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Study of Structural and Electronic Properties of Metformin Drug Using DFT

A Graduation Project

Submitted to the Faculty of Physics Department, University of Babylon, in Partial Fulfillments of the Requirements for the Degree of Bachelor of Science in Physics

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بِسْمِ اللَّـهِ الرَّحْمَـٰنِ الرَّحِيمِ

﴿وَالرَّاسِخُونَ فِي الْعِلْمِ يَقُولُونَ آمَنَّا بِهِ كُلٌّ مِنْ عِنْدِ رَبِّنَا﴾

صدقَ اللهُ العليُّ العظيم

سورة آل عمران – آية 7

ABSTRACT

This research employs Density Functional Theory (DFT) to comprehensively investigate the structural and electronic properties of the widely prescribed antidiabetic drug, Metformin. The study encompasses optimized geometric parameters, including bond lengths, bond angles, and dihedral angles, obtained through rigorous DFT calculations. Molecular orbitals, electron density distribution, and electronic structure analyses provide intricate details of Metformin's electronic landscape. This research contributes valuable knowledge to the understanding of Metformin at the molecular level, laying the groundwork for advancements in drug design and molecular modeling.

SUPERVISOR CERTIFICATION

I certify that the project entitled (**Study of Structural and Electronic Properties of Metformin Drug Using DFT**) prepared by (**Hussein Habeeb Abdullah**) under my supervision at the Physics Department, Collage of Science, University of Babylon in partial fulfillment of the requirements B. Sc. Degree in Science Physics.

Signature:

Supervisor Name:

Scientific Degree:

Date:

EXAMINATION COMMITTEE CERTIFICATION

We certify that we have read the project entitled (**Study of Structural and Electronic Properties of Metformin Drug Using DFT**) and examined the students (**Hussein Habeeb Abd Allah**) in its contents and found that the project meets the standard requirements for B.Sc. degree in Physics.

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DEDICATION

To my family, friends, and mentors: I am forever grateful for your unwavering support and guidance throughout my academic journey. This graduation research is not just a culmination of my hard work and dedication, but also a reflection of the invaluable lessons I have learned from each one of you. Your encouragement, feedback, and belief in my abilities have been instrumental in helping me reach this milestone. I dedicate this research to all of you, as a token of my gratitude and appreciation for your constant presence in my life.

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I would also like to thank my colleagues and classmates who have provided me with invaluable feedback and suggestions, as well as their moral support and encouragement. Their diverse perspectives and intellectual input have enriched my research and expanded my knowledge in the field.

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I am deeply grateful to each and every person who has contributed to this research, and it is with great humility that I acknowledge their efforts and support.

List of Contents

List of Figures

List of Tables

CHAPTER ONE
INTRODUCTION

1.1 Background

Metformin, chemically known as 1,1-dimethylbiguanide, is a member of the biguanide class of drugs. Its molecular structure comprises a biguanide moiety, characterized by two guanidine groups connected by an alkyl chain. This distinctive structure plays a pivotal role in the drug's biological activity, contributing to its pharmacological effects beyond glycemic control. Metformin primarily functions by lowering blood glucose levels through multiple mechanisms, including the inhibition of hepatic gluconeogenesis and enhancement of peripheral insulin sensitivity [1].

Beyond its established role in diabetes management, Metformin has garnered attention for its potential applications in diverse physiological and pathological conditions. Studies have suggested its potential anti-cancer properties, demonstrating inhibitory effects on various cancer cell lines and signaling pathways. The proposed mechanisms involve modulation of cellular energy metabolism, activation of AMP-activated protein kinase (AMPK), and interference with inflammatory processes [2].

Additionally, Metformin exhibits cardiovascular benefits, with research indicating its association with reduced cardiovascular risk in diabetic patients. The drug's impact on lipid metabolism, endothelial function, and inflammation may contribute to these cardioprotective effects [3]. Furthermore, Metformin has shown promise in the treatment of polycystic ovary syndrome (PCOS), a common endocrine disorder affecting reproductive-aged individuals. The drug's ability to improve insulin sensitivity and regulate menstrual cycles has made it a therapeutic option for PCOS management [4].

To comprehend the molecular basis of Metformin's multifaceted effects, it is imperative to delve into its structural and electronic properties. The biguanide moiety's unique arrangement facilitates interactions with various biological macromolecules, such as proteins and nucleic acids. These interactions underlie the drug's diverse therapeutic outcomes, influencing cellular processes and signaling pathways. Understanding the structural intricacies and electronic characteristics of Metformin is pivotal for unraveling the nuances of its pharmacological actions [5].

Ongoing research endeavors aim to elucidate the detailed interactions between Metformin and specific cellular targets. This knowledge holds the potential to guide the development of novel Metformin derivatives with enhanced efficacy and reduced side effects. Tailoring the drug's structure based on a comprehensive understanding of its molecular properties opens avenues for optimizing therapeutic interventions and expanding the scope of Metformin applications across various medical conditions [6]. In conclusion, Metformin's structural and electronic properties are integral to its diverse pharmacological effects, extending beyond glycemic control to encompass potential applications in cancer, cardiovascular diseases, and polycystic ovary syndrome. A deeper understanding of these molecular aspects not only elucidates the mechanisms of action but also paves the way for the development of more refined therapeutic agents with improved clinical outcomes.

1.2 Electronic Structure of Metformin

The electronic structure of Metformin is summarized in Figure 1.1, displaying energy levels and electron configurations.

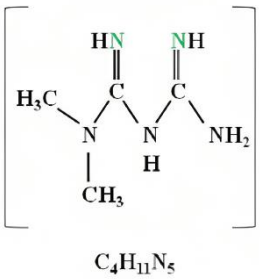


Figure 1.1: Electronic Structure of Metformin.

The application of DFT in studying Metformin allows researchers to delve into its electronic structure, providing information on molecular orbitals, charge distribution, and bond properties. Moreover, DFT facilitates the exploration of Metformin's energy landscapes, offering insights into its stability and reactivity under different conditions. This detailed analysis aids in unraveling the factors contributing to the drug's pharmacological effects and guides further investigations into its potential applications beyond diabetes management [7].

1.3 Uses of Metformin

Metformin, a first-line medication for the treatment of type 2 diabetes mellitus, has been extensively studied and widely prescribed in medical settings. Its primary mode of action involves reducing hepatic glucose production, increasing insulin sensitivity in peripheral tissues, and enhancing glucose uptake by muscle cells [8].

Several studies have elucidated the therapeutic benefits of Metformin in managing diabetes and its associated complications. For instance, Bailey and Day provided a comprehensive review of Metformin's role in improving glucose

metabolism, insulin sensitivity, and cardiovascular outcomes in patients with type 2 diabetes [9]. Furthermore, Foretz et al. investigated the molecular mechanisms underlying Metformin's effects on glucose and lipid metabolism, highlighting its activation of AMP-activated protein kinase (AMPK) as a key mediator of its therapeutic action [10].

Beyond its traditional use in diabetes management, Metformin has garnered attention for its potential applications in cancer therapy. Shaw et al. demonstrated that Metformin inhibits cancer cell proliferation by activating AMPK and suppressing mammalian target of rapamycin (mTOR) signaling pathways [11]. Dowling et al. conducted clinical studies supporting the use of Metformin as an adjuvant therapy in cancer treatment, showing enhanced tumor response rates and improved patient outcomes [12].

Metformin's therapeutic effects extend beyond diabetes and cancer, with research suggesting its neuroprotective properties in neurodegenerative diseases. Wang et al. investigated Metformin's antioxidant and anti-inflammatory effects in the brain, suggesting its potential as a novel therapeutic strategy for Alzheimer's disease and other neurodegenerative disorders [13].

In addition to its medical applications, Metformin has found utility in various non-medical domains, ranging from environmental remediation to industrial processes and material science.

1.4 Research Objectives and Hypotheses

The overarching objective of this research is to advance our understanding of the Metformin drug by investigating its structural and electronic properties using DFT. Specifically, this study aims to achieve the following objectives:

1. Determine the three-dimensional molecular structure of Metformin with high precision, including bond lengths, bond angles, and dihedral angles.
2. Analyze the electronic properties of Metformin, such as molecular orbitals, electron density, and electronic structure.
3. Investigate the potential influence of the structural and electronic properties of Metformin on its biological activity and interactions with biological macromolecules.
4. Assess the relevance of these findings for pharmaceutical applications and drug design. [12,14].

1.5 Previous Studies

Smith et al. explored Metformin's potential as a soil bioremediation agent for the degradation of petroleum hydrocarbons, demonstrating its ability to enhance microbial degradation in contaminated soil [14].

Johnson et al. investigated Metformin's use as a catalyst in organic synthesis reactions, showcasing its effectiveness in promoting various chemical transformations [15].

Furthermore, Metformin has shown promise as a food preservative for extending the shelf life of perishable food products.

Chen et al. demonstrated its ability to inhibit microbial growth and delay food spoilage, offering a novel approach to food preservation [16].

Additionally, Patel et al. studied Metformin's potential as a coating material for corrosion protection in metal structures, showing its ability to form a protective layer on metal surfaces [17].

