

# Use Ferrocene as a drug carrier: Density functional theory study

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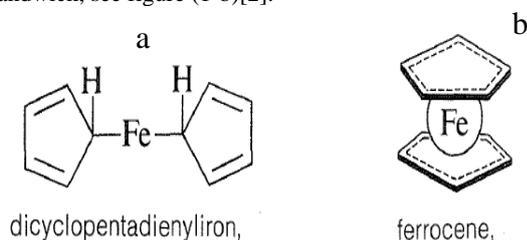
## Abstract

In this manuscript, Quantitative Mechanical Characterization In the structural and vibrational properties of the Ferrocene we studied, drug Aciclovir and Ferrocene bonded with drug Aciclovir. The physical properties were investigated by using theory of density functional the basis set B3LYP/6-31G (d), which included polarization functions basis set and created using Gaussian 09 program auxiliary by Gaussian view 5.08. Energy gap, electrostatic potential, density of states, tetrahedral angle, dihedral angle, bond length, IR intensity, Raman spectrum, UV/Visible and electrostatic potential in order to fully investigate. Ferrocene structure, high stability and inertness, it can be used as a drug carrier. The results show that length of the bond of Ferrocene equal to 1.09Å. A Ferrocene dihedral angle is completely true for the angles (-60° and 60°). The density of geometrically optimized energy states of the Ferrocene energy gap value (0.79eV). It has big energy gap as expected in this nano range. Excitation energy of Ferrocene is (0.4653 eV), Maximum absorption(2664.39 nm). Electrostatic potential of Ferrocene, the green color signifies, and the neutral electrostatic potential reflect the stability of Ferrocene structures.

**Keywords:** Ferrocene, drug carrier, Density functional theory

## 1. INTRODUCTION

Ferrocene represents an essential molecule. The recognition of the epitaxial structure compound with the formula C<sub>10</sub>H<sub>10</sub>Fe in 1951 produce organic metallic transition metals based on metals. Ferrocene shows properties of a characteristic aromatic molecule, it is stable for more than 500 °C, doesn't react easily with both acids or bases, and it is sensitive to oxidizing agents. All the atoms of carbon in the two cyclopentadiene rings were bonded equally (by the π electrons of the two rings) to the central ferrous ion [1]. The reaction product was a very stable, beautiful, and orange crystalline material, so that Pauson formulated as a simple combination of two cyclopentadienide anions and ferrous ion with two Carbon-Iron bonds, see figure (1-a) However, the product soon appeared in a variety of physical methods for the structure of the sandwich, see figure (1-b)[2].



Figs. (1): show (1-a) combination of two cyclopentadienide and (1-b) sandwich structure [2].

The scientists have stimulated interest of Ferrocenophanes because of its many desirable characteristics.

- 1- Dissimilar many compounds of organometallic, ferrocene and ferrocenophanes have high stability in air, thus, ferrocene-based materials can be used in different applications without degradation fear.
- 2- Both Ferrocene and ferrocenophanes can subjected to an oxidative reverse to give stable and deep green ferrocenium cations. This characteristic makes the systems of ferrocene and ferrocenophanes attractive electrochemical agents for using in chemical sensing [3].

The medicinal inorganic chemistry field is progressing rapidly, such as in spatial organometallic complexes that had great potential as agents of therapeutic and diagnostic. The carbon bond and other ligands permit the metal ion thermodynamic and kinetic reactivity to be controlled and also provide a scaffold for functionalization. The establishment of structure activity relationship and the speciation elucidation of complexes under condition relevant to drug testing and formulation are crucial for the further development of organometallic complexes promising

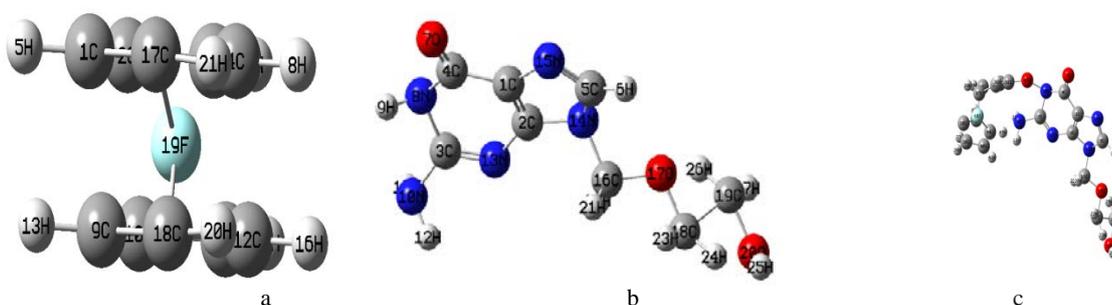
medicinal application [4]. Numerous reports have shown that some of derivatives of ferrocenyl are very active against many diseases, including cancer [5]. In this study it can be used ferrocene as a carrier of the drug, when bonded with Aciclovir. Aciclovir (ACV), also known as acyclovir, is an antiviral drug. It is primarily used for the treatment herpes simplex infections, chickenpox, and shingles. Other uses include prevention of cytotoxic virus infection after transplantation and severe complications of Epstein-Barr virus infection. It can be taken orally, applied as a cream, or injected. The physical properties were investigated using density functional theory the basis set B3LYP/6-31G (d), which included [6]. Polarization functions basis set which created using Gaussian 09 program auxiliary by Gaussian view 5.08

