REVIEW ARTICLE

CONTENTS

Features of the proteo-peptidome composition and the influence of the scorpion venom toxins on the structure of the heart of mammals (review)

Andrii Yanchyshyn[1], Inha Samborska[2], Oleksandr Maievskyi[3], Iryna Dzevulska[1]

[1] BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE

[2] NATIONAL PIROGOV MEMORIAL MEDICAL UNIVERSITY, VINNYTSYA, UKRAINE

[3] CLINICAL MEDICINE DEPARTMENT, EDUCATIONAL AND SCIENTIFIC CENTER "INSTITUTE OF BIOLOGY AND MEDICINE" OF TARAS SHEVCHENKO NATIONAL UNIVERSITY OF KYIV, KYIV, UKRAINE

ABSTRACT

Aim: To determine the profound influence of scorpion venom toxins on the intricate structure of the heart of mammals, a topic of utmost importance in toxicology and cardiovascular health.

Materials and Methods: A meticulous and comprehensive literature analysis was conducted using PubMed, Google Scholar, Web of Science, and Scopus databases. We meticulously selected the newest publications up to 5 years old or the most thorough publications that vividly described our topic's essence, ensuring our findings' credibility and reliability.

Conclusions: Scorpion venom is a complex of biologically active substances that have a wide range of effects on the vital systems of the victim's body. Violations of the normal functioning of the cardiovascular system occur both as a result of disorders of the conduction system of the heart and as a result of pronounced morphological changes in the tissues of the organ. In particular, the development of inflammatory processes of the myocardium, the formation of blood clots in the heart vessels, degeneration of myofibrils, fragmentation of fibres, haemorrhages, etc., are characteristic under these conditions. In addition, these changes are accompanied by the production of pro-inflammatory cytokines, apoptosis factors, and the development of OS.

KEY WORDS: scorpions, toxins, heart, inflammation, oxidative stress

Wiad Lek. 2024;77(9):1782-1788. doi: 10.36740/WLek/191323 DOI

INTRODUCTION

Poisoning due to scorpion bites is one of the current medical problems that pose a threat to the health and life of people, especially children and older people with a severe medical history [1]. The epidemiology of scorpionism worldwide is staggering. Every year, about 1.2-1.5 million people suffer from the bites of these animals, which leads to 2,600 deaths. Until recently, it was believed that poisoning due to scorpion bites is characteristic mainly of poorly developed tropical and subtropical countries, namely Africa, India, the Middle East, Mexico, and Latin America. However, the significant expansion of their usual distribution area is currently well known, so fatal cases are also recorded in countries with a high standard of living [2, 3]. Data from scientific sources testify to more than 1,500 different species of scorpions, among which 50 are poisonous subspecies [4]. It has been established that the toxic components of their venom cause the appearance of not only local symptoms (redness at the site of bites, pain, swelling) but also the development of severe neurological and haematological disorders, disorders of the cardiovascular, respiratory, excretory systems, etc. Clinical manifestations, as indicated, depend on the dose of toxin that entered the victim's body, age, season, when the case occurred, the time between the actual bite, and the speed of providing medical assistance. The results of experimental studies show that among the leading causes of death under these conditions are heart failure and pulmonary oedema [5]. In modern sources of scientific literature, it is stated that among all arthropods, the genome of scorpions contains the most significant number of genes (almost 32,016) encoding proteins. The last ones are essential structural components of their venom and have extremely toxic properties [6].

AIM

This crucial research aimed to determine the profound influence of scorpion venom toxins on the intricate structure of the heart of mammals, a topic of utmost importance in toxicology and cardiovascular health.

MATERIALS AND METHODS

A thorough literature analysis was conducted using PubMed, Google Scholar, Web of Science, and Scopus databases. When searching for information on the features of the scorpion venom composition peculiarities of the influence of scorpion venom toxins on the structure and functions of the organs and systems of the mammalian body, we used the following combinations of keywords: "scorpions", "toxins", "heart", "inflammation", "oxidative stress". When processing the search results, we chose the newest publications up to 5 years old or the most thorough publications that vividly described the essence of our topic. After conducting a detailed review of the abstracts of the articles and getting acquainted with their entire content, 36 sources were selected that fully corresponded to the results of the request.

