POLITECNICO DI TORINO

Department of ELECTRONIC AND TELECOMUNICATION ENGINEERING (DET)

Master of Science in Nanotechnology for ICT's engineering

Master Degree Thesis

Analyzing, studying and comparing the applications of graphene, carbonic nanotubes and other 1 and 2 dimensional materials as an alternative of drugs in cancer treatment

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"The best and most beautiful things in the world cannot be seen or even touched -

They must be felt with the heart."

— Helen Keller

TO MY HUSBAND
&
MY FAMILY. . .

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Thanks for believing me.

Abstract

We intend to introduce a high-level article on drug delivery with carbon nanotubes and how to use nanoscale nanotubes in drug delivery. To achieve this goal, we first introduce the drug Nimesulide, and it is said that if it does not reach the target tissue and elsewhere, it is highly toxic and dangerous and has irreparable effects, as prohibited by many countries. , But using closed carboxyl nanotubes, it is possible to place the Nimesulide drug into these nanotubes, and when we reach the target tissue, we use external light radiation to release the nanotubes and release the drug precisely into the tissue the goal is to have no other toxic effects for other tissues in the body.

In this way, we will introduce the Siesta software in the third chapter of the thesis, and we will describe how to simulate and behave the system. Of course, since this software is very high and heavy, we will only simulate a part of the article so that the reader will get familiar with how this simulator works and how to research nanoscale drug delivery. In Chapter 6, the results of our simulation and the main results of the essay article are presented.

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Chapter 1

Introduction

1.1 Introduction

One of the most important topics in pharmacy industry, is the topic of delivering controlled drugs to the body. As you know, in the common approaches of consuming drugs, weather injectable or other methods, the drugs distributes all over the body and so all the body is influenced, and as a result, some unpleasant side effects will appear. Therefore, if we want to have a high efficiently, we must consume a huge amount of this drug. Until now, a lot of researchers tried to solve this issue. With entrance of nanotechnology to medical sciences, and by using this technology, researchers became more interest in this field. Due to the fact that particles that contain drugs have special importance in the production of drugs, and particles in Nano size will have special characteristics that can be very effective in eliminating the common problems in delivering drugs; so creating these particles needs very complicated methods [1].

In the past decade, the fast growth of nanotechnology has created interesting ideas and opportunities for detection and treatment of the illnesses. Carbonic materials specially the zero dimensional of fullerence and the one dimensional structure of carbon and graphene nanotubes has attracted the attention of many researchers in different areas. Among them, graphene and graphene oxide, due to their special and unique characteristics, are considered proper for different applications including pharmacy.

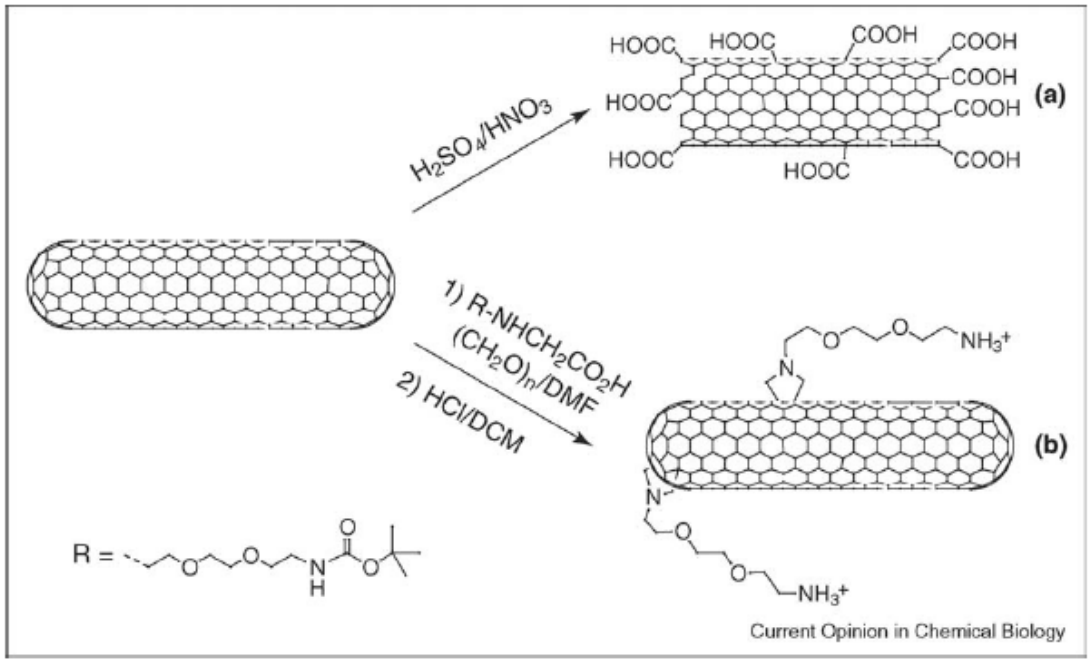

Fig. 1.1 application of carbon nanotubes in delivering drugs [8]

1.2 Purposeful delivering of drugs in treatment- of the cancer

The main problem in treating many of illnesses is delivering the needed drugs to a special point in the body. The traditional methods of delivering drugs may have some unpleasant effects such as limited effect of the drugs, unpleasant biological distribution, and not having the power of choice. By controlling the drug delivery we can overcome these issues and limitations. In under-controlled drug delivery systems, the drug is transmitted directly to the related position in body. And as a result, its effect on vital parts of the body and also its side effects will be minimized. Further, in this method the fast corruption of the drugs is reduced and the density of the drug in the target part of the body is increased. Therefore, in this method there is no need to use high-doze drugs [3].

In delivering the drugs, one of the most important factors, is decreasing side effects and increasing the effect of drugs in target parts of the body. There are many anti-cancer drugs that are very effective but due to the fact that they can be very poisoning, they have no usage [2].

Considering the fact that in the normal drug delivery method, in order to make the density of the drug constant, we must inject a huge amount of drug in different times, so this can be harmful. Further, these drugs can impact the healthy cells, so we can't use them. If we can inject these drugs using a purposeful system, then there is a possibility that with overcoming to their poisoning problem, we can introduce a wide range of new anti-cancer factors for human usage. The results of the studies in the field of cells, shows that with combining anti-cancer drugs with nanoparticles, we can deliver the drugs to the tumor cells and we can increase the efficiency of the method. With this method of targeting directly the cancerous cells, the amount of receiving these drugs in natural cells will be increased. In purposeful drug delivery for curing cancer, usually some drug delivery carriers are used that have a diameter of a couple of nanometers and can cross the very small parts in cells and can go and reach for the cancerous cells[2].

1.3 Categorizing drugs Nano-carriers

In recent years, creating nanoparticles as carriers for delivering the drugs, has attracted much attention. Nano carriers, can change the pharmacokinetic characteristics of the drugs, and as a results, they can cause improvement in performance of the drugs and reduction of the side effects. For transferring the drugs, we use different materials in the structure of the Nano particles, like polymers, metal particles, lipids and so on. Depending upon their method of creation we can create different shapes and sizes of them. Drug delivery systems that are based on Nano carriers, are now entering the drug market and their usage in pharmacy is rapidly increasing. In the future, the performance of some particles with the capability of targeted drug delivery will be the topic of research [4, 5].

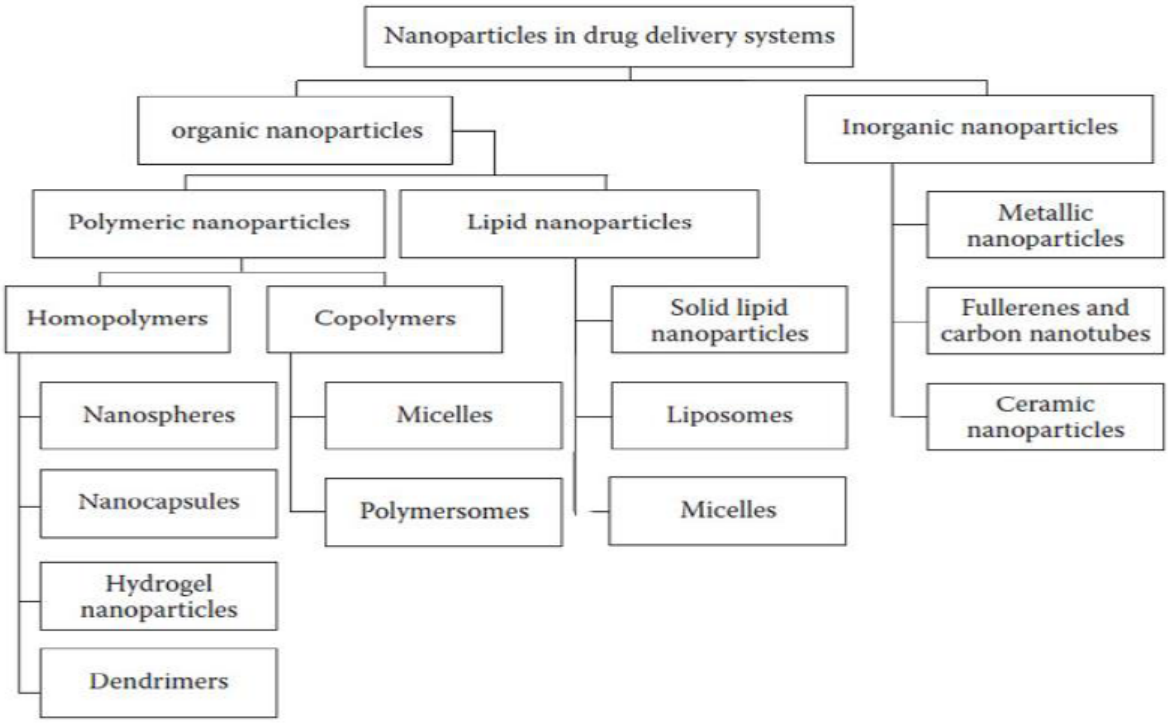

Fig. 1.2 categorization of drug Nano-carriers [31]

Drug transfer systems are created on the basis of improving the feathers of the drugs that is been used by patients. These systems are generally like a container and they contain the drug. These systems can release the drugs with a specific amount and they can release it in special conditions. And as a result, they can be effective in the distribution of the drug in body. Nano particles are widely used in drug delivery systems [6].

With the advancement of the Nano-technology, and its entrance to other sciences, many kinds of nanoparticles with different structures are introduced. That each one of them has its own advantages and disadvantages. And they could make the performance of the particles better. One of the best fields that nanoparticle have entered, is the field of drug delivery. In this field, the nanoparticles in different systems like polymer carriers, lipids, metals and so on; have a big part in improvement of drug delivery in treating different types of illnesses specially cancers. Since the first dendrimer was analyzed, the growing interest in dendrimer chemistry was created. Advancement in controlled polymerization and analyzing techniques, caused advancement of structured with a great number of analyzing groups. Dynasties may contain drugs or lively particles on the surface or in their wholes. They have the feather that the guest molecules can release themselves in target part, and in a controllable manner. And this procedure can cause reduction of the drug use and sometimes its bad effects. Although dendrimer drug delivery is a science that is in its first stages, but it has some feathers that makes it very interesting.

The controllable features in dynasties, like size, shape, the length of the parts, and surface feathers allows us to change them for any usage and we can also adopt them as ideal carriers for every application. The drug loading mechanisms in dendrimer carriers are different and transferring of the drug, depending upon the kind of the drug and the dendrimer, may be via skin, mouth, eye, or even lungs. Dynasties can also be good for detecting the illness and they may contain anti-cancer drugs. In recent years, using Nano structures as carriers for transferring the drugs, have been the subject of interest. Because these structures, due to their property of controlling and slowing the growth of the drug, protecting the drug molecule, the particle size less than the cells, the capability of crossing of the biological blockages, increasing the durability of the drug in blood vessels, purposeful drug transfer and adoptability with biological conditions; can be considered as a very effective drug transfer system that can increase the performance of the drug. During the last 50 years, different advances in different sciences, like polymer and chemistry, biology and mechanic science and physic, has affected the variation of all kinds of Nano-carriers. And they have introduced different categorizations from carriers with unique characteristics and different applications. The drug carriers can be categorized in two different types' carriers: organic and non-organic carriers. Each one of these groups can be categorized to different sub-group that is shown in figure 1.2.

1.4 The targets of the thesis

A wide range of studies are done on carbon Nano-pipes and graphene. These studies consider them as a tool for targeted drug delivery for attacking cancerous cells. Our aim here in this thesis is to gather the results of these studies in the form of a comprehensive study. Many of one and two dimensional materials like gallium Nano-materials, can be used as a replacement for carbon nanotubes. And if they are not poisonous, they can act much better than carbon nanotubes in pharmacy. Our innovation in this study is analyzing the possibility of using other nanotubes as a drug transfer system for treating cancer. Very few studies are done on the basis of this study.

1.5 Field of the study

The field of this study is hierarchy and it is common in pharmacy, medicine, Nano technology and physics. And the researchers of these four fields can use the results of this study.

The results of this study is important for those researchers that are working on treating cancer.

1.6 The structure of the thesis

Chapter 2 is about the basic concepts such as introducing carbon Nano-tubes, other two-dimensional materials, transferring drugs with Nano-technology and so on.

Chapter 3 is about analyzing the previous researches about purposeful drug delivery with carbon Nano pipes and the related challenges.

In chapter 4, the replacement nanotubes and other two-dimensional materials like two-dimensional Nano sheets are analyzed and the possibility of using these materials in drug delivery will be discussed. In chapter

5, we will conclude and we will make some propositions about continuing this studies by interested researchers. And we will present the difficulties and challenges.

Chapter 2

Base concepts about nanomaterials and purposeful drug delivery

2.1 Introduction

In recent years, sheet nanomaterials like graphene, boride nitride with hexagonal structure and other two-dimensional materials; due to their vast application in electronic, optoelectronic and catalyst and power saver industry; and due to having pleasant feathers, are becoming the subject of many researches. And by studying them, we achieved wonderful electronic feathers and high thermal conductance and electrical conductance feathers. This two dimensional Nano-material, plays an essential role in development of electrochemical sensors. The high area of graphene sheets, leads to high capacity of it in gathering elite molecules with high sensitivity. Also, strong factor groups in the level of graphene derivatives, creates different methods for pairing chemical-biological molecular receivers for assessing electrochemical proteins and nucleic acids.

Carbon is one of the fantastic elements of nature. This element, constitutes the structure of life on earth and until now, about ten million mixtures of it are known. Carbon has a great tendency to bond with small atoms like hydrogen and carbon. Carbon, exist in nature as graphite and diamond and sometimes it's like gas. Graphite is one of the most important and durable structures of the natural carbon and it consists of carbonic hexagonal in a plane. Each carbon atom has a covalence bond with 3 atoms in the same plane. And has a vender walls bonds with the adjacent plane. Graphite is the most durable allotrope of carbon. In very high temperature and high pressures, carbon is as stable as diamonds. In diamond, each atom of carbon has a bond with four other atoms. Diamond, because of having a strong covalence bond of carbon-carbon, can be considered as one of the hardest materials that exist in nature. This structure creates strong feathers in diamonds. Fullerene is one of the other shapes of carbon that has been discovered recently.

Fullerenes are much like graphite's but in their structures, instead of hexagonal, are heptagonal of pentagonal. Fullerenes are big combinations of carbon atoms that are in spherical, pipe-like and other complicated forms. Two-dimensional Nano-tubes, due to their thickness and due to their dimensions in Nano and macro scales, are known as the thinnest materials. There are various forms of these sheet structures with strong bond in surface and weak bond between layers like graphene, hexagonal boride nitride, Broken and DiCalcogene and the medium metals. Due to their special shape, Researchers have done many attempts to create two dimensional Nano-sheets via analyzing these mixtures to different layers. As we mentioned earlier, the constituent element of graphene is carbon. Each carbon atom, share three of its four free atoms through covalence bonds and makes a plane consisting integrated hexagonal. Among these planes, which are called graphene planes, and they are like honeybee hives, the weak Van der Waals force is the dominant force. This force causes these planes to cross each other very easily; and this feather causes the production of some kind of a trace on the plane. It's like a trace of a pencil on a paper. When we are writing, as a result of the pressure of your hand on the paper, the graphene planes will move and will be separated from the graphite structure of the pencil brain and they will stick on the paper.

