Semi-Empirical Study Of Rotenone Stemonone: HOMO, LUMO and Reactivity Descriptors

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Abstract— Agricultural evolution is directly related to the transformations of land and tools created. One of these tools is the use of agrochemicals to combat pests in order to increase productivity in order to obtain the highest possible profit. It is currently looking for new compounds less aggressive to human health and the environment that are efficient in pest control. In this context, the Clitoria fairchildiana arises, a tree native to Brazil, popularly called a hat, used in the forestation of squares, gardens and roads. In its composition it presents rotenones that have crystalline, colorless and odorless characteristics with pesticidal properties. One of the rotenones present in Clitoria fairchildiana is Stemonone, aromatic compound with molecular formula C19H14O8. The aim of this work is the initial characterization of rotenone stemonone, through semi-empirical calculations. It was possible to generate the table of chemical properties of rotenone Stemonone, such as electronegativity, ionization potential, chemical hardness, chemical sofness, electronic chemical potential and electrophilicity index. The data generated in this work consists of an initial step to serve as a basis for future studies on the relationships between the three-dimensional structure of rotenone and its biological activities.

Index Terms— *Agriculture, Agrotoxics, Rotenone, Stemonone, characterization.*

1 INTRODUCTION

One of the oldest activities developed by humans is agriculture, since it is carried out from the Neolithic period. Agricultural evolution is directly related to the transformations of land and tools created. One of these tools is the use of agrochemicals to combat pests in order to increase productivity in order to obtain the highest possible profit [1].

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Agrochemicals are agents consisting of a large variety of primarily chemical compounds designed to kill, combat and control specific processes, such as growth regulators. However, they cause harm to human health and the environment [2]. There are an estimated 3 million cases of poisoning annually in the world, with 220,000 deaths [3]. We are currently looking for new compounds that are less aggressive to human health and the environment, which are efficient in pest control.

In this context, the *Clitoria fairchildiana* arises, a tree native to Brazil, used in the forestation of squares, gardens and roads. In its composition it presents rotenones that have crystalline, colorless and odorless characteristics with pesticidal properties [4]. One of the rotenones present in *Clitoria fairchildiana* is the stemonone, aromatic compound with molecular formula C19H14O8 [5].

Currently, the molecular modeling allows structural and electron characterization [6] [7], the molecule of interest, as well as identifying the interaction sites, electro-donor regions, electro-receptors, making it possible to carry out structure-activity relationship (SAR) studies [8], generating data relevant to the study and planning of the use of new molecules [9] [10].

In this context, the present work aimed to characterize rotenone stemonone, generating data for future development studies of new molecules and molecular docking studies.

2 METHODOLOGY

The methodology used was modified from the methodology used by Dewar et al. [11], where the two-dimensional structure of the stemonone was initially obtained in the PubChem virtual repository © https://pubchem.ncbi.nlm.nih.gov/] [12] and physicochemical properties of rotenone stemonone in the

ChemSpider virtual repository [13]. Then the MarvinSketch © code [14] was used for the calculation of pKa. In order to perform the electronic / structural characterization a conformational analysis was performed using the code ArgusLab © [15] [16] [17] [18], configured to perform semi-empirical calculations (based on the theory of quantum mechanics with Hamiltonian PM3 [19] [20]). After the optimization, the single point calculations were performed to obtain the dipole moment, electrostatic potential map, electron density map, HOMO and LUMO orbital and heat of formation, Mulliken atomic charges.

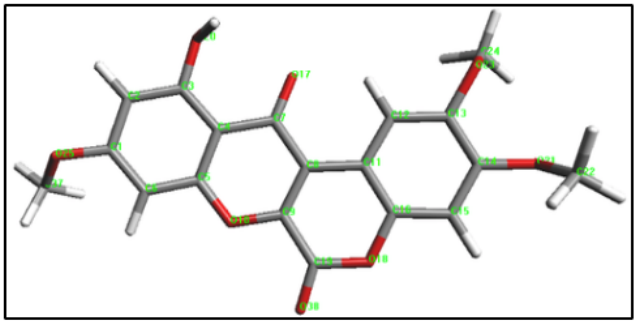

Figure 1: Three-dimensional structure of rotenone stemonone

3 Results and Discussions

In the ChemSpider© virtual repository, we obtain some physico-chemical properties of rotenone stemonone (Table 1) that are of paramount importance for the study of molecular modeling. Among these properties we can mention the polarizability (35.6 ± 0.5 10^{-24} cm^3), because the greater the increase in polarizability the greater the polar character of the species and the LogP (2.04) that refers to the lipophilicity of the compound from an octanol system / water, and the lower the more hydrophilic value will be the compound [21].

