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INTERACTION OF VALPROIC ACID VS. NEUROTRANSMITTERS AND THE RELATIONSHIP TO NICOTINE BY THE QUANTUM METHOD

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ABSTRACT

Background: Valproic acid (VPA) is a widely used antiepileptic drug with adequate safety and efficacy in the treatment of pediatric patients with various types of seizures. Nicotine (NIC) is a toxic alkaloid found in the leaves and stems of Nicotiana tabacum tobacco. The NIC is known for its adverse effects on health and directly affects the Central Nervous System (CNS) because of its highly addictive. **Method:** It used HyperChem molecular simulator for Windows Serial # 12-800-1501800080. Semi-empirical parametric method 3 (SE-PM3) to extracting the molecules. When comparing the interaction of two substances by this theory, there is a range between the ETC of a substance A and an ETC of substance B. **Result:** We observe how the NT and NIC act as an antioxidant of the VPA. Lowest ETCs have 5-HT: VPA and NIC: VPA, their affinity is considered to be very high. **Conclusion:** We conclude, in general, that patients with VAP treatment is contraindicated exposure to tobacco smoke.

KEYWORDS: Valproic acid, Nicotine, quantum methods.

INTRODUCTION

Epilepsy is a chronic neurological disease, and long-term pharmacological treatment is usually necessary.[1] There are more than twenty antiepileptic medications.[2] VPA is a widely used antiepileptic drug with adequate safety and efficacy in the treatment of pediatric patients with various types of seizures.[3] VPA was marketed after 1967 and patients have consumed it for nearly 50 years for this disease.[4]

VPA is a fatty acid with anticonvulsant properties used in the treatment of epilepsy and mood stabilizer.[5] VPA, a histone deacetylation inhibitor, is primarily used to treat epilepsy and bipolar disorder with few complications. [6-8] Studies have shown that VPA decreased brain injury.[9] VPA acts by increasing the concentration of gamma-aminobutyric acid (GABA) in the brain.[10]

Scientists have recently been substantially concerned about the neuropsychiatric safety of smoking cessation medications.[11] A cigar contains about 4,000 substances harmful to the body and NIC is one of the substances found to be in the highest proportion.[12]

NIC is a toxic alkaloid found in the leaves and stems of Nicotiana tabacum tobacco.[13] The NIC is known for its adverse effects on health and directly affects the CNS because of its highly addictive.[12,14] This alkaloid modifies the concentration of some neurotransmitters (NT) and their particular function.[15-16] NIC consumption develops tolerance and withdrawal symptoms.[17-18]

The release of several NT mediated the action of the alkaloid: acetylcholine, beta endorphin, dopamine, norepinephrine, and serotonin (5-HT).[19] R. Johnston, M. Crowe and K. Doma in 2017 reported physiological responses showing that CIN significantly increased heart rate compared to placebo and increased cardiac output and pressure significantly.[20]

Hyperchem is a molecular modeling program.[21] Hyper Chem's graphical interface allows researchers to perform chemical simulations that facilitate multiple data entry.[22-25]

The primary objective of this work is to determine the interaction between VPA and NIC using the QM using quantum analyzers SE-PM3.

MATERIALS AND METHODS

Software and simulation

It used Hyper Chem molecular simulator for Windows Serial # 12-800-1501800080 SE-PM3 to extracting the molecules.

General setting

SE-PM3 a total load of around 0. Multiplicity1. Pairing turns the RHF. State under the Convergent limit of 0.01.50. Limit iteration accelerates convergence Yes. Polarizability. Geometry Optimization: Algorithms Polak-Ribiere (conjugate gradient). RMS termination condition gradient 0.1kcal/Amol. Algorithm Polak-Ribiere (conjugate gradient), the termination condition or 1000 cycles Maximum. Algorithm Polak-Ribiere (conjugate gradient).

PARTICULAR SETTING

Table: 1. Parameters used for quantum computing molecular orbitals – HOMO and LUMO.[12]

Parameter	**Value**	Parameter	Value
Total charge	0	Polarizability	Note
Spin multiplicity	1	Geometry optimization algorithm	Polka-ribera (conjugated gradiente)
Spin pairing	RHF	Termination condition RMS gradient of	0.1Kcal/Amol
State lowest convergent limit	0.01	Termination condition or	195 Maximum cycles
Internation 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.[12]

Parameter	**value**	**Parameter**	**Value**
Molecular Property	Property Electrostatie 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	

Hardware

Hardware ATA ST500DM002 IDB14SCSI. 6.1.7600.16385.

ETC theory

When comparing the interaction of two substances by this theory, there is a range between the ETC of a substance A and an ETC of substance B. Therefore; there are 3 zones in which the ETC value of its cross bands can fall. One in range and two out of range (Figure 1). The area of greatest electronic interaction is I. In this zone I a chemical reaction has a very high probability of being carried out. Zone II is of medium probability; While Zone III is the very little likelihood of interaction between these two substances.

