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Comparison of structural parameters in antiparkinson's drug: Procyclidine & its nano carrier based on fullerene with calculation chemistry

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Abstract

Parkinson's disease is a degenerative disorder of the central nervous system. It results from the death of dopamine-containing cells in the substantia nigra, a region of the midbrain; the cause of cell-death is unknown. Procyclidine is used to treat parkinsonism (slowed movements, stiffness of the body, uncontrollable body movements, weakness, tiredness, soft voice, and other symptoms caused by damaged nerves in the brain). Procyclidine is also used to treat problems with moving and drooling that may be caused by certain medications for mental illness. Procyclidine is in a class of medications called antispasmodics or antimuscarinics. It works by preventing sudden tightening of the muscles. In this Study at the first compounds $[C_{60}$- Procyclidine–Cn-2X$]^+$ and [Procyclidine-Cn-2X$]^+$ (X=F,Cl,Br) were optimized (n is similar to in two compound). All calculations is done in 6-31g* basis set in HF method and in gas phase. The results showed that the energy levels of molecular orbital (HOMO & LUMO) in the RF has the lowest value. C_{62}-X, C_{62}-N_{61} has a length of the shortest bond and the bond has most power. Comparison of the dipole moments of compounds shows this trend: R-2Br > R-2Cl> R-2F.This is noticeable that the trends in these compounds are quite similar but the values in only drug are more intense than drug with fullerene.

Keywords: Procyclidine, Parkinson , nano carrier, fullerene

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. Procyclidine is an antidepressant of the selective serotonin reuptake inhibitor (SSRI) class. Procyclidine 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 [3]. Procyclidine 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 [4]. In addition, Procyclidine is used to treat trichotillomania if cognitive behavior therapy has been successful [5]. Procyclidine's mechanism of action is predominantly that of a serotonin reuptake inhibitor [6]. Procyclidine delays the reuptake of serotonin, resulting in serotonin persisting longer when it is released. Procyclidine may also produce some of its effects via its weak 5-HT2C receptor antagonist effects [7]. In addition, Procyclidine has been found to act as an agonist of the σ1-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 [8]. Procyclidine also functions as a channel blocker of anoctamin 1, a calcium-activated chloride channel.

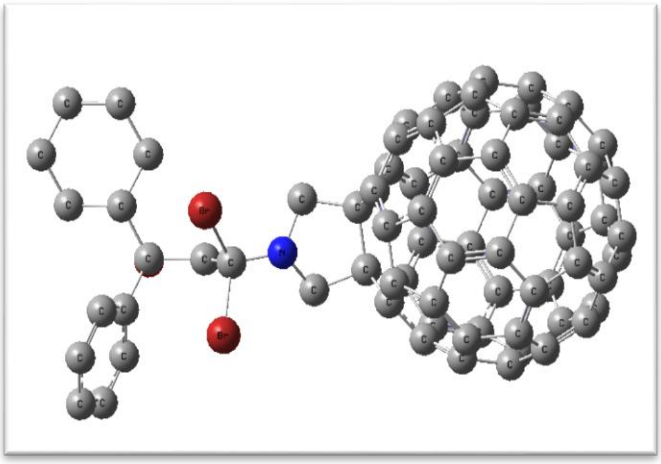

Fig 1. View of Procyclidine with Fullerene

2. Computational details

All Computations are performed by means of GAUSSIAN 03 packing [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 Procyclidine 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 Procyclidine 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 [10].

3. Results

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

Table (2) combines 2Br -C60-Procyclidine with Br substituents at carbon position 62

* In the base series 6-31G

```
      (Occupancy)   Bond orbital/ Coefficients/ Hybrids
-------------------------------------------------------------------------------
   1. (1.97082) BD ( 1) C   1 - C   2
              ( 50.27%)   0.7090* C   1 s( 36.45%)p 1.74( 63.55%)
                                        0.0000  0.6037  0.0077  0.5747 -0.0035
                                        0.4387  0.0207 -0.3350 -0.0079
              ( 49.73%)   0.7052* C   2 s( 36.23%)p 1.76( 63.77%)
                                        0.0000  0.6018  0.0094 -0.7460 -0.0188
                                       -0.1532  0.0134  0.2392 -0.0009
   2. (1.67180) BD ( 2) C   1 - C   2
              ( 49.41%)   0.7029* C   1 s(  0.01%)p 1.00( 99.99%)
                                        0.0012 -0.0091  0.0000 -0.6586  0.0021
                                        0.7260 -0.0169 -0.1967  0.0082
              ( 50.59%)   0.7113* C   2 s(  0.00%)p 1.00(100.00%)
                                        0.0016 -0.0036  0.0014 -0.2998  0.0159
                                        0.8843 -0.0122 -0.3574  0.0031
   3. (1.96676) BD ( 1) C   1 - C  13
              ( 50.05%)   0.7075* C   1 s( 31.27%)p 2.20( 68.73%)
                                       -0.0001  0.5592 -0.0053 -0.1713 -0.0061
                                        0.0709  0.0188  0.8078  0.0000
              ( 49.95%)   0.7067* C  13 s( 31.17%)p 2.21( 68.83%)
                                       -0.0001  0.5583 -0.0048  0.0166 -0.0064
                                        0.2311  0.0187 -0.7964  0.0020
   4. (1.96593) BD ( 1) C   1 - C  14
              ( 50.16%)   0.7083* C   1 s( 32.17%)p 2.11( 67.83%)
                                       -0.0001  0.5672 -0.0036 -0.4542 -0.0074
                                       -0.5246  0.0126 -0.4432 -0.0110
              ( 49.84%)   0.7060* C  14 s( 32.11%)p 2.11( 67.89%)
                                       -0.0001  0.5666 -0.0020  0.2743 -0.0069
                                        0.7232  0.0177  0.2832 -0.0068
```

