P: ISSN NO.: 2394-0344 RNI No.UPBIL/2016/67980 VOL-3* ISSUE-12* (Part-1) March- 2019
E: ISSN NO.: 2455-0817 *Remarking An Analisation*

Study of Electronic Structure Properties of Netropsin Molecule through Computational Method

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Abstract

The molecule Netropsin, a DNA minor groove binder, is a natural polyamide which exhibit antibiotic and antiviral activities. Its analogs are used in tumor and cancer related diseases. In the present work, the molecular geometry of the netropsin molecule has been optimized in *gaseous phase* using B3LYP density functional in conjunction with 3-21G basis set. The molecular geometry and its conformations have been compared with that of crystallographic structure. Comparison of torsion angles shows that the conformations of the core rings do not differ considerably from the crystallographic values while conformational changes have been observed for the side chains and groups. The normal modes of vibrational frequencies in the range of 300 to 4000 cm^{-1} have been assigned. Non-existance of negative frequencies indicated the true minima of the molecule in gaseous state. Molecular electrostatic potential, fractional charges, HOMO- LUMO and thermodynamic properties of the molecule have also been investigated using same level of theory and discussed in detail.

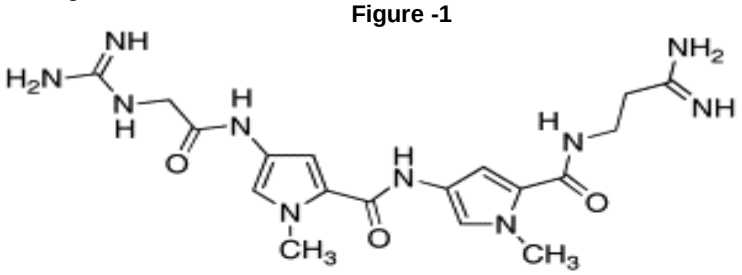
Keywords : Optimization, Electronic structure, HOMO-LUMO,IR Spectra.

Introduction

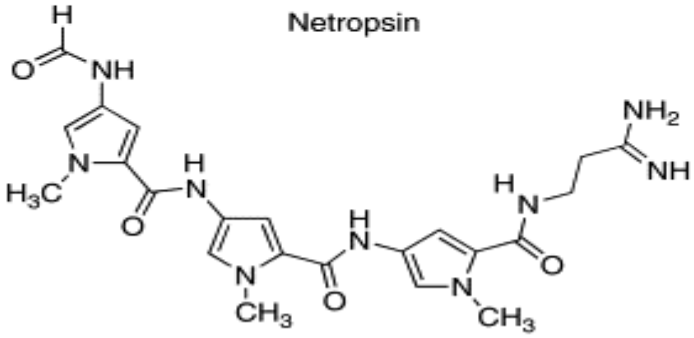
Netropsin, Distamycin and Related Compounds

There is found minor groove interaction in netropsin and distamycin A.These compounds have antitumor and anticancer properties these are the prototype minor groove binders (MGBs) . This is the reason why, I shall briefly discuss below. binding of these molecule is non-covalent to the minor groove of DNA, this is the reason why preventing DNA synthesis by inhibition of the corresponding polymerase reaction , leading to much current interest in them.[1]

Figure -1



Netropsin



Distamycin A

Here specific properties of only netropsin molecule has been done and related compounds, which have shown a pronounced specificity

for AT sequences. Recognition molecule by the minor groove is done, in the first place, interactions of hydrogen bonding, acceptor groups in DNA bases, mainly $N_3$and C_2=O of the adenine-thymine or guanine-citosine pairs. As shown in Fig.these interactions are hampered in the latter , due to steric reasons. Hydration of the ligand molecules is also a very important factor in the understanding of differences in binding affinity.

Computational Detail

The electronic structure of netropsin in ground state has been optimized using DFT(density functional theory) withB3LYPG basic set.DFT is used in this paper .Form of DFT is given below

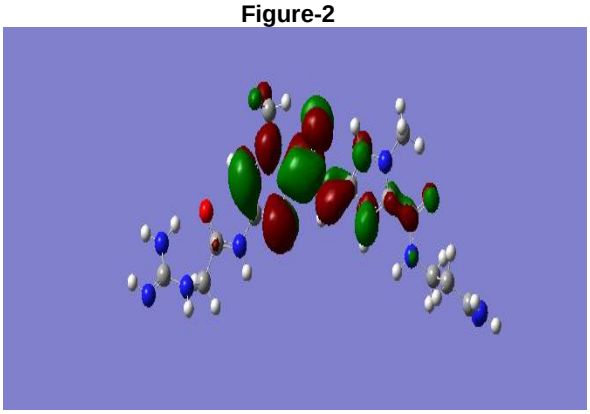
$E_{xc=}(1-a_0)E_x^{LSDA} + a_oE_x^{HF} + a_0E_X^{B88} + a_cE_C^{LYP} + (1-a_c)E_C^{VWN}$

In this equation energy terms are , Slater , Hertree-Fock exchange, Becke's exchange .functional correction, the gradient corrected correlation functional of Lee yang, Paar and, the local correlation functional of Vosco, Wilk and Nusair

Geometry of the molecule is fully optimised resulting no imaginary frequency which indicates that the optimized molecule has true minimum potential energy. In this work all the parameters are calculated using optimised geometry of the molecule with the help of B3LYP/3-2IG theory using GAUSSIAN.