REVIEW AND DISCUSSION

Even though more than 800 peptides have been identified to date, the composition of scorpion venom is considered poorly researched. In addition, it can vary significantly even within a species. Therefore, the variables are the features of biological action, impact on target organs, and morphological changes in body systems. Therefore, a detailed study of the structural elements of scorpion toxins is a promising area of toxicology, molecular biology, morphology, etc. Expanding ideas about the influence of scorpion venoms will make it possible to establish the pathogenetic mechanisms of the development of certain complications and patterns of histological and biochemical changes in target organs. It may also be essential in developing treatment methods, prevention, and producing medicines and antidotes.

Scorpion venom contains a whole arsenal of biologically active substances, including polypeptides, enzymes (phospholipases A, B, acid phosphatase, phosphodiesterase, acetylcholinesterase, 5'-nucleotidase, hyaluronidase, ribonucleases, metalloproteinases), mono- and polysaccharides, lipids, nucleotides, biogenic amines, in particular, histamine and serotonin. Scientists know the classification of the peptides of their venom into those containing disulfide bridges (disulfide-bridged peptides – DBP) and those without them (non-disulfide bridged peptides – NDBP) [7]. Most DBPs exhibit neurotoxic activity, having the ability to change the permeability of ion channels and block or reduce the action potential. Among these peptides, toxins of Na^+, K^+, Ca^{2+}, and Cl^- channels are distinguished [8]. Blockers of Na^+ channels contain 58 to 76 amino acid residues in the structure and are stabilised by four disulfide bridges. They are classified into α and β-toxins. α-Na toxins (α-NaTx) affect the nervous system of victims by prolonging the depolarisation time of ion channels, while β-Na toxins (β-NaTx) cause changes in their activation threshold [9].

DBPs acting on K^+ channels comprise 20-70 amino acid residues and 3-4 disulfide bridges. According to the molecular weight and the number of disulfide bridges, α-KTx, β-KTx, γ-KTx, κ-KTx are distinguished. As a result of the blockade of K^+ channels, there is a delay in their repolarisation, a prolongation of the action potential, and an increase in the refractory period [10].

Inhibitors of Cl^- channels are currently less studied than the previously mentioned types. However, 30-40 amino acid residues and four disulfide bridges in their composition have been established. The interaction of toxins with low-conductance chlorine channels leads to suppression or complete inhibition of their activity. In the body of the victims, it becomes the cause of the development of convulsions and paralysis. The latter mainly affects the respiratory muscles, sometimes leading to severe respiratory dysfunction [11].

Scientists have established that the enzymatic activity of scorpion venom is much lower than the venom of snakes and vipers. Still, most of them have adverse effects on the victim's body. In particular, hyaluronidase is involved in the rapid systemic distribution of toxins. This property is characterised by enzyme degradation of the extracellular matrix, vessel walls, and poison entering the bloodstream. A high content of hyaluronidase was found in the venom of scorpions Tityus serrulatus and Tityus stigmurus [12]. Metalloproteinases (MMPs) have demonstrated the ability to cleave neuropeptides and affect synaptic vesicles of the presynaptic membranes of neuromuscular junctions. Scorpion venom phospholipases belong to the III class of secretory phospholipases. These have a particular heterodimeric structure built from a long polypeptide chain connected to a short one by a disulfide bridge. Neurotoxic, myotoxic, hemolytic, anticoagulant, anticarcinogenic, and antiangiogenic activities are among their biological effects on the human body [13].

Experimental studies of recent years prove that the toxins of almost all species of scorpions have a high tropism to the cardiovascular system [14, 15]. A series of cardiac conduction disturbances occur in approximate-

ly one-third of patients in case of systemic distribution of venom components. The most common conditions are atrial tachycardia, ventricular extrasystole, T-wave inversion, ST segment changes, and bundle branch block (bundle of His) [16]. Probable causes of the appearance of these complications are pronounced sympathetic stimulation. Hypertension is also a common consequence. Hypotension, on the other hand, is rare and is associated with a severe course of poisoning characterised by vasodilatation, hypovolemia, and suppression of the contractility of the heart [17].

