RESEARCH PAPER

Adsorption of Bupropion on C60 Nanocage: Thermodynamic and Electronic Properties

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ABSTRACT

Bupropion is a drug primarily used for treating major depressive disorder and helping smokers quit smoking. Bupropion is a fairly effective antidepressant, but it leads to restlessness and palpitations at relatively high doses. In addition, it is used as an adjunct in cases where the patient has an incomplete response to first-line SSRI antidepressants. Bupropion is also the only drug approved for seasonal affective disorder. In the present work, the properties of bupropion related to reactivity and the chemical structure regarding its medicinal properties were obtained in the adsorption process of bupropion on fullerene (as an adsorbent) in the gas phase using DFT / B3LYP / 6-311 + G (d, p). Further, the adsorption phenomenon on the fullerene molecule was chemically studied and the adsorption energy was calculated. Chemical structure parameters including dipolar moment (μ=1.2151), thermodynamic properties including Gibbs free energy (G=-2879.11 kJ), enthalpy (H=-2879.45 kJ), entropy (+75.26 kJ/mol) as well as thermodynamic capacity (98.32 kJ/mol)), and electronic parameters (σ (0.51), μ(-4.06), ω(4.20), χ(4.06), and η(1.96) all data in eV) which are effective in justifying the chemical behavior of the compound were calculated. Calculating stability and reactivity by HOMO (-6.03 eV) and LUMO (-2.03 eV) bupropion energies, five chemically active regions for bupropion were found, all of which had thermodynamic stability. This study indicated that his adsorption helps to transfer bupropion to biological systems.

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INTRODUCTION

One of the psychoactive substances which is commonly used worldwide is alcohol. The 12-month prevalence of alcohol consumption in European countries such as Spain has recently been 94.1% among its population aged 15-64 years [1]. Bupropion is in commercial use under the approval of the FDA for depression, cessation of smoking, and lose of weight. At present, some effects of this medication includes inhibiting the reuptake of norepinephrine and dopamine as well as inhibiting cation-selective Cys-loop ion channels such as nicotinic acetylcholine and serotonin type 3 A (5-HT3A) receptors.

This paper aimed to evaluate the ability of bupropion to inhibit the 5-HT3A receptor, which belongs to the superfamily of pentameric ligand-gated ion channels which includes nicotinic acetylcholine, g-aminobutyric acid type A (GABAA), as well as glycine receptors. Five homologous subunits around a central ion channel pore make the above-mentioned channels. Extracellular, transmembrane, and intracellular domains make up every subunit. Any dysfunction of this superfamily is associated with neurological problems, including anxiety, depressive disorders, epilepsy, Alzheimer's and Parkinson's diseases.

Recently, clinical targeting of the 5-HT3 receptor has been conducted using anti-emetics

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and irritable bowel syndrome therapies. In addition, this receptor may be targeted to treat anxiety, psychosis, and bipolar disorder, along with some other neurologic complications. Engineering amino acids were carried out in the a-helical M2 and M3 transmembrane segments around the M2M3 loop at the transmembrane and extracellular domains interface. Docking investigations and site-centered mutagenesis were employed in the analysis of binding site residues for bupropion. The impacts of mutations on inhibiting bupropion in these engineered 5-HT3A channels whose expression happens in Xenopus oocytes were examined using two-electrode voltage-clamp recordings [2].

In the United States, for one example, significant economic and social burdens are incurred by methamphetamine, with approximately the total annual cost of 23 billion dollars [3]. The first approval for the clinical application of bupropion, which inhibited the reuptake of norepinephrine and dopamine, was in 1989. Applying the immediate release (IR) and sustained-release (SR) methods was common with two and three doses a day before introducing the bupropion extended-release (XL) method with one dose a day in 2003 [4].

Computational chemistry is a branch of theoretical chemistry which can predict the structure, energy, and other known or unknown properties of molecules. Digital computers which simulate chemical systems must be used for calculations. On the other hand, not all computational methods are suitable for studying a molecule. Therefore, first, a suitable theoretical method should be selected for studying a molecule. In computational chemistry, systems that are precisely solvable are single- or two-particle systems, in which a two-particle system can be transformed into two single-particle problems using a center-mass coordinate system. In the case of multi-particle systems, mathematical calculations are very complex and lengthy.

