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Computational Study of Doping in Dopamine with Halogens to Control Optical and Spectroscopic Properties

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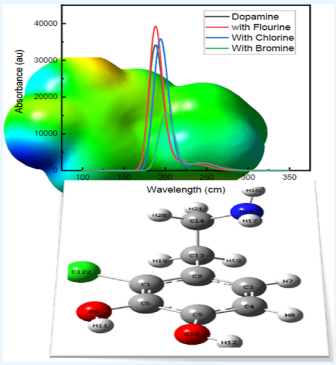
ABSTRACT: In this research, a comprehensive study of dopamine was conducted using the theoretical first principles method due to its crucial importance as a hormone for the neurotransmission process in the animal body. Many basis sets and functionals were used for optimization of the compound to attain stability and find the appropriate energy point for the overall calculations. Then, the compound was doped with the first three members of the halogen family (fluorine, chlorine, and bromine) to analyze the effect of their presence in terms of change in their electronic properties, such as band gap and density of states, and spectroscopic parameters, such as nuclear magnetic resonance and Fourier transform infrared. It was found that the band gap of the system changes depending on the doping of halogens.



1. INTRODUCTION

One of the main functions of dopamine in animals, especially human beings, is the neurotransmission process, which is the ability to send signals from the brain to nerve cells and vice versa.[1,2] Some researchers suggested that dopamine serves to control memory storage in the brain, controls incoming noise in the body, and regulates human characteristics.[3] Most diseases associated with the brain and nervous systems are related to the malfunction of dopamine in the body. Such diseases include Parkinson's disease (PD), resulting from improper or insufficient release of dopamine into the brain, and Schizophrenia disease (SD), resulting from the change in the level of dopamine in the body system.[4−7] Decreasing dopamine activity in the human and animal bodies results in attention deficit hyperactivity disorder.[8] Nowadays, the majority of the research on dopamine molecules is moving in the direction of developing a sensitive method to analyze dopamine for curing many related diseases,[9−11] and that is why it is important to understand the reactivity, structure, and stability of the dopamine molecule.[12,13] Combined nuclear magnetic resonance (NMR) and density functional theory (DFT) studies give details about electrochemical properties of dopamine and its activity as a neurotransmitter.[14] Neurotransmitters and their metabolites in the human body are all guided by the presence of well-functioning and active dopamine molecules. Dopamine also aids in the production of molecules that have radical potency in the human body to serve as a defense against oxidation of cells in the central and peripheral nervous systems (anti-radical scavenging effect) (see Figure 1).

Dopamine also has anti-radical activity. The molecules with anti-radical potential have a great tendency to reduce oxidative stress in the central and peripheral nervous systems. Dopamine is an optically acive molecule and exists in different forms based on the arrangement of two hydroxyl groups that are attached to the benzene moiety, but in this study D1 dopamine (normal dopamine or L-DOPA) was investigated for its activity as a hormone. It can help the body to develop neurons and also plays a very crucial role in the reward and movement regulation of the nervous system, especially the brain, that has been studied in detail experimentally.[15−19]

Nowadays, the increase in many diseases, such as irregular heartbeats, shortage of breath, and PD, that is happening not only among old people but also in young people is what motivates this study. As the band gap is the threshold for photons to be absorbed, determination of the variation of the band gap will give us a measure of effectiveness of dopamine for curing.[20−27] Research in band gap control can provide a complete control in the activity of the title molecule in the reaction mechanism of the molecule in the human body.[28−34] Free radicals and harmful chemical species in the human body always originate from aerobic metabolism and other processes, like smoking, use of pesticides, herbicides, and drugs, and

