WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 6.647
Volume 6, Issue 8, 2467-2477 Research Article ISSN 2278 – 4357

INTERACTION OF METILENDIOXIMETANFETAMINA VS. NEUROTRANSMITTERS AND THE RELATIONSHIP BY THE QUANTUM METHOD.

Jesús Francisco Mondragón-Jiménez[1], Bernardo Ojeda-Lara[1], Adrián Alvarez-Aguilar[1], Carlos Arturo Brito-Pérez[1], Francisco José Rosales-Hernández[1] and Manuel González-Pérez*[2,3]

[1]Universidad Juárez Autónoma de Tabasco (UJAT). División Académica de Ciencias de la Salud (DACS).

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

[3]Sistema Nacional de Investigadores. Nivel I.

Article Received on
19 June 2017,

Revised on 11 July 2017,
Accepted on 31 July 2017,

DOI: 10.20959/wjpps20178-9912

***Corresponding Author**
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

Background: Methylenedioxymethamphetamine (MDMA) is a psychostimulant derived from amphetamines, commonly known as "ecstasy. MDMA causes the release of serotonin, dopamine (DA) and norepinephrine (NA) by blocking presynaptic reabsorption transporters. MDMA causes prolonged toxic effects to the serotonergic nerve terminals and, more recently. A neurotransmitter (NT) is a chemical released selectively from a nerve ending by the action of an action potential. The AD by B-adrenergic stimulus increases the contractile force of the myocardium and enhances the frequency of myocardial contraction. AD is involved in various signaling processes in the central nervous system (CNS). **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 of the Electron transfer coefficient (ETC) of a substance (A) and an ETC of substance (B). **Result:** when comparing MDMA with the NTS we find that it has a strong affinity with the following NTS: AD, DA, ASP, and GLU due to its low ETC. **Conclusion:** We conclude that the MDMA has a high electronic transfer to the NTSs: AD principally, DA, Asp, Glu.

KEYWORDS: MDMA, adrenaline, dopamine, glutamic acid and aspartic acid, SE-PM3 and quantum methods.

INTRODUCTION

MDMA is a psychostimulant derived from amphetamines, commonly known as "ecstasy.".[1] MDMA formerly had a use, as a psychotherapeutic adjuvant was also important in the treatment of various psychiatric illnesses by mental health professionals, however.[2] MDMA causes the release of serotonin, DA, and norepinephrine by blocking presynaptic reabsorption transporters.[3,4] MDMA causes prolonged toxic effects on the nerve terminals Serotonergic and more recently, has been shown to reduce the number of gamma-aminobutyric acid neurons in the hippocampus of rats.[5, 6] In recent decades, several molecular imaging studies directly examined in vivo the effects of ecstasy / MDMA in neurotransmitter systems.[7]

An NT is a chemical released selectively from a nerve ending by the action of an action potential, which interacts with a specific receptor in an adjacent structure and which, if received in sufficient quantity, produces a certain physiological response.[8, 9]

AD (or also epinephrine) is synthesized and stored in the adrenal medulla.[10] AD occurs in more than 80% in the adrenal medulla.[11] AD by B-adrenergic stimulus increases the contractile force of the myocardium (positive inotropic action) and enhances the frequency of myocardial contraction (positive chronotropic action).[12] AD produces vasoconstriction in many vascular beds (precapillary resistance) of the skin, mucosa, and kidney along with venous constriction.[13]

DA is an important neurotransmitter of catecholamines in the brain. DA is involved in various signaling processes in the CNS, such as motivation, reward titration and endocrine regulation.[14,15] The action of AD proceeds through DA receptors, D1-5.[16] AD reduces the influence of the indirect neuronal pathway and increases the actions of the direct path within the core ganglia.[17] Amphetamines inhibit re-uptake of AD.[18]

Aspartic acid (Asp) is a free amino acid found in neuroendocrine tissues of invertebrates and vertebrates where it performs essential physiological functions.[19,20] Asp occurs naturally as an L or D form. L-Aspartic acid (L-Asp) belongs to the endogenous human amino acids involved in the formation of peptides and proteins that also participate in the synthesis of purines and pyrimidines. D-Aspartic acid (D-Asp) occurs in organisms in free form and does

not create proteins. He D-Asp plays a major role in the endocrine and nervous system (functioning as a neurotransmitter and a neuromodulator).[21]

