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Physical and Electrical Properties of Sandwich Compound as Drug Delivery to Transport Chlorpheniramine Medication Using Density Functional Theory

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ABSTRACT

Sandwich compounds have widespread applications in fields such as medicine, molecular electronics, and pharmacology. This study is an attempt to design drug delivery by using a di-benzene chromium sandwich compound $Cr(\eta^6\text{-}C_6H_6)_2$ to transport chlorpheniramine medication ($C_{16}H_{19}ClN_2$). Some of the electronic and spectrum properties of the sandwich compounds and chlorpheniramine medication using density functional theory (DFT) and the B3LYP/6-31G(d,p) basis set were investigated. The sandwich compound, chlorpheniramine, and the sandwich compound bonded with chlorpheniramine were evaluated by studying the geometry optimization and calculating the HOMO and LUMO, bond length, energy gap, UV-VIS, IR spectrum, and force constant for the three compounds. These calculations highlight several features of the new compound, including strength and higher stability. In the investigation, it was observed that the UV-VIS and IR spectra for the new compound exhibits shifts towards longer wavelengths absorptions. The energy gap values for the three compounds were determined to be 2.1768 eV, 4.813 eV, and 3.0557 eV, respectively, while the force constant values were measured as 3 mDyne/Å, 2.7 mDyne/Å, and 4 mDyne/Å.

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1. Introduction

Sandwich systems have numerous uses because of their redox properties, which make it easy to form stable or reactive ions [1-3]. The redox behavior is mainly due to the sandwich molecules' low ionization energies (IEs), which depend on the type of metal atom and the ligand structure [4, 5]. Sandwich compounds as transition organometallic compounds with biological activity have been introduced as new prospective therapeutics against malaria, HIV, and cancer. These substances have also already found use in medicine as radiopharmaceuticals and antibiotics [6-9]. For example, platinum complexes make up more than 50% of the drugs used to treat patients receiving cancer chemotherapy [6, 10, 11]. Metallocenes, which have the formula, $M(C_5H_5)_2$ are a special class of sandwich complexes that have been widely studied in the field of chemistry [12]. They have several applications in medicine and can be utilized to deliver drugs to particular receptors, known as target-specific drugs [13-15].

Ferrocene $(C_5H_5)_2Fe$ is the prototype and the best-known of metallocenes. This compound was prepared for the first time in 1951 [16]. It consists of two rings parallel to each other, with an iron ion in the center between them [17]. It has shown potential in a number of medical applications. Many investigations have shown that some of the derivatives of ferrocenyl are highly active against a number of diseases, including cancer [18]. One study reported the synthesis and characterization of ferrocene when the sandwich compound bonded with Aciclovir (ACV), using the compound as a drug carrier in the treatment of herpes simplex infections, shingles, and chickenpox [19]. Along with other metallocenes, di-benzene chromium, the organometallic compound with the formula $Cr(\eta^6\text{-}C_6H_6)_2$, has also been studied for its medical applications. This compound has two benzene ligands that are coordinated to a central chromium atom [20].

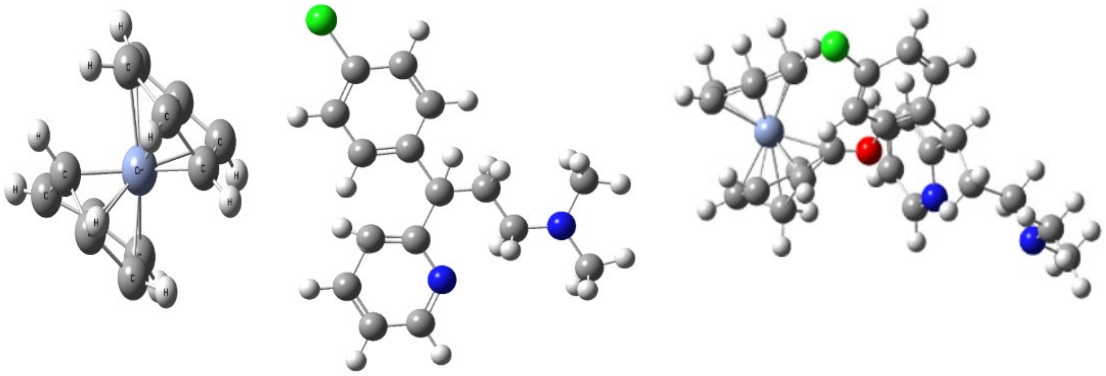
On the other hand, chlorpheniramine, also known as chlorphenamine, which has the chemical formula $C_{16}H_{19}ClN_2$, is an antihistamine medicine that relieves symptoms of allergy, cold, and hay fever. Among these symptoms are itchy watery eyes, a runny nose, and sneezing [21]. Despite the fact that chlorpheniramine can help control the symptoms of allergies, it cannot treat the cause of the symptoms or speed recovery. Chlorpheniramine works by blocking the action of a substance in the body that causes allergic symptoms called histamine [22].

