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# ANALYSIS OF THE MOLECULAR INTERACTION OF LEVODOPA VS. AMINO ACID USING QUANTUM METHOD

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## ABSTRACT

The pharmacological treatment of Parkinson's disease through the drug Levodopa (Lev) is used to control the symptoms and signs of it for as long as possible, minimizing the adverse effects. To date, no treatment has demonstrated modifying impact on the course of the disease. The objective of the study is to determine, using the semi-empirical parametric method 3 (SE-PM3), which amino acid has a higher affinity with Lev. The Hyperchem Professional software performed a Molecular Modeling and Analysis of Lev and different Amino Acids. The result of the simulations shows the loss of Guanine amino acid, which can be correlated with multiple pathologies linked with the side effects of said drug.

**KEYWORDS:** Levodopa, Amino Acid, Quantum Method, Hyperchem, SE-PM3.

## INTRODUCTION

Lev is a medication for the most efficient systematic treatment available to reduce the motor symptoms of Parkinson's disease and better tolerated.[1, 2, 3] The diet or supplements with amino acids like Leucine or Phenylalanine compete with conveyor, altering its availability.[4]

Only 1% of an oral dose of Lev reaches the brain.[5] Due to the intense metabolic effect of the first step and the decarboxylation of dopamine.[3]

Treatment with oral Lev long-term is complicated by the appearance of motor fluctuations and dyskinesias, mainly due to the pulsatile stimulation of dopamine receptors.[6, 7] During the decade from 1980 to 1990 were worrying data regarding the potential presenting the Lev to accelerate the progression of the disease. However, the concerns raised about this amino acid remain utterly untested today.[8]

The process of Parkinson's disease is associated with decreased levels of dopamine, tyrosine hydroxylase, norepinephrine and serotonin.[9, 10] This decrease causes wear of the L-DOPA. The imbalance of the amino acids can generate a disorder in the generation of vital substances, affecting the metabolism and transport of the same and the following function of the Central Nervous System.[11, 12]

The objective of the study is to determine, using the semi-empirical quantum method parametric 3 (is-PM3), what amino acid has a higher affinity with the Lev. Hyperchem is a program for molecular modeling graphic interface, which allows researchers to carry out chemical simulations that facilitate multiple data entry. Through the program, it is possible to analyze the electron transfer coefficient (ETC) of every interaction. The ETC is the parameter that identifies the probability of a union between several compounds.[13, 14]

## MATERIALS AND METHODS

SE-PM3 is a program for molecular modeling used by scientists to analyze the quantum composition of molecules for HOMO-LUMO, BG, EP, ETC and other properties. These data are used to form the table where the interaction of Lev and amino acids. Hyperchem Professional software performed Molecular modeling and analysis of Lev and amino acids. (Hyperchem, Hypercube, Multi On for Windows, series 12-800-1501800080. Multi On, southern 1236-301 Col. Insurgentes Tlacoquemecatl del Valle, Benito Juárez, Mexico City, Mexico CP 03200).

**Table 1. Parameters used for quantum computing molecular orbitals-HUMO and LUMO.[14, 15]**

| Parameter | Value | Parameter | Value |
|---|---|---|---|
| **Total charge** | 0 | Polarizability | Not |
| **Spin Multiplicity** | 1 | Geometry Optimization algorithm | Polak-Ribiere (Conjugate Gradient) |
| **Spin Pairing** | RHF | Termination condition RMS gradient of | 0.1 Kcal/Amol |
| **State Lowest Convergent Limit** | 0.01 | Termination condition or | 1000 maximum cycles |
| **Interaction Limit** | 50 | Termination condition or | In vacuo |
| **Accelerate Convergence** | Yes | Screen refresh period | 1 cycle |

**Table 2. Parameters used to visualize the map of the electrostatic potential of the molecules.[14, 15]**

| Parameter | Value | Parameter | Value |
|---|---|---|---|
| **Molecular Property** | Property Electrostatic Potential | Contour Grid increment | 0.05 |
| **Representation** | 3D Mapped Isosurface | Mapped Function Options | Default |
| **Isosurface Grid: Grid Mesh Size** | Coarse | Transparency level | A criteria |
| **Isosurface Grid: Grid Layout** | Default | Isosurface Rendering: Total charge density contour value | 0.015 |
| **Contour Grid: Starting Value** | Default | Rendering Wire Mesh | |

## RESULTS AND DISCUSSION

Table 3, shows the comparison between the amino acids with their own ETC´s, stressing that the Arg (Arg) presents less than everyone else. It means that the Arg has a high possibility of being altered by Lev.