Buckyball (C60) has been used as an absorbent [5] for several poisonous and nonpoisonous chemicals [6] in dies [7] as well as wastewater [8-11]. Theoretical calculations of field studies [12], including nanocage[5], were all conducted using density functional theory [12-16] and molecular dynamic calculation [17-20].

The present research utilized buckyball(C60) as the bupropion absorbent in the gas phase based on the density functional theory with a 6-311+G(d, p) basis set.

MATERIALS AND METHODS

Computational method

The Gaussian 03 [21] package implemented on the supercomputer was used for quantum chemical calculations. Employing the density functional theory (DFT) with three-parameter hybrid functional of Becke B3LYP and the 6-311+g(d, p) basis set aimed at optimizing the complete geometry, and measuring electric field gradient, thermodynamic characteristics, and electrical parameters. Buckyball C-C (C60 ih) was used as an absorbent in the present research. The following formula was applied for the calculation of adsorption energy:

$$E_{ads}=E_{(B\text{-}Bup)}-(E_{Bupropion}+E_{buckyball})$$

RESULTS AND DISCUSSION

Based on the results in the literature, nanocage's adoption with metallic atoms has the potential of modifying their electrical features in an efficient way, along with chemical activities and the potential for reacting [22]. Thus, B3LYP/6-311+G (d, p) was utilized to optimize all structures, including bupropion, buckyball (C60, fullerene), and adopted bupropion on buckyball in the present research. The optimized structure of bupropion is shown in Fig. 1. Bupropion has four active sites, in which there are one N, one Cl, one O, and one phenyl ring, all of which show distinct chemical and electrochemical

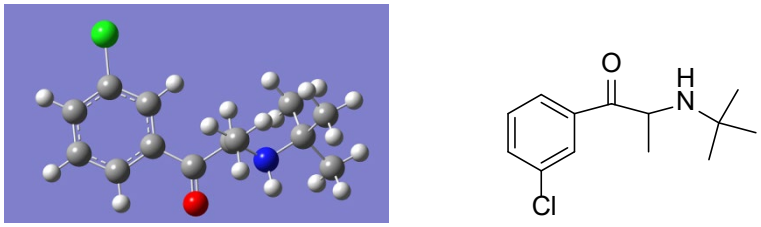

Fig. 1. Optimized structure of Bupropion by B3LYP/6-311+G(d, p)

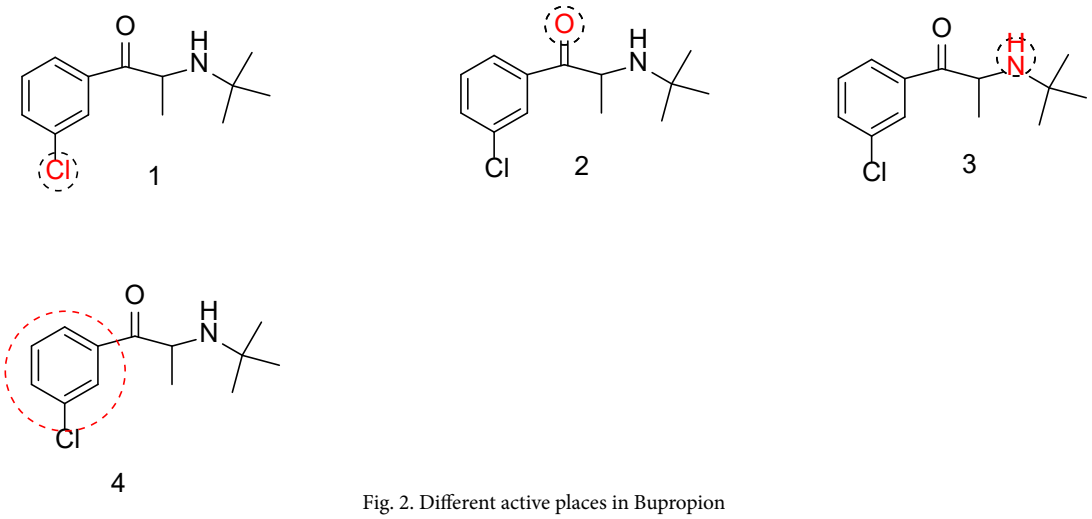

Fig. 2. Different active places in Bupropion

positions in bupropion. Additionally, its overall active positions are shown in Fig. 2 where a variety of effects are associated with the density of electrons in the chemical reactions in every position. Better behaviors can be obtained in the gas phase when one phenyl ring is present.