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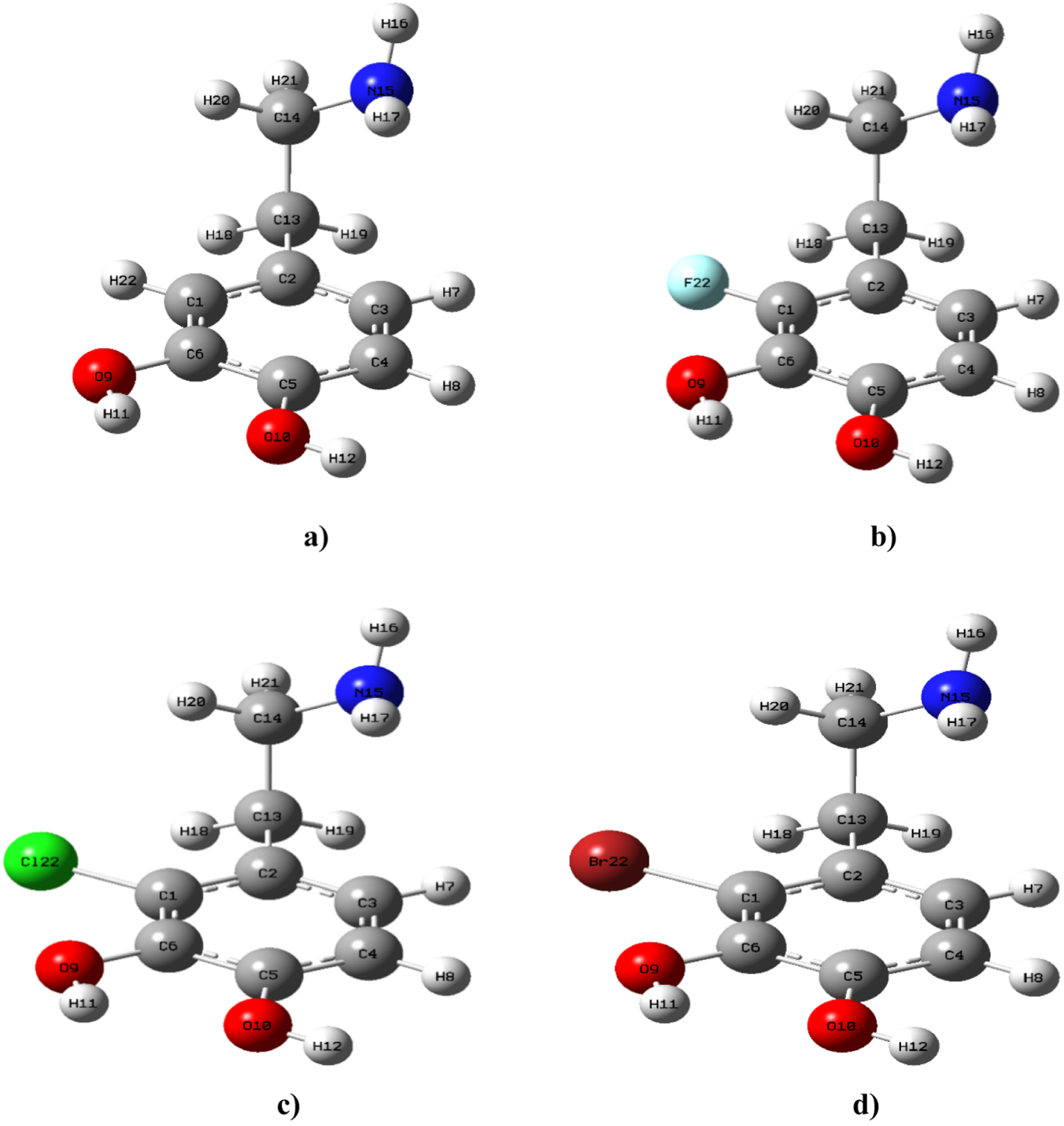

Figure 1. Optimized molecular structures of (a) dopamine, (b) dopamine doped with fluorine, (c) dopamine doped with chlorine, and (d) dopamine doped with bromine.

ionization radiation.[5,35−41] All these process can change the balance of the oxidation−reduction reaction in the body, which leads to problems like hypertension, cancer, cardiovascular diseases, and neurodegenerative disorders such as PD and Huntington's disease.[42−45] That is why this research focuses on improving the efficiency of dopamine activity to produce molecules that will balance oxidants and anti-oxidants present in the body, which will be helpful for curing many detected and undetected diseases. Also, we investigated the behavior of doping of ascorbic acid with halogens and the effect of changes in the band gap when doping took place and concluded that the band gap of ascorbic acid responded to the introduction of halogen atoms based on their position in the electronegative series, thus increasing the effectiveness of ascorbic acid in radical scavenging in the human body.[46]

In this work, the dopamine molecule was doped with the first three members of the halogen family (fluorine, chlorine, and bromine) to analyze their effects on some spectroscopic and electronic properties, such as NMR, Fourier transform infrared (FT-IR) spectroscopy, band gap energy, potential energy map, and density of states (DOS). The obtained theoretical results were compared with those in the literature.

