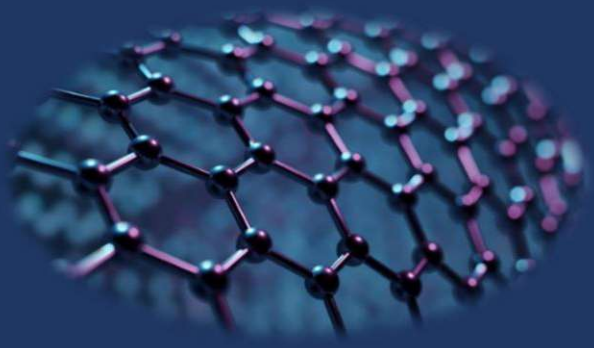
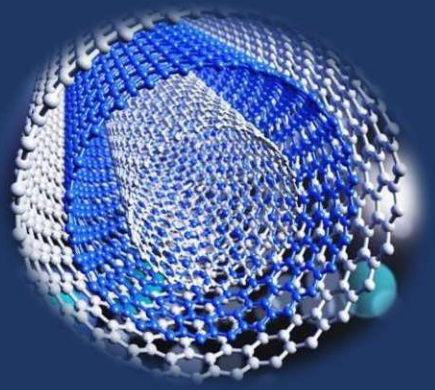
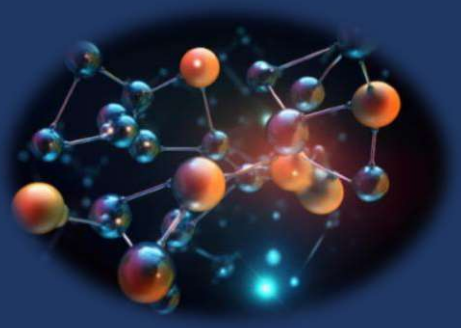
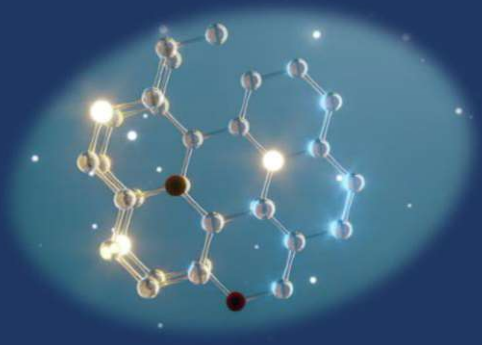
# Chapter 1

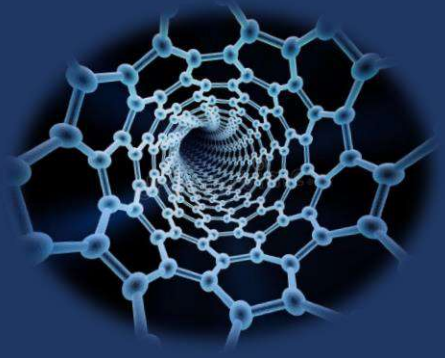
# Introduction to Organic Materials











## 1.1 Importance of Organic Materials

A symphony of organic materials orchestrates the beat of existence in the complex tapestry of life's molecular dance. The relevance of organic materials in the world of biomolecules and pharmacological molecules reveals a profound tale of interconnection, adaptability, and therapeutic potential [1-2]. Let's explore the subtleties that highlight their significance and resonate across scientific domains as we dig into this interesting world.

The vital significance of organic materials' function is highlighted by biomolecules, those complex macromolecular components that make up life's blueprint. The foundation upon which life exhibits its myriad expressions is composed of the delicate dance of proteins, nucleic acids, lipids, and carbohydrates. A tribute to nature's craftsmanship is the supple ballet of amino acids shaping proteins, DNA encoding genetic inheritance, lipids preserving cellular structure, and carbs supplying essential energy [3-4].

The orchestra of biological elements takes on the role of something close to a transforming conductor when the stage opens up to medication molecules. An in-depth knowledge of molecular interactions in biological systems is essential for the design and identification of effective therapeutic medicines. Due to their varied structural and functional properties, organic molecules open up new possibilities for developing precise treatments, battling diseases, and reestablishing balance in biological ecosystems [3-5].

