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Computational Study of Chemical Properties of Xylometazoline and the Connected form to Fullerene (C₆₀) as a Medicine Nano Carrier

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ABSTRACT

In this research at the first, xylometazoline hydrochloride drug (XY) and its fullerene connected form (FXY) were optimized. Natural Bond Orbital (NBO) calculations for these compounds were carried out at the B3LYP/6-31G* quantum chemistry level, in the gas phase and the liquid phase. These calculations can be performed at different accuracy levels depending on the aim of the theoretical study. For instance, Density Functional Theory (DFT) can be used to calculate an accurate electronic structure, HOMO and LUMO energies, Mulliken charge of atoms, energetic orbital levels, chemical hardness, chemical potential and electrophilicity of systems, and finally chemical, physical, biological, pharmacological and industrial of fullerene and fullerene derivatives. Theoretical calculations such as NBO are very important to understand the pathways of electron transfer in assemblies. Consequently, the obtained results showed that energy orbital levels decreased considerably by linking structure of xylometazoline hydrochloride to structure of fullerene C₆₀. In the study some other characteristics such as chemical potential, chemical hardness, electrophilicity in these structures; it was found that they changed considerably. These changes show dependency of the results, on the power of electron affinity of C₆₀. In another part, the valence electrons populations for carbons, nitrogen, oxygen and hydrogen atoms in similar position for FXY and XY were compared. Finally the data were compared and discussed.

Keyword: DFT; Electrophilicity; Chemical hardness; Chemical potential; Xylometazoline Hydrochloride.

1. INTRODUCTION

In the recent years, many studies have been done on the structure of fullerene and their derivatives form to drug as medicine nano-carrier compounds. The theoretical study of the electronic structure has used to

predict physic-chemical properties of donor-acceptor systems. xylometazoline Hydrochloride is The drug works by constricting the blood vessels in the nose. The vasoconstriction means that there is less pressure

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in the capillaries and less water can filter out, thus less discharge is made [1]. (If the colour of the nasal passage is observed, it is visibly paler after dosage. Xylometazoline is an imidazole derivative which is designed to mimic the molecular shape of adrenaline. It binds to α -adrenergic receptors in the nasal mucosa [2]. Due to its sympathomimetic effects, it should not be used by people with high blood pressure, or other heart problems. Extended usage of xylometazoline can result in decreased effectiveness or a buildup of tolerance against the drug [3]. The number of receptors decreases, and when the administration of the drug is ceased, chronic congestion can occur; this is called rhinitis medicamentosa, commonly referred to as rebound congestion. Moreover long-term overdosing can cause degenerative changes in nasal mucous membranes that pose another health problem.

It is worth mentioning that, it has no significant effect on Beta Adrenergic receptors. However, it is important to study the Pentagonal ring of Imidazole activity caused by the variation of the halogen branches or Bind the nanoparticles carrier [4]. As, the Imidazole ring contain an acidic nitrogen and a base nitrogen. The study on the change or branched aryl or alkyl compound on the Carbone between two nitrogen and hydrogen within the pentagonal ring, seems to be indispensable. This can be a measure for assessing the strength of the acid compound. It is conspicuous that, the longer the bond length, the easier hydrogen dissociation occurs. This will lead to increase the acidic strength of this compound.

Xylometazoline hydrochloride is used alone or in combination with other drugs for the Function of narrowing vessels [5]. Fullerene is one of the other artificial forms of carbon element which is made by heating graphite. Due to its similarity to ball, it is called buckyball. Fullerene has different types and can be as spherical, elliptical and cylindrical. Kroto and Curl are known as discoverers of fullerene [6]. In 1990, Wolfgang Kratschmer and Donald Huffman et al described the first practical method C_{60} [7-9]. This material was prepared for the first time with formula C_{60} in 1985 by Richard Smalley, Robert Curl, James Heath, Sean O'Brien, and Harold Kroto at Rice University of Texas State [10]. Low solubility of the fullerenes in fluids limits application of these materials as medi-

nal effective material. But hydrophobic size, three-dimensionality and electron properties cause its use as medicine. For example, their spherical form causes ability and position of fullerene molecules in enzymes or cells hydrophobic solutions [11]. This action causes interesting medicinal properties which increases the rate of such characters by adding nano properties of these structures [12]. The electrophilicity concept was expressed for the first time in 1999 by Parr and et al [13]. The electrophilicity and the maximum amount of electronic charge indices are related to electronic charge; when the system acquires an additional or removal electronic charge.