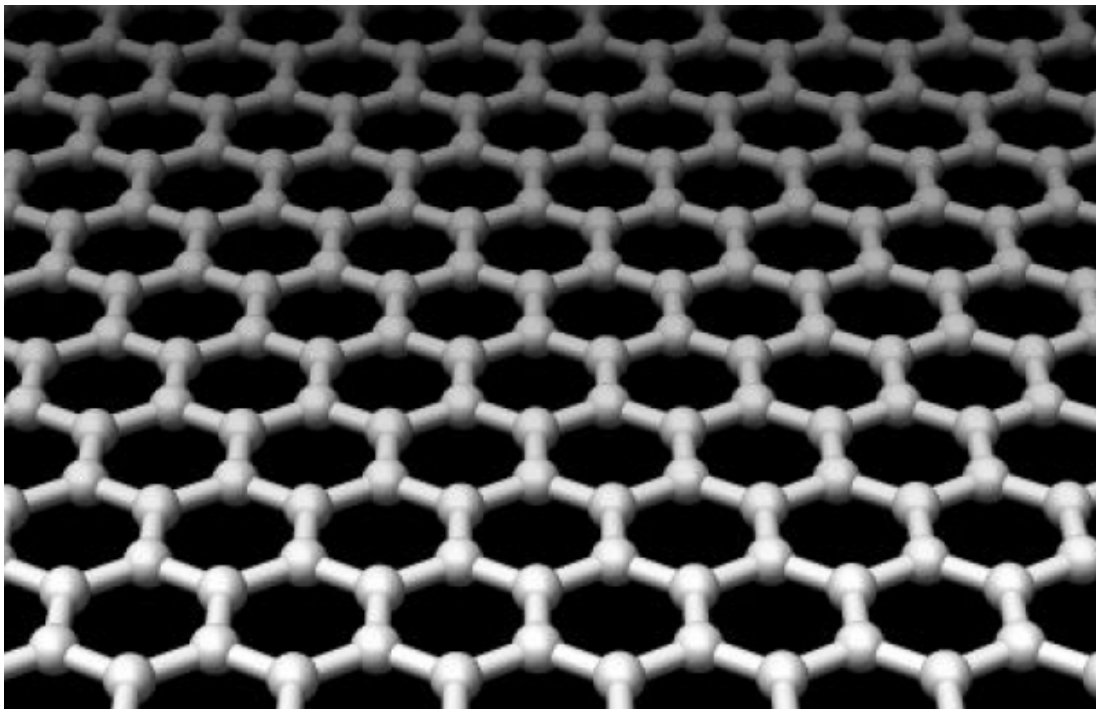

Fig. 2.1 graphene (two-dimensional material) [2]

The biochemical application of graphene-based materials, like drug delivery, in recent years, is increasing dramatically. In the past few years, studies about graphene and graphene oxide in bio-medical applications, has grown rapidly. This is because of the unique properties of these materials; such as: two-dimensional plane structure, big available area, high mechanical and chemical stability, very high chemical and mechanical conductivity and so on.

Because of these feathers, designing drug delivery systems has developed and a new spectrum of graphene-based cure is created. In the past few years, new Nano-carriers like carbon nanotubes, graphene and graphene oxide, have been analyzed widely for loading different types of special drugs including anti-cancer drugs, unsolvable drugs in water, anti-biotic, anti-bodies, peptides, DNA, and RNAs. Graphene. Graphene oxide, and other derived group from graphene, are analyzed widely in the past five years for their application in drug delivery.

2.2 Analyzing and studying of graphene and carbon nanotubes

Carbonic mixtures (organic mixtures) are very widespread and they are very important. Carbon (C) is a special element in. the widespread chemistry of carbonic mixtures is such that chemistry majors called organic chemistry, analysis this element of the periodic table. The covalence bond of each carbon atom with other atoms or other carbon atoms, creates various structures. In nanotechnology also, carbonic mixtures are studied under the title of carbonic nanostructures. Carbonic nanostructures have some unique physical and chemical characteristics. And they have an important role in the field of new technologies. The study of the base chemistry

of carbonic mixtures (organic chemistry) can show us many of carbonic nanostructures and can help us to improve them.

Diamond, is a crystal carbonic structure with hybrid SP3 (which does not participate in hybrid SP2); that is vertical on graphite plane and creates the π bond between planes (figure 2.3). The strength of the bond between carbon atoms (sigma σ bonds) in the graphite plane, comparing to weaker π bonds in the planes, causes the graphite to be like a plane. The existence of the π electrons in the graphite structure, causes the great conductance that is not seen in the diamond structure with the hybrid carbon of SP3. Because of the lack of π electrons, the electrical gravity doesn't appear in diamonds. As we stated earlier, carbon does exist in different microscopic forms. Some examples are: The mixtures like graphite, diamond, non-shaped carbons, fullerene, carbonic nanofibers, carbonic Nano pipes, and graphene. Graphene is the newest member of the graphite carbonic and two dimensional materials family. Fullerene are considered as a zero-dimensional (D-0) nanomaterial, carbonic Nano pipes as a one-dimensional nanomaterial (1-D) and graphite as a three dimensional material (3-D). In figure 2.2, feathers and characteristics of different forms of carbon, are seen.

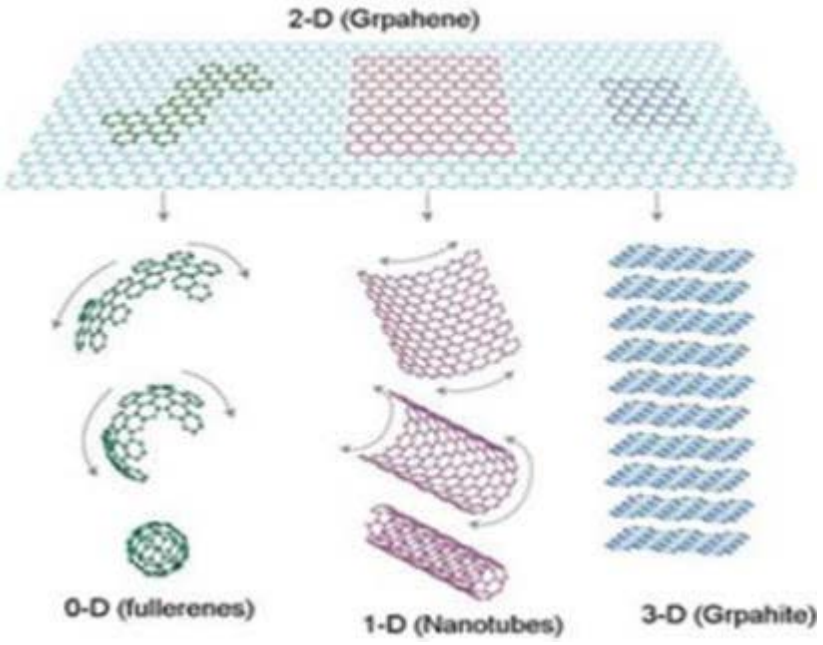

Fig. 2.2 different carbonic forms [32]

Graphite consists of a hexagonal structure with carbonic atoms that are in a body with hybrid sp2 bonds [6]. This atomic structure causes the creation of layered planes of sheeted planes of graphene with the distance of 3.354 angstrom. There is a strong covalence bond between atoms in graphene sheet. Unlike diamond, there is a weak Vander walls force between layered planes that can't keep them together. And because of these weak interactions, graphene sheets (one mono-

layer of graphite) can slip over each other all over each layer and this gives good lubricant feathers to this material.

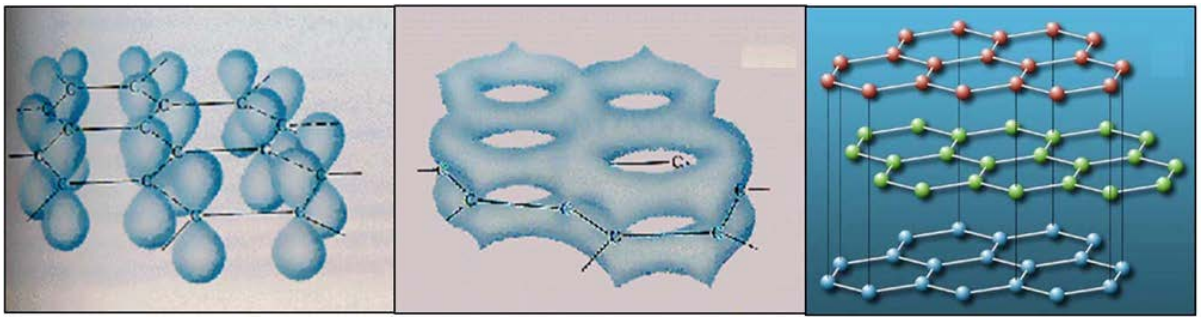

Fig. 2.3 the graphite plane structure: from left to right: the p perpendicular to the plane orbitals. The π cloud containing the planes. The π bond among the planes [32]

2.2.1 Hexagonal crystal device

In 1912, the internal structural study of the crystals in atomic scale, with x rays, was invented. In crystals, atoms (in general the constituent particles), are formed together. Today, using X-ray, measuring the distances between the crystal planes, with the accuracy less than angstrom, is possible.

The hexagonal network, is one of the seven crystal coordinates (a coordinate that consists of 3 vector) and one of the complex structures in which the empty space between the atoms is minimized. Most of the metals, alloys and even ceramics has cubical structures and there are not many metals and alloys that have these sort of hexagonal structures. The studies have shown that all the crystals can be classified to seven basic structures (geometrical shape) (fig 2.4); that with replacing the atoms in these seven structures, we can achieve 14 networks.

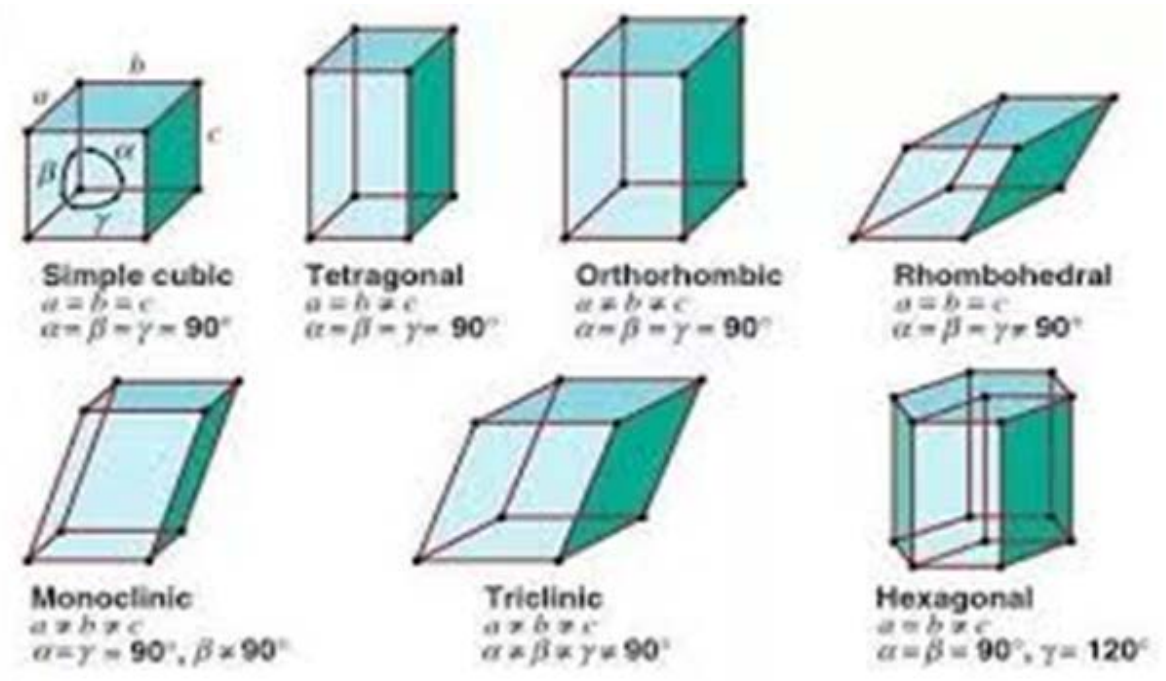

Fig. 2.4 seven basic structures (geometrical shape) [32]

In figure 2.5, the 3 dimensional view of the configurations in the cubical unit networks are shown.

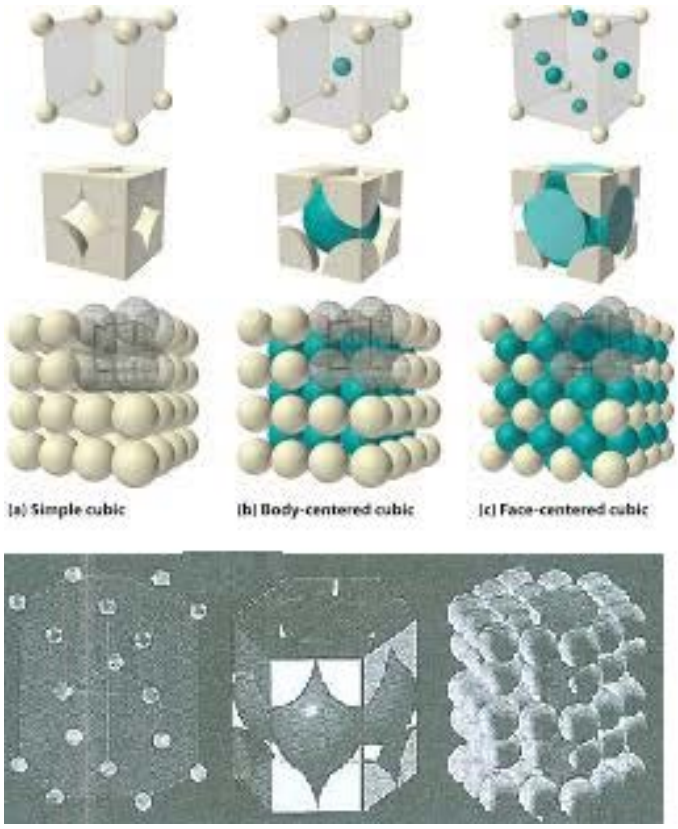

Fig. 2.5 the 3 dimensional view of the configurations in the cubical unit networks [32]

2.3 Drug delivery systems

The common methods of drug delivery systems is in the form of taking a pill or injecting drugs. In these methods, there is not control on the effective amount of the drugs of the place of the effect of the drugs. Entering the drugs in the body with these methods, causes some problems and limitations. And due to this fact, scientists are seeking a way to solve the above problems. As a results of these studies, the controlled releasing of the drugs is introduced that has a lot of advantages. One of the most important of its advantages is the ability to maintain the doze of the drug in a relatively constant level and for a relatively constant time; the ability to control the speed of releasing the drugs and the dependence to the place of drug delivering, the possibility of delivering the drug to one special organ or part of the body, the ability to deliver some of the drugs with the same formulation, the possibility to delivering the drugs with nanometer dimensions and so on. These systems made a progress in the field of curing many illnesses and these systems are increasing rapidly.

2.3.1 Releasing the drugs

The controlled release of the drugs, is a process in which a polymeric factor, ceramic or metallic, will be mixed with the drug or the active factor; and as a result, the active factor in the body will be released from this material, in a predetermined way. The biomaterial engineering as a great role in the releasing systems of the drugs and the most important part of these systems consists of materials that are used as a substrate for the drugs of as a container for enclosing it. And they have an important role in the process of releasing the drug, the rate of releasing, type of releasing, the density of the drug in the blood and in general in directing the controlled process of drug delivery. Normally, after using the drug, a huge amount of it will enter the body. And after a few hours, its amount will reduce. And the patient will have to consume it again and this cycle will continue. With the advancement of technology, new methods for solving this issues are invented. In this method, the patient, won't receive a high doze of the drug, after consuming it. And this amount, will remain constant, in a relatively long period. The focus of drug delivery technology is on delivering drugs to the correct part of the body in a correct time and with correct effects. This technology has many advantages:

- Reducing the amount of the drug
- Reducing of the side effects; because the drug only goes to a special part and doesn't influence other parts
- Increasing the effectiveness of the drug; because of concentrating of the drug in a special part
- Reducing the time of the treatment and safer treatment
- More satisfaction from the patients in accepting the drugs.

- Reducing the costs of the treatment

Today, releasing the drug, is one of the widespread fields in biomaterial engineering. And it is also studied by scientists in: genetic, nanotechnology, and so on. The level of treatment in the patient must be such that until the next time of consuming the drug, it must meets the patient's needs. But unfortunately it is observed that the wasteful reduction or wasteful increasing of the level of the drugs in body, will affect its effectiveness. In fact, after sudden entrance of the drug in the body, the amount of the drug in the circulation system or the place of injection will increase. And this could make some drugs, poisonous. Therefore, technologies of the slow and controlled releasing of drugs; with the aim of controlling the rate of releasing the drugs and making the releasing of the drugs purposeful, has invented. Of course using these systems will create some limitations that may include appearing some poisoning as a result of using new material in body, of delaying in distribution of the drugs, and needing for new experiments for analyzing the drug factors. The studies done in the field of cell culture, showed that with sticking anti-cancer drugs to Nano-particles, we can purposely deliver the drug to tumor cells and we can increase the effectiveness of the treatment. Therefore the need for studying and analyzing different kinds of drug delivery systems, seems crucial.

2.3.2 Different types of drug delivery

With the advancement of nanotechnology, more effective systems are introduced for drug delivery. Below are some of these systems:

Stimuli-sensitive drug delivery systems

In this systems, the carries will answer the existed stimulations like temperature, Ph., existent ammonia in body and so on. And this system will cause releasing the drug.

Targeting drug delivery systems

These systems, use peptide signal, antibody-antigen interactions or ligand-receiver. In other words, in these systems, a molecule will be on the surface of a carrier and this molecule will be a complementary of the other molecule. The potential mechanisms of releasing the drugs include:

- Retreating And releasing the banded drug to the surface
- Diffusion from the carrier matrixes
- Diffusion from the carries wall for micro-particles and micro-capsules
- Erosion and destruction of the carrier matrix
- A mixture mechanism from the erosion/diffusion process

Drug delivering is done by two main methods:

- Putting the drug in releasing systems and smartening these systems

- Smartening the drug

2.4 Biocompatibility and poisoning of the graphene used as drug carrier

In order to use graphene and graphene oxide in medical application in the real world, we must analyze their biocompatibility and poisoning via vast laboratory and non-laboratory experiments using animal cells and models. The two dimensional structure of graphene is a unique structure comparing to spherical Nano-particles. And the physical and chemical factors determining its cellular interaction and it is biocompatibility are unknown. Therefore, the problem of safety and poisoning of graphene based materials has not been solved completely and much attention must be paid to the determination of its biocompatibility and poisoning.

Many of the past reports shows that graphene, graphene oxide and its hybrid structure has little cellular poisoning for drug delivery; but now, the results are a paradox.

