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Investigation of UV-Visible Absorption Quantum Effects Doped of Norepinephrine, Mg^{+2} Atom by Using DFT Method

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ABSTRACT

The research focused on investigating and optimizing the interaction of the hormone Norepinephrine (Noradrenaline), which acts as a neurotransmitter, with Mg^{+2} atoms at the molecular level. To do this, we used GaussView 6.0.16 to generate the molecular structure. Then, it employed Gaussian 09: AS64L-G09RevD.01 program to optimize the molecular structures of Norepinephrine using the DFT method and SDD basis set, and the Mg atom doped molecule using the DFT method and LanL2MB basis set. Various quantum mechanical calculations were conducted on the molecule, including Fourier Transform Infrared spectroscopy (FT-IR), Nuclear Magnetic Resonance Spectroscopy (NMR), HOMO-LUMO structure with the energy level diagram, UV-visible absorption, and density of states (DOS). These calculations provide important insights into the behavior and properties of the Norepinephrine-Mg^{+2} complex at the molecular level.

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1. Introduction

Norepinephrine, also known as noradrenaline, is a hormone and neurotransmitter that occurs naturally in the body. It is synthesized in the locus coeruleus region of the brain and the sympathetic nervous system [1]. Its main function is as a neurotransmitter, facilitating communication between nerve cells in the brain. During stress and arousal, norepinephrine is released in higher quantities and spreads throughout the body along nerve fibers [2]. This hormone plays a crucial role in stress responses, alertness, attention, focus, and various cognitive processes. Additionally, it regulates blood pressure and constricts blood vessels. When faced with a stressful situation, norepinephrine release leads to an increase in blood pressure and heart rate, preparing the body for potential danger. This response is known as the "fight or flight" response. Moreover, norepinephrine aids in memory formation and maintenance due to its stimulating effects. It also has a significant role in regulating emotional states and moods. On the other hand, Magnesium (Mg) is an essential mineral that plays a vital role in various biochemical reactions within the body. It is involved in regulating crucial functions such as nervous system activity, muscle contractions, energy production, protein synthesis, and DNA replication [3]. In this study, the researchers opted for the SDD basis set in conjunction with the DFT method to analyze the Norepinephrine molecule most effectively. Additionally, they used the same method and the LanL2MB basis set to study the Mg-doped Norepinephrine molecule, which provided the most optimal representation of the complex.

2. Material And Method

Norepinephrine Molecule Structure and Function

Magnesium (Mg) is a crucial mineral necessary for numerous biochemical reactions in the body. It actively participates in various enzymatic reactions and plays essential roles in numerous biological processes [4]. The functions of magnesium encompass the regulation of vital processes, including those related to the nervous system, muscle contractions, energy production, protein synthesis, and DNA replication. Fig. 1(b) depicts the formation of a norepinephrine-magnesium complex, which occurs when magnesium (Mg) is bonded to the norepinephrine molecule [4]. This complex represents a structural arrangement resulting from the combination of the norepinephrine molecule with a magnesium ion.

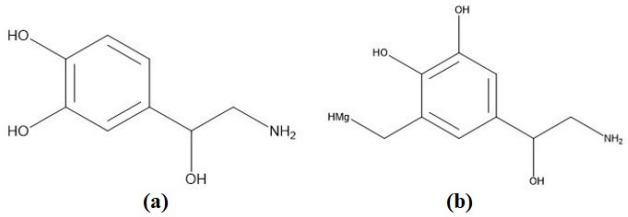


Figure 1. Skeletal formula of **(a)** Norepinephrine **(b)** Mg-Norepinephrine by ChemOffice drawing

3. RESULTS AND DISCUSSIONS

3.1. Geometry Optimization

The molecular structure was generated using GaussView 6.0.16 [5]. Theoretical calculations were conducted using the Norepinephrine molecule Gaussian 09: AS64L-G09RevD.01 program package [6]. The optimized version of the molecule, shown in Fig. 2(a), underwent a process where 9H hydrogen atoms were removed, and the Mg atom was bonded, as illustrated in Fig. 2(b).