Think of penicillin as an illustration of the powerful effects of antibiotics. A new age of focused pharmaceutical innovation was sparked by Alexander Fleming's accidental discovery of this organic compound, which revolutionised medicine. To avoid the one-size-fits-all approach and to embrace the field of personalised medicine, researchers can create customised therapeutic molecules thanks to the organic chemistry inherent to these chemicals [4].

Organic materials unfold a variety of tactics in the area of cancer therapies. The organic canvas develops as a platform for innovation, from small molecule inhibitors that selectively shut down abnormal signalling pathways to antibody-drug conjugates that deliver payloads with razor-sharp accuracy. A multidisciplinary approach to illness care is supported by the incorporation of biomolecules as therapeutic agents, such as monoclonal antibodies, which blur the distinctions between the fields of biology and pharmacology [6-7].

The function of organic materials goes beyond their chemical structure in the constantly changing story of biomolecules and pharmacological compounds. The development, adaptability, and interaction of these materials with the natural environment are captured in their legacy. As we learn more about this story, we discover the ties that bind organic components to the narrative of life itself [7-8].

In essence, the significance of organic materials resonates as a melodious symphony—infused with variety, connectivity, and the capacity for transformation. Organic materials play a crucial role in this vast story, from the delicate dance of biomolecules moulding the shapes of life to the dynamic potential of medicinal molecules curing illnesses. We pay respect to their heritage and add to the on-going story of exploration, healing, and scientific enlightenment with each discovery, every scientific achievement, and each beautiful design. These biological ingredients work together to influence science and medicine in the same way as the components of a symphony work together to produce a masterpiece.

## 1.2 Introduction of Nano Materials (from 2D to 0D)

Due to its excellent qualities and many uses, carbon-based materials have attracted a lot of attention in the field of nanoscience. Among these, the remarkable class of materials known as carbon nanostructures has come to light. These nanostructures, which can change from two-dimensional (2D) to zero-dimensional(0D) forms, display unique properties [9]. This metamorphosis not only causes notable changes in their electrical, mechanical, and optical properties, but it also creates new opportunities for ground-breaking innovations across a range of disciplines.[10] Carbon has recently been studied in all of its allotropes, including 3D graphite[11], 1D nanotubes[12], 0D fullerenes[13] , and the most well-known form, 2D graphene[14-15] , for use in technology and fundamental science. Graphene, a two-dimensional sheet of carbon atoms arranged in a tightly woven honeycomb pattern, serves as the fundamental structure underlying all carbon variations. This captivating material has captivated researchers due to its remarkable array of qualities, including remarkable carrier mobility[14][16-17] , the phenomenon of quantum electron transport[16-17] , exceptional elasticity[18], modifiable bandgap[19] , and superb electrochemical characteristics [20]. These distinctive attributes position it as a material of great promise in the realms of biosensing, biomedical applications, and nano-bioelectronic devices[21]. There are two forms of hybridization in the carbon family of materials, $sp^2$ and $sp^3$, with $sp^2$ type carbon dominating

in the technological sector. The $sp^2$ hybridization occurs in a wide variety of geometric structures, including fullerenes (zero dimensional, 0D), carbon nanotubes (one dimensional, 1D), graphite (3D), and graphene (2D). Recent advances in sp and $sp^2$ hybridization have led to the emergence of a new class of carbon allotropes, including graphyne and graphdiyne[22-23] . Distinct geometries have distinct electrical characteristics. For example, graphite, in its bulk form, has a semi-metallic nature [24] in addition to having a high resistance perpendicular to the layer plane [25]. As a zero-gap semimetal with a massless carrier in 2D form, graphene [14] possesses a metallic or semiconducting nature, but in 1D carbon nanotubes, chirality determines the properties of the material[26]. Fullerenes have a quantum dot-like character[27]. The $sp^3$ crystal form of carbon (diamond) has entirely different electrical characteristics from the $sp^2$ form; they have a broad band gap, which gives them semiconducting or insulating nature[28]. This tetrahedral geometry, which precludes the possibility of any weakly coupled or delocalized electrons, is what causes this behaviour in $sp^3$ hybridization.

