International Journal of New Chemistry, 2015, 2 (1), 17-26.
Published online January 2015 in http://www.ijnc.ir/.
Original Article

Online ISSN 2383-188X
Open Access

Computational study of Chemical properties in fullerene Derivatives of Enalapril drug

Roya Ahmadi, Alireza rezaie asl

Department of Chemistry, Faculty of Science, Islamic Azad University, Shahr-e-Rey Branch, Tehran, Iran.

*Corresponding Author e-mail Address: *roya.ahmadi.chem@hotmail.com*
Received: 6 December 2014; Accepted: 28 January2015; Published 30 January 2015

Abstract

In this research at the first Enalapril drug and its fullerene derivative were optimized. NBO calculations and NMR for the complexes were carried out at the B3LYP/6-31G* quantum chemistry level. Different parameters such as energy levels, the amount of Chemical Shift in different atoms, the amount of HOMO/LUMO, chemical potential (μ), chemical hardness (η), the coefficients of hybrid bonds (π, σ) and the orbital portion of the bonds p (π, σ) was performed. In another part, the valence electrons of atoms were compared. this drug as a major therapeutic category is Antihypertensive drug. In this study of fullerenes, we used nano drug carriers. The data in tables and graphs and shapes were compared and discussed.

Keywords: Enalapril, fullerenes, chemical potential, nano drug carriers.

1. Introduction

Nanostructures can be categorized into following forms according to their structures: diamonds with sp^3 hybridization, Graphite with sp^2 hybridization, Hexagonal diamonds with sp^3 hybridization, fullerenes with SP^2 hybridization, Nanoparticles, Graphene, single-layer and multi-layer nanotubes, Crystal Nanostructures. All these forms of nanostructures produce unique Pharmaceutical and electronic properties. Graphenes have a two-dimensional structure of a single layer of carbon chicken wire [1-5]. A fullerene is any molecule composed of carbon in the form of a hollow sphere, ellipsoid, tube, and many other shapes. Spherical fullerenes are also called Bucky balls, and they resemble the balls used in football (soccer). Cylindrical ones

are called carbon nanotubes or Bucky tubes. Fullerenes are similar in structure to graphite, which is composed of stacked graphene sheets of linked hexagonal rings; but they may also contain pentagonal (or sometimes heptagonal) rings. The first fullerene molecule to be discovered, and the family's namesake, buckminsterfullerene (C60), was prepared in 1985 by Richard Smalley, Robert Curl, James Heath, Sean O'Brien, and Harold Kroto at Rice University. The discovery of fullerenes greatly expanded the number of known carbon allotropes, which until recently were limited to graphite, diamond, and amorphous carbon 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. Enalapril is an angiotensin-converting-enzyme (ACE) inhibitor used in the treatment of hypertension, diabetic nephropathy, and some types of chronic heart failure. ACE converts the peptide hormone angiotensin. I to angiotensin II One of the actions of angiotensin II is the vasoconstriction of blood vessels, resulting in an increase in blood pressure. ACE inhibitors such as enalapril prevent this effect. Enalapril has been shown to lower the death rate in systolic heart failure. Enalapril was the first member of the group known as the dicarboxylate-containing ACE inhibitors. It is on the World Health Organization's List of Essential Medicines, the most important medications needed in a basic health system [6]. Enalapril is used to treat hypertension, symptomatic heart failure, and asymptomatic left ventricular dysfunction [7]. It has been proven to protect the function of the kidneys in hypertension, heart failure, and diabetes, and may be used in the absence of hypertension for its kidney protective effects [8]. It is widely used in chronic kidney failure [9].

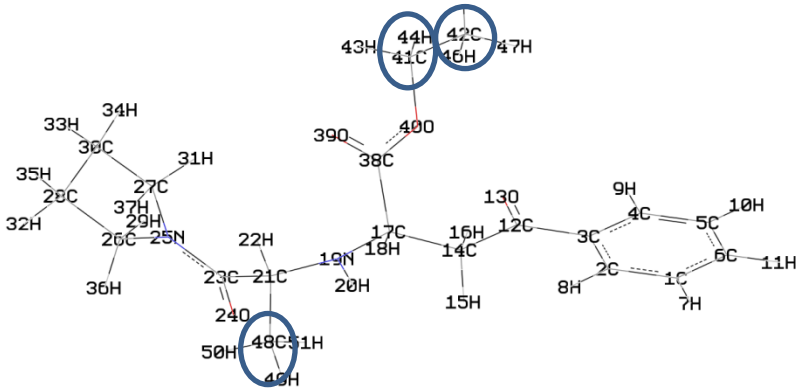

Fig 1. View of Enalapril alone and location of connectable (C42, C41, C48) to Fullerene and shown briefly EN.