Summary of Natural Population Analysis:

Atom	No	Natural Charge	Natural Population Core	Valence	Rydberg	Total
C	1	-0.00432	1.99870	3.99155	0.01407	6.00432
C	2	-0.00625	1.99868	3.99301	0.01456	6.00625
C	3	-0.00284	1.99868	3.98978	0.01438	6.00284
C	4	0.00090	1.99868	3.98606	0.01436	5.99910
C	5	0.00265	1.99868	3.98425	0.01442	5.99735
C	6	-0.00331	1.99868	3.99026	0.01437	6.00331
C	7	-0.00262	1.99870	3.98964	0.01428	6.00262
C	8	-0.00712	1.99867	3.99408	0.01437	6.00712
C	9	-0.00875	1.99863	3.99533	0.01479	6.00875
C	10	0.04044	1.99878	3.94282	0.01795	5.95956
C	11	-0.00073	1.99868	3.98769	0.01435	6.00073
C	12	-0.00068	1.99868	3.98764	0.01436	6.00068
C	13	-0.00549	1.99870	3.99273	0.01406	6.00549
C	14	0.03142	1.99879	3.95263	0.01716	5.96858
C	15	-0.00063	1.99868	3.98748	0.01447	6.00063
C	16	-0.00707	1.99867	3.99403	0.01437	6.00707
C	17	0.00286	1.99868	3.98404	0.01442	5.99714
C	18	0.00279	1.99868	3.98410	0.01444	5.99721
C	19	-0.00199	1.99868	3.98894	0.01436	6.00199
C	20	0.00031	1.99868	3.98665	0.01436	5.99969
C	21	-0.00927	1.99867	3.99620	0.01440	6.00927
C	22	-0.00290	1.99868	3.98984	0.01438	6.00290
C	23	-0.00121	1.99868	3.98813	0.01440	6.00121
C	24	0.00041	1.99868	3.98656	0.01434	5.99959
C	25	-0.01695	1.99865	4.00366	0.01463	6.01695
C	26	0.00659	1.99869	3.98039	0.01432	5.99341
C	27	-0.00614	1.99868	3.99290	0.01455	6.00614

