

## **Theoretical study of molecular mechanics methods on clonidine drug-carbon nano cone**

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### **ABSTRACT**

In this study, geometrical optimizations of Clonidine Drug were carried out with the HF/6-31g basis sets. Then, drug was put covalently to carbon nanocone with (5, 1) structure and a length of 15<sup>0</sup>Å. We use chem Office software and hyper chem at the end data will be presented as tables and Figs. Simulation was done in MM<sup>+</sup>, AMBER and OPLS force fields by Monte Carlo method. Three important energy parameters – Potential Energy, Kinetic Energy and Total Energy- calculated in five different simulating temperatures (308, 310, 312, 314 and 316 Kelvin) were used for computation and good results were obtained.

**Keywords:** Theoretical; Molecular Mechanic; Clonidine Drug; Nano Cone

### **INTRODUCTION**

Nanotechnology is an advancing method with many ways for unlocking problems, specially in medical science. By performing more research on this technology, treat can be found for diseases that have no cures until now. Therefore, nanotechnology can effect on life like a revolution. One of the exciting classes of nano materials is carbon nano cones (CNCs), which possess characteristics suitable for many applications as delivery vehicles of biologically important molecules in view of possible biomedical applications, such as vaccination and gene or drug delivery. Scientists from different fields of science are just beginning to solve

the mysteries and hypothesize about CNC-gen complexes [1]. A useful devise to achievement these purposes is theoretical methods. Since the first observation [2] of Carbon Nano Cones (CNCs), large progress has been made on synthesis, characterization, and manipulation of CNCs [3-7]. Differently from a planar graphene, the CNCs show a mixing of geometric, topological, and symmetry aspects that are exhibited in a non-homogeneous distribution of the electronic states through the structure. Particular effects of such feature are the charge accumulation at the cone apix and the selective polarized light absorption that

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may be used in technological applications [8].

Carbon Nano Cone has a high asymmetric geometry that in our simulations, classical non-equilibrium molecular dynamics method is adopted. The cone is entirely characterized by its cone angle. When one pentagon is introduced into a hexagonal carbon network, a  $60^\circ$  disclination defect is formed, leading to the formation of a Nano Cone with cone angle of  $118^\circ$  and the equilibrium carbon-carbon bond length is  $1.418 \text{ \AA}$ . In this work, we focus on the cone with the cone angle of  $180^\circ$ , which is the largest angle observed experimentally [9, 10] and theoretically. Moreover, in all theoretical models so far, the rectification efficiency decreases quickly as the structure length increases.

The primary goal of this study was to examine the binding of Clonidine drug ( $C_9H_9Cl_2N_3$ ) was put covalently to Carbon Nano Cone (CNC) with (5, 1) structure and a length of  $15^0\text{A}$ . The secondary goal of this study was to investigate Energy parameters of Drug-CNC complex.

## METHODOLOGY

The Carbon Nano Cone that used in this study containing 84 carbon atoms, with ends opened. In our model, Clonidine drug was put covalently to carbon nanocone (CNC) with (5, 1) structure and a length of  $15^0\text{A}$ .

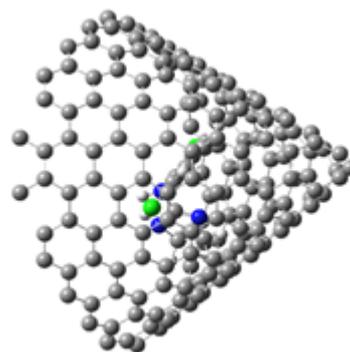
Geometrical optimizations of Drug were carried out with the Hartee -Fock method coupled to 6-31g basis sets for all atoms. Also, in this study we use chem Office software (chem3D and chem draw) and hyper chem at the end data will be presented as tables and figs. Simulation was done in  $MM^+$ , AMBER and OPLS force fields. Molecular Mechanics calculations were assessed by Monte Carlo method [11]. Three important energy

parameters – Potential Energy, Kinetic Energy and Total Energy- in five different simulating temperatures (308, 310, 312, 314 and 316 Kelvin) were used for computation.