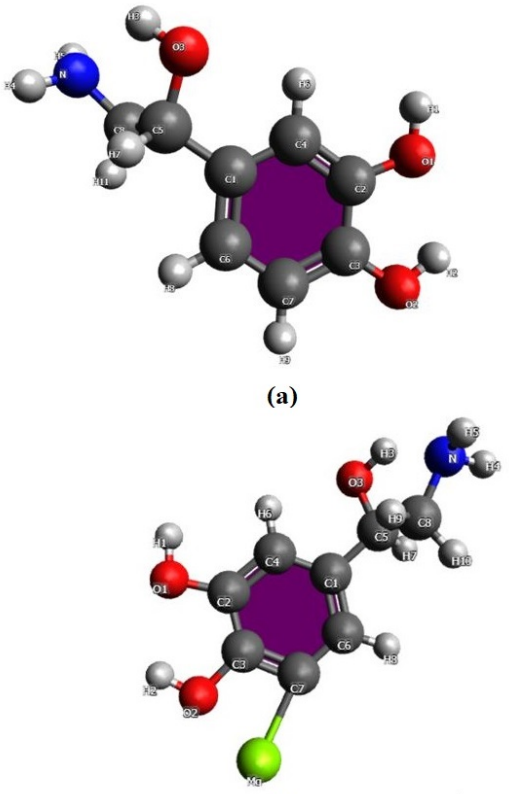


Figure 2. Optimize structure of **(a)** Norepinephrine **(b)** Mg-Norepinephrine

3.2. Frontier Molecular Orbital Analysis (FMO)

The forbidden energy gap refers to the range of energy levels in a molecule where electrons can be found. When Mg is attached to the norepinephrine molecule, there is a decrease of 2.991 eV in the E energy gap. This reduction in the forbidden energy gap is linked to the transition of electrons to lower energy levels. The smaller forbidden energy gap makes electronic transitions in the molecule easier, increasing the likelihood of changes in its electronic structure [7]. Additionally, this reduction can lead to alterations in the optical, electronic, or magnetic properties of the molecule [8, 9]. Fig. 3 illustrates that binding Mg to the norepinephrine molecule causes changes in its molecular structure, geometry, or bond lengths, resulting in the decrease of the forbidden energy gap. The descriptors in Table 1 are all calculated using quantum chemical methods. These methods are based on the Schrödinger equation, which describes the behavior of electrons in atoms and molecules. The descriptors in Table 1 provide information about the electronic structure of Norepinephrine and Mg doped Norepinephrine.

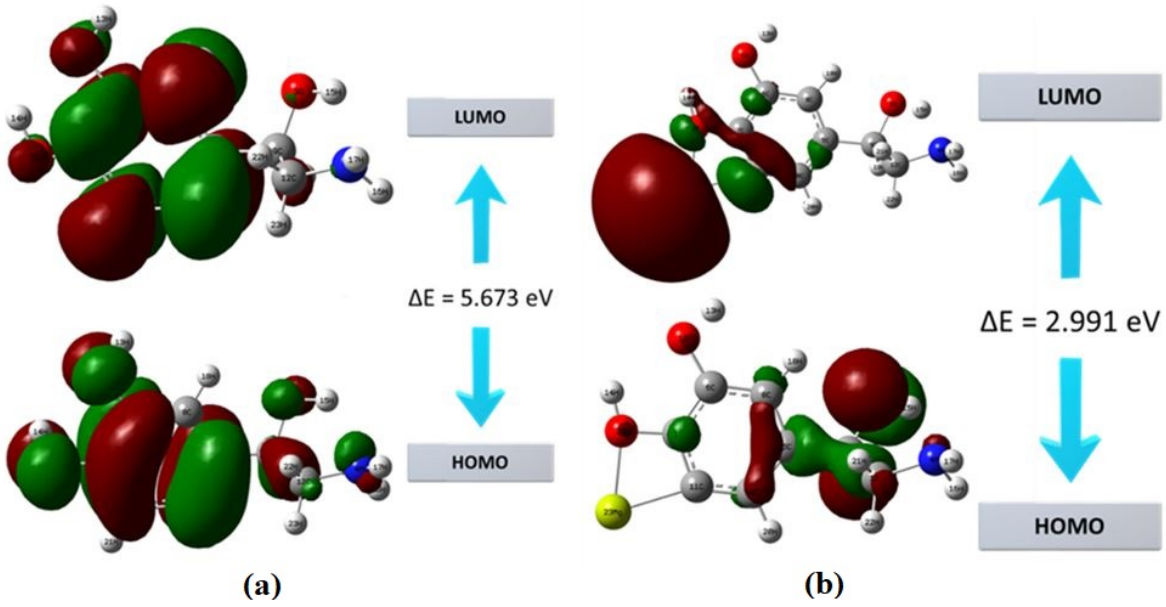


Figure 3. HOMO-LUMO structure with the energy level diagram of **(a)** Norepinephrine **(b)** Mg-Norepinephrine