## 2- THEORY

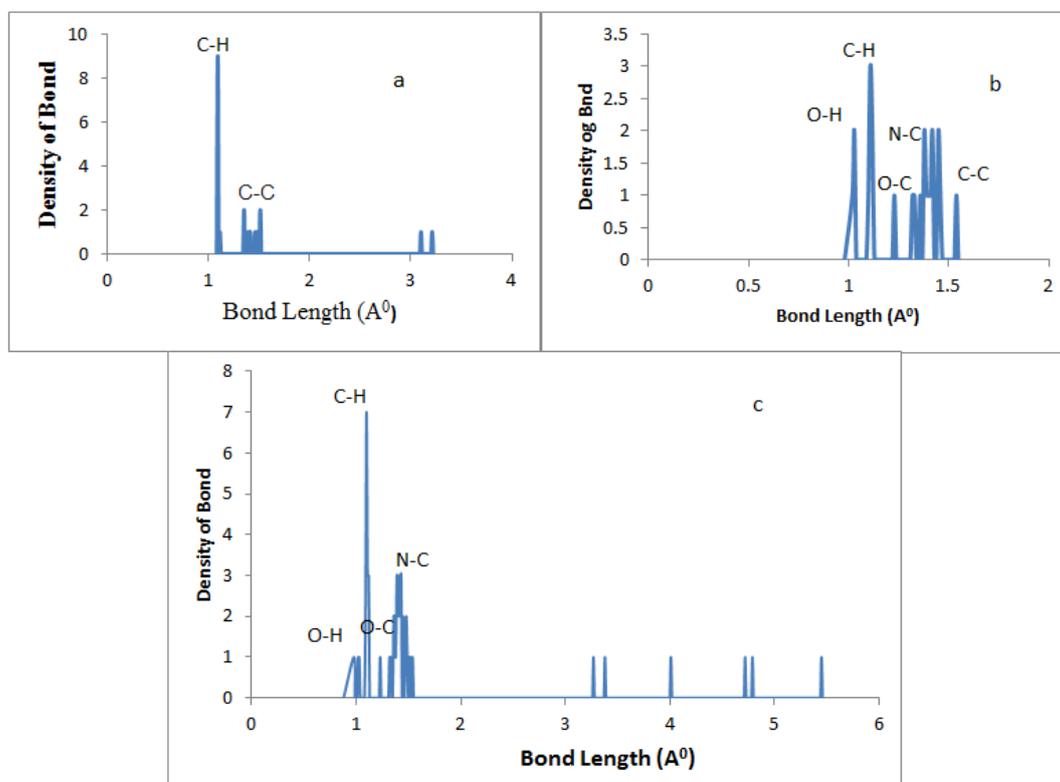
The underlying theoretical analysis and computational treatment of molecular problems have revealed permanent growth in the molecular complexity degree as the earliest chemists efforts to use computer calculations in advancing understanding. This will definitely continue right along with rapid increment in computing power and computer availability for example we've seen over the last decade. Computational study has reached a point where it is realistic to envision, predictive simulations of complex biological phenomena along the way to the cellular level [7]. Furthermore, the computational methods depends on approximations to density functional theory (DFT) which had the ability to provide computationally efficient methods for modeling where non-covalent interactions play a central role [8]. The essential problem in the describing the materials electronic structure is to solve the Schrödinger equation of a multi-electronic system in the presence of a nuclei field. According to the estimate of Born-Oppenheimer, nuclei kinetic energy is neglected and the nucleus-nucleus interactions can be considered constant. So that, Schrödinger equation for a system consisting of N nuclei with constant coordinates [9]. In this article, quantum mechanical study focused on the properties of Ferrocene, Aciclovir and Ferrocene bonded with Aciclovir.

