A PROJECT REPORT ON

"STUDY OF CHEMICAL REACTIVITY OF 4-HYDROXY BENZAMIDDE"

SUBMITTED TO THE

DEPARTMENT OF PHYSICS

FACULTY OF SCIENCE

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226026

IN PARTIAL FULFILMENT OF REQUIREMENTS

FOR THE DEGREE OF

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IN PHYSICS

SUBMITTED BY-

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M.Sc. PHYSICS (IV SEMESTER)

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UNDER THE SUPERVISION OF

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TO WHOM IT MAY CONCERN

This is to certify that **KAVITA YADAV** is a bona fide student of M.Sc. (II Year /IV semester) Session 2021-2022 to 2022-23 at Integral University, Lucknow. She completed her project entitled **"STUDY OF CHEMICAL REACTIVITY OF 4-HYDROXYBENZAMIDE (4HBAM) USING A QUANTUM CHEMICAL APPROACH"** successfully under the supervision of **Dr. Anuradha Shukla**, Assistant Professor, Department of Physics, Integral University.

I wish her good luck and a bright future.

Date: **(Dr. Seema Srivastava)**

Place: Lucknow **Head Department of Physics**

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CERTIFICATE

This is to certify that **KAVITA YADAV,** a student of M.Sc.(Physics-IV Semester) has completed the project on **"STUDY OF CHEMICAL REACTIVITY OF 4-HYDROXY BENZAMIDE (4HBAM) USING A QUANTUM APPROACH"** under my supervision during the year 2022-2023.

I wish her good luck and a bright future.

Date: **(Dr. Anuradha Shukla)**

Place: Lucknow **Supervisor**

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KAVITA YADAV

TOPIC

STUDY OF CHEMICAL REACTIVITY OF 4-HYDROXY BENZAMIDE (4HBAM) USING A QUANTUM CHEMICAL APPROACH

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- **Density functional theory (D.F.T.)**
- **Basis Sets**
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- **Total density**
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- **Homo Lumo**
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- **Molar refractivity(MR)**

LIST OF SYMBOLS AND ABBREVIATIONS

- **D.F.T. = Density Functional theory**
- **P.C. = Pharmaceutical Compounds**
- **A.P.I.= Active Pharmaceutical Ingredients**
- **H.F.= Hartee-Fock**
- **S.T.O.= Slatter Type Orbitals**
- **G.T.O.-= Gaussian Type Orbital**

ABSTRACT

Co-crystals were first found about a century ago, but their capacity to alter the physical characteristics of solid-state materials, particularly semiconductors, has made them increasingly popular in recent years pharmaceuticals. An increase in the number of potential uses for cocrystals has coincided with an intensification of research activities in this field. Cocrystals have lately been proven to offer appealing possibilities for flavour masking, mechanical property improvement, and intellectual property development and extension, whereas solubility modification was long thought to be the main driver for cocrystal formation. With a handful of cocrystal products now available on the market and more in the registration and clinical trial stages, cocrystals are quickly becoming a commercial reality. Additional study on cocrystal production techniques is now necessary as a result of increased commercialization, with a focus on cutting-edge technology that may provide ecologically friendly and effective alternatives. This article reviews techniques for creating cocrystals and utilising the customised physical property adjustment offered by cocrystals, with a focus on recent developments in both fields.

CHAPTER 1: INTRODUCTION

1.1 CO- FORMER - A co-former (also known as a co-crystal former or co-crystallizing agent) is a compound that is used to form a co-crystal with a drug molecule or other active pharmaceutical ingredient (API). A co-crystal is a crystalline material that contains two or more components in a well-defined stoichiometric ratio, and in which the individual components are bound together through non-covalent interactions, such as hydrogen bonding.

When two or more different molecular and/or ionic compounds are combined in a stoichiometric ratio, the result is a solid called a cocrystal that is neither a solvate nor a simple salt.1. It is recognised as a pharmaceutical cocrystal2 if at least one of the co-formers is an API and the other is pharmaceutically acceptable.

As demonstrated by the carbamazepine:4-aminobenzoic acid cocrystal system, which can exist in 1:1, 2:1, and 4:1 stoichiometric configurations3, cocrystals of varied stoichiometry with the same co-former are possible. Cocrystals differ from either of the beginning materials in terms of their crystal structure, and as a result, their physicochemical characteristics. Because the cocrystal solid can be constructed to have better physical qualities than either of the pure starting materials, crystals are appealing.