## RESULTS AND DISCUSSION

### Molecular Geometry

Fig. 1, Shows the graphical representations of the optimized geometry of drug- CNC. In the figure, the Cl atoms are shown by green colors, white spheres are H atoms, blue sphere is N atoms and gray sphere is C. Selected geometrical parameters for Clonidine drug SWCNT are also shown in Fig.1.



**Fig. 1.** Optimized geometries of Clonidine drug-CNC obtained at HF/6-31G level.

### Energy Parameters

In current study computations were done in sophisticated and appropriate molecular modeling environment of Hyper Chem™ which is well known for its quality and flexibility [12, 13]. It is known that atoms are held together by forces. Function of biological systems arises from interaction of resilient bonds between atoms and electron motion. The main purpose is to seek for the lowest energy, in which the molecule is in its most stable state [14, 15]. In this study AMBER,  $MM^+$  and OPLS force fields were chosen. The total Potential Energy is the sum of mentioned

contribution interactions based on the force fields.

Therefore, force fields are a series of functional energy parameters that evaluate performance and calculate the Potential Energy of molecule in various positions of its constituent atoms and bonds [16].

MM<sup>+</sup> is a proper parameter for attaining vibration motion of atoms, related bond stretching potential, and angles bending. AMBER force field has extensive application for proteins and nucleic acids. It assigns all conformational energies and treats with hydrogen bond energy, and torsion term [17]. Like AMBER, OPLS is designed for computation of proteins and nucleic acids. In this force field bonded potentials are similar to AMBER and its non-bonded potentials involves vanderwaals and electrostatics. Similar to AMBER and OPLS it has been designed to study macromolecules [18].

Clonidine drug to Nano Cone was simulated in mentioned force fields in 5 different temperature (308K, 310K, 312K, 314K and 316K). To elucidate the effect of Clonidine drug to Nano Cone energy on molecular mechanic calculation, the most usual expression for total potential energy is given by the following equation:

$$E_{total} = \sum_i^{bonds} E_i^{stretch} + \sum_i^{bondangles} E_i^{bend} + \sum_i^{dihedralangles} E_i^{torsion} + \sum_{ij}^{atompairs} E^{vanderwaals} + \sum_{ij}^{atompairs} E^{electrostatics} \quad (1)$$

$E_{total}$  is the sum of bonded and non-bonded interactions

$E_{bond}$  is stretching bond energy between two atoms

$E_{angle}$  is energy of bending an angle

$E_{torsion}$  is torsion energy of rotation around a bond

$E_{electrostatic}$  and  $E_{van\ der\ Waals}$  are two energies which are exponent distribution, and repulsion or attraction between non-bonded atoms, respectively.

The other two calculated energy quantities are kinetic and total energy values. In symbols the total energy equals:

$$E_{total} = \sum E_{potential} + \sum E_{kinetic} \quad (2)$$

From a statistical point of view, the obtained valuable data for three basis sets of thermodynamic parameters ( $E_{potential}$ ,  $E_{kinetic}$ ,  $E_{total}$ ), analyzed under the different simulation procedure, various temperatures values every 10 ps span are listed in tables 1, 2 and 3. According to results observed in table 1, the amount of minimum potential energy calculated by MM+ force filed have been reported. Minimum potential energy level in normal body temperature (310K) was 316.2 for MM+ force filed. Also, comparison of potential energy levels in different temperatures are displayed in Figs. 2a-c.

