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TOXOPLASMA GONDII: KYNURENIC ACID QUANTUM ANALYSIS IN NEUROTRANSMITTERS

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ABSTRACT

Toxoplasma gondii (TG), a Protozoan parasite intracellular, which causes disorders that affects the brain and has been linked to the disease of schizophrenia. Infection with Toxoplasma gondii stimulates the degradation of tryptophan and is involved in producing neurodegenerative metabolites such as the kynurenic acid. The objective of the study is to determine, using the quantum semi-empirical method parametric (SE-PM3/1), which neurotransmitter has a higher affinity with the acid kynurenic, so understanding the neuronal oxidative effect. Hyperchem Professional software performed Molecular Modelling and analysis of the molecules of cGMP/AMPc and 9 of the major neurotransmitters. (Hyperchem, Hypercube, Multi on for Windows, series 12-800-1501800080. Multi On, southern 1236 -301 Tlacoquemecatl insurgent Col. del Valle, Mexico, Benito Juárez,

CP 03200). The result of simulations of quantum wells reveals that this metabolite is a likely media, which can oxidize the neurotransmitter Adrenaline.

KEYWORDS: Neurotransmitters, Toxoplasma Gondii, Quantum Method, Hyperchem, SE-PM3.

INTRODUCCTION

The TG is an intracellular parasite obliged, without the specific host (eurixeno);[1] its size varies according to the organ where appropriate, between 2-12 micrometers.[2] This parasite has developed several potential routes of transmission include sporozoites, coming from the feces of cats infecting; the Bradyzoites in tissue and cysts the Tachyzoites which are free parasites that infect the fetus[3] directly. It is estimated that you infect chronic way at approximately one-third of the world's population, with a higher incidence in tropical areas with environmental and cultural conditions that favor transmission.[2,4]

For some years, has collaborated with the TG with schizophrenia, psychiatric disorders, disorders of behavior and other neurological diseases.[5,6,7,8] Recent studies using magnetic resonance imaging techniques have revealed that toxoplasmosis in schizophrenic produces specific morphological changes in some regions of the brain (occipital cortex, thalamus, and cerebellar hemisphere left) of patients, and that alters the levels of various neurotransmitters.[9]

For studies in rodents infected with TG, are changes in behavior that forces them to interact with cats to be eaten.[10] The mechanisms responsible for the changes in the behavior of the carrier are unknown, but some evidence suggests that the parasite alters neurotransmitters[11] signal transduction and infects neurons in the nervous system.[12] It has been reported that TG infection increases the levels of kynurenic acid (KYNA) in the brains of infected mice; it has also been shown that this metabolite of tryptophan is present in schizophrenia.[13,14,15,16]

The objective of this study is to determine, using the quantum parametric semi-empirical method (SE-PM3/1), that neurotransmitter has a high affinity for the metabolite KYNA, to understand the TG neurodegenerative effects. In this study were analyzed nine neurotransmitters which they are: Adrenaline, Serotonin, Dopamine, GABA, Glutamic acid, Histamine, Glycine, Norepinephrine, and Acetylcholine.

Hyper Chem 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 transfer of electrons (ETC) of every interaction coefficient.

The theory of ETC is based on defining the band gap or Bandgap (BG), which is the energy difference between the valence band and the conduction band. In quantum theory, it is known as HOMO and LUMO, and in the old theory known as E_- and E_+. On the other hand, the quantum well is defined as the area in which can drop the value of, ETC. These areas are divided into 3 Zones (fig.1). The area of high probability (zone I), two. The area's average probability (ZONE II), 3. the area of low-probability (zone III).[17,18]

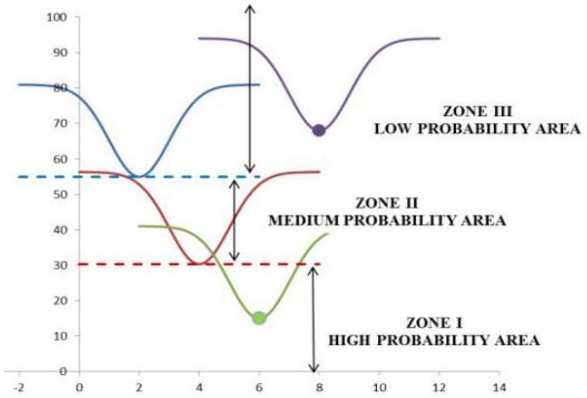


Figure 1: Areas of probability in quantum well, according to the ETC´s theory.

