



Investigation of Fullerene effect on reactivity of 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid with NMR parameters

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Abstract

In this research at the first 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid drug and its fullerene derivative were optimized. NMR calculations 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), Thermodynamic Properties was determined and the coefficients of hybrid bonds (π , σ) and the orbital portion of the bonds p (π , σ) was performed. In another part, the core and the valence electrons of atoms were compared. This drug as a major therapeutic category is antidepressant drug. In this study of fullerenes, we used nano drug carriers. The data in tables and graphs and shapes were compared and discussed.

Keywords: 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid, 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]. 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 (C_{60}), 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. 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid is an antidepressant of the selective serotonin reuptake inhibitor (SSRI) class. 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid was first documented in 1974 by scientists from Eli Lilly and Company [2]. It was approved by the U.S. Food and Drug Administration for the treatment of major depressive disorder in December 1987 [7]. 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid is used for the treatment of major depressive disorder (including pediatric depression), obsessive-compulsive disorder (in both adults and children), bulimia nervosa, panic disorder and premenstrual dysphoric disorder [9]. In addition, 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid is used to treat trichotillomania if cognitive behavior therapy has been unsuccessful [10]. 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid's mechanism of action is predominantly that of a serotonin reuptake inhibitor [3-4]. 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid delays the reuptake of serotonin, resulting in serotonin persisting longer when it is released. 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid may also produce some of its effects via its weak 5-HT_{2C} receptor antagonist effects [5]. In addition, 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid has been found to act as an agonist of the σ_1 -receptor, with a potency greater than that of citalopram but less than that of fluvoxamine. However, the significance of this property is not fully clear [6]. 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid also functions as a channel blocker of anoctamin 1, a calcium-activated chloride channel.

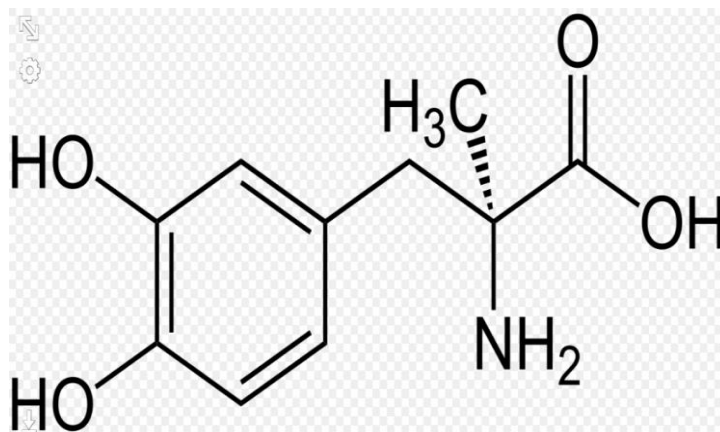


Fig 1. View of 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid alone

2. Computational details

All Computations are performed by means of GAUSSIAN 03 packing [7-9]. 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 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid 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 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid 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 and a Core i5 processor.

3. Results

In this study, 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid drug and its 3 fullerene derivatives investigated. The related structures are named in the following way:

2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid is useful in the treatment of mild to moderately severe hypertension. It lowers blood pressure chiefly by reducing peripheral vascular resistance, with a variable reduction in heart rate and cardiac output. Most cardiovascular reflexes remain intact after administration of 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid, and blood pressure reduction is not markedly dependent on maintenance of upright posture. Postural (orthostatic) hypotension sometimes occurs, particularly in volume-depleted patients. One potential advantage of 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid is that it causes reduction in renal vascular resistance. Fullerenes, the hollow carbon cages discovered in 1985[1], have fascinated scientists. The most prominent representative of the fullerene class is C₆₀, which is the most abundant cluster in the solvent-extracted carbon soot and the smallest fullerene that satisfies the isolated pentagon rule. Since macroscopic samples of C₆₀ became available in 1990. many applications [3,4] have been suggested, particularly in the bio-area.

This class of compounds can be active as HIV-protease inhibitors. As antibacterial and neuroprotective agents, and can also induce the photocleavage of DNA