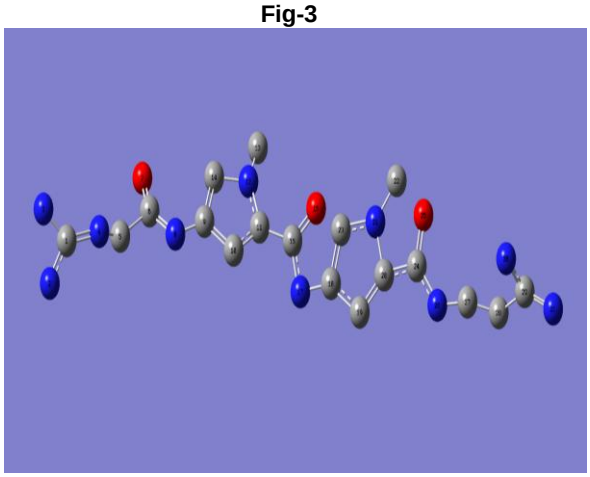
Homo Lumo of Netropsin Molecule is Given Below

Figure-2



Optimized Structure of Netropsin Molecule

Fig-3



HOMO-LUMO

The highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) are the terminology used to determine the band gap in organic/inorganic semiconductors, molecular reactivity and understand the reaction mechanisms[13]. The HOMO and LUMO as calculated using B3LYP/3-21G method are shown in Figure 3. The HOMO portion of the molecule is greatly concerted on furone rings linking carbon atoms and same is less focused on the oxygen and nitrogen atoms. Complete covering of nitrogen atom wave functions on the neighboring carbon atom decreases the length of the central bridge of HOMO. In LUMO, there are delocalization of valence (virtual) orbitals throughout the molecule. Nitrogen atoms of the connection group overlap each other and carbon atoms of the central connection overlap adjacent carbon atoms of the furone rings. The HOMO energy is directly associated to the ionization potential, while LUMO energy is directly associated to the electron affinity. Energy gapis defined as the difference between HOMO and LUMO orbital.

Table 1

Comparison of bond length bond angle and Dihedral Angle obtained from computation and theoretical values.

S.No.	atom	Atom No.				Bond length A^0		Bond angle DEG		dihedral Angle DEG	
			$Atom_1$	$Atom_2$	$Atom_3$	Exp.	Theo.	Exp.	Theo	Exp	Theo
1	C	1									
2	N	2	1			1.3866	1.2899				
3	N	3	1	2		1.3933	1.3847	130.44	130.32		
4	N	4	1	2	3	1.4357	1.4065	118.12	117.47	-177.46	-179.66
4	C	4	4	1	2	1.5132	1.4621	122.66	122.28	148.22	147.60
6	C	6	5	4	1	1.5444	1.5390	111.86	111.47	92.84	92.24
7	O	7	6	5	4	1.3712	1.2531	121.92	122.03	-58.42	-56.38
8	N	8	6	5	4	1.4362	1.3664	115.21	115.71	124.88	124.62
9	C	9	8	6	5	1.3868	1.4063	122.26	124.72	178.76	179.14
10	C	10	9	8	6	1.5061	1.4190	125.87	125.32	-179.55	-179.69
11	C	11	10	9	8	1.3763	1.3958	106.75	107.61	-178.92	-179.34
12	N	12	11	10	9	1.3644	1.3894	106.75	107.34	0.56	0.37
13	C	13	12	11	10	1.4711	1.4806	126.33	126.59	-178.11	-178.69

14	C	14	12	11	10	1.3857	1.3762	109.94	109.58	-0.57	-0.57
15	C	15	11	10	9	1.4987	1.4678	129.22	128.95	176.86	178.29
16	O	16	15	11	10	1.3124	1.2553	124.49	124.58	-165.09	-165.09
17	N	17	15	11	10	1.3249	1.3794	112.78	114.32	14.12	14.68
18	C	18	17	15	11	1.4277	1.4021	126.24	124.43	-176.08	-176.58
19	C	19	18	17	15	1.3988	1.4199	123.84	124.97	178.55	179.62
20	C	20	19	18	17	1.3766	1.3953	107.36	107.77	179.33	179.89
21	N	21	20	19	18	1.3949	1.3894	107.36	107.31	-0.33	-0.33
22	C	22	21	20	19	1.4568	1.4800	128.68	126.52	177.22	179.65
23	C	23	21	20	19	1.3996	1.3767	109.21	109.58	0.41	0.36
24	C	24	20	19	18	1.3699	1.4671	129.58	128.95	-176.35	-179.43
25	O	25	24	20	19	1.2765	1.2580	122.99	124.58	172.42	170.19
26	N	26	24	20	19	1.3721	1.3721	115.38	115.47	-9.23	-9.62
27	C	27	26	24	20	1.4522	1.4704	120.92	119.65	178.52	177.61
28	C	28	27	26	24	1.5386	1.5406	112.55	112.15	75.66	74.77
29		29	28	27	26	1.5489	1.5299	113.65	113.00	175.56	177.94
30	N	30	29	28	27	1.2534	1.2871	129.42	127.98	5.08	5.44