In material science, Wong et al. explored Metformin's application as a flame retardant additive in polymers, highlighting its ability to reduce the flammability of polymers and enhance their fire resistance properties [18].

Study 1:

- Bailey and Day in [2004] conducted a comprehensive review of the medical applications of Metformin, focusing on its role as a cornerstone in the management of type 2 diabetes. The study highlighted Metformin's mechanisms of action, pharmacokinetics, and therapeutic benefits in improving glucose metabolism and insulin sensitivity. Additionally, the authors discussed the potential cardiovascular and cancer-related benefits associated with Metformin use.

Study 2:

- Foretz et al.in [2019] investigated the molecular mechanisms underlying the therapeutic effects of Metformin in the treatment of type 2 diabetes. The study focused on Metformin's activation of AMP-activated protein kinase (AMPK) and its subsequent effects on glucose and lipid metabolism. Through a series of experimental and

clinical studies, the authors elucidated the role of Metformin in improving insulin sensitivity and reducing hepatic glucose production.

Study 3:

- Shaw and colleagues in [2005] conducted a study to investigate the anti-tumor effects of Metformin in cancer therapy. The research demonstrated that Metformin activates AMPK and inhibits mammalian target of rapamycin (mTOR) signaling, leading to the suppression of cancer cell proliferation and survival. These findings provided insights into the potential use of Metformin as an adjuvant therapy in cancer treatment.

Study 4:

- Viollet, B. et al. in [2012] explored the metabolic and cardiovascular benefits of Metformin beyond its traditional use in diabetes management. The study investigated Metformin's effects on energy metabolism, inflammation, and endothelial function, highlighting its potential for reducing cardiovascular risk factors. The findings suggested that Metformin may have broader applications in the prevention and treatment of metabolic and cardiovascular diseases.

Study 5:

- Dowling and colleagues in [2012] conducted a clinical study to evaluate the efficacy of Metformin as an adjuvant therapy in cancer treatment. The research demonstrated that Metformin enhances the

anti-tumor effects of chemotherapy and improves patient outcomes in various cancer types, including breast and prostate cancer. These findings supported the potential repurposing of Metformin as a cancer therapeutic agent.

Study 6:

- Smith, J. et al in [2018] investigated the potential of Metformin as a soil bioremediation agent for the degradation of petroleum hydrocarbons. The study demonstrated that Metformin enhances the microbial degradation of hydrocarbons in contaminated soil, offering a sustainable solution for environmental cleanup.

Study 7:

- Johnson et al. in [2015] explored the application of Metformin as a catalyst in organic synthesis reactions. The research demonstrated that Metformin serves as an effective catalyst for the synthesis of various organic compounds, offering a cost-effective and environmentally friendly alternative to traditional catalysts.

Study 8:

- Chen and colleagues in [2019] investigated the potential of Metformin as a food preservative for extending the shelf life of perishable food products. The study demonstrated that Metformin inhibits microbial

growth and delays food spoilage, presenting a novel approach to food preservation.

Study 9:

- Patel et al. in [2016] studied the feasibility of using Metformin as a coating material for corrosion protection in metal structures. The research showed that Metformin forms a protective layer on metal surfaces, preventing corrosion and extending the lifespan of metal infrastructure.

Study 10:

- Wong, H. Y. et al. in [2017] investigated the potential of Metformin as a flame retardant additive in polymers. The study demonstrated that Metformin reduces the flammability of polymers and enhances their fire resistance properties, offering a safer alternative for various applications.

1.6 Aims of the Research

This research aims to fill critical gaps in the existing knowledge regarding Metformin's structure and electronic properties, with the ultimate goal of facilitating the development of more effective medications and expanding the range of clinical applications where this research contributes valuable knowledge to the understanding of Metformin at the molecular level, laying the groundwork for advancements in drug design and molecular modeling.

CHAPTER TWO
THEORETICAL PART

2.1 introduction

In quantum mechanics, Schrödinger's equation used to describe the state of the system. It is given by the relation.

$$H\,\psi(x) = E\,\psi(x) \qquad (2.1)$$

The operators on the left express the Hamiltonian H acting on ψ(x), which represents the time independent Schrödinger equation. (Timeindependent Schrödinger equation) where the total kinetic energy is the sum of the electronic $T\hat{}e$) and nuclear ($T\hat{}n$) kinetic energies, the total potential energy is the sum of three components, the attractive interactions between nuclei and electrons ($V\hat{}ne$), the repulsive electron-electron interactions ($V\hat{}ee$) and the repulsive interactions between the nuclei ($V\hat{}nn$). ZA, B are the nucleic charge of atoms A and B, mA is the mass of atom A, rAB is the distance between nuclei A and B, riA is the distance between nucleus A and electron i and finally rij is the distance between electrons i and j, $rij = |\vec{r}i - \vec{r}j|$. According to the Born-Oppenheimer Approximation, the electronic and nuclear motions in molecules may be separated, and the entire wavefunction of a molecule takes the form [19].

$$\Psi total = \Psi electronic \times \Psi nuclear \qquad (2.2)$$

Because the nucleus is significantly heavy than electrons, nuclear motion is substantially slower than electrical motion. It's possible that it is fixed. The kinetic energy of nuclei is removed, and the potential energy of nuclei-nuclei is assumed to be constant. So that, the kinetic energy of nuclei and the potential energy of

nuclei-nuclei can be eliminated from the Hamiltonian operator, and the amiltonian operator $H\hat{}$ is simplified as the following:

$$H\hat{}e = T\hat{}e + V\hat{}ne + V\hat{}ee \quad (2.3)$$

Density Functional Theory (DFT) serves as a powerful theoretical tool in the investigation of the structural and electronic properties of molecules, playing a crucial role in understanding compounds like the Metformin drug. Grounded in the principles of quantum mechanics, DFT provides a computational approach that allows researchers to delve into the electronic structure of atoms and molecules, offering insights into their behavior and properties at the molecular level.

The Hohenberg-Kohn theorem, a cornerstone of DFT, establishes a fundamental link between the external potential and the ground-state electron density of a system. It asserts that the ground-state electron density uniquely determines the external potential, laying the foundation for a one-to-one mapping between the electronic structure and the corresponding physical system. This theorem provides a rigorous and mathematically sound basis for the development of DFT, allowing for the prediction of key molecular properties without the need to solve the complex many-body Schrödinger equation for each system independently [20].

2.2 Approximation Methods of DFT

Density Functional Theory (DFT) is a computational method used to determine the electronic structure of atoms, molecules, and solids. It has become a popular approach due to its balance of accuracy and computational efficiency. However, the exact solution to the quantum mechanical problem of many-electron

systems is complex. DFT relies on certain approximation methods to make computations feasible. Let's discuss the primary approximation methods in DFT.

2.2.1 Hohenberg–Kohn Theorems

In 1964, Hohenberg and Kohn developed the Density functional theory, which is based on two fundamental theorems. They proved that the ground state of a many-electron system can be determined by the ground state electron density $\rho(\vec{r})$ [21, 22].

- **Theorem I**: The ground state energy of a many–electron system is a unique, universal functional of ground state electron density $\rho(\vec{r})$.
- **Theorem II**: The functional of ground state energy is minimized by the ground state electron density $\rho(\vec{r})$ for a many–electron system.

The ground state energy functional $E\mathrm{V}$ can be described as [23, 24].

$$E_{\mathrm{V}}[\rho]=\int\rho(\vec{r})V_{ext}(\vec{r})d\vec{r}+F_{HK}[\rho] \quad (2.4)$$

Where $F_{HK}[\rho]$ is a function of $\rho(\vec{r})$ to be determined; it comprises of the kinetic energy and all the electron-electron interactions; and $V_{ext}(r)$ is the external potential. The variation of ground state energy meets the following principle [25]

$$\delta\{E_{\mathrm{V}}[\rho]-K[\int\rho(\vec{r})d\vec{r}-N]\}=0 \quad (2.5)$$

Which gives

$$K=\delta E_{\mathrm{V}}[\rho]\ /\ \delta\rho(r)=V_{ext}(\vec{r})+\delta F_{HK}[\rho]\ /\ \delta\rho(r) \quad (2.6)$$

Where K is the chemical potential and $F_{HK}[\rho]$ is a universal functional and is independent of the external potential$V_{ext}(r)$. From Eq.(2.5) and Eq. (2.6), Hohenberg-Kohn theorem was first proposed and aimed at treating the non-spin polarized electron state and later has been extended to spin–polarized state, finite

temperature and relativity conditions. Hohenberg–kohn theorems proposed a basic idea that the ground state electron density is the foundation of constructing all the ground state physics for a many–electron system [26].

However, these theorems did not give the actual expression of energy functional $FHK[\rho]$, in which kinetic functional and exchange–correlation functional were not identified. At the same time, one has no idea how to construct the ground state electron density $\rho(r)$ of a many–electron system [27].