The maximum amount of electronic charge index, ΔN_{\max} , describes the charge capacity of the molecule that the electrophone system may accept, it is given by (1) equation [14]. A positive value of ΔN_{\max} index (a.u.) for system indicates that acts as an electron acceptor, whereas a negative value of ΔN_{\max} index indicates that acts as an electron donor. The electrophilicity Index, ω , in atomic units is a measure of electrophilic power of a molecule it is given by (2) equation. When two molecules react with each other, one molecule behaves as a nucleophile, whereas the other one acts as an electrophile. A higher electrophilicity index shows higher electrophilic power of a molecule. So the quantity of ω describes the propensity of the system to acquire additional electronic charge from the environment, which is described by (1) equation [26]. In equations (3) and (4), μ and η are the chemical potential and the chemical hardness respectively. Both quantities may be approximated based on the energies of frontier molecular orbital's (EHOMO and ELUMO) as (equations 3 and 4). The low values of μ and η , characterize a good electrophile species [16].

$$\Delta N_{\max} = \frac{-\mu}{\eta} \quad (1)$$

$$\omega = \frac{-\mu^2}{2\eta} \quad (2)$$

$$\mu = \frac{1}{2(E_{\text{HOMO}} + E_{\text{LUMO}})} \quad (3)$$

$$\eta = \frac{(E_{\text{HOMO}} - E_{\text{LUMO}})}{2} \quad (4)$$

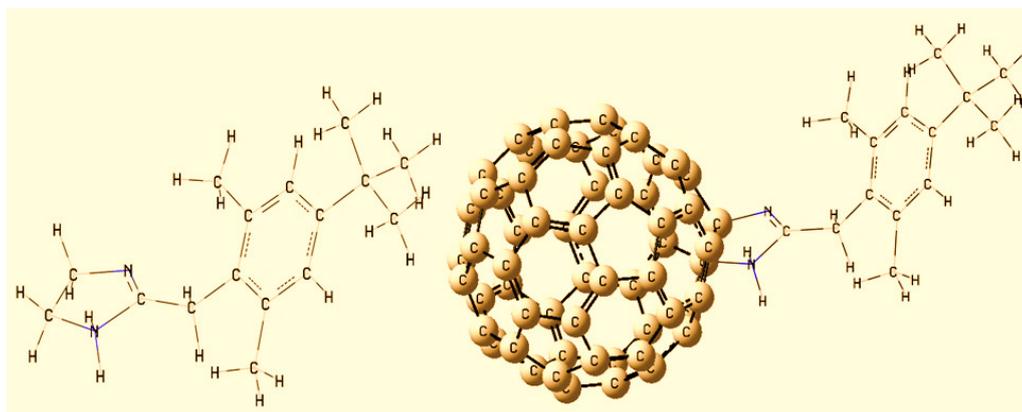


Figure 1: Show of XY and FXY obtained by B3LYP/6-31G* level of theory.

2. COMPUTATIONAL METHODS

The structures of xylometazoline hydrochloride (XY) and nano fullerene xylometazoline hydrochloride (FXY) were designed primarily using of Gauss View 3.1 and nanotube modeler 1.3.0.3 soft wares (Figure 1). The optimization and natural bond orbital (NBO) calculation were done with water solvents with Polarized Continuum Model (PCM) and then in the gas phase. Finally obtained results were compared with each other. The optimization and NBO calculations of all systems are done by density functional theory

(DFT) using B3LYP method and the standard 6-31G* basis set, by Gaussian W98 suit of programs. Total computations were done under 1 atmosphere pressure and 298 Kelvin temperature [17-18].

3. RESULT AND DISCUSSION

On the basis of these results, some separate issues such as energetic characters, electrophilicity, chemical potential, chemical hardness values were discussed of which results in this section.

Table 1: Calculated E_{HOMO} and E_{LUMO} (a.u.), chemical hardness η , chemical potential μ , electrophilicity index ω , and the maximum amount of electronic charge index ΔN_{max} in atomic units and dipole moment (Debye) for XY and FXY obtained by B3LYP/6-31G* level of theory.

	Gas Phase		Liquid Phase	
	XY	FXY	XY	FXY
HOMO (a.u.)	-0.409	-0.378	-0.322	-0.288
LUMO (a.u.)	-0.007	-0.107	0.130	-0.019
HLG (a.u.)	0.402	0.271	0.452	0.269
Hardness (a.u.)	0.402	0.271	-0.096	-0.1535
Chemical Potential (a.u.)	-0.208	-0.243	-2.6041	-0.1628
Electrophilicity (a.u.)	-11.949	-0.668	-35.319	8.6401
ΔN_{max} (a.u.)	0.517	0.895	-27.1260	-10.610
Dipole moment (Debye)	10.4741	18.5391	22.1082	16.4857

