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Entitled

NEUROTOXICOLOGICAL EFFECTS OF CHLORPYRIFOS AND DELTAMETHRIN ON DOPAMINE AND ACETYLCHOLINE SYSTEMS IN DROSOPHILA MELANOGASTER

by

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Abstract

Emerging evidence suggests a positive association between pesticide exposure and sporadic Parkinson's disease (PD) development. The molecular mechanisms of PD and other neurodegenerative diseases are not fully understood, which hinders the development of therapeutic agents to cure or prevent the development of such diseases. *Drosophila* has been widely used as a model organism to study various neurodegenerative diseases and to screen for promising therapeutic agents. The aims of this study were: (i) investigating the toxic effect of 24 hours exposure to chlorpyrifos (CPF) and deltamethrin (DLM) on the dopaminergic system and AChE activity in *Drosophila melanogaster*; (ii) comparing different methodologies to test negative geotaxis behavior in *D. melanogaster*; and (iii) investigating the combined neuroprotective effects of ferulic acid (FA), and Thymoquinone (TQ) natural compounds on DLM induced neurotoxicity. Adult male wild-type flies were exposed to either CPF, DLM, for 24 hours, or concomitantly exposed to DLM and individual neuroprotective agents, or their mix for 72 hours in 10% sucrose on a cotton swab. CPF/DLM-treated flies climbed shorter distances in the negative geotaxis assay as well as had a higher incidence of mortality when compared to the control group. Evidently, CPF/DLM exposure caused a disturbance in the expression of DA-related genes. The DLM exposure for 72 hours caused a higher incidence of mortality and severe locomotor defects. Co-treatment with neuroprotective agents offered protection against these toxic effects of DLM after 72 hours. DLM caused significant inhibition of AChE which was ameliorated with the concomitant exposure with FA. Our results suggest that FA and TQ were effective in reducing the toxicity induced by DLM in *D. melanogaster* as well as confirm the utility of this model to investigate potential therapeutic strategies on movement disorders, including PD. The present study indicates that a single molecule can interact and affect multiple systems that are not related to their main mechanism of action. Data gathered in the present study may be important for the assessment of the safety of insecticides that we are at risk of daily exposure to them. Moreover, this study presents a potential natural compound that can ameliorate and protect against the neurotoxicity that is caused by these insecticides.

Keywords: Sporadic Parkinson's disease, Neuroprotective agents, Pesticides, *Drosophila melanogaster*