## 3- RESULTS AND DISCUSSION

Figs. (2-a, 2-b and 2-c) shows geometrically optimized of Ferrocene, Aciclovir and Ferrocene bonded with Aciclovir. The molecular approach to nanostructure crystal is an interesting approach. It can be used to determine many properties that are from time to time difficult to determined using theories of solid-state. In part because of the ab initio molecular programs that have existed since the 1970s. These programs were always developing to reach a higher number of atoms with higher precision; one of them is the program of Gaussian 09 [10].



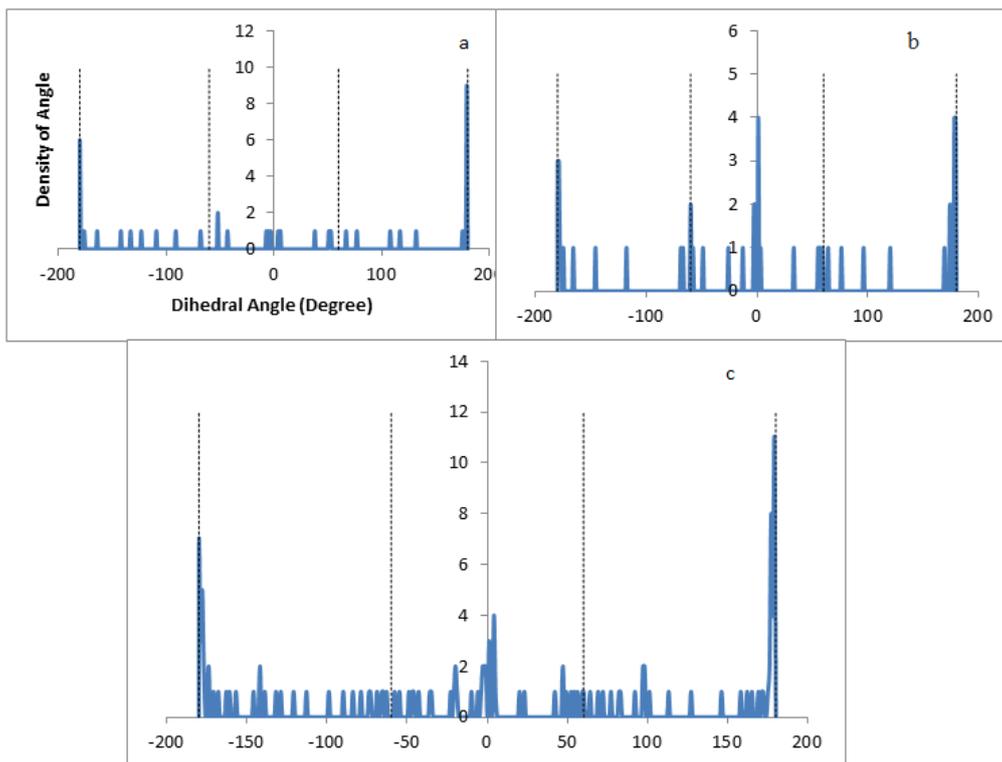
Figs. (3-a, 3-b and 3-c) shows the distribution of bond lengths at Fig. (3-a) bond length of Ferrocene the carbon-hydrogen bonds are the shortest bonds. It equals ( $1.09\text{\AA}$ ) and equal experimental value of the carbon-carbon bonds it equal to ( $1.35\text{\AA}$ ) is nearly the experimental value ( $1.5\text{\AA}$ ). At fig. (3-b) Oxygen-hydrogen bonds are the shortest bond it ( $0.97\text{\AA}$ ) has the same experimental values the carbon-carbon bond. Either the bond between oxygen- carbons is ( $1.22\text{\AA}$ ) is nearly the experimental value ( $1.4\text{\AA}$ ) [11]. At Fig. (3-c) Note that the values of the above mentioned bonds are either equal or there is a slight change. This reflects a high degree of constancy and unresponsiveness of the current Ferrocene structure [12].