Table-2

Electronic energy	-1466.66	Hartree
Dipole moment	-0.858085	debye
Polarizability	273.04	au
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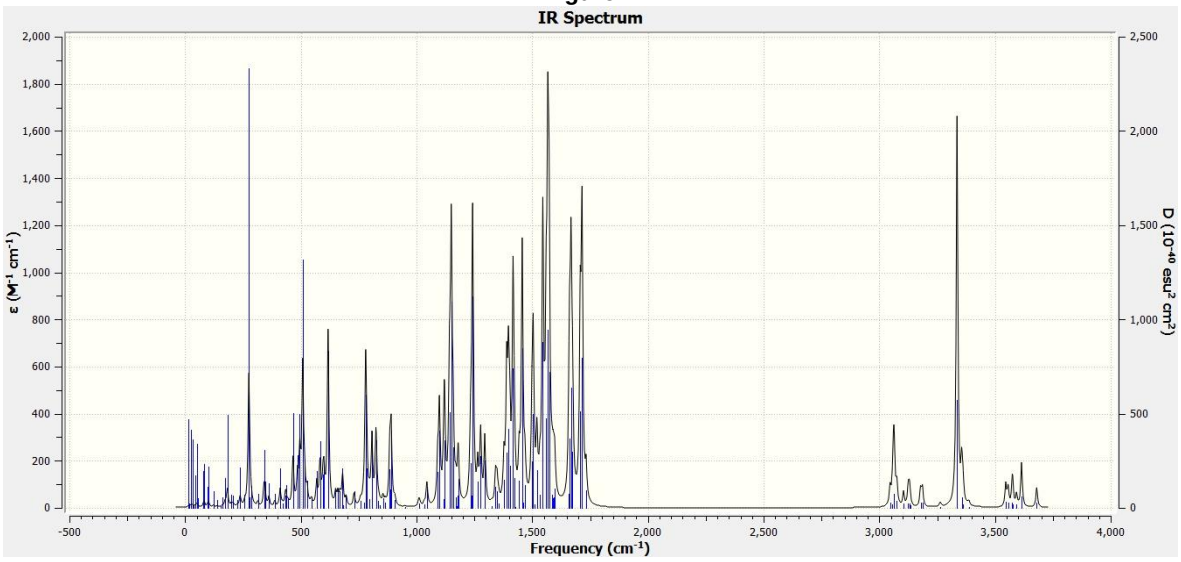
Dipole moment	-0.858085	debye
Polarizability	273.04	au

IR Spectrum of Netropsin Molecule

Figure-4



Result and Discussion

Optimized structure of netropsin obtained fromB3LYP/3-21G method is given in the fig .comparison of bond length, bond angles and torsion angles of the optimized molecular structure with those data from crystallographic structure ,as shown in the table. from the result ,it clear that there is a very small difference between computational value and value obtained from crystallographic data.

In the table it is clear that experimental and theoretical values are nearly same. There is a very small variation in experimental values and theoretical values.The normal modes of vibrational frequencies are in the range of 300 to 4000 cm^{-1} have been find out in the spectrum .Peak intensities are at 300,1550and3350$cm^{-1.}$

Analysis of IR Spectra

Infrared spectroscopy is due to transition of molecule between its vibrational energy levels due to absorption of radiation. These spectra is due tochange in dipole moment within the molecules. Frequency versus absorption intensity plot of the netropsin molecule is studied as shown in Figure 4. Theoretically calculated vibrational (IR) frequencies of the given molecule is assigned and compared with the experimental values reported in theliterature . The IR spectrum of the molecule gives the details regarding the ring out of plane deformation, C-H out of plane

bending, rocking, scissoring, bending, symmetric and anti-symmetric NH vibrations etc.

Aim of the study

DRUG-DNA interaction through computational technique. molecules that bind major groove or minor groove of DNA they can be effective anticancer, antibiotic and antiviral therapeutic agents affect the well-being of millions of people worldwide.

Conclusion

Geometrical parameters calculated through B3LYP/3-21G method are in very good agreement with experimental values having a very little deviated conformations. The MEP map gives evident that electrophilic ability strengthens and nucleophilic ability become poor as one move radially outwards from the center of the molecule. Small values of HOMO and LUMO energy gaps explain the ultimate charge transfer interactions taking place within the molecule. Computed IR assignments are in good correlation with those of experimental values.

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