In spite of all of its astounding qualities, cytotoxicity is what prevents carbon-based nanomaterials from being used in biological applications [29] Last but not least, carbon quantum dots, which exist in zero dimensions, provide a playground of quantum phenomena for cutting-edge applications. The path of innovation presented by this change in dimensions offers a stimulating setting for the conception and creation of revolutionary nanotechnologies.

## 1.3 Biomedical Applications of Carbon Nanomaterials

Recent advances in nanotechnology have produced a broad range of nanoscale materials, including carbon allotropes, which have been used in several applications due to their fundamental characteristics[30]. There were only three known carbon allotropes prior to the 1980s: graphite, diamond, and amorphous carbon. Since then, fullerenes[31], carbon nanotubes (CNTs)[32] and graphene[33] have all been found and characterised, contributing to the development of several scientific areas. Fullerenes were discovered for the first time in 1985, and its discoverers were awarded the 1996 Nobel Prize in Chemistry [34]. The synthesis of carbon allotropes is said to have been revolutionised by this accomplishment[35]. Fullerenes are variously sized $sp^2$-carbon atom cages with single or double bonds **(Figure 1.1).**[36] In comparison to other carbon nanostructures, fullerenes have the highest degree of symmetry and, as a result, are highly stable in terms of both structure and chemical composition. For

targeted delivery in applications such as drug delivery, diagnostics, imaging, and biosensing, fullerene surfaces can be decorated with a variety of functional groups.[36][38] Fullerenes, in particular $C_{60}$, have photoelectrochemical characteristics that make them appropriate for photodynamic treatment **(Figure 1.2).** Fullerenes are hydrophobic; their limited solubility in polar solvents like water prevents them from being employed in biomedical applications. Various techniques, such as synthesising fullerene derivatives, have been explored to get around this problem[36][39].

