AMHSR ORIGINAL ARTICLE

Ab initio studies of fullerene effect on chemical properties of naphazoline drop

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ABSTRACT

Purpose: To evaluate the effect of fullerene on chemical properties of naphazoline drug in water by density functional theory (DFT) methods.

Materials and Methods: Naphazoline belongs to the imidazoline class of sympathomimetics. The present study on naphazoline drug and its fullerene connected form were carried out using computerized calculations of Gaussian program in b3lyp/6-31g level in water.

Results: Impact of fullerene on naphazoline was analyzed as changes in level of some properties including energetic levels, stability, high occupancy molecular orbital (HOMO), low unoccupancy molecular orbital (LUMO) levels, chemical hardness and electrophilicity properties. Results indicated that joint of medicine and C_{60} considerably decreases the energy level and the dipole moment. Therefore, reacting ability of the medicine is increased but its solubility is decreased in solution phase.

Conclusion: Combined fullerene structure with naphazoline, as a nano-carrier, enhances reacting ability of the medicine and its low solubility in the water phase of human body.

Keywords: imidazoline; naphazoline; fullerene; density functional theory (DFT) methods; nano-particles.

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INTRODUCTION

Naphazoline is a sympathomimetic agent with alpha adrenergic activity.[1] Its uses include Clear Eyes and Naphcon eye drops.[2] It has the molecular formula $C_{14}H_{14}N_2$. HCl and a molecular weight of 246.73 g/mol.[3] Naphazoline can be synthesized from (1-naphthyl) acetonitrile, which in reaction with ethanol transforms into iminoester and with ethylene diamine heterocyclization into the naphazoline (Figure 1).[4]

Many studies have been performed on fullerene and its drug derivatives. Fullerene is a molecule composed of only carbon, in the form of a buckyballs with pentagonal and heptagonal rings. The first fullerene molecule to be discovered, (C_{60}), was prepared in 1985 by Harold Kroto at Rice University.[5] Fullerenes have since been found to occur in nature.[6] More recently, fullerenes have also been detected in outer space. The discovery of fullerenes greatly expanded the number of known carbon allotropes, which until recently were limited to graphite, diamond and amorphous carbons such as soot and charcoal. Buckyballs and buckytubes have been the subject of intense research, both for their unique chemistry and for their technological applications, especially in materials science, electronics and nanotechnology.[7] This action

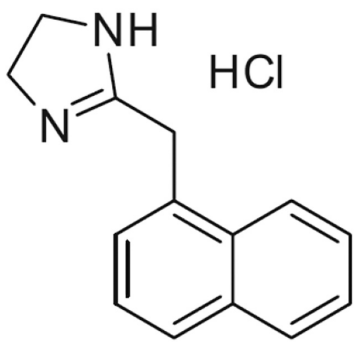

Figure 1. The structure of naphazoline hydrochloride.

INTRODUCTION

Naphazoline is a sympathomimetic agent with alpha

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causes interesting medicinal properties which increase rate of such characters by adding nano properties of this structure.[8]

The aim of this study was to evaluate the effect of fullerene on chemical properties of naphazoline drug in water by density functional theory (DFT) methods.

MATERIALS AND METHODS

The structures of naphazoline and nano fullerene naphazoline were designed primarily using Gauss View 3.1 and nanotube modeler 1.3.0.3 softwares. The optimization and natural bond orbital calculation were done with water solvents with polarized continuum model and then in the gas phase. The obtained results were compared with each other. The optimization and natural bond orbital calculations of all systems were done by density functional theory using B3LYP method and the standard 6-31G basis set, by Gaussian W98 suit. All computations were done under 1 atmosphere pressure and 298 Kelvin temperature.

In this report some properties including energetic levels, stability, high occupancy molecular orbital (HOMO), low unoccupancy molecular orbital (LUMO) levels, chemical hardness and electrophilicity properties were investigated.