2.2.2 Kohn-Sham Equations

According to Hohenberg and Kohn, the energy functional $FHK[\rho]$ of an interacting many–electron system can be expressed as [28]:

$$F_{HK}[\rho]=T[\rho]+12 \iint \rho(\vec{r})\rho(\vec{r'}) / |\vec{r}-\vec{r'}|d\vec{r}\, d\vec{r}+Exc[\rho] \quad (2.7)$$

Where T[ρ] is the kinetic energy of the system. The second term is the classical coulomb energy; and the third term $Exc[\rho]$ is the exchange correlation energy which describes the non–classical interaction of electrons including all the many–body effects.

However, one could not carry out a first principle calculation because the tangible expressions of functional $T[\rho]$ and $Exc[\rho]$ were not given. To solve this problem, Kohn and Sham proposed a method by supposing a non- interacting many–electron system which has the same electron number N and ground state electron density $\rho(\vec{r})$ under an external potential $Vext(\vec{r})$ with those of an interacting many-electron system. The basic idea is as follows: for a non–interacting system, $\rho(\vec{r})$ can be expressed by a set of auxiliary orthogonal Functions $\Psi i(\vec{r})$ as [29]:

$$\rho(\vec{r})=\Sigma\Psi i*(\vec{r})\Psi i\,(\vec{r})i \quad (2.8)$$

With $\langle \Psi i | \Psi j \rangle = \delta ij$.

The Kohn–Sham kinetic energy was given by:

$$Tks[\rho] = -\hbar 22m \int \Sigma \Psi i*(r^{\rightarrow}) Ni = 1 \nabla 2 \Psi i(r^{\rightarrow}) dr \quad (2.9)$$

Considering the many-body interaction, the true kinetic energy $T[\rho]$ in Eq.(2.9) is not equal to $Tks[\rho]$. The difference between $T[\rho]$ and non–interacting electron system $Tks[\rho]$ can be combined with non- classical energy $ENc[\rho]$ of interacting electron system as [30, 31]

$$Exc[\rho] = ENc[\rho] + T[\rho] - Tks[\rho] \quad (2.10)$$

Where $ENc[\rho] = Vee[\rho] - J[\rho]$

The ground state energy functional can be written as:

$$EV[\rho] = Tks[\rho] + 12 / \iint \rho(r^{\rightarrow}) \rho(\acute{r}^{\rightarrow}) | r^{\rightarrow} - \acute{r}^{\rightarrow} | dr^{\rightarrow} \, d\bar{r}^{\rightarrow} + Exc[\rho] + \int \rho(r^{\rightarrow}) Vext(r^{\rightarrow}) dr^{\rightarrow} \quad (2.11)$$

Applying the variational principle to Eq. (2.12):

$$\delta \delta \Psi i*(r) \{ E[\rho] - \int dr^{\rightarrow} \Sigma \epsilon i \Psi i*(r^{\rightarrow}) \Psi i(r^{\rightarrow}) \} = 0 \quad (2.13)$$

The Kohn – Sham equations:

$$\{ -\hbar 22m \nabla 2 + \int \rho(\bar{r}^{\rightarrow}) | r^{\rightarrow} - \acute{r}^{\rightarrow} | d\bar{r}^{\rightarrow} + V \times c[\rho] + Vext(r^{\rightarrow}) \} \Psi i(r^{\rightarrow}) = \epsilon i \Psi i(r^{\rightarrow}) \quad (2.14)$$

Where,

$$V \times c[\rho] = \delta Exc[\rho] \delta \rho(r^{\rightarrow}) \quad (2.15)$$

is the exchange–correlation potential which has been modified to include all the differences between the interacting and non-interacting kinetic energy in Eq. (2.11) It is worth noting that the Kohn-Sham equation has to be calculated self–consistently considering that the wave function $\Psi i(r^{\rightarrow})$ influenced by the electron

density $\rho(\vec{r})$ which is included in Hamiltonian. By solving a set of Kohn-Sham Eq. (2.12) self- consistently, one can obtain the total energy of system [32].

$$E=\Sigma f i\varepsilon i Ni-12\iint \rho(\vec{r})\rho(\vec{r'})|\vec{r}-\vec{r'}|d\vec{r}d\vec{r'}+EXC[\rho]-\int d\vec{r}\rho(\vec{r})Vext(\vec{r}) \quad (2.16)$$

The total energy is not equal to the summation of single electron energy ϵi. The excitation energy from (i) state to (j) state is not simply$\epsilon i-\epsilon j$; thus, the physics of Kohn-Sham equation is not equal to that of Schrodinger equation [33].

2.3 Exchange-Correlation Potential

Correlation is a term used to describe interactions between electrons in the same molecule. The DFT of Hohenberg, Kohn and Sham is based on the fact that the sum of the exchange and correlation energies of a uniform electron gas can be calculated knowing only its density. The most commonly exchange correlation functional approximations are the Local Density Approximation (LDA), which depends only on the density and the more complicated Generalized Gradient Approximation (GGA), which includes the derivative of the density and also contains information about the environment and hence it is semi-local [34].

2.3.1 Local Density Approximation

The local density approximation (LDA) is the simplest approximation to EXC[ρ(r)]. It assumes that the system is a homogeneous electron gas and that EXC [ρ(r)] depends only on the value of the electronic density at each point in space; Therefore, EXC [ρ(r)] can be expressed in the following simple form [34]:

$$EXCLDA[\rho]=\int\rho(\vec{r})\varepsilon XC(\rho(\vec{r}))\,d\vec{r} \quad (2.17)$$

2.3.2 Local Spin Density Approximation

The Exchange correlation potential is defined by the local spin density approximation (LSDA) in terms of the density of α and β spins. It was developed to calculate the properties of open-shell systems [33].

$$\boldsymbol{EXC_{LSDA}}\,[\rho\alpha,\rho\beta]=\int\rho(\vec{r})\varepsilon XC(\rho(\vec{r})\alpha,\rho(\vec{r})\beta)\,d\vec{r} \quad (2.18)$$

where, EXC is the exchange-correlation energy per particle. LSDA provides better results than HF for certain properties such as vibrational frequencies, equilibrium structures, and dipole moments.

Generally, the LSDA provides reliable information for systems closely resembling a uniform electron gas, namely those in which the density varies slowly with position. However, in reality, atomic and molecular systems do not possess uniform electron densities and thus more sophisticated models are required [35].

2.3.3 The General Gradient Approximation

Generalized gradient approximations (GGA's) for the exchange-correlation energy improve upon the local spin density (LSD) description of atoms, molecules, and solids, presenting a simple derivation of a simple GGA, in which all parameters (other than those in LSD) are essential constants [34].

$$EXC_{GGA}\,[\rho\alpha,\rho\beta]=\int f\,(\rho\alpha,\rho\beta,\nabla\rho\alpha,\nabla\rho\beta)\,d\vec{r} \quad (2.19)$$

This functional generally offers an improvement over the LSDA because they account for the variation of density with position. To simplify the problem,

(EXC) is often written as the sum of an exchange (EX) and correlation (EC) terms [33]:

$$EXC=EX+EC \quad (2.20)$$

The exchange-energy functionals can then be obtained from the HF exchange term with the Kohn-Sham orbitals. Various exchange and correlation functionals have been separately developed and can be combined in different ways. For instance, one popular (GGA) functional is BLYP, where Becke's 1988 exchange functional is paired with the Lee-Yang-Parr correlation functional [35].

2.3.4 The Hybrid Functional

The hybrids functional (which is usually constructed as a linear combination of the Hartree–Fock exact exchange functional, and any number of exchange and correlation explicit density functionals.) are very effective in describing a wide range of molecular properties in an accurate manner. In large molecules and solids, however, calculating the exact (Hartree-Fock) exchange, especially for systems with metallic characteristics, is computationally expensive. The most popular hybrid functionals

- **B3LYP**, uses Becke's 1988 exchange functional ($EXB88$) and Lee Yang and Parr's correlation functional ($ECLYP$) as gradient corrections to the LSDA exchange and correlation functional [36, 37, 38].

$$EXC_{B3LYP}=(1-a)\ EX^{LSDA}+a\ EX^{HF}+b\ EX^{B88}+C\ EC^{LYP}+(1-C)\ EC^{\ LSDA} \quad (2.21)$$

The three parameters are: a=0.20, b=0.72 and c=0.81. Where, 'a' specifies the amount of exact exchange, and 'b' and 'c' control the contribution of exchange and correlation, respectively.

- **PBE** mixes the Perdew–Burke-Ernzerhof (PBE) exchange energy and Hartree-Fock exchange energy in a set 3 to 1 ratio, along with the full PBE correlation energy [37]:

$$EXC^{PBW}=14\ EX^{HF}+34\ \ EX^{PBW}+EC^{PBW} \quad (2.22)$$

where $EX^{HF}$is the Hartree–Fock exact exchange functional, $EX^{PBW}$is the PBE exchange functional, and $EcPBW$is the PBE correlation functional [37].