HOMO and LUMO energies play a significant role in chemical reactivity, and A considerable amount of LUMO energy is associated with accepting more electrons in molecules. HOMO and LUMO energies are capable of recognizing and predicting how strong and stable the chemical compounds are. Based on these frontier orbital energies, as the nearby orbitals with different energy levels, the place at which the greatest electron excitations take place shows the HOMO-LUMO bandgap energy. Especially, in the case of large chemical aromatic systems, small HOMO-LUMO band gaps lead to the mobility of π electrons; thus, the electrons are capable of jumping quickly to a higher level of energy close to themselves. Energy is distributed across the molecule and leads to more stable conditions by greater π electrons mobility in large conjugated π orbital systems.

The mobility of π electrons and good conductivity of large aromatic systems (such as graphene nanoribbons) lead to excellent semiconductors due to the small bandgap of conduction and subsequent electrical current of the electrons movement. HOMO and LUMO create an exciting dimension of chemistry, providing striking insights regarding the workings of reactions according to the interaction of orbitals to control the reaction outcomes. For example, weak electrons are supplied by HOMO energy to engage in chemical reactions. Given the bupropion HOMO energy, it can engage excellently in chemical reactions while playing the role of electron donator due to the electronegative atoms (O, Cl, N) present in its chemical structure. The data associated with the Bupropion frontier (HOMO and LUMO) orbitals are shown in Table 1.

The compound's polarity is introduced into the reaction media by dipole momentum. Based on Table 1, Bupropion dipole momentum equals 1.2152 D in the gas phase. Since electronegative atoms are present in the chemical structure of bupropion (N atom), it imposes polar effects.

Fig. 3 indicates bupropion's active position to adopt C60. All positions of C60 provide an equal chance for participation in chemical reactions due to its (ih) symmetric structure. None of the considered positions makes a difference in the reaction. Buckyball's major and optimized structure is shown in Figs. 4 and 5.

Energy is the ability to do work and supply heat. Chemical potential energy can be defined as the energy saved in the chemical bonds which is of considerable importance regarding thermodynamic characteristics and can be applied

Table 1. Energy data and dipole momentum of Bupropion by B3LYP/6-311+G(d, p)

Bupropion	gas
Energy	-2879.11 kJ
Dipole moment (Debye)	1.2152 D
HOMO	-6.03 eV
LUMO	-2.103 eV

