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ANALYSIS OF THE EFFECT OF LEVODOPA ON NEUROTRANSMITTERS USING QUANTITY METHOD

Manuel Aparicio-Razo*[2,3], Oscar Sánchez-Parada[1], Javier Flores-Mendez[2,4], Jorge Tzompantzi-Texis[3], Nora Mercedes Sánchez-Parada[5] and Manuel González-Pérez[3, 4]

[1]Escuela de Medicina Universidad Popular Autónoma del Estado de Puebla.

[2]Benemérita Universidad Autónoma de Puebla, Facultad de Ciencias de la Electrónica.

[3]Universidad Popular Autónoma del Estado de Puebla A.C. (UPAEP). Centro Interdisciplinario De Posgrados (CIP). Posgrado en Ciencias de la Ingeniería Biomédica.

[4]Sistema Nacional De Investigadores. Nivel 1.

[5]Maestria en Ciencias de la Salud, Universidad Popular Autónoma del Estado de Puebla.

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***Corresponding Author**
Dr. Manuel González-Pérez
Universidad Popular Autónoma del Estado de Puebla A.C. (UPAEP). Centro Interdisciplinario De Posgrados (CIP). Posgrado en Ciencias de la Ingeniería Biomédica.

ABSTRACT

The Benefit of the Levodopa or L-Dopa (LEV) to reduce the symptoms of Parkinson's disease and have been studied and presented a concern for promoting the acceleration of neurodegeneration. The objective of the study is to determine, using the parametric semi-empirical quantum method 3 (SE-PM3), that neurotransmitter (NT) has a higher affinity with LEV through Hyperchem professional software; it is possible to perform molecular models and analysis of the LEV and the nine primary NT. The result of the simulations of the quantum sediments reveals that Serotonin is the primary NT oxidized by the presence of LEV, correlating with multiple pathologies linked to the side effects of that drug.

KEYWORDS: Levodopa, Neurotransmitters, Quantum Method, Hyperchem, SE-PM3.

INTRODUCTION

Parkinson's disease is a progressive and disabling neurodegenerative disorder that manifests clinically by various symptoms, such as bradykinesia, tremor, rigidity, flexed posture, postural instability and freezing of gait. It is characterized by the loss of dopaminergic neurons pigmented in the black substance. The course of clinical decline parallels the

progressive degeneration of the remaining dopaminergic neurons.[1] The use of LEV as a replacement therapy for Dopamine is highly effective in improving the detection of symptoms of the disease and remains the standard drug with which it is compared with other treatments.[2,3]

Because the LEV and Dopamine can generate reactive oxygen reactions and induce the degeneration of cultured dopaminergic neurons, the concern has been raised that the LEV can increase oxidative stress and accelerate the degeneration of dopaminergic neurons in patients with the disease. Of Parkinson.[4-6] However, LEV is non-toxic in animals and can be trophic and promote functional recovery of damaged nigral neurons.[7-10]

Several studies show that the dose in humans is Parkinson's disease that is exposed to mild neurobiology,[11,12] however it has been observed that it has higher oxidative stress in their neurons that are localized. The black substance. Whether the law is harmful, beneficial or without effect on the rate of progression of Parkinson's disease is unknown and extremely important, both from a scientific and clinical point of view.

For this reason, the present work focuses on performing a quantum simulation using parametric methods, to evaluate the effect of Lev concerning the oxidation that presents the various neurotransmitter and relational receptors with the side effects present in Parkinson's disease. Hyperchem is a molecular modeling program with a graphical interface, which allows researchers to carry out simulations in a tree that facilitate the entry of multiple data. Through the program, it is possible to analyze the Electron Transfer Coefficient (ETC) of each 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 molecular modeling program used by scientists to analyze the quantum composition of molecules and obtain HOMO-LUMO, BG, EP and other properties. These data are used to form the table where the ETC of the interaction of Lev and the nine main neurotransmitters are located. Hyperchem Professional software performed Molecular Modeling and Lev Analysis and Neurotransmitters (Hyperchem, Hypercube, Multi On for Windows, Series 12-800-1501800080. Multi On, South 1236-301 Tlacoquemecatl Insurgentes Col. Del Valle, Benito Juárez, DF, Mexico CP 03200).