In this study, we show the ability of using a di-benzene chromium sandwich compound as a carrier of chlorpheniramine. This work aims to examine the theoretical aspects of the electronic and structural properties of the sandwich compound, chlorpheniramine, and the sandwich compound bonded with chlorpheniramine using the DFT method. 6-31G (d,p) basis set which was created using Gaussian 09 program auxiliary by Gaussian view 5.08.

2. Computational Details

Both the density functional theory (DFT) and time-dependent density functional theory (TD-DFT), at the B3LYP/6-31G (d,p) level of theory, were the two computational approaches used in this study. They are frequently employed in computational chemistry and make precise forecasts of molecule characteristics like electronic structure and absorption spectra [23-25]. The computations were carried out using the Gaussian 09 and the Gauss View 5.08 molecular visualization software suite. The gradient-corrected B3LYP hybrid functional, which stands for "Becke, 3-parameter, Lee-Yang-Parr was employed in the calculations. The DFT method is useful for identifying the ground state structures of molecules as well as their electronic properties, such as total energy and electron density. However, the time-dependent density functional theory (TD-DFT) is an extension of the density functional theory DFT method, and it is used to calculate excited states of systems and predict UV-visible spectra [24, 26, 27].

The energies of HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital) were used to calculate pertinent global parameters, which describe the chemical reactivity of molecules. The same basis set was used for the B3LYP density functional theory as it was for geometry optimization [28]. Fig. 1 presents the 3D geometry of sandwich compound, chlorpheniramine, and sandwich compound bonded with chlorpheniramine. The prescription and features of di-benzene chromium sandwich compound, chlorpheniramine, and sandwich compound bonded with chlophenamine are several of the aspects of these materials that will be covered in this study



(a) **(b)** **(c)**

Fig. 1. Geometry optimization of (a) sandwich compound, (b) chlorpheniramine, and (c) sandwich compound bonded with chlorpheniramine

3. Results and Discussion

3.1. Bond length

Fig. 2 shows the bond length of sandwich compound, chlorpheniramine and sandwich compound bonded with chlorpheniramine. The bond lengths of (C-H), (O-C), (C-C), (C=C), (C-Cl), (C-Cr), and (C-N) are (1.08 Å), (1.44 Å), (1.52 Å), (1.3 Å), (1.7 Å), (2.2 Å), and (1.47 Å), respectively. In our case, the position of atoms near or far from the surface and their bonding with one or two H atoms are the primary causes of the nonequivalent bond lengths. The fact that C, N, and O are nonmetals is the cause of this variance. Nonmetal electrons exhibit great spatial localization [29-31].