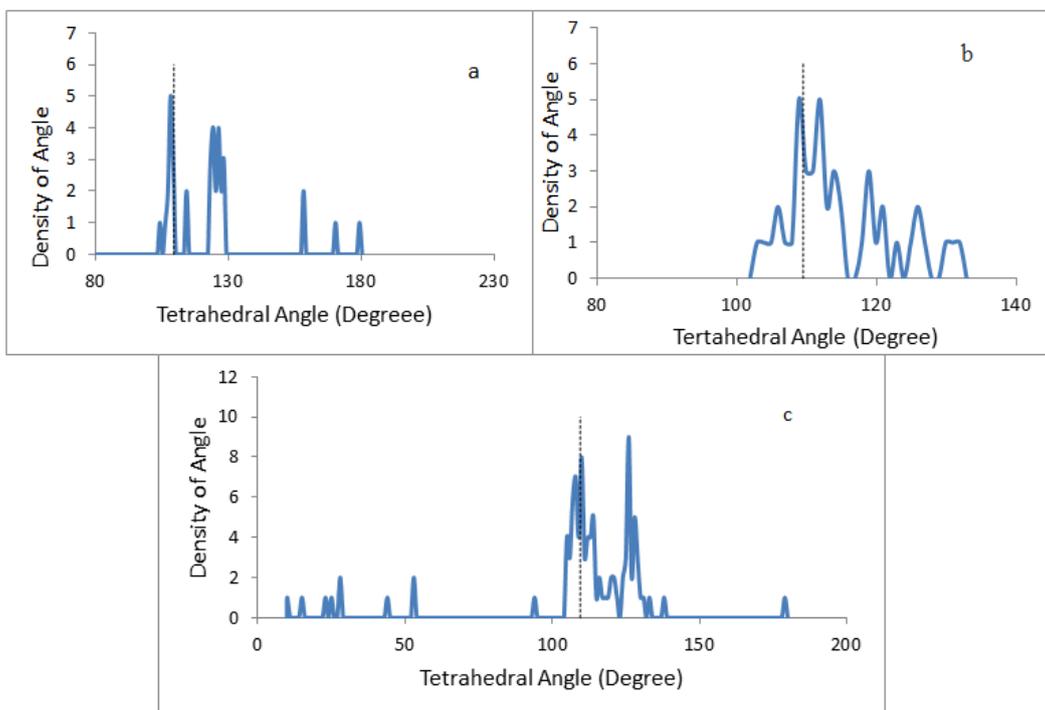
Figs: (3-a, 3-b and 3-c) Shows bond length (3-a) of Ferrocene, (3-b) Aciclovir and (3-c) Ferrocene bonded with Aciclovir.

Figs. (4-a, 4-b and 4-c) shows the dihedral angle. Zincblend's ideal bulk values for these angles are  $\pm 60^\circ$  and  $\pm 180^\circ$  [13]. Ferrocene in Fig. (4-a) it is completely true for the angles ( $-60^\circ$  and  $60^\circ$ ). For Fig. (4-b) Aciclovir the situation improves for the angles  $-60^\circ$  and  $60^\circ$  that become more closer to its ideal value. Fig. (4-c) Ferrocene bonded with Aciclovir. Again, the dihedral values reflect the stability of Ferrocene structures which is useful for our study to get the inert and no harm structures after bonding there with different drugs to use it as drugs carriers.

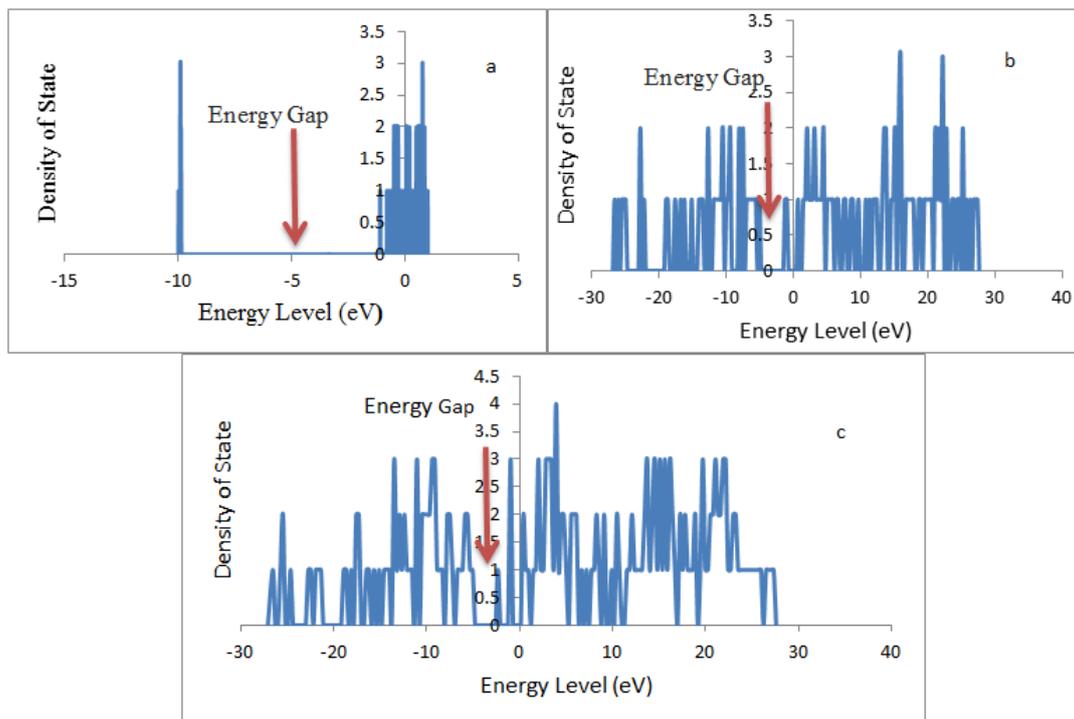
Figs. (5-a, 5-b and 5-c) illustrates the ferrocene values distribution, Aciclovir and Ferrocene bonded with Aciclovir tetrahedral angles. The maximum value of this angle displayed at  $109.47^\circ$  is shown [14]. Fig. (5-a) note the distribution of tetrahedral angle centered on the experimental value (dashed line). Figure (5-b) exhibits the distribution with the highest peak shifted one or two degrees of this value. Fig. (5-c) is also centered on the experimental value (dashed line).