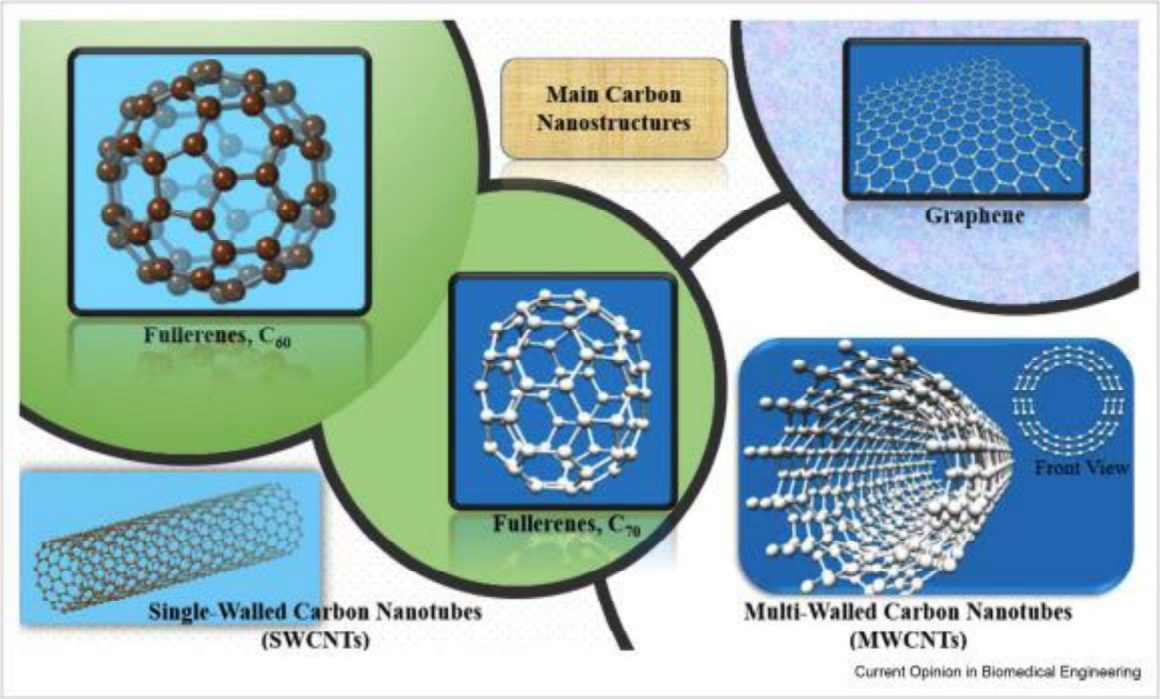



**Figure 1.1:** *An illustration depicting the fundamental carbon nanostructures encompasses fullerenes ($C_{60}$, $C_{70}$), graphene, as well as single-walled and multi-walled carbon nanotubes (SWCNTs and MWCNTs)[37].*

Carbon nanotubes have attracted a great deal of attention since their discovery because of their exceptional structural, chemical, electrical, and optical capabilities. In order to create hollow tubes with large aspect ratios, carbon nanotubes are made of either a single (single-walled carbon nanotube, SWCNT), double (double-walled carbon nanotube, DWCNT), or multiple (multi-walled carbon nanotube, MWCNT) concentric graphene cylindrical layers. Additionally, CNTs are biocompatible for conjugation with biomolecules and are excellent candidates for bioanalytical applications as they may be functionalized with various chemical groups either covalently or noncovalently.[40-41] SWCNTs in particular have a perfect balance of biocompatibility and an inherent near-infrared, non-blinking, non-photobleaching fluorescence [42]. The potential use of carbon nanomaterials, especially for biomedical

applications, is increased by using them as scaffolds for biomolecules. CNTs have been considered to be the most promising options for immobilising proteins and enzymes because of their enormous specific surface area. The protein/enzyme immobilisation is a crucial step in the construction of biosensors, which can address many of the difficulties in the healthcare-system, the creation of innovative CNT-protein/enzyme conjugates is crucial for advancing biomedical research and applications[41]. Furthermore, the special optical and electrochemical qualities of CNTs make them perfect for medicinal, imaging, sensing, and energy applications [43-44]. A two-dimensional, one atom thick carbon sheet called graphene and its oxidised derivative, graphene-oxide (GO), have a huge surface area that may be further functionalized with biomolecules for a variety of uses[45]. In order to bind proteins, enzymes, peptides, bacteria, cells, and nucleic acids to graphenes and GOs, both covalent and noncovalent binding methods have been employed.[45-46] For a variety of applications, including fluorescence- or electrochemical-based sensors, labelling and imaging, therapy and targeted delivery, and energy storage[47-48], proteins, enzymes, peptides, bacteria, cells, and nucleic acids have been bound to graphenes and GOs using both covalent and noncovalent binding[45].

Nanoparticles have an enormous capacity for loading due to their high surface-to-volume ratio, high mobility, and flexibility in functionalization. New capabilities are added to the underlying nanoparticles carriers by various biomolecule types, such as proteins, peptides, and enzymes. Nanoparticles can acquire biocompatibility, accountability for a particular target analyte, or biocatalytic capability by being loaded with customised proteins or enzymes. Here, we emphasise carbon nanomaterial scaffolds and go through several forms of surface immobilisation for diverse purposes. Since the majority of these carbon nanoparticles have a hydrophobic character, effective surface functionalization also encourages their dispersion and colloidal stability in aqueous solution, which is essential for most of the applications addressed here. Biocatalysis, one of the most potent techniques in biotechnology, is one of the main applications of nanoparticle-enzyme conjugates. It has a significant societal impact on health, food supply, environmental protection, and sustainable fuel generation[49]. This is because certain processes may be accelerated by enzymes to rates that are higher than those that can be achieved by conventional chemical or physical catalysis. Enzymes can be used in this context as selective biomolecule detection instruments, serving as enzymatic biosensors for use in the food sector, healthcare, and environmental monitoring.