The results shows that with increasing the solvability of graphene, its compatibility increases. Nevertheless, because of many hydrophilic groups like carboxyl, hydroxyl and epoxy on the graphene oxide, the biocompatibility of graphene oxide is much higher than graphene. Factorization of the plane of graphene and graphene oxide, increases its biocompatibility. Leo et al. analyzed biocompatibility of graphene based materials with controlling physical and chemical feathers. They showed the strong effect of particles, the state of particles, the amount of oxygen or the surface charge of graphene on the biological response or poisoning to red blood cell. The biocompatibility effect of graphene oxide on fibroblast cells of human and mouse, has shown that in the values more than 50 μg/mg the cellular poisoning will be induced. For the betterment of biocompatibility, Leo and his colleagues, using a reduced reactive element, developed a new method for preparing a graphene Nano-plane factored gelatin. The achieved biocompatible gelatin from graphene Nano-planes, shows high solvability, stability in physiological liquids, and high capacity of the drugs [9].

Poly ethylene glycol is been used as a hydrophilic polymer with high biocompatibility for factorizing carbon nanotubes and other Nano-materials; that increases their biocompatibility, reduced the non-linear biomolecules and cells, and betters the targeting of tumor in pharmacokinetic body. So the method of betterment of graphene and graphene oxide for achieving the same features, is been used. Some of the studies show that graphene oxide after being covered with poly ethylene glycol isn’t considerably poisonous.

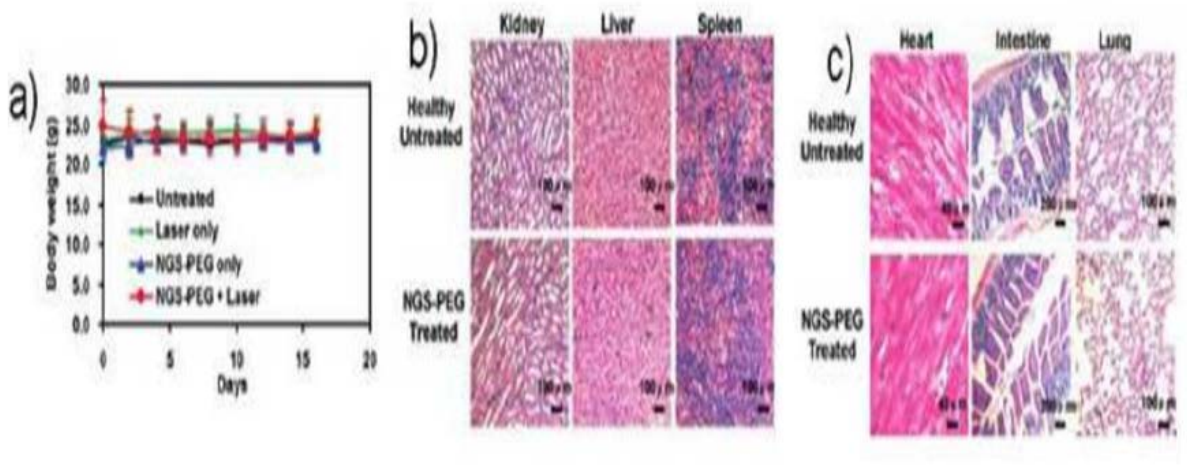

Fig. 2.6 investigating the toxicity of NGS-PEG in the body. a) Mass gravity curve after [9]

Different treatments b, c) Images of the main organs including the kidneys, liver, spleen, heart, intestine and lungs of the live mice, c image after the 40-day period of tumor treatment using the thermotherapy method.

Yang et al. Investigated peg-Nano graphene sheets by functional fluorescence experiments and NGS-PEG behavior in mice with fluorescence imaging from the inside of the body. Histological studies, blood chemistry and blood plate analysis do not show any signs of toxicity of PEG-GO injected into mice. They also studied the biological dispersion of NGS-PEG inside the body and studied the graphene's toxicity regularly over time. After intravenous infusion, it has been observed that NGS-PEG accumulates to a large extent in the liver and spleen. If the amount of injected is as much as tested (20 mg / kg) during a three-month period of treating the mice with blood biochemistry, blood and histology analysis It has been determined that this accumulation will be gradually cleansed without any toxicity.

2.5 Application of graphene and graphene oxide

The biochemical use of graphene-based materials, including drug delivery, has grown rapidly over the past few years. Over the past few years, research on graphene and graphene oxide in biomedical applications has been widespread and significant in biomedical applications due to its unique properties, such as a two-dimensional flat structure, a large surface area, high mechanical and chemical stability, high conductivity, and good biocompatibility. . These properties provide a promising approach towards the design of advanced drug delivery systems and provide a new range of graphene-based treatment. Over the past few years, new Nano-carriers, such as carbon nanotubes, graphene and graphene oxide, have been extensively investigated for loading various types of drugs, including anticancer drugs, water insoluble drugs, antibiotics, antibodies, peptides, DNAs, RNAs, and genes. They are Graphene, graphene oxide and other graphene-derived groups have been extensively surveyed for the last 5 years for drug delivery. The actual uses of each nanomaterial in medicine and treatment are based on the biocompatibility of that substance. Although many graphene preparations are widely used in various electronic

devices, few are suitable for biological applications. The only non-toxic carbon compounds are graphene materials, which must be understood as the decomposition and release time of the biological systems of these carbon derivatives.

Graphene is a safe carrier molecule in drug-related research. Graphene's high surface area makes it possible to deliver multiple medications to the target location. Polymer correction and conjugate strategy increase the biocompatibility and circulation time inside the body. Over the past few years, many studies have been conducted on the delivery of anticancer drugs, genes and peptides via graphene derivatives. Simple physical absorption with π bond is used to load many hydrophobic drugs such as doxorubicin, docetaxel with an antibody to kill selected cancer cells. Small size, high surface area, low cost, useful noncovalent bonds with aromatic drug molecules make graphene a good material for pharmaceutical applications.

A high level, high π-π accumulation, electrostatic interactions or hydrophobic graphene contributes to the high loading of low-solubility drugs without reducing efficacy.

A common strategy for achieving targeted tumor is the binding of drug carrier with specific bonds such as polyclonal antibodies, folic acid and transferrin to identify the target molecule. A simple method for direct drug delivery to the direct fixation of the drug on the graphene surface has been modified. A good example of this approach is in the studies of Yang et al., Depan et al., Mendes et al., Which shows a strong connection of DOX anticancer molecules on graphene surfaces and more drug release in acidic or tumorous environments rather than healthy tissues. Zhao et al. used a carrier with a cross-link between Nano-germanium oxide and polyethylene glycol to transport DOX. Release of DOX in an environment with pH = 5 is 6 times faster than an environment with pH = 7.

The kinetics of drug release from drug carriers are usually controlled by a diffusion process, indicating no change in its release behavior and drug release after administration. Several new accountability methods have been developed for drug carriers that can respond to internal stimulation (body temperature, pH, specific chemical reaction (or external) use of ultrasonic, magnetic field, and electric field). Recently, several graphene and Graphene oxide-based drug delivery systems, which is a response to environmental manipulation, has been reported. When binding of drugs to drug carriers such as graphene oxide with pH-sensitive connectors, drug release control is carried out by manipulating the pH of the environment. A team of collaborators of a hydrogel graphene oxide- Polyvinyl alcohol (PVA-GO) pH-sensitive for its selective loading and release. The physiological pH of the environment was prepared, and the percentage of drug release was found to depend on the pH and the concentration of saline buffering solution.

Other methods for controlling drug release are the use of ester bond hydrolysis or biodegradability of a disulfide bond designed on carriers. These chemical methods allow precise control of drug release.

In addition to intracellular changes in pH, ion and temperature concentrations are used to release the drug by other external methods such as ultrasonic, magnetism and electric field. A good example of the external factor for drug release is the study by Zhou et al. On the use of a magnetic field to release a drug from a Fe3O4 graphene nanocomposite. The weight ratio of the drug loaded to the graphene oxide carrier can be as high as 200%.

The combination therapy simultaneously targets the pharmacologically active or pre-active disturbances of pharmacology. The idea of multidrug transfer was proposed by Zhang et al. By loading DOX and camptothecin on a carboxylic acid / β-follicle acid carrier [11]. Concurrent transplantation in two drugs, better targeting and higher cell adhesion than graphene oxide loading Only with DOX or CDT.

Chapter 3

Quantum Simulation and Molecular Dynamic

3.1 Introduction

According to the Hartree model in an N-electron atom, each electron in the nucleus potential field plus the potential field (N-1) of another electron (which are considered as overlapping clouds of charge), moves With this attitude, N Schrödinger's integral-integral pair (Hartree equations), one for each electron, must be solved. Asterisk and Gantt showed that the Hartree equations are exactly the conditions for optimizing its approximate solutions in the form of a simple product of the wave functions (atomic orbits) are distinct. A modified form presented by Slater and Fock considers the atomic wave function as a deterministic function of atomic orbital spin that is compatible with Pauli's principle. Using the principle of the transformation and application of the deterministic wave function, we again find a series of coupled integral-integral equations (Hartree-Fock equations), which are completely similar to the Hartree equations and only the exchange integrals are added to them. These exchange integrals are not of the same classical nature. The inherent error in the Hartree-Fook method is related to electron correlation. An important advance in the calculation of his field-adapted method was obtained by Roothaan in 1951. Roothaan suggested that Hartree-Fock orbitals be represented as linear combinations of functions defined as base functions. Almost all calculations on atomic and molecular systems are based on this method. So far, SCF calculations have been carried out on all atoms in the periodic table and in atomic and multi-atomic molecules**.**

3.2 Molecular dynamics

Molecular dynamics simulation is one of the strongest tools for obtaining macroscopic and microscopic properties of materials. Specifically, it is possible to use the molecular dynamics simulation technique for quantities that are difficult to obtain in their experimental values under unconventional conditions. The most important part in simulating the molecular dynamics is the potential for interaction. In recent years, scientists have used many uses of the types of potentials in molecular dynamics simulation to predict the behavior of materials in different sizes and conditions. The more accurate this potential is, the more accurate the paths of the simulated system in the phase space and the more accurate simulation results [12]. Molecular dynamics is one of the branches of computational physics. In this method, the interaction between atoms and molecules in time intervals according to the laws of physics is simulated by a computer; molecular dynamics is a well-known method for simulating complex systems consisting of many components. The basis of the work of the molecular dynamics is the numerical integration of the Newtonian motion equations for the individual particles in the system.

Since molecular systems generally contain a large number of particles, it is not possible to analyze the properties of complex systems analytically. Simulation of molecular dynamics solves this problem by employing the computational method. This method creates an intermediary between experimental and theory experiments and is considered as a virtual experiment. The molecular dynamics examines the relationships between the structure of molecules, the movement of molecules, and molecular functions. Molecular dynamics is a regular method of multiplicity. Its laws and theories come from mathematics, physics and chemistry, and employ algorithms from

computer science and information theory. The molecular dynamics method is one of the most accurate simulation methods in physics used to simulate multiple-particle systems. In this method, the phase paths of systems involving thousands of interacting particles are obtained by solving the Hamilton equations under suitable boundary conditions. By analyzing the path of particles in the phase space and using statistical mechanics, which are in fact the interfaces between microscopic and macroscopic quantities, one can obtain information about the various properties of the system, including energy, structural, dynamic, mechanical properties, etc. In the simulation of molecular dynamics, the successive configuration of the system is achieved by integrating Newton's law of motion. The result is a path that shows how to change the positions and velocities of the system particles with time. Using molecular dynamic paths, time-dependent thermodynamic and time-dependent properties can be calculated.

The transformation equation describes the time of a physical system. There are several types of motion equations that examine movements in a variety of ways, as shown in the table below.

Table 3.1 Different motion equations

Motion equation	Column type
Time dependent Schrödinger equation	Quantum mechanical system
Newtonian equation	Classic mechanical system
Langevin equation	Rotary system

3.3 Molecular dynamics simulation methods

Since today theoretical reviews are usually done using modeling, simulation or both, the recognition of modeling and simulation differences will be very helpful. A model is a simple or ideal descriptor of a system or process that is often expressed by the use of mathematical concepts and phrases, and the purpose of its design is to simplify the calculations and predictions desired, and the model is usually much simpler than the actual system, and the output For some inputs, they are correct but are considered in the simulation of all modes, and, unlike modeling, the simulation of the studied system is more complicated. The simulation on a molecular scale consists of three main steps: a) making the model, b) computing molecular paths, and c) analyzing the paths and computing the thermodynamic properties.

Stage B forms the complete simulation, and the method for calculating the positions and molecular paths in step B is to distinguish between different molecular simulations. In the molecular dynamics of situations, numerical solutions of differential equations of motion are obtained, and therefore, they have a time relation. In other methods of simulation, molecular positions do not have time relations. For example, in the Monte Carlo simulation, the positions are generated in bits, so that each molecular configuration depends on the configuration before it. When the outcome of any random event in a chain depends only on the outcome of the preceding event, this chain is called a Markov chain. In some simulation methods, there is also some kind of intermediate, that is, some aspects of computing positions, such as Monte Carlo, are random and some aspects like deterministic molecular dynamics.

The following is a flowchart illustrating the molecular dynamics simulation method.

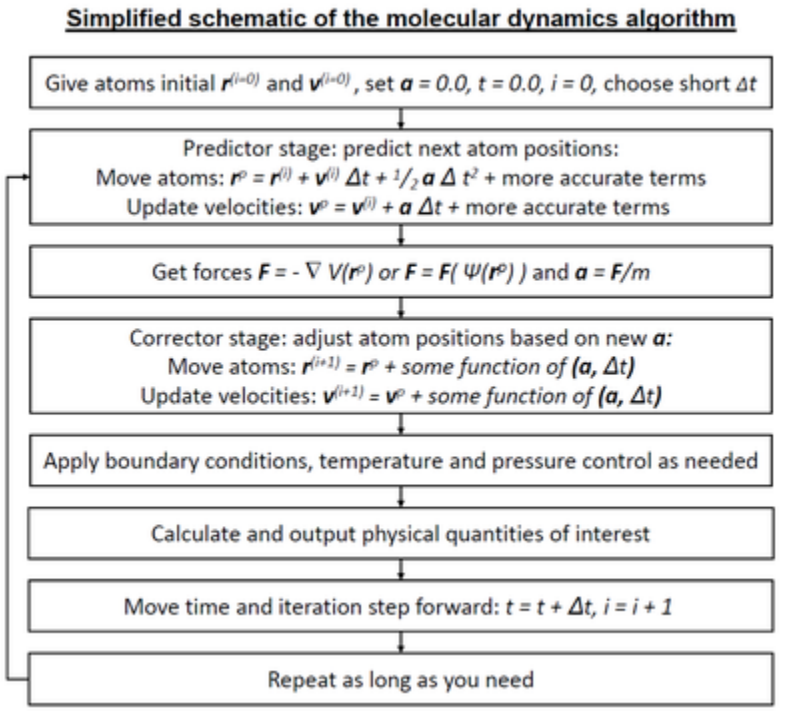

Fig. 3.1 Flowchart Dynamic Molecular Simulation Method [25]

The result of simulating the molecular dynamics of an element, the macro-molecular behavior or system over a given time period is obtained by using Newton's motion equations and potential energy functions. Simulation output is a series of structures created during the simulation

that presents the process of structural changes over time that reflects how these dynamic changes of the system or molecule. Most of the molecular dynamics simulations were carried out under the constant values of the atomic number, volume, and temperature (NVT), but the recent simulations under the constant conditions of the atomic number, pressure, and temperature (NPT) are performed because, under these conditions, the results of the simulation with more experimental conditions The actual behavior of the system is better reflected in the experimental conditions. The following figure shows the steps for a molecular dynamics simulation.

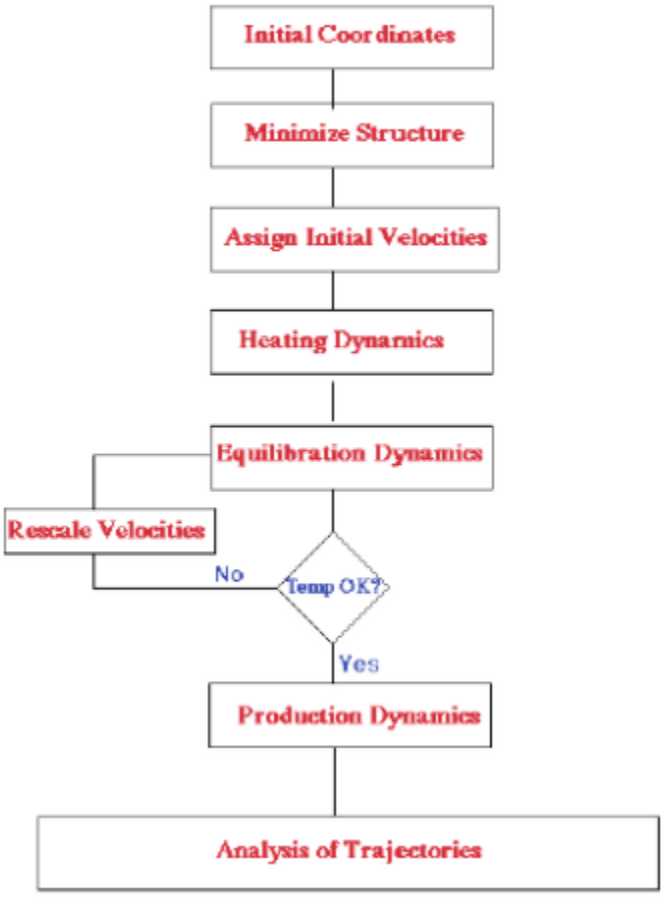

Fig. 3.2 Flowcharts of molecular dynamics simulation steps [25]

3.4 Computational methods initio AB

The Latin word initio Ab means the beginning, which is a sign of calculation based on fundamental principles. This method is the most reliable and valid method for molecular dynamics simulation, since it uses the best mathematical approximation for systems with a large number of atoms.