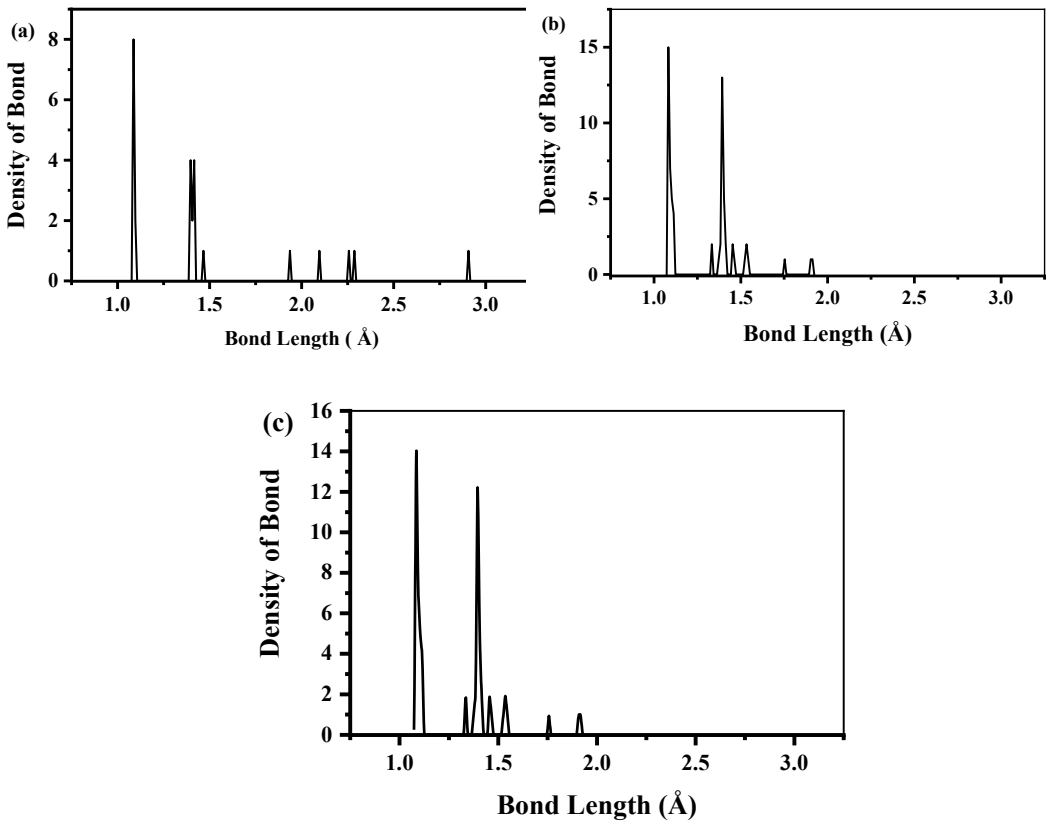


Fig. 2. Bond length of (a) sandwich compound, (b) chlorpheniramine, and (c) sandwich compound bonded with chlorpheniramine

3.2. UV-Visible spectra

Fig. 3 displays the UV excitation energy for the sandwich compound, chlorpheniramine, and for the sandwich compound bonded with chlorpheniramine, respectively. The vertical axis represents the molar absorptivity ε in (liters/mole cm), and the horizontal axis represents the wavelength.