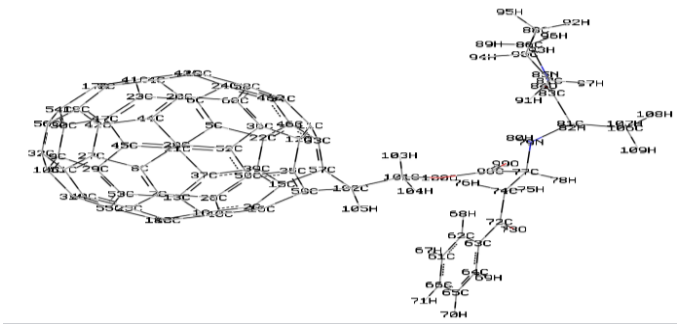

Fig 2. View of Nano-drug Enalapril has been obtained from carbon connection of Enalapril C102 to Fullerene and shown briefly FEN (1).

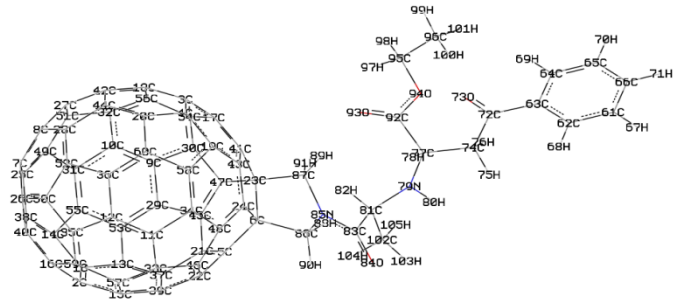

Fig 3. View of Nano-drug Enalapril has been obtained from carbon connection of Enalapril C83 to Fullerene and shown briefly FEN 2.

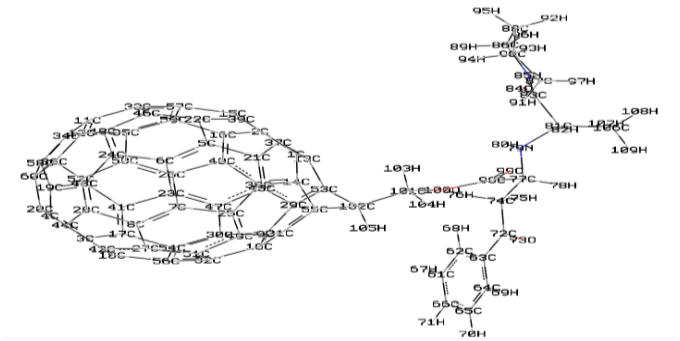

Fig 4. View of Nano-drug Enalapril has been obtained from carbon connection of Enalapril C_{101} to Fullerene and shown briefly FEN (3)

2. Computational details

All Computations are performed by means of GAUSSIAN 03 packing [10]. Geometries for all compounds are computed by means of the density functional theory (DFT) with Becke's three-parameter functional (B3) plus Lee, Yang, and Parr (LYP) correlation functional. For all atoms, the standard 6-31G basis set is utilized. The structures of Enalapril on Fullerene were designed primarily using of Gauss View 5.0.8 and nanotube modeler 1.3.0.3 soft wares. The interaction effects of Enalapril on Fullerene were investigated through attachment to three different base positions. All these calculations are done under the assumption of standard

state of gas phase, pressure of 1 atmosphere, and temperature of 25 degrees centigrade. The calculations are performed, using a Pentium 4 PC with a Windows 7 OS.

3. Results and discussion

In this study, Enalapril drug and its 3 fullerene derivatives investigated. The related structures are named in the following way:

NO	Symbol	Mater
1	EN	Enalapril
2	FEN(1)	Nano-drug from binding of Enalapril C102 to Fullerene
3	FEN(2)	Nano-drug from binding of Enalapril C83 to Fullerene
4	FEN(3)	Nano-drug from binding of Enalapril C101 to Fullerene

The results showed that the calculated energy gap is typically much higher of the Enalapril than Enalapril attached to Fullerene in each three connection is different and the other hand the amount of that in each three Enalapril binds to Fullerene to connection forms is different and mostly the same (compared with the accuracy of thousands EN> FFS (1)> FFS (3) > FFS (2) (Fig 5).

