People's Democratic Republic of Algeria

Ministry of Higher Education and Scientific Research

Higher School of Professors for Technological Education-Skikda

Department of technology

Specialization: Process Engineering

Graduation manuscript

Presented by:

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In order to obtain a diploma of Secondary Education Professor

Subject

A Computational Study of Atorvastatin Adsorption Using Natural Cellulose Materials

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JUNE 2024

Acknowledgments

First and foremost, our deep thanks and praise is to "Allah",

for granting us the opportunity, strength and patience to complete this modest research work.

We would like to extend our sincere thanks and appreciation to all the persons who participated in lighting our path with luminous knowledge candles along our university career,

those who helped us and supported us to be here;

and precisely those who encouraged us along the process of hard working and searching.

With biggest and deepest appreciation, we would like to thank our supervisor Mme. "**Aloui Amel**" and Pr. **Khoreif Nacereddine** and **Bou-Abbasi Hayat**" for his valuable guidance and insightful suggestions and encouragement.

It was a privilege to achieve this manuscript under his supervision.

We would like to express our warmest thanks to our beloved parents for their great encouragement.

With great respect, besides our supervisor we would like to acknowledge the members of Jury for giving their time to read and correct our work.

And finally,

thanks to all the educational and administrative team of "**National Higher School of Technological Education-SKIKDA-**".

Dedication

With deep gratitude to Allah the almighty for his blessings, I extend my heartfelt thanks to those who have been my guiding lights and pillars of support throughout this research. To the one who always pushed me forward towards my goals and to the one who dedicated himself to my education with immense sacrifices, revering knowledge: my dear father, may his days be long. To the one who gave her all in love and care, who endured everything, who was my rock in times of hardship: my mother, the dearest angel to my heart and eyes.

To them, I dedicate this humble work, which brings some happiness to their hearts.

To my siblings: ***Haroun, Sara*** *and* ***Yasmine***

To my supervisors: ***Aloui Amel*** *and* ***Khoreif Nacereddine abdelmalek****.*

To my dear family.

To my friends: " ***Bouthaina, Hadeel, Hasna, Basma, Achouak, Amina, Rihem, Badiaa, Ahlem, Manel*** *"*

To my lifelong friend and my partner in this work: ***Lina Rihab****, and to all who supported me, even with a word, I send my appreciation to you all. Your kindness band support means the world to me.*

AFAF

Dedication

Praise be to God, and thanks to God first for completing this work

Every challenging work needs self-efforts as well as guidance of elders especially those who are very close to our heart.

I dedicate my humble effort to my dear

Father and Mother

Whose affection, love, encouragement and prays of days and night makes me able to get such success and honor

To my siblings, "**Yahia, Idris,Intissar**", who have never left my side just wanted to say that I really appreciate this.

I dedicate this work and give special thanks to my best friends "**Hasna, Mariya**"who have supported me throught the process. I will always appreciate all they done, especially my friend of my life,who is the companion of my path and the smile of my heart,she is the partner of my memories. God will never separate us **Afaf** "thanks for her for sharing with me the difficulties of this manuscript.

I also dedicate this manuscript to my friends"**Hadil, Boutiana, Basma, Achouak, Amina, Rihem, Manel, Badiaa, Radiah**"

And to everyone who helped me in this work, from near or far.

This humble work is a sign of my love to you.

Lina

Abstract

In this manuscript, we carried out a simulation study of the adsorption of a pharmaceutical contaminant such as atovastatin by plant fibers of luffa cylindrica composed essentially of cellulose, which is formed of glucose units. We used the semi-empirical PM6 method to calculate the energetic and thermodynamic properties of the resulting complex as well as the reactants. The results obtained showed that the resulting complex is more stable than the reactants and that the reaction is exothermic, non-spontaneous and relatively reversible. The results provided by the NCI, RDG and QTAIM methods, using the Multiwfn and VMD program which are used to find the wave function in the calculation of the electron density and the deduced properties. We concluded that non-covalent interactions such as electrostatic effects and hydrogen bonds are most responsible for the stability of the cellulose-atorvastatin complex and that adsorption is physical nature. Luffa fiber can be used as an adsorbent in water treatment of atorvastatin and other products.

Key words : adsorption, luffa, atorvastatin, PM6, NCI analysis, QTAIM analysis, RDG, VMD, Multiwfn

Résumé

Dans ce mémoire, nous avons mené une étude de simulation de l’adsorption d’un contaminant pharmaceutique tel que l’atovastatine par des fibres végétales de luffa cylindrica composées essentiellement de la cellulose, qui est formée des unités de glucose. Nous avons utilisé la méthode semi-empirique PM6 pour calculer les propriétés énergétiques et thermodynamiques, du complexe résultant ainsi que les réactifs. Les résultats obtenus ont montré que le complexe résultant est plus stable que les réactifs et que la réaction est exothermique, non spontanée et relativement réversible. Les résultats apportés par les méthodes NCI, RDG et QTAIM, utilisant le programme de Multiwfn et VMD qui servent à trouver la fonction d’onde dans le calcul de la densité électronique et les propriétés déduites. Nous avons conclu que les effets non covalents tels que les effets électrostatiques et les liaisons hydrogènes sont les plus responsables de la stabilité du complexe cellulose-atorvastatine et que l'adsorption est de nature physique. La fibre de luffa peut être utilisée comme adsorbant dans le traitement des eaux d'atorvastatine et d’autres produits.

Mots clés : adsorption, luffa, atorvastatine, PM6, analyse NCI, Analyse QTAIM, RDG, VMD, Multiwfn.

ملخص

في هذه الأطروحة، أجرينا دراسة محاكاة لامتزاز أحد الملوثات الصيدلانية مثل الأتورفاستاتين بواسطة ألياف نباتية من نبات الليفا سيلاندريكا المكون أساساً من السليلوز، والذي يتكون من وحدات الجلوكوز. استخدمنا طريقة PM6 نصف التجريبية لحساب الخواص الطاقوية والديناميكية الحرارية للمعقد الناتج وكذلك المواد المتفاعلة. أظهرت النتائج التي تم الحصول عليها أن المعقد الناتج أكثر استقرارًا من المواد المتفاعلة وأن التفاعل ناشر للحرارة وغير تلقائي وعكوس نسبيًا. النتائج المقدمة بواسطة طرق NCI و RDG و QTAIMباستخدام برنامج Multiwfn و VMDوالتي تستخدم لإيجاد الدالة الموجية في حساب كثافة الإلكترون والخصائص المستنتجة. لقد توصلنا إلى أن التأثيرات غير التكافؤية مثل التأثيرات الكهروستاتيكية والروابط الهيدروجينية هي المسؤولة عن استقرار

مركب السليلوز-أتورفاستاتين وأن الامتزاز له طبيعة فيزيائية. يمكن استخدام ألياف الليفا سيلاندريكا كمادة مازة في معالجة مياه الأتورفاستاتين ومنتجات أخرى.

الكلمات المفتاحية: الامتزاز، الليفا، أتورفاستاتين، PM6، تحليلNCI ، تحليلQTAIM ، RDG، VMD، Multiwfn

List of Abbreviations

MO: Molecular orbitals.

AO: Atomic orbitals.

LCAO: Linear combination of atomic orbitals.

CNDO: Complete neglect of differential overlap.

INDO: Intermediate Neglect of Differential Overlap.

AM1: Austin model1.

PM6: Parameterization Methods 6.

DFT: Density functional theory.

FMO: Frontier molecular orbital.

HOMO: Highest occupied molecular orbital.

LUMO: Lowest unoccupied molecular orbital.

NCI: Non covalent interactions index.

RDG: Reduced density gradient.

QTAIM: quantum theory of atoms in molecules.

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General introduction

General introduction

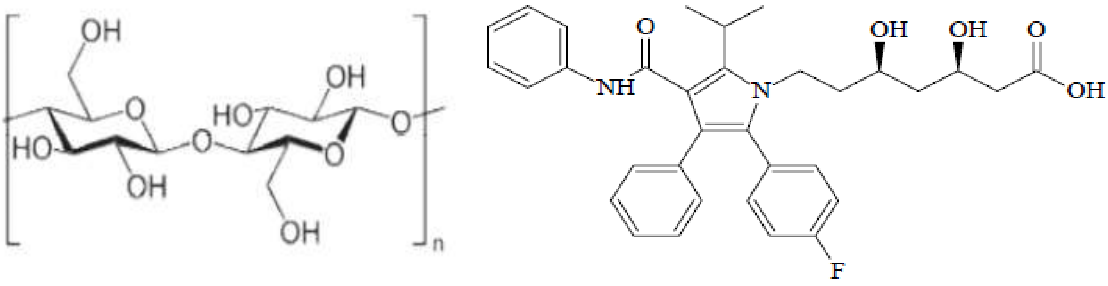
Pollution is a worldwide problem and its potential to influence the physiology of human populations are great. Studies of human growth and development in relation to pollution have increased in number and quality since the mid-twentieth century. Many studies have found that some pollutants have detrimental effects on human growth. Although worldwide–attention regarding pollution, the effect is as yet felt because of its drown-out adverse consequence[1]. The majority of researches emphasize the study of water pollution. The study discusses water pollution caused by dumping solid, carbon-based and liquid materials into lakes and waterways that comprise toxic chemicals like lead, mercury, metals and some pharmaceutical substances, such as amoxicillin, drugs and ATV (atorvastatin), which is the subject of this study[2].

Atorvastatin (ATV) is a human cholesterol-lowering statin drug that was first marketed under the trade name “Lipitor” in the United States in late 1999 and has been detected as contaminants in natural waters.

When atorvastatin is used frequently, it builds up in the body and can be extremely toxic to most of the body's live organs if the concentration is higher than what is needed (15mg/l) [3].

In light of the aforementioned, numerous physical and chemical methods, such as filtration, sedimentation, neutralization, and adsorption, have been developed to eliminate pharmaceutical compounds found in wastewater. Because of its low cost and excellent efficiency, the latter process is regarded as one of the most significant of these [4].

Due to the current development in computers, it has become possible to use the principles of quantum chemistry to study and develop reaction mechanisms and predict experimental results theoretically [5].Therefore, in this work, we conducted a computer study on the adsorption of a pharmaceutical substance contaminating drinking water, “Atorvastatin "from water using "glucose as a basic unit that makes up cellulose, which in turn is considered an essential component of the luffa cylindrical fibers (Figure1). The aim of this study is to know the type of adsorption, in addition to the type of effects that arise between the adsorbate and the adsorbent, using the theory of molecular boundary stations, effectiveness indicators, analysis of non-covalent interactions and low-density rate.



Cellulose **Atorvastatin**

Figure 1: Structure of the cellulose molecule and the atorvastatin molecule

This manuscript is divided into two parts, the first part is the bibliographic part, which is divided into two chapters:

The first chapter is a study on water pollution, its causes and types, and addresses adsorption as a treatment method followed.

In the second chapter, we will discuss the quantitative methods used in calculating the physicochemical properties of chemical systems and activity models, in addition to some analyzes used in studying non-covalent interactions inside or outside molecules.

As for the second part of this manuscript, we will address the presentation of the results obtained through the computer study of the interaction between atorvastatin (adsorbate) and cellulose (adsorbent) and then discuss them.

Finally, we end this manuscript with a general conclusion in which we collect all the results and conclusions that we obtained through this study.

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PART ONE : BIBLIOGRAPHIC STUDY

CHAPTER ONE: GENERALITIES ON WATER POLLUTION

1.1 Introduction

Water is god's precious gift on earth. This is essential to the existence and function of all forms of life on earth. Without water, there can be no life at all. It makes up about 70% of the planet. Water is extremely scarce, despite it is enormous abundance. This resource is not replenishable as per the 2021 world water development report published by UNESCO, the freshwater consumption worldwide has surged six times in the last century and has been increasing at a rate of roughly 1% year since the 1980s. Water quality is suffering greatly as a result of rising water demand. The environment has been degraded and polluted as a result of industrialization, agriculture and urbanization. This has a negative impact on the water bodies (oceans and rivers) that support life and ultimately on human health and the advancement of sustainable social development [1].

