WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 8, 234-240. Research Article ISSN 2277– 7105

ANALYSIS OF INTERACTIONS OF NEOTAME AND NITROGENOUS BASES OF DNA AND RNA USING QUANTUM METHODS

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Article Received on
12 June 2016,

Revised on 04 July 2016,
Accepted on 25 July 2016

DOI: 10.20959/wjpr20168-6839

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ABSTRACT

Neotame is a 3, 3-dimethyl substituted N-butyl group containing aspartame structural derivative. Neotame has a capacity of 7,000 to 13,000 times sweeter than sugar. The intake of sugary drinks (SD) is a concern in Mexico since 2012. Mexico ranked the first world ranking in consumption of sugary beverages. The simulation was Elaborated using HyperChem molecular simulation. The specific parameters selected for each of the simulations were done by Semi- Empirical Method (SE-PM3). The cross bands of neotame and nitrogenous bases of DNA and RNA. G: Neo shows an ETC of 24.648, it is the lowest, followed by A: Neo with 25.718 and C: Neo with 26.738 indicating increased stability, unlike other interactions. A bit ETC shows a high probability that the compounds bind. The interaction Neo: A, shows an ETC of 33.946 is unlikely to join. Because of the results indicate that the quantum simulation of Neotame vs. Nitrogenous bases of DNA and RNA is possible that neotame will be a precursor to cancer.

KEYWORDS: Neotame, Nitrogenous bases, Quantum interaction, Quantum methods.

INTRODUCTION

Neotame is a 3,3-dimethyl substituted N-butyl group containing aspartame structural derivative. Neotame has a capacity of 7,000 to 13,000 times sweeter than sugar.[1] Caloric

sweeteners aspartame, neotame, sucralose, and stevia are ingredients in many foods. These sweeteners reduce the energy content without reducing the sweetness.[2, 3] Neotame is in carbonated or noncarbonated drinks, energy drinks, juices, and nectars.[4, 5, 6]

The intake of sugary drinks (SD) is a concern in Mexico since 2012. Mexico ranked first world ranking in consumption of sugary drinks.[7] Table 1 show the consumption of sugary drinks by Mexican Children.

Table 1. Consumption of sugary drinks by Mexican children.[8]

Age (years)	Consumption per day (L)
1 to 4	0.810
5 to 11	1,040
12 to 19	1,400

Medical do not recommend neotame consumption and Stevia for the children.[9, 10]

Eating foods with sweeteners like neotame increases the risk of disease. Excessive weight gain, metabolic syndrome, diabetes and cardiovascular disease, type 2, are related to the consumption of sweeteners.[11] A third of cancers in Western countries are attributable to food consumption, nutrition, and physical activity factors.[12, 13]

ETCs values and 36 possible combinations of NB forming the theory of DNA and RNA and published before. The difference between the ETC of the 36 possible combinations of six NB is 10,620. The difference between the cross bands is only 2.38. Because of these differences, mutations are easily produced, and 88.88% of these combinations[14] is not allowed.

Quantum Chemistry has computational methods based on the identification of the most stable molecular systems that knowledge of chemistry, in general, is not enough to make definitive predictions.[14]

The principles of quantitative structure-activity relationships (QSAR) could be extended to improve the physicochemical structural indices. Molecular fragments or other design provide detailed maps of biological and chemical interactions.[15] The surfaces of the interaction of DNA[16] and protein can be identified using the computer.[17, 18]

The aim of this study is to investigate the interactions of neotame against the nitrogenous bases of DNA and RNA using the PM3 quantum method.

METHODOLOGY

a. Abbreviations

Highest Occupied Molecular Orbital (HOMO). Lowest Unoccupied Molecular Orbital (LUMO). Band Gap (BG), Negative Energy (E-). Positive Energy (E+). Electrostatic Potential (EP). Electronic Transfer Coefficient (ETC). Uracil Tautomer 1 (UT1). Uracil Tautomer 2 (UT2) figure 1.