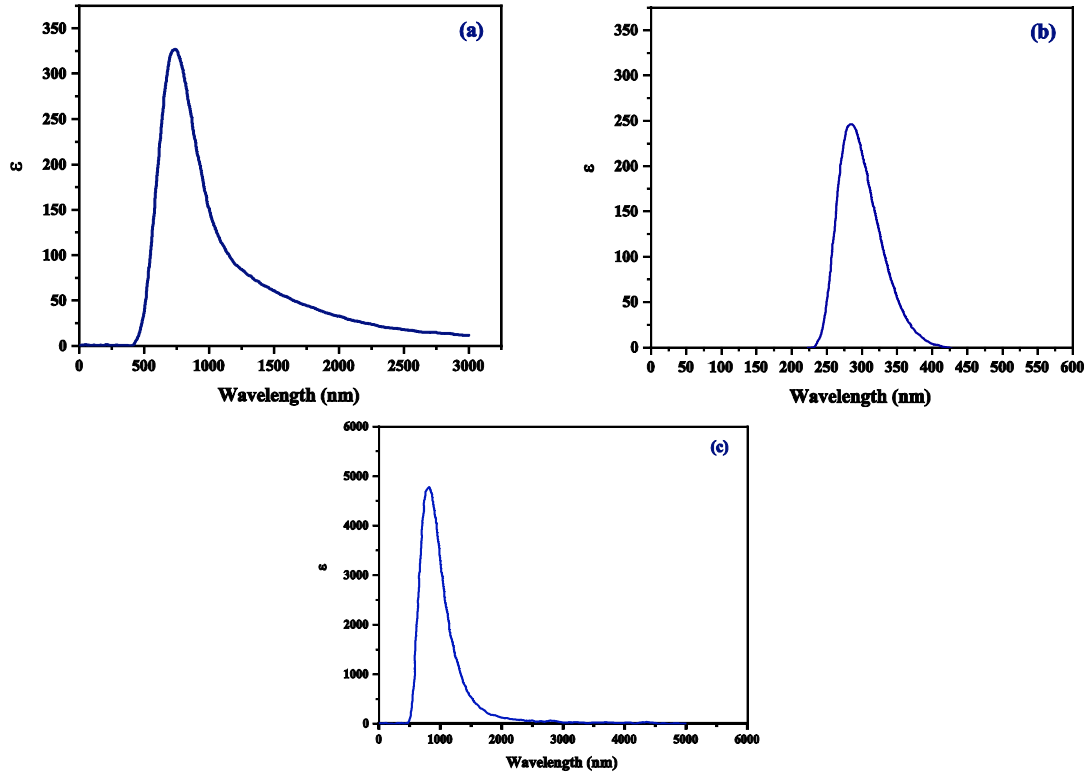


Fig. 3. Visible (VIS) and ultraviolet (UV) radiation of (a) sandwich compound, (b) chlorpheniramine, and (c) sandwich compound bonded with chlorpheniramine

Fig. 3a shows a high degree of conjugation in the UV spectra for the sandwich compound. It absorbs radiation in the range of 500-300 nm, with a λ_{max} value of about 600 nm. The UV spectra for chlorpheniramine in Fig. 3b depicts how the molecule's electronic energy levels vary, particularly in relation to the transfer of electrons from π- or non-bonding orbitals. Fig. 3c illustrates the UV spectra for the sandwich compound bonded with chlorpheniramine. With the increasing of the degree of conjugation, the spectrum shifts toward longer wavelength (lower energy) absorptions. The energy decreased and the wavelength increased due to the $\pi - \pi^*$ electronic transitions, and this led to a red shift [32-34].

3.3. Transmittance

The transmittance values for the following states are shown in Fig. 4: (a) sandwich compound, (b) chlorpheniramine, and (c) sandwich compound bonded with chlorpheniramine. For single bonds with carbon, such as C-C and C-Cr, there is a noticeable absorption and low transmittance in the range of 0-1000 cm^{-1} as shown in Fig. 4a. The carbon double bond in the benzene ring, however, exhibits strong transmittance and low absorption at 1650 cm^{-1}. Fig. 4b displays single bonds like C-C and C-N in the range of 200–1500 cm^{-1} and double bonds like C=C and C=N in the range of 1600–1800 cm^{-1}. There are no bonds between 2000 and 3000 cm^{-1}, however, at 3200 cm^{-1}, the carbon atom is connected to another carbon atom in a double bond and to hydrogen in a single bond. The SP^2 form of carbon hybridization has high transmittance and low absorption. Furthermore, the N-H bond can be seen around 3400 cm^{-1}. Fig. 4c shows the C-H and O-H bonds for the sandwich compound bonded with chlorpheniramine, having transmittance values of 2900 cm^{-1} and 3600 cm^{-1}, respectively.