1.2 Water pollution

Water pollution occurs when unwanted materials enter in to water, changes the quality of water [2] and harmful to environment and human health [3].

Major sources of water contamination include radioactive waste, atmospheric deposition, leaks from water tanks, marine dumping, and the discharge of household and industrial effluent wastes. Industrial trash and heavy metals that have been disposed of can build up in rivers and lakes, posing a threat to people and animals [4].

1.3 Types of water pollution

1.3.1 Thermal pollution

Any process that modifies the ambient water temperature can lead to thermal pollution, which is the deterioration of water quality. When heat is produced by heated industrial effluents or by anthropogenic (human) modifications that raise the water system's temperature as a result of solar radiation, it is categorized as a water pollutant. The use of water as a coolant by power plants and industrial enterprises is a common source of thermal pollution. The abrupt change in temperature that occurs when coolant-treated water is released into the natural environment at a higher temperature impacts the ecology by reducing the availability of oxygen [5].

1.3.2 Radioactive pollution

Radioactive pollutants are one of the most dangerous and newly discovered categories of pollutants. One of the most hazardous human activities in nature is radioactive pollution. Since there are no rehabilitation options for this type of pollution, it can be said that the ecosystem has been irreparably harmed [6].

1.3.3 Chemical pollution

Chemical pollution includes industrial solvents, pesticide runoff, oil spills from ships, heavy metals including mercury, lead and cadmium, among others. They are lethal and cause infertility in aquatic life forms. When metal wastes enter our bodies, they pose a threat to people as well. They may harm the kidneys, nervous system [7].

1.3.4 Pharmaceutical pollution

There are several different sources of pharmaceutical compounds that end up in water bodies, including groundwater and surface water the first of these is urban wastewater, which has a high concentration of pharmaceuticals from human waste. For instance, the majority of antibiotics are eliminated through urine and feces after intake because they are frequently very soluble in water [8].

1.3.5 Biological pollution

1.3.5.1 Algae contamination

Surface water contains many plant organisms that change the nature and quality of water, where it is confined on water surfaces causing the emission of bad odors, and it is known that sewage drainage in rivers and lakes increases this problem because residues act as a good fertilizer for algae that increases of it is immense growth [9].

1.3.5.2 Wastewater

Wastewater, often known as sewage water, is water that has had human influence adversely effect it is quality. It comprises effluents released from commercial, industrial and residential, and agricultural complexes. This kind of contaminated water contains a wide range of hazardous contaminants, including hazardous bacteria and micro-organisms, heavy metals, carbohydrates, organic and chemical compounds (like soap and industrial detergents) [10].

Figure.1.1: Thermal water pollution from nuclear power plants.

1.4 Sources of water pollution

The main causes of water pollution are industrialization, agriculture, inadequate sewage treatment facilities, and inadequate water supplies**.**

1.4.1 Human sources

1.4.1.1 Industry

Industry is the main cause of water pollution. These industries include the food, beverage, iron and steel, tannery, pulp and paper, and nuclear industries, among others. In the course of industrial production, a variety of hazardous substances, both organic and inorganic, hazardous solvents, and volatile organic compounds may be released. The industrial sector also contributes significantly to the harmful pollutants wastewater from industrial production has gradually increased as urbanization has accelerated [11, 12].

1.4.1.2 agriculture

Agriculture and water pollution are closely related. Significant contributors to water pollution include organic farm wastes, nitrogen fertilizers and pesticides [13]. Water contaminated by pesticides, nitrates, phosphorus, soil sediments, salts, and pathogens are all results of agricultural activities the presence of pollutants in sewage poses risks to the environment and human health [14].

1.4.1.3 Domestic Pollutants

The sewage contains garbage, soaps, detergents, waste food and human excreta and is the single largest sources of water pollution. Micro-organisms (bacteria, fungi, protozoa, algae) enter the water system which leads to many diseases like typhoid, cholera, polio, viral hepatitis and may cancer. As a result of drinking infected water [15].

1.4.1.4 Petroleum products

Petroleum products are widely used for fuel, lubrication, plastics manufacturing…etc, and happen to be poisonous in nature. Crude oil and other related products generally get into water by accidental spillage from ships, tankers, pipelines …etc [15].

1.4.2 Natural sources

1.4.2.1 Floods

Floods increase contaminants and sedi-ments from urban and agricultural runoff during high rainfall causing a decrease in water quality [16]. Due to a scarcity of clean water, nearly all victims use the water on a daily basis. This is because 2.5 billion people worldwide lack adequate access to better sanitation and water [17]. This is as a result of the large number of the harmful bacteria present in the floodwater.

1.4.2.2 Volcanics

The most extensively dispersed by product of violent volcanic eruptions is volcanic ash, which can fall hundreds of kilometers from the source of an eruption.

Transportation networks, power and water supplies, stormwater and sewerage systems, can all be negatively impacted by even small amounts of ash [18,19].

1.5 Pollution damage

Table 1.1: Sources of water pollutants with their effects [20].

Sources	**Components/pollutants and their effects**
Agricultural run-offs and mill-waste	NO3- and PO4-3 (in fertilizers) -Excess amount results to eutrophication
	Herbicide and **pesticide** residues -Accretion of pesticides and herbicides have lethal effects on organisms in the water and to the humans. -Level of pesticides start to build up as it passes over the food chain. -High dose of pesticides may collect in the tissues of ultimate consumers that are mostly carnivores.
Untreated sewage consisting mainly of human faeces and domestic waste	**Suspended solids** -Reduced penetration of light -If suspended solids are biodegradable, micro-organisms can decompose them and their processes require a high oxygen requirement.
	NO3- and PO4-3 -Results into eutrophication.
Domestic waste includes detergents and food waste	**Detergent** -‘Hard’ detergents create foam that reduces oxygen supply to water-borne organisms -Soft detergents are biodegradable but it may contain high phosphate levels that can sometimes give rise to eutrophication.
Animal waste from farm	Micro-organisms such as bacteria and protozoa. -If water would be used to drink, perhaps it will cause waterborne diseases namely cholera to be properly treated.
Effluents from industries	Heavy metals such as Cu, Hg, Zn and Cr

-Electronic and electroplating plants **-Food and beverage processing industry** **-Rubber product processing industry**	-Highly toxic accumulation through the food chain in the organism. -Mercury can cause acute human nervous disorder. -Waste water contains numerous contaminants, including sulphide of hydrogen.
Underground pipes	**Lead** -Lead is highly poisonous Heavy metals that could built up in living organisms tissues -Lead may affect children's mental capability

1.6 Water treatment methods

There are many techniques adopted for water treatment, including:

1.6.1 Physical methods

It is the first method used in treating wastewater and still is. It is a treatment method that relies on natural and physical forces and includes many processes, the most important of which are separation, sedimentation, filtration.

1.6.2 Chemical methods

Chemical treatment is carried out by adding chemicals to industrial wastewater, and depends on the occurrence of chemical reactions in order to get rid of pollutants or transform them into substances that are easy to separate, and one of the most common chemical methods in this field is the neutralization method.

1.6.3 Physico-chemical method

1.6.3.1 Adsorption

Adsorption is mostly utilized in drinking water treatment to get rid of substances that give off an unpleasant taste, odor, or color. It aids in the elimination of dissolved organic materials, while it may also eliminate particle matter. Adsorption is defined as the phenomenon of collecting extended particles, atoms, or ions, which is called an adsorbate, on the surface of another substance called an adsorbent. Examples of it are porous, clays and silica gel. It is natural that the states of matter that have specific surfaces in space are the two states (liquid and solid), and therefore the surface contact areas that lead to adsorption are (liquid : liquid), (solid : solid), (solid : liquid) and (solid : gas) [21].

1.6.3.2 Types of adsorption

1.6.3.2.1 Physic-sorption

Adsorption occurs on such surfaces due to natural attractive forces, also known as Vander Waals forces. The adsorbent and the adsorbate, which is estimated at less than (40 KJ/mol), therefore, this type of adsorption does not require high temperatures and does not require activation energy and occurs at low temperatures similar to the process of vapors condensation on the surfaces of liquid materials. When suitable conditions of pressure and temperature are available, adsorption can take the form of multiple layers of the adsorbent material on the surface [21].

1.6.3.2.2 Chemical adsorption

This type of adsorption occurs on surfaces that are not electronically unsaturated, as such surfaces tend to form chemical bonds with the atoms or molecules that have been adsorbed. This type of adsorption requires a high activation energy as the initial step in the chemical reaction that takes place between the adsorbent surface and the adsorbent material. It also requires high temperatures that are predicted to be larger than (40 KJ/mol) [21].

1.6.3.3 Mechanism of adsorption

The transfer of a liquid phase containing the adsorbate to a solid phase with solute retention on the adsorbent surface is done in several steps of which one or more may be determinative of the overall kinetics of the process:

1)- External mass transfer (external diffusion) corresponding to the solute transfer of the within the solution to the outer surface of the particles.

2)- Internal mass transfer in pores (internal diffusion) occurring in fluid filling the pores. Indeed, the molecules spread from the surface of the grains towards their center through the pores.

3)- Surface scattering: for some adsorbents, there may also be a contribution of diffusion of adsorbed molecules along pore surfaces to the scale of an adsorbent grain.

4)-Adsorption proper [22].

1.6.3.4 Adsorbate (atorvastatin)

The statin that is most frequently prescribed worldwide is atorvastatin. It is a member of the class of drugs known as statins, or reductase inhibitors. There functions by reducing the amount of cholesterol that the body produces, which lowers the risk of cholesterol accumulating on artery walls and obstructing blood flow to the heart, brain, and other organs. When taken in conjunction with diet, exercise, and weight loss, atorvastatin can lower the risk of heart attack and stroke as well as the likelihood that heart surgery will be required for those who already have heart disease or are at risk of getting it.
Within 2.3 hours, atorvastatin reaches it is peak plasma concentration due to it is rapid absorption. The time of day that atorvastatin is taken does not affect it is ability to lower cholesterol. This is most likely caused by the relatively lengthy 20-hour half-life. Cytochrome P-450 3A4 and P-450 3A5 metabolize atorvastatin to produce ortho-hydroxy atorvas [23].

1.6.3.4.1 Structure of atorvastatin

Atorvastatin structure Belongs to the diphenyl pyrroles class of chemical compounds. The structure of these aromatic heterocyclic compounds is based on a pyrrole ring that is connected to precisely two phenyl groups [24].

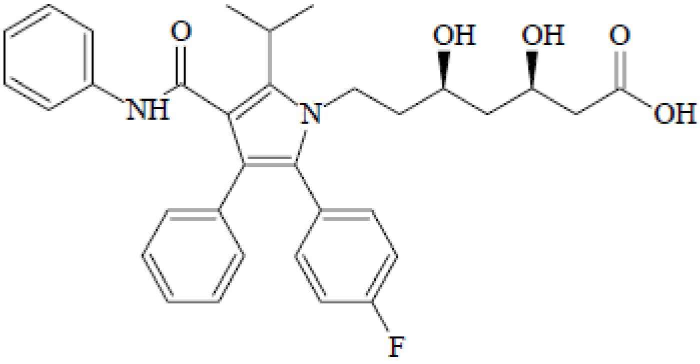

Figure 1.2: the structure of atorvastatin.

1.6.3.5 Adsorbent (cellulose)

Cellulose $(C_6H_{10}O_5)_n$ is one of the most widespread organic polymers on the planet. It is an important structural component of the primary cell wall of green plants and various forms of algae and oomycetes. It is a polysaccharide consisting of a linear chain of several hundred to several thousand β-linked d-glucose units (1 → 4).