Table 1. The calculated quantum chemical descriptors for Norepinephrine and Mg doped Norepinephrine

Compound	Norepinephrine	Mg doped Norepinephrine
E_{HOMO} (eV)	-5.741	-3.014
E_{LUMO} (eV)	-0.068	-0.023
ΔE (eV)	5.673	2.991
η (eV)	2.836	1.496
σ (eV^{-1})	0.352	0.669
χ (eV)	-2.904	-1.519
μ (eV^{-1})	2.904	1.519
ω	1.486	0.771
ε	0.672	1.297
ω^+	0.389	0.199
ω^-	3.293	1.717

3.3. Vibrational Spectroscopic Analysis Spectrum

Vibrational spectroscopic analysis is a technique that uses the absorption of infrared or Raman radiation to study the vibrations of molecules. The spectra produced by this technique can be used to identify molecules, determine their structure, and study their interactions with other molecules [10]. The vibrational spectrum of a molecule is a plot of the intensity of the absorbed radiation versus the wavenumber of the radiation[11]. The wavenumber is a unit of frequency that is inversely proportional to the wavelength of the radiation. The peaks in the spectrum correspond to the absorption of radiation by the molecule at specific wavenumbers. These peaks are caused in the molecule by the vibrations of the atoms [12]. The vibrations of a molecule can be classified into two types: stretching vibrations and bending vibrations. Stretching vibrations occur when the atoms in a molecule are pulled apart and then brought back together. Bending vibrations occur when the atoms in a molecule are bent or twisted [13]. The wavenumber of a vibrational peak in a spectrum is determined by the strength of the bond between the atoms that are vibrating and the mass of the atoms. The stronger the bond, the higher the wavenumber of the peak. The heavier the atoms, the lower the wavenumber of the peak. Vibrational spectroscopic analysis is a powerful tool for studying molecules. It can be used to identify molecules, determine their structure, and study their interactions with other molecules. This technique is used in a wide variety of fields, including chemistry, biology, and materials science [14].