Pharmaceuticals are particularly interested in physical property improvement because the vast majority of medications are administered in solid forms. The processing, transport, and ultimately the effectiveness of the medication will all be directly impacted by the physical characteristics of the solids found in pharmaceutical medicinal products. The solubility of a given material in solution is directly influenced by crystal structure, to give a well-known illustration. For drug products to be bioavailable in the body, they must have a specific solubility. According to estimates, up to 90% of new chemical entities and 40% of established therapeutic products have low water solubility13, making it impossible to transport them to the body using standard methods. By modifying the co-former during cocrystal formation, it is possible to increase solubility.

Co-formers are typically small organic molecules that have complementary functional groups to those found on the API. By selecting the appropriate co-former, it is possible to enhance the solubility, stability, and bioavailability of the API, as well as modify its physical properties, such as melting point, crystallinity, and particle size distribution. Co-crystallization is therefore an important technique for optimizing the performance of APIs and developing new drug formulations.

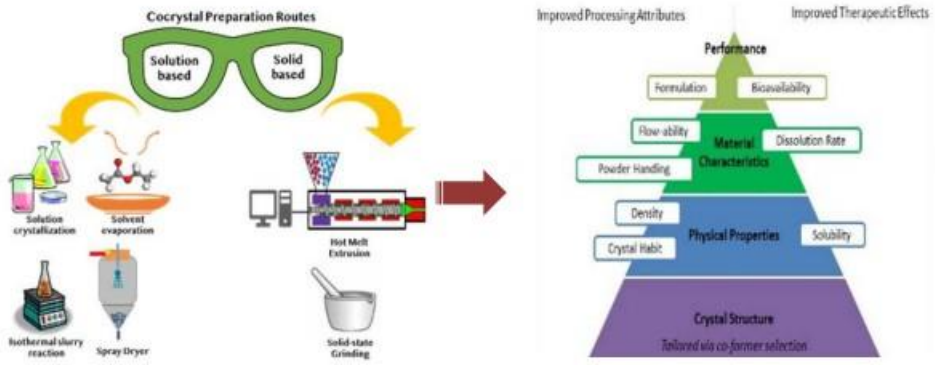

Figure 1structure of co crystals

1.2 CO-FORMER ROLE IN FORMATION OF CO-CRYSTAL

In the formation of co-crystals, co-formers play a critical role in providing a second component that can interact with the drug molecule or other active pharmaceutical ingredient (API) through non-covalent interactions, such as hydrogen bonding, π-π stacking, or van der Waals forces. These interactions can help to stabilize the crystal lattice and alter the physicochemical properties of the co-crystal, such as solubility, melting point, and dissolution rate.

Co-formers can also affect the morphology and crystal structure of the co-crystal, as well as its stability and compatibility with other excipients in the final drug formulation. The selection of an appropriate co-former is therefore crucial to the successful formation of a co-crystal, and must take into account factors such as its solubility, melting point, functional group chemistry, and potential toxicity.

Overall, co-formers are essential components in the design and development of co-crystals, as they provide a means of tailoring the physicochemical properties of APIs for improved drug performance and efficacy.

1.3 MODEL COMPOUND

The IUPAC name for 4-hydroxybenzamide is 4-hydroxybenzamide, and it can also be referred to as p-hydroxy benzamide or para-hydroxy benzamide. The compound is commonly encountered in organic chemistry and pharmaceutical research due to its diverse range of applications. 4-Hydroxybenzamide is known for its ability to inhibit certain enzymes and biological processes, making it useful in various fields. It has been studied for its potential use in drug development, particularly in the areas of cancer treatment and neurological disorders. Additionally, it has been investigated for its antioxidant and anti-inflammatory properties. The compound's physical properties include a white crystalline appearance and a melting point around 170-174°C. It is sparingly soluble in water but dissolves readily in organic solvents such as ethanol and acetone.

Overall, 4-hydroxybenzamide is a versatile chemical compound with promising applications in different scientific disciplines, and ongoing research continues to explore its potential uses and properties.