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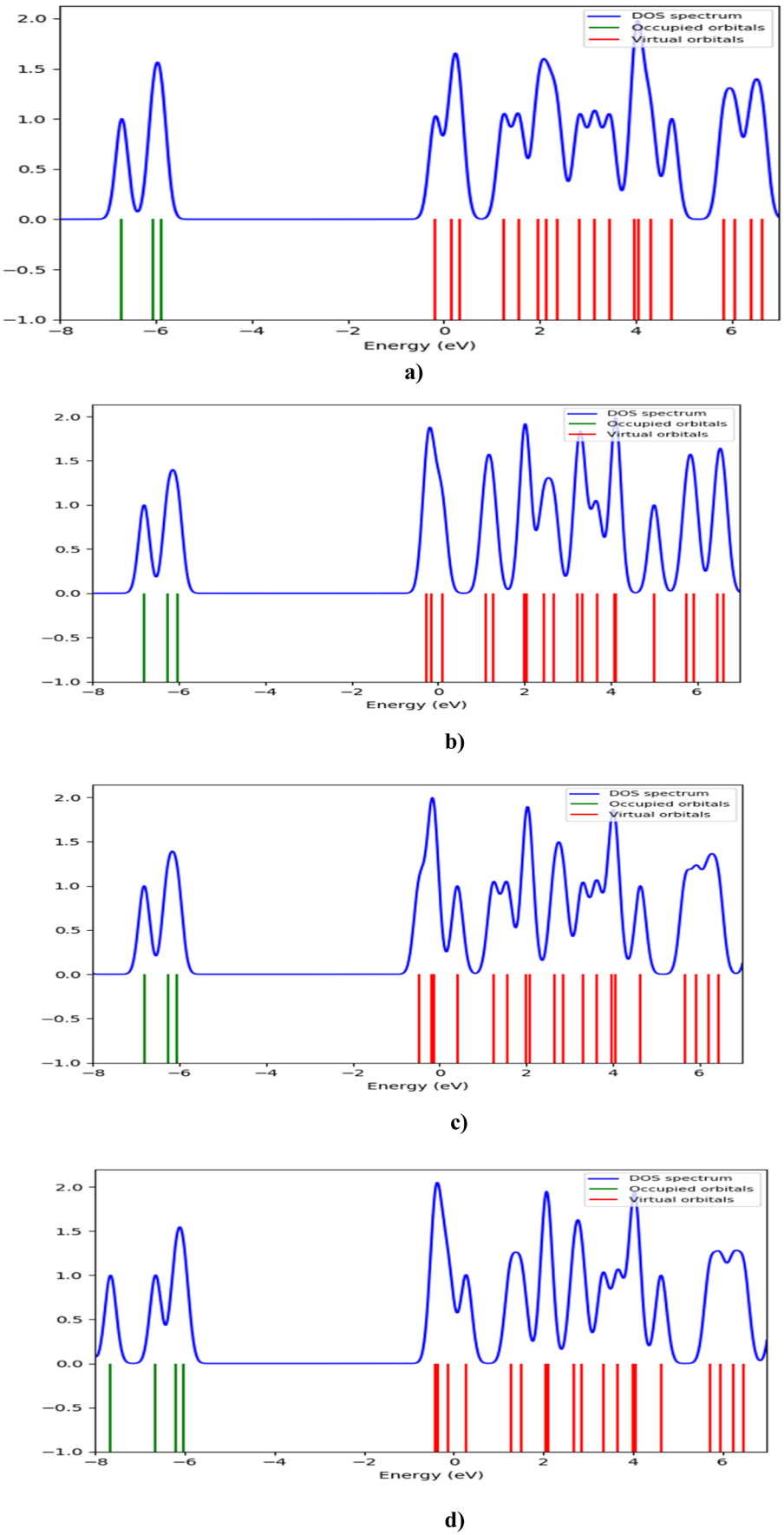

Figure 2. DOS of (a) dopamine, (b) dopamine doped with fluorine, (c) dopamine doped with chlorine, and (d) dopamine doped with bromine.

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2. COMPUTATIONAL PROCEDURE

The dopamine figure was drawn using GaussView 9.0, and two methods were applied to optimize the structure (DFT and Hartree−Fock) using eight basis sets and functionals to achieve convergence and stability of the molecule.[47,48] Different papers implemented the method to describe the geometries and energies of noncovalent systems. The ground state geometry optimization of dopamine was done with DFT using the hybrid functional B3LYP at various basis sets: STO-3G, 3-21G, 6-31G, 6-31G*, 6-311G, LanL2MB, LanL2DZ, and SDD. We found that the energy value for the 6-311G basis set is in harmony with the literature one, which is the main idea behind using it for all the rest of the quantum mechanical calculations. At the end of calculations, the FT-IR results have been multiplied by a factor of 0.2. The frequency calculation was determined using the optimized structure to obtain the minimum on the potential energy surface. Furthermore, the UV is also determined using the optimized structure. The plotting of the three-dimensional mapping of the molecular orbitals is done by the B3LYP/6-311G basis set.[49] At the B3LYP/6-311G basis sets, the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) energies are calculated. All calculations in this paper are performed using the Gaussian 09 program.[50] During the stability check, resonance appears in the benzene ring instead of the conjugated cyclic double bond, indicating a strong bond between the atoms of the molecule after optimization (Figure 2).

The DOS calculations have been obtained with the following equation

$$\mathrm{DOS}(E) = \sum g(E - \varepsilon_i) \quad (1)$$

where g is a function dependent on energy E and ε_I. ε_I is the energy level of the calculated system, which is a function of electronic orbitals.