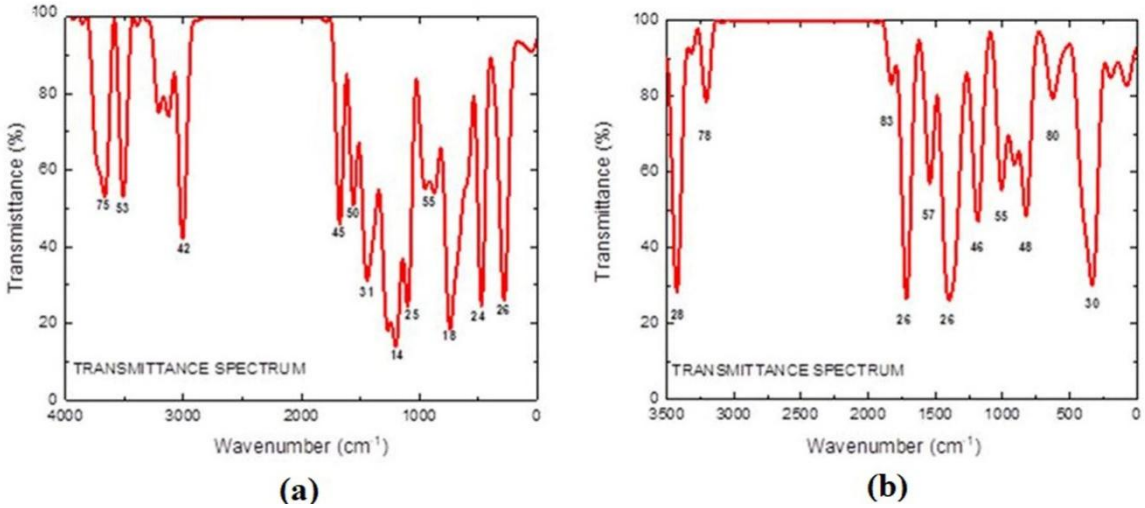


Figure 4. FT-IR analysis of **(a)** Norepinephrine **(b)** Mg-Norepinephrine

When Mg is introduced as a dopant into the molecule, FTIR analysis yields spectra within the range of 3500 cm-1 -0 cm-1 (Fig. 4b.). This energy range spans from 3424 cm-1 to 1712 cm-1 in wave numbers, while the transmittance values range from 28% to 26%. The incorporation of Mg into the molecule leads to an expansion of the energy range. This expansion is attributed to the influence of Mg on the molecule's vibration, electron affinity, translation, and rotation, which arise from the binding energy of Mg. Moreover, the formation of complexes between Mg and the neurotransmitter molecule results in an increase in peak intensity due to their interactions. The presence of relatively broad and significant shifts in wave numbers suggests the formation of norepinephrine and Mg-doped complexes.

3.4. Nuclear Magnetic Resonance Spectroscopy

NMR spectroscopy utilizes the chemical shift, measured in parts per shielding (ppm), to observe changes in resonance frequency due to environmental influences within a magnetic field. Tetramethylsilane (TMS) serves as a reference compound, with its chemical shift assumed to be zero. Chemical shifts provide crucial information about the chemical environment, electron distribution, and molecular structure of atoms. Peaks in NMR plots correspond to resonance frequencies of nuclei, each representing signals from specific atoms or groups of atoms [15]. Peak height reflects signal intensity, varying with the number of nuclei and environmental influences. Peak width indicates signal distribution and interactions. Analyzing chemical shift values helps identify functional groups and atomic bonds. Peak intensities reveal the abundance or concentration of nuclei, with greater intensity indicating more significant contributions from specific regions. Comparing intensities helps determine the proportions of different groups or bonds in the molecule. The shape and width of peaks offer insights into molecular structure [16]. Narrow, pointed peaks suggest a homogeneous environment, while peak width indicates interactions between nuclei. Doublet (multiple) peaks indicate interconnected nuclei. Analyzing peak shape and width provides information about linkages, transformations, or structural changes in the molecule. Integral analysis involves measuring the area under peaks, proportional to the number of nuclei. By using integral values, one can determine the number and proportions of different groups in the molecule. This comprehensive analysis of NMR spectra aids in understanding the chemical environment and structure of molecules.