Abroug F. et al. [18] studied cardiomyopathy associated with scorpionism. Cardiac dysfunction occurring in the early stages of poisoning is associated, according to the researchers, with the so-called "vascular phase". It is characterised by catecholamine-induced vasoconstriction, which leads to an increase in the afterload of the left ventricle, an increase in the filling pressure, a violation of its emptying and a critical rise in pressure in the capillaries, leading to the development of pulmonary oedema, an increase in the afterload of the right ventricle. In response to increased production of vasoconstrictors – epinephrine, norepinephrine, neuropeptide B, and endothelin, the contractility of the myocardium of the left ventricle and, accordingly, oxygen consumption increases, temporarily maintaining cardiac output at an acceptable level. Subsequently, the "myocardial" phase occurs, accompanied by a decrease in the contractile ability of the heart muscle, low cardiac output, and hypotension. Among scientists, there are various hypotheses regarding the mechanisms of cardiomyopathy in scorpion bites. Considering the reversibility of pathological changes and the main pathophysiological pathways of development, most hold opinions regarding the development of Takotsubo cardiomyopathy or stress cardiomyopathy. Recent clinical observations have shown that under these conditions, stress cardiomyopathy occurs more often in children and is characterised by spasms of small myocardial vessels, ischemia of the heart muscle, and microvascular vasomotor dysfunction.

A careful and comprehensive study of literature sources made it possible to establish that myocardial infarction is a frequent complication of poisoning by scorpion toxins. It is known that the active components of their venom stimulate the production and release of vasoactive pro-inflammatory and thrombogenic substances, such as histamine, serotonin, bradykinins, leukotrienes, and thromboxane. These compounds can induce spasms of coronary arteries and stimulate the aggregation of platelets and the formation of blood clots in the vessels of the heart. In addition, there is data on the possible mechanism of myocardial infarction due to IgE-induced hypersensitivity of the immediate type, which was described for the first time by Kunis and is accompanied by damage of the heart muscle and severe eosinophilia [19].

Reis M. B. et al. [20], studying the mechanisms of the cardiovascular system damage during intoxication with Tityus serrulatus scorpion venom, established the induction of the inflammatory reaction in heart tissue. Thus, flow cytometric analysis of the organ revealed an increase in neutrophils and a decrease in macrophages. This process was accompanied by activating genes that regulate the innate immune system and produce eicosanoids. The venom of Tityus serrulatus stimulated the activation of the inflammasome – NLRP3, apoptosis-associated proteins and caspase 1/11, the release of IL-1β and the production of PGE_2 in experimental animals' heart and blood serum. During the experiment, it was possible to determine that in the mechanisms of triggering inflammatory reactions, the leading role belongs to the fibroblasts of the organ and, to a lesser extent, to cardiomyocytes. Stimulation of the culture of these cells for 24 hours showed that only fibroblasts could release IL-1β and both cell types PGE_2. Cardiac fibroblasts showed higher expression of pro-inflammatory genes and CD14 and TLR_4 receptors on the surface of cell membranes. It is known that for NLRP3 and increasing of the of IL-1β, activation of pattern recognition receptors (PRR), increased release of K^+ ions from the cell, synthesis and release of PGE_2, increased levels of 3'-5'-cAMP, activation of protein kinase A and nuclear factor-kB (NF-kB) are necessary conditions. Cardiac fibroblasts treated with Tityus serrulatus scorpion venom-induced IL-1β release through the PGE2/cAMP/PKA signalling pathway. cAMP levels increased in these cells after the addition of exogenous PGE_2. Increased expression of the total and phosphorylated form of PKA was also observed in the heart lysates of poisoned mice. Therefore, the authors indicated that the fibroblasts of the heart participate in the processes of triggering the inflammatory cascade in the heart of rats after intoxication with Tityus serrulatus scorpion venom by stimulating the production of IL-1β and PGE_2.

Single studies were found in scientometric databases, accompanied by histological examination of heart samples of experimental rats exposed to the venom of various types of scorpions. Androctonus mauretanicus and Buthus occitanus were found to cause degeneration of cardiac muscle myofibrils 60 minutes after venom injection in rats. Further observations under the specified conditions revealed a deepening of the myocardial damage. The venom of Buthus lienhardi scorpions within 3 hours after administration causes significant myocardial fibres and haemorrhage frag-

mentation. Inoculation of animals with toxins from scorpions Androctonus australis hector led to dystrophy of cardiomyocytes, infiltration of the myocardium with polymorphonuclear cells, macrophages, lymphocytes, the appearance of oedema, acute haemorrhage, and necrosis [21].