Table 1: Values of energies of the frontier molecular orbitals (ε_{HOMO} and ε_{LUMO}, eV), electronic chemical potential, μ (eV), chemical hardness, η (eV), calculated at the B3LYP/6-31G* level of theory

Compound	LUMO (a. u)	HOMO (a. u)	Energy Gap= LUMO – HOMO	Dipole moment	Chemical hardness	Chemical potential
EN	0.07749	-0.35	0.42749	2.6400	0.21374	-0.13625
FEN(1)	-0.01571	-0.28875	0.27304	1.8991	0.13652	-0.15223
FEN(2)	-0.02406	-0.26479	0.24073	7.0587	0.12036	0.15188
FEN(3)	-0.01558	-0.28819	0.27261	1.4080	0.13635	-0.14442

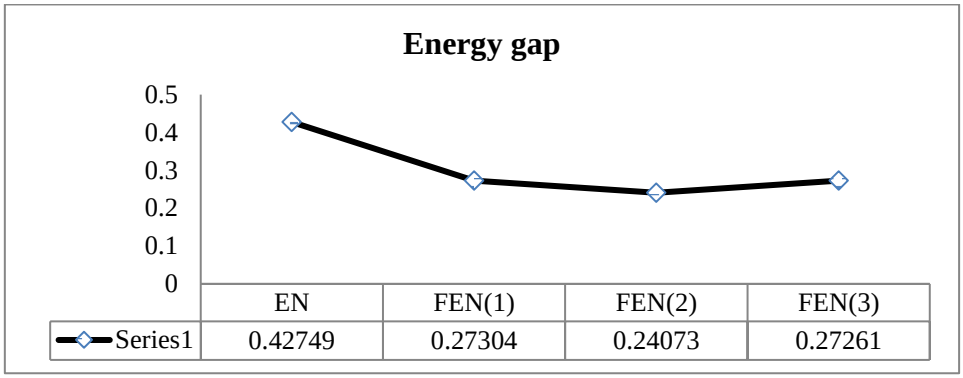

Fig 5. Results of the survey molecular orbital energy levels of the drug and three Fullerene derivative in B3 LYP/6-31G* level

Since most of the weight is composed of water and water is a polar solvent, so the amount and the process of the change in dipole moment in Nano-drugs and Enalapril in free mode is also important .the results showed that the minimum value of dipole moment in order first is related to FEN (3) next FEN (1) next Enalapril and Nano-drug (2) is little .in total the dipole moment FEN (2) alone is higher than the other combinations. so we expect that when FEN (2) arrived our body than other three combinations easily in water that is a polar solvent dissolved and has more solubility so after FFS (2) Enalapril has a dipole moment higher and higher solubility (Fig 6).

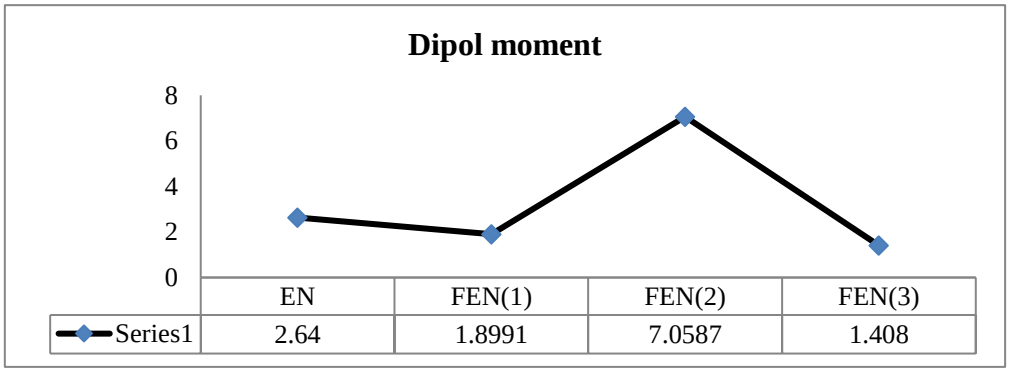

Fig 6. The amount of dipole moment in EN, FEN (1), FEN (2), FEN (3) is calculated in B3LYP/6-31G* level.