The electrophilicity concept was expressed for the first time in 1999 by Parr and colleagues.[9] The electrophilicity and the maximum amount of electronic charge indices are related to electronic charge. The maximum amount of electronic charge index, ΔN_{max}, describes the charge capacity of the molecule that the electrophone system may accept, given in equation (1). A positive value of ΔN_{max}index (a.u.) for a system indicates that it acts as an electron acceptor, whereas a negative value of ΔN_{max} index indicates that it acts as an electron donor.[10]

The electrophilicity index, ω, in atomic units is a measure of electrophilic power of a molecule, given in equation (2). When two molecules react with each other, one molecule behaves as a nucleophile, whereas the other one acts as an electrophone. A higher electrophilicity index shows higher electrophilic power of a molecule.[11] So the quantity of ω describes the propensity of the system to acquire additional electronic charge from the environment. 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 (E_{HOMO} and E_{LUMO}) as in equations (3) and (4). The low values of μ and η, characterize a good electrophone species.[12]

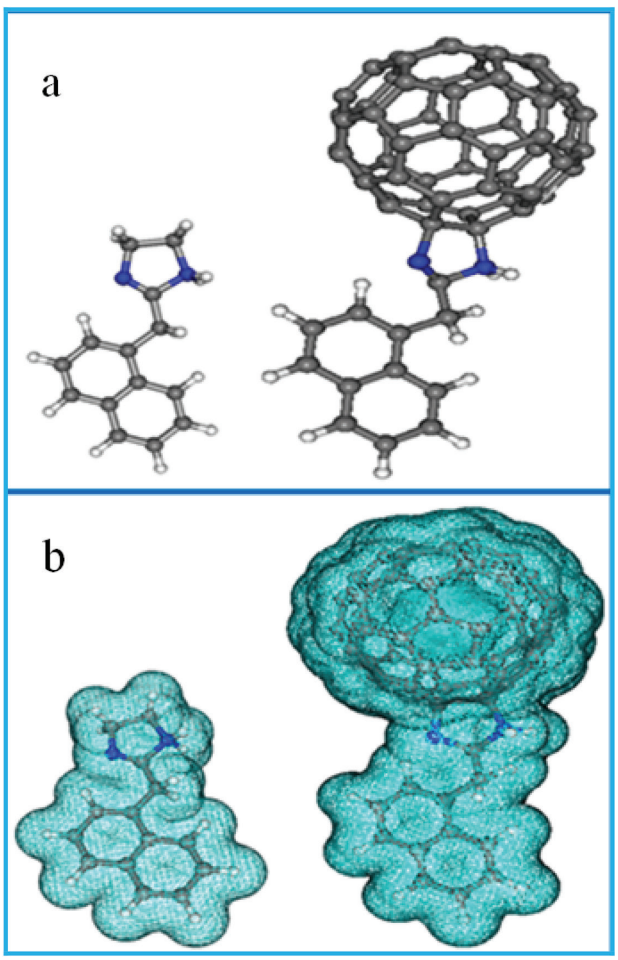

Figure 3. Naphazoline and fullerene naphazoline obtained by B3LYP/6-31G level of theory (grey atom: Carbon, blue atom: Nitrogen, white atom: Hydrogen) in the gas phase and in the liquid phase.