Bakir F. et al. [22] studied the effect of Androctonus crassicauda venom on rat heart tissue when administered intravenously to animals. Examination of the morphological state of the organ was carried out after 1, 3, 6, and 24 hours. Microscopic studies revealed hydropic degeneration of cardiomyocytes; their cytoplasm contained many vacuoles of various shapes and sizes, and pyknosis of the nuclei was characteristic. However, cardiomyocytes with signs of necrosis containing homogeneous eosinophilic granules rarely occurred among degenerated myofibrils. Some muscle fibres lost transverse striation. Myocardial capillaries had signs of whole blood and included many erythrocytes. Erythrocytes between myofibrils in many fields of view and phenomena of haemorrhages were also noted. Infiltration of heart tissue by leukocytes and macrophages was observed. Biochemical studies confirmed organ damage, as an increase in the level of cardiac troponin I (cTnI) was recorded.

Yazdkhasti M. et al. [23] proved the cardiotoxic effect of Hemiscorpius lepturus venom. Morphological studies revealed signs of multifocal fragmentation of myocardial muscle fibres, between which foci of haemorrhages were noted. In some fields of vision, the characteristic transverse striation of the heart muscle disappeared. After 3-6 hours of observation, acute myocytolysis and interstitial necrosis were characteristic. The results of parallel studies confirmed these findings and, in addition, demonstrated the development of oedema and hypertrophy of myocardial muscle fibres with their massive infiltration by leukocytes. In the blood serum of laboratory animals under these conditions, the levels of LDH, AST, CPK-MB and cTnI increased after 1, 3 and 24 hours of the study [24].

Scorpion venom leads to the activation of inflammatory processes and excess production of free radicals in the heart tissue of victims, leading to organ damage. As a rule, venom components bind to pattern recognition receptors, namely Toll-like receptors TLR_2 and TLR_4, activate the transcription factor NF-kB, stimulate the production of pro-inflammatory mediators and reactive oxygen species (ROS), which leads to the development of oxidative stress in the heart (OS) [25, 26]. Recently, it has been established that endothelin-1, the production of which increases significantly under the conditions of poisoning with scorpion toxins, also stimulates the production of superoxide anion and pro-inflammatory cytokines, including IL-1, TNF-**α**, IL-6 [27, 28]. In experiments on rats, Sifi A. et al. [29, 30] established that the introduction of venom from the scorpion Androctonus australis hector was associated with increased expression of TNF-α and IL-17 in animals. In addition, the pronounced activity of myeloperoxidase (MPO) (the main enzyme of azurophilic granules of neutrophils), matrix metalloproteinases (MMP-2 and MMP-9) was found in homogenates of rat heart and aorta. According to the authors, MPO, under these conditions, is a marker of neutrophil activation. MMPs are involved in the degradation of the extracellular matrix of the myocardium and components of the aorta walls. Scientists have proven the development of OS in the heart of experimental animals by injecting them with the venom of the specified species of scorpions. OS was characterised by an increase in the levels of H_2O_2, malondialdehyde (MDA), and NO_2 in the supernatants of the myocardium. At the same time, a decrease in the activity of antioxidant protection enzymes – catalase and glutathione peroxidase was recorded. Microscopic studies revealed damage to the myocardium, degeneration of muscle fibres, foci of haemorrhages, and oedema. Zones of myonecrosis and pronounced leukocyte infiltration were noted. The aorta was characterised by thickening of its tunica media, and in some places, signs of the development of an aneurysm of its wall were observed.

Naserzadeh P. and co-authors [31], studying the venom of scorpions Hemiscorpius lepturus, established that the last exhibits a cardiotoxic effect. Thus, the authors, through experiments on rats, demonstrated that the indicated effect of the toxins of these animals consists in the death of cardiomyocytes by apoptosis. The venom of Hemiscorpius lepturus causes the activation of caspase-3 and the development of mitochondrial dysfunction. Mitochondrial dysfunction was associated with significant production of ROS, swelling of organelles, a decrease in the potential of their membranes, activity of cytochrome c oxidase (respiratory chain complex IV), ATP levels, and ruptures of the mitochondrial outer membrane. In addition, inhibition of the activity of the II complex of the respiratory chain (succinate-CoQ-oxidoreductase) and the formation of apoptosomes – cytosolic factors of apoptosis, in response to the release of cytochrome c due to the opening of the pores of the mitochondrial membranes were recorded.