In the initio Ab quantum chemistry, three very important assumptions are used:

A) The approximate width of the oppenheimer in which the nucleus is assumed to be in comparison with the constant motion of the electron.

B) Base series (base functions), molecular orbital marker

C) Electron correlation which is considered at some theoretical level

The first computational method of initio Ab is the Hart-Factor Self-Adjustment (HF-SCF) method.

3.4.1 Ability of the initio Ab method

- Ability to calculate basic and excited modes
- Ability to compute wave functions and partial descriptions of molecular orbital
- Calculation of the vibrational frequencies of IR and Raman intensities and chemical displacement of NMR
- The ability to calculate the geometers and energies of equilibrium structures, transition structures, interfaces, and neutral and pregnant species
- Calculation of ionization and electron energy
- Perform calculations for all elements
- Ability to calculate atomic loads, bipolar and multipole moments, polarizabilities
- Consider the electrostatic effects on solvent

3.4.2 The steps to run a calculation with the initio Ab method

Read input and compute a structure:

To run the calculation, a molecular structure is required. When optimizing the structure, the calculation of energy and gradient is done for each structure.

Determine the base series:

At this point, a base series is determined that optimizes the given structure.

Total energy calculation:

By adding nuclear repulsion energy to the electron energy.

Determine the electron configuration:

The total load of the molecule and its multiplicity are specified in the given file.

Calculating Integrals:

That include all phrases in the Hamiltonian system and base series functions are computed.

Electron Density Analysis:

Atomic loads are multipolar and bipolar moments.

Repeat implementation in SCF self-compatibility field in order to calculate electron energy.

Core Refractive Energy Computation:

After determining the structure and base series, the nuclear repulsion energy is evaluated, which is equal to ε (ZA.Zb) / RAB = Eh, in which ZA and ZB are atomic numbers, and RAB is the distance between the atoms A and B.

Generate the initial guess:

A series of approximate molecular orbitals is chosen as the first guess to create molecular orbitals. Then, the energy is raised in order to use all the electrons. Then calculate the energy of the Hartree - Fock the advanced heap by calculating the first derivatives of energy, taking into account the atomic coordinates and optimizing the structure by calculating the second derivatives of energy relative to the atomic coordinates and obtaining the vibrating frequencies.

The most important form of the Hartree-Fock method is ignoring the electron correlation. In this method, the interaction of electrons is considered only through the average electron density. In fact, the momentary and simultaneous repulsion of the electrons is the same energy of correlation. There are other methods of initio Ab, in addition to the Hartree-Fock method, in which the correlation of electrons is considered.

3.4.3 Condition of the initio Ab method

Our answer must be defined both by structure and by molecular electron states.

The model should be based on the change method.

The model should not be prejudiced, that is, no chemical bond between atoms.

The model should be proportional to the size of the molecule.

The potential energy of a molecule should change continuously as it moves atomic nuclei.

3.4.4 Strengths of the initio Ab method

The initio Ab method is one of the most quantum methods for calculating the accuracy of the calculations. The so-called complete methods are also called because all interactions are considered in them, but it is very time consuming.

The strengths of this method are:

There is no experimental basis.

A calculation can be made in a logical subject with a theoretical level and base series

Provides information on the intermediate species including the relative spectral data.

Calculates new structures without the need for empirical data.

3.5 sets of bases

An atomic orbital or atomic function that explains the behavior of a wave such as a charge is a mathematical electron or a pair of electrons in an atom. This function can be used to calculate the probability of the presence of electrons in an atom in certain regions around the nucleus. The function of this function can be used to plot a three-dimensional graph of the probability of the presence of electrons in a location, which is likely to be determined by this physical area. In particular, atomic orbits may be described in a special case of a single electron, which are in a set of electrons around a single atom, with the orbital function. After the expansion of quantum mechanics, it was discovered that the circulating electrons around the nucleus cannot be described entirely as particles, but should be described in terms of the wave-particle dichotomy.

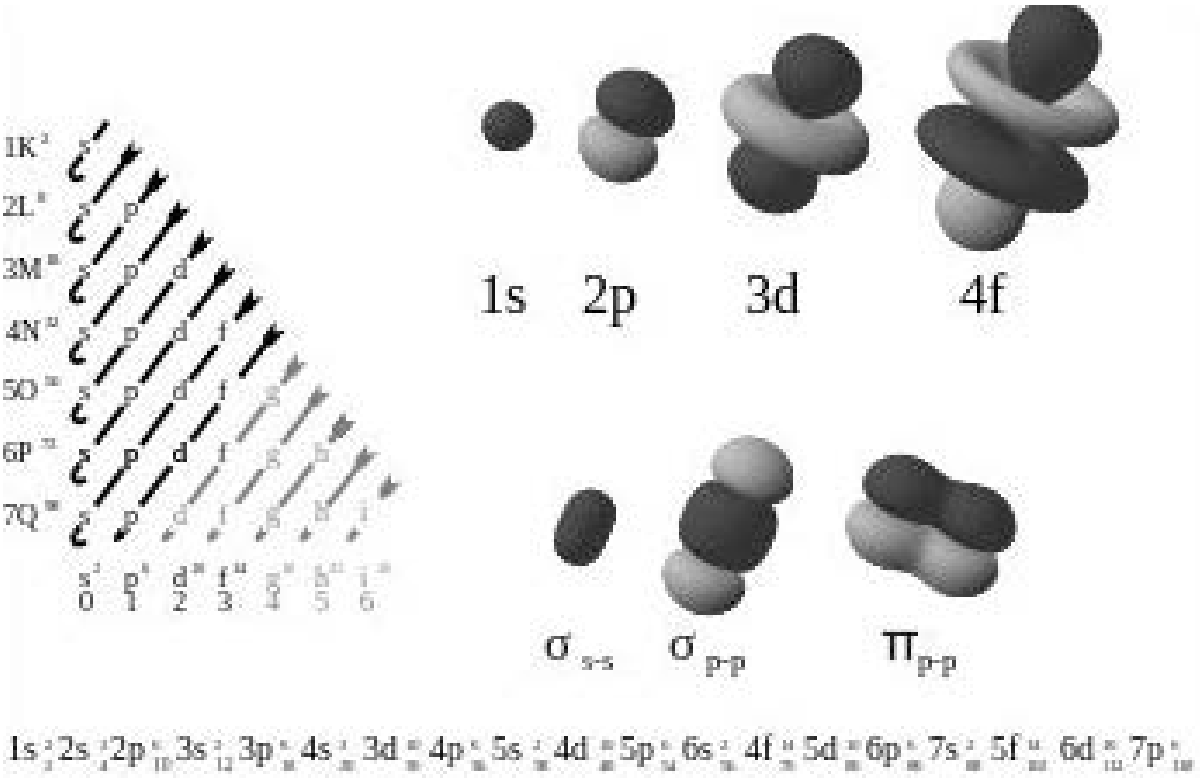

Fig. 3.3. Electron orbitals in the atom [33]

The wave function in quantum mechanics for any particle or physical system is a mixed function that includes the possible states of a particle or system in space. We describe the behavior of electrons by the wave-wave function. Since the electron has a particle behavior, we say that its wave function is positioned, and as the wave behavior is different, its wave function is widespread and diffused. There are generally two types of Gaussian and Slytherin functions that are slicker but their calculations are very difficult to use because of Gaussian. As an example to reader familiarity with the Gaussian base functions used in simulations, Figure 3.4 can be considered.

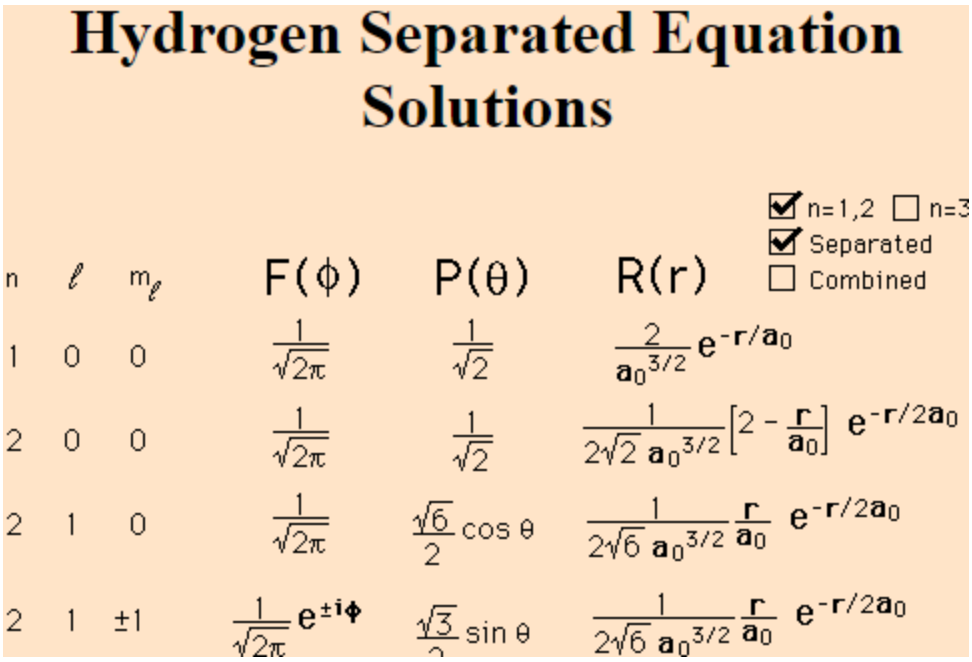

Fig. 3.4 An example of a wave function for hydrogen electrons [33]

An orbital atom in which electrons are solid particles can never be explained by the planet that is elliptical in the sun. A set of basic functions is a mathematical tool for describing molecular orbitals that form a system-wide wave function in the form of a slater determinant. Larger base assemblies obtain better results because they provide less constraints for the presence of electrons in different areas of the space. In quantum mechanics, there is always a limited possibility for the presence of electrons anywhere in space. This limit mode is well described when the base set is large enough. Several types of mathematical functions have been proposed as base sets, but only two of them have found a general application that names Slytherin functions and Gaussian functions. In modern computational chemistry, quantum computing is typically done using a finite set of basic functions. Choosing the base set in chemical quantum computing has a great impact on the quality of the results. Regarding the type of molecules that can have a simple and light structure to heavy molecules that have a complex structure, as well as polar and nonpolar molecules, choosing the type of base set can be important. Today, there are different types of sets of foundations, consisting of Gaussian orbitals of the type (GTOs). The smallest of these sets are called Minimal base units, and they typically consist of the minimum number of required base

functions representing all electrons per atom. The largest of these collections can literally be tens or hundreds of basic functions per atom.

The most commonly used Minimal Base sets is STO-nG, where n is an integer. This value n represents the number of primitive Gaussian functions consisting of a single base function. In this set of foundations, the same number of initial Gaussian include core and orbital capacity. Minimal basis sets of this type are STO-3G, STO-4G, STO-6G and STO-3G * the STO-3G polarizing version.

The next set of bases is double zeta basis units. In this series, the basic set of each internal shell of a shell is composed of a slit function and each shell orbit of the shell of two or more basic functions, which these slice functions are contractile Gaussian functions. For example, in the 6-31G split capacity base series for a particular atom, the inner shell (2S) is described by a function that contains six Gaussian functions, and can be used to describe the shell aperture (2S2P) from two functions The first consists of the initial Gaussian function and the next contains a basic Gaussian function.

The next bunch of foundations is Polarized basis sets. In the bundle of sets of foundations, we split the set due to the more fundamental analysis of the valence electrons. When the molecule moves towards polarization, the two sets of previous bases are not appropriate, so we have to set Define new foundations.

Slit-type functions provide a better quality of molecular orbitals, and to achieve a certain result, more Gaussian functions are needed compared to the Slytherin function. Also, for large r, molecular orbitals behave like Slytherin functions. On the other hand, the costly and time consuming part of self-consistent field calculations relates to the determination of four-center electron integrals. The calculation of these four-center integrals using the functions is much simpler and faster than the slide functions, since the product of the two functionality with different centers leads to a Gaussian function with a new central and the simple integral solution It's all about Another way is to use the useful features of the Slytherin functions while simultaneously implementing calculations in terms of time and cost. Instead of directly using the Slytherin functions, they approximate them with linear combinations of Gaussian functions and directly use

these linear combinations. These new functions are called Contracted Gaussian functions, and the functions derived from the linear combination of condensed functions are called primitive Gaussian functions.

The difference between the base sets is in the number and type of functions that are included and are also categorized accordingly. The smallest and simplest base compartments that are least costly in computing terms are called the Minimal Base Set. The reason for their naming is that their number of functions is the least possible number for describing molecular orbitals. These compounds are used to study large molecules with high computational volume. Of course, the results of calculations with the base set of the minimum are not very high value and are more applicable in qualitative analysis. The most famous of them are STO-NG, in which ... 1, 2,3N =. This collection consists of orbitals of the type SL-type, approximated by linear combinations of initial Gaussian functions.

The types of set assemblies considered in molecular simulations for electron orbits can be summarized in the following.

21G-3, 3-21G *, 3-21G +, 3-21G + *, 4-21G, 4-31G, 6-21G, 6-31G and 6-31G *, 6-31G + *, 6-31G (3df, 3pd), 6-311G, 6-311G *, 6-311 + G *, cc-pVDZ, cc-pVTZ, cc-pVQZ, cc-pV5Z

Chapter 4

Schrödinger equation and DFT molecular calculation method

4.1 Introduction

In recent years, extensive research has been carried out on Nano-structure systems, especially with the reduction of the components of electronic components, the study of Nano-structures is of great importance in the field of science and technology. Has found the industry.

The physical properties of these nanostructures, in particular their electronic and optical properties, depend on their behavior and electron states. Therefore, calculating the electron states of materials and determining the strip structure of energy in them is one of the most important theoretical and empirical research topics in dense material physics. Given that, in general, the electron gas in a solid is an interfering system, the basic solution for calculating the electron states of materials is to solve the particle problem. Therefore, since the inception of the physics of dense matter physics, researchers have sought to transform the problem of solid state electron gas into an equilibrium problem as an approximation. All texts relating to the dense material and the various methods for calculating the structure of the electron energy bands of solids show the application of various types of approximations that are used to solve the Schrödinger equation. Fortunately, despite the close-to-fine-particle methods, these methods have shown a great deal of practical success, and so, in cases where the complexity of the effects of electron interaction In the final behavior of the system, should, as far as possible and in different ways, interfere with the maximum effects of the particles in the calculation. In any case, it should be noted that each approximate method has a range of credibility.

4.2 Wave function

One of the goals of condensed matter physics is the theoretical study of the electron properties of materials. Understanding the behavior of systems, including atoms, molecules, and nanostructures for complex mass systems, relates to the solution of the Schrödinger equation, which solves this equation is the main and fundamental task of a parabolic problem. . Since the coil or electrostatic interactions between electrons are very strong, the analytical solution of this equation is possible only for a small number of very simple systems, and in particular, a numerical solution can only be used for a small number of Atoms and molecules. The basic and complex computational problem lies in the nature of the Hamiltonian H-type, and the control of each system formed by electrons (which is represented by the coordinates (spatial and spin) {ri}, the pixel pi, the mass mi) And the atomic nucleus (which is characterized by the coordinates {RI} and PI excitation with MI mass and atomic charge ZI):

$$H[\{r,p\}|\{R,P\}]=\sum_{i=1}^{N}\frac{p_i^2}{2m_i}+\sum_{i=1}^{M}\frac{P_I^2}{2M_I}+\sum_{I<J}\frac{e^2}{|r_i-r_j|}+$$
$$-\sum_{i<J}\frac{Z_I e^2}{|r_i-R_I|}+\sum_{I<J}\frac{Z_I Z_J e^2}{|R_I-R_j|} \qquad (4\text{-}1)$$

This Hamiltonian is applied to the wave functions,

$$\psi_{MB}=(\{r_1,...,r_n\};\{R_1,...,R_N\}) \qquad (4\text{-}2)$$

Particular states of the real system, expressed in terms of the contribution of electrons and atoms, are described by the following equation:

$$\hat{H}(\{r_i\},\{R_I\})\ \psi_{MB}(\{r_i\},\{R_I\})=E_{tot}\,\psi(\{r_i\},\{R_I\}) \qquad (4\text{-}3)$$

Given the large number of interactions in this issue, it is difficult to solve even today for the most powerful supercomputers. So, researchers have been struggling to find some approximations that simply do this. The first of these, as expressed by Boren and Oppenheimer in 1927, [26] introduces a hierarchy of approximation with respect to different energy scales. The Boren approximation - an oppenheimer or an approximate approximation-is in fact a tendency to separate nuclear and electron degrees. Since electrons move much faster than the nucleus, it can be assumed that for the given core configuration, the electrons are in the lowest state of energy: electrons and nuclei they move in energies and at different timescales, so that the electrons follow the movement of the nuclei. Therefore, with respect to the Boren-oppen-heimer approximation, we can separate the electron variable from the nucleus and write the particle-wave function in partnership with two sentences.

$$\psi_{MB}\approx\psi_{BO}=\varphi(\{r\},\{R\})\ \phi(\{R\}) \qquad (4\text{-}4)$$

Then the special equation (1-3):

$$(T_e+T_I+V_{ee}+V_{Ie}+V_{II})\psi_{MB}(\{r_i\},\{R_I\})=E_{tot}\,\psi_{MB}(\{r_i\},\{R_I\}) \qquad (4\text{-}5)$$

(In combined sentences, the kinetic energy is replaced by V by the T and the potential energy) are separated by two equal equations:

$$(T_e + V_{ee} + V_{Ie})\ \varphi(\{r\},\{R\}) = E(\{R\})\ \varphi(\{r\},\{R\})$$
$$[T_I + V_{II} + C(\{R\})]\ \phi(\{r\},\{R\}) = E_{tot}(\{R\})\ \phi(\{r\},\{R\}) \quad (4\text{-}6)$$

In fact, the electron properties are parametric dependent on the nuclear frameworks {RI}. Since the nuclei (or ions) can be assumed to be frozen, it can be seen that the ionic potential is introduced as an equation in the equation (1-6). Different methods over the last century, it has been proposed to consider the interactions of electrons. Many of the approximate theories are related to finding a good single-particle approximation for the Colombian term. The first Hartre attempt was in 1928 [2]. The main features of the Hartre approximation are:

The non-localized Coulomb potential with localized Coulomb potential (Hartree potential), which is averaged by total electrons, is replaced.

$$V_H = \sum_{N}^{j=1} \int d^3r'\, \varphi_j^*(r')\, \varphi_j(r') \frac{1}{|r - r'|} = \int d^3r'\, \rho(r') \frac{1}{|r - r'|} \quad (4\text{-}7)$$

The particle-wave function of φ ({r}, {R}) is isolated from the N-wave function of the particle, which satisfies the single-particle Schrödinger equation.

$$\varphi(\{r\},\{R\}) \approx \varphi_H = \varphi_i(r_1)\, \varphi_i(r_2)\, \varphi_i(r_3) .... \varphi_i(r_i) \quad (4\text{-}8)$$

Although the Hartre approximation provides acceptable results, but also ignores the exchange effects and correlation between electrons, it also does not consider the Pauli Exclusion Principle (the spin component effect).