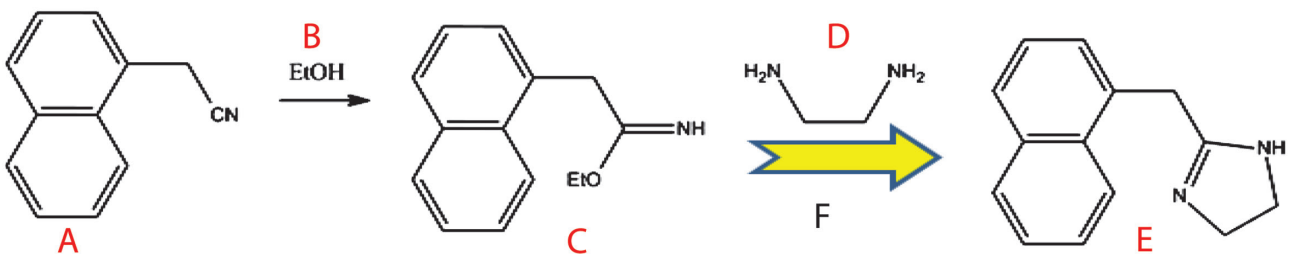

Figure 2. The synthesis of Naphazoline.
A: (1-naphthyl) acetonitrile; B: Ethanol; C: Iminoester; D: Ethylene diamine; E: Naphazoline; F: Reaction Type: Heterocyclization

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

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

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

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

RESULTS

The structure of naphazoline hydrochloride and the synthesis of naphazoline have been shown in Figures 1 and 2. In order to obtain its favorite position on fullerene, naphazoline molecule was connected to fullerene. Naphazoline and fullerene naphazoline, obtained by B3LYP/6-31G level of theory, in the gas phase and in the liquid phase have been shown in Figure 3.

Detailed information about the structure and electronic properties of the naphazoline and fullerene naphazoline, including the HOMO/LUMO energy gap (Eg), chemical hardness, h, chemical potential, μ, electrophilicity index, ω, plus the maximum amount of electronic charge index, ΔN_{max}, in atomic units and dipole moment (Debye) for naphazoline and nano fullerene naphazoline obtained by B3LYP/6-31G level of theory are shown in Table 1. HOMO/LUMO energy gap for nano fullerene naphazoline (Eg = 0.26383 a.u) was less than the naphazoline (Eg = 0.36449 a.u). Density of state (DOS) for energy gap in naphazoline and fullerene naphazoline obtained by B3LYP/6-31G level of theory has been shown in Figure 4. When the structure of naphazoline was linked to nano-fullerene, the dipole moment in nano fullerene naphazoline was decreased. This was an effective factor which had a direct relationship with solubility. The higher amount of this factor causes more solubility inside the polar solvent. The vectors of dipole moment (Debye) for naphazoline and fullerene naphazoline obtained by B3LYP/6-31G level of theory, and flow of electron density in naphazoline and