Glutamic acid (Glu) constitutes more than 60 percent of the total amino acids in the human body.[22] Glu is also an important excitatory neurotransmitter in the mammalian CNS and plays a vital role in many physiological processes. Scientists have proposed that the glutamate system plays a relevant role in various neurological and psychiatric disorders such as Alzheimer's disease, autism, schizophrenia, depression, drug addiction and more.[23]

Hyperchem is a molecular modeling program.[24] Hyper Chem's graphical interface allows researchers to perform chemical simulations that facilitate multiple data entry.[25-28]

MATERIALS AND METHODS

Software and simulation

It used HyperChem 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 0.1 kcal / 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	One 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 MDMA act as an antioxidant of the NT. Lowest ETCs have MDMA: AD, MDMA: DA, their affinity is considered to be very high. The highest recorded ETC is from MDMA: NORADRENALINE.

Cross Bands of NT and MDMA against VPA (ECTs.)

CHEMICAL REACTIVITY TABLE OF COMPOUNDS

Reducing agent	Oxidizing agent	HOMO	LUMO	BG	E-	E+	EP	ETC
MDMA	MDMA	-8.808338	0.2838469	9.0921849	-0.143	0.124	0.267	34.05312697
MDMA	**ADRENALIN**	**-8.808338**	**0.0917624**	**8.9001004**	**-0.143**	**0.198**	**0.341**	**26.10000123**
MDMA	SEROTONIN	-8.808338	-0.129448	8.6788905	-0.143	0.141	0.284	30.55947359
MDMA	**DOPAMINE**	**-8.808338**	**0.1988791**	**9.0072171**	**-0.143**	**0.189**	**0.332**	**27.13017199**
MDMA	GABA	-8.808338	0.9385893	9.7469273	-0.143	0.18	0.323	30.17624551
MDMA	GLYCINE	-8.808338	0.8744405	9.6827785	-0.143	0.188	0.331	29.25310725
MDMA	**ASPARTY ACID**	**-8.808338**	**0.5161864**	**9.3245244**	**-0.143**	**0.198**	**0.341**	**27.34464633**
MDMA	**GLUTAMIC ACID**	**-8.808338**	**0.5371279**	**9.3454659**	**-0.143**	**0.197**	**0.34**	**27.48666441**
MDMA	**NORADRENALINE**	**-8.808338**	**-0.004275**	**8.8040626**	**-0.143**	**-0.222**	**0.079**	**111.4438306**
MDMA	ACETYLCHOLINE	-8.808338	1.034277	9.842615	-0.143	0.105	0.248	39.68796371

