

HEALTH RESEARCH ABSTRACT SUBMISSIONS

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Title of Research *	Comparative Effects of Dieldrin Analogs in a Parkinson's Disease Model
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Introduction & Purpose *

Parkinson's Disease (PD), characterized by tremors, rigidity, and bradykinesia, affects more than 1 million people. This disease has been correlated to pesticide exposure, with increased concentrations of dieldrin, an organochlorine pesticide, found in the brains of PD patients. Dieldrin is one of the twelve most persistent, bioaccumulative, and toxic chemicals ranked by the US EPA. This compound has been shown to adversely affect a number of cellular processes thought to increase the likelihood of developing PD, however, the mechanism(s) responsible for dieldrin-mediated cellular dysfunction has not been defined.

Experimental Design *

The hypothesis of this study is that the toxicity profile is unique for each analog of dieldrin, indicative of a structure-activity relationship. In order to test this hypothesis, structural analogs of dieldrin (aldrin, endrin, isodrin, and cis aldrin diol) were used in various cellular assays using differentiated dopaminergic PC6-3 cells. These assays include the evaluation of mitochondrial activity, assessment of cytotoxicity of each compound, the quantification of extracellular dopamine metabolites, and reactive oxygen species production. By determining the effects of each compound on these endpoints, the toxicity profiles may be compared.

Results *

The results of these experiments indicate cis aldrin diol and aldrin were the most potent compounds, causing significant cell death and a disruption in dopamine metabolism. Dieldrin was the next most potent compound, resulting in inhibition of mitochondrial activity. Isodrin and endrin were the least potent, with no cytotoxicity, however, isodrin caused a significant increase in reactive oxygen species production.

Conclusions *

The results of these experiments indicate a structure-specific effect, implicating the relative orientation of two bridgehead carbons critical for toxicity. This information is very important for elucidating the mechanism of dieldrin toxicity as it relates to PD, and may ultimately lead to the development of treatments and the prevention of idiopathic PD.

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