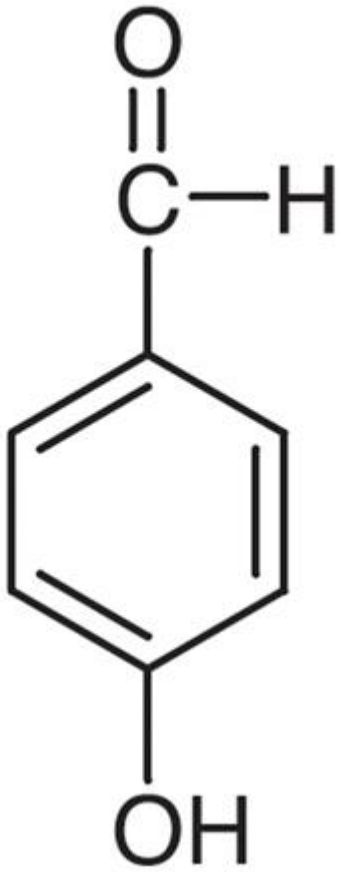

Figure 2 chemical structure of 4-Hydroxybenzamide

1.4 RESEARCH OBJECTIVE

The objective of the current study is to understand the electronic and chemical properties of 4-Hydroxy benzamide by calculating its electrostatic potential and total density with the help of the Gaussian 09 software package. In this proposed project work we focused on the structural properties of selected drugs and this work yielded essential information about new/novel compounds.

CHPATER 2: THEORETICAL CALCULATION

Density functional theory (DFT) was used to optimise and compute the co-former's molecular structure and geometry. Density functional theory (DFT) was used to optimise and compute the cocrystal's molecular structure and shape using the B3LYP correlation functional and the 6-31G(d,p) basis set. The optimised structure was confirmed and visualised using the Gauss View programme. The B3LYP/6-31G(d,p) level was used in the NBO computations to understand the charge-transfer interactions.

2.1 COMPUTATIONAL DETAILS

Mercury software, the Gaussian 09 programme package, and the Gauss view programme package were all used to perform the computations for this study. All of the chosen molecules' chemical structures and optimised geometries were calculated using the DFT approach, which makes use of the cc-pvt, correlation consistent polarised valence triple basis set, B3LYP functional, and 6311-G(d,p) basis set. In this project, electrostatic potential and total density are transformed into ".cub files" with the aid of the Gauss View software, and after the function was mapped out, it was observed. To meet the demands of both accuracy and computation, theoretical approaches and basis set must be combined. Because of this, it has been demonstrated that DFT is very useful for handling molecules with electronic structures. Using the Gaussian 09 software package, the entire vibrational spectra and molecular electrostatic potential calculations of 4 hydroxy benzamide were produced.

2.2 TYPES OF THEORETICAL CALCULATION

The experimental parameters and Schrodinger's equation interpretation made up the semi-empirical technique. Equations are parametrized by using experimental data in this way. (Structure-property relationship (SPR) example. Compared to ab initio, this approach is faster but less accurate. The equations are parameterized in order to replicate certain results, typically the geometry and formation heat rather than total energy. The Ab- initio technique, however, shows that the computations are based on fundamental ideas. No empirical parameters or experimental data are used in this procedure. A Latin phrase that means "from the beginning" is "ab initio." Ab initio quantum mechanics offers an energy function that, in theory, can be precise and is applicable to any molecule, but it must be calculated within the Born-Oppenheimer approximation because electrons move much more quickly than nuclei and react adiabatically to changes in nuclear configuration.

There are many different types of ab-initio computations, some of which are included here.

a. Hartree-Fock (HF)

b. Moller-Plesset-Perturbation Theory (MP)

c. Density functional theory (DFT)

d. Configuration Interaction (CI)

2.3 DENSITY FUNCTIONAL THEORY

Pierre Hohenberg and Hohenberg Kohn created the Hohenberg-Kohn theorem (HK) in 1964, which served as the theoretical foundation for the first application of density functional theory.

The electron density is uniquely characterised by the Schrodinger's equation. This means that all of the ground-state's attributes, including its energy and wave function, are determined only by its electron density. This approach had a lot of success in predicting, reconstructing, and explaining a variety of material phenomena. It is a quantum mechanical technique that is primarily used in the fields of physics and chemistry to determine the structure of an atom's or molecule's electrons in the form of solid crystals of many-body systems and to provide a quantitative understanding of the properties derived from the basic principles of quantum mechanics.