Chemically, it is a non-toxic, biodegradable polymer with high tensile and compressive strength. Their use in various fields such as pharmaceutical industry, food industry, cosmetics, textile and paper industry has become widespread. The high dispensability of bacterial cellulose and it is tasteless and odorless nature provide it with many industrial applications [25].

1.6.3.5.1 Structure of cellulose

Cellulose is totally insoluble in water. It is polydisperse linear homopolymer, consisting of region and enantio-selectively α-1,4-glycosidic linked D-glucopyranose units (so called anhydro-glucose units [AGU]). The Polymer contains free hydroxyl group at the C-2, C- 3 and C-6 atoms. Based on the OH groups and oxygen atoms of both the pyranose ring and the glycosidic bonds, ordered hydrogen bond systems from various types of supramolecular semi-crystalline [26].

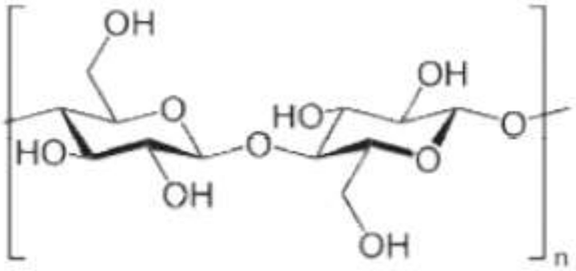

Figure 1.3: the structure of cellulose[27].

1.6.5.3.2 Hemicellulose

Hemicelluloses are polysaccharides of plant cell walls. They vary in amount and in structure, depending on the plant type and the location of the cells within the plant. Generally, they constitute 20–30% of cell walls. Hemicelluloses represent an enormous reservoir of industrial material. Hemicelluloses are defined more narrowly as plant-cell-wall polysaccharides. The commonest hemicellulose and perhaps the most abundant in annual plants, including farm crops, consists of (1 → 4)-β-D-xylopyranosyl units in the main chain with side chains of one to several α-L-arabinofuranosyl, D-galactopyranosyl, β-D-glucuronopyranosyl, or 4-O-methyl-β-D-glucuronopyranosyl units [28].

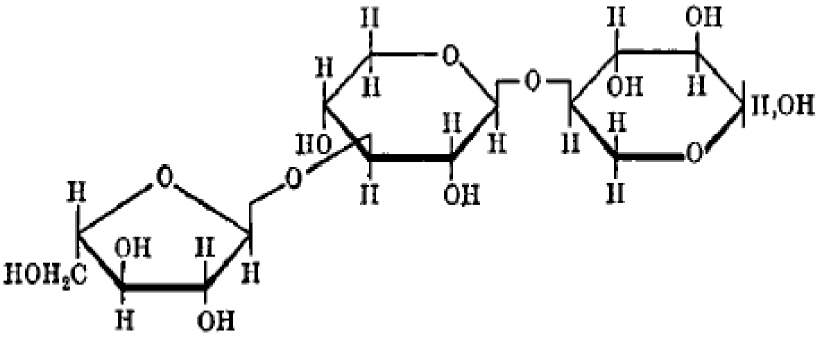

Figure 1.4: The structure of hemicellulose[29].

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CHAPTER TWO: QUANTUM METHODS AND CHEMICAL REACTIVITY MODELS.

2.1 Introduction

Computational quantum chemistry has long promised to become a major tool for the study of molecule structure, electronic properties, bond lengths, energies of molecules, transition states and reaction mechanisms…etc. It based on the solution of the time-independent Schrödinger equation, which called wave functions [1]. Those satisfy to characterize the properties of the chemical system. In this chapter we will present the quantum methods and chemical reactivity models which permit to obtain the electronic properties of the molecular chemical system.

2.2 Methods of quantum chemistry

2.2.1 Schrodinger equation

The properties of molecules and of intermolecular interactions may be understood by analysis of the electronic Schrödinger equation, which describes a different distribution of all electrons and the energy of electrons with that distribution [2] . The Schrödinger equation for a multi-electron system is given by the following equation:

$$\widehat{H}\psi = E\psi \text{ ……………...(1)}$$

Where:

ψ: the wave function.

E: the energy system.

$\hat{H}$: the Hamiltonian operator.

If no external electronic or magnetic fields are present and if the interaction between the particles is restricted to the Coulomb interaction, the molecular Hamiltonian operator is given by:

$$\hat{H}=\widehat{T}_{e}+\widehat{T}_{N}+\widehat{V}_{ee}+\widehat{V}_{eN}+\widehat{V}_{NN}\text{……..(2)}$$

Where:

$\widehat{T}_e =-\sum_{i}^{N}\frac{\overline{h^2}}{2m}\nabla_i^2$: The operator of the kinetic energy of the electrons.

$\widehat{T}_N= -\sum_{I}^{N}\frac{\overline{h^2}}{2M}\nabla_I^2$: The operator of the kinetic energy of the nuclei.

$\widehat{V}_{ee}= \frac{1}{4\Pi\varepsilon_0}\times\frac{1}{2}\sum_{i<j}\frac{e^2}{|\vec{r_i}-\vec{r_j}|}$: The Coulomb repulsion between the electrons.

$\widehat{V}_{eN}= \frac{1}{4\pi\varepsilon_0}-\sum_{i}^{I}\frac{z_j e^2}{|\vec{r}_i-\vec{R}_J|}$: The Coulomb attraction between the nuclei and the electrons.

$\hat{V}_{NN}=\frac{1}{4\Pi\varepsilon_0}\times\frac{1}{2}\sum_{I<J}\frac{z_I z_J e^2}{|\vec{R}_I-\vec{R}_J|}$: The Coulomb repulsion between the nuclei.

I,j: coefficients depend to the electrons.

I,J: coefficients depend to the nuclei.

M: the mass of the nuclei and m is the mass of the electron.

Z: the nuclear charge.

$\nabla_i^2=\frac{\partial^2}{\partial x^2}+\frac{\partial^2}{\partial y^2}+\frac{\partial^2}{\partial z^2}$: laplace operator.

$|\vec{r}_i-\vec{r}_j|$: the distance between electron i and j.

$|\vec{r}_i-\vec{R}_J|$: the distance between electron i and nuclei J.

$|\vec{R}_I-\vec{R}_J|$: the distance between nuclei I and J.

For a system with K nuclei and N electrons, the SE is an eigenvalue equation in 3K+3N independent variables, the Cartesian coordinates of the particles. Since, in general, it is impossible to solve such a problem exactly, either analytically or numerically, it should necessary to find approximate solutions, which are accurate enough to provide useful information [3].

2.2.2 Born-Oppenheimer approximation

The total wave function ψ (R, r) depends on both the positions of all the nuclei and the positions of all the electrons. Because electrons are much lighter than nuclei, and therefore it is moving is too much rapidly than that of nucleus [4]. Thereby, the electrons are essentially instantaneously responding to any changes in the relative positions of the nuclei. This allows us to separate of the total wave function into an electronic wave function ψ(r) and a nuclear wave function Φ(R).

$$\psi(R,r)=\psi(r)\phi(R)\ \ldots\ldots\ldots\ldots\ldots(3)$$

This separation means that the positions of the nuclei can be fixed and then one only has to solve the SE for the electronic part. This approximation was proposed by born and Oppenheimer in 1927 [5].

The Hamiltonian obtained after applying the Born-Oppenheimer approximation is:

$$\hat{H}=\hat{T}_e+\hat{v}_{ee}+\hat{v}_{eN}\ldots\ldots\ldots\ldots\ldots\ldots(4)$$

Even with this simplified approximation of the Schrödinger equation, the exact resolution remains impossible if the systems have two or more electrons. This is due to the bi-electronic repulsion of the Hamiltonian, which has no analytical solution. Several methods have been developed in order to approach as possible the exact solution [6].

2.2.3 Hartree-Fock approximation

The wave function depends on the coordinates of all the electrons in the molecule. In 1928, Hartree proposed a new approximation based on the postulate that the electronic wave function may be written as a product of mono-electronic functions. This wave function would solve the SE without the electron-electron repulsion term of the Hamiltonian. Hartree next rewrote this term as an expression that describes the electronic repulsion of such electron with the average position of the other electrons. In other words, the exact electron-electron repulsion is replaced with an effective field V produced by the average positions of the remaining electrons [7,8]. Therefore, the Hamiltonian operator is written as the following:

$$\hat{H} = \sum_{i=1}^{N} \hat{h}_i \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(5)$$

Where, N is the number of electrons and $\hat{h}_i$ is the one- electron Hamiltonian defined by:

$$\hat{h}_i = -\frac{1}{2}\nabla_i^2 - \sum_{I}^{N} \frac{Z_I}{r_{Ii}} + v_i^{eff} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (6)$$

The Schrödinger equation with Hartree approximation is written as the following:

$$\left(-\frac{1}{2}\nabla_i^2 - \sum_{I}^{N} \frac{Z_I}{r_{Ii}} + V_i^{eff}\right)\psi_i = E_i\psi_i \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (7)$$

In 1930, Fock demonstrated that Hartree's method does not respect the principle of antisymmetry of the wave function. Indeed, according to the Pauli Exclusion principle, two electrons cannot be simultaneously in the same quantum state. The Hartree-Fock method allows an approximate resolution of the Schrödinger equation of a quantum system with n electrons and N nuclei in which the polyelectronic wave function Ψ HF is written in the form of a determinant of Slater composed of mono-electronic spin-orbitals that respect the antisymmetry of the wave function [9].

$$\psi(r_1, r_2, r_3, \ldots r_N) = \frac{1}{\sqrt{N!}}\begin{vmatrix} \psi_1(e_N) & \cdots & \psi_N(e_1) \\ \vdots & \ddots & \vdots \\ \psi_1(e_N) & \cdots & \Psi_N(e_N) \end{vmatrix} \ldots\ldots\ldots(8)$$

Where:

ψ: The one-electron molecular orbital.

$\frac{1}{\sqrt{N!}}$: The normalization constant.

2.2.4 Hartree-Fock-Roothan method

The solution of the Hartree-Fock model, is known as the molecular orbitals (MOs). These orbitals generally cover the entire molecule, just as the atomic orbitals (AOs) cover the space of an atom. Because organic chemists consider the atomic properties of atoms in which it embedded within a molecule. Therefore, it seems reasonable to construct the MOs as an expansion of the atomic orbitals (AOs). Thus, it defines the linear combination of atomic orbitals (LCAO) approximation of Roothan [10].

These orbitals are written as:

$$\varphi_i = \sum_{\mu}^{k} C_{i\mu}\chi_{\mu} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (9)$$

Where:

μ: Spans all of the atomic orbitals.

$C_{i\mu}$: The expansion coefficient of AO in MO.

2.2.5 Semi-empirical methods

Semi-empirical methods modify Hartree-Fock calculations by introducing functions with empirical parameters. These parameters are adjusted with experimental conclusions to improve the quality of computation and to speed up calculations [11]. Semi-empirical methods such as (CNDO, INDO, AM1, PM6…) are based on two principal approximations:

. The elimination of the core electrons from the calculation.

. The reduction of the number of the Two-electron integrals [12].

2.2.6 Density function theory

The density function theory (DFT) is an alternative approach to the theory of electronic structure, which was proposed first by Fermi and Tomas in 1927. This theory based in using the electronic density distribution, rather than the many electrons wave function. The electronic wave function is dependent on 3n variables: the x, y, and z coordinates of each electron. Thereby, it is complicated and difficult to readily interpret. The total electron density is dependent on just three variables: the x, y, and z positions in space, so it is simpler than the wave function and it is also offer a more direct way to obtain the molecular energy [13].