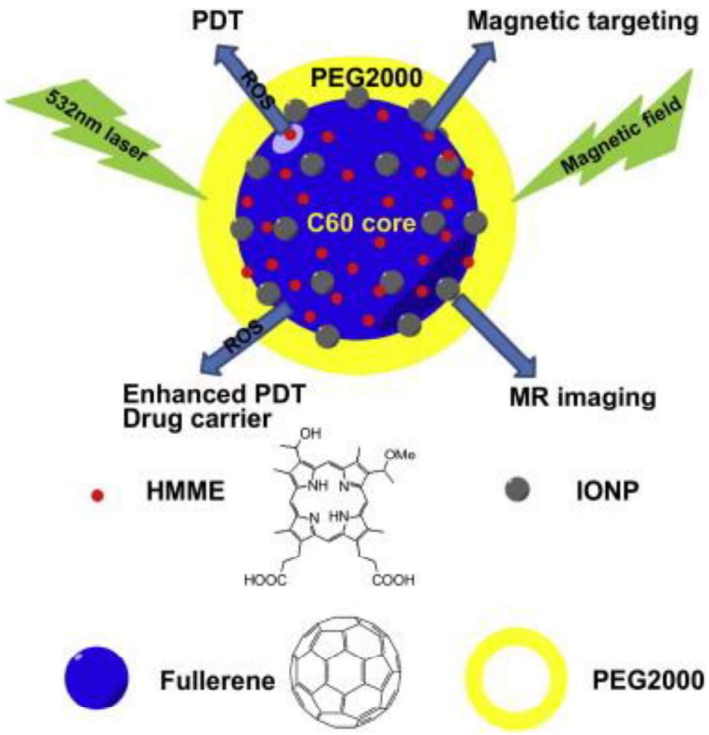



**Figure 1.2:** *Diagram portraying $C_{60}$-IONP-PEG/HMME and its biological functionalities [39].*

In particular, point-of-care sensor devices, which use enzymatic-based sensor technology, are the sole way to address numerous healthcare system shortcomings[41-50]. Despite being economical, sustainable, and selective, natural catalysts are frequently not well-suited for industrial applications. For instance, major inactivation or loss issues can seriously impair the performance of enzyme biosensors[51-52]. In order to make such biocatalysts practicable and commercially viable, enzyme immobilisation appears as a critical method [21][53]. The creation of effective industrial biocatalysts involves the immobilisation of enzymes, which calls for enhanced stability across a range of heat, pH, storage, and operational conditions. The enzyme must also have a suitable level of resistance to autolysis, organic solvents, and heat denaturation[54-55]. In broad terms, the immobilisation method is essential for developing new enzymatic and biological instruments that have appropriate performance metrics, great sensitivity, amazing selectivity, quick response times, and excellent repeatability[50]. Furthermore, it is essential that biomolecules that have been immobilised maintain their structural integrity, biological functioning, and continued adhesion to the surface throughout use**(Figure 1.3**)[21][55] .

