Investigation On Binding Affinity Of Biomolecules Over Novel Carbon Nanomaterials

A synopsis submitted to

The Maharaja Sayajirao University of Baroda
for the degree of
Doctor of Philosophy
in
PHYSICS

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Faculty	:	**Science**
Title of the Thesis	:	**Investigation On Binding Affinity Of Biomolecules Over Novel Carbon Nanomaterials**
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June 2023

Introduction:

Across a wide range of disciplines, including chemistry, biology, materials science, and environmental science, organic materials serve a crucial role in scientific study. These materials, which are mostly made of carbon-based compounds, have a variety of useful features and functions, making them a great resource for several scientific studies [1]. Organic materials serve as crucial building blocks in the synthesis of complex molecules and materials. The wide range of organic compounds available allows scientists to design and engineer structures with specific properties. Organic synthesis techniques, such as multistep reactions and functional group transformations, enable the creation of tailored molecules for applications in drug discovery, catalysis, polymers, and advanced materials[2] . The enhancement of knowledge and applications in biology and medicine are greatly aided by this. The study of biochemistry, molecular biology, and medicinal chemistry is impossible without them. The study of biological systems is made easier by organic molecules, which also help with the creation of drugs and molecular probes for imaging and sensing[3] . Fluorescence microscopy, for instance, frequently uses organic dyes to examine disease causes and observe cellular activities. Intense attention has been generated by the exceptional qualities and adaptability of carbon and materials connected to it, which have changed the scientific landscape. Due to its many diverse qualities, carbon, the fundamental component of life on Earth, has attracted scientists for ages. Researchers have recently delved into the field of nanoscience, where carbon-based nanomaterials have become an effective tool for creating unique structures with exceptional features. Due to its abundance on Earth, low cost, and presence of allotropes with distinct characteristics, the family of carbon nanostructures is regarded as one of the alternatives for the fundamental electrical sensors[4]. Due to their distinctive structural, electronic, chemical, optical, and sensing properties, the most famous sp2 hybridized allotrope of the carbon family—two-dimensional (2D) structured graphene and graphene oxide, one-dimensional (1D)

materials like carbon nanotubes, and zero-dimensional (0D) structures like fullerene nanocages—have been used in a variety of diverse fields, including biological, medical, and pharmaceutical [5] [6] [7] [8] [9] [10]. C_{60} fullerene, which was synthesized experimentally in 1985 by H. Kroto, is the first carbon nanomaterial to be identified. Because it is hydrophobic, biocompatible, has a high surface area due to its spherical form, and exhibits less toxic behavior towards living microorganisms than graphene and carbon nanotube (CNT), fullerene has received a lot of attention in the biomedical fields. It has also been successfully used as a biosensor, drug sensing, and drug delivery [11] [12] [13] [14] [15]. Here, we have used DFT and conventional MD simulations to examine the adsorption applications of the various pristine fullerenes, such as C_{70}, C_{50}, C_{36}, and C_{24}, with diverse biomolecules and pharmaceutical substances.

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.

Summary of Research Work:

The six chapters that collectively make up the full description of the research carried out with the suggested objectives are organized and presented.

Chapter 1: Introduction

This chapter gives detailed description of the importance of the organic materials and fundamentals of carbon which is the most important element for organic chemistry. The basic novel electronic and morphological properties of the carbon nano-materials from 0D to 2D have been introduced in this chapter. Particularly, the appeal of bucky ball-shaped zero-dimensional fullerenes has been addressed in great detail for their wide range of applications, including biosensing, drug sensing, and drug administration. The requirement of biosensing and drug sensing in the fluorescing environment, as well as the rationale for the selection of particular fullerenes like C_{70}, C_{50}, C_{36}, and C_{24}, have also been thoroughly reviewed in this chapter.

Chapter 2: Methodology

This chapter covers the step-by-step description regarding the theory and approach utilized for studying the proposed properties of selected nano and bio-materials .The first theoretical approach starting from Born-Oppenheimer approximation to the latest ground breaking electron density-based approximation formulated by Walter Kohn and Sham together with different exchange-correlation functionals like local density approximation (LDA) and generalized gradient approximation (GGA) for the construction of pseudopotentials is described to get detailed account on the development of the electron density-based approach. The advanced electronic structure methods like hybrid functionals. for correcting the electronic band profiles are also discussed. Apart from electronic properties, we have also evaluated the vibrational, thermodynamic properties and effect of solvent of the proposed systems with the

biomolecules and the respective approaches have been included in the present chapter. Last but not the least, the present chapter light on the classical molecular dynamics simulation based on the Newtonian mechanics for evaluating the stability and bond-forming /bond-breaking of biomolecules and selected fullerenes complexes with time evaluation in water phase at the room temperature and pressure.