Studying the sources of scientific literature showed that some components of scorpion venom have a positive effect on the structures of the heart muscle under certain conditions. Ahmed L. A. et al. [32] found that bradykinin-potentiating peptides isolated from Leiurus quinquestriatus scorpion venom protect myocardial

structures and significantly reduce the adverse effects of doxorubicin-induced acute cardiotoxicity. In their experiments, the researchers isolated a fraction of the venom and treated it by **γ**-irradiation to weaken the peptides' toxicity and potentiate the pharmacological activity. Pretreatment of the myocardium with bradykinin-potentiating peptides from Leiurus quinquestriatus scorpion venom before treatment of experimental rats with doxorubicin significantly reduced the degree of heart tissue damage and manifestations of OS, inflammation, and apoptosis. Bradykinin-potentiating peptides showed antioxidant, anti-inflammatory and immunomodulatory properties. The realisation of these effects is possible through antigen-receptor signalling pathways. Activation of bradykinin B2 receptors leads to increased production of NO, increased expression of antioxidant defence enzymes, in particular SOD (MnSOD, Cu/Zn-SOD), and reduction of NADPH oxidase, which prevents excessive production of ROS. It should be noted that the histological structure of the myocardium significantly improved under these conditions. Thus, doxorubicin led to the formation of areas of necrosis, foci of infiltration by mononuclear cells, the development of nuclear pyknosis, intercellular oedema, and hyalinosis. During preliminary treatment of heart tissue with bradykinin-potentiating peptides from Leiurus quinquestriatus scorpion venom, cardiomyocytes had an organisation similar to that of intact rats; only sporadic cases of moderate degenerative changes were recorded.

CONCLUSIONS

Scorpion venom is a complex of biologically active substances that have a wide range of effects on the vital systems of the victim's body. The toxins of their venom are tropic to the organs of the nervous, respiratory, skeletal, excretory, and cardiovascular systems. Violations of the normal functioning of the cardiovascular system occur both as a result of disorders of the conduction system of the heart and as a result of pronounced morphological changes in the tissues of the organ. In particular, the development of inflammatory processes of the myocardium, the formation of blood clots in the heart vessels, degeneration of myofibrils, fragmentation of fibres, haemorrhages, etc., are characteristic under these conditions. In addition, these changes are accompanied by the production of pro-inflammatory cytokines, apoptosis factors, and the development of OS. These data point to the need for an in-depth study of the structure, biological action, and functional activity of scorpion toxins of various species since a significant part of them remains unknown.

REFERENCES

1. Almeida ACC, Carvalho FM, Mise YF. Risk factors for fatal scorpion envenoming among Brazilian children: a case-control study. Trans R Soc Trop Med Hyg. 2021;115(9): 975-983. doi: 10.1093/trstmh/trab120. DOI
2. Cid-Uribe JI, Veytia-Bucheli JI, Romero-Gutierrez T et al. Scorpion venomics: a 2019 overview. Expert Rev Proteomics. 2020;17(1):67-83. doi: 10.1080/14789450.2020.1705158. DOI
3. Torrez PPQ, Dourado FS, Bertani R et al. Scorpionism in Brazil: exponential growth of accidents and deaths from scorpion stings. Rev Soc Bras Med Trop. 2019;52:e20180350. doi: 10.1590/0037-8682-0350-2018. DOI
4. El-Aziz FEA A, El Shehaby DM, Elghazally SA, Hetta HF. Toxicological and epidemiological studies of scorpion sting cases and morphological characterization of scorpions (Leiurusquin questriatus and Androctonus crassicauda) in Luxor, Egypt. Toxicol Rep. 2019;6:329-335. doi: 10.1016/j.toxrep.2019.03.004. DOI
5. Abroug F, Ouanes-Besbes L, Tilouche N, Elatrous S. Scorpion envenomation: state of the art. Intensive Care Med. 2020;46(3):401-410. doi: 10.1007/s00134-020-05924-8. DOI
6. Amorim FG, Longhim HT, Cologna CT et al. Proteome of fraction from Tityus serrulatus venom reveals new enzymes and toxins. J Venom Anim Toxins Incl Trop Dis. 2019;25:e148218. doi: 10.1590/1678-9199-JVATITD-1482-18. DOI
7. Batista CVF, Martins JG, Restano-Cassulini R et al. Venom characterization of the Amazonian scorpion Tityus metuendus. Toxicon. 2018;143:51-58. doi: 10.1016/j.toxicon.2018.01.006. DOI
8. Dueñas-Cuellar RA, Santana CJC, Magalhães ACM et al. Scorpion Toxins and Ion Channels: Potential Applications in Cancer Therapy. Toxins (Basel). 2020;12(5):326. doi: 10.3390/toxins12050326. DOI
9. Furtado AA, Daniele-Silva A, Silva-Júnior AAD, Fernandes-Pedrosa MF. Biology, venom composition, and scorpionism induced by brazilian scorpion Tityus stigmurus (Thorell, 1876) (Scorpiones: Buthidae): A mini-review. Toxicon. 2020;185:36-45. doi: 10.1016/j.toxicon.2020.06.015. DOI
10. Díaz-García A, Varela D. Voltage-Gated K+/Na+ Channels and Scorpion Venom Toxins in Cancer. Front Pharmacol. 2020;11:913. doi: 10.3389/fphar.2020.00913. DOI
11. Cohen G, Burks SR, Frank JA. Chlorotoxin-A Multimodal Imaging Platform for Targeting Glioma Tumors. Toxins (Basel). 2018;10(12):496. doi: 10.3390/toxins10120496. DOI