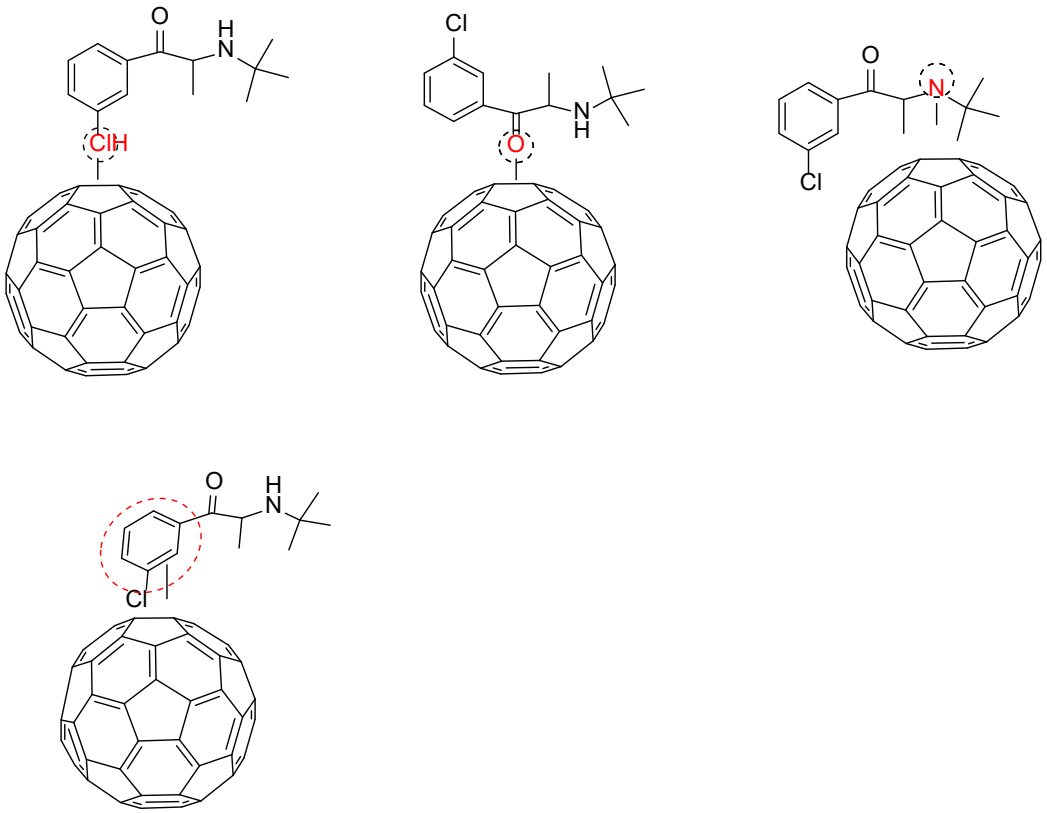

Fig. 3. Bupropion -C60 complexes in different active sides (four different positions)

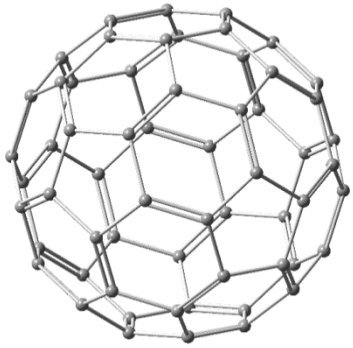

Fig. 4. Optimized structure of C60(ih) by B3LYP/6-311+G(d, p) E(-738.33kJ)

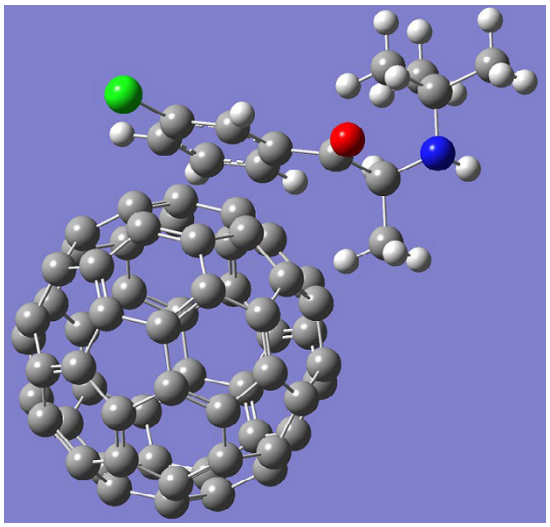

Fig. 5. The output of Bupropion-C60 complex

to different material sciences including chemistry, physics, biology, and chemical engineering. Chemical potential can be used to compute the thermodynamic parameters of materials at a specific pressure and temperature. In other words, it is possible to determine how stable the substances, chemical compounds, and solutions are by using chemical potential and considering the pressure and temperature constant. The value of 4.06- eV obtained for the chemical potential (μ) of bupropion indicates its stability in the gas phase. Negative energy reflects hidden energy in bupropion chemical bonds along with its activity.

Table 2. electronic parameters of bupropion in gas and water phase by B3LYP/6-311+G(d, p)

Bupropion	IP (eV)	EA (eV)	μ (eV)	η (eV)	χ (eV)	σ (eV)	ω (eV)
gas	6.03	2.103	-4.06	1.96	4.06	0.51	4.20

Table 3. Energy and dipole momentum in Bupropion-C60 complexes

	1	2	3	4
E(kcal/mol)	-2050.214	-2156.580	-2045.206	-2564.230
μ(D)	1.6817	1.325	1.8541	1.2879
ΔE(ads/kJ)	-4993.459	-5440.196	-4997.425	-7152.326

Losing or gaining energy by an atom due to chemical reactions produces energy. Exothermic reactions release energy while endothermic reactions absorb energy. The former results in negative energy, shown by a negative sign; however, the latter results in positive energy, denoted by a positive sign. Adding an electron to a neutral atom, which means the first electron affinity, results in releasing energy and leads to negativity. On the other hand, adding an electron to a negative ion that has the second electron affinity, needs higher amounts of energy. This case leads to the positive affinity of the second electron due to the overwhelming release of energy from the process of electron attachment.