Given the parity of the wave function relative to the exchange of both electrons, it is possible to specify the wave function as a slider retransmission in terms of single-wave wave functions by inserting the fuzzy Dirac statistics.

$$\varphi(\{r\},\{R\}) \approx \varphi_{HF} = \frac{1}{\sqrt{N!}} \det[\varphi_i(r_j)] \quad (4\text{-}9)$$

By modifying the Hartre potential and taking into account the spin electrons, we can obtain the so-called Hartre-Fock method, which appears in the Hamiltonian of a spontaneous non-localized span-free sentence [3].

$$\int d^3r' V_x(r, r')\, \varphi_i(r') = -\sum_{j=1}^{N\,occup} \int d^3r' \varphi_j^*(r') \frac{1}{|r - r'|} \varphi_j(r) \varphi_i(r') \quad (4\text{-}10)$$

In this new approach of Vx exchange engagement, it is possible to predict total energy for atoms and molecules, but it fails to describe solid state systems, in particular, the energy gap considers insulators and semiconductors too much. Factor Hartree methods do not consider the correlation between electrons with spin and hence camouflage. One possibility to go for it is the Hartre-Fock approximation and the calculation of the correlation between electrons, using the Configuration Interaction Method (CI) [27]. In this method, sets of slater determinant are considered as bases for the particle-wave function, but the number of configurations increases with the speed relative to the number of electrons, which itself It is highly debilitating the method (a linear combination of Determinant is intended to describe the lowest state, but increasing the number of configurations relative to the number of electrons means that Only low electron systems can be calculated with high precision).

All of these methods relate to the so-called mean-field approximation sets: since all electrons are an averaged potential due to the electrostatic interaction with the density of the electron-generated load others experience the system.

A different approach was proposed by Thomas and Fermi in the year (1927-1927), in which the particle problem lies in the form of a semi classical framework, and the degrees of system freedom are only in the electron density (n r) is concentrated. The development of this method was developed by Dirac in 1930, in which the exchange interaction between electrons was considered as a function of density, and also by a slider that considered the effects of correlation. These were the basis for the development of the density theory.

4.3 DFT

Although there is a possibility of correction in Thomas's model (such as the correlation and exchange effects or gradient of density with the expansion of Dirac) and can lead to really good results, it cannot be considered as the first simple method of density theory. The first scientific basis for the density function theory was introduced in 1964 by Hohenberg and Cohen in the original paper [30] which led to the award of the Nobel Prize in chemistry in 1998 to Cohen. They showed that all the electron properties of the system, in the configuration of its non-Eigen functional base state, are entirely determined by the electron density of the n (r) system: in addition, this energy and potential can only be considered as a function of the density electronically expressed. A year later, in 1965, Cohen and Shem, a self-consistent scheme for mapping the particle interaction problem into a set of non-interacting single-particle equations, and the re-formulation of the mean square method a converting principle, which is based solely on the basis of electron density [29]. Therefore, the first turning point of the density function theory can be considered on the basis of the Hohenberg-Cohen theory and the Cohen-sham equations.

4.3.1 Bourne approximation - Oppenheimer

The nuclei are much heavier and therefore move under the influence of a constant force much slower than the electrons. Hence, we can consider them frozen in fixed locations, and assume that the electrons are in equilibrium with them. When we examine the ions, we assume that the electrons are in their base position, and when we examine the electrons, we assume that the ions are frozen in their equilibrium positions. This approximation is called the Borne_ oppenheimer. In other words, in the particle's eigenvalue, only the electrons are considered to be the main actors and the presence of the nuclei is felt by their colonial potentials. So, to solve such a problem, we first think of nuclei and nuclei in We prove it there. By doing this, the first sentence is H _tot zero, and the last sentence is relative to the electron variables of a constant. By solving the Schrödinger equation, which includes the second, third, and fourth sentences, obtaining the ground state energy of such an equation and summing it with the energy term of the potential due to the interaction of the nuclei together, the total energy of the device's base state is obtained. By displacing the nucleus in a partial way and calculating the total energy from the above method and finding the minimum amount of energy from the preceding steps, we obtain the real location of the nuclei. Therefore, the Boron approximation - Oppenheimer makes us only have a Schrödinger equation it solves that its variables are only electrons, not cores. So the problem is simplified with this task than before.

4.3.2 The Hohnberg-Cohen theory

The Hohnberg-Cohen theory (H-K) states that the properties associated with the system's electron structure in the base state are expressed entirely by the electron density of the base state n (r). This theory states that the base state density n (r) can, individually, determine the external potential v (r) of the boundary system of interacting electrons. A unique term is associated with an additional constant (defined in the Hohnberg-Cohen paper). In view of the system of N-electron interactions in the presence of the external potential of Vext (r), Hamiltonian is as follows:

$$\hat{H} = \hat{T} + \hat{V}_{ext} + \hat{W} \tag{4-11}$$

Including kinetic energy as:

$$\hat{T} = -\frac{1}{2}\sum_{i}^{N} \nabla_i^2 \tag{4-12}$$

And the sentence of electron-electron interference coulomb potential as:

$$\hat{W} = \frac{1}{2}\sum_{i \neq j} v_{ij}\left(\left|\mathrm{r_i} - \mathrm{r_j}\right|\right) \tag{4-13}$$

And for the expression of the interaction with the external potential Vext (r) we will have:

$$\hat{V}_{ext} = \frac{1}{2}\sum_{i}^{N} v_{ext}(\mathrm{r_i}) \tag{4-14}$$

The base-state particle waveform function can be expressed as φ (r1 ... φN) and for the base electron density (assuming that it is non-eigenface), we will have:

$$n(\mathrm{r_1}) = N\int \varphi^{*}(\mathrm{r_1} \ldots . \varphi_N)\ \varphi(\mathrm{r_1} \ldots . \varphi_N)\ d\,\mathrm{r_2} \ldots d\,\mathrm{r_N} \tag{4-15}$$

.

4.3.3 Cohen-sham equations

An important special strategy has been introduced to solve the DFT practical problem by Cohen and Shem [28]. They are considered as a contributing system of non-interacting electrons that are exposed to potentials and described by Hamiltonian

And also the initial Hartree formulation of the Schrödinger equation for non-interacting electrons in the v_{eff} external potential and the minimum H-K principle. According to Hohenberg and Cohen's theory, for a non-interacting N-particle system, energy is a function of density:

$$E_s[n] = T_s[n] + \int v_s(\mathrm{r})\tilde{n}(\mathrm{r})\,d\,\mathrm{r} \tag{4-16}$$

The main expression used in the creation of the Cohen-Sham scheme is as follows: For each interacting system, there is a single-particle potential $v_{ks}(\mathrm{r})$, such that the precise base state density is equal to the base state density of the auxiliary system, means that
We restrict our argument to non-egalitarian systems, reference can be made to more general methods.

The minimization of the energy function for the Cohen system of an independent N-particle, with the limitation on the number of electrons, and taking into account that the density must be constructed for an independent particle system, we obtain the following equation set:

$$\left[-\frac{\mathrm{h}^2}{2m}\nabla^2+v_s(\mathrm{r})\right]\varphi_i(\mathrm{r})=\varepsilon_i\varphi_i(\mathrm{r}) \tag{4-17}$$

The unique density of the (lowest) N orbital particle is unique:

$$n(\mathrm{r})=\widetilde{n}(\mathrm{r})=\sum_{i=1}^{N}\left|\varphi_i(r)\right|^2 \tag{4-18}$$

In which the limit on density is equivalent to the interchange of wave functions:

$$\int d\,\mathrm{r}\,\varphi_j^i(\mathrm{r})\varphi_i(\mathrm{r})=\delta_{ij} \tag{4-19}$$

When the existence of the potential vs (r) produces an interacting density of n (r), it is assumed that vs (r) follows the Hohenberg-Cohen theory.

Therefore, single particle orbitals are a function of one of the densities n (r), φi (r) = φi ([n (r)], as well as non-interacting kinetic energy Ts [n (r)] is a single function of n (r).
Starting from the interacting system located at the external potential v (r), we can again re-calculate the total energy of Equation by separating the FHK [n] sentences as follows:

$$F_{HK}[n]=\frac{1}{2}\iint d\,\mathrm{r}d\,\mathrm{r}'\frac{n(\mathrm{r})n(\mathrm{r}')}{\left|\mathrm{r}-\mathrm{r}'\right|}+T_s[n]+E_{xc}[n] \tag{4-20}$$

We obtain the following equation:

$$E_v[n]=T_s[n]+\int d\,\mathrm{r}\,v(\mathrm{r})n(\mathrm{r})+\frac{1}{2}\iint d\,\mathrm{r}d\,\mathrm{r}'\frac{n(\mathrm{r})n(\mathrm{r}')}{\left|\mathrm{r}-\mathrm{r}'\right|}+E_{xc}[n] \tag{4-21}$$

This relationship is obtained by using the following three conditions for $F_{HK}[n]$:

The term "Hartree Energy" describes the interactions between electron

The kinetic energy Ts is related to the non-interference system.

Exc[n] is called "exchange energy" -consolidation, and yet it is not known exactly and is defined as follows:

$$E_{xc}[n] = F_{HK}[n] - \frac{1}{2}\iint d\,\mathrm{r} d\,\mathrm{r}' \frac{n(\mathrm{r})n(\mathrm{r}')}{|\mathrm{r}-\mathrm{r}'|} - T_s[n] \qquad (4\text{-}22)$$

But according to equation, it can be seen that E_{xc} is a potential and a kinetic part:

$$E_{xc}[n] = \left(W[n] - \frac{1}{2}\iint d\,\mathrm{r} d\,\mathrm{r}' \frac{n(\mathrm{r})n(\mathrm{r}')}{|\mathrm{r}-\mathrm{r}'|} \right) + \left(T[n] + T_s[n] \right) \qquad (4\text{-}13)$$

In Cohen's scheme, the problem of interactions is simplified, but it is still not solvable: in fact, it is necessary to find a good approximation for the exchange energy-Excision correlation. When a good approximation for Exc is obtained, the Cohen equations will be resolved in a self-consistent manner and, as a result, the density of the base state and the total energy of the interacting system, as depicted in Figure 4.1, Will be obtained.

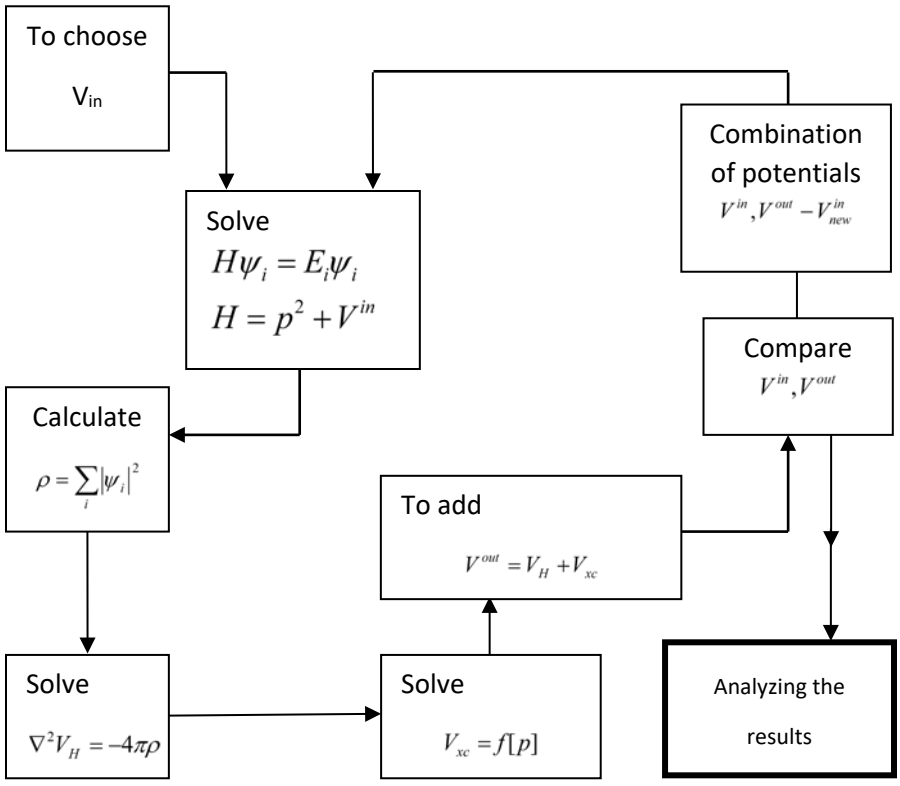

Fig. 4.1 The original self-consistent algorithm

4.3.4 The amount of E_{xc}

Since there is no exact analytical expression for the Exc function, total energy calculations require some approximations for it. The three approximations used in most of the molecular simulation software, such as Sistema and the quantum espresso, are: Local Area Approximation (LDA), Local Spin Density Approximation, and Generalized Slope Approximation (GGA).

According to the local field approximation (LDA), which is one of the simplest and most used approximations, the function xc is defined in terms of the local function of the density of an homogeneous electron gas. One of the improvements that can be made to the LDA is to consider the spin polarization, termed LSDA, especially for systems exposed to external magnetic field , Or systems that have an important relativistic effect on them. One of the ways in which LDA approximation can be approached is the expansion of the exchange-correlation function in terms of sentences of density gradient (GGA). Among the components of this type of slopes, there is the possibility of better results due to changes in density.

Chapter 5

Problem Statement and Research Method

5.1 Introduction

Among all engineered nanoparticles, carbon-based nanoparticles have attracted much attention to potential biomedical applications such as biosensors, drug design, drug delivery, tumor therapy, and tissue engineering, which is the main reason for this attention, features the electrical, apparent and mechanical properties of these nanomaterials. Primary carbon nanotubes are inert in nature, so they need functionalization to function. In this process, different active agent groups such as carboxyl, carbonyl, hydroxide and acid are added to carbon nanotubes, which makes the nanostructures reactive and prepares them for various applications. The biocompatibility of these carbon nanotubes is functional and their compounds must be tested before any use in biological systems. Investigating the toxicity of carbon nanotubes is one of the oldest questions in various fields of nanotechnology. Antitrust reports about the toxicity of carbon nanotubes in various papers and scientific findings, and the existence of a logical explanation for the toxicity reports of these compounds remains unclear. The results of various scientific experiments on the cells are so contradictory that some of them show very high toxicity and other results do not prove any sign of toxicity. Different mechanisms for causing toxicity of carbon nanoparticles are suggested to interfere with membrane electron transfer, cell wall degradation or perforation, oxidation of internal compositions, and the production of secondary products such as heavy metal insoluble ions and reactive oxygen species (ROSs)). The toxicity of a carbon nanotube sample depends on the structural formula, as well as its geometry and surface functionalization. Several studies have suggested that well-functionalized carbon nanotubes are harmless to animal cells, while raw and primary carbon nanotubes or non-functional nanotubes show even modest toxicity for animal and human cells even in dosages. [12]

5.2 Nimesulide molecule

Nimesulide is a non-steroidal anti-inflammatory drug that belongs to the class of sulfonamides with anti-inflammatory, febrile and analgesic effects. Despite a wide range of uses, Nimesulide may cause digestive disturbances [13]. In toxicity studies, it is basically a liver, kidney and digestive tract. In Switzerland, according to the number of reported cases, the most anti-inflammatory drug was hepatotoxicity. According to studies, the use of Nimesulide has stopped in some countries, such as Ireland and many European countries [15]. In addition, Nimesulide can have other effects when dosed higher than the therapeutic concentrations it can occur in the tissues in which the drug is absorbed, for example, antioxidant activity. Direct delivery of the Nimseulide molecules to specific tissues can increase the positive effects of the drug on the human body and also prevent adverse side effects. The chemical formula of the Nimesulide is C13H12N2O5S, with a molecular weight of 308.311 g / mol. In Figure 5.1, the spatial structure of the molecule of the Nimesulide drug is shown.