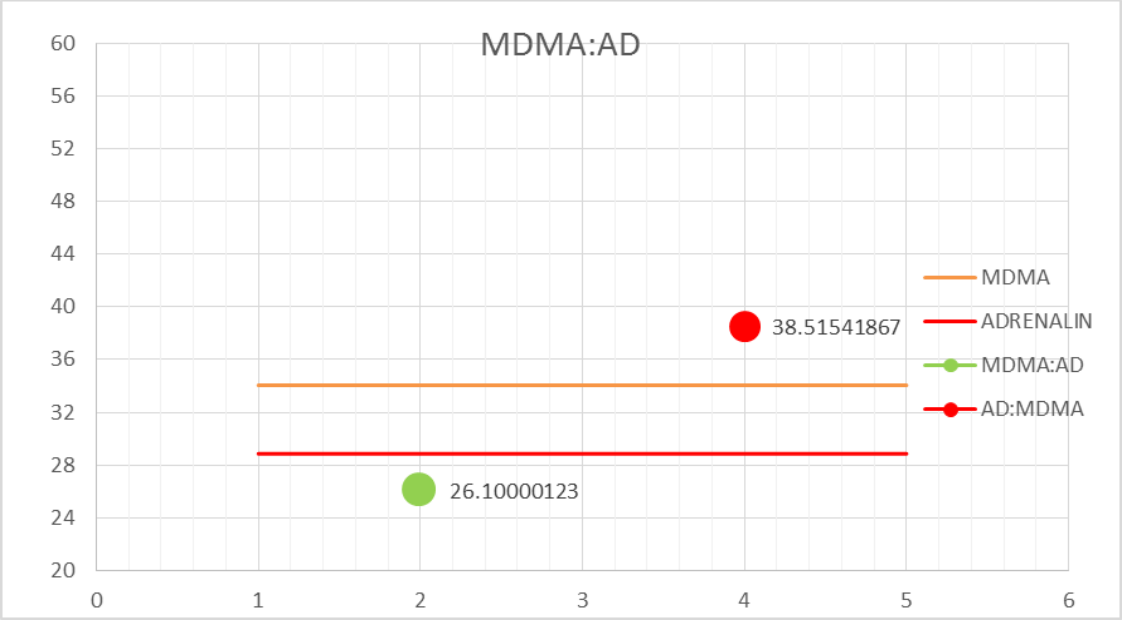

Figure 1. Quantum wells, the green dot represents the MDMA: AD ratio, this is located in a high probability zone. The red dot represents the AD: MDMA ratio, this is located in a low probability area. Green (MDMA) and red (AD) lines represent Boundaries.

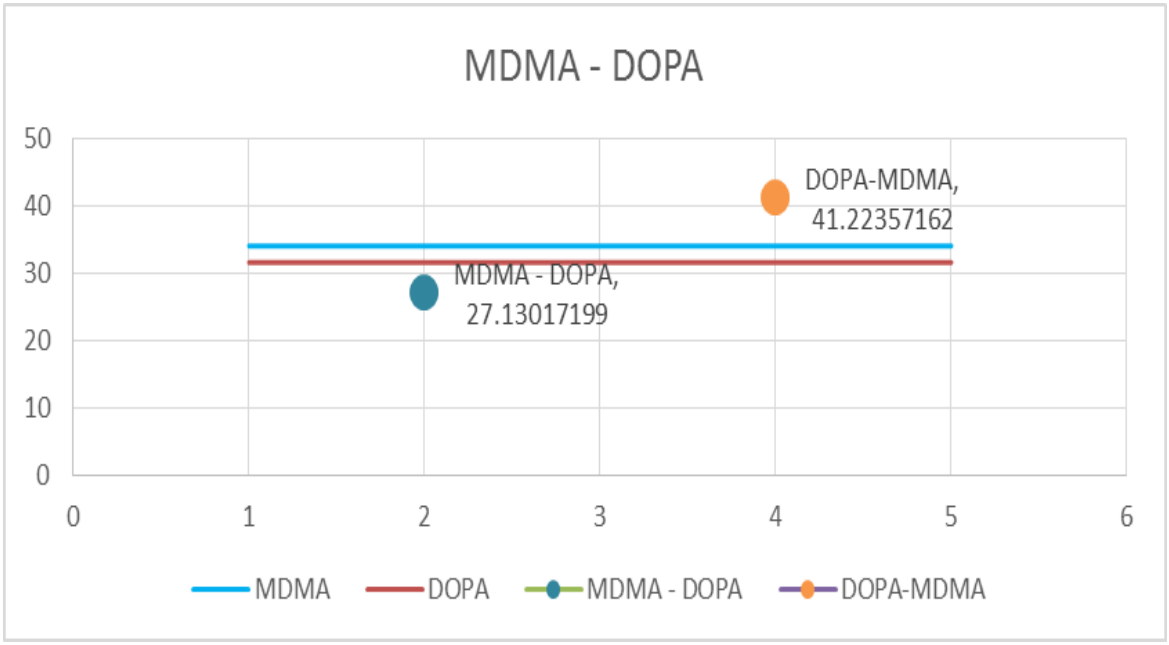

Figure 2. Quantum wells, the blue dot represents the MDMA: DA ratio, which is in a high probability zone. The orange dot represents the DA: MDMA ratio, which is in an area of low probability. The blue (MDMA) and red (AD) lines represent Boundaries.