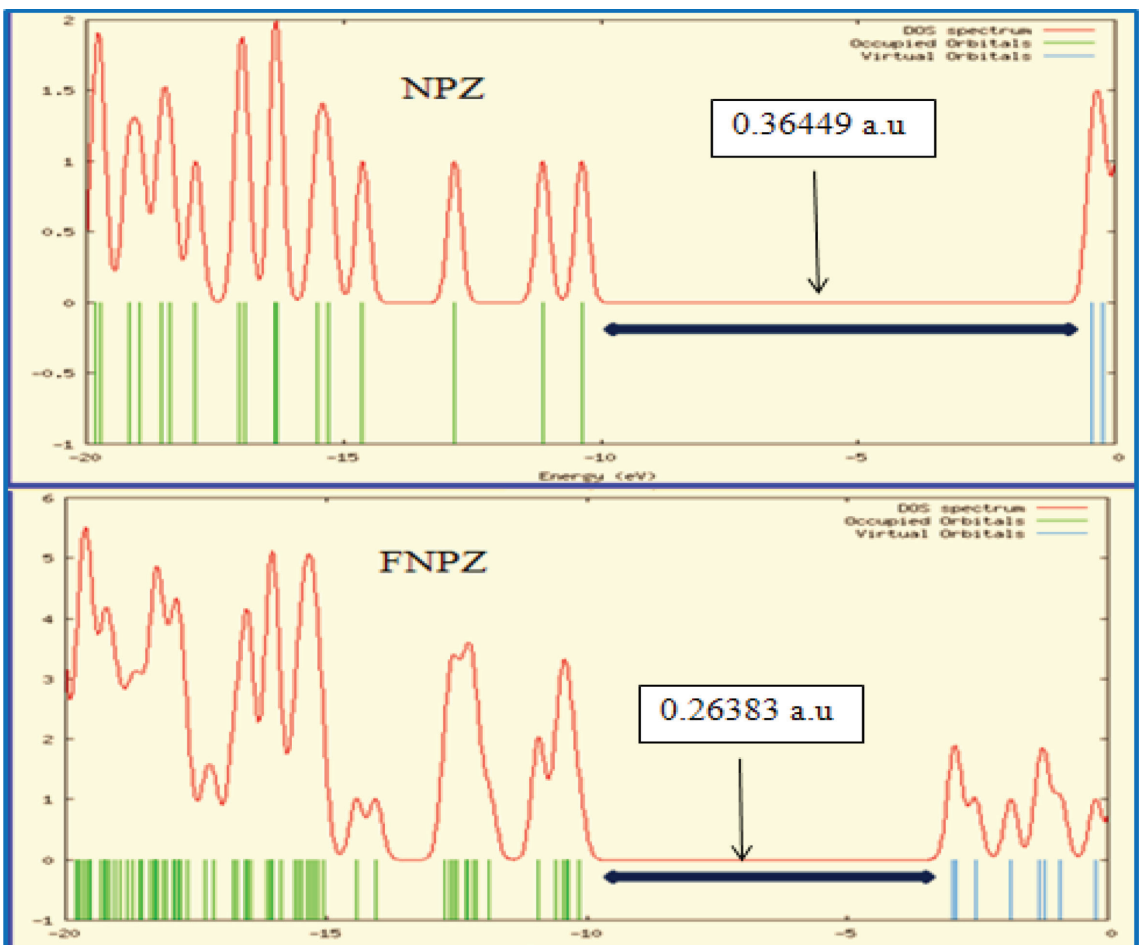

Figure 4. Density of state (DOS) diagram for energy gap in naphazoline and fullerene naphazoline obtained by B3LYP/6-31G level of theory.

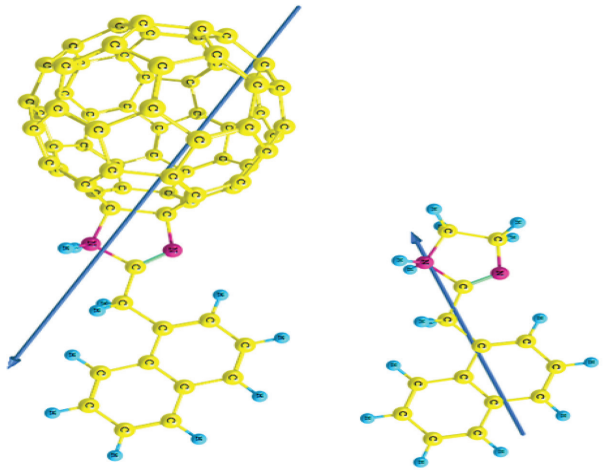

Figure 5. The vectors of dipole moment (Debye) for naphazoline and fullerene naphazoline obtained by B3LYP/6-31G level of theory.

fullerene naphazoline obtained by B3LYP/6-31G level of

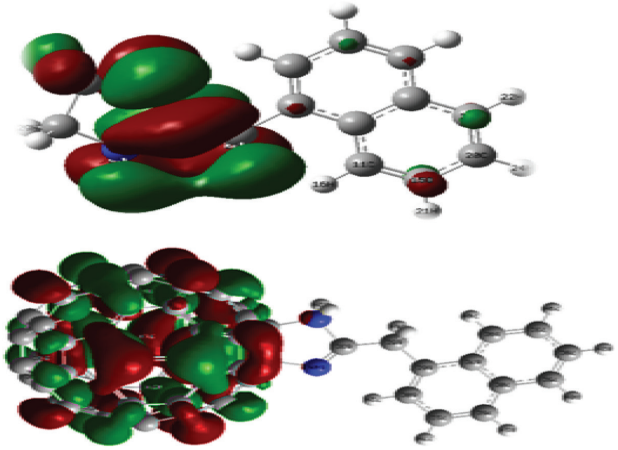

Figure 6. Flow of electron density in naphazoline and fullerene naphazoline obtained by B3LYP/6-31G level of theory.

theory have been shown in Figure 5 and 6.