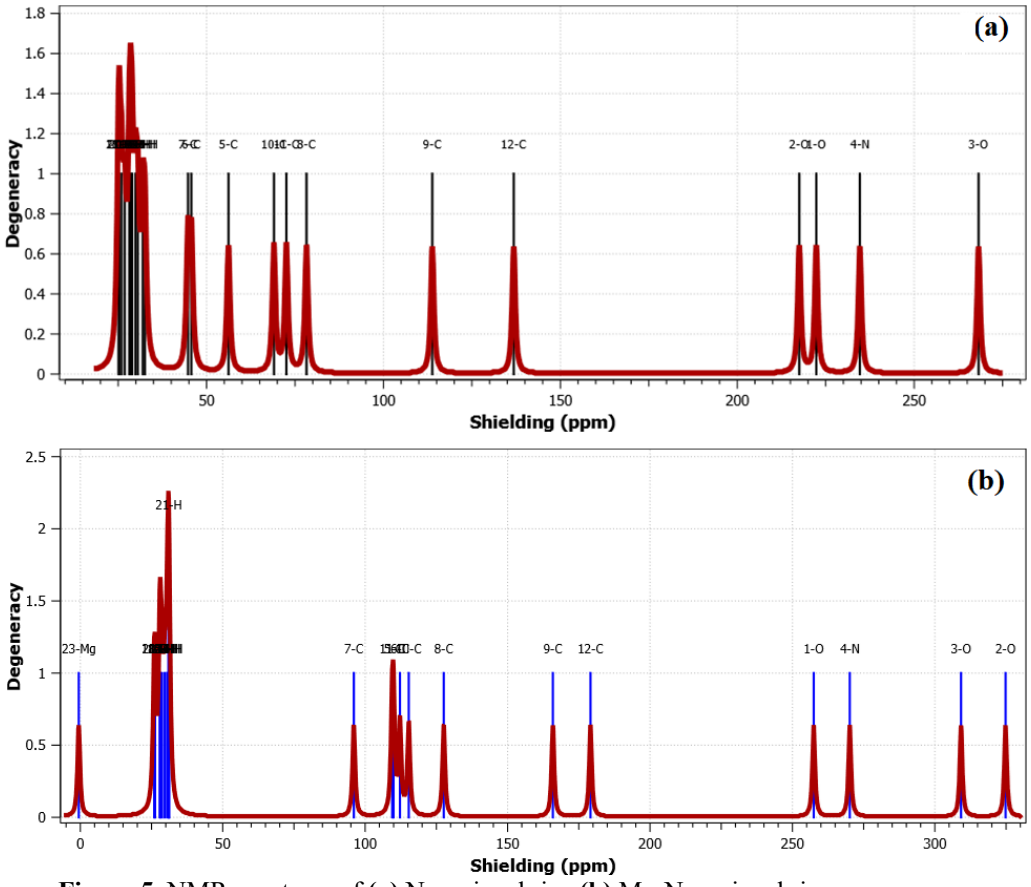


Figure 5. NMR spectrum of **(a)** Norepinephrine **(b)** Mg-Norepinephrine

Table 2. Chemical shifts of Norepinephrine, Mg-Norepinephrine

Norepinephrine		Mg-Norepinephrine	
Method	**Shielding (ppm)**	**Method**	**Shielding (ppm)**
18-H	25.0966	23-Mg	-0.5393
21-H	25.3305	18-H	25.9535
20-H	25.9606	20-H	26.2363
14-H	26.8605	14-H	27.8822
15-H	28.1527	15-H	28.0716

19-H	28.5211	13-H	28.6807
13-H	28.9583	19-H	29.6434
23-H	29.903	22-H	30.4664
22-H	30.5651	17-H	30.9342
17-H	31.9338	21-H	30.9348
16-H	32.547	16-H	31.2282
7-C	44.743	7-C	96.0262
6-C	45.6936	11-C	109.5134
5-C	56.1802	5-C	109.9545
10-C	69.0409	6-C	112.2257
11-C	72.5559	10-C	115.3106
8-C	78.2376	8-C	127.5997
9-C	113.8041	9-C	165.9033
12-C	136.8239	12-C	179.1126
2-O	217.5328	1-O	257.4745
1-O	222.3375	4-N	270.128
4-N	234.662	3-O	309.1903
3-O	268.2187	2-O	324.819

The NMR spectra of the two molecules are depicted in Fig. 5, while the calculated chemical shift values are presented in Table 2. These values correspond to the shielding positions of the constituent atoms within the molecule. It is evident from the table and graph that the sudden peaks in the graph indicate the locations of distinctive features within the molecular structure. For norepinephrine, sudden peaks are observed for atoms H18, H21, H20, H14, H15, H19, H13, H23, H22, H17, and H16. In the case of Mg-doped norepinephrine, the sudden peaks appear for atoms H20, H18, H14, H13, H19, H15, H21, H22, H17, and H16. Both norepinephrine and magnesium-doped norepinephrine share common atoms exhibiting these sudden peaks. However, H23 is absent in Mg-doped norepinephrine, as it is replaced by a Mg atom, which accounts for the difference.

3.5. UV–Visible analysis

UV-Visible analysis, also known as UV-Vis spectroscopy, is a technique used to study the absorption and transmission of ultraviolet (UV) and visible (Vis) light by a substance. It provides valuable information about the electronic structure and properties of molecules. In UV-Visible analysis, a sample is exposed to light within the UV and/or visible range, and the amount of light absorbed or transmitted by the sample is measured [17]. The principle behind UV-Visible analysis is based on the absorption of photons by molecules. When photons with energies corresponding to the UV or visible region interact with the sample, electrons in the molecules can undergo electronic transitions, moving from lower energy levels to higher energy levels. The energy difference between the electronic levels determines the wavelength of light absorbed. The absorbed light results in a decrease in the intensity of the transmitted light, which is measured using a spectrophotometer.