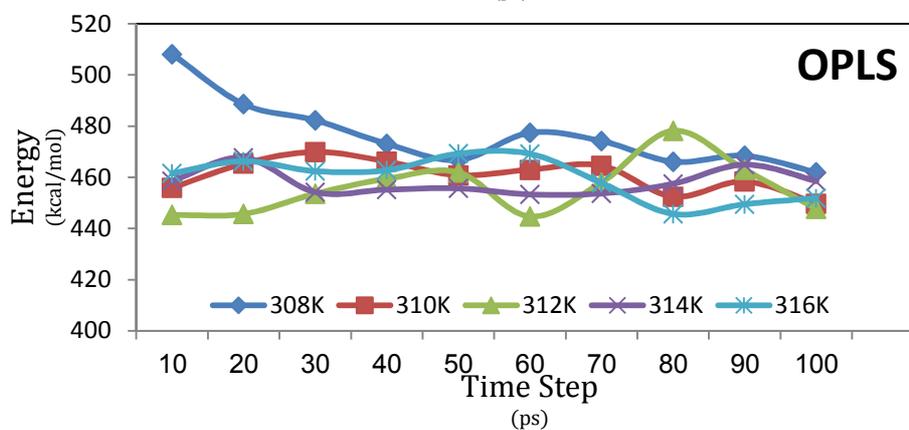
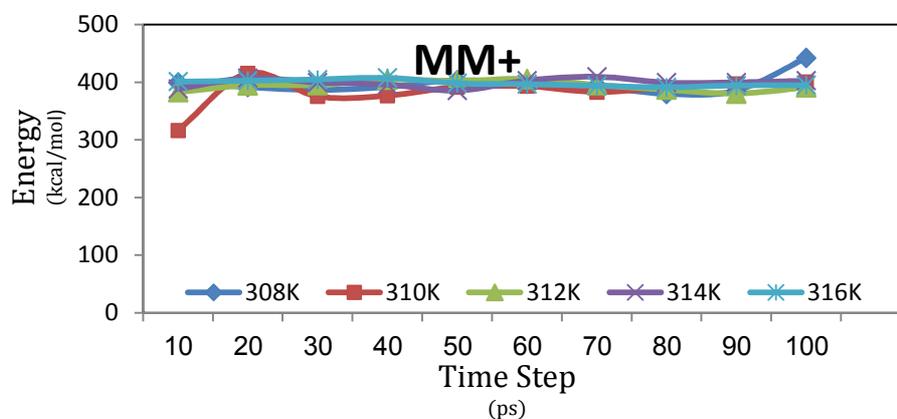
It is known that to have optimum function in biologic system, the energy levels must be in the minimum level. According to results observed in table 2 and Figs.3 for kinetic energy in different time steps and various force fields were constant and the maximum and minimum quantity observed in 310K, 285.5Kcal/mol and in 308K, 123.7 Kcal/mol, respectively.

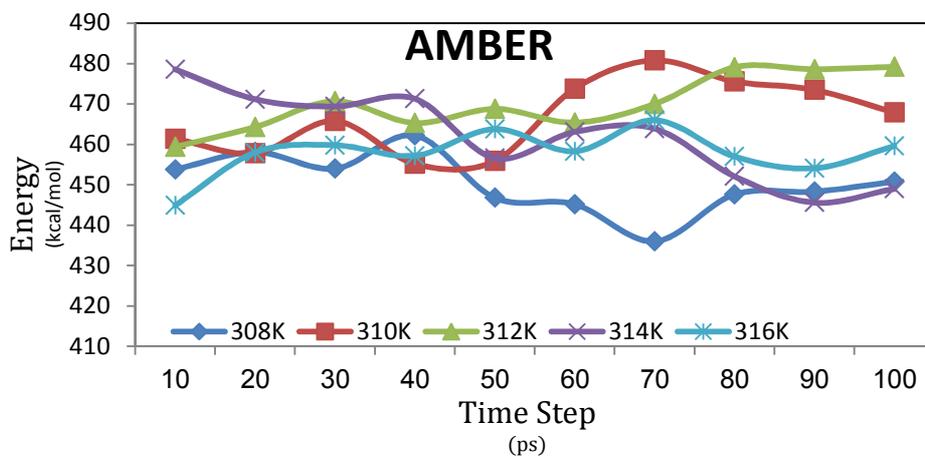
Also, data analysis of table 3 exhibited that total energy quantities were affected by increasing temperature that energy increase leads to molecular instability.

According to results observed in table 3 and Fig.4 maximum quantity total energy in different temperature was 312K, 673.4Kcal/mol in amber method.