Bond lengths, bond angles, and dihedral angles of rotation about single bonds (which determine the molecular shape) are three factors that affect a polyatomic molecule's electronic wave function. Calculating the electronic wave function for a range of values for each of these variables is necessary for a complete theoretical treatment of a polyatomic molecule. The equilibrium bond distances, bond angles, and dihedral angles are then found as those values that minimize the electronic energy including nuclear repulsion. The four main approaches to calculating molecular properties are ab initio methods, semi-empirical methods, the density-functional method, and the molecular-mechanics method. Semi-empirical molecular quantum-mechanical methods use a simpler Hamiltonian than the correct molecular Hamiltonian and

use parameters whose values are adjusted to fit experimental data or the results of ab initio calculations. As an illustration, consider the Hückel MO treatment of conjugated hydrocarbons, which employs a one-electron Hamiltonian and treats the bond integrals as movable parameters as opposed to theoretically definable quantities. The right Hamiltonian is used in an ab initio (or first principles) calculation, which employs no experimental data other than the values of the basic physical constants.

In density functional theory, functionals (functions of some other function) can be used to analyse the properties of many-electron systems. The electron probability density and electronic energy can be calculated, but the molecular wave function is not disclosed.

A wide range of ground-state molecular features, including potential barriers and reaction pathways, hydrogen bonds, vibrational frequencies, and thermodynamic properties, are

predicted by DFT. It has been used in a variety of contexts, including the study of spin-polarized systems, multicomponent systems, free energy at finite temperatures, superconductors with electronic pairing mechanisms, relativistic electrons, time-dependent phenomena, excited states, and MD, among others. Lattice dynamics, electron density, electronic structure, and various spectroscopy techniques, including Raman and Compton scatterings, photoemission spectroscopy, optical absorption spectroscopy, and magnetic resonance spectroscopy, have all found uses in the study of structural properties (such as lattice parameters, elastic constants, equilibrium geometry, and structural defects), lattice dynamics, and electronic structure. The exchange-correlation functional is selected with the utmost care because it affects how the DFT is presented.

The decision is based on how well they perform for a variety of characteristics, including reaction barriers, molecular geometry, and van der Waals interactions. The molecule electron probability density, or r, and the molecular electronic energy are calculated using the density-functional approach instead of attempting to determine the molecular wave function.

The molecular-mechanics approach does not employ a molecular Hamiltonian operator or wave function and is not a quantum-mechanical approach. As opposed to this, it sees the molecule as a group of atoms bound together by bonds and describes the molecular energy in terms of force constants for bond bending, stretching, torsion, and other factors. The Hartree-Fock calculation method is covered in this chapter along with the general concepts of electronic structure computations for polyatomic molecules.

As previously mentioned, the Hartree-Fock approach ignores electron correlation. Polyatomic Molecule Electronic Terms.

This project discusses semi-empirical approaches, the molecular mechanics, and ab initio and density-functional methods that account for electron correlation.

2.3(A) Local Density Approximation (L.D.A.)

(i) Fastest method

(ii) Provides good band structures

(iii)Gives less accurate geometry

2.3(B) Gradient corrected functionals

(i) Provides more accurate geometries

(ii) Resulted in improvements for the calculated values of the total energies of atoms and molecules.

2.3(C) Hybrid functionals

(i) Gives more accurate geometries

(ii) Gives approximation to the exchange-correlation energy functional in D.F.T.

Despite several successes, the Density Functional theory possesses certain limitations that need to be flabbergasted (resolve) before it can be preserved as an exact theory rather than a semi-empirical theory. Following are a few limitations-

(a) Neglecting or ignoring significant correlations**:** DFT predicts a metallic state despite the fact that many transition metal compounds can transfer charge in an insulator.

(b) Band Gap issues: Atoms in the excited state defy the Hohenberg-Kohn Sham theory. Semiconductor and insulator band gaps are frequently underestimated.

(c) Issues with over-binding are frequently encountered in density functional theory.

(d) No density functional theory functionals are present in Van der Waal's interactions.

2.4 BASIS SET

A basis set is a mathematical representation of a molecule's chemical orbitals.

Each electron can be thought of as being contained in a specific area of space by the basis set. Superior basis sets limit electrons less frequently and more closely resemble the chemical orbitals. The entire electrical wave function is approached by a linear grouping of the basis function. The linear combinations of Gaussian functions are called basis functions.

Basis sets are divided into Slater-Type Basis Sets and Gaussian-Type Basis Sets, or STO and GTO forms. Minimal Basis Sets, Split-Valence Basis Sets, and Polarisation Basis Sets are the three types of Slater-Type Basis Sets that can exist.