Figures (4-a, 4-b and 4-c): Distribution of Dihedral angle. (4-a) Dihedral angle of Ferrocene, (4-b) Aciclovir and (4-c) Ferrocene bonded with Aciclovir. The dashed lines show the ideal values of the zincblende structures at -180°, -60°, 60° and 180° [13].

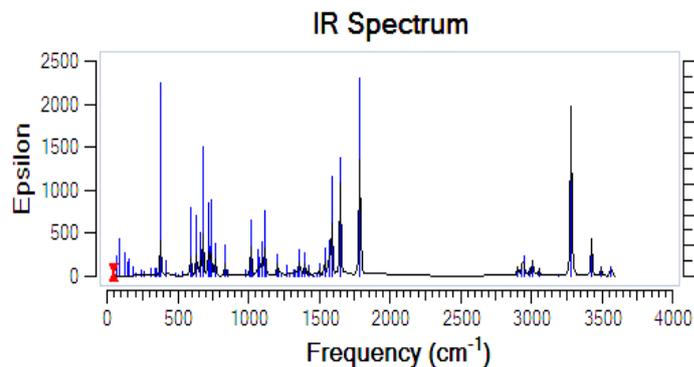


Figures (5-a, 5-b and 5-c): shows Distribution tetrahedral angle. (5-a) tetrahedral angle of Ferrocene, (5-b) Aciclovir and (5-c) Ferrocene bonded with Aciclovir. The dashed line show the ideal values of the zincblende structures at 109.47° [14].

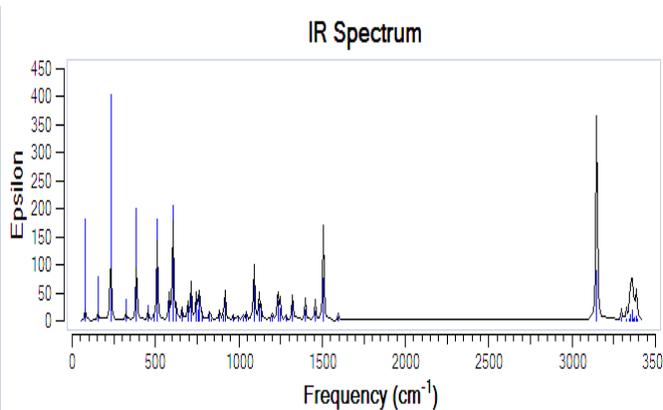


Figures (6-a, 6-b and 6-c): Density of energy states of geometrically optimized as a function of energy level. (6-a)Density of energy states offFerrocene, (6-b) Aciclovir and (6-c) Ferrocene bonded with Aciclovir.