**Table 3: Amino Acid.**

| No. | Reducer | Oxidant | HOMO | LUMO | BG | E- | E+ | EP | ETC |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Val | Val | -9.914 | 0.931 | 10.845 | -0.131 | 0.109 | 0.240 | 45.188 |
| 2 | Ala | Ala | -9.879 | 0.749 | 10.628 | -0.124 | 0.132 | 0.256 | 41.515 |
| 3 | Leu | Leu | -9.645 | 0.922 | 10.567 | -0.126 | 0.130 | 0.256 | 41.279 |
| 4 | Phe | Phe | -9.553 | 0.283 | 9.836 | -0.126 | 0.127 | 0.253 | 38.879 |
| 5 | Gly | Gly | -9.902 | 0.902 | 10.804 | -0.137 | 0.159 | 0.296 | 36.500 |
| 6 | Ser | Ser | -10.156 | 0.565 | 10.721 | -0.108 | 0.198 | 0.306 | 35.037 |
| 7 | Cys | Cys | -9.639 | -0.236 | 9.403 | -0.129 | 0.140 | 0.269 | 34.956 |
| 8 | Glu | Glu | -10.374 | 0.438 | 10.812 | -0.111 | 0.201 | 0.312 | 34.655 |
| 9 | Ile | Ile | -9.872 | 0.972 | 10.844 | -0.128 | 0.188 | 0.316 | 34.316 |
| 10 | Thr | Thr | -9.896 | 0.832 | 10.728 | -0.123 | 0.191 | 0.314 | 34.167 |
| 11 | Gln | Gln | -10.023 | 0.755 | 10.778 | -0.124 | 0.192 | 0.316 | 34.108 |
| 12 | Asp | Asp | -10.370 | 0.420 | 10.790 | -0.118 | 0.204 | 0.322 | 33.509 |
| 13 | Asn | Asn | -9.929 | 0.644 | 10.573 | -0.125 | 0.193 | 0.318 | 33.249 |
| 14 | Lys | Lys | -9.521 | 0.943 | 10.463 | -0.127 | 0.195 | 0.322 | 32.495 |
| 15 | Pro | Pro | -9.447 | 0.792 | 10.238 | -0.128 | 0.191 | 0.319 | 32.095 |
| 16 | Trp | Trp | -8.299 | 0.133 | 8.431 | -0.112 | 0.155 | 0.267 | 31.577 |
| 17 | Tyr | Tyr | -9.056 | 0.293 | 9.349 | -0.123 | 0.193 | 0.316 | 29.584 |
| 18 | His | His | -9.307 | 0.503 | 9.811 | -0.169 | 0.171 | 0.340 | 28.855 |
| 19 | Met | Met | -9.062 | 0.145 | 9.207 | -0.134 | 0.192 | 0.326 | 28.243 |
| **20** | **Arg** | **Arg** | **-9.176** | **0.558** | **9.734** | **-0.165** | **0.199** | **0.364** | **26.742** |

Figure 1 shows the interaction between Lev and Arg, showing that Lev has a high probability of being an oxidative agent, while Arg plays an anti-oxidant or reducing paper.

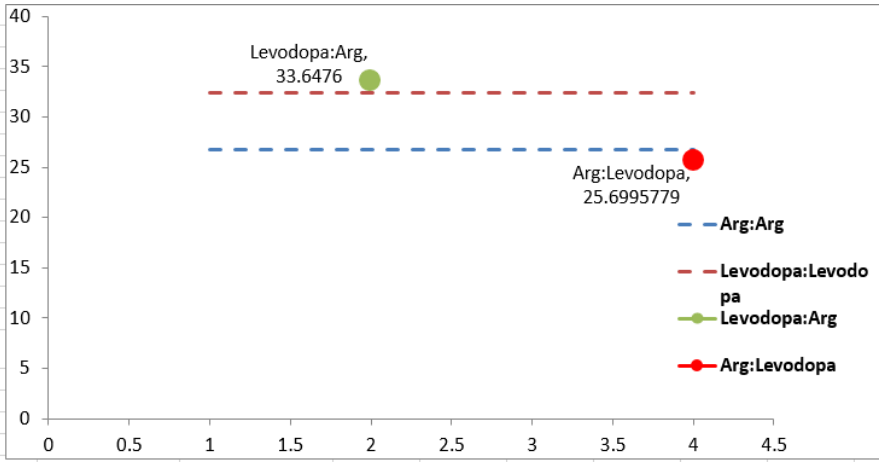


**Figure 1: Levodopa and Arginine quantum well.**

In the case of quantum grounds in cross bands, we can mention that all amino acids with the Arg are the same ETC (25.6995779), which implies that the Arg is the amino acid with increased interaction with Lev. Table 4 shows where you can see 20 bands.

**Table 4: Arg and Cross bands.**

| No. | Reducing Agent (pairs) | Oxidizing Agent | HOMO | LUMO | BG | E- | E+ | EP | ETC |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Arg:Ala | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 2 | Arg:Arg | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 3 | Arg:Asn | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 4 | Arg:Asp | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 5 | Arg:Cys | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 6 | Arg:Gln | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 7 | Arg:Glu | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 8 | Arg:Gly | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 9 | Arg:His | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 10 | Arg:Ile | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 11 | Arg:Leu | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 12 | Arg:Lys | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 13 | Arg:Met | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 14 | Arg:Phe | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 15 | Arg:Pro | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 16 | Arg:Ser | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 17 | Arg:Thr | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 18 | Arg:Trp | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 19 | Arg:Tyr | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |
| 20 | Arg:Val | Lev | -9.176235 | 0.1270122 | 9.3032472 | -0.165 | 0.197 | 0.362 | 25.6995779 |

## CONCLUSIONS

The physiological consequences of the oxidation of amino acids still a matter of great debate because in the majority of cases cannot be defined with precision if oxidation is the cause or consequence. However, this analysis helps to understand the impact of the drug Lev.

In the particular case of the oxidation of the amino acid Arg (Figure 1). The oxidation of amino acids is correlated with various conditions in the human body, of which we can highlight: premature aging, the death of neurons, problems of Alzheimer's disease, inflammatory diseases, diabetes, kidney damage and cataractogenesis, among others.

The following mechanisms can relate immune function, creatine synthesis, the release of hormone growth, insulin production, and increase in muscle mass, formation of new tissue or healing, cardiac and arterial problems, sperm motility and impotence problems.

We can mention that Arg is an amino acid that increases the production of glucagon-like peptide-1 (GLP-1), an intestinal hormone of the body that plays a role in regulating appetite

and glucose metabolism. By which its oxidation can encourage a tendency to develop principles of Diabetes type 2 and obesity problems.

The study of the quantum grounds between substances and chemicals created by the human body gives us the possibility to study and analyze the interactions among these. In the particular case of the oxidation of Arg by Lev, we can conclude that such alterations are correlated with the side effects of the drug resulting in future research.

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