Very little functions are employed to run the programme on minimal basis sets. For an accurate representation of orbitals and to characterise the electron supply between the nuclei needed to create chemical bonds, the minimal basis sets are not flexible enough.

Slater Type Orbitals (STO):

(CI)$function \rightarrow S\,(\zeta, \boldsymbol{r}) = Cx\ ny\ mz\ le\ {-\zeta r}$ ..... (2.41)

It characterizes electron density in the valence region and beyond. But, the

valuation of these integrals is difficult Gaussian Type Orbitals (GTO):

$function \rightarrow g\ (\alpha, \boldsymbol{r}) = Cx\ ny\ mz\ le\ -\alpha r\ 2$..... (2.42)

where α is a constant determining the size of the function. It is easy to evaluate but does not represent electron density well. This can be overcome by using the actual basis function as a linear combination of such primitive Gaussian-

$\chi\mu = \sum p\ d\mu pgp$ …… (2.43)

In split valence basis sets.

Where the origin lies at nucleus b, the behaviour of the Gaussian exponential factor is displayed. For tiny values of rb, a Gaussian function does not provide a good depiction of an AO because it lacks the required cusp at the nucleus. We need to utilise a linear combination of many Gaussians to properly depict an AO. Since the number of two-electron integrals is proportional to the fourth power of the quantity of basis functions, an LC-GTF SCF MO calculation entails the evaluation of very many more integrals than the comparable LC-STO SCF MO calculation. However, the computation time for Gaussian integral evaluation is substantially lower than that for Slater integral evaluation. This is because a single Gaussian centred at a third point is equal to the product of two Gaussian functions that are centred at two separate points. A0s a result, all integrals with three or four centres and two electrons are reduced to integrals with two centres.

Let's go over a few of the terms that are used to characterise STO basis sets. One STO is required for each valence-shell AO and inner shell of each atom in a minimal (or minimum) basis set (Section 14.3). For instance, a minimal basis set for C2H2 consists of a 1s STO on each hydrogen and 1s, 2s, 2px, 2py, and 2pz AOs on each carbon. Twelve basis functions overall, with five STOs on each C and one on each H. On each carbon atom, there are two s-type STOs, a set of p-type STOs, and a single s-type STO.

The notation for such a set is further simplified to 12s1p>1s2, which stands for (2s1p) for the carbon functions and (1s) for the hydrogen functions.

Additionally, minimum basis sets, split valence basis sets, and polarisation functions are subcategories of Gaussian-Type Basis Sets.

The smallest number of basis functions needed for each atom are contained in minimal basis sets. It makes use of orbitals of fixed atomic sort. A minimum basis set is frequently referred to as STO-XG, where X is an integer. This X value denotes the quantity of primitive Gaussian functions with a single basis function. The core and valence orbitals make up the equivalent number of Gaussian primitives in both basis sets. Minimal basis sets generally produce imprecise, inadequate results. The minimal basis sets STO-2G, STO-3G, STO-6G,

and STO-3G*(polarized) are frequently used. A Slater type orbital fitted with a linear combination of three Gaussian type orbitals is referred to as a STO-3G basis set. Typical split-valence basis sets with or without polarisation and diffuse functions include the following:

3-21G

3-21G*- polarization function on heavy atoms

3-21G**- polarization functions on heavy atoms and hydrogen

3-21+G- Diffuse functions on heavy atoms

3-21++G- Diffuse functions on heavy atoms and hydrogen

3-21+G*- Polarization and diffuse functions on heavy atoms

3-21+G**- Polarization functions on heavy atoms and hydrogens, as well as diffuse functions on heavy atoms

4-21G

4-31G

6-21G

6-31G

6-31G*

6-31+G*

6-31G(3df,3pd)

6-311G

6-311G*

2.5 TOOLS USED IN THE PROJECT

The use of software in research activities has grown significantly in popularity in recent years.

The value of computational research and information is greatly increased by their ability to create necessary data more precisely. Three pieces of software-Mercury, Gaussian 09, and Gauss View 06-play a key part in this study.

Software called Gaussian is used in Windows-compatible PCs.

The primary users of this software are scientists like physicists and chemists. The needed compound's molecular structure as well as its electrostatic characteristics, thermal properties, and other qualities are predicted using fundamental laws of quantum mechanics.

