WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 13, 31-38. Research Article ISSN 2277– 7105

QUANTUM ANALYSIS OF THE EFFECT OF CANNABIDIOL ON NEUROTRANSMITTERS

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Article Received on
24 August 2017,

Revised on 14 Sept. 2017,
Accepted on 05 October 2017

DOI: 10.20959/wjpr201713-9861

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ABSTRACT

Scientists suggest that Cannabis possess the potential medical benefits in the management of pain, spasticity in neurodegenerative disease, anorexia and wasting syndromes, psychiatric disorders, and epilepsy. To achieve a good molecular model and analysis of Cannabidiol and neurotransmitters, we use Hyper Chem Professional Software. The Electron Transfer Coefficient needs to be compared with two limits to determine its position between the zones of probability or quantum wells. In this research, we get that Serotonin and GABA have a lower ETC value. Nevertheless, Leucine was far away from the lower limit; that implies that CBD can have greater interaction with this neurotransmitter.

KEYWORDS: Cannabidiol, Neurotransmitters, Quantum analysis.

INTRODUCTION

Cannabidiol Scientists suggest that Cannabis possess the potential medical benefits in the management of pain, spasticity in neurodegenerative disease, anorexia and wasting syndromes, psychiatric disorders and epilepsy[1], concerns relating to abuse and other deleterious consequences of smoking marijuana have limited progress in therapeutic utility.[2,4]

Nowadays, it is possible to identify the compounds responsible for psychoactivity of cannabis and the therapeutic potential of the nonpsychoactive compounds. Δ9 -tetrahydrocannabinol

(Δ9 -THC) is the major psychoactive component of cannabis whereas cannabidiol (CBD) is the major and most widely studied of the other constituents.[4]

Cannabidiol (CBD) is one of the main components of *Cannabis sativa*, but it is not involved in its psychomimetic effects.[5]

Neurotransmitters

A neurotransmitter is a substance released by a neuron at the synapse, which specifically affects a postsynaptic cell,[6] either a neuron or an effector organ, such as a muscle cell or a gland.[7]

Scientists consider as neurotransmitters the substances that meet the following criteria:

1. Neurons can synthesize it.
2. It is present in the presynaptic terminal and is released in sufficient quantity to exert a definite action on the postsynaptic neuron or effector organ.
3. When given externally (as a drug) in reasonable concentrations, it mimics exactly the action of the endogenous release transmitter.
4. There is a specific mechanism to remove it from its place of action (the synaptic cleft)
   Adrenaline belongs to a group of neurotransmitters called catecholamines. Catecholamines are synthesized from the amino acid tyrosine[8] in a common biosynthetic pathway containing five enzymes: tyrosine hydroxylase, aromatic amino acid decarboxylase, dopamine B-hydroxylase, pteridine reductase and N-methyl phenylethanolamine Transferase.[7]

The enzyme phenylethanolamine N-methyl transferase methylates noradrenaline to form adrenaline (epinephrine) in the adrenal medulla.[8]

Serotonin and the essential amino acid tryptophan from which it comes belong to a group of aromatic compounds called indoles. It is possible to found cell bodies of the serotonergic neurons in and around the brain stem nuclei. These nuclei participate in the regulation of attention and other complex cognitive functions. Serotonin is involved in depression, the main mood disorder.[15]

Glycine is the main transmitter of inhibitory interneurons of the spinal cord and is probably synthesized from the serine.[7]

GABA is synthesized from glutamate in a reaction catalyzed by decarboxylase of glutamic acid, is present in great concentrations throughout the central nervous system and is detectable in other tissues. Several inhibitory interneurons of the spinal cord use it as a transmitter, such as the cells in the cerebellum basket, the olfactory bulb granules and the amacrine cells of the retina.[7]

Leucine is the most widely studied branched-chain amino acid. Leucine have several roles in skeletal muscle, including the regulation of translation initiation, modulation of insulin/PI3-kinase signaling, provision of metabolic fuel, and donation of nitrogen for alanine and glutamine synthesis.[7]