Chemical hardness indicate the measurement of the stability of the material as much as chemical hardness is more electron transfer from HOMO to LUMO is harder and consequently system reactivity decrease. In comparison whit chemical hardness among Enalapril and three combination of Nano-drug . we resulted like energy gap that chemical hardness is more than three other combination in the other hand Nano-drug has indicate chemical hardness can be finer species and changes in the density of the electron can occur more easily the more difficult chemical hardness is less reactive species is better and chemical hardness FEN (2) is the minimum (Fig 7).

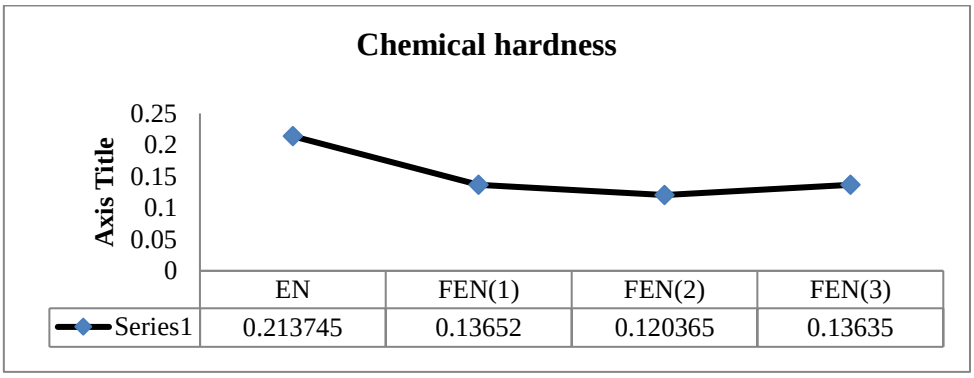

Fig 7. Result obtained from chemical hardness in FEN (3), FEN (2), FEN (1), EN is calculated in B3LYP/6-31G* level.

Negative chemical potential is a symbol of system stability. The calculated results showed that the chemical potential Nano-drug 1,2 and that is the same and the lowest and then is a chemical potential ,the calculated highest value of the chemical potential allocate to Nano-drug 3 the more chemical potential the more reaction molcouler or in the other words that type is more reactive (Fig8).

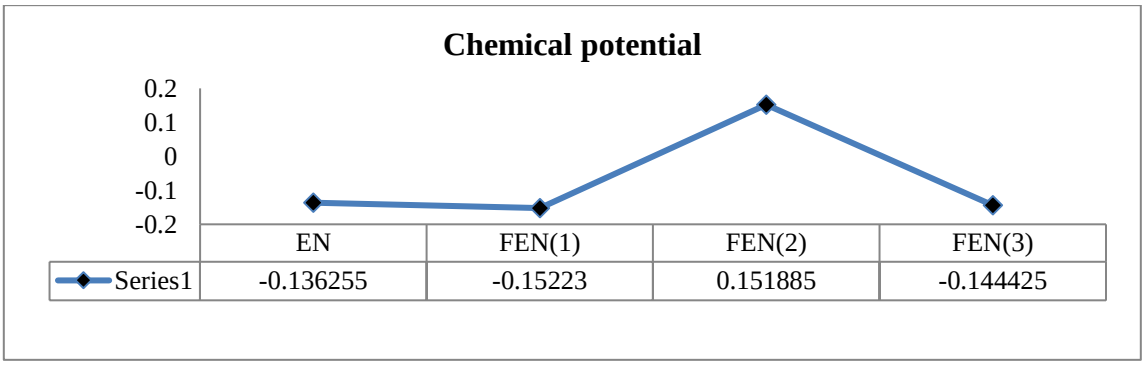

Fig 8. The result of survey of the chemical potential of Enalapril and its Fullerene derivatives.

The results of the study show that position oxygen O24 in natural charge has the negatively charge than the position O13. The number of valence electrons and constant coverage of O24 and that Nano medicines is more than O13 (Fig 9). so there is more Alkalinity in position O24.