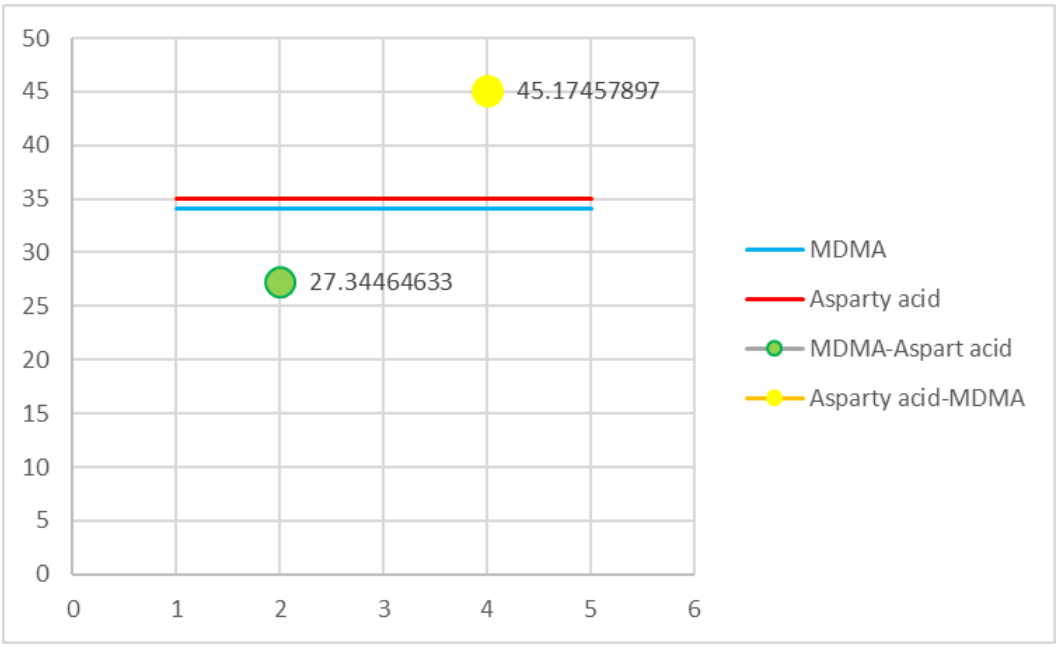

Figure 3. Quantum wells, the green dot represents the MDMA: Asp ratio, which is in a high probability zone. The yellow dot represents the ASPARTY: MDMA relationship, which is in an area of low probability. The blue (ASPARTY) and red (MDMA) lines represent Boundaries.

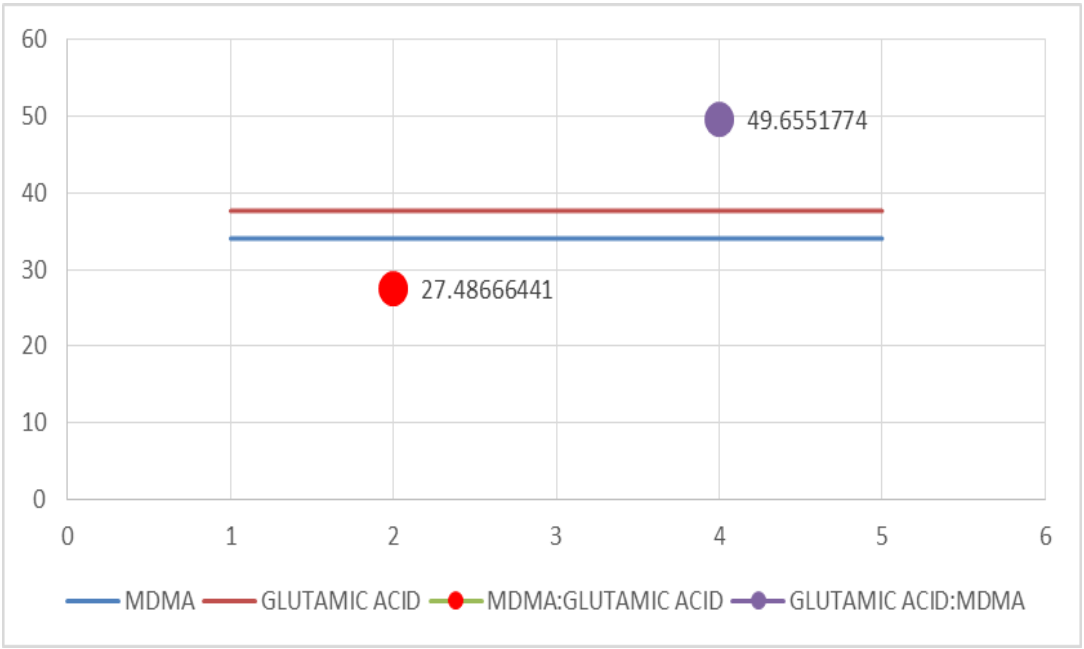

Figure 4. Quantum wells, the red dot represents the MDMA: Glu ratio, which is in a high probability zone. The purple dot represents the Glu: MDMA ratio, which is in an area of low probability. The red (Glu) and blue (MDMA) lines represent Boundaries.