12. Guerra-Duarte C, Rebello Horta CC, Ribeiro Oliveira-Mendes BB et al. Determination of hyaluronidase activity in Tityus spp. Scorpion venoms and its inhibition by Brazilian antivenoms. Toxicon. 2019;167:134-143. doi: 10.1016/j.toxicon.2019.06.019. DOI
13. Krayem N, Gargouri Y. Scorpion venom phospholipases A2: A minireview. Toxicon. 2020;184:48-54. doi: 10.1016/j.toxicon.2020.05.020. DOI
14. Khalaf MA, El-Deen MAB, Hishmat AM. Scorpion sting: N-terminal fragment of proB-type natriuretic peptide as an early predictor of pediatric cardiotoxicity. Hum Exp Toxicol. 2021;40(5):754-760. doi: 10.1177/0960327120968863. DOI
15. Ratnayake RM, Kumanan T, Selvaratnam G. Acute myocardial injury after scorpion (Hottentotta tamulus) sting. Ceylon Med J. 2016;61(2):86-87. doi: 10.1177/0960327120968863. DOI
16. Prasad R, Kumar A, Jain D et al. Echocardiography versus cardiac biomarkers for myocardial dysfunction in children with scorpion envenomation: An observational study from tertiary care center in northern India. Indian Heart J. 2020;72(5):431-434. doi: 10.1016/j.ihj.2020.07.020. DOI
17. Costal-Oliveira F, Guerra-Duarte C, Oliveira MS et al. Cardiorespiratory alterations in rodents experimentally envenomed with Hadruroides lunatus scorpion venom. J Venom Anim Toxins Incl Trop Dis. 2016;23:2. doi: 10.1186/s40409-016-0076-5. DOI
18. Abroug F, Souheil E, Ouanes I et al. Scorpion-related cardiomyopathy: Clinical characteristics, pathophysiology, and treatment. Clin Toxicol (Phila). 2015;53(6):511-518. doi: 10.3109/15563650.2015.1030676. DOI
19. Baykan AO, Gür M, Acele A et al. Scorpion envenomation-induced acute thrombotic inferior myocardial infarction. Turk Kardiyol Dern Ars. 2016;44(1):82-86. doi: 10.5543/tkda.2015.88590. DOI
20. Reis MB, Rodrigues FL, Lautherbach N et al. Interleukin-1 receptor-induced PGE2 production controls acetylcholine-mediated cardiac dysfunction and mortality during scorpion envenomation. Nat Commun. 2020;11(1):5433. doi: 10.1038/s41467-020-19232-8. DOI
21. Darkaoui B, Lafnoune A, Chgoury F et al. Induced pathophysiological alterations by the venoms of the most dangerous Moroccan scorpions Androctonus mauretanicus and Buthus occitanus: A comparative pathophysiological and toxic-symptoms study. Hum Exp Toxicol. 2022;41:9603271211072872. doi: 10.1177/09603271211072872. DOI
22. Bakir F, Ozcan O, Alcigir ME, Vural SA. Effects of Androctonus crassicauda scorpion venom on the heart tissue. J Anim Vet Adv. 2012;11(14):2594-2599. doi:10.3923/javaa.2012.2594.2599. DOI
23. Yazdkhasti M, Jalali MR, Khadjeh GH et al. Cardiotoxic effects of Hemiscorpius Lepturus scorpion venom fractions in rats. Iran J Toxicol. 2021;15(1):27-36.