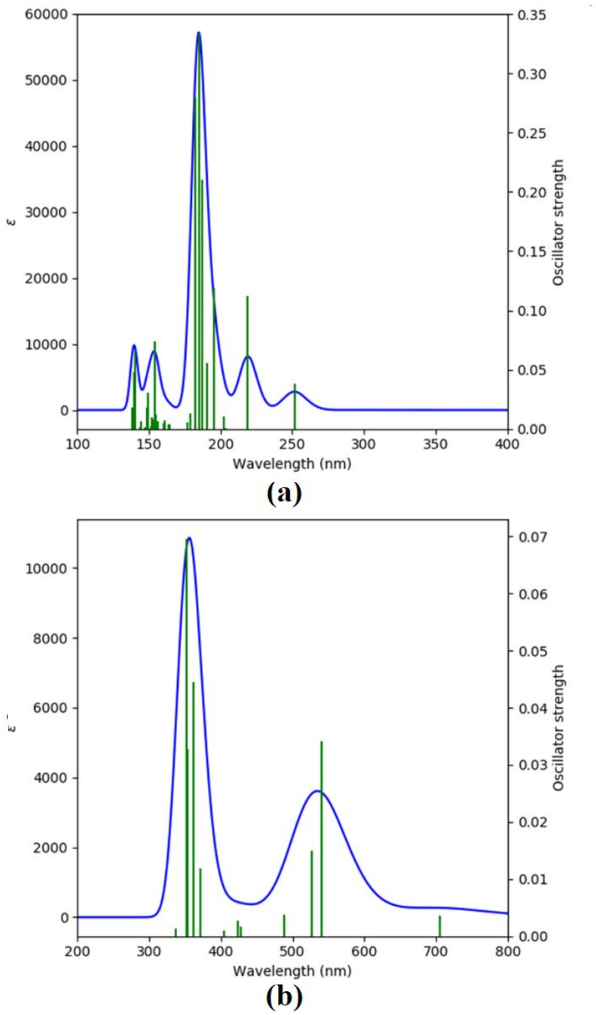


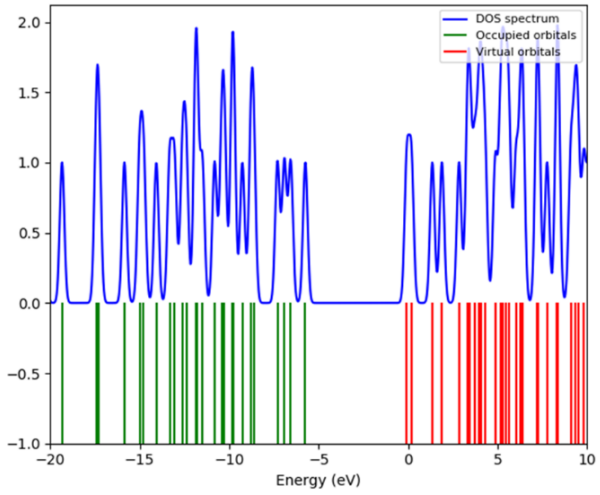
Figure 6. UV-Visible absorption of **(a)** Norepinephrine and **(b)** Mg-Norepinephrine

Fig. 6 displays the UV-visible absorption spectra of the compounds. In the case of Norepinephrine, its UV absorption spectrum spans a wavelength range of 100 nm to 400 nm. The peak absorption occurs at 175 nm, which falls below 200 nm and is considered hazardous due to its association with high-energy radiation. As for norepinephrine, its absorption spectrum extends from 200 nm to 800 nm, with the highest peak observed at 345 nm. Within the range of 200-800 nm, there is absorption

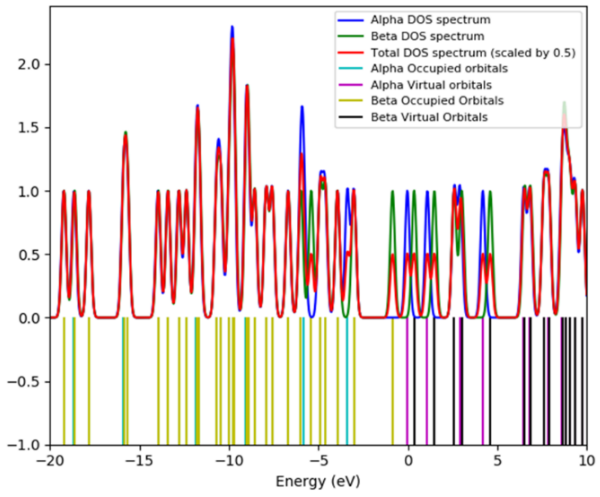
indicating the presence of double or triple bonds within the molecule, specifically in conjugated systems.