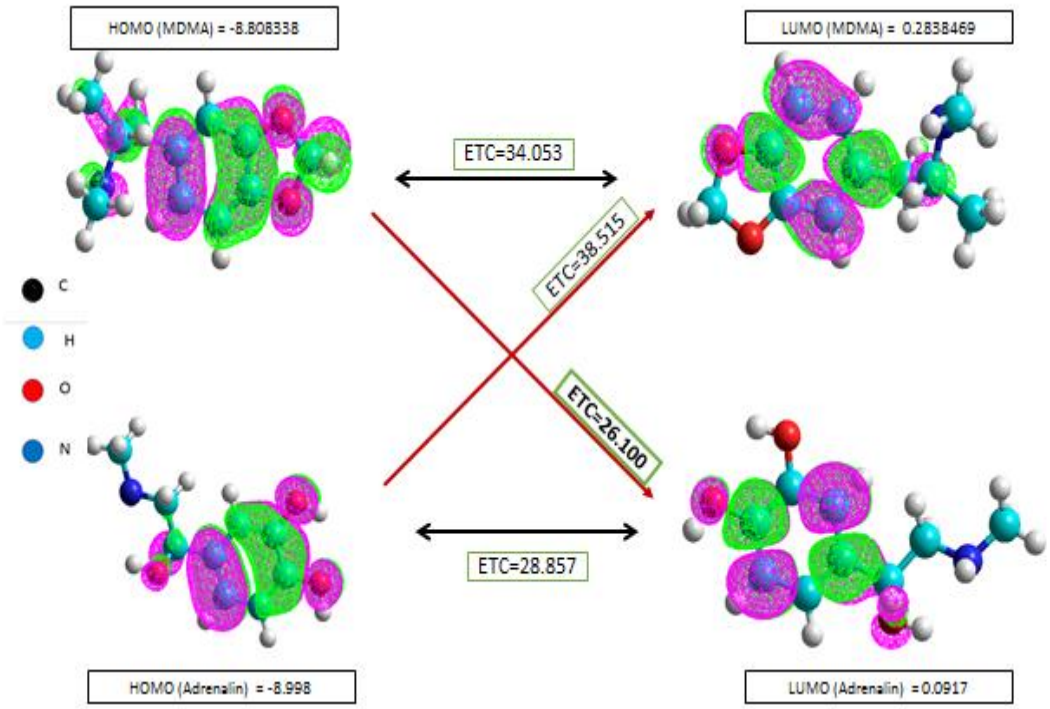

Figure 5. Electron exchange between molecules of MDMA and AD in crossed bands.

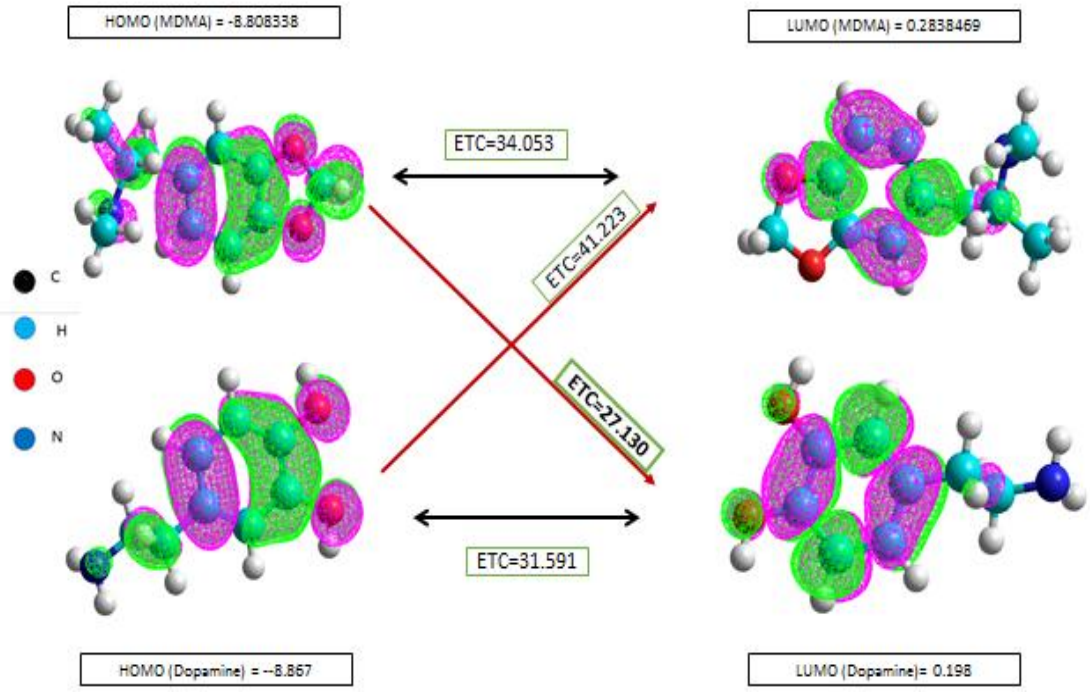

Figure 6. Electron exchange between MDMA and DA molecules in cross bands.

