Abstract
Understanding Ciguatoxin-Induced CNS Depression and Evaluating Piperine as a Therapeutic Strategy †

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Abstract: Introduction: Ciguatoxin (CTX) is a potent marine toxin known for its detrimental effects on the Central Nervous System (CNS), inducing symptoms of depression and neurological dysfunction. The nervous system’s synapses’ threshold for opening voltage-gated sodium channels is reduced by ciguatoxin. Piperine, a bioactive compound found in black pepper, has shown promise as a potential treatment for CTX-induced CNS depression due to its neuroprotective properties. Methods: This review comprehensively examines studies investigating the effects of CTX on CNS depression and the potential therapeutic role of piperine. Various cell models, including Mus musculus cells (N2A), Zalophus californianus tissues and many others have been utilized to elucidate the mechanisms underlying CTX-induced CNS depression. Studies employing proteomic techniques such as 2D DIGE, MALDI-TOF/TOF, LC-MS/MS, and nanoLC-MS/MS have provided insights into the dysregulated proteins, pathways, and cellular responses associated with CTX toxicity. Additionally, investigation into the therapeutic effects of bioactive compound such as piperine has been conducted for marine toxins. Results: Studies have revealed that CTX exerts its CNS-depressant effects through dysregulation of calcium homeostasis, membrane depolarization, and disruption of neurotransmitter pathways. Furthermore, CTX-induced toxicity is associated with dysregulated proteins involved in neurodegenerative pathways, apoptosis, and excitotoxicity. Piperine has been shown to mitigate CTX-induced CNS depression by modulating oxidative stress, inflammation, and neurotransmitter imbalances. Mechanistically, piperine’s neuroprotective effects involve activation of NRF2 pathways, inhibition of apoptotic signaling, and modulation of neuronal excitability. Conclusions: The findings from this review underscore the potential of piperine as a therapeutic agent for mitigating CTX-induced CNS depression. More large-scale studies and clinical trials are required for subsequent research to demonstrate piperine’s effectiveness and safety as a treatment for CTX intoxication. Understanding the intricate mechanisms underlying CTX-induced CNS depression and the therapeutic effects of piperine could pave the way for novel interventions in managing ciguatera fish poisoning.

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