Chapter 3: Biosensing Activity of C_{24} Fullerene towards DNA Nucleobases

This chapter focus on the interaction of different nucleobases (Adenine (A), Thymine (T), Guanine (G), Cytosine (C) and Uracil (U)) with the C_{24} fullerene (D_{6d} symmetry) and to get the binding sequence of these nucleobases using dispersion (D3) corrected density functional theory (DFT). To evaluate the interaction between the nucleobases with the C_{24} fullerene, we have calculated adsorption energy, NBO analysis, Mulliken charge analysis, density of state, sensing response and recovery time. We observe that the adsorption sequence of nucleobase follows the trend as A > C > G > T > U. Due to interaction between the nucleobases and the C_{24} fullerene charge redistribution is taking place between them which also induces the dipole moment. Adenine can be enisled from the other DNA nucleobase molecules, while cytosine and guanine can be sensed with the recovery time of 10^{-14} s in gas phase. The interaction energy increases for adenine and cytosine with solvent effect confirms their application as carrier [16].

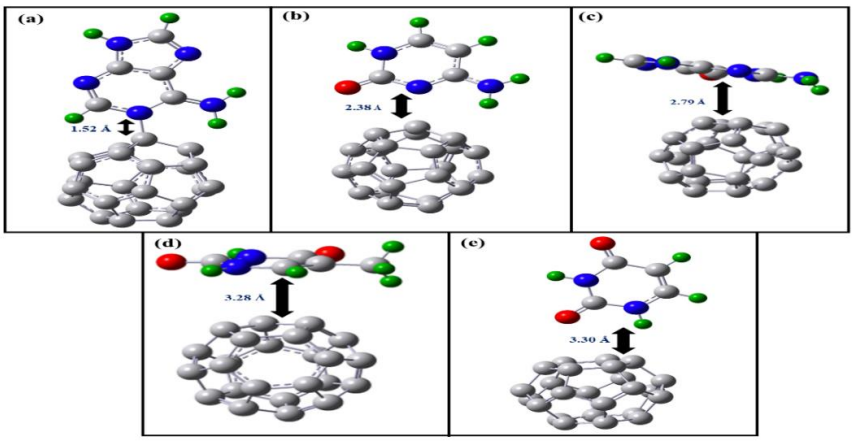

Figure 1: Minimum energetic geometry of Adenine (a), Cytosine (b), Guanine (c), Thymine (d) and Uracil (e) adsorbed over C_{24} fullerene, respectively.

Chapter 4: Exploring C_{24} Fullerene as an illicit Drug sensor

This chapter provides the explanation on the utilization of both density functional theory (DFT) and the classical molecular dynamics simulation calculations to evaluate and understand the interaction mechanism between three illicit drug molecules Amphetamine (AMP), Ketamine (KET) and Mercaptopurine (MER) and pristine C_{24} fullerene. We observe that the adsorption sequence of the drug molecules in the case of gas phase is AMP > KET > MER. However, on the application of the solvent effect adsorption energy increases for the AMP and KET drug molecules over C_{24} indicating chemisorption behavior. This suggests the possibility of using C_{24} as potential candidate for the removal application of AMP and KET drugs from environment. In the case of MER drug molecule, the interaction is a physisorption with a suitable interatomic distance and hence can be used for the detection purpose. The structural and dynamical stabilities of sensing material C_{24} at the room temperature has been confirmed by classical MD Simulation study. The MD calculations such as time evaluation of RMSD, RDF, energy profiles and temperature validate the DFT results [17].

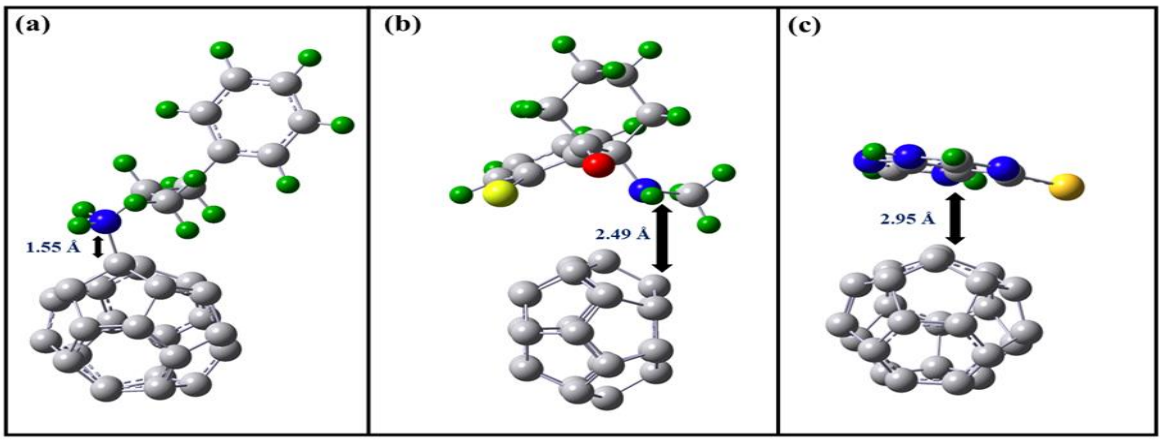

Figure 2: Minimum energetic geometry of AMP(a), KET (b) and MER (c) adsorbed over C_{24} fullerene, respectively.