Table 1: Parameters used for quantum molecular computing HOMO 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 Vacuum
Accelerate Convergence	Yes	Screen Refresh Period	1 cycle

Table 2: Parameters used for visualizing 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 ETCs of the NT. The lowest calculated ETC are adrenaline, serotonin, and dopamine respectively. This is the same order of chemical stability. In contrast, the Lev has a higher value of ETC than the three NTs, which indicates that the LEV can more easily attack these three NTs.

Table 3: ETCs Neurotransmitters, and LEV.

No.	Reducer agent	Oxidant agent	HOMO	LUMO	BG	E-	E +	EP	ETC
1	Acetylcholine	Acetylcholine	-9.241984	1.034277	10.276261	-0.028	0105	0133	77.26512
2	Noradrenaline	Noradrenaline	-9.151818	-0.0042754	9.1475426	-0083	-0222	0139	65.809659
3	Glutamic acid	Glutamic acid	-10.14479	0.5059321	10.650722	-0136	0161	0297	35.861017
4	Glycine	Glycine	-9.853025	0.8744405	10.727466	-0126	0188	0314	34.163903
5	Histamine	Histamine	-9.190549	0.675378	9.865927	-0134	0163	0297	33.218609
6	Gaba	Gaba	-9.561541	0.9385893	10.50013	-0.14	0.18	0.32	32.812907
7	**Dopamine**	**Dopamine**	**-8.867786**	**0.1988791**	**9.0666651**	**-0098**	**0189**	**0287**	**31.591168**
8	**Serotonin**	**Serotonin**	**-8.948424**	**-0.129448**	**8.8189765**	**-0145**	**0141**	**0286**	**30.835582**
9	**Adrenalin**	**Adrenalin**	**-8.998369**	**0.0917624**	**9.0901314**	**-0117**	**0198**	**0315**	**28.85756**
10	**LEV**	**LEV**	**-8.897056**	**0.1270122**	**9.0240682**	**-0082**	**0197**	**0279**	**32.34433**

Figure 1, It shows that the interaction of the quantum well Serotonin with the LEV presenting an ETC of ***26.536363***, implying that LEV has a high probability of being an oxidative agent, while Serotonin plays a role of antioxidant or reducer.

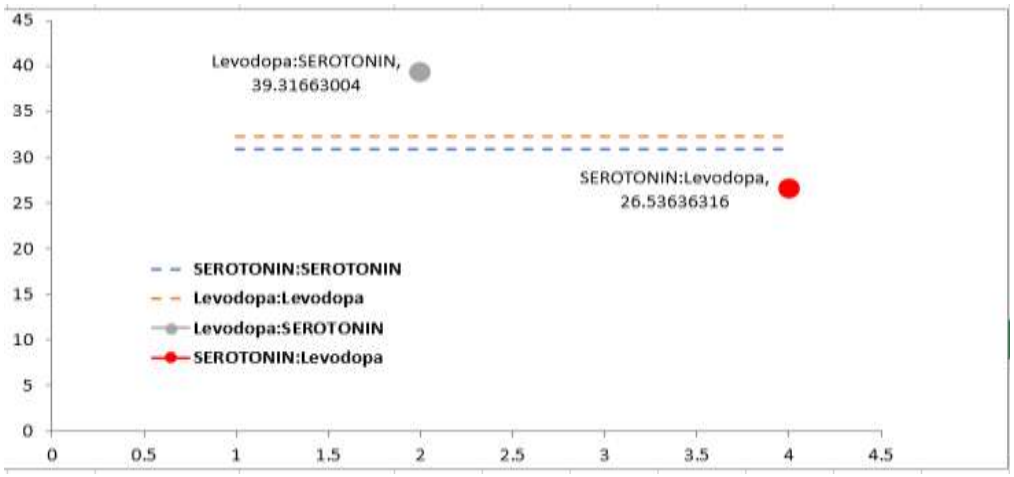

Figure 1: LEV and Serotonin Quantum well.