This theory based on the existence of a unique functional which link the energy with the electronic density:

$E_{ele} = f\big(\rho(r)\big)$………..……………………………….(10)

Where:

E_{ele} : the total electronic energy.

2.3 Chemical reactivity models

Chemistry is generally the science where we study the processes of formation or broken of bonds. Thus, to understand these processes, it is necessary to know the energy necessary for their creation or the energy to be supplied by this system. The study of the stability of the formed molecules and the selectivity of the chemical reactions allowing their formation always require the application of the theories of quantum chemistry. Thus, the latter offers the possibility of studying the reactivity of the reagents in the ground state (separated molecules) and the selectivity of the reactions as well as their reaction mechanisms. Various theories have been discovered to study these chemical phenomena, in particular, transition state theory, frontier molecular orbitals theory and DFT-based reactivity indices.

2.3.1 Frontier Molecular Orbital Theory

The theory of frontier molecular orbitals (FMO) was developed in the 1950s by F. Fukui in order to explain the observed regioselectivity of organic reactions. The original idea of Fukui consists that during the reaction between a nucleophile and an electrophile, the charge transfer which takes place at the transition state involves mainly the electrons of the highest occupied molecular orbitals (HOMO) of the nucleophile and the lowest unoccupied molecular orbitals (LUMO) of the electrophile [14].

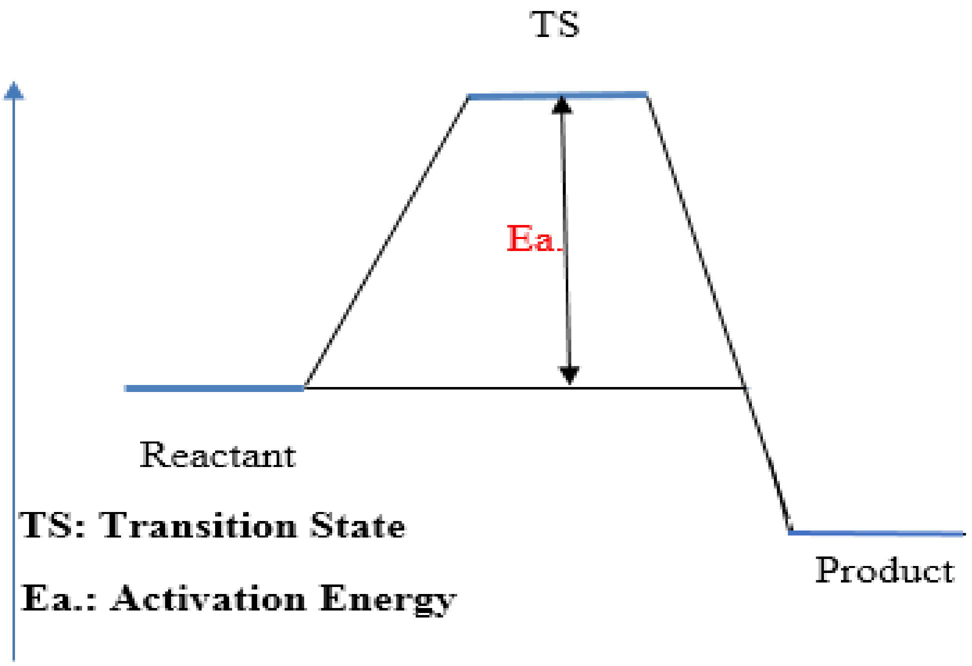
2.3.1.1 Energy of molecular orbitals

According to Pearson’s classification of Lewis acids and bases in hard and soft species, it appears that hard species are highly charged, and have highly contracted orbitals [15] . Unlike soft species are weakly charged and have weakly contracted orbitals. In addition, the hard acids have a very high energy of LUMO and the hard bases a very low energy of HOMO.

2.3.2 Transition state theory

The transition state theory is one of important methods within the field of chemical reactions, and it is the most used theory for the calculation of the reaction rates. The principal of this theory is based on the principal of active complex, in which that the reactants before they react and become products, they should pass through an active complex called ‘’the transition state’’ (Scheme 2.1) [16] . The activation energy is given by the following relation:

$E_a = E_{TS} - E_{Reactant}$……………………….(11)[17].



Scheme 2.1: Scheme of Energy reaction profile.

This theory was proposed in 1930 by Eyring and coworkers, in which the most common equation of this theory is [18]:

$$k = \frac{T.k_B}{h} e^{-\left(\frac{\Delta G}{RT}\right)} = \frac{T.k_B}{RT} e^{\left(\frac{\Delta H}{RT} + \frac{\Delta s}{R}\right)} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots.. (12)$$

Where:

K: The velocity constant.

K_B: Boltzmann's canstant.

h: Plank's constant.

R: The gaz constant.

T: The absolute temperature.

ΔG: The activation free energy.

ΔH: The activation enthalpy.

ΔS: The activation entropy.

2.3.3 DFT-based reactivity indices

In recent years, important approaches in quantum chemistry based on Kohn's and Hohenberg's theorems have emerged [19]. Thus, this first theorem shows that the electronic density $\rho(r)$ determines the number of electrons N of the system by the relation:

$$N=\int \rho(r)dr \ \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (13)$$

During it is development, it provided a formal basis for a number of concepts such as electronic chemical potential μ and chemical hardness η [20]. Both quantities may be approached in one-electron energies of the frontier molecular orbital HOMO and LUMO, ε_H and ε_L.

2.3.1.2 Coefficients of atomic orbitals

If the reaction is under electrostatic control, the most favorable approach is that involves the high charges with opposite signs. Therefore, in a reaction between a nucleophile and an electrophile, the most favored interaction is that between the most negative center of the nucleophile and the most positive center of the electrophile. It removes also high loads from same sign. We find the well-known rule that during a reaction under electrostatic control, among all the possible interactions between the electrophile and the nucleophile, the most favorable is the one that involves the most positively charged site of the electrophilic and the most negatively charged site of the nucleophile.

If the reaction is under charge transfer control, according to Hook's rule, the coefficients of the atomic orbitals at the frontier molecular orbitals that determining the favorable interaction [21]. The rule indicates that the most favorable interaction for a charge transfer controlled reaction is that involving the atom with the largest coefficient in the HOMO of the nucleophile and the atom with the largest coefficient in the LUMO of the electrophile.

2.3.3.1 Global indices

2.3.3.1.1 Electronic chemical potential (μ)

Parr shows that for every chemical system, there is a quantity μ , called the electronic chemical potential, which is associated with feasibility of a molecule to exchange electron density with the environment, it is defined within the conceptual DFT as [22, 23]:

$$\mu = \left(\frac{\partial E}{\partial N}\right)_{v(r)} \approx \frac{\varepsilon_H+\varepsilon_L}{2} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(14)$$

Where:

E : The total electronic energy.

N : The number of electrons.

$v(r)$: The external electrostatic potential.

ε_H : Energy of the frontier molecular orbital HOMO.

ε_L : Energy of the frontier molecular orbital LOMO.

2.3.3.1.2 Chemical hardness

The chemical hardness η have been introducing by Bop Bar, it was defined by the following expression [24]:

$$\eta = \left(\frac{\partial \mu}{\partial N}\right) v(r) = \left(\frac{\partial^2 E}{\partial^2 N}\right) \approx \varepsilon_L - \varepsilon_H \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(15)$$

2.3.3.1.3 Electrophilicity and Nucleophilicity

A specific electrophile is able to accept a specific amount of charge along the reaction and nucleophile is a molecule able to give an amount of electron density. This amount of charge transfer called electrophilicity for electrophile and nucleophilicity for nucleophile [25].

Electrophilicity

Parr and coworkers introduced the following expression to defined the electrophilicity [26] :

$$\omega = \frac{\mu^2}{2\eta} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(16)$$

Where:

μ : The chemical potential.

η: the absolute hardness.

It is defined as the energy stabilization due to the transfer charge when the system acquires an electronic charge [27]

Nucleophilicity

Nucleophilicity is based on the HOMO energies obtained within the Kohn-Sham scheme, is defined by:

$$N = E_{HOMO_{(nuc)}} - E_{HOMO_{(TCE)}} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (17)$$

Where nucleophilicity is referred to Tetracyanoethylene ‘’TCE’’ because it presents the lowest HOMO energy in large series of molecules [28].

2.3.3.2 Local indices

2.3.3.2.1 Fukui function

The Fukui function is given as the change of density function $\rho(r, N)$ of the molecule as a consequence of the numbr of electrons [29] :

$$f(r) = \left(\frac{\partial\rho(r)}{\partial N}\right)_{v(r)} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots(18)$$

A different approach to the fukui function was proposed based on the Mulliken gross charges q(r) of an atom of a molecule with **N-1, N** and **N+1** electrons [30].

For an electrophile:

$$f_k^+ = q_k(N+1) - q_k(N) \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots(19)$$

For a nucleophile:

$$f_k^- = q_k(N) - q_k(N-1) \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots(20)$$

Where:

q_n(N+1): The charge of atom k when it accepts an electron.

q_k(N): When the atom is electrically neutral.

$q_k(N-1)$: The charge of atom k when it donates an electron.

2.3.3.2.2 Local electrophilicity and local nucleophilicity

The local indices have been proved to be useful tools in the study of the regioselectivity of cycloaddition reaction [31].

Local electrophilicity

Defined by[32]:

$\omega_k = \omega \times f_k^+$ ……………………………………………………………………(21)

Local nucleophilicity

Defined by[33]:

$N_k = N \times f_k^-$ ……………………………………………………(22)

2.3.3.2.3 Parr function

Parr function is a new local reactivity index P(r), it is based on the spin density distribution at the radical anion and cation of a neutral molecule. There are two local functions $P^-_k(r)$ for nucleophilic attacks and $P^+_k(r)$ for electrophilic attacks [33].

2.4 Study of asymmetric effects

2.4.1 Analysis of non-covalent interactions (NCI analysis)

This method is based on analyzing the density of electrons in space as they appear on low-density surfaces and is used to find out (non-covalent interactions), electrostatic effects, Vander-Waals forces, and hydrogen bonding [34].

2.4.2 Low density rate map RDG

It is one of the maps derived from the analysis of non-covalent interactions to clarify the location and type of bonds based on the low electronic density and the electronic density gradient according to the relationship:

$$RDG = \frac{|\nabla \rho|}{2(3\Pi^2)^{1/3}\rho^{4/3}} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(23)$$

In RDG analysis, colors such as red, green, and blue determine what type of effects are present (Figure 2.2) [35].

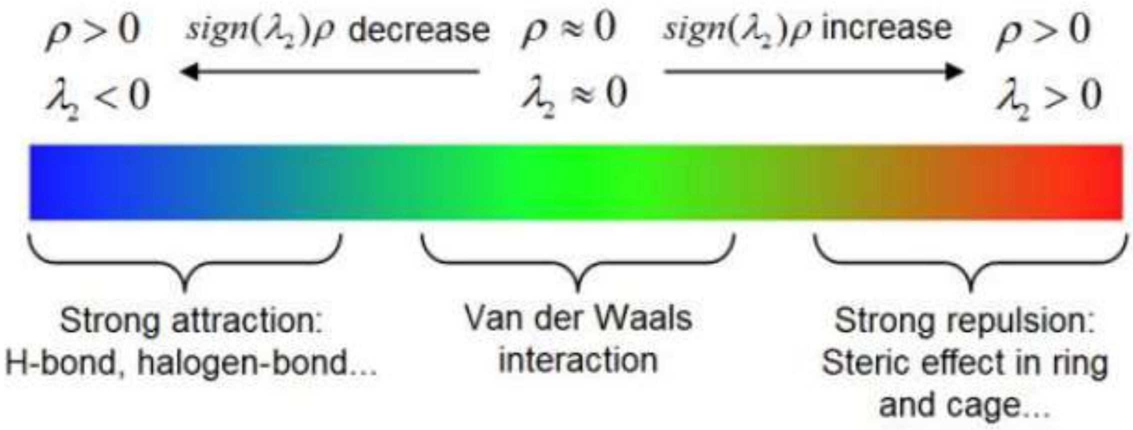


Figure 2.2: Determine the type of non-covalent interactions in the analysis RDG.