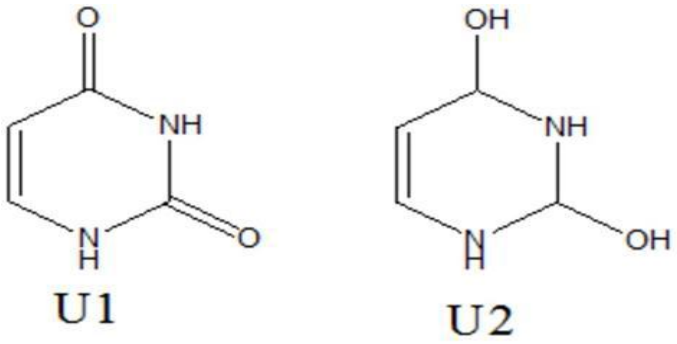

Fig. 1. Tautomers of U. U tautomer U T1 has ketone links. U tautomer U T2 has hydroxyl links.[20]

b. Computational Methods: The simulation was Elaborated using HyperChem molecular simulation (HCL). (Hyper Chem. Hypercube, MultiON for Windows. Serial #12-800-1501800080. MultiON. Insurgentes Sur 1236 - 301 Tlacoquemecatl Col. del Valle, Delegación Benito Juárez, D. F., México CP. 03200.[19]

The computational model was; HC Semi-Empirical Parameterized Model number 3 (SE-PM3) to draw the corresponding molecules. The data processed by SE-PM3. The geometry is optimized with Polak Ribiere method. The computational quantum chemistry variables were calculated: HOMO-LUMO, BG, EP and other properties, resulting in a delimited table tab for BG and EP.[19]

The specific parameters selected for each of the simulations were as follows: SET UP. Semi-Empirical Method: PM3. Semi-Empirical Options: Charge and Spin. Total Charge 0. Spin Multiplicity 1. SCF Control. Converge limit 0.01. Interaction limit 1000. Accelerate converge Yes. Spin Pairing Lowest. Overlap Weighting Factors Sigma-Sigma 1, Pi-Pi 1. Polarizabilities do not calculate.

Computation 1. Geometry Optimization. Algorithm Polak Ribiere (conjugate gradient). Options Termination conditions. RMS gradient of 0.1 kcal/mol or 1000 maximum cycles. In vacuo yes. Screen refresh period one cycles.

Computation 2. Orbitals. Plot Orbital Options Isosurface Rendering. Orbital Contour Value 0.05. Rendering Wire meshes Isosurface Grid. Grid meshes size Coarse. Grid layout Default. Gird contour Default. Transparency level Default.

Computation 3. Plot Molecular Graphs. Plot Molecular Options. Molecular Properties. Properties. Electrostatic Potential Yes. Representations. 3D Mapped Isosurface. Grid Mesh Size Coarse. Grid layout Default. Contour gird Default. Isosurface Rereading. Total Charge Density Contour Value (TCDCV) 0.015. Rendering Wire mesh. Transparency level Default. Mapped Options Functions Default.[19, 20]

c. Formulas: The quantum calculation based on the theory ETC.[15] This theory is calculating the ratio of dividing the BG / EP. This ratio indicates the multiples of the EP that the electron jumps its BG.

$$\mathrm{ETC} = \left|\frac{BG}{EP}\right| \qquad (1)$$

The EP is equal to the absolute value of the difference (E+) – (E-).

$$\mathrm{EP} = |E_+ - E_-| \qquad (2)$$

The BG is equal to the absolute value of the difference (HOMO) – (LUMO).[14, 19]

$$\mathrm{BG} = |HOMO - LUMO| \qquad (3)$$

RESULTS

Table 2. Electronic interactions between molecules of the same chemical species

Interaction number	Gives Electron cloud	Get Electron cloud	HOMO (eV)	LUMO (eV)	BG (eV)	E- (eV/a0)	E+ (eV/a0)	EP (eV/a0)	ETC [a]
I	G	G	-8.537	-0.206	8.331	-0.150	0.172	0.322	25.872
II	C	C	-9.142	-0.344	8.799	-0.174	0.161	0.335	26.265
III	U2	U2	-9.910	-0.415	9.495	-0.147	0.202	0.349	27.208
IV	A	A	-8.654	-0.213	8.441	-0.140	0.156	0.296	28.518
V	T	T	-9.441	-0.475	8.966	-0.123	0.169	0.292	30.707
VI	U1	U1	-9.710	-0.511	9.200	-0.126	0.171	0.297	30.975
VII	**Neo**	**Neo**	-9.684	0.09	9.774	-0.123	0.2	0.323	30.260

Source: Gonzalez-Perez 2016[20]

Table 3. Cross Band neotame sweetener and nitrogenous bases.