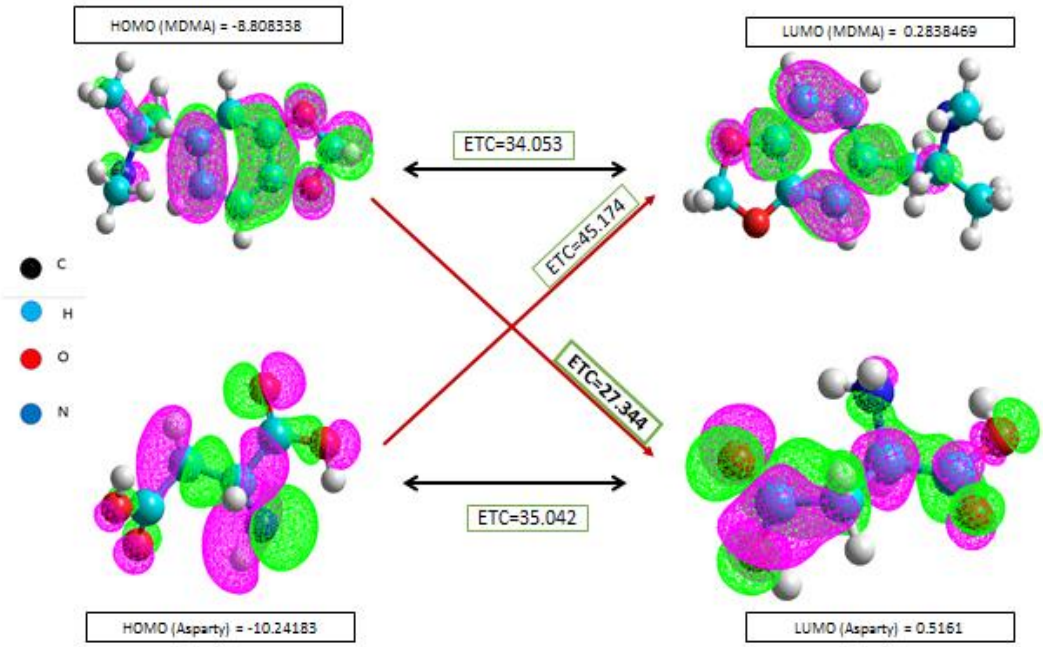

Figure 7. Electron exchange between MDMA and ASP molecules in cross bands.