Gaussian09 offers new features and performance enhancements that will enable you to model molecular systems of increasing size, with more accuracy, under a broader range of real-world conditions. Some of these features include;

Model Reactions of Very Large Systems with ONIOM.

- Study Excited States in the Gas Phase and Solution.
- Additional Spectra Prediction.
- New and Enhanced Methods and Algorithms.
- Ease-of-Use Features.
- Performance Improvements.

Gauss View is a graphical user interface made to make it easier for you to prepare input for Gaussian and to visually inspect the output that Gaussian generates. Instead of being integrated into Gaussian's computing module, Gauss View serves as a front-end/back-end processor to facilitate the use of Gaussian. Users of Gaussian can gain three key advantages from Gauss View.

- Gauss View makes it easy to set up many types of Gaussian calculations.
- Gauss View lets you examine the results of Gaussian calculations using a variety of graphical techniques.
- Gauss View offers you an advanced visualization facility.

Chapter 3
Result and discussion

3.1 GEOMETRY OPTIMIZATION

Geometry optimization is a very important step of almost all the quantum calculations that are related to the structure of molecule. The molecular geometry optimization for the molecules has been done by energy minimization using calculation method B3LYP and basis set 6-31G(d,p). The structure of 4-Hydroxy Benzamide is optimized to minimum energy. After the optimization of structure there is change in bond lengths.

This figure consists of The optimized structure of 4-hydroxy benzamide has been shown in the following fig.

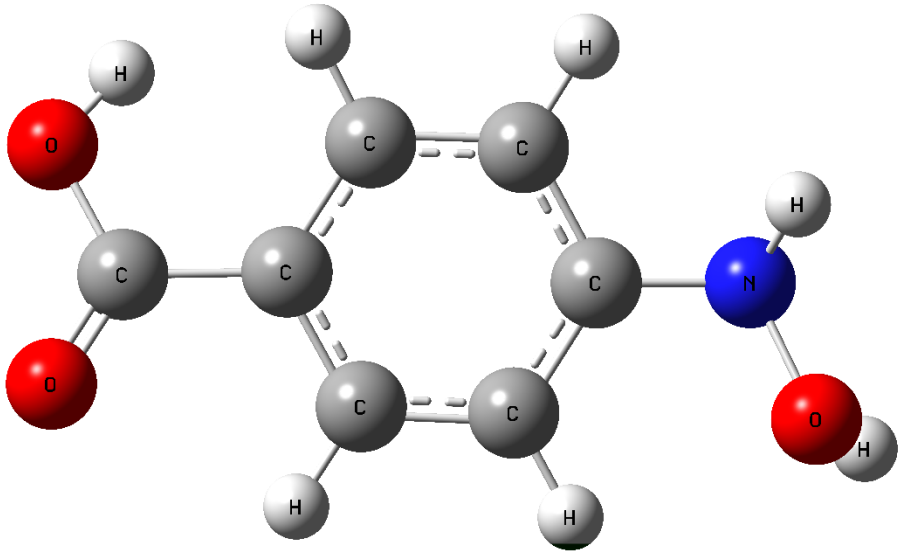

Figure 3 optimized structure of 4-hydrpxybenzamide

The ground state optimised structure of 4-Hydroxy benzamide was optimised for geometry in unessential internal coordinates, as illustrated in the relevant figures above. At DFT, initial geometry for 4-hydroxy benzamide was reduced using B3LYP and a basis set of 6-31G(d,p).

The optimised 4-hydroxy benzamide structures have molecular energies of – 551.34468295 a.u. The dipole moment was 6.3047 Debye.

3.2 ELECTROSTATIC POTENTIAL

A highly helpful characteristic or quantity to describe charge transfer and polarisation within molecules is the electrostatic potential. The explanation of reactivity, the analysis of the hydrogen bonds between electrons, and electrophilic and nucleophilic characteristics. Chemical reactions are expected to happen in these procedures. Using a basis set of 6-31G(d,p) and the B3LYP technique, the electrostatic potential of 4-Hydroxy Benzamide is calculated. The 4-Hydroxy benzamide's electrostatic potential is depicted in the following figures.