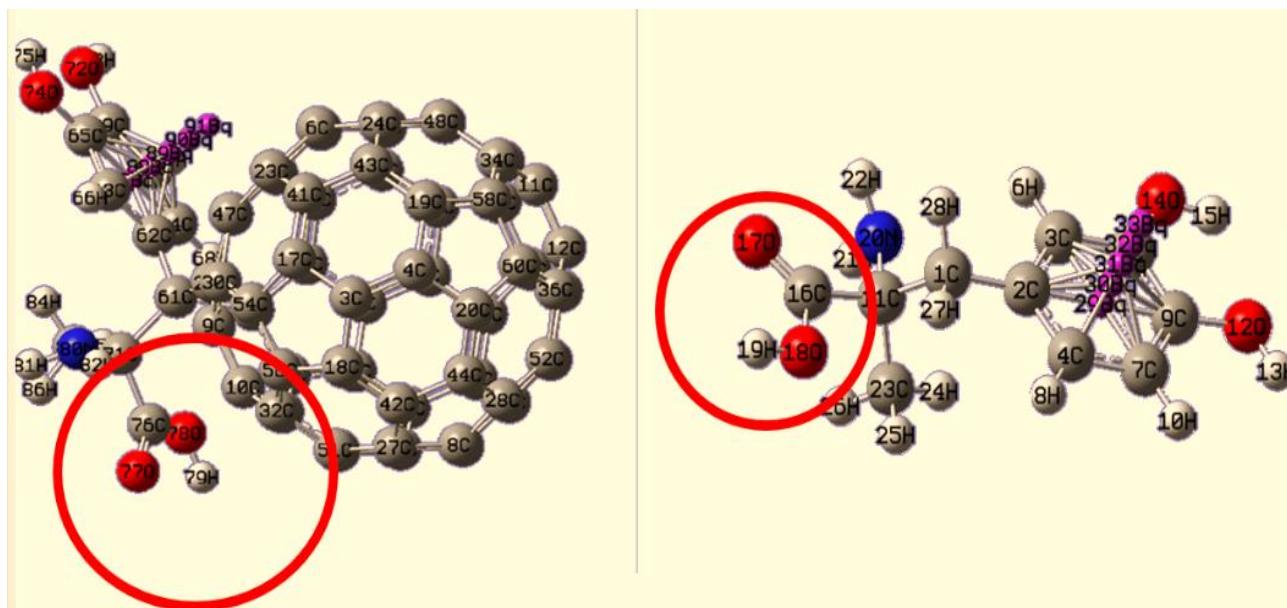


Fig2. Nano fullerene-2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid & 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid

4. Materials and methods:

All structure relating to structure of 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid and nano fullerene-2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid were designed primarily with use of Gauss view 4.1. In order to do final optimization, Gaussian 98 program of package HF method were used. However, for this purpose, 6-31G basis set was used. computation were done in gas phase.


5. Apparatus:

Total computations were done with use of Pentium III with processor Intel® core i3 with memory of 4 gigabytes and inside the operating system of windows SEVEN®. All computations were performed under gas phase, 1 atmosphere and 298 Kelvin temperature

4. Result and discussion:

In this work 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid was linked to the fullerene, then compare Gap Energy, Hardness, chemical potential, dipole moment parameters between 2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid alone and nano- fullerene-2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid. It's found that Gap Energy and Hardness were decreased in nano- fullerene but chemical potential and dipole moment were increased. In other hand compare between chemical shielding isotropy(σ_{iso}) and chemical shift(δ) in H79, H19 (that is similar in two compound) showed that chemical shielding isotropy was decreased in acidic hydrogen of nano-fullerene-2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid but chemical shift of it was increased.

Table.1. Some Chemical properties

compound	Gap Energy	Hardness	Chemical potential	dipole moment			
					iso σ	δ	
R-C ₆₀ -X	0.26499	0.132495	-0.146065	5.6772	H ₇₉	27.8210	4.7766
R-X	0.44659	0.223295	-0.081765	4.3526	H ₁₉	28.0984	4.4992

Conclusion:

The result showed that reactivity and solubility in polar solvent were increased. With increasing of chemical shift in H79 can find when electronic density of around H79 decrease, this hydrogen will be more than positive and it can easily separate in the field water (acidity). This is a support for increasing of reactivity of nano-fullerene-2-amino-3-(3,4-dihydroxyphenyl)-2-methyl-propanoic acid in the human body.

Reference

- [1] N. Noma, T. Tsuzuki, Y. Shirota, *Adv. Mater.*, 7, 647 (1995); C. Videlot, A. El Kassmi, D. Fichou, *Solar Energy Mater. Solar Cells*, 63, 69 (2000); K. Hara, M. Kurashige, Y. Dan-Oh, C. Kasada, A. Shinpo, S. Suga, K. Sayama, H. Arakawa, *New J. Chem.*, 27, 783 (2003); J. Ackermann, C. Videlot, A. El Kassmi, R. Guglielmetti, F. Fages, *Adv. Mater.*, 16, 1709 (2004).
- [2] A.D. Becke, *J. Chem. Phys.*, 98, 5648 (1993).
- [3] R. Ditchfield, W.J. Hehre, J.A. Pople, *J. Chem. Phys.*, 54, 724 (1971).
- [4] W.J. Hehre, R. Ditchfield, J.A. Pople, *J. Chem. Phys.*, 56, 2257 (1972).
- [5] P.C. Hariharan, J.A. Pople, *Mol. Phys.*, 27, 209 (1974).
- [6] M.S. Gordon, *Chem. Phys. Lett.*, 76, 163 (1980).
- [7] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J.A. Montgomery, Jr., K.N. Kudin, J.C. Burant, J.M. Millam, S.S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G.A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J.E. Knox, H.P. Hratchian, J.B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, G.A. Voth, P. Salvador, J.J. Dannenberg, V.G. Zakrzewski, S. Dapprich, A.D. Daniels, M.C. Strain, O. Farkas, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J.V. Ortiz, Q. Cui, A.G. Baboul, S. Clifford, J. Cioslowski, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, C. Gonzalez, J.A. Pople, *GAUSSIAN 03*, Revision B.04, Gaussian, Inc., Pittsburgh PA, 2003.
- [8] J. Casado, V. Hernández, F.J. Ramirez, J.T. López, *Navarrete*, 463, 211 (1999).