2.4.3 Quantum theory of atoms in molecules (QTAIM)

2.4.3.1. Definition

It is a model of quantum chemistry used to distinguish chemical systems, as it is based on the topological analysis of electronic density. The method was developed to study the properties of atoms, bonds, and other interactions between atoms and molecules, and to determine the electronic density values, the Laplacian, and the potential energy values for critical points.

2.4.3.2 Critical points

In the QTAIM analysis, most of the properties are deduced based on the electronic density ρ(r), and the gradient in the electronic density is zero at the critical points (cp) and it can be divided into four types of critical points according to the second derivative of the electron density (Hess matrix).

Critical point type (3, -3): Or NCPs, these points are characterized by the fact that all second derivatives with respect to the three negative directions point to the location of the nucleus.

Critical point type (3, -1): Or BCPs. At these points, the second derivative with respect to two directions is negative and the third direction is positive, as it indicates the presence of a chemical bond.

Critical point type (3, 1): Or CCPs, the second derivative with respect to two directions is positive and the third direction is negative and indicates the presence of a loop.

Critical point type (3, +3): Or RCPs where all second derivatives with respect to the three directions are positive and indicate the presence of a cage [35].

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PART TWO

CHAPTER THREE : RESULTS AND DISCUSSION

3.1 Introduction

Pollution is one of the biggest threats to life as we know it. Pollution affects the air we breathe, the water we drink, and the ecosystems we depend on. The major types of pollution include water pollution. Water gets polluted when toxic substances like chemicals and plastic waste are discharged into the water bodies. Deteriorating water quality is damaging the environment, health conditions and the global economy, so we must study and develop effective methods for treating polluted water, one of the treatment methods is adsorption, we must study and develop effective methods for treating polluted water. One of these methods is adsorption, so in this chapter we will conduct a computer study on the adsorption of a pharmaceutical substance (atorvastatin) from water contaminated by cellulose as a basic material of luffa cylindrica. The main objective of this study is determining the type and the nature of adsorption as well as the type of interactions between these two reactants.

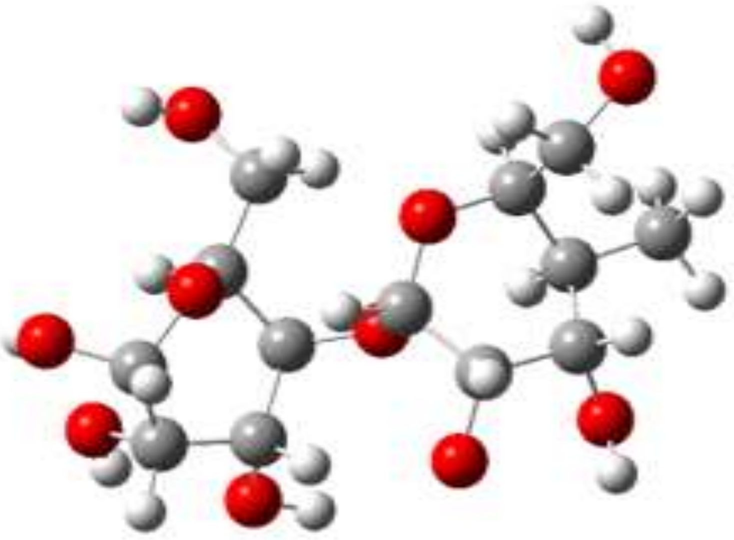
In this study, we relied on the most important models used in theoretical and computational chemistry, which are the theory of molecular border stations, activity indicators, the theory of non-covalent interactions, the quantum theory of atoms in molecules, in addition to the theoretical study of thermodynamics. In this study, we used the Gaussian 09 program, where we adopted the semi-empirical quantitative chemistry method PM6 in finding the most stable structure and calculate thermodynamic properties. We also relied on the Multiwfn program and the VMD program to perform an analysis of non-covalent interactions (QTAIM, RDG and NCI).

3.2 Energy study

Since the reaction occurs under experimental conditions of normal temperature T=298.15k and pressure p=1atm, that is why we conducted a computer study of the thermodynamic properties (enthalpy, entropy, free energy) under these conditions. The results obtained were collected in **(Table 3.1).** In this table, the relative values were calculated considering the sum of the values of the reactants as reference. The most stable structure obtained using the Gaussian program for cellulose and atorvastatin is shown in **(Figure 3.1),** and the results of the complex resulting from the reaction between them are shown in **(Figure 3.2).**

Table 3.1: Energy values and thermodynamic properties of the adsorption reaction of atorvastatin by cellulose

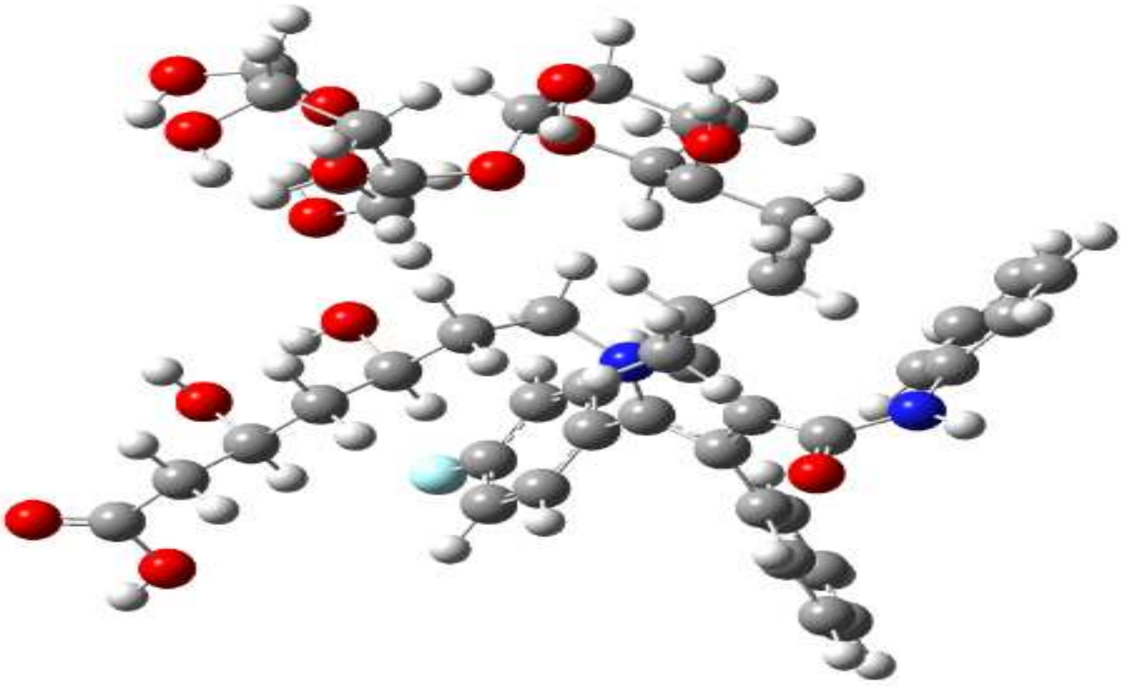
	Energies (Kcal/mol)	Enthalpies ΔH (Kcal/mol)	Free Energies ΔG (Kcal/mol)	EntropiesΔS (Kcal/mol. Kelvin
Atorvastatin	135	135.59	62.54	0.245
Cellulose	-254.94	-254.35	-304.26	0.167
Complex	-121.03	-120.44	-231.15	0.371
Change in Energy	-1.09	-1.68	10.57	-0.041



Cellulose

ATV

Shape 3.1 : The most stable structure obtained using the Gaussian program for cellulose and atorvastatin.



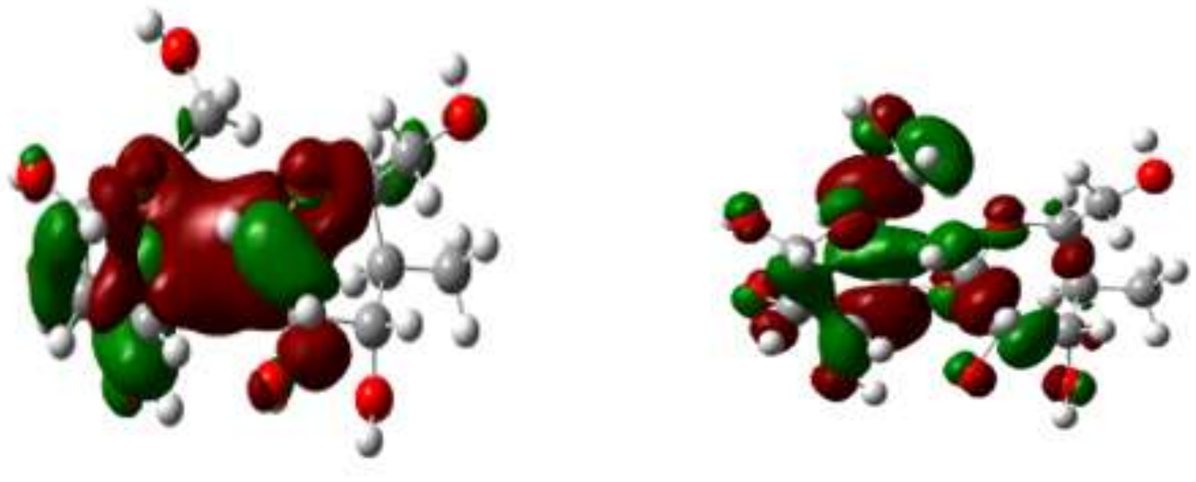
Shape 3.2 : The most stable structure obtained using the Gaussian program of complex.

Through the values shown in (Table 3.1) we notice that the reaction is possible to occur because the relative energy value of the resulting complex is negative **(-121.03 Kcal/mol)** and the resulting compound is stable,this is due to the fact that the energy of the latter is smaller than the sum of the energy of the reactants with the **(-1.09 Kcal/mol).** We also note that the value of the change in enthalpy is **(-1.68 Kcal/mol),** which indicates that the reaction is a heat dissipator, and the value of the change in entropy is **(-0.041)**, which indicates that the reaction contains vacuum crowding but at a very small percentage, almost non-existent, and this does not impedes the meeting of the reactants,. In addition, the value of change in free energy is higher than zero **(10.57)** which indicate that the reaction is reversible and non- spontaneous (Energically catalyzed reaction).

Based on these results, since the reaction is reversible and non-spontaneous and occurs at normal temperature, adsorption is possible and it is probably of a physical type.

3.3 The nature of the interaction

The theory of frontier molecular orbitals (FMO) enables us to determine the nucleophilic reactant and the electrophilic reactant by calculating the energy required to transfer the electron from the HOMO and LUMO orbitals of the reactants atorvastatin and cellulose. The border orbitals for cellulose are shown in **(Figure 3.3)**, while those for atorvastain are placed in **(Figure 3.4)**.