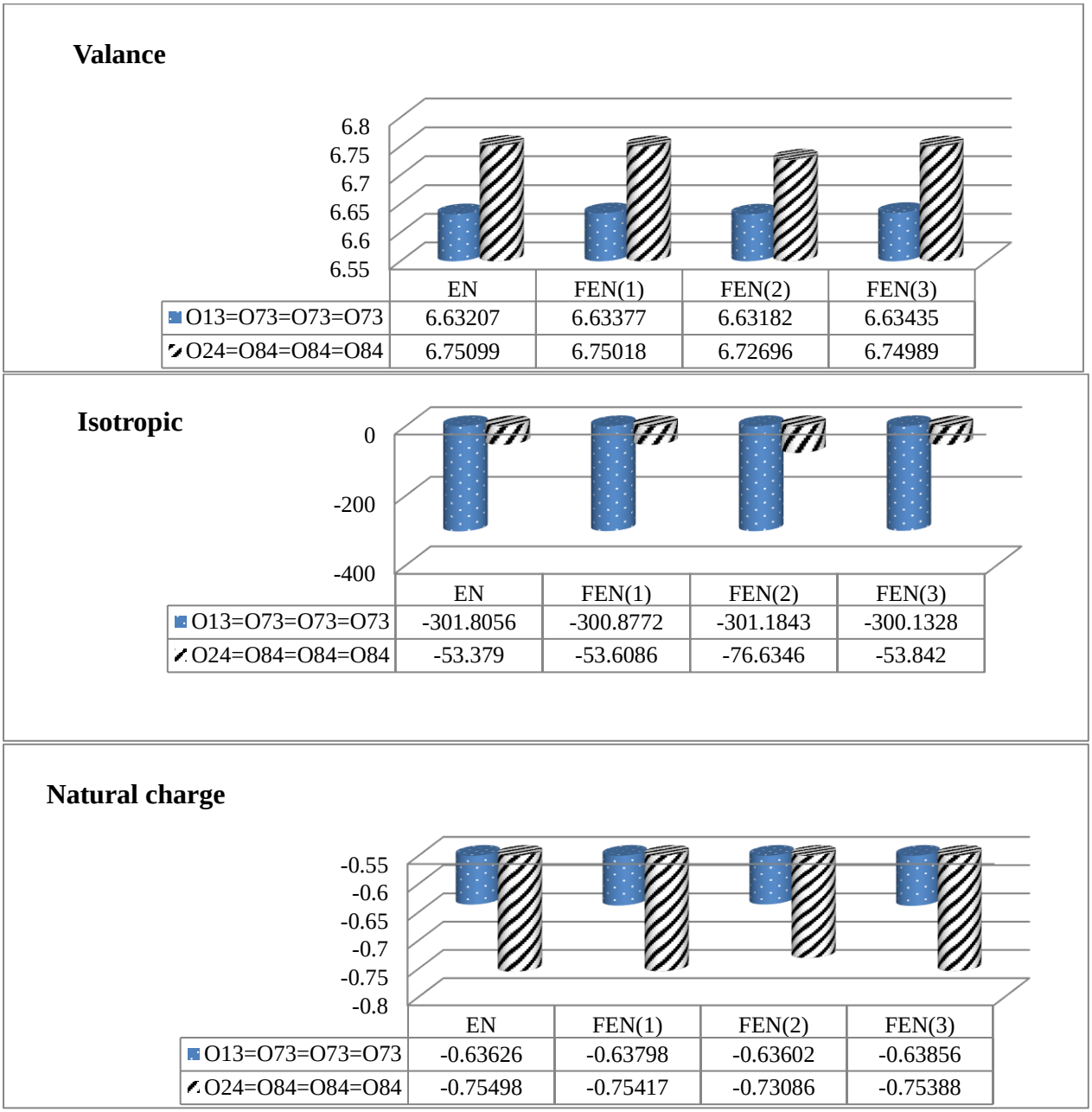

Fig 9. The comparison chart of natural charge, the number of valence electrons, covering factor, the combination of 1,2,3 Nano- drug in level B3LYP/6-31G* level

According to the survey Carried out calculation the natural charge of N in FEN(2) in order is higher than EN, FEN (1), FEN (3) the process about valence electrons, which acts as reverse the natural charge is evident, so valence electrons of FEN (3) is higher . Occupation number follow such process and the nature of nitrogen can be discussed (Fig 10).