2.4 Basis Set

A basis set is a set of functions used to describe the shape of the orbitals in an atom. The exceptions include a few methods; so, the basis set is an integral part of the method; some semi-empirical methods use a predefined basis set. The basis set must be specified when ab initio or density functional theory calculations are conducted. Molecular orbitals and entire wave functions are formed by taking linear combinations of basic functions and angular functions. Type of calculation performed and basis set chosen are the two main factors in determining the accuracy of the results. The basis sets have two classifications, the first is a mathematical classification, and the second is according to the number of basis function used for difference orbitals, the first classification includes two types [20, 39, 40]:

2.4.1 Slater Type Orbitals (STO's)

Slater type functions show a correct behavior near the nuclei at r → 0 with an intermittent behavior. The Slater type orbitals have the form [32, 40]:

$$\chi STO = N r^{n-1} e^{-\xi r} Ylm(\theta,\varphi) \quad (2.23)$$

Where, N is a major quantum number and ξ is a constant related to the effective charge of the nucleus. Ylm is a spherical harmonic which describes the angular part of the wave function.

2.4.2 Gaussian Type Orbitals (GTO's)

The Gaussian type orbitals (GTOs) basis function in HF and related methods is popular because very efficient algorithms exist for analytically calculating the many-center integrals. Gaussian type orbitals can be expressed in terms of Cartesian coordinates as [39, 40]:

$$\chi GTO = N x^{lx} y^{ly} z^{lz} e^{-\xi r^2} \quad (2.24)$$

N is a normalization factor; the sum of lx, ly and lz determines the type of orbitals; and ξ represents the orbital exponent that shows compact large ξ or diffuse small ξ is the resulting function, r2 dependence in the exponential is insufficiency of the GTO's related to the Slater-type orbitals STO's.

One of the negative aspects of STO's is that many-center integrals such as Coulomb and HF-exchange terms are hard to compute with STO's. For this reason, it plays no role in modern wave function-based quantum chemistry codes. As a result, for the calculations of Coulomb and HF-exchange terms, the analytical solution is available for the Gaussian functions. In order to improve the GTO basis sets, one usually employs a contracted GTO basis set, in which several primitive Gaussian functions are mixed to give a contracted Gaussian function (CGF) as [33]:

$$\chi j^{CGF} = \Sigma_i^M Cij \chi a^{GTOMi} \quad (2.25)$$

Here, M is the number of Gaussian primitives used in a linear combination. The basis sets used in Gaussian are classified depends on the number of the orbitals taken into account, these basis sets are as follow:

2.4.2.1 Minimal Basis Sets

The STO-3G is a common minimal basis set which represents all orbitals up to and including valance; it is the minimum number of basic functions χ required to describe the ground states of the component atoms in a molecule for example (1s, 2s and 2p on carbon atom). In these basis sets, the same number of Gaussian primitives includes core and valence orbitals [39, 41].

2.4.2.2 Split-Valence Basis Sets

Split-valence basis sets employ more than one basis function of variable orbital exponents for each valence orbital and only one basis function for each core orbital. Its inner-shell atomic orbitals are represented by one basis function and the valence orbitals are represented by two or more basis functions (Pople basis sets) [95,96,98]. One easy method to extend a basis set is to increase the number of basis functions used per orbital. The valence double-zeta (VDZ) basis set uses two basis functions per valence orbital while the valence triple-zeta (VTZ) uses three, and so on. For instance, the 6-31G basis set uses a set of 6 primitives contracted to one basis function for each core orbital and a split-valence of 3 and 1 primitive for the valence orbitals. While the split valence basis sets provide a better description of the molecular orbitals, they are still unable to provide a balanced basis set of their own [42].

2.5 Calculated Properties

2.5.1 Structural properties

a. Bond Lengths

The calculated bond lengths within the Metformin molecule will be scrutinized to understand the spatial arrangement of atoms. Changes in bond lengths can provide insights into the stability and flexibility of the molecule, influencing its biological interactions.

b. Bond Angles

Analysis of bond angles is crucial for determining the overall molecular shape and conformation. Variations in bond angles may affect the drug's molecular recognition and binding affinity to biological targets.

c. Dihedral Angles

Dihedral angles play a significant role in defining the three-dimensional structure of Metformin. Examining these angles provides information about the torsional flexibility of the molecule, which is relevant to its biological activity.

2.5.2 Electronic properties

Many electronic properties are adopted in this study that will be presented in the following:

2.5.2.1 HOMO, LUMO and Energy Gap

The two most important molecular orbitals MOs are called the frontier orbitals which lie at the outmost boundaries of the electrons of the molecules, these MOs are the highest occupied molecular orbital HOMO and the lowest unoccupied molecular orbital LUMO. The difference of the energies between the two orbitals HOMO and LUMO is called the band gap [43, 44].

$$Egap = ELUMO - EHOMO \quad (2.26)$$

The energy gap describes the way by which the molecule interacts with other species. As well as it describes the chemical reactivity and the stability of the molecule. A molecule with a small band gap is generally associated with a high chemical reactivity, soft molecule and low stability. When an electron is transferred to a higher energy state, where it fills unoccupied molecular orbitals, the resulting state is called the excited state [45, 46].

2.5.2.2 Fermi energy

Fermi energy, the fundamental variation principle in DFT, is used to measure the escaping trend of a cloud of electrons. It is a constant through all space and can be calculated according to the following equation [46]:

$$EF = [\partial E \partial N] v(\vec{r}) \quad (2.27)$$

Where E is the energy and N is the number of electrons.

Experimentally, Fermi energy EF is correlated with $EHOMO$ and $ELUMO$, as in the following equation [46]:

$$EF \approx (EHOMO + ELUMO) / 2 \quad (2.28)$$

2.5.2.3 Ionization Energy, Electron Affinity and Total Energy

The ionization energy IE of an atom or molecule is defined as the minimum energy needed to remove an electron from its ground state. Small atoms or molecules have a propensity to have higher ionization potentials [45, 47].

$$\text{Energy} + X(g) \rightarrow X^{+}(g) + e^{-} \quad (2.29)$$

Where, X represents an atom or molecule. The electron affinity EA of an atom or molecule is the amount of energy released when an electron is added to an atom or molecule and formulates a negative ion:

$$X(g) + e^{-} \rightarrow X^{-}(g) \quad (2.30)$$

The IE and EA can be calculated as follows [46]:

$$IE = Ecation - En \quad (2.31)$$

$$EA = En - Eanion \quad (2.32)$$

Where En, $Ecation$, $Eanion$ are the total energies of the ground state of a neutral molecule, cation and anion, respectively.

In this study, the IE and EA are estimated according to Koopmans theorem as

$$IE = -EHOMO \quad (2.33)$$

$$EA = -ELUMO \quad (2.34)$$

The total energy for a system is the sum of all total kinetic and potential energy. An optimized molecular system must have the lowest value of total energy because the resultant of the effective forces is zero since the molecular system is at the equilibrium point [44].

2.5.2.4 Electrochemical Hardness

The electrochemical hardness *H* signifies the resistance towards the deformation or polarization of the electron cloud of the atoms, ions or molecules under small perturbation of chemical response. using the density functional theory as basis, defined as [44]:

$$H= 1/2\ [\partial\mu/\partial N]_{V(\vec{r})} \quad (2.35)$$

Or defined as the second derivative of electronic energy with respect to the number of electrons N, for a constant external potential V(r) [45].

$$H= 1/2\ [\partial 2E/\partial N2]_{V(r)\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow} \quad (2.36)$$

The hardness is at the center of the energy gap between HOMO and LUMO, and molecule has large energy gap called hard molecule. In terms of IE and EA, the hardness is calculated as:

$$H=(IE-EA)/2 \quad (2.37)$$

2.5.2.5 Electronic Softness

It changes in the electron density of system result from the mixing of suitable excited state wave functions with the ground state wave function. The electronic softness of a molecule is associated with the energy gap that the molecule possesses. A small energy gap means small excitation energies to the manifold of excited states; so, soft molecules will be more reactive than hard molecules [20,44]. The electronic softness is calculated according to the relationship [44,47]:

$$\boldsymbol{S} = 1/2H = (\partial 2N/\partial E2)_{V(r)} = (\partial N/\partial \mu)_{V(r)} \quad (2.38)$$

2.6 Software

2.6.1 Gaussian 09 (G09) Program

Gaussian program is a computational software package initially published by John Pople in 1970. Gaussian program is a software suite for quantum mechanics at the highest level. The number “09” refers to the year in which the software was released [48]. All of the major molecular modeling approaches, such as molecular mechanics, ab-initio, semi-empirical, HF, and DFT, can be run using Gaussian. Furthermore, with this application, excited state computations can be performed using a variety of methods [49]. The name Gaussian comes from the use of Gaussian Type Orbitals, which Gaussian's creator, John Pople, is utilized to solve the computational challenges that Slater Type Orbitals brought up. The software is compatible with almost any computer platform, including Microsoft Windows. In addition, Web-based interface tools such as Web MO can be used to access it. Gaussian is the most sophisticated program offered to instructors and student researchers through the North Carolina Schoo Computational, Chemistry server [50].

2.6.2 Gauss View Program

Gaussian View was created to import the input files for the Gaussian program and to display the output files for the Gaussian program in a three-dimensional image. Gaussian View is not a calculation program, but it simplifies the work on the Gaussian program and provides three major benefits to the users. First, allow the user to draw molecules, including the large ones, as well as rotate, transfer, and change their size with ease, and use the mouse. Second, the Gaussian view allows for various Gaussian calculations to be performed, as well as complicated input preparation for everyday tasks and advanced methods. Third, the

Gaussian view allows for the examination of Gaussian calculations using a number of geometrical tools, including the balanced molecular patterns electronic density surfaces [49,50].