When structure of naphazoline was linked to nano fullerene, the dipole moment and the chemical potential in nano fullerene naphazoline increased. Also, the band gap and chemical hardness of nano fullerene naphazoline were less than naphazoline. However, the electrophilicity value in nano fullerene naphazoline increased more than naphazoline, whereas ΔN_{max} for nano fullerene naphazoline was increased. The result for nano fullerene naphazoline and naphazoline show that generally in nano fullerene naphazoline, electron population is pushed to C_{60}. So C_{60} has power of electron affinity.

DISCUSSION

This study was conducted to evaluate the effect of fullerene on chemical properties of naphazoline drug in water by DFT methods. Its findings show that nano fullerene naphazoline has less band gap than naphazoline. A small HOMO-LUMO Gap (HLG) in atomic units automatically means small excitation energies to the excited states. Therefore nano fullerene naphazoline is more reactive than naphazoline. A C_{60} cage is formed from twenty 6-membered rings (6-MR) and twelve 5-membered rings (5-MR) with spherical symmetry (Figure 2). The natural bond orbital analysis reveals that the hybridization of C and C atoms is nearly sp^3 and sp^2, respectively. After linking C_{60} on the naphazoline, the HOMO/LUMO energy gap decreases and therefore a substantial increase occurs in conductivity and this phenomenon can be explain in equation (5).[13]

$$\sigma \propto \exp(-E_g/2kT) \quad (5)$$

In this equation σ is conductivity, T is temperature, k is Boltzmann constant. So, as often as E_g is smaller, there is more conductivity. Density of state (DOS) diagram clearly shows that when naphazoline is doped on the C_{60}, it will become a semiconductor (Figure 4). Optimization of these types of interactions is desirable for gas detection, since such strong interactions mean that the nano fullerene naphazoline is a suitable absorbent for molecule. If E_{ad} is significantly increased then it is expected that recovery will be so long. The transition state theory and recovery time can be explained in equation (6):[14]

$$\tau = \upsilon_0^{-1} \exp(-E_{ad}/kT) \quad (6)$$

where T is the temperature, k is the Boltzmann's constant, and υ_0 is the attempt frequency.[15]

According to this equation, as often as adsorption energy (E_{ad}) is increasing, the recovery time becomes longer. So nano fullerene naphazoline is more conductive than naphazoline.

The results of this study show that when structure of naphazoline is linked to fullerene, the chemical potential (a.u.) of nano fullerene naphazoline is decreased in the liquid phase (Table 1). Nano fullerene naphazoline has chemical hardness less than naphazoline. 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 nano fullerene naphazoline is softer than naphazoline. Soft molecules with a small gap will have their electron density changed more easily than a hard molecule. So nano fullerene naphazoline is more reactive than naphazoline (Table

1). The dipole moment in nano fullerene naphazoline was decreased. This was an effective factor which has a direct relationship with solubility and its increase can cause less solubility inside the polar solvent (Table 1).

Also, electrophilicity value (a.u.) in nano fullerene naphazoline was increased. The electrophilicity index is a measure of electrophilic power of a molecule. A higher electrophilicity index shows higher electrophilicity of a molecule. So nano fullerene naphazoline has higher electrophilicity than naphazoline, therefore nano fullerene naphazoline is a stronger Lewis acid (Table 1). 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, which had increased in nano fullerene naphazoline. A positive value of ΔN_{max} indicates that charge flows to system, or the system acts as an electron acceptor, whereas a negative value of ΔN_{max} indicates that charge flows from system or the system acts as an electron donor. So nano fullerene naphazoline is an electron acceptor or a Lewis acid (Table 1).