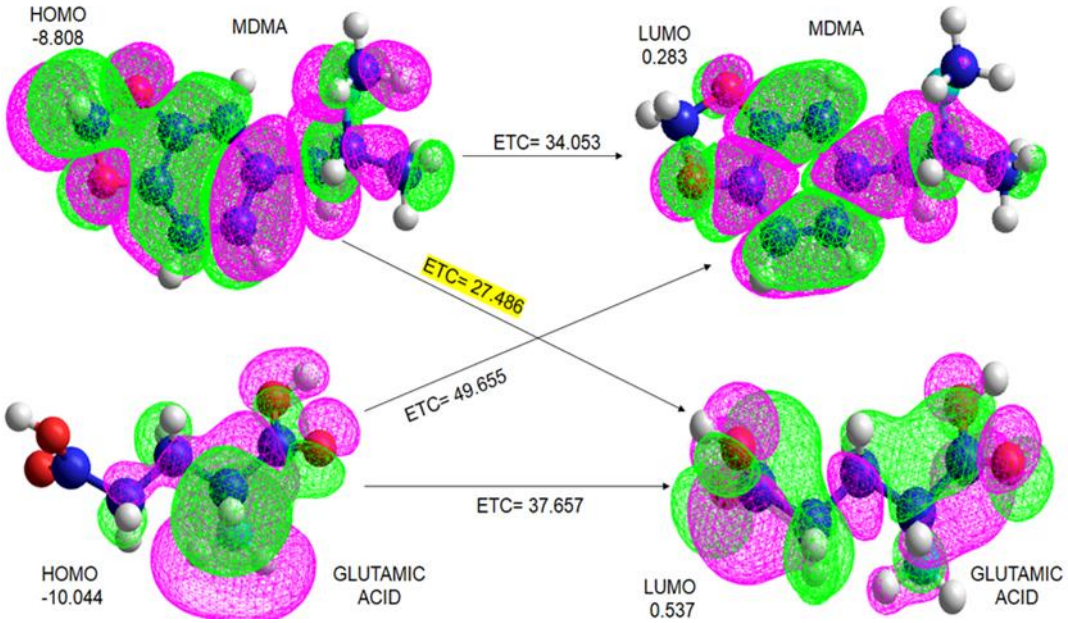

Figure 8. Electron exchange between MDMA and Glu molecules in cross bands.

CONCLUSION

1. - We conclude that MDMA acts as a good antioxidant agent for NTS: AD (26,100), DA (27,1301), Asp (27,3446) AND Glu (27,4866) MDMA has a high electron transfer To these NTS.

2. – We found that the MDMA-AD interaction has the lowest ETC (26,100)

3. – We found that the interaction MDMA-NORADREANLINE has the highest ETC (111,443) and as a consequence, there is a low electron transfer.

4.- We believe that MDMA interacts with DA. This concordance is by the medical literature.

5.- Through the quantum method, we reaffirm that this drug is a potent neurotoxic agent and causes cognitive impairment due to its low ETC.

ACKNOWLEDGEMENTS

We thank the UJAT. Academic Division of Health Sciences for its support during the stay in the city of Puebla to carry out this summer of scientific research and for the UPAEP especially the Interdisciplinary Postgraduate Center for its facilities.

BIBLIOGRAPHY

1. Duman, B., Sedes, N., & Baskak, B. (2017). Additive Effects of Former Methylenedioxymethamphetamine and Cannabis Use on Subclinical Psychotic Symptoms. *Archives of Neuropsychiatry*, *54*(1): 38.
2. Amoroso, T. (2015). The psychopharmacology of ±3, four methylenedioxymethamphetamine and its role in the treatment of posttraumatic stress disorder. *Journal of psychoactive drugs*, *47*(5): 337-344.
3. Hysek, C. M., Schmid, Y., Simmler, L. D., Domes, G., Heinrichs, M., Eisenegger, C., ... & Liechti, M. E. (2013). MDMA enhances emotional empathy and prosocial behavior. Social cognitive and affective neuroscience, 9(11): 1645-1652.
4. Hysek, C. M., Simmler, L. D., Schillinger, N., Meyer, N., Schmid, Y., Donzelli, M., ... & Liechti, M. E. (2014). Pharmacokinetic and pharmacodynamic effects of methylphenidate and MDMA administered alone or in combination. International journal of neuropsychopharmacology, 17(3): 371-381.
5. Anneken, J. H., Collins, S. A., Yamamoto, B. K., & Gudelsky, G. A. (2016). MDMA and Glutamate: Implications for Hippocampal Neurotoxicity. In Stimulants, Club and Dissociative Drugs, Hallucinogens, Steroids, Inhalants and International Aspects. Elsevier Inc..
6. Roberts, C. A., Jones, A., & Montgomery, C. (2016). Meta-analysis of executive functioning in ecstasy/polydrug users. Psychological medicine, 46(8): 1581-1596.
7. . Vegting, Y., Reneman, L., & Booij, J. (2016). The effects of ecstasy on neurotransmitter systems: a review on the findings of molecular imaging studies. Psychopharmacology, 233(19-20): 3473-3501.