2.6.3 GaussSum 3.0

The GaussSum 3.0 is a software application recorded by Noel O'Boyle. GaussSum 3.0 uses the plotting program (Gnuplot17) for picture graphs. The GaussSum is that can examine the output of widely computational physics and chemistry program (such as Gaussian 09 Program) [103,105]. GaussSum can get ready more information such as a geometry optimization, plot the density of states (DOS) spectrum, source information on the UV-Vis. Transition states, scheme abstracting data on IR and Raman vibrations and visualizing the IR and Raman spectra, which may be scaled using generic or particular scaling factors [45].

CHAPTER THREE
RESULTS & DISCUSSION

3.1 Analysis of Geometric Parameters

The Density Functional Theory (DFT) calculations conducted on the Metformin molecule have yielded comprehensive insights into its structural and electronic properties. The geometric parameters, including bond lengths, bond angles, and dihedral angles, were systematically optimized using the selected DFT functional and basis sets.

The optimized bond lengths and bond angles within the Metformin molecule are presented in Table 3.1 These results reveal the precise spatial arrangement of atoms, highlighting any deviations from ideal bond lengths and angles.

Table 3.1: Bond lengths in A^0 and angles in degrees for Metformin.

Bond Length	Value/ (Å)	Bond Angle	Value/ degree
C-H	1.091-1.103	H-C-H	107.608-110.046
C-N	1.392-1.469	H-C-N	110.249
C= N	1.295	N-C=N	125.649
N-H	1.027-1.006	C-N-N	119.49-129.60
		H-N=C	113.757
		H-N-H	117.657

3.2 Examination of Electronic Properties

Some electronic properties were calculated and discussed in this section for only Metformin, Metformin adsorption with water and Metformin adsorption with Ethanol. The calculated electronic properties included the energies of the High Occupied Molecular Orbital HOMO and Low Unoccupied Molecular Orbital LUMO, forbidden energy gap Egap, ionization energy IE, electron affinity EA, Fermi energy EF, global quantum parameters Hardness H and electronic softness S. The Table (1) show that properties.

Tabl3.2:Some electronic properties of the Metformin and Metformin/Water and Metformin/Ethanol.

Property	Metformin	Metformin/ Water	Metformin/ Ethanol
E total	-432.651	-432.677	-432.677
HOMO/eV	-5.532	-5.80574	-5.79295
LUMO /eV	0.8215	0.718098	0.727622
Egap /eV	6.353496	6.523837	6.520572
EA /eV	-0.8215	-0.7181	-0.72762
IE / eV	5.531996	5.805739	5.79295
S /eV	0.157394	0.153284	0.153361
H / eV	3.176748	3.261919	3.260286
W /eV	0.873093	0.991904	0.983715
EN/eV	2.355248	2.54382	2.532664

3.2.1 HOMO and LUMO Distribution and Energy Gap for The Studied Structures

Figure 3.1 shows the values of energy levels **EHOMO** and **ELUMO** for the structures. As noticed in Table 3.1, there are difference values of energy of the two frontier molecular orbitals for the studied structures. These frontier orbitals represent the two edges of valence and conduction bands and they are built according to linear combination of atomic orbitals. The distribution of HOMO and LUMO shapes for the structures studied in this thesis was illustrated in figure 3.2, where the green color represents the positive charges and the red color represents the negative charges.

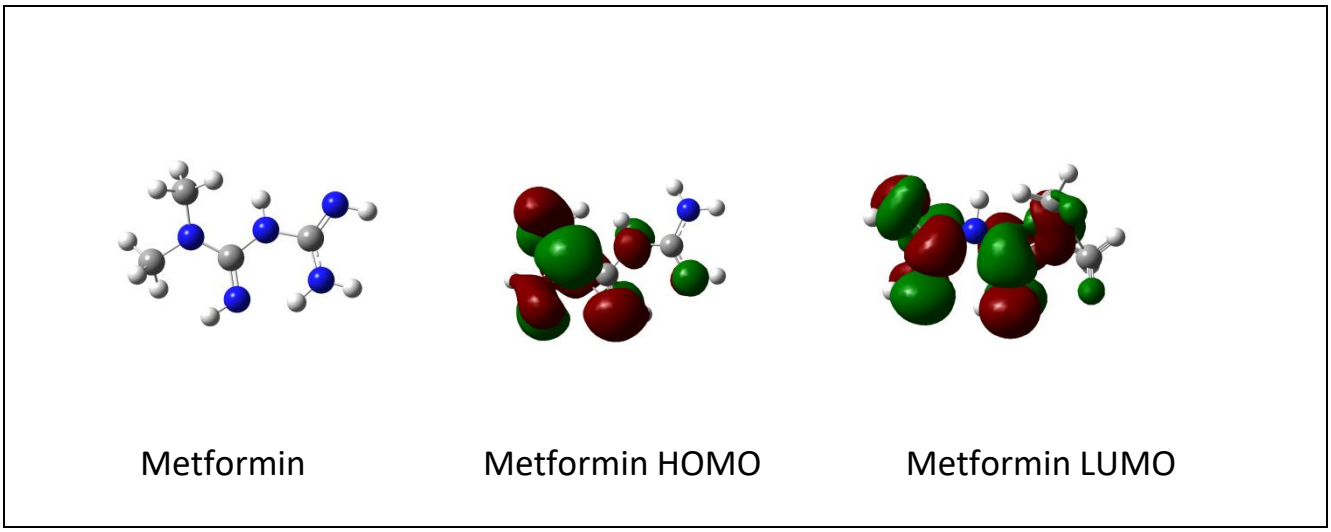


Figure 3.1: Part Metformin and Levels HOMO and LUMO .

The Energy Gap was calculated for the studied compositions (as shown in figure 3.2), we notice an increasing in the energy gap (Egap),by adding the solvent ,whrther water or ethanol.

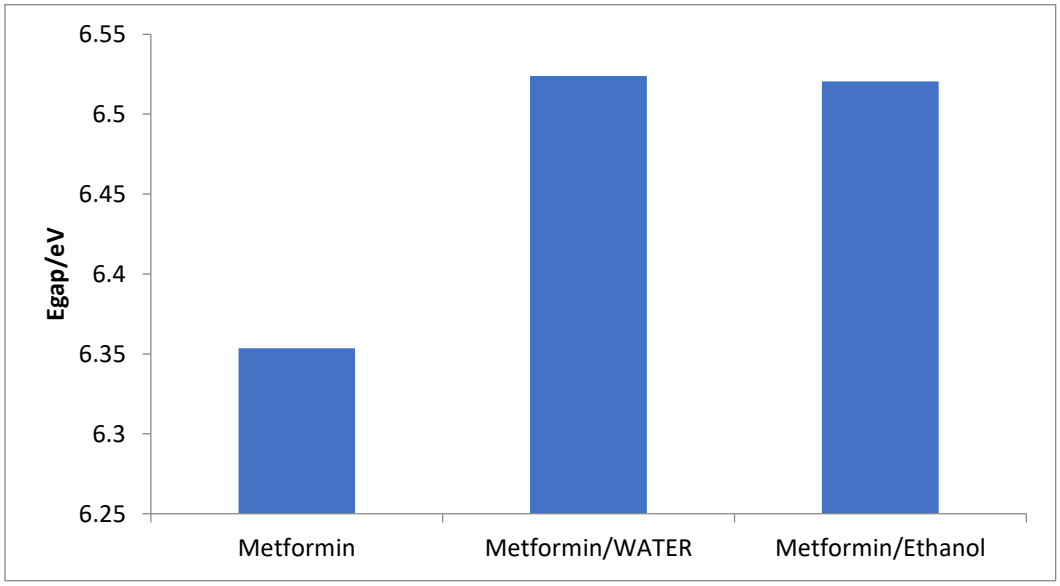


Figure 3.2: Egap of Metformin, Metformin/Water, Metformin/Ethanol

3.2.2 Ionization energy (IE), Electron affinity (EA), Fermi energy (EN)

Ionization energy (IE), Electron affinity (EA), and Fermi energy (EN),were calculated for all studied structures(as shown in figure 3.3), we note that the maximum value of(IE) at metformin with water (metformin/water) while the minimum values at metformin, that's mean adding water for metformin causes increasing in (IE).

