Establishing the Parkinson's-Pesticide Connection through Computational Molecular Modeling

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Parkinson’s Disease (PD) is the second most common neurodegenerative disease, and is defined by the loss of dopamine-producing cells and the presence of Lewy bodies and Lewy neutrites. Dopamine helps control muscle movement, so without it symptoms such as unprecedented tremors and loss of movement arise. Recent studies have found that there is a positive correlation between exposure to pesticides and PD. Pesticides are believed to increase the amount of Lewy bodies. Alpha-synuclein, Dardarin, PINK1, and UCHI-1 are presynaptic neuronal proteins involved in the UPS and are linked genetically to PD. The stereo-chemical orientation between the proteins and their corresponding ligands and their degradation can construct a link and provide deeper insight between PD and pesticides. The novel QSAR analysis approach gives the solution for selective specificity of ligands in inhibiting complex1 and damaging neurons. The structural orientation of the pesticide molecules with the target proteins involved in ubiquitin proteasome system and autophagy lysosomal pathway is studied by performing molecular modeling studies using SYBYLS2.0. Molecules are downloaded and placed in docking sites of the optimized target proteins. The placement of the ligands is then analyzed and recorded based on binding affinities and scores. There is a strong correlation between certain ligands to certain target proteins as shown by the binding scores. The data revealed that many ligands bound with the proteins and yielded high affinities. This approach can be used for other neurodegenerative diseases and is also much easier, cheaper, and widely available for use than physical trials.

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