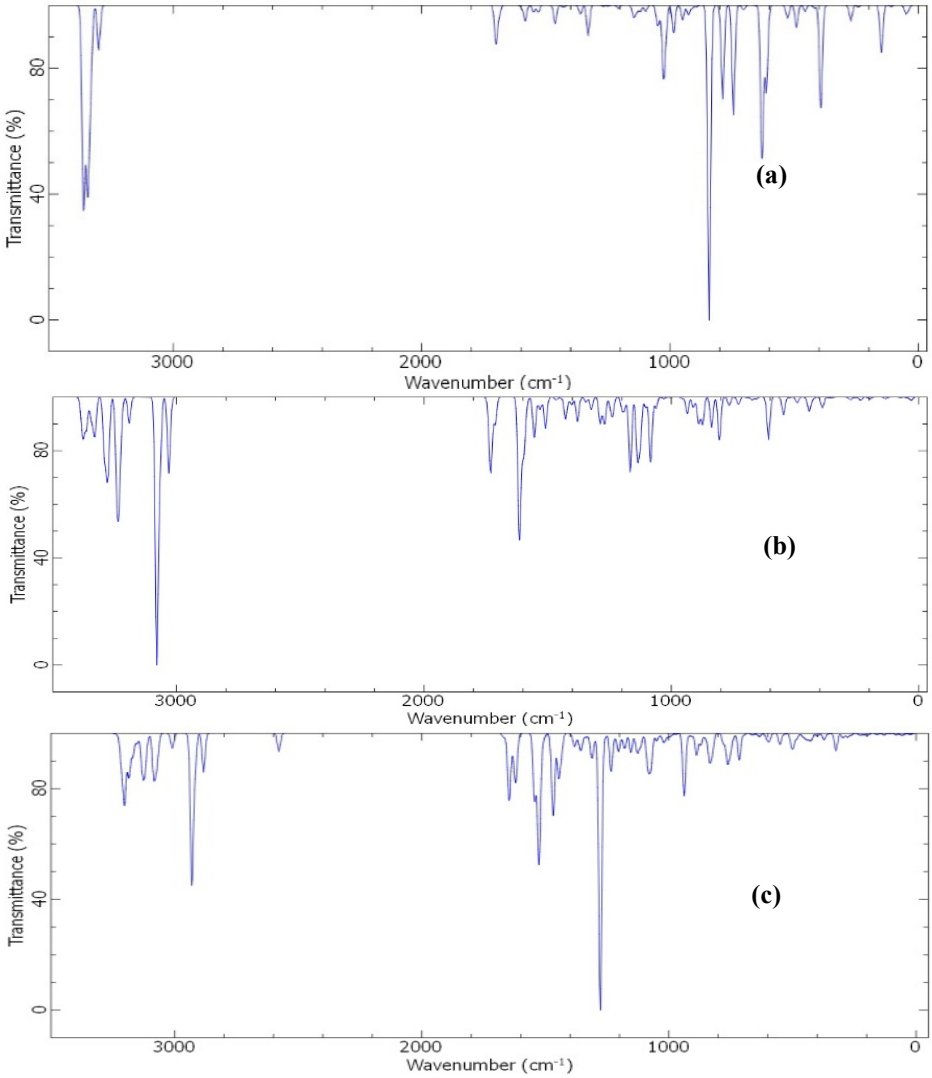


Fig. 4. Transmittance of (a) sandwich compound, (b) chlorpheniramine, and (c) sandwich compound bonded with chlorpheniramine.

3.4. Electronic Circular Dichroism (ECD)

Electronic Circular Dichroism (ECD) can be studied using the DFT/B3LYP method. DFT methods provide a practical means of reaching high prediction accuracy in such calculations. The ECD spectra of the sandwich compound, chlophenamine, and the sandwich compound bonded with chlorpheniramine are shown in Fig. 5. As seen in Fig. (4-a),

there are two peaks for the ECD spectra of the sandwich molecule, a positive region at 650 nm and a negative region at 1357 nm. These peaks can be attributed to the benzene ring's orientation, with one being up and the other being down. The chlorpheniramine's ECD spectrum is shown in Fig. 4b. The curve has a single negative peak at 342 nm. The sandwich molecule bonded to chlorpheniramine exhibits two positive peaks at 650 nm and 1357 nm in the ECD spectra, as seen in Fig. 4c.