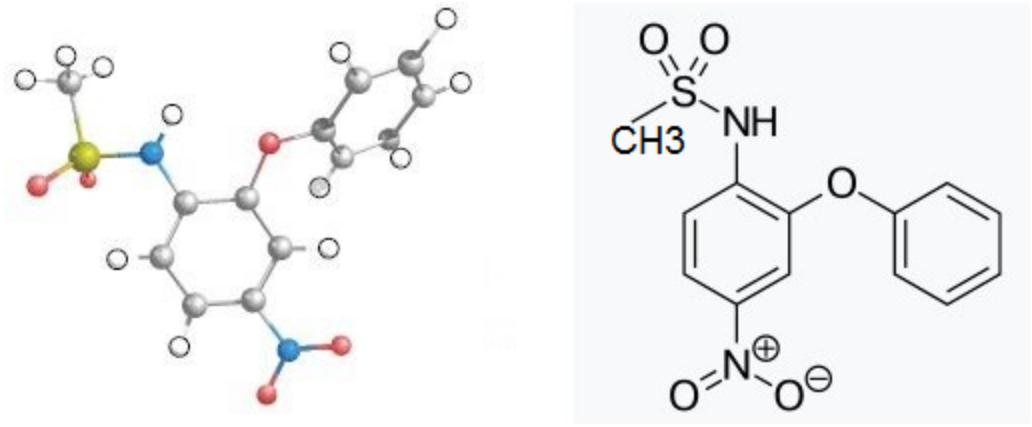

Fig. 5.1 the spatial structure of the molecule of the Nimesulide drug [34]

The possibility proposed here is the proposed interaction of Nimesulide molecules with carbon-carbon carbohydrate carbon nanotubes (CCCNs). These nanoscale materials can provide an alternative route for delivering medication to a specific body part, and the carboxyl group may represent a way to control the insolubility and incompatibility of CN [10].

Nimesulide is a nonsteroidal anti-inflammatory drug belonging to the class of sulfonamides with anti-inflammatory, antipyretic, and analgesic effect. Despite a wide range of applications, the Nimesulide may cause some gastrointestinal disorders. In toxicity studies, it presents essentially liver, renal, and gastrointestinal damage. In Switzerland, based on the number of cases reported, it was considered the most hepatotoxic anti-inflammatory drug. Due to studies like this, the use of Nimesulide was discontinued in some countries, such as Ireland and many other European countries.

Moreover, Nimesulide can cause other effects when it is in higher dose than therapeutic concentrations, which can occur in tissues where the drug is absorbed, for example, antioxidant activity. The direct delivery of Nimesulide molecules to specific tissues could maximize and enhance the positive effects of the drug on the human body as well as avoid the undesirable side effects. The possibility here proposed is the interaction of Nimesulide molecules with carboxylate capped carbon nanotubes (CCCN).These nanomaterials can provide an alternative route of drug delivery to a specific part of the body and the carboxyl group may represent a way to control the insolubility and incompatibility of CN.

Another point to be considered for the successful use of nanotubes in biological medical devices is the fact that in the initial form they are water-proof and biological fluids are juicy [19]. It has been reported that the introduction of functional groups at the pipe surface can overcome these problems, and the carboxyl group is most used for this purpose [20].

In fact, the root cause of the use of carboxylic acid is the same as hydrophilic, which means it has a great desire to react and to bind to water molecules, and as we all know, all bio organisms in the body have an environment full of water molecules and for drug delivery And performing drug

delivery to the defective and diseased target tissue, the carbon-nanotube water-friendliness is important.

In addition to operating the CNs, some interactions are facilitated by the use of electric fields, where the polarization of the system causes a bipolar motion magnitude and a change in the non-polar property of the tube [21].
In fact, this is an innovative way of using the electric field applied to the carbon nanotube structure. This electric field causes the polarization of non-polar water molecules and leads to better reactions for our drug delivery goals.

5.3 Proposed structure for carboxylation of carbon nanotubes

The unit cell had 120 carbon atoms, along with radical carboxyl, and a tube (0.10) with an appropriate diameter to close the end of the tube with parts of the fullerene C60. All geometric optimizations have been made without any convergence limit.
A single cell of a carbon nanotube that is attached to a C60-like quaternary segment is as follows, consisting of 120 carbon atoms with covalent bonds.

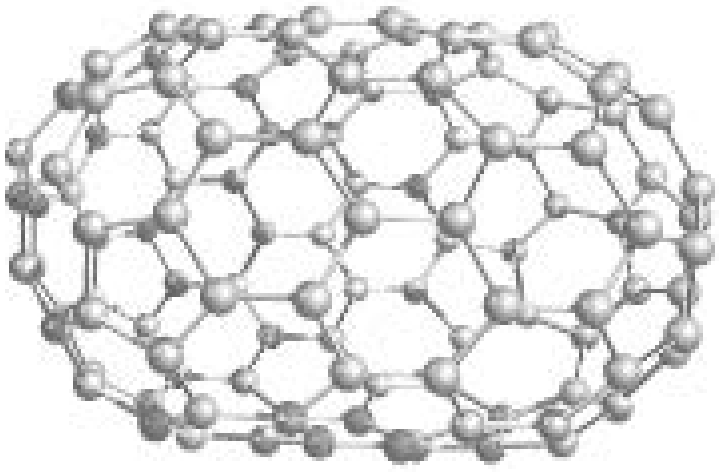

Fig. 5.2 The structure of the carbon nanotube plus the Fullerene that closed the nanotube [8]

In fact, one can imagine that a Fullerene C60 structure would be split from the middle to two parts and closed with them the first and the end of the carbon nanotube. Figure 5.3 shows the

structure of carbon fluoride. Fullerene has many medicinal properties and is used in the treatment of cancer and other diseases in Nano-drugs.

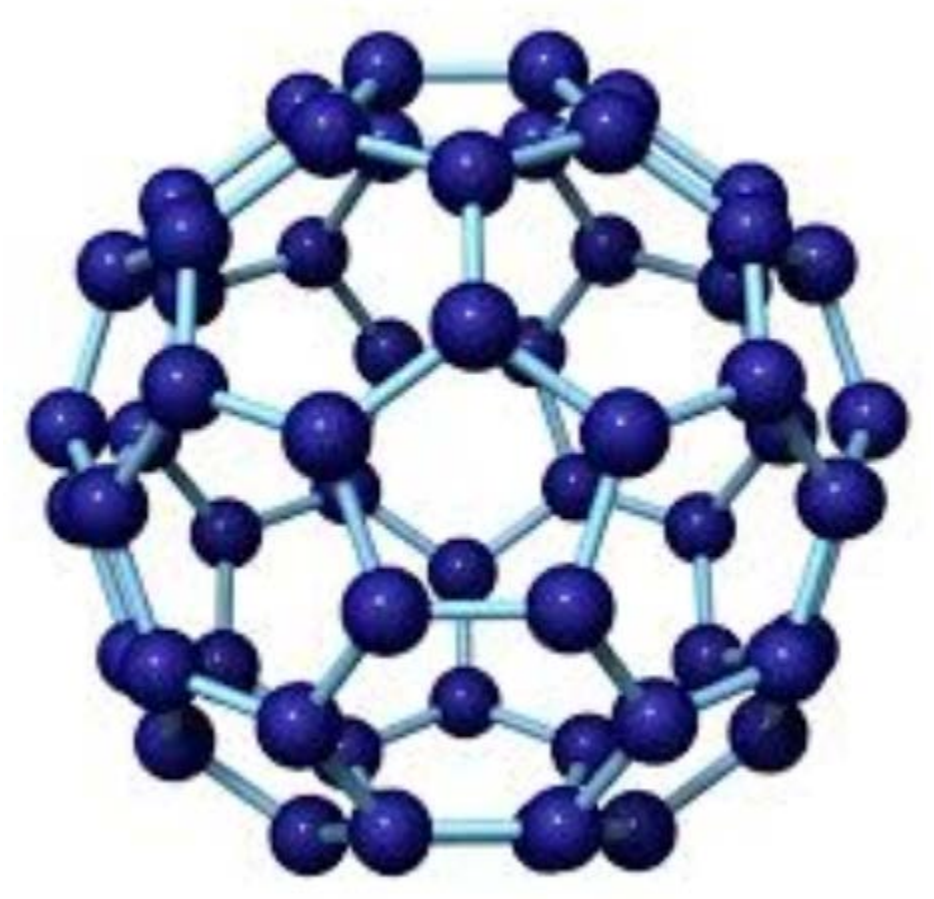

Fig. 5.3 Fullerene C60 structure [8]

The term nanotube (10.0) is a nanotube with carbon atoms, which is located on a circle on a cylindrical environment of 10 carbon atoms in the form of a Zigzag form (in fact, it shows the size of the cross-section of the nanotube). In the figure below, two other forms of carbon nanotubes called Chiral and Armchair have been shown to the reader.

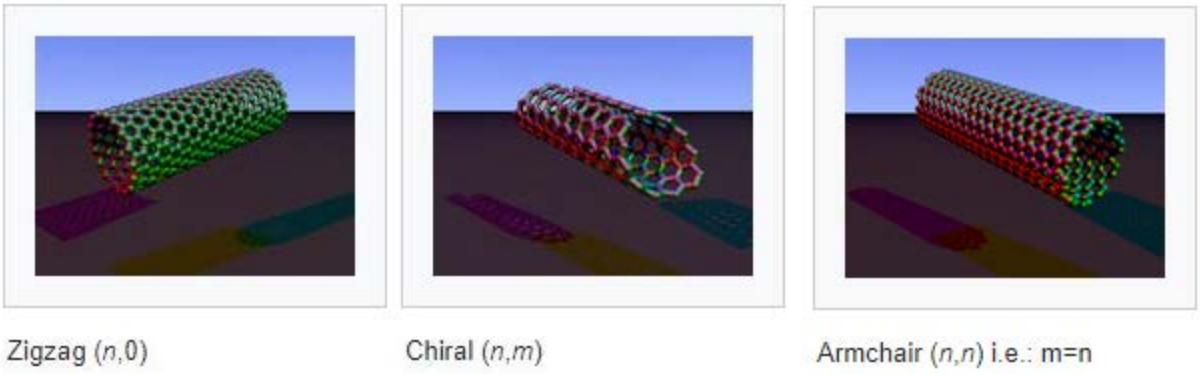

Fig. 5.4 three common forms of carbon atoms in carbon nanotubes

5.3.1 Carboxylated capped carbon nanotubes (CCCN)

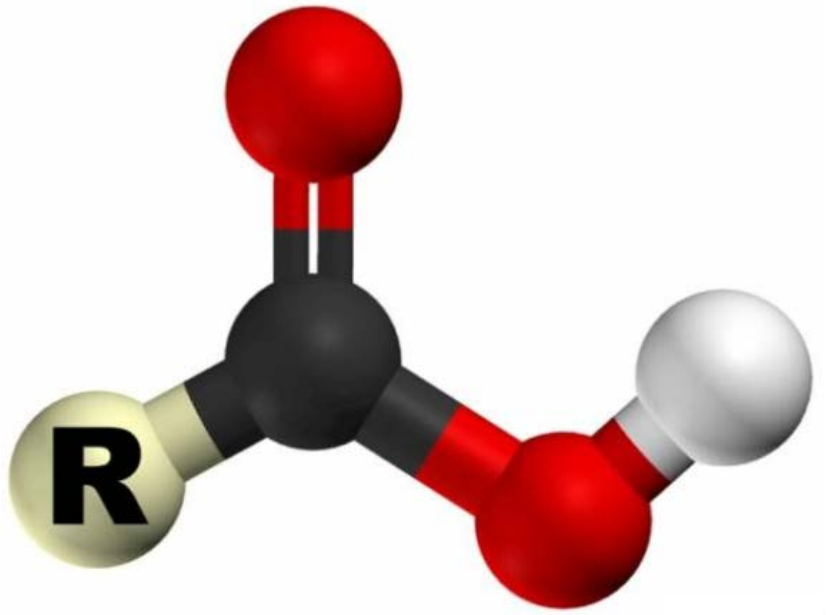

Fig. 5.5 carboxylic agent having a COOH formula that acts on the R molecule

If, in a short sentence, we want to explain carboxyl, a functional group with the formula COOH is a carbon atom and two oxygen atoms and a hydrogen atom that is attached to a carbon

nanotube (closed with a fluorine), which causes the new large molecule (Carboxylate Carbon Nanotubes) prepared and capable of participating in chemical reactions. In fact, the COOH binds to the nanotube, and on the other hand interacts with the other nanotubes. In Figure 5.5, the carbon-carbonated carbon nanotube is displayed. Closed carboxylate carbon nanotubes can provide an alternative route for delivery of the drug to a specific body part, and the carboxyl is used to control the insolubility and incompatibility of carbon nanotubes [16]

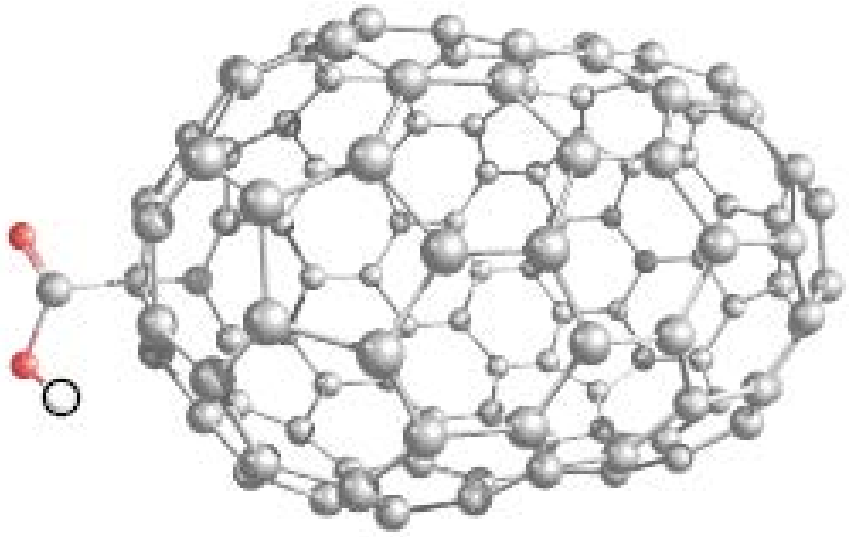

Fig. 5.6 the Carboxylate Capped Nanotube Spatial Structure [34]

Carboxylic acids are a group of organic compounds that are found in one or more carboxyl "cooh" functional groups. Carboxylic acids (up to four carbon atoms) dissolve well in water, with the lengthening of the carbon chain length decreasing their solubility in water, many of which are practically insoluble in water. Carboxylic acids are weak acids and when dissolved in water, a number of their molecules release their acidic proton to water molecules and quickly reach the equilibrium.

5.3.2 Nimesulide bond with CCCN

To attach the Nimesulide drug to the carbonaceous carbon nanotube donor, the molecular-chemical bonding of the three different binding states can be considered. The first configuration is a link between NO2 oxygen in Nimesulide and oxygen of carboxylic, shown in the following figure as the spatial structure of this bond.

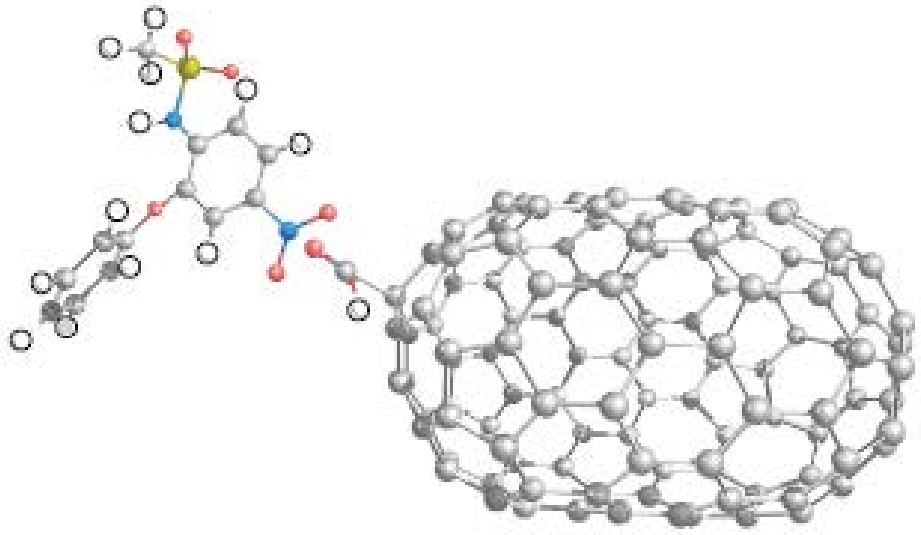

Fig. 5.7 the spatial structure of a Capped carbon nanotube bonded with Nimesulide by O (of the -NO2 group), O atoms [34]

This configuration was first investigated by Zanella et al. [17]. The interaction of Nimesulides with primary CN and impregnated with silicon was investigated by Zanella et al. By calculating the basics, in which a physical absorption regimen was observed. In this paper, repulsive forces have been found in the interactions studied and we are discussing overcoming the weakness using an electric field that changes the energy of the bond. Previous studies have shown that the applied electric field can cause polarization of the system, increase CN interactions with polar molecules, or even allow covalent bonds between these systems. [18, 19].