3. RESULTS AND DISCUSSION

Table 1 explains the comparison between two quantum methods and their basis set (Hartree−Fock and DFT) in order to find a better basis set for the calculation of DOS, atomic orbitals, and other spectroscopic parameters, such as NMR, ultraviolet (UV), and FT-IR. The DFT method along with the 6-311G/B3LYP basis set was selected, and all the calculations were obtained with the basis set (see Table 2).

Table 1. Comparison of Different Methods during Convergence of the Dopamine Molecule

basis set	Hartree−Fock (eV)	DFT (eV)
STO-3G	1.32	0.57
3-21G	3.54	5.07
6-31G	4.43	5.49
6-31G*	4.43	5.49
6-311G	4.81	5.69
LanL2DZ	5.07	5.53
LanL2MB	0.899	0.57
SDD	5.081	5.53

3.1. Frontier Molecular Orbitals. The analysis of molecular orbitals plays a vital role in understanding the band gap and energy distribution in a chemical reaction. Figure 3 depicts the energy distribution of HOMO and LUMO of the

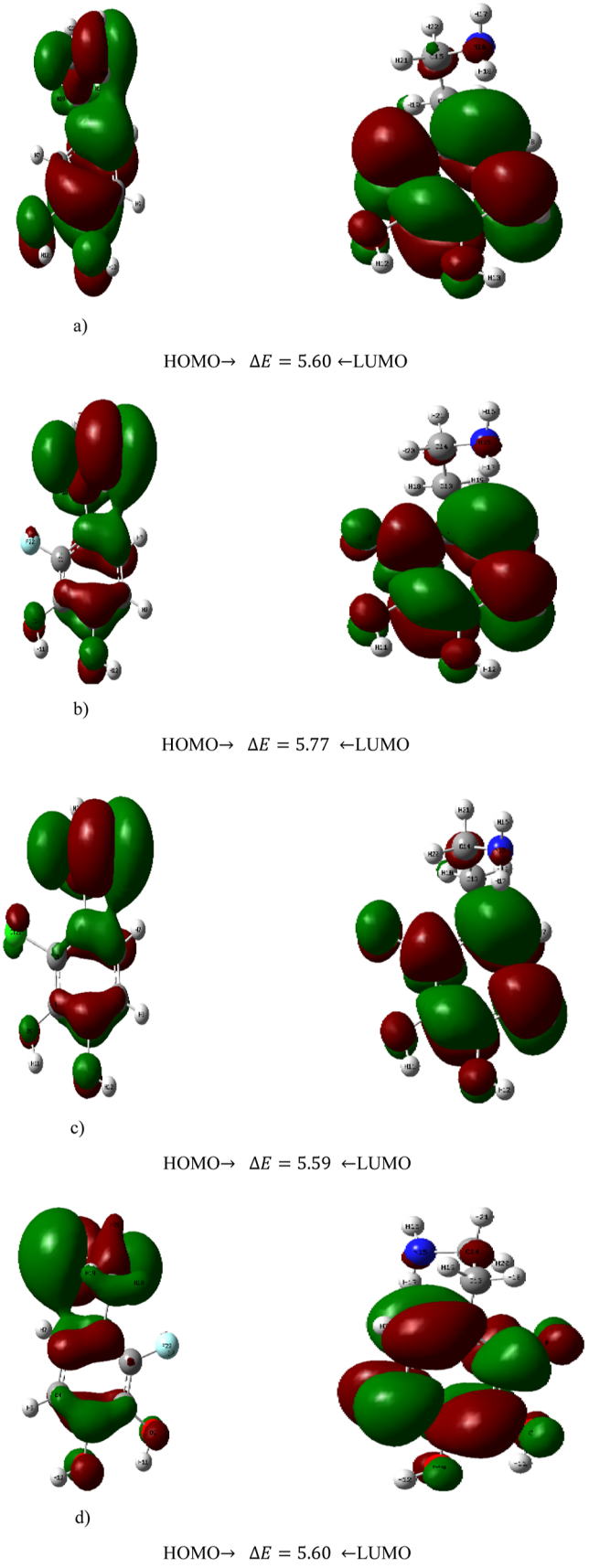

Figure 3. Frontier molecular orbitals of (a) dopamine, (b) dopamine doped with fluorine, (c) dopamine doped with chlorine, and (d) dopamine doped with bromine.

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normal dopamine molecule and dopamine doped with the first members of ascorbic acid. The band gap between the atomic orbitals is used as a pointer for the creation of the relationship between the chemical and biochemical systems.