Table 1: Physical-chemical properties of the stemonone, taken from the ChemSpider virtual repository.

Properties Name	Value of properties
Density	1,5 ± 0.1 g / cm^3
Boiling point	628.5 ± 55.0 ° C a 760 mmHg
Steam pressure	0.0 ± 1.9 mmHg a 25 ° C
Enthalpy of Vaporization	96.4 ± 3.0 kJ / mol
Flash point	231.2 ± 25,0 ° C
Refractive index	1.673
Molar Refractivity	89.7 ± 0.4 cm^3
Connection Acceptors #H	8
Donors of titles	1
Freely rotating connection	3
Polar surface area	101 Å2
Polarisability	35.6 ± 0.5 10 -24 cm^3
Superficial tension	72.1 ± 5.0dine / cm
Molar Volume	239.3 ± 5.0 cm^3
LogP	2.04
ACD / LogD (pH 5.5)	2.96

Drawing a molecule three-dimensionally or withdrawing it from an online repository, it is not found with a more stable conformation, requiring a geometric optimization for the fidelity of the minimum energy calculations possible to find the most stable structure [22]. Therefore, using the ArgusLab® program [15], it was possible to design the three-dimensional structure (Figure 1) and perform geometric optimization calculations of stemonone, generating -111009.5782 kcal / mol as the lowest and stable energy.

The calculations of energies, based on the Hamiltonian PM3 in order to obtain the electron density map, Homo orbitals (Highest Occupied Molecular Orbital) and Low Unoccupied Molecular Orbital (LUMO), heat of formation and atomic charges of Mulliken. We obtained that the heat of formation is -223.8274 kcal / mol, dipole moment is equal to 3.68827466 D and the orbitals 69 and 70 represent HOMO with value -9.24864 eV and LUMO with value -1.68833 eV, respectively. The border orbitals are descriptors that act as an intermediate of the stability of the structures and of the chemical reactivity of the molecule [23]. Since they are information about fundamental characteristics of the chemical reactivity, such as ionization potential, electronegativity, hardness and softness of the molecule, electronic affinity, electronic potential among others (Table 2) [24]. Electronegativity and molecular hardness help predict the formation of chemical bonds and the physical and chemical properties of the substance [25] [26]. The electron affinity is the energy change when a neutral atom in the gaseous state and the ionization potential according to Koopman's theory can be used in the Density Functional Theory (DFT) method [27].

Table 2: Chemical properties found from the boundary orbits HOMO and LUMO

Parameters	Values
HOMO	-9.24864 eV
LUMO	-1.68833 eV
Electronic affinity	1.68833 eV
Vertical ionization potential	9.24864 eV
Electronegativity	5,46848 eV
Chemical hardness	0,138918 eV
Chemical softness	3,78015 eV
Electronic chemical potential	-5,46848 eV
Electrophilicity index	3,95542 eV

The HOMO orbital, or higher occupied molecular orbital, is directly associated with the electrospray character of a compound and the LUMO orbital, or lower free-energy molecular orbital is directly associated with the electron-acceptor character of a compound [28]. The difference between the values of the border orbitals, called GAP, is the most important in determining the chemical stability. The molecules have larger

band gaps, making them more stable. Those with smaller gaps are reactive, due to the ease in interacting with the reagents [25]. The GAP obtained a -7.56031 eV. They are shown by HOMO (Figure 2) and LUMO (Figure 3) with the positive phases represented in blue and negative in red. We can highlight the symmetry, since both the HOMO orbital showed to be symmetrical between the positive and negative phases as the LUMO orbital was shown to be symmetrical.