The second mode is to create a bond between the Nimesulide and the carboxylate carbon nanotubes, which is the chemical bond between the carboxylic oxygen sticking to the carbon

nanotube and the oxygen atom sticking to the sulfur in the Nimesulide molecule. In Figure 5.8, the spatial structure for the second topology is shown. In fact, a bond between S and O is broken down and sulfur is bonded to carboxylic oxygen.

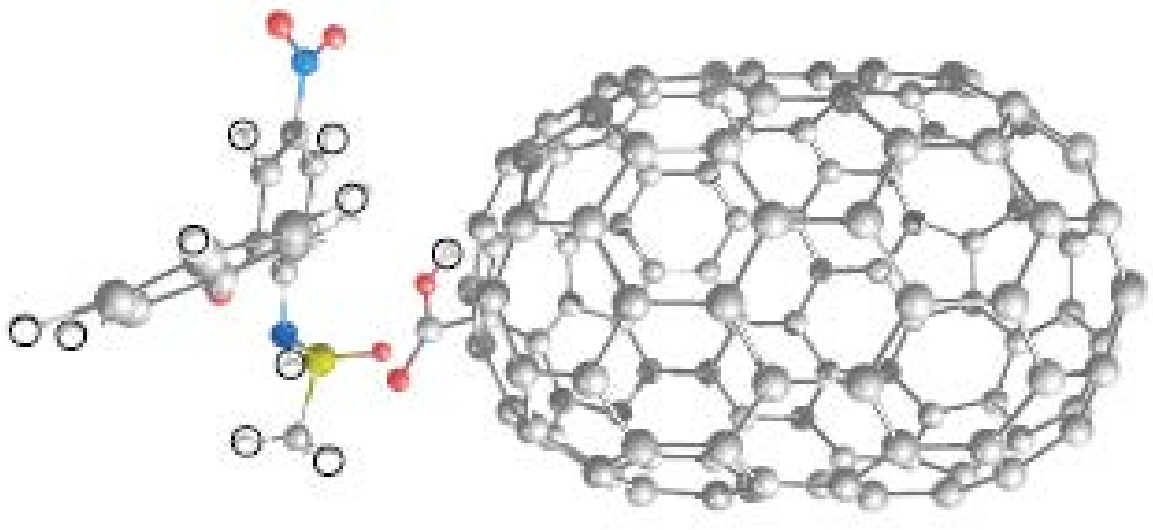

Fig. 5.8 the spatial structure of a capped carbon nanotube bonded with Nimesulide by O **(of** the -SO2 group), O atoms [34]

The third mode is to link the drug carboxylate Nimesulide and carbon nanotubes to the bond between the carboxyl oxygen bonding to the carbon nanotube and the CH3 carbon atom (which is, of course, a hydrogen that is removed from the carbon and carbon bonded to carboxylic acid instead of this hydrogen) It is produced in the Nimesulide molecule. In Figure 5.9 the spatial structure for the third topology is shown.

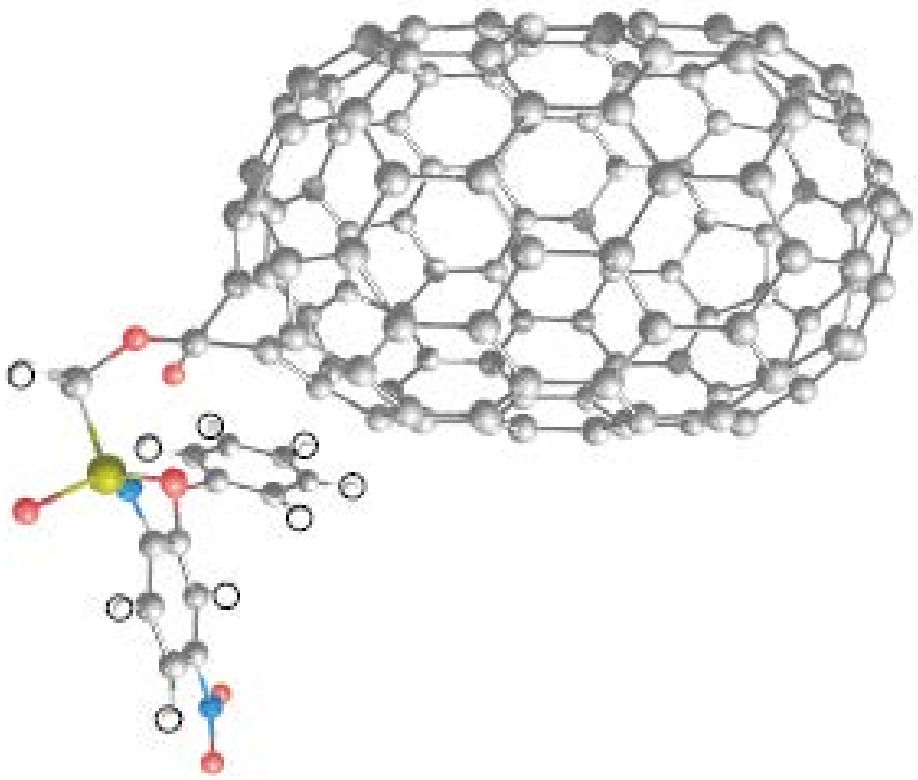

Fig. 5.9 the Spatial Structure of Carbon Nanotubes Coupled Carboxylic with Semisolid by Atoms C, O [34]

5.4 The bonding distance and transplant energy in 3topologies of the bond between the Nimesulide and the proposed CCCN structure

The structural and energetic results for CCCN interacting with Nimesulide were performed by ab initio density functional theory (DFT) calculations[15 ,14] .

The DZP wave function (double-zeta basis) is used as a base function to increase accuracy, and the polarization of external orbital is considered in the calculations. DZP is used to describe valence electrons. In the description and description of the DZP wave function, it can be stated that a set of basic functions is used to describe the electron orbits in quantum equations (Schrödinger equation), the more basic these functions are, and the more precise the simulation will be. The first step to magnifying a base set is to increase the number of base functions. The base capacity set separates this step by doubling or multiplying the number of descriptive functions of the capacitive layer electrons.

Of course, the size of these functions is not the same, that is, they have different ε views. A

base set that has twice the functions of a minimum set of bases is called a dual-zeta base set. Similarly, you can increase the number of members of the collection and create three-zeta, four-zeta sets, and so on. In a pure dual zeta base set, each member of a base set is replaced by at least two functions. As a result, the minimum number of functions is doubled compared to the base set. Of course, in some cases, the number of dual zeta bases may be slightly less than double. By doubling the number of functions, better answers will be obtained than the base set. In triple zeta bases, three primary functions are used to describe each orbital

In quantum mechanics, one main purpose is to determine how a particular type of wave propagates and behaves. In this application, the wave is called the wave function, and the governing equation for wave behavior is called the Schrödinger wave equation. The first way to calculate the behavior of the function of the waveguide is to write the waveform function over superfluous (called quantum superposition). Several (or perhaps infinite) functions of a particular state are static, whose behavior is simple. Since the Schrödinger wave equation is linear, the behavior of the original wave function can be calculated using the superposition principle. This approach is called BSSE (basis set superposition error), and we can calculate the energy of the bond between atoms using this principle. The equation for calculating the energy of the links is given below.

$$E_b = [E_T(CCCN+X) - E_T(CCCN+X_{ghost}) - E_T(CCCN_{ghost}+X)] \quad ; \qquad (5\text{-}1)$$

In Equation 5-1, X represents the Nimesulide molecule, and $E_T(CCCN+X)$ is the total energy of the interaction between the carboxylate carbon nanocrystal line structure and the Nimesloide molecule; the meaning of the ghost index alongside X, CCCN is the set of basic functions added without any potential function.

In this thesis, we intend to change the interactions between the CCCN and the Nimesolide by observing the electric field in the CCCN and the NIMZ direction along the carbon nanotube axis (Fig. 5.10) and see how the energy band diagram changes in the intensity of the different electric fields. Of course, we have to apply the values of the applied electric field intensity in a range that cannot break the carbon bonds in the structure of the nanotube.

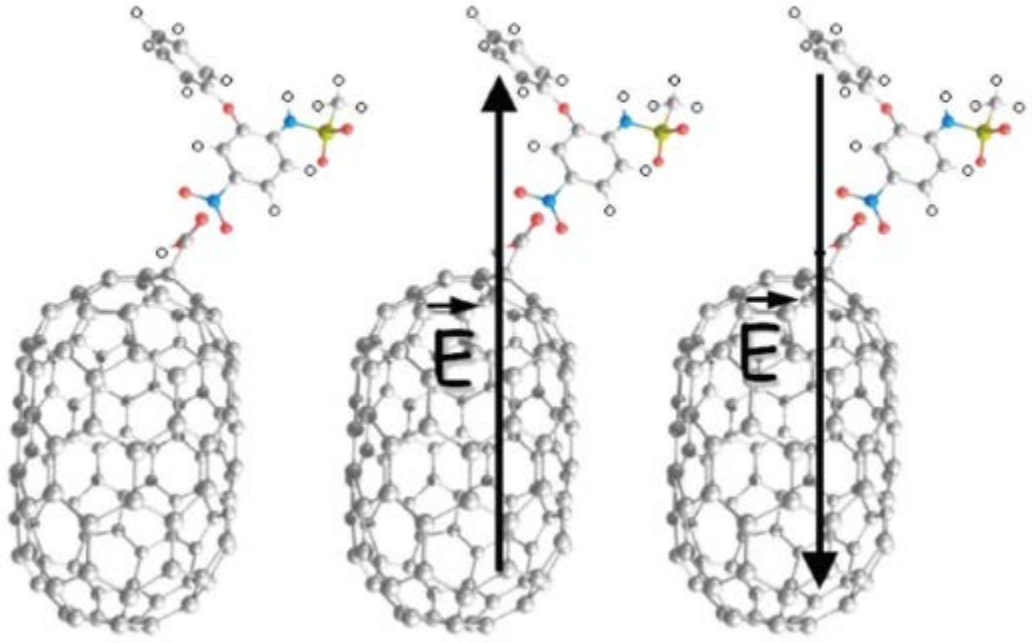

Fig. 5.10 putting an electric field in the CCCN and NIM field along the carbon nanotube axis [34]

We define the relative energy of the structure of CCCN and Nimesulide as the difference between the total energy of the system in the presence of the electric field and the absence of an electric field.

$$E_r = E_E - E_0 \quad ; \quad (5\text{-}2)$$

All simulation calculations should be done in the periodic boundary conditions, taking into account the supercell approximation.

Chapter 6

Simulation and Discussion

6.1 Introduction

In Chapter 5, the proposed structure was introduced using a carboxylate carbon nanotube packed to carry the Nimesulide drug. In this section, we try to examine the different states of the bond between the Nimesulide molecule and the carbon nanotube in terms of the energy band. In this regard, we will examine the external electric field to assist in the transfer of Nimesulide molecules and the corresponding energy band diagrams. To simulate the molecular dynamics of atomic bonds, we will use the molecular simulator of Siesta, in which a brief explanation is given of this simulator.

6.2 Siesta simulation software

There are many simulation software available to simulate atomic structures based on molecular dynamics and Schrödinger equations, including for example wasp, quantum spresso, and Siesta. The simulation software used in this thesis is Siesta software, a powerful software for simulating solids with the density function theory in a periodic system with a large number of atoms. Siesta's software stands for the initiation of a Spanish initiative for the simulation of electron with thousands of atoms. Siesta is software based on the Fortran 90 programming language, which is used for computing electronic structures and molecular dynamics simulations of molecules and solids. This program is based on self-consistent density citizenship theory using standard pseudo-potentials. The linear combination of atomic orbitals leads to the creation of a numerical and stable base set which, in order to improve the results, can be considered as the polygonal condition of orbital and multi-zeta. Approximation required to achieve the citizenship of the exchange-correlation in solving Kohn_sham equations is applied using local density approximation or generalized gradient approximation. The base functions and electron density are projected into a fixed space network, which minimizes them to orthogonal functions of energy and density, which, like the results of taking Kohn_sham energy, without the explicit need for orthogonal condition Is becoming. In addition, the use of localized quasi-wave electron wave functions allows large systems, with a large number of atoms, to be calculated over a shorter time period without the need for high memory. This advantage is due to the linear scaling of memory and runtime with the size of the system as a result of the use of these electronic wave functions. A powerful Siesta software program for parallel systems is also available. Implementing the computer program and performing the calculations of the electron structure and simulating the molecular dynamics with the initial methods are the methods that this software implements. Sistema is also used to run a computer program by simulating molecules and solids in comparison to atoms. In calculating electron structures, quantum number solving equations mechanically operates on the behavior of electrons and simulates the dynamics of the molecule in physical processes And chemical at the atomic scale.

Main features of Cisco Software:

1-Quickly execute computations in a system with a large number of atoms compared to Gaussian software

2-Use of the Cohen-Sohn standard method, the method of self-consistent density functions in local density or generalized gradient approximation.

3- Preserve perfect pseudopotential shapes.

4- The use of atomic orbitals as base sets, unlimited application of multi-zeta, and angular, polar, and inactive orbital size, have radial shape for each orbital, and each shape can be provided by the user.

5- Projects of electron wave and density functions on a real network of space in order to calculate Hartree and the equivalence potential and element matrix.

6- Run chains or parallelization under MPA.

7- The use of local linear combinations of occupied orbits and the creation of computer time and linear memory scale with a number of atoms.

6.3 Calculate energy band structures with Siesta

First, we must simulate each of the structures separately and obtain the energy band of each of them in isolation and in the states of the Nimesulide, so that we can calculate the energy of each structure using equation (5-1). And compare. All simulations are based on periodic boundary conditions and to prevent interactions between atoms in distinct nanotubes (the interaction between valence electrons of carbon atoms in a nanotube with electrons and atoms of carbon nanotubes adjacent to the volume of matter), the distance between the axes of the nanotubes From 40 angstroms.

Each unit has a structure of 120 carbon atoms, which is adhered to a covalent bond by a radical carboxyl (COOH) bond.

6.3.1 The energy diagram of a separate Nimesolide molecule

Figure 6-1 shows the energy structure of the Nimesulide molecule. This molecule is simulated using the LDA approximation in the Siesta simulator, and its energy band diagram is obtained.

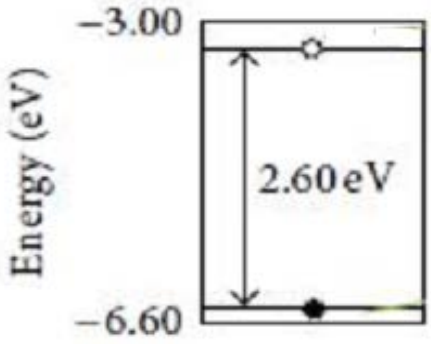

Fig. 6.1 The energy structure of the Nimesulide molecule

As shown in Fig. 6.1, the total energy of the Nimesulide molecule structure is in the pure state between -6.6 and -3, and according to the random distribution methods, the placement of electrons in the molecular orbitals of this energy varies between these two quantities. These two molecular energy quantities are called Homo and Lomo. In fact, in chemistry, according to the energy level of orbital molecules, the highest molecular orbitals with electrons are called HOMO and the lowest molecular unrelated molecular orbital LUMO. The hollow circles in the diagram represent the molecule orbital capacity layer electrons, and solid circles represent valence layer electrons.

6.3.2 Carbon nanotube energy diagram

Figure 6.2 shows the structure of the Carboxylated Capped Carbon Nanotubes energy structure. This molecule is simulated using the LDA approximation in the Siesta simulator, and its energy band diagram is obtained.

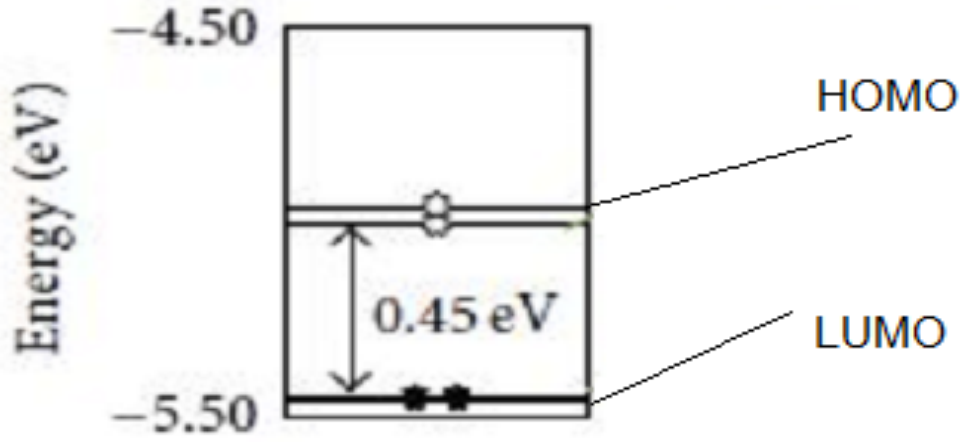

Fig. 6.2 CCCN Balancing Structure

6.3.3 Energy Diagram The structure of CCCN bonded to the Nimesulide molecule

In the previous chapter, we said that the Nimesulide bond is carried out with a different form or topology carboxylated nanotube, which in the first case the Nimesulide molecule through the oxygen atom carries out NO2 itself with the oxygen carboxyl, COOH, of the covalent bond, and in the second case, the oxygen atom is the SO2 agent It binds to oxygen COOH, in the third case, the carbon atom is linked to the oxygen atom of the COOH from the CH2 molecule of Nimesulide (initially CH3). In Fig. 6-3, these three structural modes are shown in terms of energy.