LUMO **HOMO**

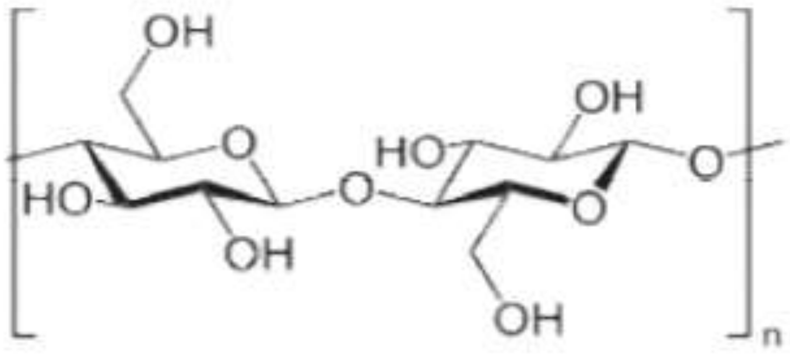
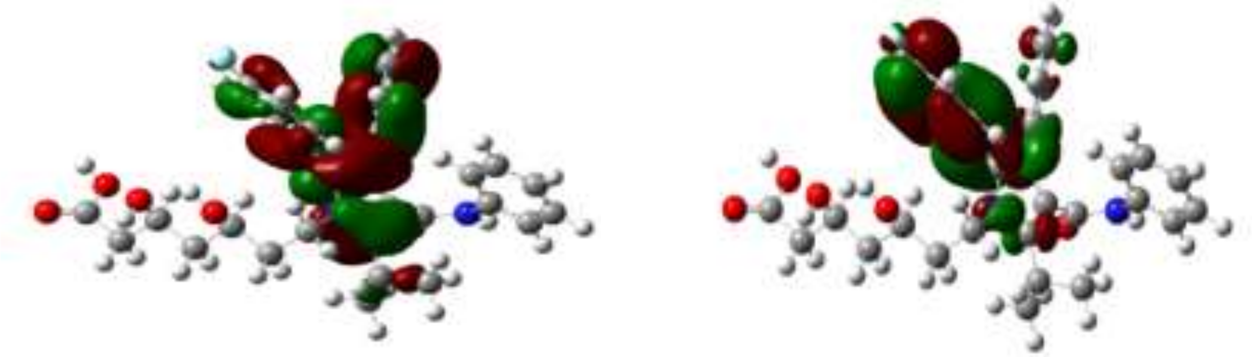


Figure 3.3: Molecular border orbitals of cellulose.



HOMO **LUMO**

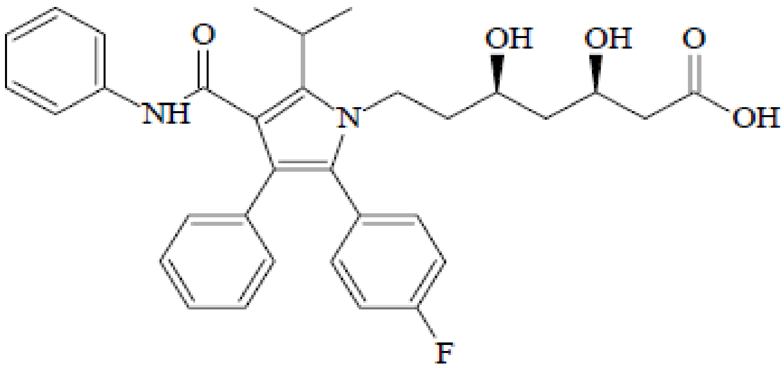


Figure 3.4: Molecular border orbitals of atorvastatin.

We notice from **(Shape 3.4)** that the border molecular orbital HOMO of ATV is the most abundant compared to the LUMO orbital, it is concentrated in the pyrrole ring, the benzene ring, and the fluorobenzene, as they are electron donor compounds, which indicates that the molecule ATV interacts as a nucleophile.

In relation to the border orbitals of the cellulose molecule, we notice from **(Shape 3.3)** that the HOMO orbital is located in parts of the two glucose units, especially those that have the hydroxyl function, while the LUMO orbital is located in each of the two glucose units, it is present in a greater percentage compared to the HOMO orbital ,which indicates that the cellulose molecule interacts as an electrophile.

From these results, the most effect is between the HOMO orbital of ATV and the LUMO orbital of cellulose.

Table 3.2: Molecular boundary orbital energy and chemical activity indicators for atorvastatin and cellulose.

The reactant	HOMO	LUMO	μ	η	N
ATV	-0.31	-0.01	-0.16	0.3	0.034
Cellulose	-0.38	0.03	-0.175	0.41	-0.035

Figure 3.5: It shows the possible effects between the border orbitals of atorvastatin and cellulose and energy values transfer of electrons where E1,E2 calculated as follows:

$$\boldsymbol{E_1} = LUMO_{(ATV)} - HOMO_{(\mathrm{CELLULOSE})} = -0{,}01 - (-0{,}38) = 0{,}37\ (\mathrm{eV})$$

$$\boldsymbol{E_2} = LUMO_{(CELLULOSE)} - HOMO_{(ATV)} = 0{,}03 - (-0{,}31) = 0{,}34\quad(\mathrm{eV})$$

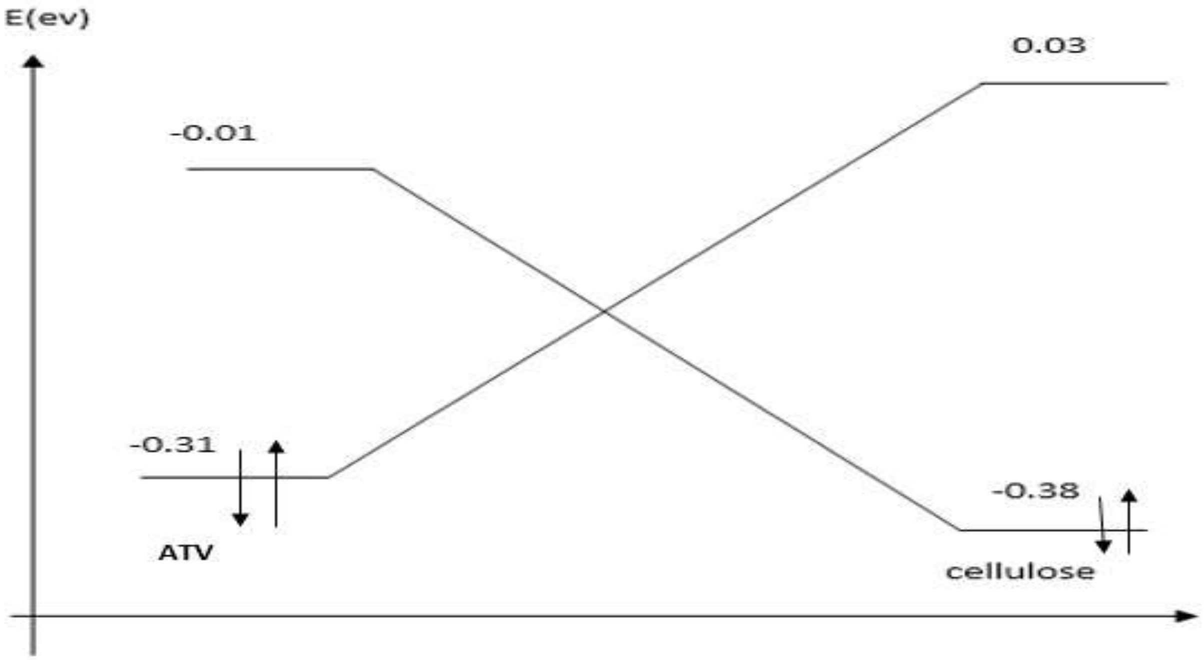


Figure 3.5 : Possible states of electron transfer between the molecular border orbitals of ATV and cellulose and transfer energy values.

We note from the shape and the results of the obtained transfer energy values that $\mathbf{E_1} > \mathbf{E_2}$**,** that mean atorvastatin reacts as a nucleophilic compound and cellulose reacts as an electrophilic compound, where atorvastatin is the compound that will provide the electronic charge, in other hand, the charge transfer will be from the HOMO orbital of ATV to the LUMO orbital of cellulose.

These results are consistent with the previous analysis using the size and position of the border molecular orbitals of the two compounds.

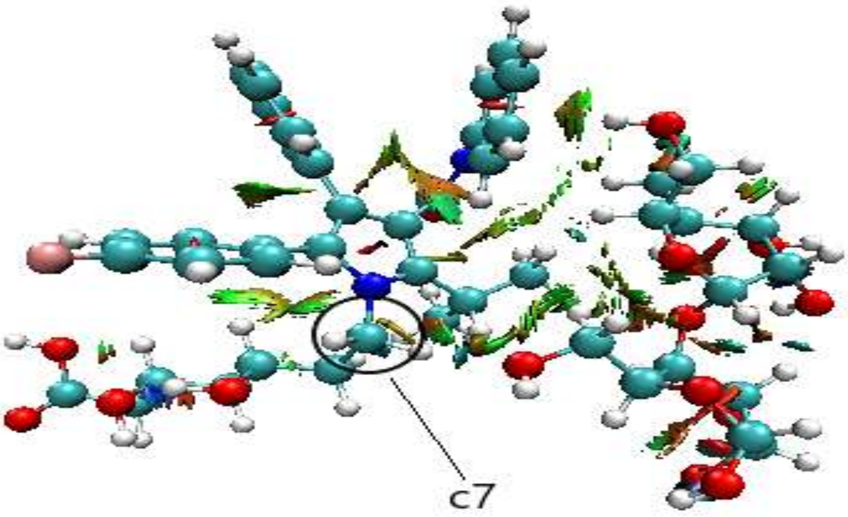
Comparing between the general effectiveness indicators for both compounds listed in **(Table 3.2)**, we note that the chemical potential of atorvastatin **(-0.16 eV)** is bigger than the chemical potential of cellulose **(-0.175 eV),** which indicates that the charge transfer will be from the atorvastatin molecule to the cellulose molecule. In addition, we note that the nucleophilic index of atorvastatin **(0.034 eV)** is bigger than the nucleophilic index of cellulose **(-0.035 eV)**, which indicates that atorvastatin interacts as a nucleophile (electron-rich), while cellulose reacts as an electrophile (electron-poor).

These results are consistent with those obtained using the theory of molecular boundary orbitals.

3.4 Analysis of non-covalent interaction (NCI)

The non-covalent interactions method is one of the most widely used methods for studying weak effects. we can determine the nature of the effects through the equal surfaces that appear in the resulting (figure 3.6).

By analyzing the stable three-dimensional structure of the complex **(Figure 3.2),** we note that there is a possibility of the formation of several hydrogen bonds between the atorvastatin part and the cellulose part, such as the O−H and N−H hydrogen bonds, in addition to the presence of several other effects. For this reason, we performed the NCI analysis of the structure. This complex was determined using the Multiwfn program. The structure obtained from the NCI analysis of the atorvastatin-cellulose complex with iso-surfaces is shown in **(Figure 3.6)**.



Shape 3.6 : NCI analysis of the complex resulting from the interaction between ATV-cellulose with iso-surface for possible non-covalent interactions.

From the **(Shape 3.6)**, we notice the appearance of two equal surfaces of turquoise blue between the hydrogen atom of the iso-propyl group attached to the pyrrole ring of atorvastatin molecule and the hydrogen atom of glucose. Also between the hydrogen atom linked to carbon atom number 7 of atorvastatin compound and the oxygen atom linked to the alcohol function of glucose, this indicates the presence of a weak hydrogen bond. We notice the presence of a group of equal surfaces in the compound of green color, the most important of them is between the group of benzene ring atoms of the atorvastatin molecule and the hydrogen atom of the alcohol function linked to the glucose molecule. In addition, between the ethyl group of atorvastatin molecule and alcohol function of cellulose, this indicates an effect of Vander-Waals.

We notice the presence of red color inside all the rings in the compound, this indicates the presence of vacuum congestion. As well, we notice the presence of an equal surface of blue color between the hydrogen atom of the alcohol function of the glucose molecule and the oxygen atom of another alcohol function of the same glucose molecule. this indicates the presence of a strong hydrogen bond.