Quantum chemistry is a tool that helps through simple methods such as SE-PM3 to calculate the nuclear reorganization during the electronic coupling.[9-14]

MATERIALS AND METHODS

To achieve a good molecular model and analysis of Cannabidiol and neurotransmitters, we use Hyper Chem Professional Software (Windows Serial: 12-800-1501800080 acquired at MultiON Insurgentes Sur 1236-301 Tlacoquemecatl Col. del Valle, Delegación Benito Juárez, DF, México CP 03200). The method used for the little geometric calculations was Polak-Ribiere method. Also, we used SE-PME for the optimization of the molecular geometry.[9,10]

Finally, we set the following parameters to standardize[11] each of the quantum calculations.

Table 1: Parameters used in Hyper Chem for Orbitals simulation.

Parameters used for quantum computing molecular orbits -HOMO and LUMO.	
Parameter	**Value**
Total Charge	0
Spin Multiplicity	1
Spin Pairing	RHF
Convergent Limit	0.01
Iteration Limit	50
Accelerate Convergence	YES
Polarizability	NOT
Algorithm	POLAK-RIBIERE
RMS gradient	0.1 kcal/Å mol
Maximum cycles	795 cycles
Screen refresh period	1 cycle

Table 2: Parameters used to visualize the map of electrostatic potential.

Parameter	Value
Molecular Property	Electrostatic Potential
Representation	3D Mapped Isosurface
Grid Mesh Size	Coarse
Grid Layout	Default
Starting Value	Default
Contour Grid Increment	Default
Mapped Function Options	Default
Alpha Level	Default
Total charge density contour value	0.015
Rendering	Wire Mesh

RESULTS AND DISCUSSION

With the data obtained in Hyper Chem we calculate the Electron Transfer Coefficient (ETC) using the following equations.

$BG = \lvert HOMO - LUMO \rvert$	Eq 1
$EP = \lvert E^{+} - E^{-} \rvert$	Eq 2
$TC = {}^{BG}/_{EP}$	Eq 3

In Table 3, we show the ETC values of the main neurotransmitters and Cannabidiol. Then, we use those values to make cross-bands calculations between the NT and CBD. First, we took CBD as the reducer and de NT as oxidizers, and then we invert the roles, we chose CBD as an oxidizer and NT as reducers.

Table 3: Electron Transference Coefficient Table of CBD and principal neurotransmitters.

Compound	Training Energy	HOMO	LUMO	BG	E-	E+	EP	ETC
Adrenaline	-53276.4	-8.998382	0.0918	9.0901	-0.11	0.2	0.31	29.323
Noradrenaline	-49831.7	-9.152911	-0.0037	9.1492	-0.08	0.219	0.299	30.5993
Serotonin	-42500.4	-8.948444	-0.1294	8.819	-0.138	0.139	0.277	31.8376
Dopamine	-43061.1	-8.86781	0.1989	9.0667	-0.094	0.188	0.282	32.1514
Gaba	-31442.5	-9.561555	0.9386	10.5001	-0.135	0.182	0.317	33.1235
Glycine	-24545.6	-9.853027	0.8744	10.7275	-0.117	0.189	0.306	35.0571
Asparty Acid	-44279.6	-10.24183	0.5162	10.758	-0.102	0.2	0.302	35.6226
Glutamic Acid	-47731	-10.04444	0.5371	10.5816	-0.077	0.196	0.273	38.7603
Cannabidiol	-81516.4	-8.090646	0.6509	8.7415	-0.027	0.185	0.212	41.2337
Leucine	-34888.4	-9.786279	1.0023	10.7885	-0.139	0.11	0.249	43.3275
Acetlycholine	-38320.4	-9.241997	1.0343	10.2763	-0.031	0.105	0.136	75.5608

Here, in Table 4, we show the results of the first set of calculations, assuming CBD as reducer and NT as oxidizers.