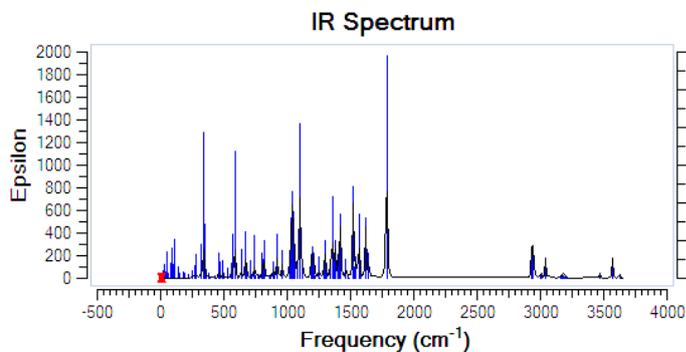
Figs. (6-a, 6-b and 6-c), the density of energy states of geometrically improved significantly from Ferrocene, Aciclovir and Ferrocene bonded with Aciclovir. Fig. (6-a) note the energy states density of ferrocene the value of the energy gap (0.79eV) as expected in this nano range. And this is agreement with all researches which tell us that the energy gap of nanomaterials is bigger than bulk of the same materials. Fig. (6-b) note the the density of energy states of Aciclovir (3.86 eV)the energy gap of the smallest than ferrocene. Fig. (6-c) show the density of energy states of Ferrocene bonded with Aciclovir, the levels of energy were almost separate in ferrocene. As the number of energy levels increases, separate behavior in the ferrocen turns into approximately the continues band in Ferrocene bonding with Aciclovir. The energy gap reduces from 2.58eV.



b



a



c

Figures (7-a, 7-b and 7-c): I.R intensity as a function of frequency using PBE/6-31G (d) basis sets(7-a)ofFerrocene, (7-b) Aciclovir and (7-c) Ferrocene bonded with Aciclovir.

Figs. (7-a, 7-b and 7-c) display analysis of oscillation modes in terms of IR intensity is performed. Fig. (7-a) show the I.R spectrum of ferrocene structure using PBE/6-31g(d) basis sets which can be divided into two regions depending on the properties of vibration or the gap separation them. In first region, (0 – 1500)  $\text{cm}^{-1}$  region is characterized by carbon and iron atoms. The region around the broad peak at  $248\text{cm}^{-1}$  has one cyclopentadienide with iron. The second region (3150-3202) $\text{cm}^{-1}$  this includes the hydrogen atoms vibrations include stretching (symmetric and asymmetric) and the bending mode of vibration (wagging, scissoring, rocking and twisting)[15]. Fig.(7-b))show the I.R spectrum of Aciclovir and Fig.(7-c)Ferrocene bonded with Aciclovir. The infrared vibrational frequency due to increase of number of atoms.

Figs. (8-a, 8-b and 8-c) show the Raman spectrum of Ferrocene, Aciclovir and Ferrocene bonded with Aciclovir structure molecule. It can be shown from the figure that the active region in IR is within less activity in Raman and this is due to different in selection rule as the different in intensity between IR and Raman for the same frequency and symmetry [16]. Fig. (8-a) show the Raman spectrum of Ferrocene as mentioned above, vibrational frequency between (3150-3202) $\text{cm}^{-1}$  is concerned with the vibration of hydrogen atoms. Fig. (8-b) show the Raman spectrum of Aciclovir and Fig (8-c) the Raman spectrum of Ferrocene bonded with Aciclovir