COMBINATIONS		HOMO	LUMO	BG	E-	E+	EP	ETC
GUANINE	NEOTAME	-8.537	0.090	8.627	-0.150	0.200	0.350	24.649
ADENINE	NEOTAME	-8.654	0.090	8.744	-0.140	0.200	0.340	25.718
CYTOSINE	NEOTAME	-9.910	0.090	10.000	-0.174	0.200	0.374	26.738
NEOTAME	URACIL T2	-9.684	-0.415	9.269	-0.123	0.202	0.325	28.520
URACIL T2	NEOTAME	-9.910	0.090	10.000	-0.147	0.200	0.347	28.818
TIMINA	NEOTAME	-9.441	0.090	9.531	-0.123	0.200	0.323	29.508
URACIL T1	NEOTAME	-9.710	0.090	9.800	-0.126	0.200	0.326	30.061
NEOTAME	NEOTAME	-9.684	0.090	9.774	-0.123	0.200	0.323	30.260
NEOTAME	URACIL T1	-9.684	-0.511	9.173	-0.123	0.171	0.294	31.201
NEOTAME	TIMINA	-9.684	-0.475	9.209	-0.123	0.169	0.292	31.538
NEOTAME	GUANINE	-9.684	-0.206	9.478	-0.123	0.172	0.295	32.129
NEOTAME	CYTOSINE	-9.684	-0.344	9.340	-0.123	0.161	0.284	32.887
NEOTAME	ADENINE	-9.684	-0.213	9.471	-0.123	0.156	0.279	33.946

Table 2 presents the cross bands of neotame and nitrogenous bases of DNA and RNA. G: Neo shows an ETC of 24.648, it is the lowest, followed by A: Neo with 25.718 and C: Neo with 26.738 indicating increased stability, unlike other interactions. A bit ETC shows a high probability that the compounds bind. The interaction Neo:A shows an ETC of 33.946 is unlikely to join.

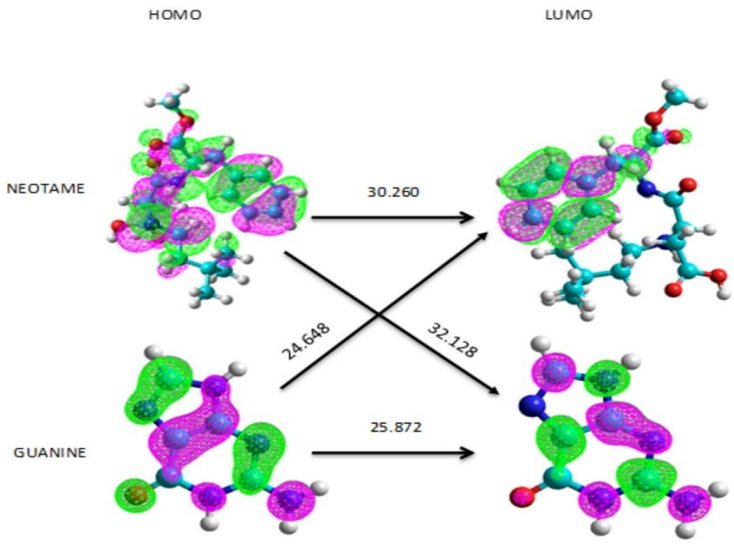

Fig. 2 Shows the guanine interaction: neotame with the value of 24,648 and is the lowest of the cross bands.

CONCLUSIONS

Because of the results show that the quantum simulation of Neotame vs. Nitrogenous bases of DNA and RNA is possible that neotame will be a precursor to cancer.

It was found that the interaction most likely is G:Neo with an ETC of 24.648. The interplay G: Neo indicates that these two substances come together at a particular time. The Interactions A: Neo and C: Neo has similar values.

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