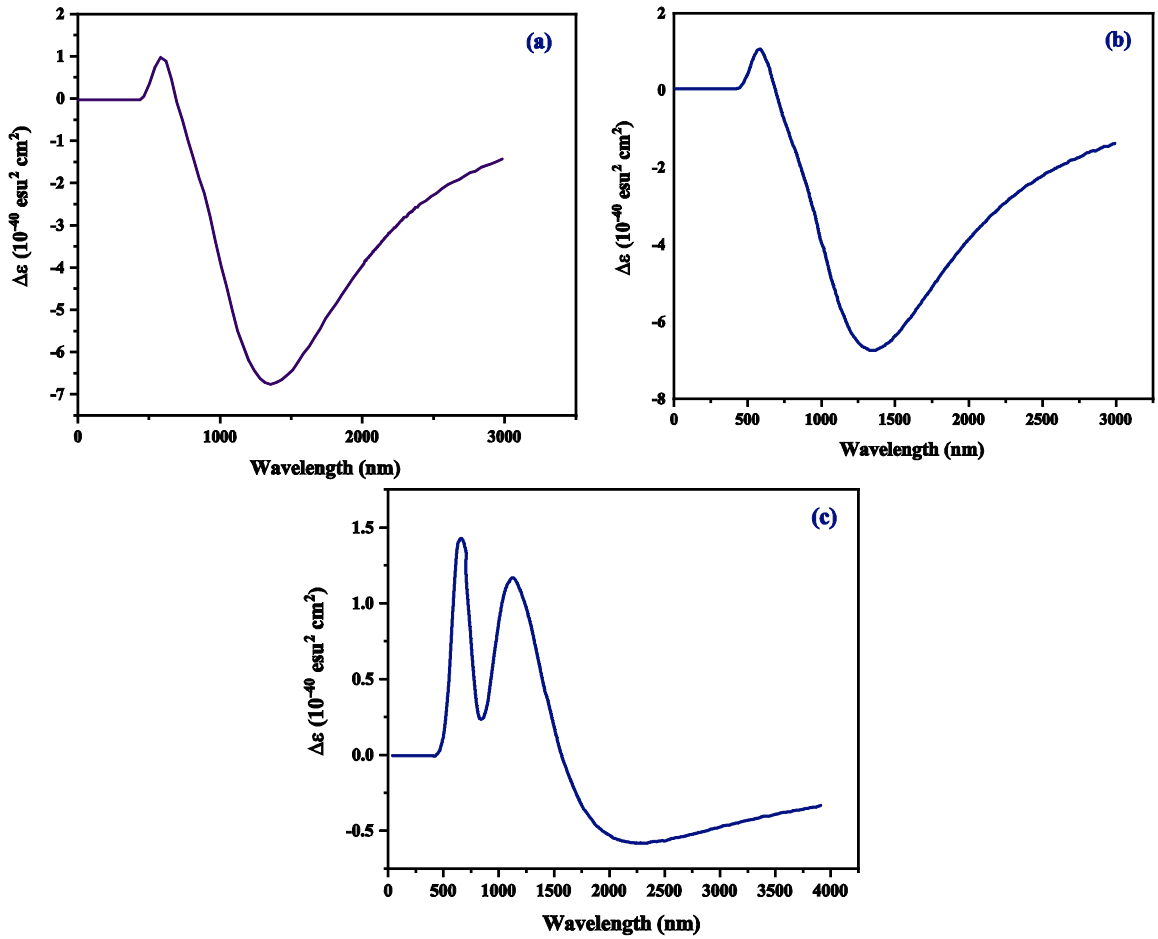


Fig. 5. (ECD) spectra of (a) sandwich compound (b) chlorpheniramine and (c) sandwich compound bonding with chlorpheniramine

3.5. HOMO–LUMO Level

The difference in energy between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) is called the energy gap [35].

Energy Gap = HOMO – LUMO (1)

The energy gap values of the sandwich compound, chlorpheniramine, and the mixture of the sandwich compound with chlorpheniramine were computed using B3LYP/631G(d,p). The calculated energy of the lowest unoccupied molecular orbital (LUMO), the highest occupied molecular orbital (HOMO), and the values of the energy gap for the three different compounds are listed in Table 1. This energy gab can be used to predict the strength and stability of transition metal complexes [36]. The magnitude of the energy gaps in nanomaterials is a key factor in influencing their electrical and optical characteristics [37].