24. Ait Laaradia M, El Hidan MA, Marhoume F et al. Buthus lienhardi venom and pathophysiological effects at the histological, hematological, biochemical and motor skills levels. Toxicon. 2018;146:106-113. doi: 10.1016/j.toxicon.2018.03.001. DOI
25. Ahmed AE, Hassan MH, Rashwan NI et al. Myocardial injury induced by scorpion sting envenoming and evidence of oxidative stress in Egyptian children. Toxicon. 2018;153:72-77. doi: 10.1016/j.toxicon.2018.08.008. DOI
26. Zoccal KF, Bitencourt Cda S, Paula-Silva FW et al. TLR2, TLR4 and CD14 recognize venom-associated molecular patterns from Tityus serrulatus to induce macrophage-derived inflammatory mediators. PLoS One. 2014;9(2):e88174. doi: 10.1371/journal.pone.0088174. DOI
27. Al-Asmari AK, Riyasdeen A, Islam M. Scorpion Venom Causes Apoptosis by Increasing Reactive Oxygen Species and Cell Cycle Arrest in MDA-MB-231 and HCT-8 Cancer Cell Lines. J Evid Based Integr Med. 2018;23:2156587217751796. doi: 10.1177/2156587217751796.
28. Corzo G, Espino-Solis GP. Selected scorpion toxin exposures induce cytokine release in human peripheral blood mononuclear cells. Toxicon. 2017;127:56-62. doi: 10.1016/j.toxicon.2017.01.007. DOI
29. Sifi A, Adi-Bessalem S, Laraba-Djebari F. Involvement of the Endothelin Receptor Type A in the Cardiovascular Inflammatory Response Following Scorpion Envenomation. Toxins (Basel). 2020;12(6):389. doi: 10.3390/toxins12060389. DOI
30. Sifi A, Adi-Bessalem S, Laraba-Djebari F. Role of angiotensin II and angiotensin type-1 receptor in scorpion venom-induced cardiac and aortic tissue inflammation. Exp Mol Pathol. 2017;102(1):32-40. doi: 10.1016/j.yexmp.2016.11.006. DOI
31. Naserzadeh P, Mehr SN, Sadabadi Z et al. Curcumin Protects Mitochondria and Cardiomyocytes from Oxidative Damage and Apoptosis Induced by Hemiscorpius Lepturus Venom. Drug Res (Stuttg). 2018;68(2):113-120. doi: 10.1055/s-0043-119073. DOI
32. Ahmed LA, Abdou FY, El Fiky AA et al. Bradykinin-Potentiating Activity of a Gamma-Irradiated Bioactive Fraction Isolated from Scorpion (Leiurus quinquestriatus) Venom in Rats with Doxorubicin-Induced Acute Cardiotoxicity: Favorable Modulation of Oxidative Stress and Inflammatory, Fibrogenic and Apoptotic Pathways. Cardiovasc Toxicol. 2021;21(2):127-141. doi: 10.1007/s12012-020-09602-5. DOI

CONFLICT OF INTEREST

The Authors declare no conflict of interest

CORRESPONDING AUTHOR

Inga Samborska
National Pirogov Memorial Medical University
56 Pirogov st, 21018, Vinnytsya, Ukraine
e-mail: samborska1990@gmail.com

ORCID AND CONTRIBUTIONSHIP
Inga Samborska: 0000-0002-6812-489X B D
Oleksandr Maievskyi: 0000-0002-9128-1033 A E
Andrii Yanchyshyn: 0000-0003-1598-8106 F
Iryna Dzevelska: 0000-0002-8043-6626 A E

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

RECEIVED: 11.12.2023
ACCEPTED: 17.07.2024

CREATIVE COMMONS 4.0