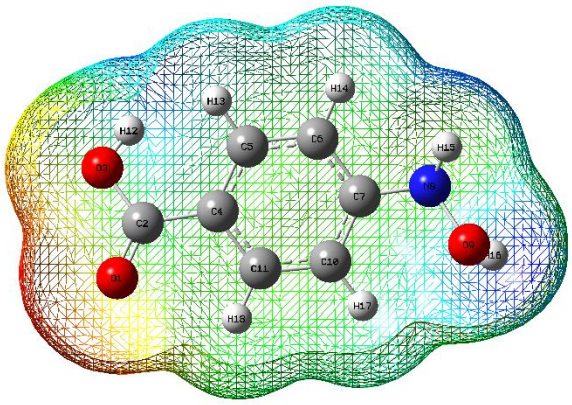

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Figure 4 Electrostatic potential

The hydroxyl group (-OH) in 4-Hydroxybenzamide is likely to have a slightly negative electrostatic potential due to the electronegativity of oxygen. Oxygen is more electronegative than hydrogen, so it attracts electrons more strongly and develops a partial negative charge. The amide group (-CONH2) consists of a carbonyl group (C=O) and an amino group (-NH2). The carbonyl oxygen in the amide group is also electronegative, resulting in a partially

negative charge. The amino group is expected to have a partially positive charge. Overall, the electrostatic potential of 4-Hydroxybenzamide may show areas of relatively high electron density around the hydroxyl and carbonyl oxygen atoms, indicating a negative potential, and areas of relatively low electron density around the amino group, indicating a positive potential.

The ESP maps enable visualization of a complex's variously charged regions. The interactions between two molecules are governed by their respective charge distributions. The Figures show the B3LYP-mapped ESP of 4-Hydroxy benzamide, which explains the charge distributions of the molecule in three dimensions. The surface of the figure displays various colours that correspond to various electrostatic potential levels. The colours zero, most electronegative and most positive electrostatic potential are represented by green, red, and blue, respectively. Potential drops from blue to green to yellow to orange to red. Blue colour indicates a high attraction, while red colour indicates a high repulsion.

3.3 HOMO LUMO

Highest occupied molecular orbitals (HOMO) and lowest unoccupied molecular orbitals (LUMO) of 4 hydroxybenzamide were determined using B3LYP functional and 6-31G(d,p) basis set. We may, however, give a broad explanation of what the HOMO and LUMO orbitals signify. The lowest energy level an electron can occupy in a molecule is represented by the LUMO (lowest unoccupied molecular orbital), while the highest occupied molecular orbital (HOMO) depicts the greatest energy level an electron can inhabit in a molecule.

The HOMO-LUMO gap, or the energy difference between the HOMO and LUMO orbitals, is a crucial characteristic of a molecule since it can reveal information about the molecule's reactivity, including its capacity for chemical reactions or its electrical characteristics.

In the case of 4-hydroxybenzamide, the HOMO and LUMO orbitals would depend on the specific conformation and electronic structure of the molecule. Therefore, a quantum chemical calculation would be necessary to obtain an accurate calculation of the HOMO-LUMO gap and corresponding energies. Figure illustrates the HOMO-LUMO energy gap, which reveals the chemical reactivity of the molecule.

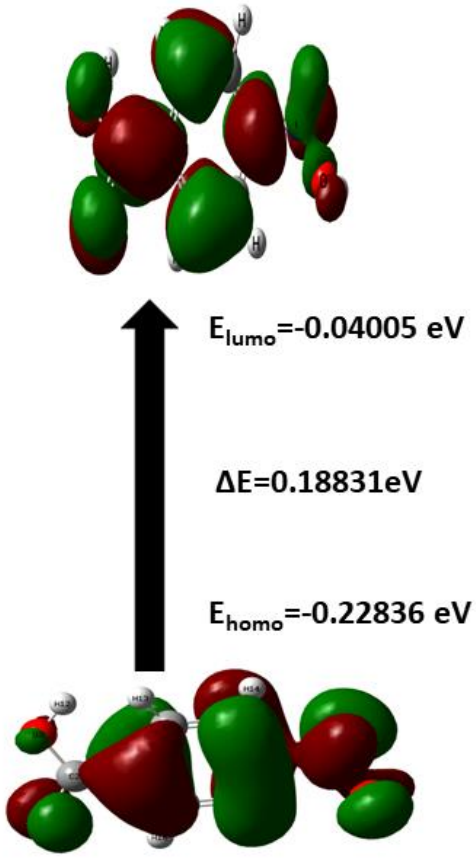

Figure: 5 Homo Lumo energy representation

The hardness of a molecule can be correlated with its stability; a lower stability (smallgap) denotes a softer and more chemically appealing molecule. Figure 5 depicts the orbital for the aforementioned molecule's homo and lumo atoms. A small gap suggests weak stability, while a wide distance suggests strong stability. A molecule with a large homo lumo gap is highly polarisable (reactive) and is typically associated with a low degree of chemical stability. The difference in energy between lumo and homo is 0.18831eV.