Figure 2, shown the interaction of the quantum well of Dopamine with LEV presenting an ETC of ***30.490841***, which means that LEV has a high probability of being an oxidative agent, while Dopamine plays a role of antioxidant or reducer.

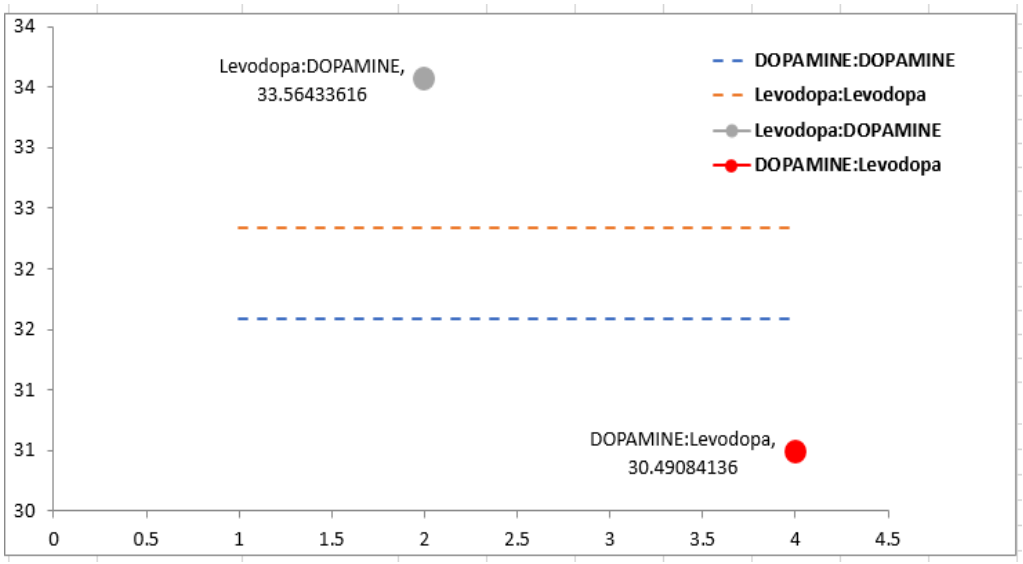

Figure 2: LEV and dopamine Quantum well.

Figure 3 shows that the interaction of the quantum well of Adrenalin with LEV presenting an ETC of ***29.061724*** suggesting that LEV and Adrenaline have a median probability of being an oxidizing agent or antioxidant.