Table 4: Cross-band Table of CBD as a reducer and principal neurotransmitters as oxidizers.

Reducer	Oxidizer	HOMO	LUMO	BG	E-	E+	EP	ETC
CBD	Noradrenaline	-8.0906	-0.0037	8.0869	-0.027	0.219	0.246	32.8737
CBD	Adrenaline	-8.0906	0.0918	8.1824	-0.027	0.2	0.227	36.0460
CBD	Asparty Acid	-8.0906	0.5162	8.6068	-0.027	0.2	0.227	37.9156
CBD	Dopamine	-8.0906	0.1989	8.2895	-0.027	0.188	0.215	38.5560
CBD	Glutamic Acid	-8.0906	0.5371	8.6277	-0.027	0.196	0.223	38.6894
CBD	Cannabidiol	-8.0906	0.6509	8.7415	-0.027	0.185	0.212	41.2337
CBD	Glycine	-8.0906	0.8744	8.9650	-0.027	0.189	0.216	41.5048
CBD	Gaba	-8.0906	0.9386	9.0292	-0.027	0.182	0.209	43.2021
CBD	Serotonin	-8.0906	-0.1294	7.9612	-0.027	0.139	0.166	47.9593
CBD	Leucine	-8.0906	1.0023	9.0929	-0.027	0.11	0.137	66.3718
CBD	acetlycholine	-8.0906	1.0343	9.1249	-0.027	0.105	0.132	69.1283

In the same order of ideas, in Table 5, we show the results of the second set of calculations, assuming CBD as oxidizer and NT as reducers.

Table 5: Cross-band Table of CBD as an oxidizer and principal neurotransmitters as reducers.

Reducer	Oxidizer	HOMO	LUMO	BG	E-	E+	EP	ETC
Serotonin	CBD	-8.9484	0.6509	9.5993	-0.138	0.185	0.323	29.7193
Gaba	CBD	-9.5615	0.6509	10.2124	-0.135	0.185	0.32	31.9139
Leucine	CBD	-9.7862	0.6509	10.4371	-0.139	0.185	0.324	32.2135
Adrenaline	CBD	-8.9983	0.6509	9.6492	-0.11	0.185	0.295	32.7094
Dopamine	CBD	-8.867	0.6509	9.5187	-0.094	0.185	0.279	34.1172
Glycine	CBD	-9.8530	0.6509	10.5039	-0.117	0.185	0.302	34.7812
Noradrenaline	CBD	-9.1529	0.6509	9.8038	-0.08	0.185	0.265	36.9955
Asparty Acid	CBD	-10.241	0.6509	10.8927	-0.102	0.185	0.287	37.9537
Glutamic Acid	CBD	-10.044	0.6509	10.6953	-0.077	0.185	0.262	40.8219
Cannabidiol	CBD	-8.0906	0.6509	8.7415	-0.027	0.185	0.212	41.2337
Acetlycholine	CBD	-9.2419	0.6509	9.8928	-0.031	0.185	0.216	45.8004

We know that higher values of ETC result in a greater difficulty for the electrons to pass from molecule to molecule of the same chemical species. In the other hand, lower values of ETC indicate easier electron transference.

However, we compare each ETC of the cross-band tables with the ETC obtained in for each molecule in Table 3. We divide the interactions of the molecules into three zones named “quantum wells” according to the following figure.