MATERIAL AND METHOD

The metabolite KYNA simulation was carried out through the Software Hyperchem (Hypercube, Multi on for Windows, series 12-800-1501800080 Multi On, South 1236-301 Col. Insurgentes Tlacoquemecatl del Valle, Benito Juárez, the city of Mexico, Mexico CP 03200). The simulation was carried out using the Semiempirical method for the calculation of the BG, the electrostatic potential (EP), ETC. When drawing the entire molecule, the values of HOMO (-), LUMO (+), E - and E + are obtained, in value to zero and a density of 0.015. The values that are recorded is captured in an Excel sheet, and he will be performing operations for BG, EP, etc. To get the cross-band of the compounds is taking the HOMO and E - of the first compound and the value of LUMO and E + the second compound. Lower transverse band ETC will be the value which determined what compound will be more reactive and will serve as data to be placed in the quantum well graphics to set the boundaries

of graphics, wholesale ETC will be placed in the upper limit and lower ETC, the lower limit of the compounds to compare.[18,19]

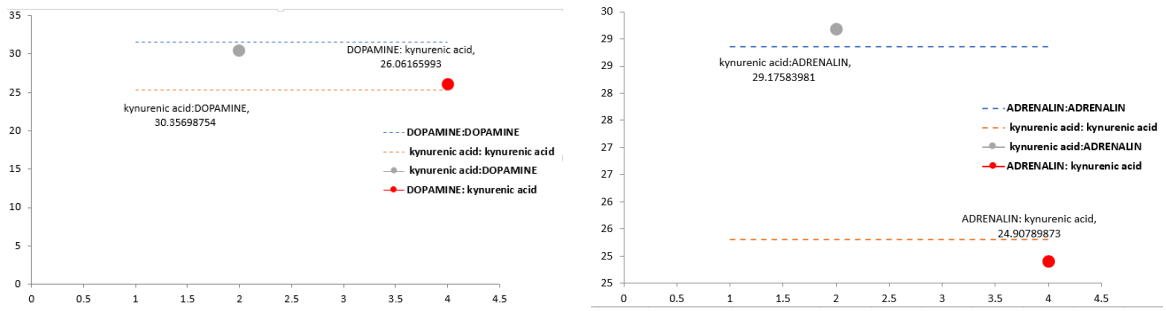
RESULTS AND DISCUSSION

Table 1 shows the interaction of KYNA against vital neurotransmitters with their respective ETC´s, stressing that the adrenaline and dopamine presented one minor for electrons jump power.

Table 1: KYNA vs Neurotransmitters.

Antioxidant	Oxidant	HOMO	LUMO	BG	E-	E+	EP	ETC
kynurenic acid	ACETYLCHOLINE	-9.302858	1.034277	10.337135	-0.124	0.105	0.229	45.1403275
kynurenic acid	NORADRENALINE	-9.302858	-0.00427538	9.29858262	-0.124	-0.222	0.098	94.8834961
kynurenic acid	GLUTAMIC ACID	-9.302858	0.5059321	9.8087901	-0.124	0.161	0.285	34.4168074
kynurenic acid	GLYCINE	-9.302858	0.8744405	10.1772985	-0.124	0.188	0.312	32.6195465
kynurenic acid	HISTAMINE	-9.302858	0.675378	9.978236	-0.124	0.163	0.287	34.7673728
kynurenic acid	GABA	-9.302858	0.9385893	10.2414473	-0.124	0.18	0.304	33.6889714
kynurenic acid	***DOPAMINE***	***-9.302858***	***0.1988791***	***9.5017371***	***-0.124***	***0.189***	***0.313***	***30.3569875***
kynurenic acid	SEROTONIN	-9.302858	-0.1294475	9.1734105	-0.124	0.141	0.265	34.6166434
kynurenic acid	***ADRENALIN***	***-9.302858***	***0.09176242***	***9.39462042***	***-0.124***	***0.198***	***0.322***	***29.1758398***

Below is the interaction of Adrenaline and Dopamine and KYNA in quantum wells (Figure 1), showing that there is a low probability of oxidation in the case of adrenaline and a mean for dopamine probability.