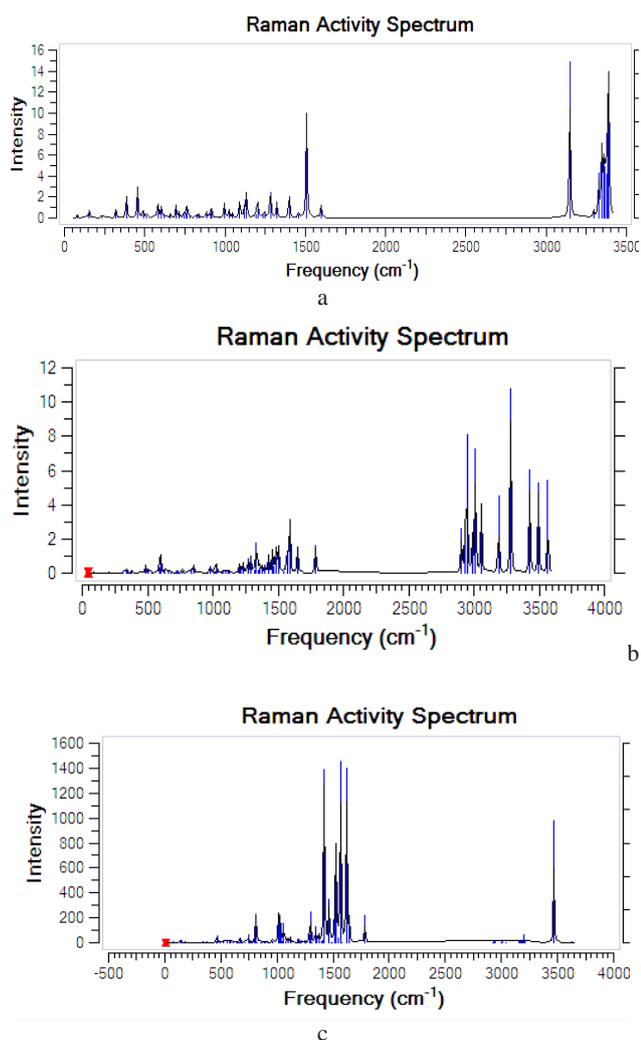
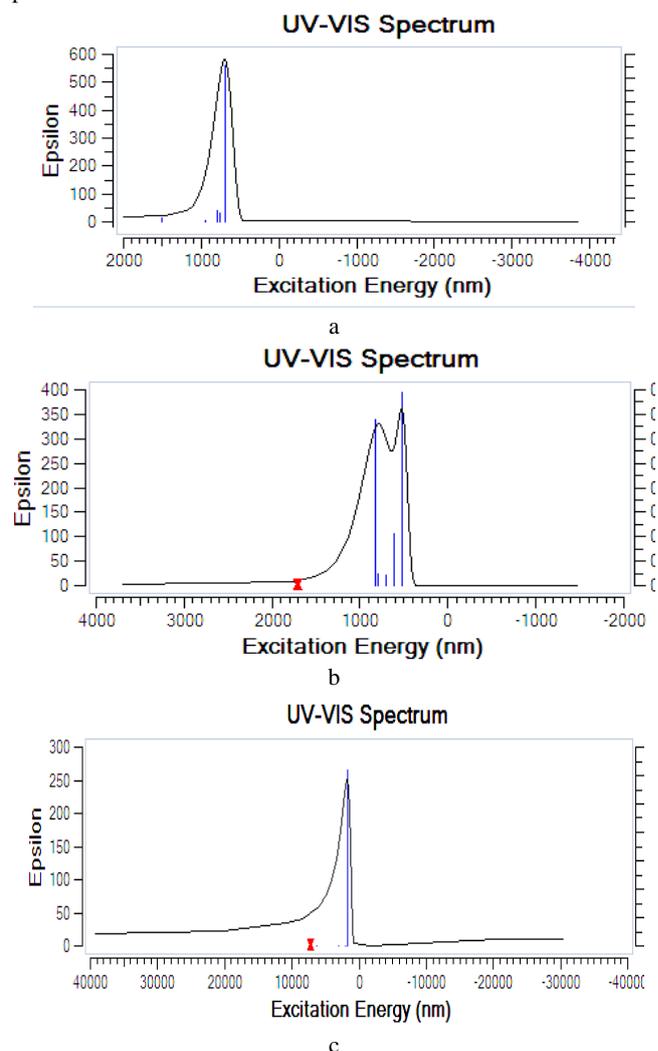
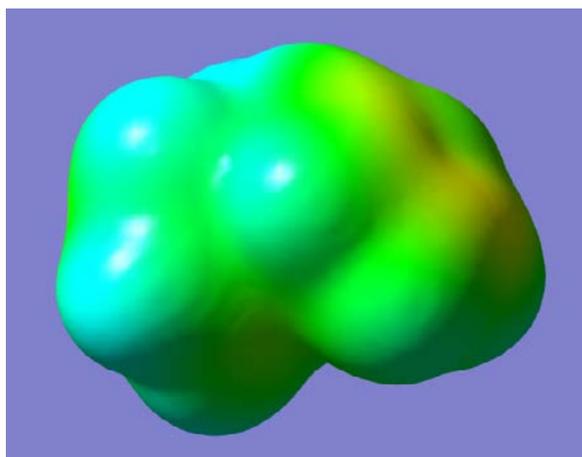


Figure 8: Raman intensities of infrared spectrum as a function of frequency using PBE/6-31G (d) basis sets of (8-a) of Ferrocene, (8-b) Aciclovir and (8-c) Ferrocene bonded with Aciclovir.