This calculation proves that the dopamine molecule has 42 molecular orbitals already occupied by the electrons. The HOMO is localized on the benzene ring, while the LUMO is not localized on the benzene ring but close to it. As seen in Figure 3, HOMO − 1 and LUMO + 1 are delocalized on the nitrogen atom. The HUMO−LUMO energy values of dopamine and dopamine doped with the three first members of the halogen family are shown in Figure 3. In the attempt to create a close relationship between the biochemical system and chemical reactions, the band gap energy of HOMO−LUMO is always used as a factor (i.e., quantum chemical descriptor).[49] The doped atoms F, Cl, and Br have their own electronic configurations as $1s^2\ 2s^2\ 2p^5$, [Ne] $3s^2\ 3p^5$, and [Ar] $3d^{10}\ 4s^2\ 4p^5$, respectively. The numbers of electrons and orbitals for Cl and Br are quite close to each other, which may not have a big effect on the band gap. Yet, the F atom has a $1s^2\ 2s^2\ 2p^5$ electronic configuration, which has the smallest energy level that may cause the band gap energy to be bigger. The wide difference in the band gap energy indicates the high stability of the complex compound under investigation. Another property associated with band gap energy is polarizability. Soft molecules are less polarizable than hard molecules. The difference in HOMO−LUMO band gap energy in normal dopamine in the gas phase is 5.70 eV (Table 2).

Table 2. Comparison of the Band Gap of Dopamine Doped with the First Three Members of the Halogen Group

S/N	atom doped with dopamine	energy of the 6-311G basis set (eV)
1	fluorine	5.77
2	chlorine	5.59
3	bromine	5.60

3.2. Electronic and Optical Studies of Dopamine and Dopamine Doped with the First Three Members of the Halogen Group. The vibrational frequencies of the dopamine molecule in this work were analyzed using DFT/B3LYP along with a 6-311G basis set. GaussView molecular visualization software was initially used to plot the infrared; then, Origin graphing and analysis software was used to plot the FT-IR vibrational band spectra. The comparison between normal dopamine and dopamine doped with members of the halogen group can be observed in Figure 4.

The benzene ring present in the dopamine molecule can be investigated from the bonds of C−H, C−C and C═C ring vibrational modes. The C−H stretching vibrations of dopamine occur at about 3000 cm^{-1}, and there is also a presence of weak to moderate bands (multiplicity) when compared with normal C−H stretching.[16−18] In this work, the vibrational modes were calculated theoretically in the range of 3065−3124 cm^{-1}. This shows excellent and precise agreement with experimental results.

The normal aliphatic C−H stretching was detected theoretically at about 2867−2973 cm^{-1}.[21] In the work, C−H stretching in ascorbic acid was calculated at 2979−3046 cm^{-1} for B3LYP, while 1259, 1193 and 1147 cm^{-1} bands are for C−H in-plane bending vibration in the dopamine molecule. The theoretical results obtained from the B3LYP model are close to the true value, which indicates the model's accuracy.