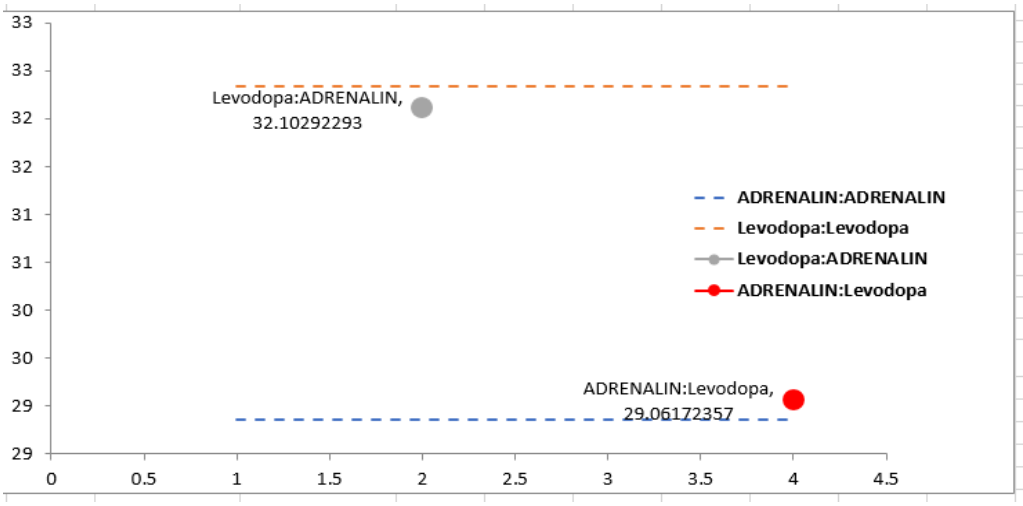

Figure 3: LEV and Adrenalin Quantum well.

After analyzing the interaction of the primary neurotransmitters and LEV we can emphasize that Serotonin presents a minor interaction in the ETC, it implies that this neurotransmitter is more likely to correlate with LEV and therefore be oxidized.

In the case of the crossbands, It presents a complex interaction, since all combinations of neurotransmitters with Serotonin present an equal ETC between them and equal the thrown between Serotonin and LEV (Figure 1), which says that there is a high probability of oxidation of Serotonin alone and its interaction among other neurotransmitters. In the following table 4, the results are shown mentioned.

Table 4. Serotonin-Neurotransmitters-LEV.

No.	Reducer	Oxidant	Homo	Lumo	Bg	And-	E +	Ep	etc
1	Serotonin--Adrenaline	LEV	-8.9484	0127	9.0754	-0145	0197	0342	**26.5364**
2	Serotonin--Dopamine	LEV	-8.9484	0127	9.0754	-0145	0197	0342	**26.5364**
3	Serotonin--Serotonin	LEV	-8.9484	0127	9.0754	-0145	0197	0342	**26.5364**
4	Serotonin--Gaba	LEV	-8.9484	0127	9.0754	-0145	0197	0342	**26.5364**
5	Serotonin--Glutamic acid	LEV	-8.9484	0127	9.0754	-0145	0197	0342	**26.5364**
6	Serotonin--Glycine	LEV	-8.9484	0127	9.0754	-0145	0197	0342	**26.5364**
7	Serotonin--Histamine	LEV	-8.9484	0127	9.0754	-0145	0197	0342	**26.5364**
8	Serotonin--Noraadrenaline	LEV	-8.9484	0127	9.0754	-0145	0197	0342	**26.5364**
9	Serotonin--Acetylcholine	LEV	-8.9484	0127	9.0754	-0145	0197	0342	**26.5364**

CONCLUSIONS

Serotonin is a monoaminergic neuromodulator that participates in a plethora of physiological processes and behaviors, including emotionality, sleep, locomotion, perception, cognition, sexual behavior aggression, and appetite. It is understood that its oxidation or degradation involves alterations related to said functions.

The most relevant disorders of the degradation of this NTs are associated with depression, substance addiction, attention deficit, irregular sexual cycles, inflammation and dysfunction of the gastrointestinal tract, disorders of sleep cycles, anxiety, fibromyalgia, dizziness, nausea, obesity, chills, tremors, confusion, delirium and tachycardia or fluctuations in blood pressure.

The process of Parkinson's disease is associated with a decrease in the concentrations of Dopamine, Serotonin, Tyrosine Hydroxylase and Norepinephrine. This reduction causes LEV wear when entering the body. However, the results of the quantum well reveal that LEV is an oxidative agent of Serotonin (Figure 1), which causes a disparity in the use of LEV for said pathology.

The study of the quantum deposits between substances and chemical compounds created by the human body gives us the possibility of studying and analyzing the interactions between them. In the particular case of the oxidation of Serotonin by LEV, we can conclude that this alteration correlates with the side effects of said drug leading to future investigations.

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