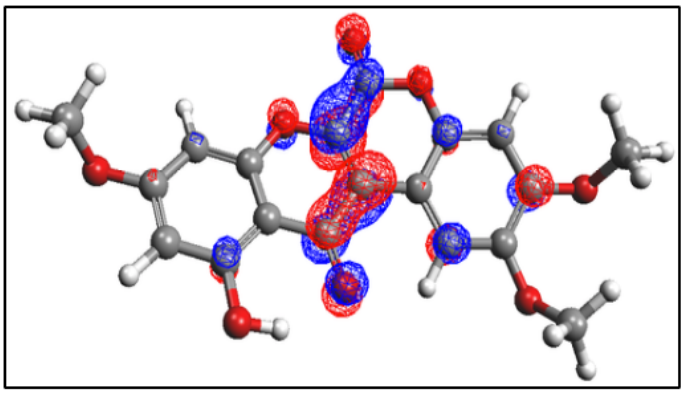

Figure 2: Representative image of the positive and negative phases of the HOMO orbital of rotenone stemonone

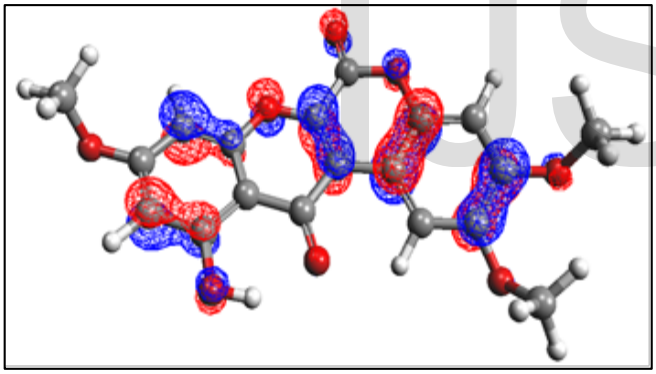

Figure 3: Representative image of the positive and negative phases of the LUMO orbital of rotenone stemonone.

The atomic charges are important in the correlational study between the structure of the molecule and its biological activity, because the charge density of a chemical species describes the distribution of the electrons responsible for the chemical behavior of each species. For the calculation of atomic loads, we used the Mulliken Population Analysis, or simply Mulliken's atomic charges (Table 3). This method divides, regardless of electronegativity, the charge density between two atoms uniformly. Table 3 shows that there were variations of the atoms of the same element, since the oxygen with the highest charge was O9 with -0.0684 and lower with O14 with -0.3738. The highest value carbon was C12 with 0.4582 and lower C3 value with -0.3294. The lowest value hydrogen was H41 with -0.3294 and higher value was H33 with 0.2868.

Table 3: Mulliken atomic charges for the C, O and H atoms of rotenone stemonone

ATOMS	CHARGES	ATOMS	CHARGES
O1	-0.2154	C22	-0.2573
C2	0.1765	O23	-0.3057
C3	-0.3294	O24	-0.1928
C4	0.2474	C25	-0.1477
C5	-0.3893	O26	-0.1913
C6	0.1728	C27	-0.1453
C7	-0.3227	H28	0.2460
C8	-0.1396	H29	0.2477
O9	-0.0684	H30	0.1198
C10	0.0143	H31	0.0938
C11	-0.1416	H32	0.0933
C12	0.4582	H33	0.2868
O13	-0.2605	H34	0.2559
O14	-0.3738	H35	0.2373
C15	0.4258	H36	0.0959
O16	-0.1604	H37	0.1208
C17	0.0907	H38	0.0876
C18	-0.0995	H39	0.0952
C19	-0.1459	H40	0.1181
C20	0.0240	H41	0.0903
C21	0.0886		

By calculating the map of electrostatic potential it is possible to identify the areas of higher nucleophilicity and electrophilicity of the stemonone molecule and to calculate the surface of electrostatic potential (figure 4) on the surface of electronic density (figure 5). In analyzing the potential electrostatic map (Figure 6), we can highlight a greater concentration of electrons, red nucleophilic region, in the areas where the oxygen (O1, O9, O13, O14, O16, O23, O24 and O26) are located, but the remainder of the structure is lacking electrons, a white electrolytic region, except for the regions that find rings and cycles formed by the carbons that remain in an area of neutrality in violet color [30].