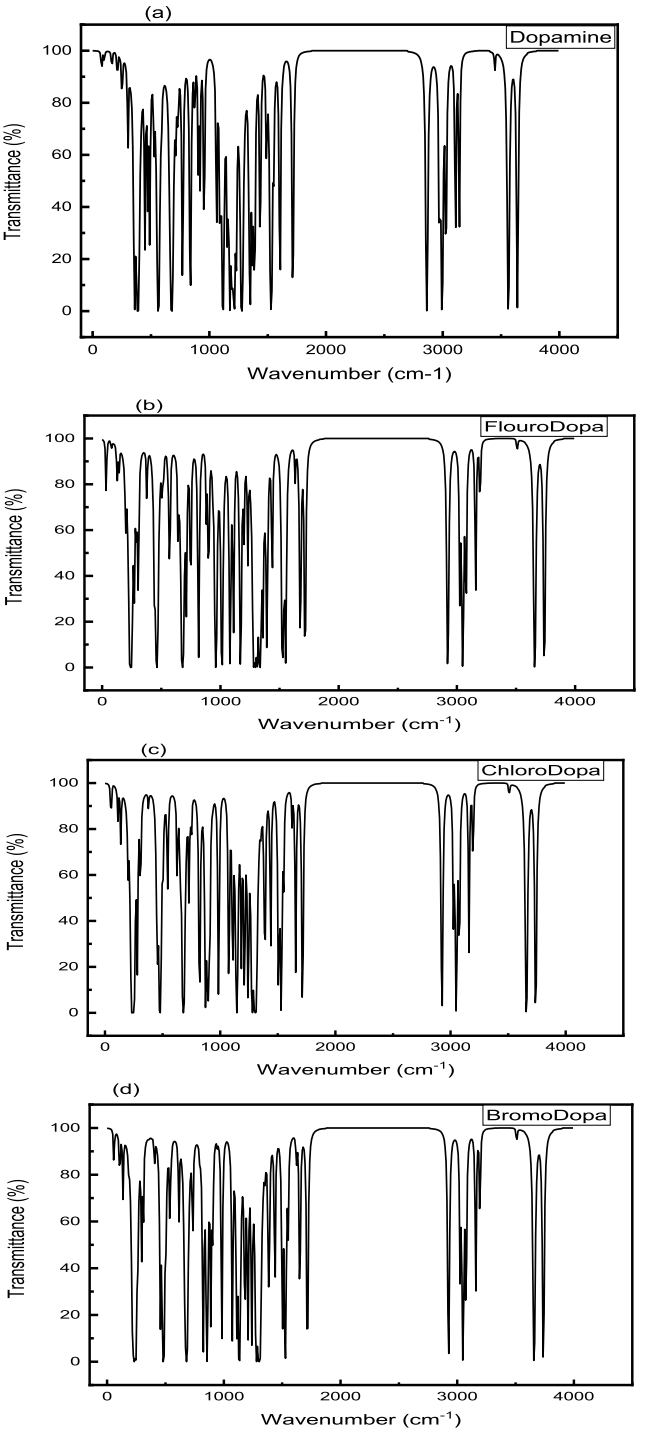

Figure 4. FT-IR absorbance spectra of comparison between (a) dopamine, (b) dopamine doped with fluorine, (c) dopamine doped with chlorine, and (d) dopamine doped with bromine.

The C−C stretching vibration in the ring has different values due to the nature of the ring, but in most cases, it ranges from 1600−1350 cm^{-1}.[17] The value has little increase due to the DFT method approximation in this work and was found to be at 1680, 1444, and 1365 cm^{-1}.

3.3. Ultraviolet Spectroscopy (UV−Vis). Ultraviolet spectroscopic (UV−vis) analysis is an important method for measuring a molecule's absorption. From Figure 5, the fluorine has the highest intensity at 39,263.78 with a wavelength of 188.50 cm. At the lowest intensity is the bromine, with

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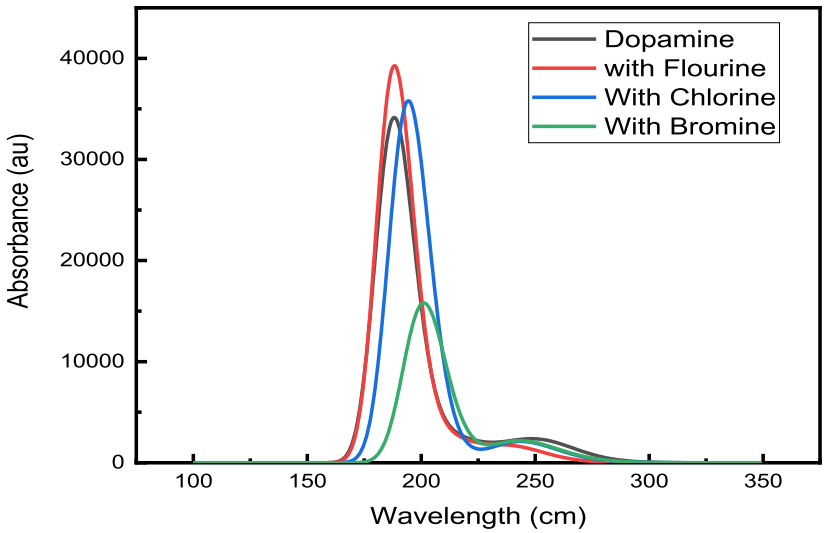

Figure 5. UV−Vis absorbance spectra of comparison between dopamine and doped with the first three members of the halogens.

absorption at 15,801.00 and a wavelength of 195.00 cm. The intermediate in the absorption is chlorine, with an intensity of 35,723.9772 and a wavelength of 195.00 cm. There is a second band at around 250 cm, which may come from the more excited states of the system. Comprehensive data comparisons have been given in Table 3. All these variations in the

Table 3. Comparison of the UV−Vis spectra of Dopamine Doped with the First Three Members of the Halogens Group

S/N	molecule (12 states)	intensity	wavelength (cm)
1	dopamine	34,140.6548	188.50
2	with fluorine	39,263.7831	188.50
3	with Chlorine	35,723.9772	195.00
4	with bromine	15,801.00	201.00

wavelengths and intensities of the dopamine doped with the first three members of the halogen group are attributed to the electronegativity of the halogens as arranged in the periodic table. Fluorine is the most electronegative element, followed by chlorine and then bromine. The increasing negativity in the group started from the top members down to the lowest members.