**Table1.** Computed drug to Nano Cone Potential Energy ( kcal/ mol ), belong to AMBER, MM<sup>+</sup> and OPLS force fields under five different temperature

| Potential Energy ( kcal/ mol ) |                |       |       |       |       |                 |       |       |       |       |                  |       |       |       |       |
|--------------------------------|----------------|-------|-------|-------|-------|-----------------|-------|-------|-------|-------|------------------|-------|-------|-------|-------|
| Method                         | MM+/Mont Carlo |       |       |       |       | OPLS/Mont Carlo |       |       |       |       | AMBER/Mont Carlo |       |       |       |       |
| Time (PS)                      | 308K           | 310K  | 312K  | 314K  | 316K  | 308K            | 310K  | 312K  | 314K  | 316K  | 308K             | 310K  | 312K  | 314K  | 316K  |
| 10                             | 399.2          | 316.2 | 382.6 | 388.4 | 400.9 | 508.1           | 455.9 | 445.3 | 458.6 | 461.6 | 453.8            | 461.4 | 459.4 | 478.6 | 444.9 |
| 20                             | 391.7          | 415.4 | 394.6 | 407.2 | 402.6 | 488.6           | 465.4 | 445.7 | 467.7 | 466.3 | 458.1            | 457.8 | 464.3 | 471.2 | 458   |
| 30                             | 386.3          | 375.4 | 395   | 399.5 | 404.6 | 482.3           | 469.9 | 453.6 | 454.2 | 462.4 | 454              | 465.8 | 470.7 | 469.4 | 459.8 |
| 40                             | 392.1          | 376.6 | 404.7 | 395.8 | 407.5 | 473.1           | 466.2 | 459.4 | 455.2 | 462.8 | 462.2            | 455.2 | 465.3 | 471.3 | 457.2 |
| 50                             | 403.2          | 391.6 | 402.1 | 385.4 | 398.1 | 466.8           | 460.8 | 461.9 | 455.7 | 469.3 | 446.8            | 455.9 | 468.8 | 456.6 | 463.8 |
| 60                             | 397.3          | 393.1 | 405.7 | 402.8 | 396.6 | 477.4           | 463   | 444.7 | 453.3 | 469.2 | 445.2            | 473.8 | 465.4 | 463.1 | 458.3 |
| 70                             | 392.7          | 383.1 | 395.1 | 409.4 | 393.8 | 474.2           | 464.6 | 458   | 453.7 | 457.8 | 436              | 480.8 | 470   | 463.9 | 466   |
| 80                             | 379.7          | 390.8 | 387.2 | 399.2 | 391.2 | 466.1           | 452.5 | 478.2 | 457.5 | 445.7 | 447.6            | 475.6 | 479.1 | 452.1 | 457   |
| 90                             | 385.3          | 397.2 | 380.2 | 399.6 | 394.1 | 468.4           | 458.4 | 463   | 465   | 449.5 | 448.3            | 473.5 | 478.6 | 445.6 | 454.1 |
| 100                            | 442.3          | 400.6 | 391.1 | 402.5 | 395   | 461.9           | 449.7 | 447.7 | 458.5 | 451.9 | 450.8            | 467.9 | 479.2 | 449   | 459.6 |

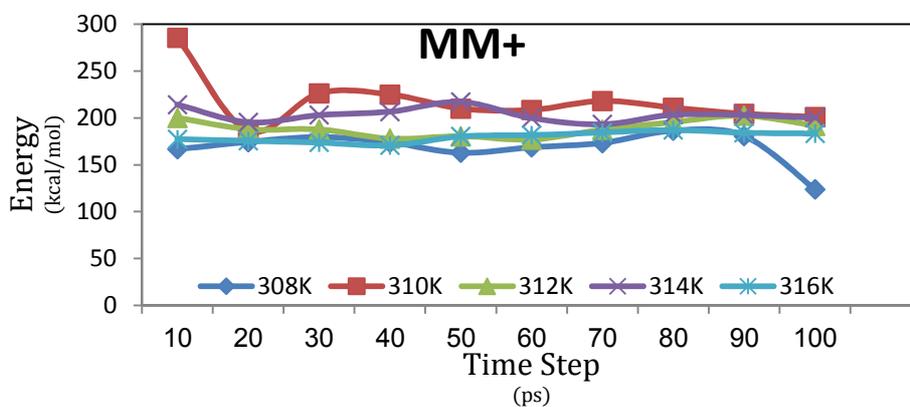




**Fig. 2.** The graphs of Clonidine drug-CNC potential energy

**Table1.** Computed drug to Nano Cone Kinetic Energy (kcal/ mol), belong to AMBER, MM<sup>+</sup> and OPLS force fields under five different temperature