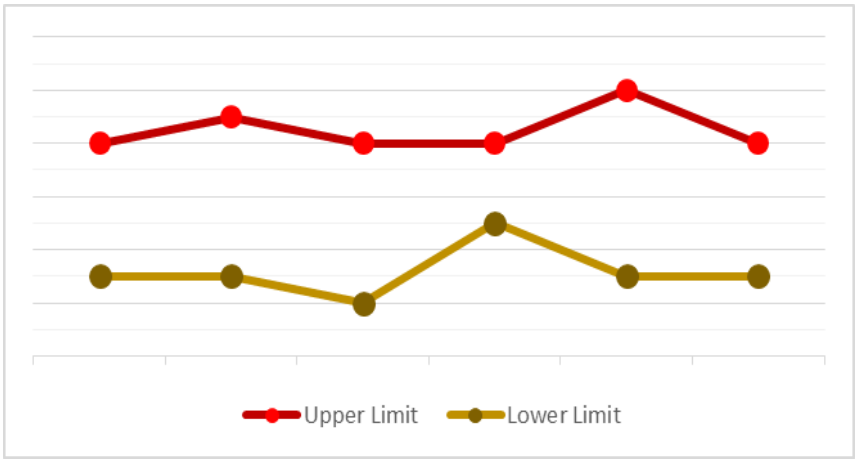

Figure 2: Quantum wells explanation.

The area above the upper limit is a shallow probability zone of interaction. The area between both limits is the area of the average likelihood of interaction. Moreover, the area under the lower limit is a high probability zone of interaction.

Table 6: Quantum wells of high probability using CBD as a limit.

Reducer	Oxidizer	HOMO	LUMO	BG	E-	E+	EP	ETC
Cbd	CBD	-8.0906	0.6509	8.7415	-0.027	0.185	0.212	41.2337
Glycine	CBD	-9.8530	0.6509	10.5039	-0.117	0.185	0.302	34.7812
Dopamine	CBD	-8.867	0.6509	9.5187	-0.094	0.185	0.279	34.1172
Adrenaline	CBD	-8.9983	0.6509	9.6492	-0.11	0.185	0.295	32.7094
Leucine	CBD	-9.7862	0.6509	10.4371	-0.139	0.185	0.324	32.2135
Gaba	CBD	-9.5615	0.6509	10.2124	-0.135	0.185	0.32	31.9139
Serotonin	CBD	-8.9484	0.6509	9.5993	-0.138	0.185	0.323	29.7193

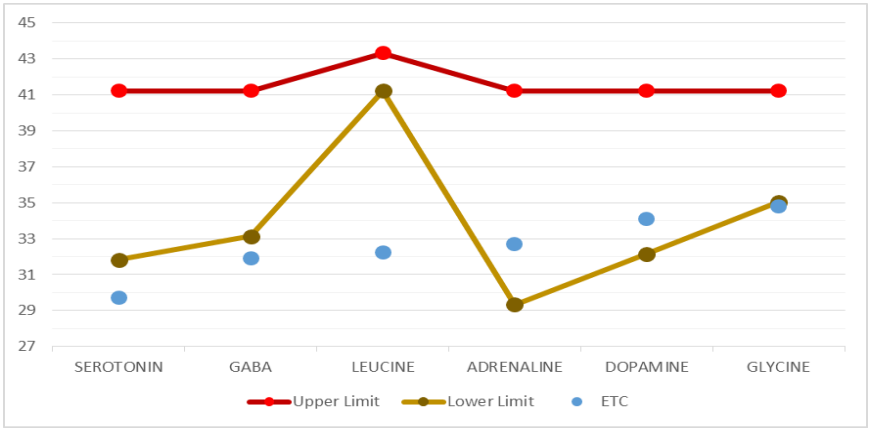

Figure 3: Comparision of ETC according to quantum wells.

As we can observe in Figure 3, the neurotransmitters that are in high probability zone, are Serotonin, GABA, Leucine and Glycine. However, Leucine ETC value is far away from the lower limit. Thus, indicates that CBD and Leucine have the highest probability of interaction above other neurotransmitters.

CONCLUSION

The Electron Transfer Coefficient needs to be compared with two limits to determine its position between the zones of probability or quantum wells.

In this research, we get that Serotonin and GABA have a lower ETC value. Nevertheless, Leucine was far away from the lower limit, which implies that CBD can have greater interaction with this neurotransmitter.