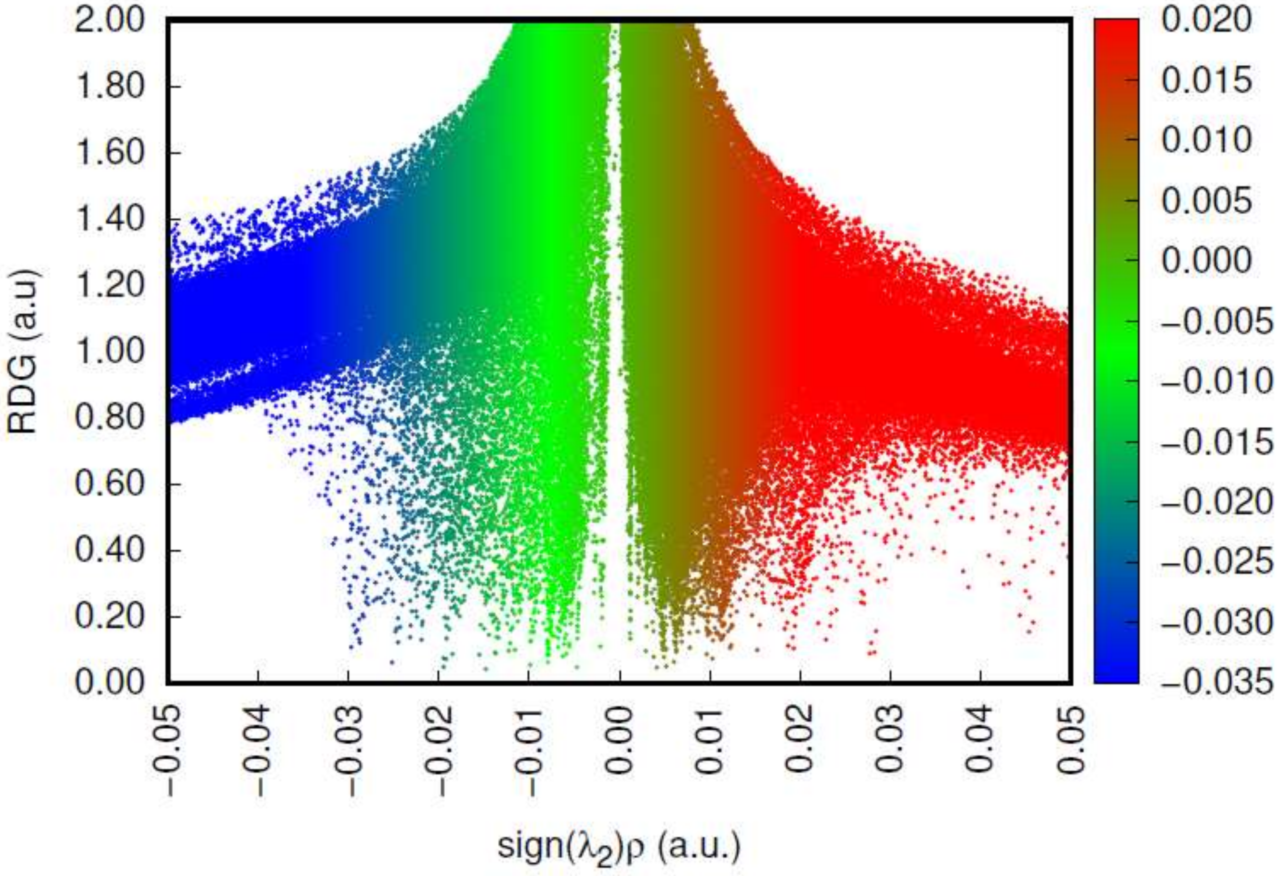
3.5 Low density rate analysis RDG

Reduced density gradient (RDG) analysis is performed to further confirm the presence of non-covalent interactions on specifically. Low density gradient analysis of the complex cellulose-atorvastatin shown in **(Shape 3.7).**

We note from the analysis of **(Shape 3.7)** that green gradations of equal surfaces are limited in the field **[-0.018, 0.00]** which indicates the presence of Vander-Waals type electrostatic effects. Also, shades of blue gradiation are limited to the field **[-0.025, -0.018]** which indicates the presence of strong hydrogen bonds.

As well, shades of red graduation confined to the field **[0.008, 0.018]** which indicates the presence of vacuum congestion in all rings of the complex atorvastatin-cellulose.

This analysis demonstrated the presence of hydrogen bonds as well as electrostatic effects of the Vander-Waals type in the structure the complex is atorvastatin-cellulose, which leads to the stability of the complex.



Shape 3.7: RDG analysis of atorvastatin-cellulose complex.

3.6 Quantum theory of atoms in molecules (QTAIM)

The QTAIM analysis using the program Multiwfn of the complex resulting from the reaction between cellulose and atorvastatin is shown in **(Figure 3.8)**, which shows the numbers of atoms of the complex and the critical points of type (3, -1). **Figure 3.9** shows the structure of the complex and the numbers of the atoms, in addition to the critical points and their numbering. The values of the electronic density and the total electronic density in addition to the Laplacian density for the critical points (3,-1) were calculated using the program Multiwfn and collected in **(Table 3.3)**.

From **(Figure 3.6)** we notice that the surfaces obtained through the NCI analysis and colored in green correspond to the critical points of type (3, -1) obtained in the QTAIM analysis.

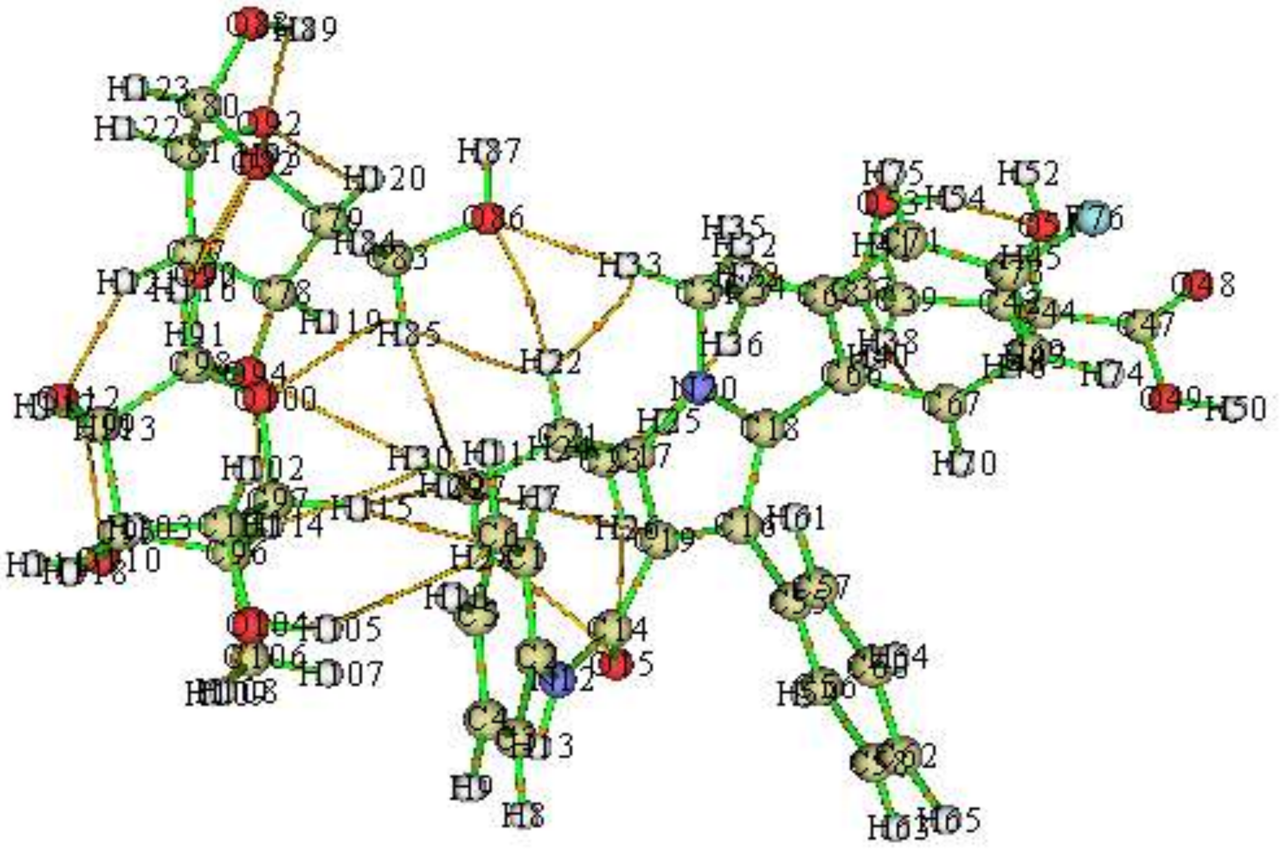


Figure 3.8: QTAIM analysis of the complex resulting from the reaction between cellulose and atorvastatin using software Multiwfn.

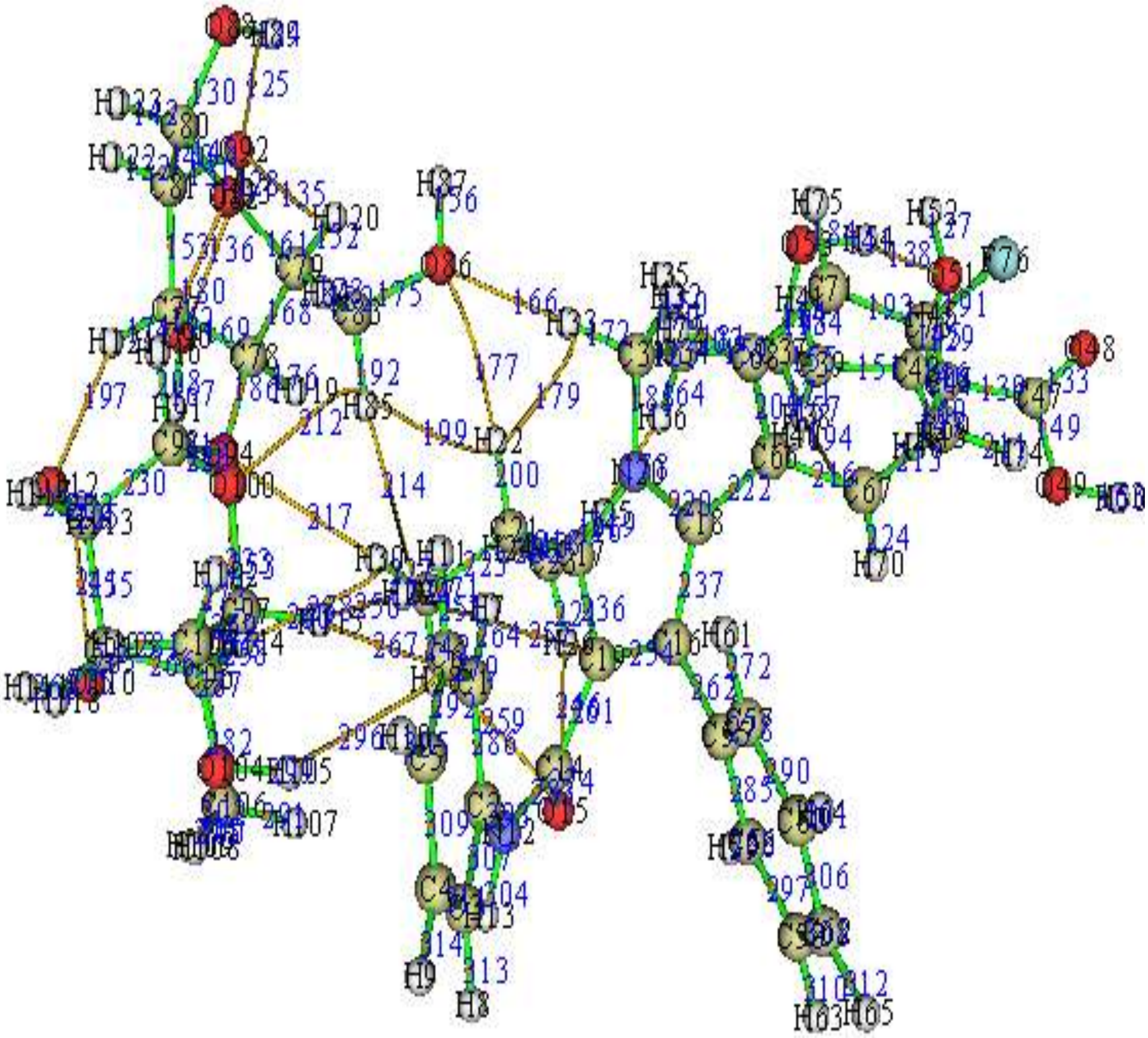


Figure 3.9: QTAIM analysis of the complex using Multiwfn program with critical points numbering.