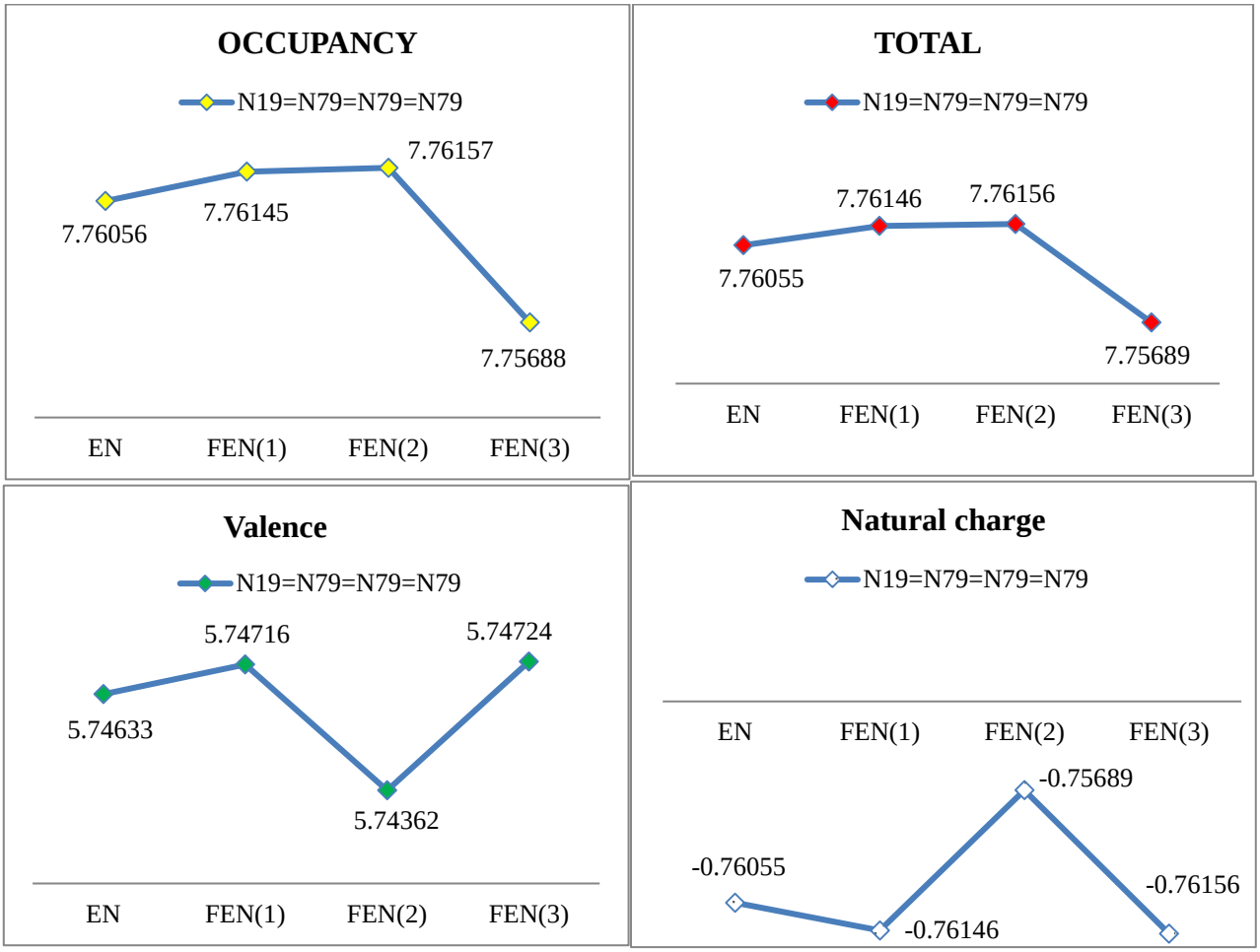

Fig 10. The comparison chart of natural charge, the covering factor and occupancy of similar nitrogen atoms in Enalapril, the combination of 1, 2, 3 Nano- drug in level B3LYP/6-31G* level.

Current ring creates a magnetic field perpendicular to the ring and the effect of H ring outside circle of caused more chemical shift for H, consequently reduce the amount of covering factor. Survey results of the calculations show that among of derivatives Fullerene Enalapril the most positive value of NICS is related to FEN (2) so the Hydrogen of ring 1 in FEN (2) has more chemical shift then this Hydrogen are better than others that participate in electrophilic substitution reaction (Table2).