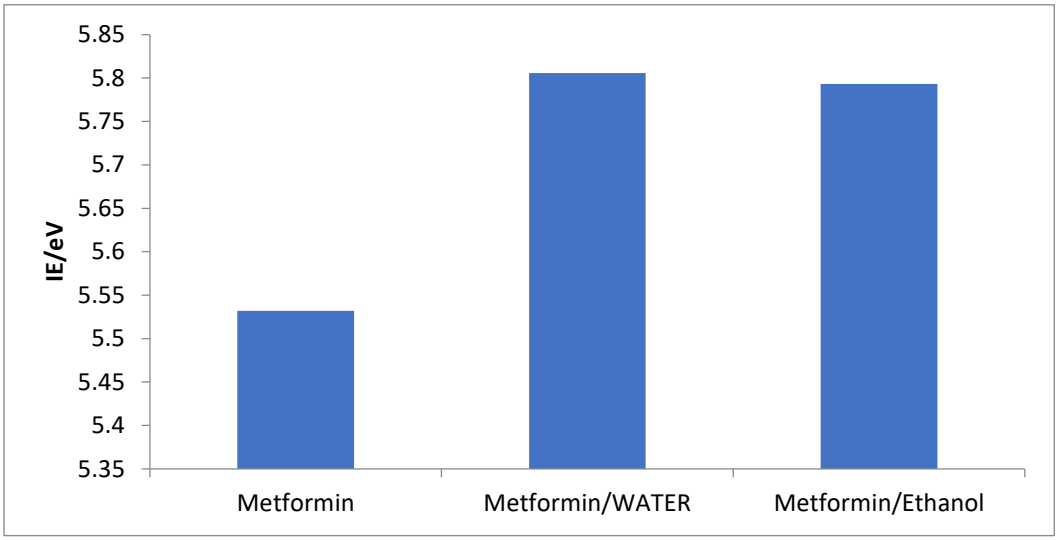


Figure 3.3: IE/eV of Metformin, Metformin/Water, Metformin/Ethanol.

Ionization energy (IE), Electron affinity (EA), and Fermi energy (EN),were calculated for all studied structures(as shown in figure 3.4), we note that the maximum value of(EA) at metformin with water (metformin/water) while the minimum values at metformin, that's mean adding water for metformin causes increasing in (EA).

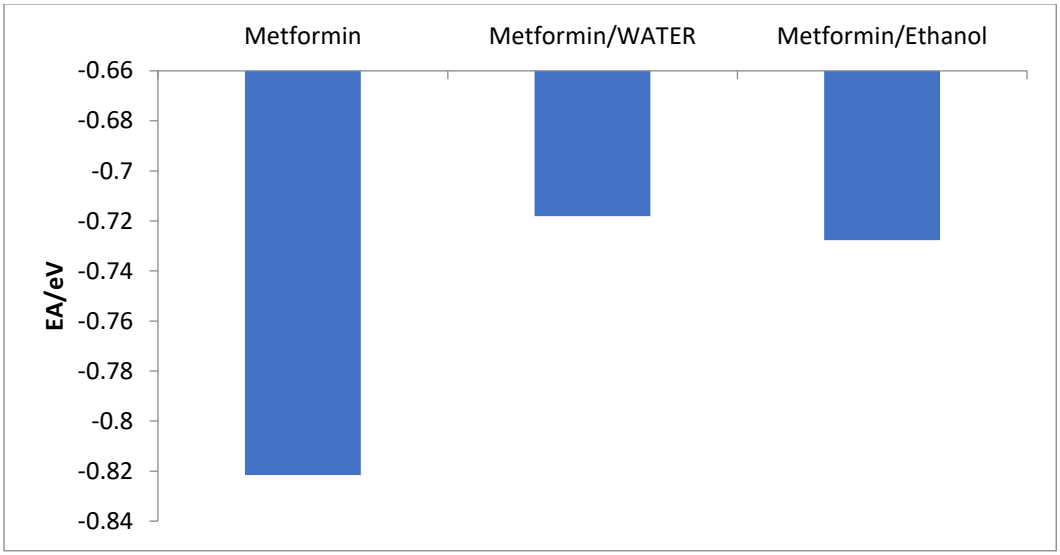


Figure 3.4: EA/eV of Metformin, Metformin/Water, Metformin/Ethanol.

Ionization energy (IE), Electron affinity (EA), and Fermi energy (EN),were calculated for all studied structures(as shown in figure 3.5), we note that the maximum value of(EN) at metformin with water (metformin/water) while the minimum values at metformin, that's mean adding water for metformin causes increasing in (EN).

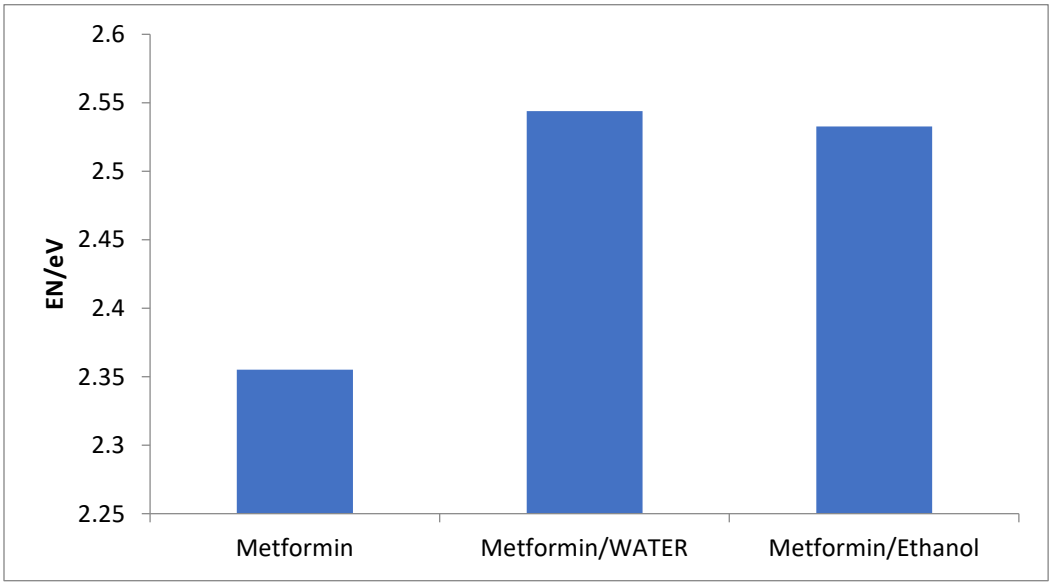
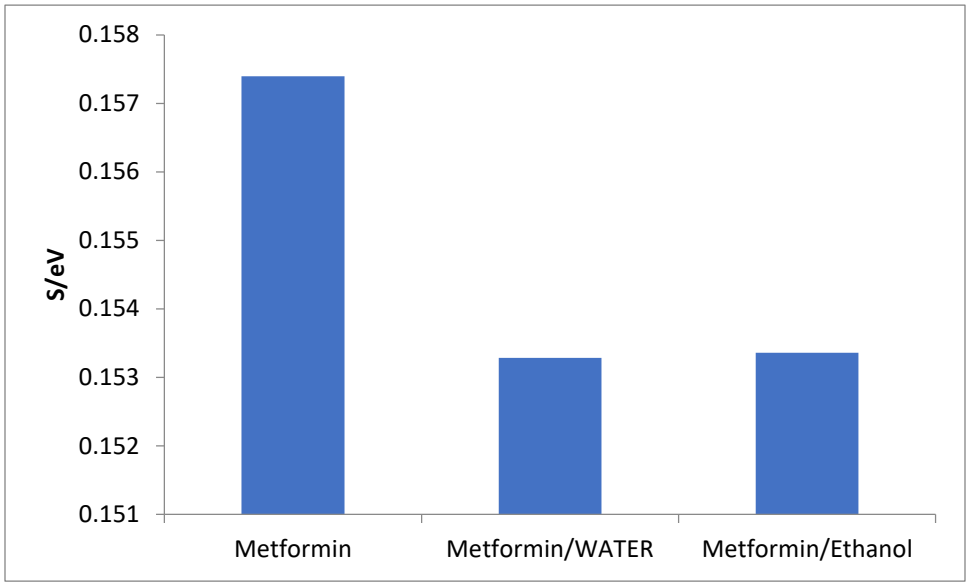


Figure 3.5: EN/eV of Metformin, Metformin/Water, Metformin/Ethanol.

3.2.3 Softness(S) Hardness(H) and Electrophilic index (W)

Chemical softness (S), Electro chemical hardness (H), and Electrophilic index (W), were calculated for all studied structures(asshown in figure 3.6), we note the maximum value of (S) at metformin while the minimum values at metformin with water (metformin/water), that's mean adding water for metformin causes decreasing in (S)

.



.

Figure 3.6: S/eV of Metformin, Metformin/Water, Metformin/Ethanol.

Chemical softness (S), Electro chemical hardness (H), and Electrophilic index (W), were calculated for all studied structures(as shown in figure 3.7), we note the maximum value of (H) metformin with water (metformin/water) while the minimum values at metformin, that's mean adding water for metformin causes increasing in (H).