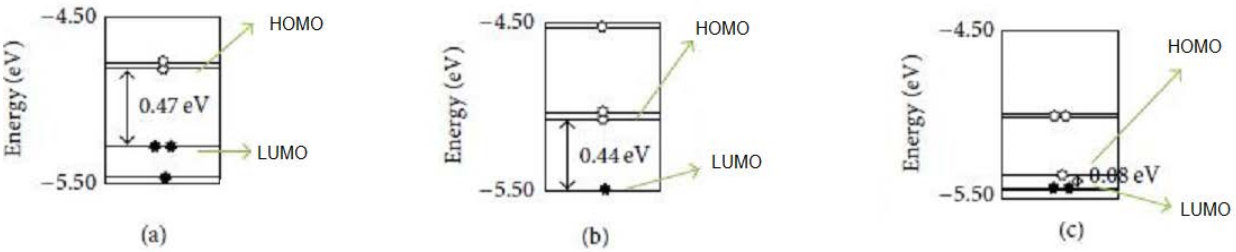

Fig. 6.3 Energy structure CCCN + Nimesulide a- First state, b- Second state and c- Third mode

As shown in Figure 6.3, the energy bandgap between LUMO, HOMO in the first and second modes is 0.47 and 0.44, but in the third case, the bandgap has a low value of 0.08, which is not suitable. In fact, the more bandgap is, the stronger the link is made and the link length becomes smaller. The bond length and bond energy in all three structural modes are given in Table 6-1.

Table 6.1 Energy $\boldsymbol{E_b}$ for Three Structural Modes

System	Bond distance (Å)	E_b (eV)
First type	1.99 (O-O_{tube})	2.09
Second type	2.15 (O-O_{tube})	0.62
Third type	1.36 (C-O_{tube})	−3.85

As we see in Table 6.1, the energy difference E_b is negative for the third-order structure, which means that there is a thrust between atoms and never has such a stable bond. So, we will only look at the first two structural modalities.

6.4 Calculation of energy band 2. Proposed structure mode by applying electric field

As we said earlier, the better the Homo-Lumo bandgap, the stronger the link structure is. In this thesis, we intend to investigate the impact on the stability of the structures and the Homo-Lumo bondage by applying different electric fields.

For the proposed structure, we apply the electric field along the axis of the nanotube. We change the values of the electric field in the simulation from 0.05 to 0.4, and we calculate the Homo-Lumo Gap band and show in Fig. 6.4. We must bear in mind that the excessive increase in the electric field may result in failure of covalent bonds between the carbon nanotubes.

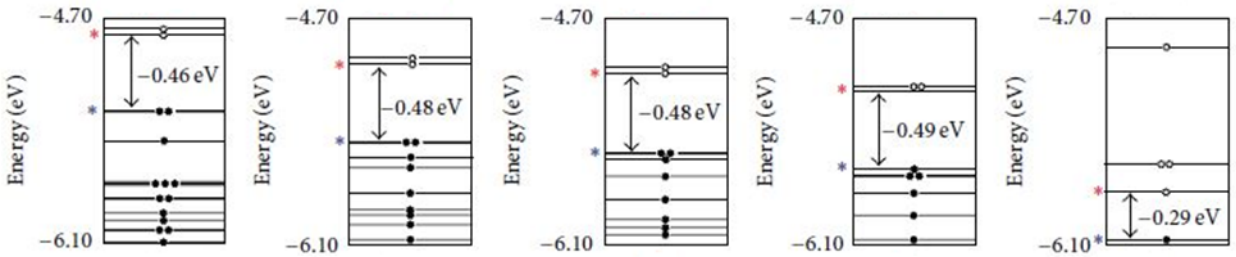

Fig. 6.4 The energy band diagram in the proposed structure with the intensity of the electric field 0, 0.05, 0.1, 0.2, 0.4 V on Angstrom first structure

For the proposed structure, we apply the electric field along the axis of the nanotube. We change the values of the electric field in the simulation from 0.05 to 0.4, and we compute the Homo-lumo Gap band and depict in Fig. 6.5.

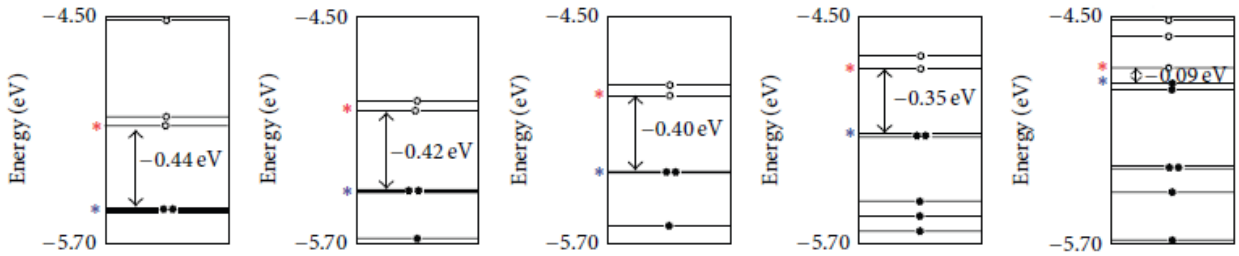

Fig. 6.5 The energy band diagram in the proposed structure with the intensity of the electric field 0, 0.05, 0.1, 0.2, 0.4 V on Angstrom second structure

In Table 6.2, the energy values of E_b are calculated for both structural states.

Table 6.2 Relative energies, binding energies, and ΔHL values for CCCN interacting with Nimesulide in two structure

	Electric field (V/Å)	E_r (eV)	E_b (eV)	ΔHL (eV)
First type structure	0	—	2.09	0.46
	0.05	−0.14	2.06	0.48
	0.10	−0.41	1.94	0.48
	0.20	−1.40	1.41	0.49
	0.40	−5.38	−1.02	0.29
Second type structure	0	—	0.62	0.44
	−0.05	−0.07	0.61	0.42
	−0.10	−0.20	0.58	0.40
	−0.20	−0.66	0.49	0.35
	−0.40	−2.34	0.19	0.09

6.5 Use Nanoribbon Graphene instead of Carbon Nanotube

Carbon nanotubes have more toxic effects than graphene, and it is harmful to the body and healthy cells of the body, so the use of Nano-ribbon graphene instead of carbon nanotube as a carrier of the molecules of Nimsulide can reduce the toxicity of drug delivery. Also, the carbon fabrication process has more complexity than graphene, and the cost of making carbon nanotubes is much higher than that of graphene. In Fig. 6.6, nanotubes are proposed graphene with 12 carbon atoms and a zigzag edges structure that has been linked with hydrogen atom.

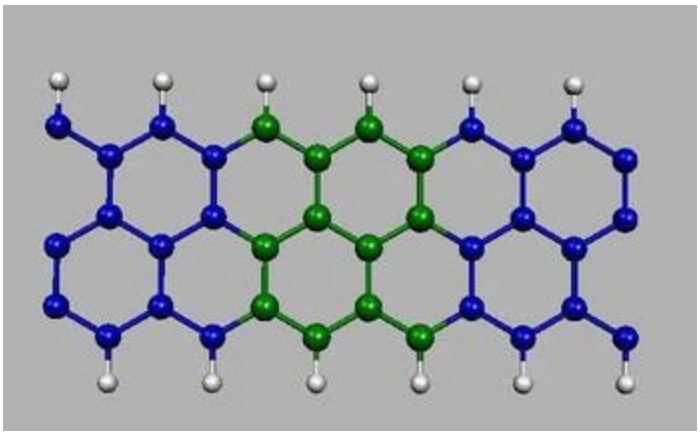

Fig 6.6 zig-zag graphene nanoribbon

For the reasons mentioned, the use of graphene nanoribbons instead of nanotubes can be a great suggestion. In Fig 6.7, the nanoparticle bonding graphene is plotted using the Siesta software.

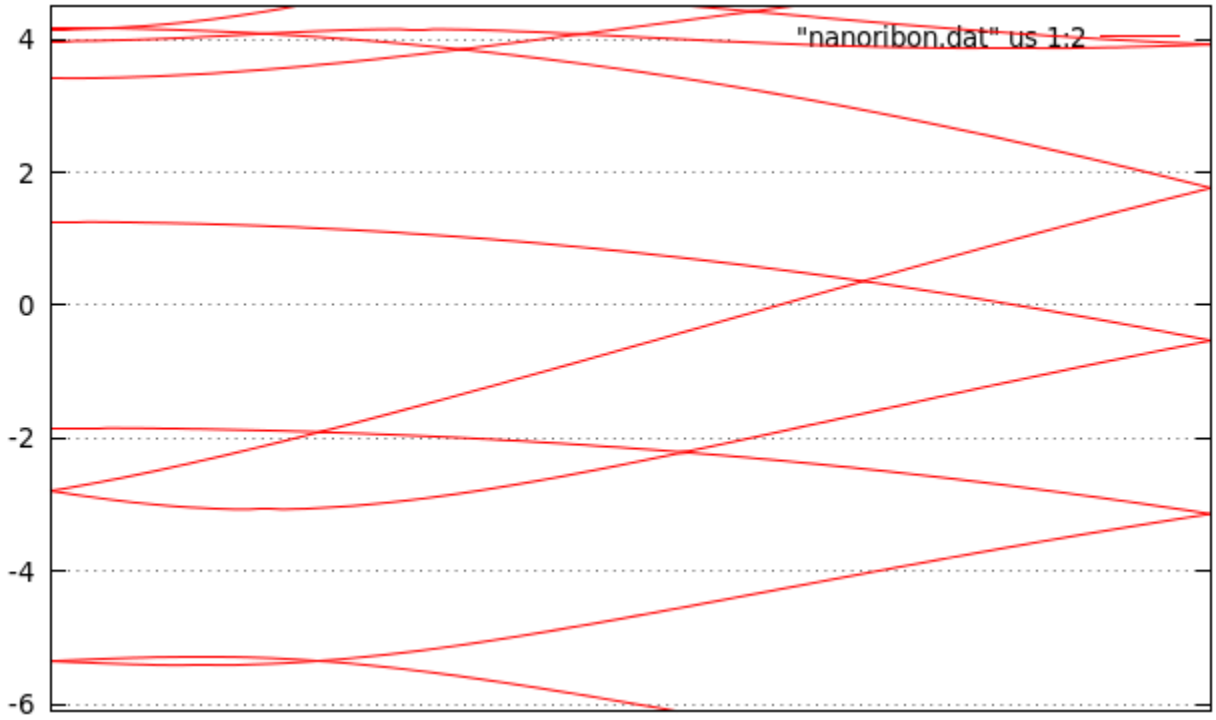

Fig 6.7 band structure of zig-zag graphene nanoribbon

The graphene Nano-ribbon structure consists of the periodic placement of 12 carbon atoms, shown in Fig. 6.6, in green colors, in which these periodic structures are repeated to a large extent, and therefore there are many places for the binding of the carboxyl agent, as well as the binding of Nimsulide molecules, which examines all These points are beyond the scope of this research and the study of the continuation of work is being done by readers and other researchers.

It should be noted that according to Fig. 6.7 and initial simulations of graphene delivery instead of carbon nanotubes, the results showed relatively acceptable results. The obtained homologous bandgap for the synthesis of graphene and isoenzoyl in several randomly selected link locations only slightly less than the hologram bandgap in carbon nanotube and semisolid, due to the greater benefits of graphene application, this insignificant difference in many applications can be neglected and will greatly reduce the cost of treatment.

6.6 Conclusion

As we have seen, using the electrical fields applied to the structure of carbon nanotubes and semisolid can enhance the stability of the drug delivery system. In the first state structure with an intensity of 0.05 electron volts on the angstrom, we were able to achieve a higher degree of stability than the second structural mode (even with the electric field).

Chapter 7

Conclusions

7.1 Introduction

Drug delivery with nanotechnology is one of the important research topics that we tried to introduce and analyze in this dissertation in different ways. In this regard, by introducing carbon nanotubes and using carboxylic agent, we examined the subject and tried to carry the drug Nimesulide. In the drug carrying case, the sustainability of the bond between the drug and the DNA molecule (CNT) is a very important issue so that the drug can deliver the drug to the desired location. In this thesis, we showed that by applying electric fields of the size and the proper direction, it is possible to improve the stability of the structure and therefore, it performs the drug delivery correctly.

7.2 Conclusions

The simulation results indicate that the proposed structure is more suitable for the delivery of Nimesulide molecules, since the length of the Homo-Lumo chain in this structure is the highest with the application of an electron field of 0.02 eV on the astronomer and has a higher stability. The rest of the states and the various values of the electric field and their effect on the Homo-Lumo distance and structural stability were also investigated. By using different electrical fields, it can be used to increase the bonding stability during the delivery time, and after reaching the drug and the carrier to the target site in the body, by applying the appropriate electric field in the early breakup of the graft and release of the drug.

7.3 Offers

For further research, other researchers are recommended to consider other non-toxic nanotubes, such as boron nanotubes or Nitride boron nanotubes, as a drug delivery agent, and also consider the proposed nanocomposite system in this thesis with other drugs.

Appendices

FDF for CCNT
SystemName 80NPH

SystemLabel 80NPH

NumberOfAtoms 48

NumberOfSpecies 2

MeshCutoff 270.0 Ry

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1 6 C

2 1 H

%endblock ChemicalSpeciesLabel

PAO.EnergyShift 0.050 eV

PAO.SplitNorm 0.15

%block PAO.Basis

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0.000 0.000

1.000 1.000

n=2 1 2 P

0.000 0.000

1.000 1.000

n=3 0 1 P

4.500

1.000

H 1

0 2 P

0.000 0.000

1.000 1.000

%endblock PAO.Basis

AtomicCoordinatesFormat NotScaledCartesianAng

LatticeConstant 4.26 Ang

%block LatticeVectors # Lattice vectors in units of LatticeConstant

3.521127 0.000000 0.000000

0.000000 3.521127 0.000000

0.000000 0.000000 3.521127

%endblock LatticeVectors

%block AtomicCoordinatesAndAtomicSpecies

3.13067920 0.00000136 0.29349785 2 H

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3.17198182 -0.00000125 1.40423392 1 C

2.92083213 1.21020715 3.53601850 1 C

3.17239469 0.00000086 4.21452565 1 C

3.13119221 0.00000023 5.32555621 2 H

2.21381807 2.21381494 0.29247760 2 H

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2.24343905 2.24343736 1.40375415 1 C

1.21020542 2.92083248 3.53601661 1 C

2.24371826 2.24371824 4.21470034 1 C

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2.21391802 -2.21391638 5.32586961 2 H

%endblock AtomicCoordinatesAndAtomicSpecies

DFT, Grid, SCF

XC.functional LDA

XC.authors CA

SpinPolarized .false.

MaxSCFIterations 1000

DM.MixingWeight 0.05

DM.RequireEnergyConvergence

DM.Tolerance 1.d-5

DM.EnergyTolerance 1.d-5 eV

DM.NumberPulay 5

#####Eigenvalue problem: order-N or diagonalization

SolutionMethod diagon

ElectronicTemperature 0 K

Optical Properties

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%endblock Optical.Mesh

Optical.EnergyMinimum 0 eV

Optical.EnergyMaximum 12 eV

Optical.Scissor 0 Ry

Optical.Broaden 0.05 eV

Optical.NumberOfBands 240

Optical.PolarizationType polarized

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%endblock Optical.Vector

Output options

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WriteCoorInitial

WriteCoorStep

WriteForces

WriteKpoints

WriteEigenvalues

WriteKbands

WriteBands

WriteMullikenPop 1

WriteCoorXmol .false.

WriteMDCoorXmol .false.

WriteMDhistory

WriteCoorXmol .false.

WriteWaveFunctions .true.

COOP.Write .true.

Fdf input file for graphene nanoribbon

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SystemLabel         nanoribbon
NumberOfAtoms       16
NumberOfSpecies     2
%block ChemicalSpeciesLabel
 1   6  C
 2   1  H
%endblock ChemicalSpeciesLabel
%block PAO.Basis                # Define Basis set
C           2                   # Species label, number of l-shells
 n=2   0   1                      # n, l, Nzeta
   4.088
   1.000
 n=2   1   1                    # n, l, Nzeta, Polarization, NzetaPol
   4.870
   1.000
H           1
 n=1   0   1
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    1.000
%endblock PAO.Basis
XC.functional GGA
XC.authors    PBE
LatticeConstant     1.433600 Ang
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   0.000000000       14.0000000000        0.0000000000
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```

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   0.0000000000   2.0000000000   0.0000000000  1
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   0.0000000000  -0.2500000000   2.5980762120  2
   0.0000000000   1.0000000000   1.7320508080  1
   0.0000000000   2.0000000000   1.7320508080  1
   0.0000000000   3.5000000000   0.8660254040  1
   0.0000000000   2.5000000000   0.8660254040  1
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   0.0000000000   2.5000000000   2.5980762120  1
   0.0000000000   4.0000000000   1.7320508080  1
   0.0000000000   4.7500000000   1.7320508080  2
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%block kgrid_Monkhorst_Pack
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   0   1   0  0.0
   0   0  30  0.5
%endblock Kgrid_Monkhorst_Pack
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MaxSCFIterations     500
DM.MixingWeight      0.2
DM.NumberPulay       5
DM.Tolerance         1.d-4
WriteCoorXmol .true.
BandLinesScale ReciprocalLatticeVectors
%block BandLines
1   0.0 0.0 0.0 \Gamma
100 0.0 0.0 0.5 X
%endblock BandLines
SolutionMethod       diagon
SolutionMethod   diagon
TS.WriteHS  .true.
```

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