3.4 Global Reactivity Descriptors

DFT computation makes it feasible to define and make clear the chemical reactivity theories. Global DFT characteristics such as the chemical potential (μ), hardness (η), softness (s), and electronegativity (χ). The investigation of the molecule's reactivity by () and the electrophilicity index (ω) has successfully established this. Global DFT descriptors were derived using the following formula inside the DFT theoretical framework.

$$\textbf{Electronegativity } (\chi) = -\frac{1}{2}(E_{HOMO} + E_{LUMO})$$

$$\textbf{Chemical Potential } (\mu) = -\chi = \frac{1}{2}(E_{HOMO} + E_{LUMO})$$

$$\textbf{Global Hardness } (\eta) = \frac{1}{2}(E_{HOMO} - E_{LUMO})$$

$$\textbf{Softness } (S) = \frac{1}{2\eta}$$

$$\textbf{reactivity index } (\omega) = \frac{\mu^2}{2\eta}$$

This novel reactivity index (ω) gauges the energy stabilisation that occurs when the system picks up more environmental electronic charge (ΔN). The maximum electronic charge (ΔN_{max}) that an electrophile can take in from its environment is defined as:

$$\Delta N_{max} = -\frac{\mu}{\eta}$$

Table: lists the calculated values for the AMP's HOMO, LUMO, energy band gap, chemical potential, electronegativity, global hardness, global softness, and global electrophilicity index.

Molecule	E_H (eV)	E_L (eV)	E_H-E_L (eV)	χ (eV)	μ(eV)	η(eV)	S (eV)	ω(eV)	ΔN_{max}

4HBAM(CO-Former)	-0.22836	-0.04005	-0.18831	0.134205	-0.134205	-0.094155	-5.31039	0.095645	-1.42536

Table contains the energies of the 4-hydroxybenzamide's frontier molecular orbitals (E_{LUMO}, E_{HOMO}), energy band gap (E_{LUMO}-E_{HOMO})χ, μ, η, S, and ω . A excellesnt indicator of a molecule's chemical stability is its chemical hardness (η) and softness (S). Hard molecules are those that have a big energy gap, whereas soft molecules are those that have a small energy gap. In comparison to hard molecules, soft molecules are more polarizable. While S gives a measure of a molecule's electrophilic reactivity, the is a direct indicator of a molecule's electrophilic stability. The value of χ, μ, η, S, and ω for 4-Hydroxy benzamide is 0.134205 eV,-0.1.4205 eV,-5.31039 and 0.095645 eV.

3.5 Molar refractivity (MR)

According to the mass, charge, and polarizability of the molecule, MR indicates the dispersivity of the valence electrons. The London dispersive force and molecule volume, which are involved in ligand-receptor interactions, are also connected to MR. This characteristic is crucial for determining the biological action of 4-Hydroxy Benzamide. The subsequent range for (MR) is 40 to 130 e.s.u. with an average value of 97.61. According to the levels of theory B3LYP6-31G(d,p), the MR for 4-Hydroxy Benzamide is 23.548 e.ss.u. respectively. The polarizability and reactivity of 4-Hydroxy Benzamide in this case are caused by this value of MR, which is a crucial characteristic from a pharmacological perspective.

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CONCLUSION

This project optimised the electro-static potential and total density of 4-hydroxybenzamide to produce the most stable structure possible. Density Functional Theory is the methodology applied in this project. Geometrical refinement utilising the Gaussian 09 software package. of the 4-Hydroxy benzamide. As we can see, 4-Hydroxy benzamide is a generic version of the drug that is readily available today. The characteristics of 4-hydroxybenzamide, both physically and chemically, are well known. The conclusion was that 4-Hydroxybenzamide is thermodynamically stable.

Given that this medication is readily available and reasonably priced, it is possible to predict that an increase in 4-Hydroxy benzamide's purity will aid in the field of medical sciences in the near future.

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