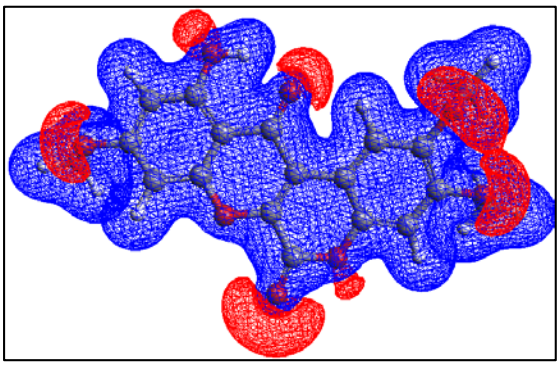

Figure 4: Surface of electrostatic potential of rotenone stemonone

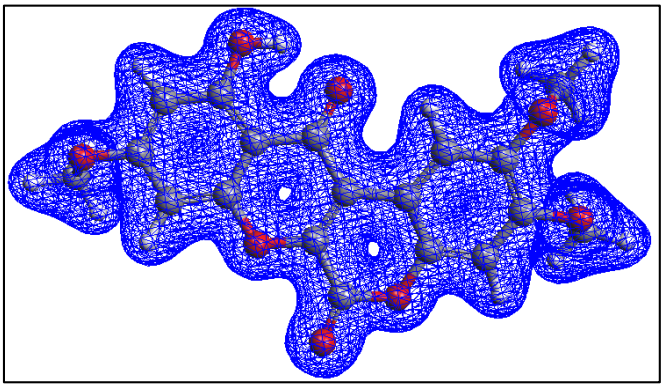

Figure 5: Surface of electronic density of rotenone stemonone

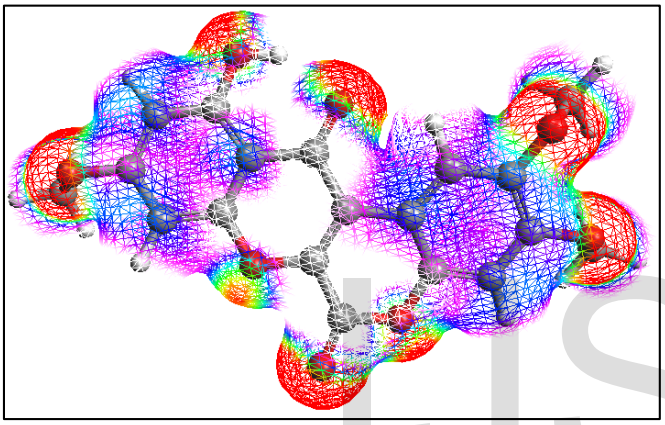

Figure 6: Surface of electronic density of rotenone stemonone

Using the MarvinSketch © software [14], it was possible to calculate the pKa of rotemonone, obtaining the value of 7.28 in the hydroxyl present. This value implies that when at pH 7.28, there will be release of H + from the hydroxyl, leaving the molecule with charge -1, being an important data for future molecular docking studies (Figure 7).

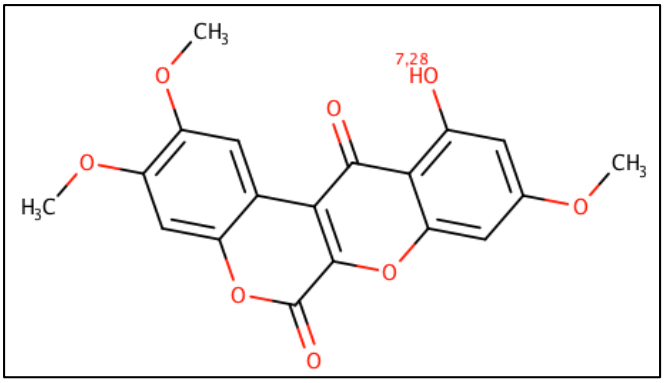

Figure 7: two-dimensional structure and pKa of rotenone stemonone

4 Conclusion

The structure of rotenone Stemonona was geometrically optimized by the ArgusLab® software, based on the semiempirical method and PM3 quantum mechanics, until reaching the point of least potential energy, seeking the most stable and close conformation of its native form, obtaining at the end of the process the energy of -111009.5782 kcal / mol, formation heat of -223.8274 kcal / mol and dipole moment 3.68827466. It was possible to tabulate some molecular properties of rotenone Stemonone, such as electronegativity, ionization potential, chemical hardness, chemical sofness, electronic chemical potential and electrophilicity index. Through the map of electrostatic potential, it is possible to determine the areas where nucleophilic connections will occur which comprises all areas of the oxygen. With the geometrization it is possible to obtain the atomic charges of Mulliken for the atoms of C, H and O, highlighting the variation of charges between atoms of the same element.

The data generated in this work consists of an initial step to serve as a basis for future studies of the relationships between the three-dimensional structure of rotenone and its biological activities.

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