Table 2. Amount of NICS

Distance	0.0	0.5	1.0	1.5	
EN	8.1707	10.9245	11.8326	8.637	Ring 1
	bq110	bq111	bq112	bq113	
FEN(1)	8.0095	10.8034	11.7487	8.5803	
	bq106	bq107	bq108	bq109	
FEN(2)	8.2023	10.9553	11.9702	8.7785	
	bq110	bq111	bq112	bq113	
FEN(3)	8.085	10.8624	11.7983	8.6229	
	8.1707	10.9245	11.8326	8.637	

The relate of bond length and orbital p participation show that Whenever orbital p participation increase bond length is increased.

Table 4. Bond length and orbital p participation

Bond	**Compound**	**B3LYP/6-31G***	**Occupancy**	**Orbital p participation**	**Bond length**
C41=C42	EN	σ =0.7099(sp^2.39)C41 + 0.7043(sp^2.67)C 42	1.99143	1.788571	1.51124
C57=C102	FEN (1)	σ =0.7081(sp^ 2.19)C57 + 0.7062(sp^3.12)C102	1.94775	1.877042	1.49309
C81=C102	FEN (2)	σ =0.7167(sp^ 2.56)+ 0.6974(sp^2.71)C102	1.9852	1.862353	1.52997
C53=C102	FEN (3)	σ = 0.7087(sp^2.20)c53 + 0.7055(sp^3.12)C102	1.94985	1.88015	1.48932
C41=C42	EN	σ=0.7099(sp^2.39)C41 + 0.7043(sp^2.67)C42	1.99143	1.788571	1.51124
C59=C102	FEN (1)	σ= 0.7079(sp^2.19)C59 +0.7063(sp^3.12)C102	1.94739	1.876979	1.49231
C81=C102	FEN (2)	σ =0.7167(sp^ 2.56)+ 0.6974(sp^2.71)C102	1.9852	1.862353	1.52997
C55=C102	FEN (3)	σ=0.7084(sp^2.20)C55 + 0.7058(sp^3.14)C102	1.94849	1.887346	1.49045

4. Conclusion

Computational Quantum Mechanics at the theory level of B3LYP/6-31G* on the structure of Fullerene and Fullerene Derivatives of Enalapril drug was done separately and only when the structure of Enalapril was attached to Fullerene and the results of this computation can be classified as follows:

-The investigation of all the parameters show that the attachment of Enalapril structure to Fullerene structure will influence the energy levels and dipole moment changes and these changes are able to be investigated in the electrical and chemical parameters of Fullerene Derivatives structure.

-The results showed that energy gap of EN is the highest and FEN (2) is the lowest. It should be noted that conductivity of FEN (2) is the highest and EN is the lowest.

-Chemical potential of FEN (2) is more than EN and after of them is FEN (3) and (1).

-Chemical hardness of EN is the highest and the lowest value is related to FEN (2).

-Dipole moment of FEN (2) is first and EN is the second.

-Bond length in FEN (2) in each bond is the most.

5. Acknowledgment:

We are appreciating and thanking Islamic Azad University of Yeager-e-Imam Khomeini (Rah) Share - Rey.

References

1. K. S. Novoselov, A. K. Geim, S. V. Morozov, D. Jiang, Y. Zhang, S. V. Dobonos, Science, 306, (2004), 666.

2. K. S. Novoselov, A. K. Geim, S. V. Morozov, D. Jiang, Nature, 438, (2005), 1970.

3. M. Terrones, A. Botello-Mendez, J. Campos-Delgado, F. Lopez-Urias, Nano Today, 5, (2010), 351.

4. B. C. Brodie, Ann. Chim. Phys, 59, (1860), 466.

5. W. S. Hummers, R.E. Offeman, J. Am. Chem. Soc, 80, (1958), 1339.

6. World Health Organization. October 2013. Retrieved 22 April 2014.

7. U.S. National Library of Medicine. Last Revised October, MedlinePlus: Enalapril, 1, 2010.

8. J. J. V. McMurray, "Clinical Practice: Systolic Heart Failure". N Engl J Med 362, (2010), 228.

9. Y.M. He, et al, Nephrology (Carlton), Sep;18 (2013) 605.

10. W. Gao, L. B. Alemany, L. Ci, P.M. Ajayan, Nature Chemistry, 1, (2009).