3.4. Nuclear Magnetic Resonance. Figure 6 explains the theoretical H NMR and C NMR structures of dopamine and dopamine doped with the first members of the hydrogen group, respectively. The Gaussian 09 software package was used to calculate the NMR, and then the Origin software package was used to plot the figures. The figures show that the shielding for normal ascorbic acid is 0 to 250 ppm. There was a shift in ppm when fluorine was introduced to the compound, from 0 to 350 ppm. The changes in ppm also continued when fluorine was replaced with chlorine, from 0 to 800 ppm. The changes in ppm were intense when bromine was introduced, from 0 to 2500 ppm. This clearly indicates that the shielding range increases with an increase in the electronegativity of the halogen family. The figures above (a, b, c, and d) compare the chemical shifts that occur when dopamine is doped with halogens (F, Cl, and Br). There is always a change in the orientation of the dopamine molecule when doped. In Figure b, the highest peak (fluorine peak) is about 225 ppm, and the carbons have little shift in the ppm due to the introduction of the fluorine atom. The same happened in Figure c, where the highest peak is attributed to the chlorine atom at about 770 ppm, and subsequently, the carbons also changed chemical environment due to deshielding by a less electronegative atom. Finally, in Figure d bromine has the highest peak at about 2300 ppm due to the shielding effect of more electrons in its outermost shells. In results, the trend follows that the more electronegative the atom, the less absorption there is in a chemical environment, and the reverse is also the case.

In Figure 5, it is clear that the normal NMR peaks of the dopamine molecule have more carbon at the upfield and less carbon at the downfield. The whole orientation of the molecules changed when fluorine was introduced. There is an appearance of the sharp medium peak of fluorine at 318.6168 ppm, and also the carbons and the hydrogens changed their chemical environment due to inductive and neighboring effects. The same trends happened when fluorine was replaced with chlorine and later bromine, with peaks at 783.5461 and 2150.7061 ppm, respectively. This proves that NMR peaks generated by the halogen family in ascorbic acid have a close linear relationship with their electronegativity. Table 4 gives the precise individual positions of the halogen members in terms of ppm.

3.5. Potential Energy Map. The potential energy map plays a crucial role in determining the concentration of electrons in a particular molecule. It can also be used to understand the electrical and optical properties of the molecule. The electron in the undoped dopamine molecule is concentrated toward the two hydroxyl groups attached to the benzene ring (blue portion) due to the electronegativity of the oxygen atom. When one of the hydrogens of the benzene is replaced with a fluorine atom, the orientation of the molecule is completely changed due to the presence of a more electronegative element (red part). As a result, some electrons have migrated from the oxygen to the fluorine part of the molecule. The same happened with chlorine and bromine (Figure 7), but the migration depends on the electron affinity of the incoming molecule.

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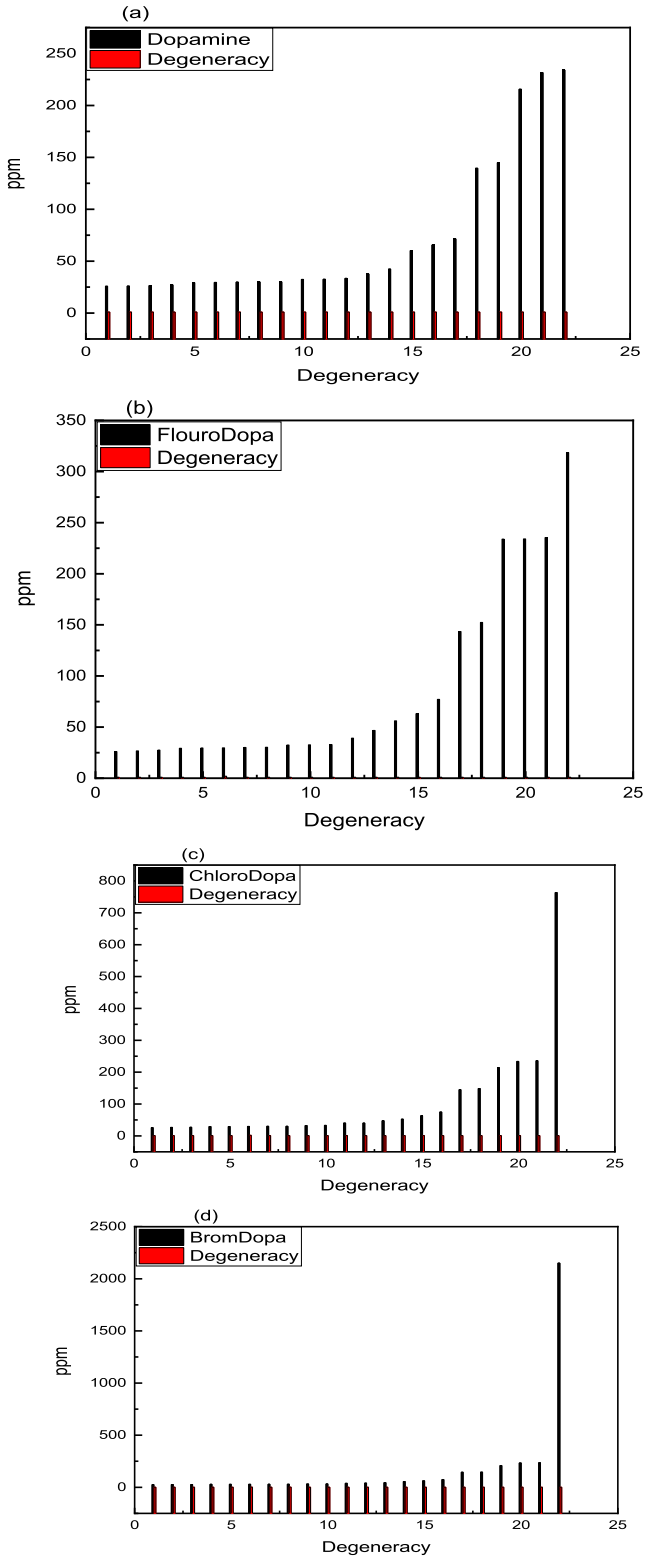

