Therapeutic Potential of Gedunin on the Effects of Parkinson's Disease in a Drosophila melanogaster Model

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Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor dysfunction and neuron loss, with limited current treatments, revealing a critical gap. Heat shock proteins (HSPs) maintain protein homeostasis and protect against neurodegeneration; as a result, the heat shock response (HSR) pathway offers a novel pharmaceutical agent for PD. This experiment evaluated the effects of a novel HSP-inducing compound, gedunin, on a PD model of Drosophila melanogaster (D.melanogaster). Male and female F1 flies, PD (genetically modified with a dj-1ß mutation, analogous to the human PARK7 gene causing PD) and wild-type flies, were exposed to DMSO (-/ vehicle control), celastrol (+ control), or two different volumes of gedunin (2.5 µl and 10 µl) beginning at 10 days old. Locomotor performance was quantified weekly for five weeks using the startle-induced negative geotaxis assay. Supplemental evidence was gathered using tyrosine hydroxylase immunofluorescence. Gedunin significantly improved locomotor performance in PD D. melanogaster, with effects varying by sex and dosage. Statistically significant findings $p<0.0001$ (two-way ANOVA) for both treatment and treatment and sex interaction. While survival was unaffected and neurodegeneration could not be quantified due to imaging limitations, these findings suggest that Hsp90 inhibition via gedunin may mitigate PD-associated motor deficits. The findings of this experiment demonstrate promise for the use of gedunin as a novel pharmaceutical therapeutic agent for PD, as well as established a foundation for future investigations into gedunin as a potential disease-modifying therapy for PD.

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