Threshold for printing: 0.50 kcal/mol

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j)-E(i) a.u.	F(i,j) a.u.
within unit 1				
1. BD (1) C 1 - C 2	/308. RY*(1) C 13	1.34	2.16	0.048
1. BD (1) C 1 - C 2	/314. RY*(3) C 14	1.50	2.12	0.051
1. BD (1) C 1 - C 2	/316. RY*(1) C 15	1.32	2.13	0.048
1. BD (1) C 1 - C 2	/318. RY*(3) C 15	0.54	2.13	0.031
1. BD (1) C 1 - C 2	/320. RY*(1) C 16	1.32	2.11	0.047
1. BD (1) C 1 - C 2	/609. BD*(1) C 1 - C 13	5.01	1.68	0.082
1. BD (1) C 1 - C 2	/610. BD*(1) C 1 - C 14	5.61	1.70	0.087
1. BD (1) C 1 - C 2	/611. BD*(1) C 2 - C 15	4.74	1.68	0.080
1. BD (1) C 1 - C 2	/612. BD*(1) C 2 - C 16	5.04	1.70	0.083
1. BD (1) C 1 - C 2	/645. BD*(1) C 13 - C 53	1.54	1.70	0.046
1. BD (1) C 1 - C 2	/648. BD*(1) C 14 - C 55	2.06	1.57	0.051
1. BD (1) C 1 - C 2	/651. BD*(1) C 15 - C 57	1.59	1.68	0.046
1. BD (1) C 1 - C 2	/654. BD*(1) C 16 - C 59	1.79	1.68	0.049
2. BD (2) C 1 - C 2	/310. RY*(3) C 13	1.67	1.51	0.049
2. BD (2) C 1 - C 2	/312. RY*(1) C 14	1.46	1.47	0.045
2. BD (2) C 1 - C 2	/318. RY*(3) C 15	1.55	1.53	0.047
2. BD (2) C 1 - C 2	/322. RY*(3) C 16	1.66	1.53	0.049
2. BD (2) C 1 - C 2	/609. BD*(1) C 1 - C 13	1.09	1.07	0.033
2. BD (2) C 1 - C 2	/610. BD*(1) C 1 - C 14	1.01	1.10	0.032
2. BD (2) C 1 - C 2	/611. BD*(1) C 2 - C 15	1.11	1.07	0.033
2. BD (2) C 1 - C 2	/612. BD*(1) C 2 - C 16	1.17	1.09	0.035
2. BD (2) C 1 - C 2	/644. BD*(2) C 13 - C 37	24.25	0.52	0.100
2. BD (2) C 1 - C 2	/647. BD*(2) C 14 - C 38	25.47	0.54	0.108
2. BD (2) C 1 - C 2	/650. BD*(2) C 15 - C 39	23.68	0.53	0.101
2. BD (2) C 1 - C 2	/653. BD*(2) C 16 - C 40	27.20	0.52	0.106
3. BD (1) C 1 - C 13	/265. RY*(2) C 2	2.17	2.04	0.060
3. BD (1) C 1 - C 13	/313. RY*(2) C 14	1.91	2.14	0.058
3. BD (1) C 1 - C 13	/405. RY*(2) C 37	2.19	2.04	0.060
3. BD (1) C 1 - C 13	/469. RY*(2) C 53	1.96	2.13	0.058
3. BD (1) C 1 - C 13	/607. BD*(1) C 1 - C 2	5.16	1.72	0.084
3. BD (1) C 1 - C 13	/610. BD*(1) C 1 - C 14	2.72	1.62	0.059
3. BD (1) C 1 - C 13	/612. BD*(1) C 2 - C 16	3.82	1.62	0.070
3. BD (1) C 1 - C 13	/643. BD*(1) C 13 - C 37	5.11	1.72	0.084

Table (4) examines the bond lengths of carbon atoms with fluorine, chlorine, bromine in

Compound 2X-C60-Procyclidine in Base Series 6-31 G * in HF Method

Atom	2F	2Cl	2Br
C_{62} - C_{63}	1.5157	1.53685	1.5304
C_{62} - N_{61}	1.4118	1.47262	1.4245
C_{63} - C_{72}	1.5494	1.54973	1.5558
C_{66}- N_{61}	1.4493	1.46340	1.4593

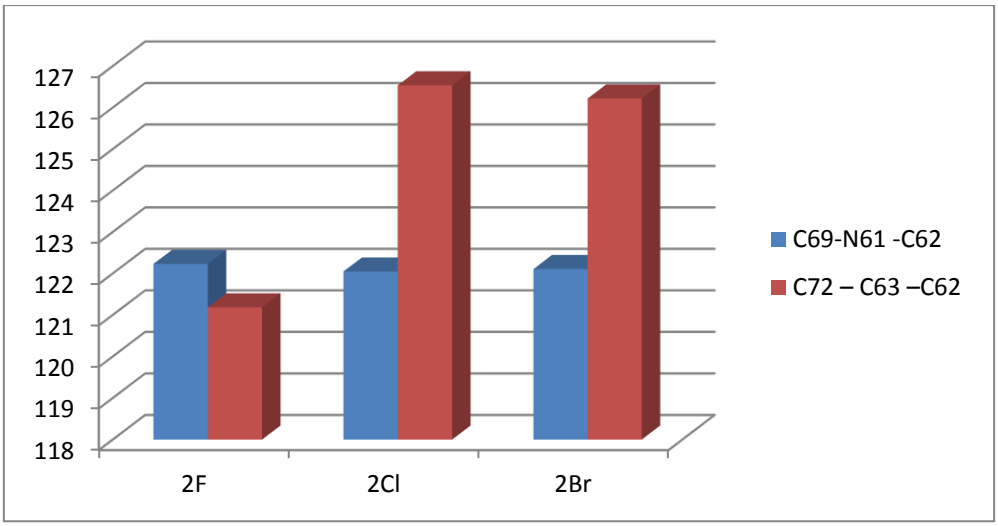

Diagram (4-5) Evaluation of the angle of bonds of carbon atoms with fluorine, chlorine, bromide in Compound 2X-C60-Procyclidine in Base Series 6-31 G * in HF Method

5. Conclusion:

Computational Quantum Mechanics at the theory level of B3LYP/6-31G on the structure of Fullerene and Fullerene Derivatives of Procyclidine drug was done separately and only when the structure of Procyclidine 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 Procyclidine 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.

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