3.6. Density of States (DOS)

The Density of States (DOS) was calculated using the GaussSum program, and the resulting DOS is displayed in Fig. 7. The DOS spectrum provides information about the molecular orbital contributions from different components of the compound's entire system [18]. In the spectrum, the HOMO (Highest Occupied Molecular Orbital) and LUMO (Lowest Unoccupied Molecular Orbital) levels are represented by the blue and green lines, respectively. The spatial redistribution of electron density, depicted in a three-dimensional manner, shows the boundary trajectories, and provides insights into the local density of states [19]. The DOS spectrum is useful for confirming the variation in the HOMO-LUMO energy range [20]. It calculates the number of available positions at specific energy levels. On the energy axis of the graph, the occupied and filled orbitals are represented by the initial lines ranging from -20 eV to 10 eV, while the virtual and unfilled orbitals are represented from -5 eV to 0 eV. These occupied and virtual orbitals can also be referred to as donor and acceptor orbitals, respectively. A high density of DOS at a particular energy level suggests the presence of numerous available positions for occupancy. Conversely, a zero density of DOS indicates the absence of any states that the system can occupy.



(a)



(b)

Figure 7. The density of states (DOS) with the contribution of **(a)** Norepinephrine **(b)** Mg-Norepinephrine

4. Discussion

The doping of magnesium into norepinephrine resulted in several notable observations. Firstly, the formation of the Mg-Norepinephrine complex led to an increase in the HOMO-LUMO value, indicating a higher level of chemical stability in the compound. This suggests that the electrons in the complex have a reduced ability to transfer energy to higher energy levels. The increased stability implies that the interaction of the reactants becomes more difficult, making the molecule less reactive. This makes the compound a "hard" molecule in terms of chemical reactions. In terms of Nuclear Magnetic Resonance (NMR) analysis, there were no distinctive features observed for the Mg atom, as it behaved similarly to a carbon (C) atom. The presence of hydrogen (H) atoms, with their single proton and electron spin, did not provide any distinguishing characteristics. However, the nearby carbon (C) and oxygen (O) atoms exhibited more significant changes in their behavior compared to others. Overall, the doping of Mg into norepinephrine resulted in a chemically stable compound with reduced reactivity. The Mg atom did not exhibit distinct features in Nuclear Magnetic Resonance (NMR) analysis, behaving similarly to a carbon atom. The nearby C and O atoms showed more noticeable changes.

UV-Visible analysis of the Mg-doped norepinephrine revealed significant findings. The presence of Mg in the compound resulted in notable changes in the absorption spectra compared to pure norepinephrine. The UV-Visible analysis indicated a shift in the absorption peaks towards higher wavelengths, suggesting a redshift in the electronic transitions. This shift indicates a modification in the electronic structure of the compound due to the interaction between magnesium and norepinephrine. The redshift in the absorption peaks can be attributed to the formation of a complex between Mg and norepinephrine, which alters the energy levels and electronic transitions within the compound. The interaction between Mg and the aromatic ring in norepinephrine likely plays a significant role in these observed changes. Furthermore, the intensity of the absorption peaks may also vary due to the presence of magnesium. This indicates that the electronic coupling between magnesium and norepinephrine affects the overall absorbance of the compound. Overall, UV-Visible analysis demonstrates that the doping of Mg into norepinephrine causes significant changes in the absorption spectra, indicating alterations in the electronic structure and electronic transitions of the compound. These findings provide valuable insights into the interaction between Mg and norepinephrine, shedding light on the chemical behavior and properties of the Mg-doped compound.

Competing interests

The authors declare that they have no competing interests.

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