERENCES

Abdullahi, Z. U., Musa, S. S., He, D., & Bello, U. M. (2021). Antiprotozoal effect of snake venoms and their fractions: A systematic review. *Pathogens*, *10*(12), 1632.

Akhtar, B., Muhammad, F., Sharif, A., & Anwar, M. I. (2021). Mechanistic insights of snake venom disintegrins in cancer treatment. *European journal of pharmacology*, *899*, 174022.

Alfonso, J. J., Kayano, A. M., Garay, A. F. G., Simões-Silva, R., Sobrinho, J. C., Vourliotis, S., ... & Gómez, M. C. (2019). Isolation, biochemical characterization and antiparasitic activity of BmatTX-IV, a basic Lys49-phospholipase A2 from the venom of Bothrops mattogrossensis from Paraguay. *Current Topics in Medicinal Chemistry*, *19*(22), 2041-2048.

Almeida, J. R., Gomes, A., Mendes, B., Aguiar, L., Ferreira, M., Brioschi, M. B. C., ... & Gomes, P. (2023). Unlocking the potential of snake venom-based molecules against the malaria, Chagas disease, and leishmaniasis triad. *International journal of biological macromolecules*, *242*, 124745.

Alves, R. D. C., Vieira, J. R., Freire, T. C., Fonseca, A. S. D., Sangi, S. C., Barbieri, F. D. S., ... & Fernandes, C. D. F. (2020). Snake venoms and purified toxins as biotechnological tools to control Ralstonia solanacearum. *Pesquisa Agropecuária Brasileira*, *55*, e01756.

Alyan, M. S., Shalaby, M. A., El-Sanousi, A. A., Mohamed, A., & Shebl, R. (2014). Antiviral and anticancer potentials of snake and scorpion venom derivatives. *Inventi Rapid: Mol Pharma*, *2*, 15-22.

Averin, A. S., Nenov, M. N., Starkov, V. G., Tsetlin, V. I., & Utkin, Y. N. (2022). Effects of cardiotoxins from Naja oxiana cobra venom on rat heart muscle and aorta: A comparative study of toxin-induced contraction mechanisms. *Toxins*, *14*(2), 88.

Bedraoui, A., Suntravat, M., El Mejjad, S., Enezari, S., Oukkache, N., Sanchez, E. E., ... & Daouda, T. (2023). Therapeutic potential of snake venom: Toxin distribution and opportunities in deep

learning for novel drug discovery. *Medicine in Drug Discovery*, 100175.

Bocian, A., & Hus, K. K. (2020). Antibacterial properties of snake venom components. *Chemical Papers, 74*(2), 407-419.

Bongomin, F., Ekeng, B. E., Kibone, W., Nsenga, L., Olum, R., Itam-Eyo, A., ... & Baluku, J. B. (2022). Invasive fungal diseases in Africa: a critical literature review. *Journal of Fungi, 8*(12), 1236.

Cañas, C. A. (2022). Biological and Medical Aspects Related to South American Rattlesnake Crotalus durissus (Linnaeus, 1758): A View from Colombia. *Toxins.* 2022; 14.

da Silva, E. F. T., Barbosa, M. A. P., de Figueirêdo Marinho, T. A., Lima, G. C., dos Santos, W. L., Espindola, M. T. A., ... & Moreira, K. A. (2023). Ten years of research on bioactive peptides in Brazil: a scientometric analysis. *Food Science and Technology, 43.*

da Silva, G. J. J., Altara, R., Booz, G. W., & Cataliotti, A. (2021). Atrial natriuretic peptide31–67: a novel therapeutic factor for cardiovascular diseases. *Frontiers in Physiology, 12*, 691407.

de Oliveira, D., Guerra-Duarte, C., Stransky, S., Scussel, R., de Castro, K. L. P., Costal-Oliveira, F., ... & Machado-de-Ávila, R. A. (2023). Toxic and antigenic characterization of Peruvian Micrurus surinamensis coral snake venom. *Toxicon, 225*, 107056.

Diniz-Sousa, R., Caldeira, C. A. D. S., Pereira, S. S., Da Silva, S. L., Fernandes, P. A., Teixeira, L. M., ... & Soares, A. M. (2023). Therapeutic applications of snake venoms: An invaluable potential of new drug candidates. *International Journal of Biological Macromolecules,* [illegible]

El-Bitar, A. M. (2019). Antiviral Activity of Egyptian Snake, Cerastes cerastes Venom Against Hepatitis C Virus. *Egyptian Academic Journal of Biological Sciences, G. Microbiology, 11*(2), 51-66.

Ferreira, I. G., Pucca, M. B., de Oliveira, I. S., Cerni, F. A., da Silva Jacob, B. D. C., & Arantes, E. C. (2021). Snake venom vascular endothelial growth factors (svVEGFs): Unravelling their molecular structure, functions, and research potential. *Cytokine & Growth Factor Reviews, 60*, 133-143.

Galli, S. J., Metz, M., Starkl, P., Marichal, T., & Tsai, M. (2020). Mast cells and IgE in defense against lethality of venoms: Possible "benefit" of allergy. *Allergo journal international, 29*, 46-62.

Guo, Z. M., Yadav, M. B., Khan, M., Hao, C. W., Lin, C. Y., Huang, T., ... & Bian, Z. X. (2021). Bradykinin-Potentiating Peptide-Paclitaxel Conjugate Directed at Ectopically Expressed Angiotensin-Converting Enzyme in Triple-Negative Breast Cancer. *Journal of Medicinal Chemistry, 64*(23), 17051-17062.

Hayashi, M. A., Campeiro, J. D., & Yonamine, C. M. (2022). Revisiting the potential of South American rattlesnake Crotalus durissus terrificus toxins as therapeutic, theranostic and/or biotechnological agents. *Toxicon, 206*, 1-13.

Hus, K. K., Buczkowicz, J., Pietrowska, M., Petrilla, V., Petrillová, M., Legáth, J., ... & Bocian, A. (2024). Venom diversity in Naja