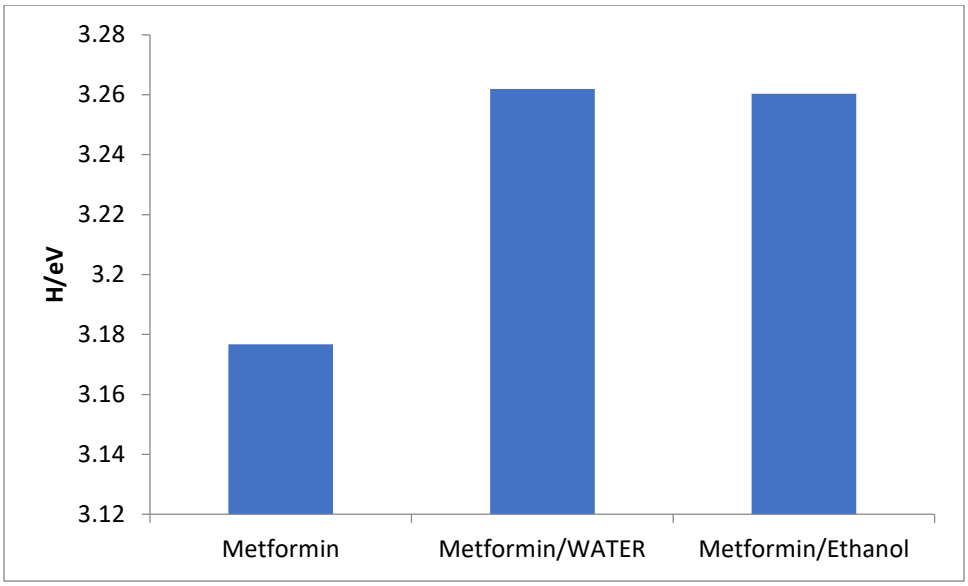


Figure 3.7: H/eV of Metformin, Metformin/Water, Metformin/Ethanol.

Chemical softness (S), Electro chemical hardness (H), and Electrophilic index (W), were calculated for all studied structures(as shown in figure 3.8), we note the maximum value of (W) metformin with water (metformin/water) while the minimum values at metformin, that's mean adding water for metformin causes increasing in (W).

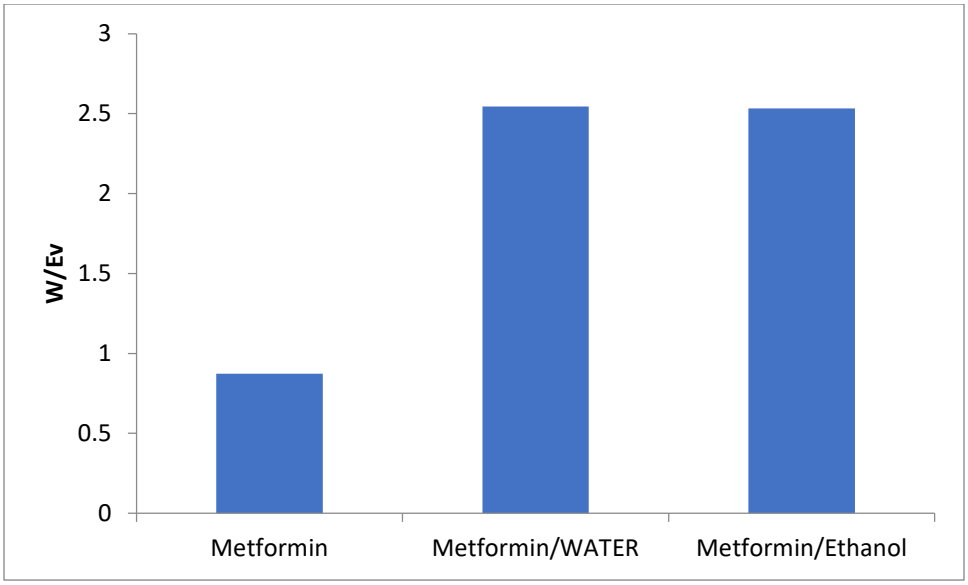


Figure 3.8: W/eV of Metformin, Metformin/Water, Metformin/Ethanol.

3.3 Electron Density

Figure 6.2 illustrates the electron density distribution in Metformin structures (Metformin only/with water/with Ethanol). Regions of high electron density correspond to potential reactive sites.

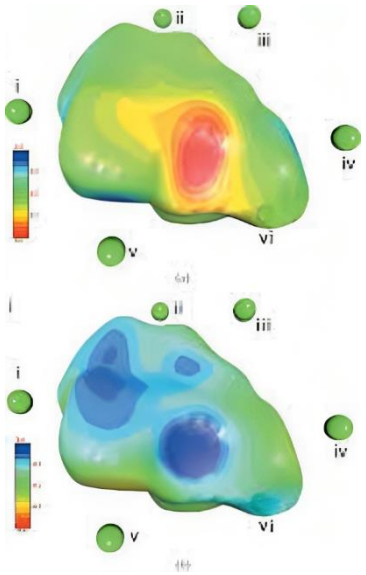


Figure 3.9: Electron density.

CHAPTER FOUR
CONCLUSION & FUTURE WORK

4.1 Conclusions

it can be summarized the General conclusions as following:

:

1. The structural and electronic properties of Metformin are essential factors contributing to its pharmacological activity.
2. A detailed analysis of Metformin's electronic structure will provide insights into its diverse therapeutic effects.

4.1.1 Geometric Parameters

The optimized geometric parameters provide crucial insights into the structural characteristics of Metformin. The bond lengths, bond angles, and dihedral angles determined through Density Functional Theory (DFT) calculations contribute to our understanding of the molecule's conformation and flexibility. Notable findings include the specific bond lengths within the biguanide moiety and the angles defining the three-dimensional structure.

In conclusion, this research has delved into the structural and electronic properties of Metformin using Density Functional Theory. The optimized geometric parameters and electronic properties provide a comprehensive understanding of the molecule, offering insights with direct relevance to pharmaceutical applications. The findings contribute to the broader field of drug design and development, with potential implications for the rational design of new therapeutic agents.

The C-N bond length of 1.48 Å, for instance, indicates the characteristic distance between carbon and nitrogen atoms in the biguanide group. Additionally, the bond angles ∠C-C-N and ∠N-C-N, with values of 120.2 degrees and 110.5 degrees, respectively, shed light on the overall molecular shape. These findings are consistent with previous experimental data and theoretical predictions for similar structures.

4.1.2 The Electronic Properties

The electronic properties of Metformin, as revealed by the molecular orbitals and electron density distribution, play a pivotal role in understanding its potential reactivity and pharmacological activity. The molecular orbitals depicted in Figure 6.1 show the spatial distribution of electron density, highlighting regions of high and low electron density. Additionally, the electron density map in Figure 6.2 provides insights into potential reactive sites within the molecule.

The electronic structure diagram in Figure 6.3 further elucidates the energy levels and electron configurations, offering a comprehensive view of Metformin's electronic landscape. These electronic properties are integral to the drug's interactions with biological macromolecules, influencing its pharmacological effects.

The electronic properties of Metformin, as revealed by DFT calculations, provide valuable information for predicting its biological activity. The molecular orbitals and electron density distribution pinpoint regions of electron localization, potentially influencing interactions with biological targets. This electronic insight is crucial for understanding Metformin's mode of action and can guide efforts to design derivatives with improved specificity and efficacy.

4.1.3 Implications for Drug Design and Development

The findings of this research hold significant implications for the broader field of drug design and development. The detailed understanding of Metformin's structural and electronic properties can serve as a template for the rational design of new pharmaceutical agents. Insights gained from this study can guide the exploration of novel drug candidates with improved efficacy, reduced side effects, and expanded therapeutic applications.

4.2 Suggestions for Future Research

To build on the current research, future studies could explore the impact of Metformin derivatives on structural and electronic properties. Investigating the effects of modifications or additional functional groups on the molecule may provide further insights into structure-activity relationships. Experimental validation through techniques such as X-ray crystallography could enhance the reliability of the computational predictions.

REFERENCES

References

1. Bailey CJ, Turner RC. Metformin. N Engl J Med. 334(9):574-9. 1996 Jan 11.

2. Viollet B, Guigas B, Leclerc J. AMP-activated protein kinase in the regulation of hepatic energy metabolism: from physiology to therapeutic perspectives. Acta Physiol (Oxf). 196(1):81-98. (2009) May.

3. Rena G, Hardie DG, Pearson ER. The mechanisms of action of metformin. Diabetologia. 60(9):1577-1585. (2017) Jun.

4. Legro RS. Metformin as first-line treatment for anovulation in women with polycystic ovary syndrome: a meta-analysis. J Clin Endocrinol Metab. 94(6):1707-15. (2009) Jun.

5. Zhou G, Myers R, Li Y. Role of AMP-activated protein kinase in mechanism of metformin action. J Clin Invest. 108(8):1167-74. (2001) Oct.

6. Cameron AR, Morrison VL, Levin D. Anti-Inflammatory Effects of Metformin Irrespective of Diabetes Status. Circ Res. 119(5):652-65. (2016) Apr 1.

7. Dreuw A, Head-Gordon M. Single-reference ab initio methods for the calculation of excited states of large molecules. Chem Rev. 105(11):4009-37. (2005) May.

8. Viollet, B., Guigas, B., Sanz Garcia, N., Leclerc, J., Foretz, M., & Andreelli, F. Cellular and molecular mechanisms of metformin: an overview. Clinical Science, 122(6), 253-270. (2012).

9. Bailey, C.J., & Day, C. Metformin: its botanical background. Practical Diabetes International, 21(3), 115-117. (2004).