CONCLUSION

The structural and electronic properties of naphazoline and fullerene naphazoline were investigated theoretically by performing DFT calculations at the B3LYP/6-31G level in the liquid phase in this study. The results show that nano fullerene naphazoline has band gap less than naphazoline. Also, chemical hardness in nano fullerene naphazoline is lower than naphazoline, so nano fullerene naphazoline with notice to electrophilicity and ΔN_{max} parameter, is a stronger acid than naphazoline. In terms of chemical reactivity it can be concluded that soft molecules will be more reactive than hard molecules for unimolecular reaction such as isomerization and dissociation. These results may open a new gate to chemically modify the nanostructure in a way to expand the fields of their applications in industry, technology and pharmaceutical research.

CONFLICT OF INTEREST

None Declared.

REFERENCES

1. Mohamed GG, Nour El-Dien FA, Frag EYZ, et al. In situ modified screen printed and carbon paste ion selective electrodes for potentiometric determination of naphazoline hydrochloride in its formulation. *J Pharm Anal*. 2013;3:367-75.
2. Ghoreishi SM, Behpour M, Nabi M. A novel naphazoline-selective membrane sensor and its pharmaceutical applications. *Sensor Actuat B-Chem*. 2006;113:963-9.
3. Zhu S, Liu Y. Spectroscopic analyses on interaction of naphazoline hydrochloride with bovine serum albumin. *Spectrochim Acta A: Mol Biomol Spectrosc*. 2012;98:142-7.
4. Meloun M, Syrový T, Vrána A. The thermodynamic dissociation constants of ambroxol, antazoline, naphazoline, oxymetazoline and ranitidine by the regression analysis of spectrophotometric data. *Talanta*. 2004;62:511-22.
5. Kroto HW, Heath JR, O'Brien SC, et al. C_{60}: Buckminsterfullerene. *Nature*. 1985;318:162-3.
6. Anafcheh M, Ghafouri R. Mono- and multiply-functionalized fullerene derivatives through 1,3-dipolar cycloadditions: A DFT study. *Physica E*. 2014;56:351-6.
7. Abe Y, Yokoyama T, Matsuo Y. Low-LUMO 56π-electron fullerene acceptors bearing electron-withdrawing cyano groups for small-molecule organic solar cells. *Org Electron*. 2013;14:3306-11.
8. Yang Y, Nakada N, Tanaka H. Adsorption of fullerene nC_{60} on activated sludge: Kinetics, equilibrium and influencing factors. *Chem Eng J*. 2013;225:365-71.
9. Parr RG, Szentpály LV, Liu S. Electrophilicity index. *J Am Chem Soc*. 1999;121:1922-4.
10. Beheshtian J, Peyghan AA, Bagheri Z. Functionalization of [60] fullerene with butadiene: A DFT study. *Appl Surf Sci*. 2012;258:8980-4.
11. Peyghan AA, Aslanzadeh SA, Noei M. A density functional study on the acidity properties of pristine and modified SiC nano-sheets. *Physica B*. 2014;443:54-9.
12. Baei, MT, Peyghan AA, Bagheri Z. Covalent functionalization of AlN nanotubes with acetylene. *Physica E*. 2013;47:147-51.
13. Peyghan AA, Soleymanabadi H, Moradi M. Structural and electronic properties of pyrrolidine-functionalized [60] fullerenes. *J Phys Chem Solids*. 2013;74:1594-8.
14. Beheshtian J, Peyghan AA, Bagheri Z. Theoretical investigation of C60 fullerene functionalization with tetrazine. *Comput Theor Chem*. 2012;992:164-7.
15. Ahmadi R, Soleymani R, Yousofzad T. Study on effect of addition of nicotine on nanofullerene structure C60 as a medicine nanocarrier. *Orient J Chem*. 2012;28:773-9.

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