RESULTS AND DISCUSSION

Table 3 shows the calculation of the ETCs of each substance involved in this research. In this, we observe how the NT and NIC act as an antioxidant of the VPA. Lowest ETCs have 5-HT: VPA and NIC: VPA, their affinity is considered to be very high. The highest recorded ETC is from acetylcholine: VPA.

Tabla3. Cross Bands of NT and NIC against VPA (ECTs.)

Reducer agent	Oxidizing agent	HOMO	LUMO	BG	E-	E+	EP	ETC
VPA	VPA	-11.22108	1.016351	12.237431	-0.087	0.19	0.277	44.178
ACETYLCHOLINE	VPA	**-9.241984**	**1.016351**	**10.258335**	**-0.028**	**0.19**	**0.218**	**47.056**
GLUTAMIC ACID	VPA	-10.04443	1.016351	11.060781	-0.084	0.19	0.274	40.367
ASPARTY ACID	VPA	-10.24183	1.016351	11.258181	-0.109	0.19	0.299	37.652
NORADRENALINE	VPA	-9.151818	1.016351	10.168169	-0.083	0.19	0.273	37.246
GLYCINE	VPA	-9.853025	1.016351	10.869376	-0.126	0.19	0.316	34.396
DOPAMINE	VPA	-8.867786	1.016351	9.884137	-0.098	0.19	0.288	34.319
ADRENALIN	VPA	-8.998369	1.016351	10.01472	-0.117	0.19	0.307	32.621
GABA	VPA	-9.561541	1.016351	10.577892	-0.14	0.19	0.33	32.054
NIC	VPA	**-9.19734**	**1.016351**	**10.213691**	**-0.141**	**0.19**	**0.331**	**30.857**
5-HT	VPA	**-8.948424**	**1.016351**	**9.964775**	**-0.145**	**0.19**	**0.335**	**29.745**

FIGURE: 1. Quantum wells, The green dot represents the VPA: NIC ratio, this is located in a low probability zone. The red dot represents the NIC: VPA ratio, this is located in a high probability area. Green (VPA) and red (NIC) lines represent Boundaries.

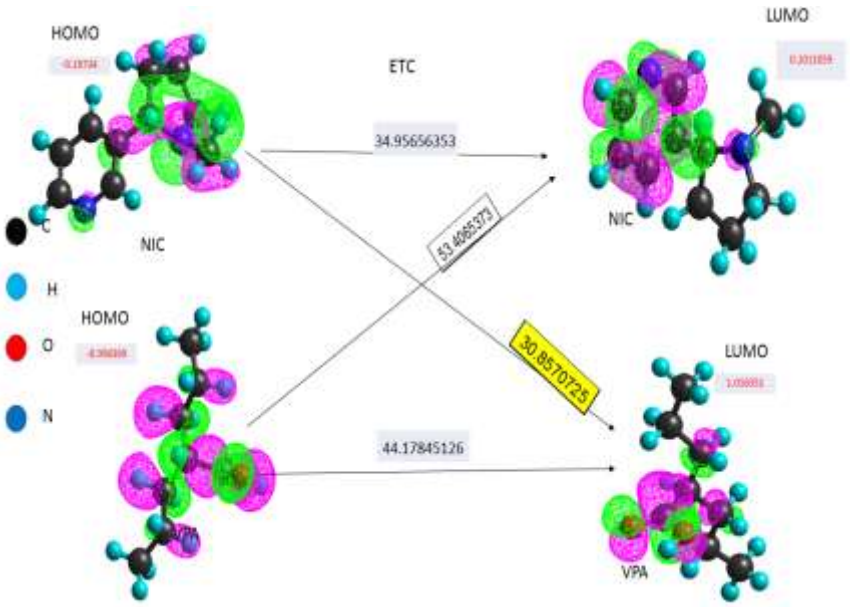

Figure: 2. Electron exchange between molecules of VPA and NIC in crossed bands. The yellow icon represents the lowest ETC NIC: VPA.

CONCLUSION

According to Table 3, we conclude that the 5-HT, NIC acts as an antioxidant for the VPA because of its small ETC, with higher affinity, demonstrating a high electron transfer from NIC to VPA. Of these NTs the 5-HTs obtained the lowest ETC with 29,745. The likelihood that NIC interacts with the VPA antioxidant is highly likely because of its small ETC (30,857). An antioxidant is a substance that can prevent the adverse effects of reactive species on the normal physiological functions of humans. However, the NIC is known to be highly harmful. The NIC: VPA interaction possibly causes havoc to the mechanism of action of the drug. We conclude, in general, we conclude, in general, that patients with VAP treatment is contraindicated exposure to tobacco smoke.

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