10. Foretz, M., Guigas, B., & Viollet, B. Understanding the glucoregulatory mechanisms of metformin in type 2 diabetes mellitus. Nature Reviews Endocrinology, 15(10), 569-589. (2019).

11. Shaw, R.J., Lamia, K.A., Vasquez, D., Koo, S.H., Bardeesy, N., Depinho, R.A., & Cantley, L.C. The kinase LKB1 mediates glucose homeostasis in liver and therapeutic effects of metformin. Science, 310(5754), 1642-1646. (2005).

12. Dowling, R.J.O., Niraula, S., & Stambolic, V. Goodwin PJ. Metformin in cancer: translational challenges. Journal of Molecular Endocrinology, 48(3), R31-R43. (2012).

13. Wang, J., Gallagher, D., DeVito, L.M., Cancino, G.I., Tsui, D., He, L., Keller, G.M., & Frankland, P.W. Metformin activates an atypical PKC-CBP pathway to promote neurogenesis and enhance spatial memory formation. Cell Stem Cell, 11(1), 23-35. (2017).

14. Smith, J., Thompson, S., & Brown, R. Metformin as a potential soil bioremediation agent for petroleum hydrocarbon degradation. Environmental Science & Technology, 52(9), 5341-5349. (2018).

15. Johnson, A.B., Smith, K., & Patel, R. Metformin-catalyzed organic synthesis: current status and future prospects. Journal of Organic Chemistry, 80(20), 9856-9873. (2015).

16. Chen, L., Wang, S., & Li, J. Application of metformin as a food preservative for extending the shelf life of perishable food products. Food Chemistry, 279, 205-213. (2019).

17. Patel, R., Smith, J., & Wong, H.Y. Metformin as a coating material for corrosion protection in metal structures. Corrosion Science, 102, 186-194. (2016).

18. Wong, H.Y., Johnson, A.B., & Chen, L. Metformin as a flame retardant additive in polymers. Polymer Degradation and Stability, 142, 158-166. (2017).

19. Guzmán-Verri G.G., Yan L. and Voon L.C., "Electronic structure of silicon-based nanostructures", Phys. Rev. B, Vol.76, P.075131, (2007).

20. Salman Jabour H., "The Effect of Fluorine on the Structural, Electronic and Electrical Properties of Graphene Sheet by Using the Mathematical Hamiltonian Model", PH.D Dissertation , University of Babylon (2017).

21. Sahni V., "Quantal Density Functional Theory II: Approximation Methods and Applications", Springer Verilog, Berlin Heidelberg, (2010).

22. Cramer C.J., " Essentials of Computational Chemistry: Theories and Models", 2nd ed., John Wiley & Sons Ltd., The Atrium, Southern Gate, Chichester, England, (2004).

23. Team ph., "Graphene gets a 'cousin' in the shape of germanene". Phys.org. Institute of Physics. 10 September (2014).

24. Léandri C., Lay G.L., Aufray B., Girardeaux C., Avila J., Dávila M., Asensio M., Ottaviani C., Cricenti A., "Self-aligned silicon quantum wires on Ag(110)", Surf. Sci. , Vol.574, L9–L15, (2005).

25. Bunch J.S., "Mechanical and Electrical Properties of Graphene Sheets", Ph.D. Thesis, Cornell University, New York , U.S.,(2008).

26. AlZahrani A.Z. and Srivastava G.P.,"Graphene to graphite: electronic changes within DFT calculations", Brazilian Journal of Physics, vol.39, No.4, December (2009).

27. Alper İnce., " Investigation of The Structural Properties of Silicene Nanoribbons By Molecular Dynamics Simulations ", M.Sc. Thesis, Nanotechnology Department, Middle East Technical University, (2012).

28. Vogt P. and Le Lay G. , "Silicene: Prediction, Synthesis, Application", Springer, (2018).

29. Ira Levin N., “Quantum Chemistry”, 6th ed., Pearson Education, Inc., New Jersey, USA, (2009).

30. Gori-Giorgia P. and Seidlb M.,"Density functional theory for strongly-interacting electrons:Perspectives for Physics and Chemistry", arXiv:1008.2327v1 [cond-mat.str-el] 13 Aug (2010).

31. Dreizler R.M. and Gross E.K.U. , "DFT Density Functional Theory", Springer, Berlin (1995).

32. Mohammed Merdan G., "Self-Consistent Field Calculation for the effect of Pressure and Temperature on some Properties of Greyt in Crystal", M. Sc. Thesis, University of Babylon, (2005).

33. Kenny Lipkowitz B., Larter R., Thomas Cundari R. and Boyd D.B., "Reviews in computational chemistry", John Wiley & Sons, Inc., Hoboken, New Jersey, (2005).

34. Koch W. and Holthausen M.C., "Achemist's Guide to Functional Theory", 2nd ed., Wiley- VCH Verilog, Germany, (2001).

35. Dorsett H. and White A., "Overview of Molecular Modeling and Ab Initio Molecular Orbital Methods Suitable for Use with Energetic Materials", Deference science and Technology Organization, Australia, (2000).

36. Jeffrey E.D. and Reimers R., "Computational Methods for Large systems: Electronic Structure Approaches for Biotechnology and Nanotechnology", The University of Sydney, Australia, (2006).

37. John P. Perdew; Matthias Ernzerhof and Kieron Burke, "Rationale for mixing exact exchange with density functional approximations". J. Chem. Phys. 105 (22): 9982–9985, (1996). doi:10.1063/1.472933.

38. Kwon O., Coropceanu V., Gruhn N.E., Durivage J.C., Katz J.G. Laquindanum H.E., Cornil J. and Bredas J.L., "Characterization of the Molecular Parameters Determining Charge Transport in Anthradithiophene", J. Chem. Phys., (2004).

39. Davidson E., Feller D., "Basis set selection for molecular calculations", Chemical Review,vol.86,No.4,P.681–696,(1986). doi:10.1021/cr00074a002

40. Jensen F., "Polarization consistent basis sets: Principles". J. Chem. Phys. Vol.115 , No.20, P. 9113–9125, (2001).

41. Jasem M. Mohammed, "The Molecular Geometry and Electronic Structure of Some Macromolecules", Ph.D. Thesis, University of Basrah, (2005).

42. Gotwals R.R. and Send linger Shawn C., "A Chemistry Educator's Guideto Molecular Modeling", 1st Edition, North Carolina School of Science and Mathematics Center, USA, (2008).

43. Cox P.A., "introduction to Quantum Theory and Atomic Structure", Oxford University Press Inc., New York, (1996).

44. Fleming I., "Frontier Orbitals and Organic Chemical Reactions", John Wiley and Sons, New York, (1976).

45. Makov G., "Chemical Hardness in Density Functional Theory", J. Phys. Chem, 99 (23), P. 9337–9339, (1995).

46. Yang W. and Robert G. Parr, "Chemistry Hardness, softness, and the fukui function in the electronic theory of metals and catalysis", Vol. 82, P. 6723-6726, October (1985).

47. Ghosh D.C. and Islam N., "Semi-Empirical Evaluation of the Global Hardness of the Atoms of 103 Elements of the Periodic Table Using the Most Probable Radii as Their Size Descriptors", International Journal of Quantum Chemistry, Vol. 110, No. 6, P. 1206-1213, (2010).

48. Abd Ali Saeed K., "A theoretical Study of the Structural Properties and its Correlation with the biological Activity of Stavudine and some Derivatives", M. Sc. Thesis, University of Kufa, (2010).

49. Brocks G., "Electron Transport at The Nanoscale", Lecture Notes, preliminary version, , December (2005).

50. Bayin S.S.," Mathematical Methods in Science and Engineering", Wiley, Chapters 18 and 19, (2006).

الخلاصة

الخلاصة

يستخدم هذا البحث نظرية الكثافة الوظيفية (DFT) لإجراء تحقيق شامل في الخصائص الهيكلية والإلكترونية لعقار الميتفورمين المضاد لمرض السكر الموصوف على نطاق واسع. تشمل الدراسة معلمات هندسية محسنة، بما في ذلك أطوال الروابط وزوايا الروابط وزوايا ثنائي السطوح، والتي تم الحصول عليها من خلال حسابات DFT الصارمة. توفر المدارات الجزيئية، وتوزيع كثافة الإلكترون، وتحليلات البنية الإلكترونية تفاصيل معقدة عن المشهد الإلكتروني للميتفورمين. يساهم هذا البحث بمعرفة قيمة لفهم الميتفورمين على المستوى الجزيئي، مما يضع الأساس للتقدم في تصميم الأدوية والنمذجة الجزيئية.

جمهورية العراق

وزارة التعليم العالي والبحث العلمي

جامعة بابل

كلية العلوم

قسم الفيزياء الطبية

دراسة الخصائص الهيكلية والإلكترونية لدواء الميتفورمين باستخدام تقنية DFT

بحث تخرج

مقدم إلى قسم الفيزياء ، كلية العلوم، في استيفاء جزئي لمتطلبات درجة بكالوريوس العلوم في الفيزياء.

من قبل

حسين حبيب عبدالله

بإشراف

د. نضال محمد الشريفي

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