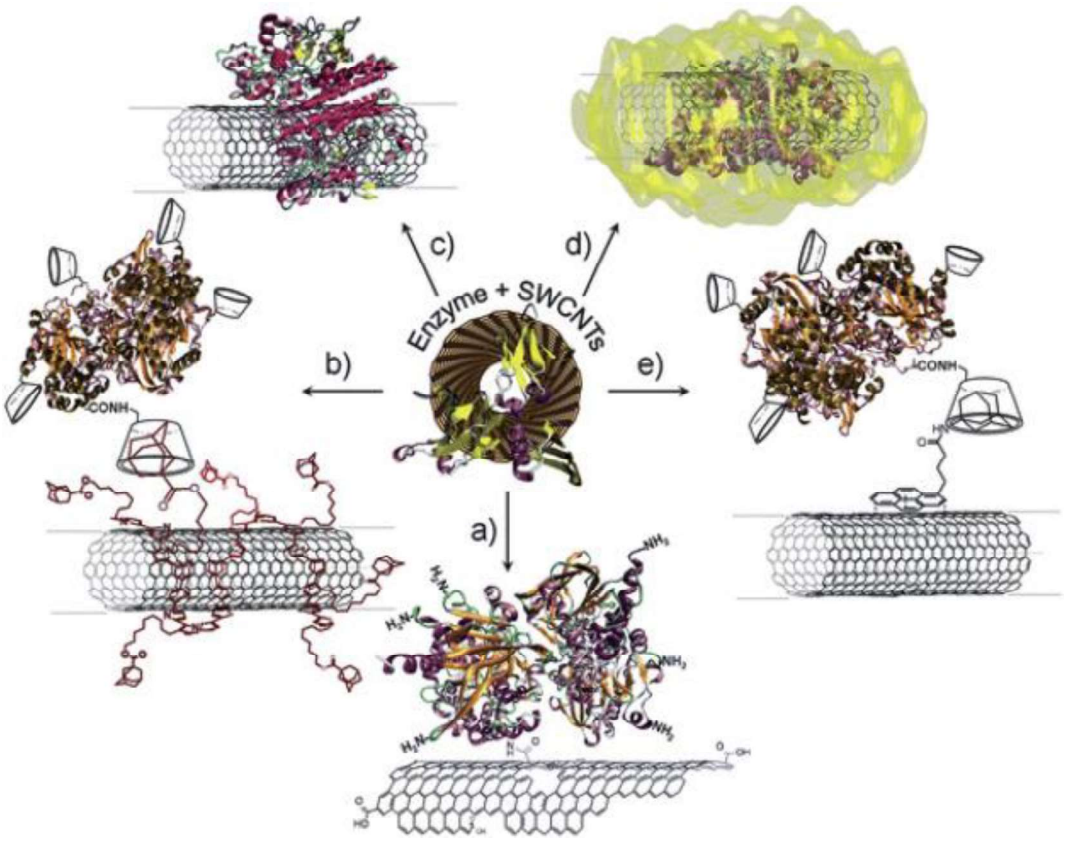



**Figure 1.3:** *Various approaches for immobilizing enzymes on single-walled carbon nanotubes (SWCNTs) include(a) Covalent binding through amide coupling involving the carboxylic acid groups of oxidized nanotubes. (b and e) Immobilization through interactions onto functionalized nanotubes using different linker molecules. (c) Adsorption of enzymes onto SWCNTs through hydrophobic or electrostatic interactions. (d) Entrapment of enzymes within a polymer matrix formed around SWCNTs[56].*

The creation of innovative nanoparticle-protein conjugates, which are important actors in imaging, targeting, sensing, drug delivery, and treatment, is also extremely beneficial for many medicinal applications. Enhancing biocompatibility and targeting capabilities for in-vivo applications is frequently the primary function of surface immobilised biomolecules[57]. On the other hand, in a sensing application, the surface coating must make the nanoparticle selectively receptive to the desired target[58], acting as the signal transducer of a binding event. Last but not least, the protein or enzyme coating is used in treatment applications as either the therapeutic agent or the targeting agent that travels with the medication payload[59].

## 1.4 Research Objectives

The foremost objective of the present research work is to investigate interaction mechanism of novel carbon nanomaterials with the different biomolecules.

The specific objectives of the present study are as under:

1. To screen the biological molecules for their binding affinity on carbon nano-material surface.
2. To delineate the relationship between binding affinity of the molecule and surface characteristics of carbon nano-materials.
3. To predict the conformational changes in the adsorbed molecule upon adsorption over carbon nano-materials.
4. To elucidate the electronic and molecular basis of biomolecule-nanomaterial interactions using DFT and molecular dynamic simulations.