| Kinetic Energy ( kcal/ mol ) |                |       |       |       |       |                 |       |       |       |       |                  |       |       |       |       |
|------------------------------|----------------|-------|-------|-------|-------|-----------------|-------|-------|-------|-------|------------------|-------|-------|-------|-------|
| Method                       | MM+/Mont Carlo |       |       |       |       | OPLS/Mont Carlo |       |       |       |       | AMBER/Mont Carlo |       |       |       |       |
| Time (PS)                    | 308K           | 310K  | 312K  | 314K  | 316K  | 308K            | 310K  | 312K  | 314K  | 316K  | 308K             | 310K  | 312K  | 314K  | 316K  |
| 10                           | 166.8          | 285.5 | 200.1 | 214.2 | 177.4 | 128.7           | 180.9 | 204.1 | 184.2 | 176   | 204.2            | 187.2 | 214   | 163.8 | 204.7 |
| 20                           | 174.3          | 186.3 | 188   | 195.4 | 175.7 | 148.3           | 171.4 | 203.7 | 175.1 | 171.3 | 199.9            | 190.9 | 209.1 | 171.3 | 655.6 |
| 30                           | 179.7          | 226.3 | 187.7 | 203   | 173.7 | 154.5           | 166.9 | 195.8 | 188.6 | 175.2 | 203.9            | 182.8 | 202.7 | 173.1 | 194.1 |
| 40                           | 173.9          | 225.1 | 177.9 | 206.7 | 170.7 | 163.7           | 170.6 | 190.1 | 187.6 | 174.8 | 195.8            | 193.4 | 208.1 | 171.1 | 197.8 |
| 50                           | 162.8          | 210.1 | 180.5 | 217.1 | 180.2 | 170.1           | 176   | 187.6 | 187.1 | 168.3 | 211.2            | 192.7 | 204.6 | 185.8 | 189.7 |
| 60                           | 168.7          | 208.6 | 176.9 | 199.8 | 181.7 | 159.4           | 173.8 | 204.8 | 189.6 | 168.4 | 212.8            | 174.8 | 208   | 179.4 | 200.4 |
| 70                           | 173.3          | 218.2 | 187.6 | 193.2 | 184.5 | 162.4           | 172.2 | 191.4 | 189.1 | 179.8 | 221.9            | 167.8 | 203.4 | 178.5 | 199.7 |
| 80                           | 186.4          | 210.9 | 195.5 | 203.4 | 187.1 | 170.7           | 184.3 | 171.2 | 185.4 | 191.9 | 210.3            | 173.1 | 194.3 | 190.3 | 181.8 |
| 90                           | 180.7          | 204.5 | 202.4 | 203   | 184.2 | 168.4           | 178.4 | 186.5 | 177.8 | 188.1 | 209.7            | 175.1 | 194.8 | 196.9 | 174.7 |
| 100                          | 123.7          | 201.1 | 191.6 | 200.1 | 183.3 | 175             | 187.1 | 201.7 | 184.3 | 185.7 | 207.2            | 180.7 | 194.2 | 193.5 | 180   |