Table 1. HOMO, LUMO, and the energy gap for the three different compounds

Structure	HOMO (a.u)	LUMO (a.u)	Energy Gap (eV)
Sandwich compound	-0.0915	-0.1715	2.1768
Chlophenamine	-0.0306	-0.2075	4.813
Sandwich compound bonded with Chlophenamine	-0.0662	-0.1785	3.0557

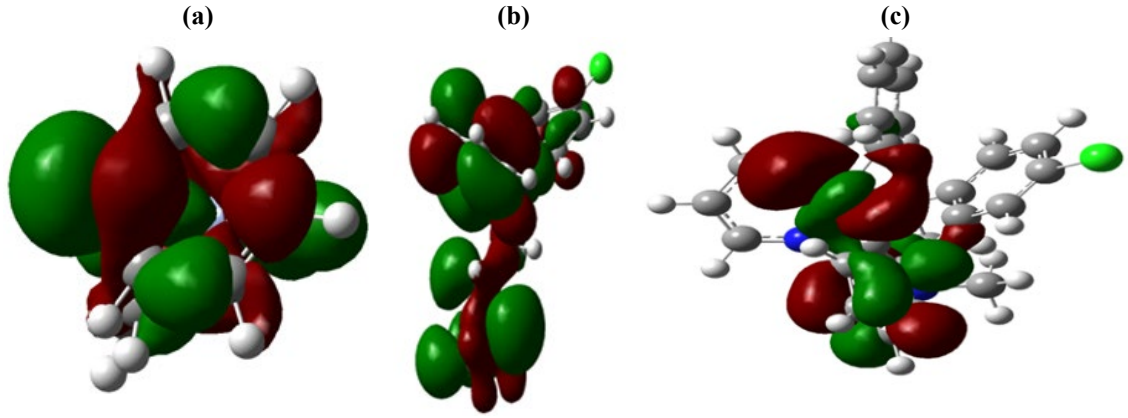


Fig. 6. HOMO-LUMO energies and energy gap of (a) sandwich compound, (b) chlorpheniramine, and (c) sandwich compound bonding with chlorpheniramine

3.6. Force constants

Vibrational modes can be analyzed using one of two techniques. While the first one is dependent on force constants, the second one depends on reduced masses. Since atom masses are better known than vibrational force constants, the second one is simpler [38]. Figs. (6-7) are related to the vibrational spectroscopy of (a) sandwich compound, (b) chlorpheniramine, and (c) sandwich compound bonded with chlorpheniramine. For a diatomic molecule A−B, the vibrational frequency is given by:

$$\nu = \frac{1}{2\pi}\sqrt{\frac{k}{\mu}} \tag{2}$$

where k is the force constant in dyne/cm and μ is the reduced mass. The dashed line in Fig.s 6a, 6b, and 6c represent the force constant, whose values for the sandwich compound, chlorpheniramine, and the sandwich compound bonded with chlorpheniramine are (3 mDyne/Å), (2.7 mDyne/Å), and (4 mDyne/Å), respectively. The higher force constant shown in Fig, 6 means higher stability and a stronger bond. This shows that higher force constant requires more energy to expand the bond and increase the difficulty of breaking it.

