Protective Immunoprophylaxis in Severe Scorpion Envenomation: Inflammatory Modulation and Multi-Organ Functional Integrity

L. Boussag-Abib, and F. Laraba-Djebari

***Abstract*—** Scorpion envenomation represents a critical medical emergency characterized by a complex multifactorial pathophysiology that contributes to significant morbidity and mortality, particularly in endemic regions such as Algeria. This study aimed to develop a prophylactic vaccine-based approach to mitigate the systemic effects of *Androctonus australis hector* (Aah) venom. A detoxified antigen formulation (Aah-FtoxG50) adsorbed onto alum adjuvant was evaluated for its protective efficacy in a murine model. Mice were immunized according to a standard schedule, and three months after the final booster, they were challenged with lethal doses of Aah venom (5 and 8 LD_{50}). The systemic inflammatory response was assessed by quantifying neutrophil and eosinophil infiltration, as well as their enzymatic activities — myeloperoxidase (MPO) and eosinophil peroxidase (EPO), respectively. Histopathological examinations of liver, kidney, heart, and lungs were performed to evaluate tissue integrity and venom-induced lesions. Results showed that vaccinated mice challenged with 5 LD_{50} of native venom exhibited complete (100%) protection, whereas a partial (50%) protection was observed in mice subjected to severe envenomation with 8 LD_{50}. Immunized mice challenged with 5 LD_{50} of Aah venom exhibited a mild inflammatory response, marked by moderate recruitment of inflammatory cells and elevated MPO and EPO levels, with no significant histological damage observed in vital organs. In contrast, mice exposed to 8 LD_{50} of venom displayed a moderate inflammatory reaction with slight histopathological changes in vital organs. Notably, these alterations remained significantly less severe than those recorded in non-immunized mice exposed to sublethal doses (<1 LD_{50}) of native venom. Collectively, these findings demonstrate that immunization with a detoxified Aah venom-based vaccine confers substantial protection against high-dose envenomation, effectively attenuating both systemic inflammation and organ-specific toxicity.

***Index Terms*—** *Androctonus australis hector* venom, Detoxified vaccine, Histopathology, Inflammation.

Manuscript received 6 November, 2025. This work was supported in part by the Ministry of Higher Education and Scientific Research of Algeria.

L. B-A Author is a researcher at University of Science and Technology Houari Boumediene (USTHB), Faculty of Biological Sciences, Department of Cellular and Molecular Biology, Laboratory of Biochemistry and Immunology, Algiers, Algeria. BP 32, El-Alia Bab Ezzouar, 16111, Algiers, Algeria

F. L-D Author is a researcher at the University of Science and Technology Houari Boumediene (USTHB), Faculty of Biological Sciences, Department of Cellular and Molecular Biology, Laboratory of Biochemistry and Immunology, BP 32, El-Alia, Bab Ezzouar, 16111 Algiers, Algeria

ACKNOWLEDGMENT

The authors acknowledge the technical support of the Laboratory of Cellular and Molecular Biology, Faculty of Biological Sciences (USTHB) and the Algerian Ministry of Higher Education and Scientific Research for funding.

REFERENCES

[1] L. Abib and F. Laraba-Djebari, "Effect of gamma irradiation on toxicity and immunogenicity of *Androctonus australis hector* venom," *Can. J. Physiol. Pharmacol.*, vol. 81, no. 12, pp. 1118–1124, 2003. https://doi.org/10.1139/y03-115

[2] M.-F. Martin-Eauclaire, S. Adi-Bessalem, D. Hammoudi-Triki, F. Laraba-Djebari, and P. E. Bougis, "Serotherapy against voltage-gated sodium channel-targeting α-toxins from *Androctonus* scorpion venom," *Toxins (Basel)*, vol. 11, no. 2, p. 63, Jan. 2019, doi: 10.3390/toxins11020063. https://doi.org/10.3390/toxins11020063

[3] L. Boussag-Abib and F. Laraba-Djebari, "Enhanced immune sera and vaccine: Safe approach to treat scorpion envenoming," *Vaccine*, vol. 29, no. 48, pp. 8951–8959, Nov. 2011, doi: 10.1016/j.vaccine.2011.09.044. https://doi.org/10.1016/j.vaccine.2011.09.044

[4] A. Nouri and F. Laraba-Djebari, "Enhancement of long-lasting immunoprotective effect against *Androctonus australis hector* envenomation using safe antigens: Comparative role of MF59 and Alum adjuvants," *Vaccine*, vol. 33, no. 43, pp. 5756–5763, Oct. 2015, doi: 10.1016/j.vaccine.2015.09.045. https://doi.org/10.1016/j.vaccine.2015.09.045

[5] N. Bachsais, L. Boussag-Abib, and F. Laraba-Djebari, "Safety and efficiency of active immunization with detoxified antigen against scorpion venom: side effect evaluation," *Inflammation Research*, vol. 66, no. 9, pp. 765–774, Sep. 2017, doi: 10.1007/s00011-017-1055-1. https://doi.org/10.1007/s00011-017-1055-1

[6] L. Boussag-Abib and F. Laraba-Djebari, "Long-term antibody response and protective effect induced by attenuated scorpion toxins: Involvement of memory plasma cells," *Immunobiology*, vol. 226, no. 4, p. 152108, 2021. https://doi.org/10.1016/j.imbio.2021.152108

[7] N. Bachsais, L. Boussag-Abib, and F. Laraba-Djebari, "Assessment of inflammatory response of developed vaccine against scorpion envenomation using attenuated venom," *Proceedings of the Medical Technologies Conference, Medical Technologies Journal*, vol. 2, no. 2, pp. 224–225, 2018.

Author Biography

L. Boussag-Abib was born in Algiers, Algeria. She received her Bachelor's degree in Biological Sciences in 1993, an Engineer's degree in Biological Engineering in 1998, a Magister in Biochemistry-Immunology in 2002, and a Ph.D. in Biochemistry and Immunology in 2012 from the University of Science and Technology Houari Boumediene (USTHB), Algiers, Algeria. She obtained her University Habilitation (HDR) in 2021. She is currently a teacher–researcher at the Faculty of Biological Sciences, USTHB, and a member of the Laboratory of Cellular and Molecular Biology. Her research focuses on the characterization of bioactive molecules and their therapeutic applications, particularly in immunopathology and toxinology She has published several papers in indexed international journals, including *Vaccine*, *Immunobiology*, and *Inflammatory Research*. Her current research interests include immunopathology, toxinology, and the biotechnological valorization of bioactive compounds from scorpion and marine species.