Bupropion shows positivity regarding electron affinity energy (EA). In other words, bupropion tends to donate electrons rather than receive them. The theory of Koopman were used to extract the molecule reactivity parameters such as electronegativity (χ), softness (σ), hardness (η) and electrophilicity index (ω) with the help of the DFT technique. Power attraction of the atom or molecule obtained from HOMO and LUMO is indicated by electronegativity (χ) values. The stable and reactive conditions of chemical molecules are shown by η, and the potential of chemical molecules for accepting electrons is represented by σ. Bupropion reactivity parameters in both gas and aqua phases are shown in Table 2. Accordingly, bupropion showed a significantly stable and reactive state in chemical reactions and was adopted on C60. The energy related to the complexes of Fig. 3 can be observed in Table 3. In contrast, based on every complex dipole momentum, all active sides are also capable of acting in polar media. According to the relative adoption of energy, all active sides led to the stability of structure 4 in the chemical media. Since the position of each part of bupropion (different orientations of active positions) has a different chemical space and different dihedral angles, this is effective both in the energy of the composition and in the production of the adsorption product as a complex.

The energy of an electron in a single atom can be determined solely by the principal quantum number. However, the energy of an electron in multi-electron atoms depends on both its principal quantum number (n) and its azimuthal quantum number. This difference in energy of various subshells residing in the same shell is mainly attributed to the mutual repulsion among the electrons in a multi-electron atom. In multi-electron atoms, there is a repulsive force acting between various electrons apart from the attractive force between the nucleus and the electrons. Thus, the stability of an electron in a multi-electron atom is dependent on the total attractive and repulsive interactions. The electron in an atom is only stable when the total attractive interaction is more than the total repulsive interaction. For bigger atoms, due to the presence of electrons in the inner shells, the electrons in the outer shell are deprived of experiencing the full positive charge of the nucleus. This effect is known as the shielding of the outer shell electrons from the nucleus by the inner shell electrons. The net positive charge experienced by the outer shell electrons is termed the effective nuclear charge.

CONCLUSION

The present paper considered the chemical reactivity of bupropion and its adoption on buckyball (C60) with DFT B3LYP/6-311+G(d, p) in the gas phase. Regarding chemical structure, bupropion showed activity in terms of electronic parameters, with the ability of being adsorbed on C60 with stability. In this study, chemical structure parameters including dipolar moment (μ=1.2151), thermodynamic properties including

Gibbs free energy (G=-2879.11 kJ), enthalpy (H=-2879.45 kJ), entropy (+75.26 kJ/mol) as well as thermodynamic capacity (98.32 kJ/mol), and electronic parameters (σ (0.51), μ(-4.06), ω(4.20), χ(4.06), and η(1.96) all data in eV) ,which are effective in justifying the chemical behavior of the compound, were calculated. Stability and reactivity calculations by HOMO(-6.03 eV) and LUMO (-2.03 eV) bupropion energies, revealed four chemically active regions for bupropion , all of which represent thermodynamic stability (ΔE(ads/kJ), -4993.459, -5440.196, -4997.425,-7152.326 for the structure 1,2,3,4 respectively) and structure 4 had the highest stability. According to the obtained data, the HOMO (-2.34 eV) and LUMO (-1.53 eV) for the complex of bupropion on C60 (structure 4), and the bandgap of the complex is 0.81 eV. The electronic properties of bupropion on C60 are σ (2.47), μ(-1.935), ω(4.62), χ(1.935), and η(0.405) all data in eV. Obtained results showed that the adsorption of bupropion on C60 is satisfactory.

CONFLICT OF INTERESTS

The authors declare no conflict of interests.

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