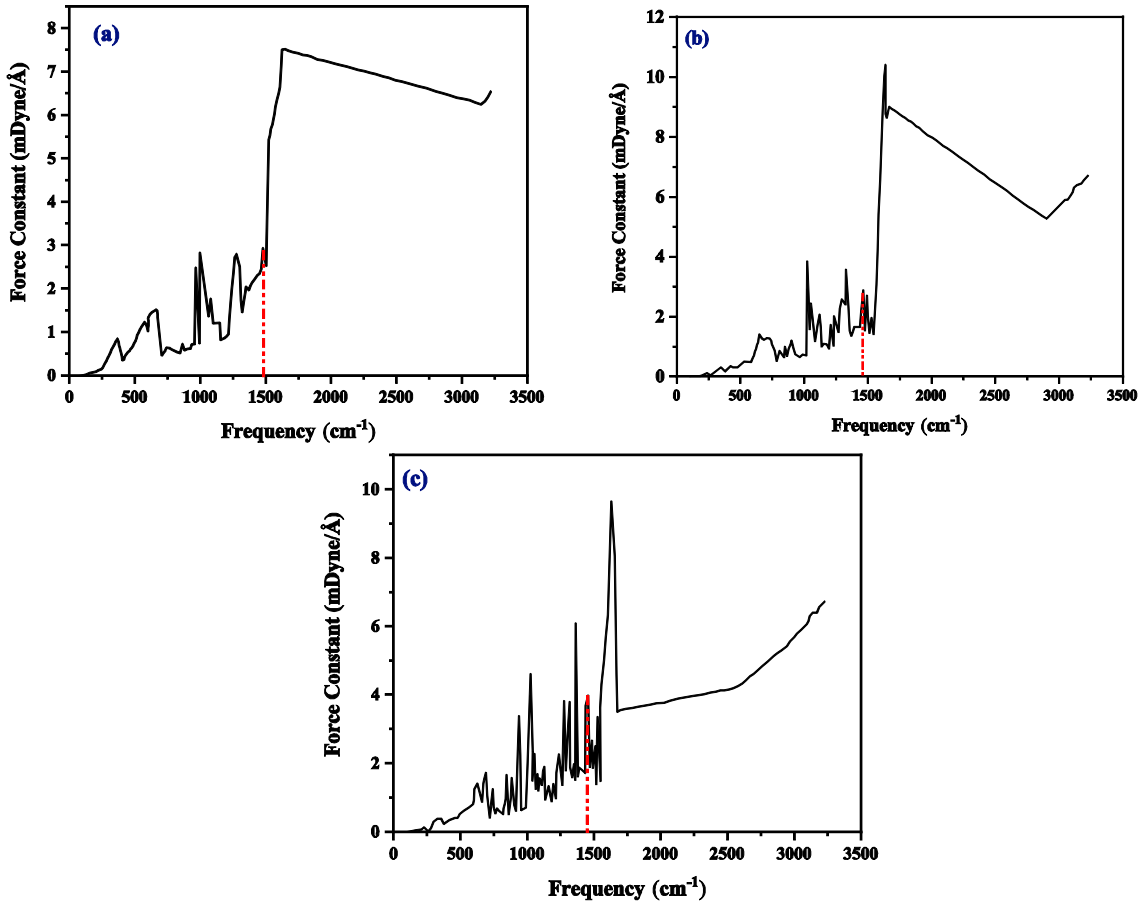


Fig. 7. Force constant of (a) sandwich compound, (b) chlorpheniramine, and (c) sandwich compound bonded with chlorpheniramine

4. Conclusions

The dibenzene chromium sandwich compound $Cr(\eta^6 - C_6H_6)_2$ is designed as a drug carrier to transport chlorpheniramine medication ($C_{16}H_{19}ClN_2$). The theoretical calculations of the HOMO and LUMO, bond length, energy gap, UV-VIS, IR spectrum, and force constant for the sandwich compound and chlorpheniramine in this work were calculated. The sandwich compound bonded with chlorpheniramine was tested for stability by using density functional theory (DFT) and the B3LYP/6-31G (d,p) basis set. The study shows that the UV-VIS and IR spectra for the new compound shift toward longer wavelength (lower energy) absorptions, while the energy gap values for the three compounds are 2.1768 eV, 4.813 eV, and 3.0557 eV, respectively. On the other hand, the force constant values are 3 mDyne/Å, 2.7 mDyne/Å, and 4 mDyne/Å. All these values reflect many aspects of the new compound, including strength and stability.

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Author Contributions

H. M. Jawad performed computations.

H. M. Jawad, and T. A. Husain wrote the manuscript.

I. N. Qader scientific and technical improvements.

All authors checked the last version of the manuscript.

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