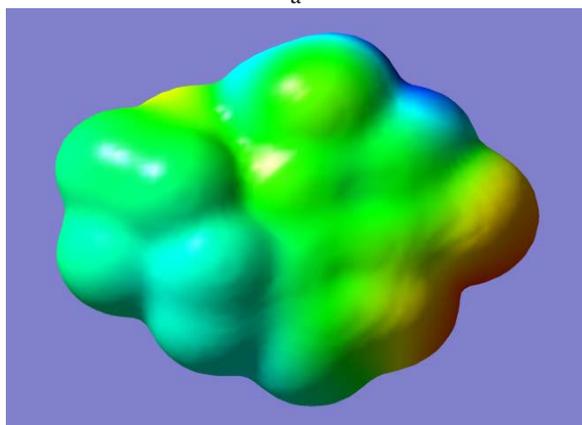
Figs. (9-a, 9-b and 9-c) show the UV/Vis absorption of light in the range of the wavelength (200–900) nm. The transitions produced by the electromagnetic radiation absorption in this spectrum region are transitions between levels of electronic energy. Commonly, the most likely transition is from highest to lowest occupied molecular orbital [17]. Fig. (9-a) note excitation energy of ferrocene is (0.4653 eV), Maximum absorption (2664.39 nm). Fig. (9-b) note excitation energy of Aciclovir is (0.7260 eV), Maximum absorption (1707.82 nm). Fig. (9-c) note excitation energy of ferrocene bonded with Aciclovir. Fig. (10-a, 10-b and 10-c) show the electrostatic potential of Ferrocene, Aciclovir and Ferrocene bonded with Aciclovir structure molecules using PBE/6-31G (d) basis sets drug. The molecular electrostatic potential (MEP) mapping is extremely functional in the study of the molecular structure with its physicochemical possessions relationships. Part of the molecule has a negative electrostatic potential is vulnerable to electrophilic attack. The red and blue regions in the MEP map indicate negative and positive potential areas and correspond to the electron-rich and electron-deficient regions respectively while the green color indicates neutral electrostatic potential that reflect the stability of Ferrocene structures and inert to use it as drugs carriers as illustrate in fig (10-a) [18]. Fig. (10-b) show electrostatic potential of Aciclovir has red and blue regions that means electron-rich and electron-deficient. It active material. Fig. (10-c) Show electrostatic potential of Aciclovir bonded with Ferrocene.



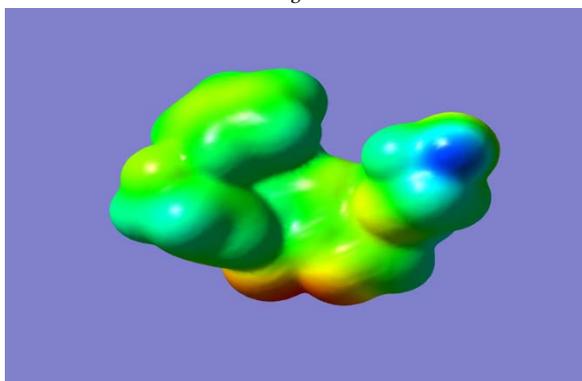
Figures (9-a, 9-b and 9-c): shows the UV/Visible. (9-a) Ferrocene, (9-b) Aciclovir and (9-c) Ferrocene bonded with Aciclovir



a



b



c

Figures (10-a, 10-b and 10-c): show the electrostatic potential of (10- a)Ferrocene,(10-b) Aciclovir and(10-c) Ferrocene bonded with Aciclovir.structure molecules using PBE/6-31G (d) basis sets.

#### CONCLUSIONS

- 1- Ferrocene structure high stability and inertness it can be used as a drug carrier.
- 2-Bond length of ferrocene the C-H bonds are the shortest bonds. It equals ( $1.09\text{\AA}$ ) and equal experimental value of the carbon-carbon bonds it equal to ( $1.35\text{\AA}$ ) is nearly the experimental value ( $1.5\text{\AA}$ ).
- 3-Zincblend's ideal bulk values of dihedral angles are  $\pm 60^\circ$  &  $\pm 180^\circ$  [13]. Ferrocene is completely true for the angles ( $-60^\circ$  and  $60^\circ$ ).
- 4-The distribution of tetrahedral angle of Ferrocene centered on the experimental value (dashed line).

5-The density of energy states of geometrically optimized ferrocene the value of the energy gap ( $0.79\text{eV}$ ). It has big energy gap as expected in this nano range.

6-I.R spectrum of ferrocene structure using PBE/6-31g (d) basis sets which can be divided into two regions depending on the properties of vibration or the gap separation them.

7-Raman spectrum of ferrocene as mentioned above, vibrational frequency between ( $3150-3202\text{cm}^{-1}$ ) is concerned with the vibration of hydrogen atoms.

8-Excitation energy of ferrocene is ( $0.4653\text{ eV}$ ), Maximum absorption ( $2664.39\text{ nm}$ ).

9-Electrostatic potential of ferrocene the green color signifies the neutral electrostatic potential reflect the stability of ferrocene structures

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