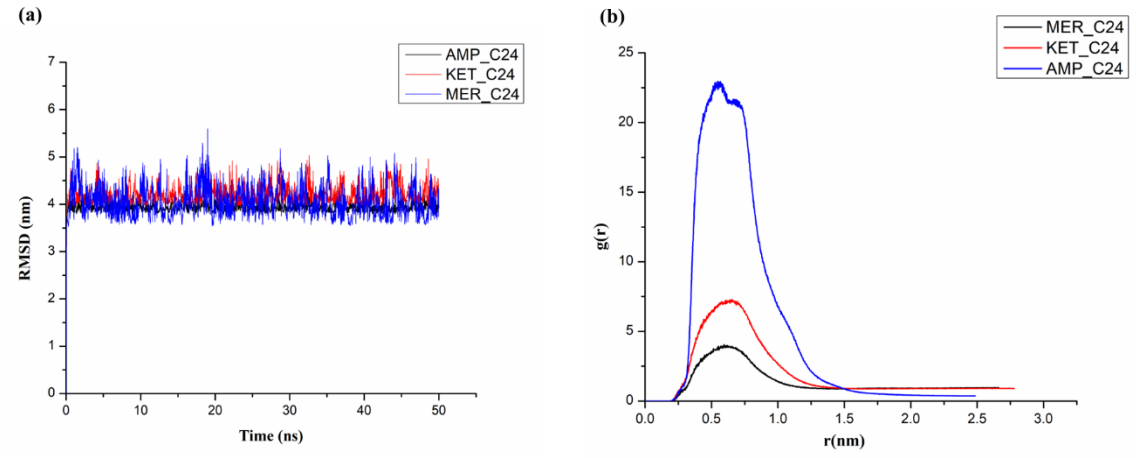

Figure 3: (a)RMSD curves for the interacted drug molecules and C_{24} fullerene as a function of time and (b)comparison of radial distribution (g(r)) of drug molecules around the C_{24} fullerene surfaces versus distance.

Chapter 5: Size dependent Activity of Carbon-based Fullerenes with L-leucine

This chapter explores on the interaction behavior of L-leucine with size-dependent fullerenes such as C_{70}, C_{50}, C_{36} and C_{24} utilizing the combined DFT and MD simulation approach. We have implemented the DFT investigation in order to understand the enhanced interaction mechanism of size dependent fullerenes such as C_{70}, C_{50}, C_{36} and C_{24}. Additionally, utilizing the DFT study, a thorough investigation of electronics properties including NBO, Mulliken charge, and DOS analysis was performed. The binding kinetics and sensitivity of L-leucine to the aforementioned fullerenes in the gas phase, as well as the solvent effect, have also been determined by the DFT analysis. Finally, the classical molecular dynamics simulation study has been carried out to justify the stability and bond-forming/bond-breaking of l-leucine and fullerene complexes with time evaluation in water environment at room temperature(310K).

Chapter 6: Summary and Future Prospects

The last chapter of the thesis summarizes the entire work. It consists of a summary of results, conclusion, application, and future scope of work.

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List of publications Related to the Thesis:

1. Jana, Sourav Kanti, Darshil Chodvadiya, Narayan N. Som, and Prafulla K. Jha. "A quantum mechanical prediction of C24 fullerene as a DNA nucleobase biosensor." Diamond and Related Materials 129 (2022): 109305. (Published)

2. Jana, Sourav Kanti, Narayan N. Som, and Prafulla K. Jha. "Theoretical appraisements on the interaction behaviour of Amphetamine, Ketamine and Mercaptopurine drug molecules over C24 fullerene: A combined dispersion corrected DFT and MD simulation Study." Journal of Molecular Liquids (2023): 122084. (Published)

3. Jana, Sourav Kanti, Narayan N. Som, and Prafulla K. Jha. “The size-dependent fullerenes C70, C50, C36 and C24 for enhanced interaction of L-leucine: A combined DFT and MD Simulation approach”. (Under preparation)

Date: /06/2023

Place: Vadodara

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