8. Duman, B., Sedes, N., & Baskak, B. (2017). Additive Effects of Former Methylenedioxymethamphetamine and Cannabis Use on Subclinical Psychotic Symptoms. *Archives of Neuropsychiatry*, *54*(1): 38.
9. Goldberg, E., Grau, J. B., Fortier, J. H., Salvati, E., Levy, R. J., & Ferrari, G. (2017). Serotonin and catecholamines in the development and progression of heart valve diseases. *Cardiovascular Research*, *113*(8): 849-857.
10. Nagatsu, T. (2017). Richard Kvetnansky: His Great Contributions to Research on Catecholamines and Other Neurotransmitters in Relation to Stress.
11. Scott, A. L., Pranckevicius, N. A., Patal, P., Nurse, C. A., & Scott, G. R. (2017). Catecholamine secretion from the adrenal medulla is blunted in high-altitude deer mice (Peromyscus maniculatus). *The FASEB Journal*, *31*(1 Supplement): 841-3.
12. Gai, Y., Zhang, J., Wei, C., Cao, W., Cui, Y., & Cui, S. (2017). miR-375 negatively regulates the synthesis and secretion of catecholamines by targeting Sp1 in rat adrenal medulla. *American Journal of Physiology-Cell Physiology*, *312*(5): C663-C672.
13. Fu, Q., Wang, Q., & Xiang, Y. K. (2017). Insulin and b Adrenergic Receptor Signaling:[488_TD $ DIFF] Crosstalk in Heart. *Insulin*, *44:* 47.
14. Kaya, C., Block, ER, Sorkin, A., Faeder, JR, y Bahar, I. (2016). Simulaciones espaciales multi-escala revelan el efecto de la localización del transportador de dopamina en la neurotransmisión de dopamina. *Biophysical Journal*, *110*(3): 632a.
15. Covey, D., Mateo, Y., Sulzer, D., Cheer, JF, & Lovinger, DM (2017). Modulación endocanabinoide de la neurotransmisión de la dopamina. Neurofarmacología.
16. Dupuis, J. P., Bioulac, B. H., & Baufreton, J. (2014). Long-term depression at distinct glutamatergic synapses in the basal ganglia. *Reviews in the Neurosciences*, *25*(6): 741-754.
17. Oldenburg, I. A., & Sabatini, B. L. (2015). Antagonistic but not symmetric regulation of primary motor cortex by basal ganglia direct and indirect pathways. *Neuron*, *86*(5): 1174-1181.
18. Dinis-Oliveira, R. J. (2017). Metabolomics of Methylphenidate and Ethylphenidate: Implications in Pharmacological and Toxicological Effects. *European journal of drug metabolism and pharmacokinetics*, *42*(1): 11-16.
19. Roshanzamir, F., & Safavi, S. M. (2017). The putative effects of D-Aspartic acid on blood testosterone levels: A systematic review. International Journal of Reproductive Bio Medicine, 15(1).

20. D'Aniello, A., Luongo, L., Romano, R., Iannotta, M., Marabese, I., Boccella, S., ... & D'Aniello, B. (2017). d-Aspartic acid ameliorates painful and neuropsychiatric changes and reduces β-amyloid Aβ 1-42 peptide in a long lasting model of neuropathic pain. Neuroscience Letters, 651: 151-158.
21. Ładyga, M., & Obmiński, Z. (2013). D-aspartic acid: biological role and potential applications as dietary supplement in sport. Medicina Sportiva, 17(4).
22. Krishnamurthy, R. V., Suryawanshi, Y. R., & Essani, K. (2017). Nitrogen isotopes provide clues to amino acid metabolism in human colorectal cancer cells. Scientific Reports, 7(1): 2562.
23. Okon, S. L., & Ronkainen, N. J. (2017). Enzyme-Based Electrochemical Glutamate Biosensors. In Electrochemical Sensors Technology. In Tech.
24. González-Perez, M., Pacheco-Bautista, D., Ramirez-Reyes-Montaño, H. A., Medel-Rojas, A., González-Murueta, J. W., & Sánchez, C. ANALYSIS OF THE INTERACTIONS OF N-(L-A-ASPARTIL)-L-PHENYLALANINE, 1-METIL ESTER (ASPARTAME) AND THE NITROGEN BASES OF DNA AND RNA USING QUANTUM METHODS, 2017.
25. González-Pérez, M. CHEMICAL-QUANTUM ANALYSIS OF THE AGGRESSIVENESS OF GLUCOSE AND ITS APPEASEMENT WITH ATP INSIDE THE CELL, AND WATER AS AN EXCELLENT ANTIOXIDANT, 2017.
26. Ibarra Medel, D., Meléndez Gámez, P., López Oglesby, J. M., & González-Pérez, M. molecular analysis of strychnine and the glycine receptor using quantum chemistry methods, 2016.
27. González-Pérez, M. applied quantum chemistry. analysis of the rules of markovnikov and anti-markovnikov. international journal of science and advanced technology, 2015; 5(5).
28. González-Perez, .. g., barrera, f. a. g., diaz, j. f. m., torres, m. g., & oglesby, j. m. l. theoretical calculation of electron transfer coefficient for predicting the flow of electrons by pm3, using 20 amino acids and nicotine. european scientific journal, esj, 2014; 10(27): 690.