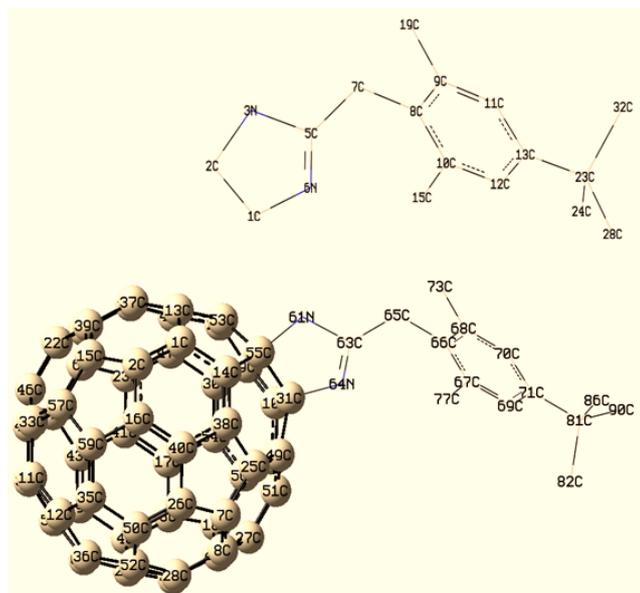


Figure 2: Show of XY and FXY obtained by B3LYP/6-31G* level of theory without Hydrogen.

3.1. Dipole moment

The results show that when structure of xylometazoline hydrochloride is linked to nano fullerene, the dipole moment in FXY increased. This parameter is an effective factor which has direct relationship with solubility and the more amount of this parameter, causes the more solubility inside the polar solvent (Table 1).

3.2. HOMO and LUMO indices

The FXY has band gap less than XY. A small HOMO-LUMO Gap (HLG) in atomic units automatically

means small excitation energies to the excited states. Therefore FXY is more conductive than XY (Table 1).

3.3. Chemical potential

In order to compare the obtained results, consider them. The results show that when structure of xylometazoline hydrochloride is linked to fullerene, the chemical potential (a.u.) of FXY decreased, in the gas and liquid phase (Table 1).

3.4. Chemical hardness

FXY has chemical hardness less than XY. A concise definition of chemical hardness (a.u.) offers that a hard molecule has a large HOMO-LUMO gap and a soft molecule has a small HOMO-LUMO gap, so FXY is softer than XY. Soft molecules with a small gap will have their electron density changed more easily than a hard molecule. So FXY is more reactive than XY (Table 1).

3.5. Electrophilicity index

Electrophilicity value (a.u.) in FXY increased. The electrophilicity index is a measure of electrophilic power of a molecule. When two molecules react with each other, one molecule behaves as a nucleophile system, whereas the other one acts as an electrophile system. A higher electrophilicity index shows higher electrophilicity of a molecule. So FXY has higher electrophilicity than XY, therefore FXY is a more strong Lewis acid (Table 1).

Table 2: Valance electron population in atomic units, for carbon, nitrogen, sulfur, oxygen and hydrogen atoms in similar position for FXY and XY obtained by B3LYP/6-31G* level of theory in the gas phase.

Atoms		valance population (a.u.)	
FXY	XY	FXY	XY
C ₃₁ =C ₁		3.874	4.28169
C ₅₅ =C ₂		3.82836	4.25316
C ₆₃ =C ₅		3.47831	3.48964
C ₆₅ =C ₇		4.50342	4.50742
C ₆₆ =C ₈		4.06331	4.06455
N ₆₁ =N ₃		5.70253	5.7269
N ₆₄ =N ₆		5.37441	5.37859

(^a) left atom related to FXY; (^b) right atom related to XY

3.6. Maximum amount of electronic charge index

As mentioned above, most electron charge which a system accepts can be calculated by ΔN_{\max} parameter. The obtained results for this parameter were obtained like the previous parameters, For FXY it is increased. A positive value of ΔN_{\max} indicates that charge flows to system, or our system acts as an electron acceptor, whereas a negative value of ΔN_{\max} indicates that charge flows from system or our system acts as an electron donor. So FXY is an electron acceptor or a Lewis acid (Table 1).

3.7. Natural Charges and valence electrons

The result of valence electron population in atomic units, for carbons, nitrogen, oxygen and hydrogen atoms in similar position for FXY and XY show that generally in FXY valence electron population is lower than XY, so C_{60} has power of electron affinity (Table 2, Figure 2).

4. CONCLUSIONS

In this paper, the structural and electronic structures of XY and FXY have been investigated theoretically by performing DFT calculations at the B3LYP/6-31G* level, in the gas phase and the liquid phase. The results show that FXY has band gap less than XY, also chemical hardness in FXY is lower than XY, so FXY with notice to electrophilicity and ΔN_{\max} parameter, is more soft strong acid than XY. In terms of chemical reactivity we can conclude that soft molecules will be more reactive than hard molecules for unimolecular reaction such as isomerization and dissociation. This work can be useful for pharmaceutical researches because this action causes interesting medicinal properties.

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