## 1.5 Structure of the Present Thesis

In the subsequent sections of this thesis, the arrangement is as follows: **Chapter 2** outlines the theoretical framework underpinning the computational techniques employed in this study. It encompasses a comprehensive elucidation of the density functional theory (DFT) for first-principles calculations, as well as an in-depth exploration of Molecular Dynamics (MD) simulations rooted in Newton's second law of motion.

In **Chapter 3**, the primary emphasis lies in examining how various nucleobases (namely Adenine (A), Thymine (T), Guanine (G), Cytosine (C), and Uracil (U)) interact with the $C_{24}$ fullerene, which possesses $D_{6d}$ symmetry. The objective is to ascertain the binding sequence of these nucleobases through the application of dispersion-corrected density functional theory (DFT), specifically using the GD3 correction method**.** To assess the interplay between the nucleobases and the $C_{24}$ fullerene, we conducted a comprehensive analysis encompassing adsorption energy calculations, NBO (Natural Bond Orbital) analysis, Mulliken charge analysis, examination of density of states, as well as the evaluation of sensing response and recovery time. Our observations reveal a distinctive adsorption pattern among nucleobases, with the sequence being A > C > G > T > U. This phenomenon is attributed to the interaction between nucleobases and the $C_{24}$ fullerene, leading to a redistribution of charges and the subsequent induction of dipole moments. Adenine can be distinctly separated from other DNA

nucleobases, whereas in the gas phase, cytosine and guanine can be detected with a rapid recovery time of $10^{-14}$ seconds. The rise in interaction energy for adenine and cytosine in the presence of a solvent underscores their suitability for use as carriers.

In **Chapter 4**, we delve into the utilization of two distinct methodologies: density functional theory (DFT) and classical molecular dynamics simulations. These approaches are employed to scrutinize and gain insights into the interaction mechanisms between three illicit drug compounds—Amphetamine (AMP), Ketamine (KET), and Mercaptopurine (MER with the pristine $C_{24}$ fullerene Our findings show that in a gas phase environment, drug molecules adsorb in the following order: AMP > KET > MER. Nonetheless, when the impact of solvent is taken into account, we see an increase in adsorption energy for AMP and KET drug molecules when interacting with $C_{24}$, indicating a change towards chemisorption behaviour. This implies that $C_{24}$ could be a promising candidate for applications involving the removal of AMP and KET drugs from the environment. For the MER drug molecule, the interaction primarily involves physisorption, characterized by an appropriate interatomic distance, making it well-suited for detection applications. Furthermore, classical Molecular Dynamics (MD) simulations have verified the structural and dynamic stability of the sensing material $C_{24}$ at room temperature. The MD calculations, including the assessment of time-dependent Root Mean Square Deviation (RMSD), Radial Distribution Function (RDF), energy profiles, and temperature, provide validation for the DFT findings.

In **Chapter 5**, using dispersion corrected density functional theory (DFT-D3) calculation and classical molecular dynamics (MD) simulation to assess and comprehend the interaction tendencies of size-variable fullerenes ($C_{24}$, $C_{36}$, $C_{50}$, and $C_{70}$) towards L-Leucine (LEU), one of the essential amino acids. The LEU biomolecule adsorbed in the following order in the gas phase: $C_{24} > C_{70} > C_{36} > C_{50}$. The LEU biomolecule, however, exhibits chemisorption behaviour across $C_{24}$ and $C_{36}$ when solvent effect is applied, increasing its adsorption energy. This raises the prospect of employing $C_{24}$ and $C_{36}$ as viable candidates for the isolation application of LEU from other amino acid sequences. In order to support the interaction between LEU and fullerenes, calculations for adsorption energy, NBO analysis, Mulliken charge analysis, DOS calculation, RDG analysis, sensing response, and recovery time were made. The stability of the biosensing materials $C_{24}$ and $C_{36}$ fullerene in terms of structure and dynamics at room temperature has been verified by classical MD simulation analysis. The DFT

results are validated by the MD calculations, which include time evaluations of RMSD, RDF, energy profiles, and temperature.

**Chapter 6** of the thesis summarizes the entire work. It consists of a summary of results, conclusion, application, and future scope of the work.

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