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Mechanistic insights into Monocrotophos Induced Neurotoxicity

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Abstract

The plethora of literature has reported the vulnerability of neuronal cells to environmental toxicants. Among such toxicants, pesticides, especially organophosphorus (OPs), have been demonstrated to exhibit severe neurotoxic effects on the brain. Monocrotophos, a widely used OP has been implicated in the onset of perilous systemic effects, in particular neurotoxicity. Neurotoxicity has been one of the emerging fields in neuroscience but their progress has been largely hindered by reliable and reproductive screening tools. Stem cells with their inherent ability for pluripotency and unlimited proliferation serve as one of the best tools to address the aforementioned issue. We have employed the pluripotency of Neural stem cells (NSCs) to assess MCP induced neurotoxicity. To gain insight into the toxicity mechanism of MCP we evaluated the potential effects of the compound on NSC derived neuronal cells in culture using a battery of cytotoxicity parameters. MCP exerted concentration dependent cytotoxicity on neuronal cells manifested by reduced cell viability, increased lipid peroxidation and reduced glutathione levels. These changes were also accompanied by excessive reactive oxygen species generation and membrane depolarization with simultaneous alterations in markers of neuronal injury and dose dependent reduction in the expression of anti apoptotic protein Bcl-2 implicating cell apoptosis. Together these findings implicate the vulnerability of neuronal cells to MCP exposure that warrants stringent use of the pesticide. Our studies have established to some extent the neurotoxicity mechanisms of MCP in rat brain neural stem cell derived neuronal cells which would further help us to delve deeper and further into the molecular and cellular insights of pesticides induced neurodegeneration.