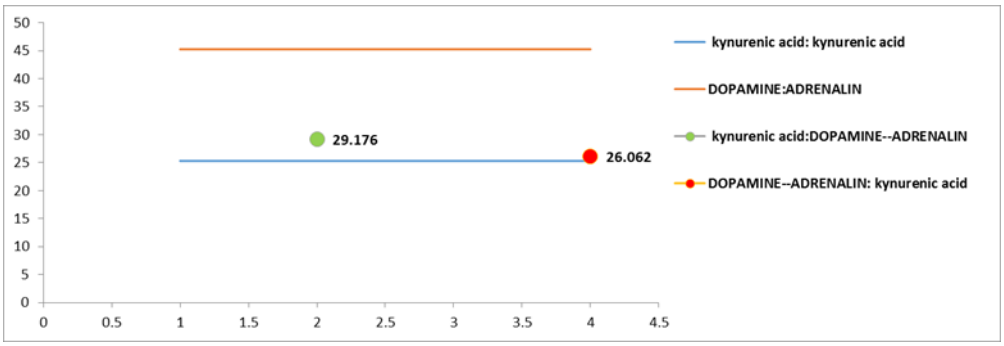
Graphic 1. Quantum well of KYNA vs Adrenaline & Dopamine.

Other interactions are cross bands of neurotransmitters with KYNA, crossbands simulate the interaction between the same neurotransmitters from the simulated substances, allowing you to analyze the molecular combination most likely oxidized or reduced. The results of cross banding can be appreciated in table 2.

Table 2: KYNA vs bands crusades of Neurotransmitters.

Antioxidant	Oxidant	HOMO	LUMO	BG	E-	E+	EP	ETC
kynurenic acid	ADRENALIN--ADRENALIN	-9.3029	0.0918	9.3946	-0.124	0.198	0.322	**29.1758**
kynurenic acid	SEROTONIN--ADRENALIN	-9.3029	0.0918	9.3946	-0.124	0.198	0.322	**29.1758**
kynurenic acid	DOPAMINE--ADRENALIN	-9.3029	0.0918	9.3946	-0.124	0.198	0.322	**29.1758**
kynurenic acid	GABA--ADRENALIN	-9.3029	0.0918	9.3946	-0.124	0.198	0.322	**29.1758**
kynurenic acid	GLUTAMIC ACID--ADRENALIN	-9.3029	0.0918	9.3946	-0.124	0.198	0.322	**29.1758**
kynurenic acid	GLYCINE--ADRENALIN	-9.3029	0.0918	9.3946	-0.124	0.198	0.322	**29.1758**
kynurenic acid	HISTAMINE--ADRENALIN	-9.3029	0.0918	9.3946	-0.124	0.198	0.322	**29.1758**
kynurenic acid	NORADRENALINE--ADRENALIN	-9.3029	0.0918	9.3946	-0.124	0.198	0.322	**29.1758**
kynurenic acid	ACETYLCHOLINE--ADRENALIN	-9.3029	0.0918	9.3946	-0.124	0.198	0.322	**29.1758**

The cross bands (table 2), shows all combinations with adrenaline to give a 27.1758 ETC, which indicates that any combination that comes with this neurotransmitter will have the same possibility of being oxidized by KYNA. In chart 2 below quantum wells, where you can see that interaction falls into the area of average probability.



Graphic 2: Quantum well of KYNA vs Adrenalin & Dopamine.

CONCLUSIONS

We can say that KYNA presents an average probability for it can corrode adrenaline and other neurotransmitters. There are several studies regarding the impact of this substance in the brain of rats, without reaching conclusive results. We believe that a more precise picture gives the quantum simulations to determine the probability that there is a substance to alter some neurotransmitter. In our case, we can say that this substance can activate some mechanisms that cause neuronal damage associated with schizophrenia. It is necessary to investigate further the effects of the neurotoxic segregated by various microorganisms since today found that many neurological diseases are related to altered microbiota.

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