Figure 6. NMR spectra of the comparison between dopamine and dopamine doped with the first three members of the halogens group: (a) dopamine, (b) dopamine doped with fluorine, (c) dopamine doped with chlorine, and (d) dopamine doped with bromine.

4. CONCLUSIONS

In this work, we have focused on increasing the efficiency of dopamine in the cure of PD and SD by controlling the band gap as a result of doping with the first three members of the halogen group (F, Cl, and Br). Most diseases of humans and animals are caused due to the bond breakage of some molecules in the body. As a result of understanding the band gap and movement of electrons in the dopamine molecule, its efficiency can be increased, and it might decrease the rate at which PD and SD attack the human body. We investigated the properties of dopamine (including the band gap, DOS, and spectroscopic properties) and dopamine doped with the first

Table 4. Comparison of the NMR of Dopamine Doped with the First Three Members of the Halogen Group

s/n	doping atom	NMR (ppm)
1	fluorine	318.6160
2	chlorine	783.5461
3	bromine	2150.7061

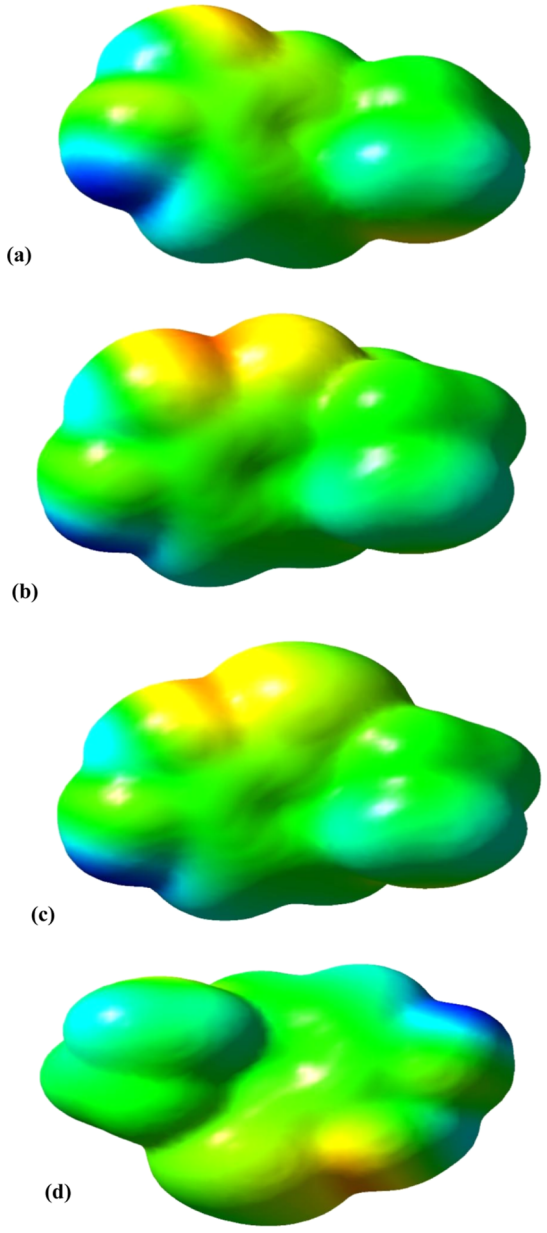

Figure 7. Potential energy map of comparison between dopamine and dopamine doped with the first three members of the halogens group: (a) dopamine, (b) dopamine doped with fluorine, (c) dopamine doped with chlorine, and (d) dopamine doped with bromine.

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three members of the halogen group to compare the changes in electronic and other spectroscopic parameters. Different basis sets in DFT and Hartree−Fock were used in the optimization process to determine the lowest energy and a suitable basis set for the whole calculation of the ascorbic acid; then, the compound was doped with the first three halogen members separately. Spectroscopic properties, such as UV−vis and NMR, for both doped and undoped dopamine were determined. Finally, the theoretical method investigated the FT-IR spectra of dopamine with different doping with halogen groups. It was found that the band gap is sensitive to doping as we moved down the group members (the band gap depends on the electronegativity of the halogen members)..

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Notes

The authors declare no competing financial interest.

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