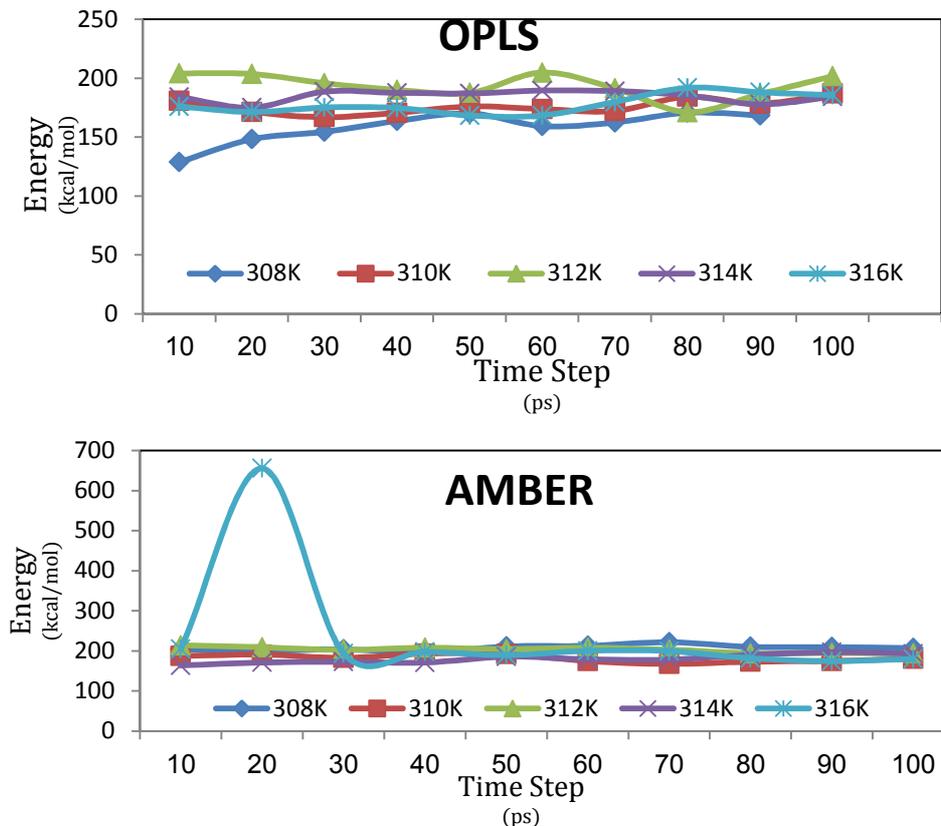


Fig. 3. The graphs of Clonidine drug-CNC kinetic energy.

Table 3. Computed Clonidine drug-CNC total energy ( kcal/ mol ), belong to AMBER, MM<sup>+</sup> and OPLS force fields under five different temperature

| Total Energy ( kcal/ mol ) |        |        |       |       |       |
|----------------------------|--------|--------|-------|-------|-------|
| Method                     | 308K   | 310K   | 312K  | 314K  | 316K  |
| MM <sup>+</sup>            | 566.1  | 601.7  | 582.7 | 602.6 | 578.3 |
| OPLS                       | 636.92 | 636.90 | 649.5 | 642.9 | 637.6 |
| AMBER                      | 658    | 648.7  | 673.4 | 642.5 | 655.6 |

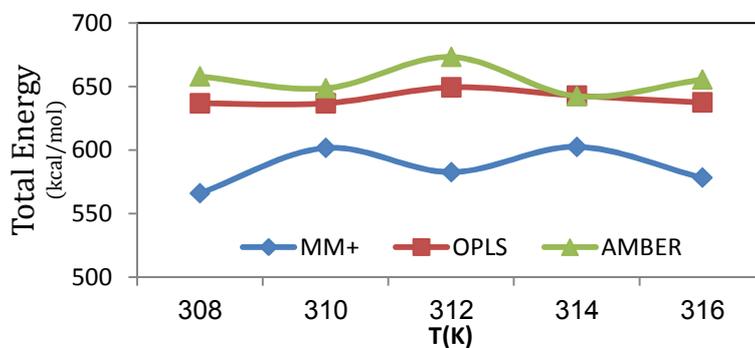


Fig. 4. The graphs of Clonidine drug-CNC Total Energy.

## CONCLUSION

After conducting the Molecular Mechanic study and gaining the potential energy by Monte Carlo method and studying the Nano cone that were involved with the drug in different temperature, the following results were concluded: The study showed that the system has the different level of energy and the different stability which is caused by the forces from inside the system and Nano cone because this Nano cone should find the best spatial conformity which means the highest stability level or the lowest level of energy. Also, you see in above diagrams, we have maximum amount of potential energy in 308K, OPLS method and the highest level of total energy observed in amber method. So with considering high amount of total energy, there will be minimum stability in this method.

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