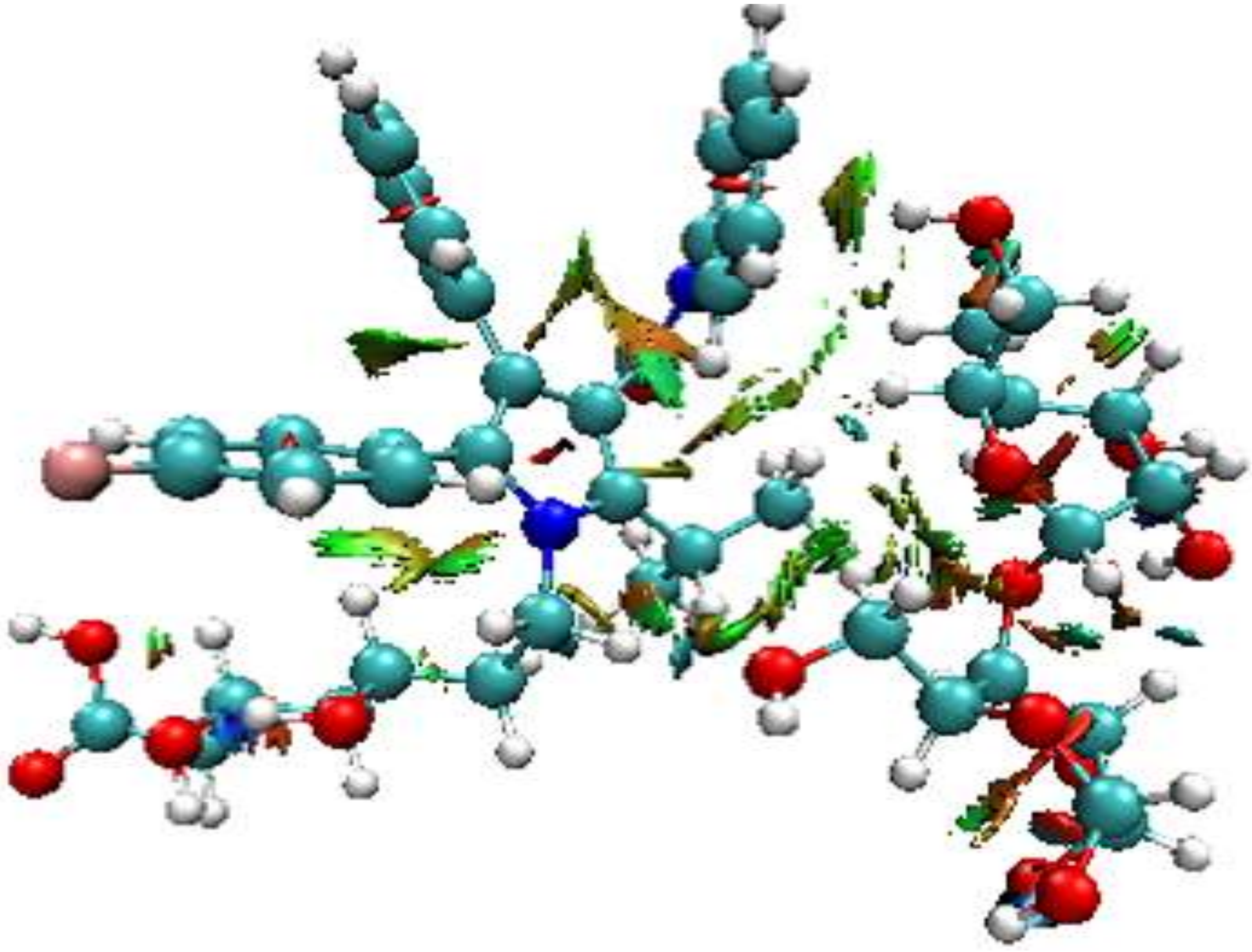
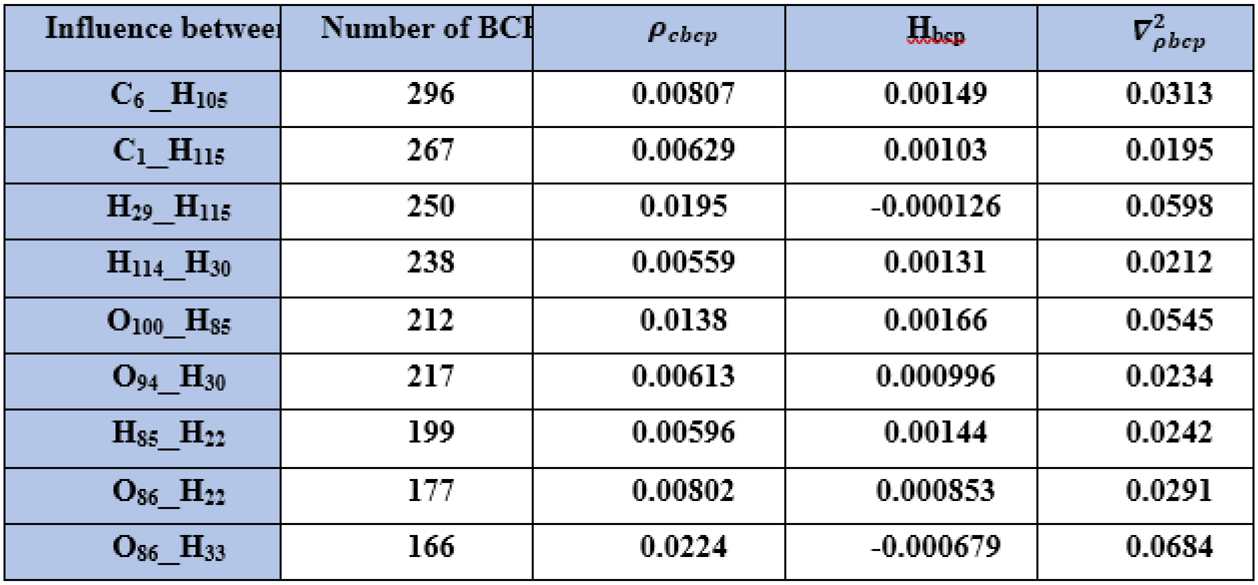


Figure 3.6: NCI analysis of the complex resulting from the interaction between ATV-cellulose with iso-surface for possible non-covalent interactions.

Table 3.3: Values of electronic density and total electronic density as well as Laplacian density for points.



Influence betwee	Number of BCI	ρ_{cbcp}	H_{bcp}	$\nabla^2_{\rho bcp}$
C_6_H_{105}	296	0.00807	0.00149	0.0313
C_1_H_{115}	267	0.00629	0.00103	0.0195
H_{29}_H_{115}	250	0.0195	-0.000126	0.0598
H_{114}_H_{30}	238	0.00559	0.00131	0.0212
O_{100}_H_{85}	212	0.0138	0.00166	0.0545
O_{94}_H_{30}	217	0.00613	0.000996	0.0234
H_{85}_H_{22}	199	0.00596	0.00144	0.0242
O_{86}_H_{22}	177	0.00802	0.000853	0.0291
O_{86}_H_{33}	166	0.0224	-0.000679	0.0684

Non-covalent interactions are characterized by critical points with a Laplacian (∇_{ρ}^{2}) , a total electronic density(ρ_{cbcp}) and energy density (H), while to study and analyze these non-covalent interactions, they are divided according to the values of the energy density (H) and ($\nabla_{\rho_{bcp}}^{2}$) to:

Electrostatic effects, when ($\nabla_{\rho_{bcp}}^{2}$) and (H) are greater than zero, and hydrogen bonds when ($\nabla_{\rho_{bcp}}^{2}$) is greater than zero and (H) is less than zero.

By analyzing the results recorded in **(Table 3.3)**, we notice that the values of ($\nabla^{2}_{\rho \mathrm{bcp}}$) for all critical points of type (3, -1) are positive and therefore they represent non-covalent interactions between molecules that stimulate the stability of this complex. In addition, we also note that the critical points numbered 296, 267, 238, 212, 217, 199 and 177 are characterized by a Laplacian and a total electronic density greater than zero, so, they represent the electrostatic effects. On the other hand, we find that the critical points numbered 250 and 166 are characterized by a Laplacian ($\nabla^{2}_{\rho \mathrm{bcp}}$) greater than zero and a total electronic density (H) smaller than zero, which indicates that they are critical points corresponding to formation of hydrogen bonds.

This analysis confirmed the presence of electrostatic effects and hydrogen bonds in ATV-cellulose complex, in addition to the large number of these electrostatic effects and hydrogen bonds that make it stable, which explains the results obtained previously.

Conclusion

Conclusion

The exacerbation of the problem of pollution, especially water pollution, has led to a continuous search for appropriate ways to remove these pollutants. In the first part of this manuscript, we discussed some of the causes of this problem and methods for treating it, including the adsorption method, which is considered one of the most important techniques used in treating water pollution due to its high efficiency. But there is always a search for new ways that are economical and not harmful to the environment. Because our study was a computational study, we shed light on the quantitative chemistry methods used to describe chemical systems and calculate physical properties, including semi-empirical methods, density functional theory, molecular boundary stations theory, and activity indicators, as well as methods for analyzing non-covalent interactions.

In the second part, we conducted a computer study (simulation) of the adsorption of one of the pharmaceutical compounds polluting water, namely atorvastatin, using cellulose, which in turn is considered the main component of the fiber plant. The aim of this study was to know the type of adsorption, as well as the type of possible effects between these two compounds, based on the semi-empirical method PM6, and based also on energy analysis and thermodynamic properties, frontier orbit theory and effectiveness indicators derived from DFT, and to determine the type of emerging bonds by conducting quantum theory analysis of atoms in molecules and analysis of non-covalent interactions and low density rate.

Regarding energy analysis, the results showed that this reaction is energetically favorable because the complex is more stable than reactants cellulose and atorvastatin. An analysis of the borderline molecular stations shows that cellulose interacts as an electrophile while atorvastatin interacts as nucleophilic.

Analysis using the theory of non-covalent interactions (NCI), Low density rate analysis (RDG) and quantum theory of atoms within molecules (QTAIM) showed the presence of several hydrogen bonds, including strong and weak ones, as well as some effects electrostatics, which is considered a source of stability for the resulting complex cellulose-atorvastatin.

The free energy values of the complex and the type of effects in the cellulose-atorvastatin complex indicate this type of adsorption it is physical adsorption.

In addition, through this study, we arrived at the following prospects:

. This study can be developed by using the method DFT instead of the method semi-emperical PM6 in order to obtain more accurate results.

. The results we obtained through simulation enabled us to confirm the laboratory results they reached last year.

. This study can be generalized to any chemical coumpound

. We concluded that it is possible to theoretically predict laboratory results through the semi-emperical method in order to save time and avoid losses.