REFERENCES

1. Sulak, D., Saneto, R., & Goldstein, B. The current status of artisanal cannabis for the treatment of epilepsy in the United States. Epilepsy & Behavior, 2017; 70: 328-333.
2. Goldenberg, M., Reid, M. W., IsHak, W. W., & Danovitch, I. The impact of cannabis and cannabinoids for medical conditions on health-related quality of life: A systematic review and meta-analysis. Drug & Alcohol Dependence, 2017; 174: 80-90.
3. Walsh, Z., Gonzalez, R., Crosby, K., Thiessen, M. S., Carroll, C., & Bonn-Miller, M. O. Medical cannabis and mental health: A guided systematic review. Clinical psychology review, 2017; 51: 15-29.
4. Fasinu, P. S., Phillips, S., ElSohly, M. A., & Walker, L. A. Current status and prospects for cannabidiol preparations as new therapeutic agents. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 2016; 36(7): 781-796.
5. Chagas M Hortes, Zuardi Antonio, Tumas Victor, Pena-Pereira Márcio, Sobreira Emmanuelle T, Begamschi Mateus M, dos Santos Antonio, Teixeira Antonio, Hallack Jaime and Crippa José Effects of cannabidiol in the treatment of patients with Parkinson's disease: An exploratory double-blind trial. Journal of Psychopharmacology, 2014; 28(11): 1088 – 1098.
6. Crawford, D. C., Ramirez, D. M., Trauterman, B., Monteggia, L. M., & Kavalali, E. T. Selective molecular impairment of spontaneous neurotransmission modulates synaptic efficacy. Nature Communications, 2017; 8: 14436.
7. Kandel Eric R., Schwartz James H., Jessell Thomas M. Principios de Neurociencia. Madrid, España. McGraw-Hill, 2011.
8. Bondarenko, N. S., Murtazina, A. R., Nikishina, Y. O., Sapronova, A. Y., & Ugrumov, M. V. (January). Molecular mechanisms of synthesis of noradrenaline as an inducer of development in the adrenal glands of rats in ontogenesis. In Doklady Biochemistry and Biophysics Pleiades Publishing, 2017; 472(1): 23-26.

9. 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. World Journal of Pharmacy and Pharmaceutical Science, 2016; 6(2): 1437-1446.
10. González-Pérez, M. Interaction analysis of four Chemotherapeutic Drugs vs. Nitrogenous Bases of DNA and RNA, using Quantum Methods. World Journal of Pharmaceutical Research. 2016; 5(6): 309-320.
11. Cabrera-Lara, M. D. R. L., Cortazar-Moya, S., Rojas-Morales, E., del Carmen Palma-Ruanova, L., & González-Pérez, M. Molecular Interactions Of Glucose, Metformin, And Water Using Improved Quantum Methods. World Journal of Pharmacy and Parmaceutical Sciencie, 2016; 5(11): 1675-1686.
12. Fernandez-Ibanez, P., Malato, S., & De Las Nieves, F. J. Oxide/electrolyte interface: Electron transfer phenomena. Boletín de la Sociedad Española de Cerámica y Vidrio, 2000; 39(4): 498-502.
13. Van der Ham, C. J., Koper, M. T., & Hetterscheid, D. G. Challenges in reduction of dinitrogen by proton and electron transfer. Chemical Society Reviews, 2014; 43(15): 5183-5191.
14. Amini, A., & Harriman, A. Computational methods for electron-transfer systems. Journal of Photochemistry and Photobiology C: Photochemistry Reviews, 2003; 4(2): 155-177.
15. Kitsy A., Carney S., Vivar J., Knight M., Pointer M., Gwathmey J., Ghosh S. Effects of Leucine Supplementation and Serum Withdrawal on Branched-Chain Amino Acid Pathway Gene and Protein Expression in Mouse Adipocytes. PLoS ONE, 9(7): e102615.