RJC

RASĀYAN *J. Chem.*
Vol. 11 | No. 1 |127-134 | January - March | 2018
ISSN: 0974-1496 | e-ISSN: 0976-0083 | CODEN: RJCABP
http://www.rasayanjournal.com
http://www.rasayanjournal.co.in

DFT BASED ANALYSIS OF N-(3-METHYL-2, 6-DIPHENYL-PIPERIDIN-4-YLIDINE)-N'-PHENYL HYDRAZINE (3-MDPYP) MOLECULE

M. Dinesh Kumar[1*], P. Rajesh[2], M. Ezhil Inban[3] and P. Kumaradhas[4]
[1]Department of Chemistry, Karpagam Academy of Higher Education,
Coimbatore-641 021, (Tamilnadu) India
[2]Department of Chemistry, Government Arts College, Coimbatore-641 018, (Tamilnadu) India
[3]Department of Physics, Government Arts College, Coimbatore-641 018, (Tamilnadu) India
[4]Department of Physics, Periyar University, Coimbatore-641062 (Tamilnadu) India
*E-mail: dinemca@gmail.com

ABSTRACT

To analyze the geometrical and topological parameters of the3-MDPYP molecule, the quantum chemical calculations using Density Function Theory (DFT) is performed. This method along with the 6-311G** basis set, confirms the exact geometry of the selected molecule. The vital role of Piperidin-4-ones and its derivatives are found to have great potential in terms of becoming potent compounds in drug design. In this regard, characterizing such compounds to study theoretically and their structure becomes important and economical in performing the suitability test. This paper is a record of such research attempt on studying geometrical properties like the bond angle, bond lengths, torsion angles and bond topological properties of the 3-MDPYP molecule.

Keywords: 3-MDPYP, DFT, Bond topology, Deformation density, Laplacian electron density

INTRODUCTION

In today's drug discovery, it is a task challenging to understand the drug-receptor interaction[1]. Many methods have been proposed in the previous years to investigate the drug-receptor interactions[2]. However, *in silico* computer modeling techniques along with in vitro studies are playing an important role and helps confirm the drug-receptor mechanism. Always the drug and receptor molecules will have complementary charges, so that the drug molecule may be well inside the binding pocket of the receptor[3,4]. The drug-receptor plays an important role in three-dimensional structures and also in the atomic level interaction of the molecule[5]. It is based on the strength of electrostatic interaction and charge distribution of atoms in the binding of sites. Further, the same electrostatic interaction of molecule is used to verify the variable regions of the active drug molecule. This regard could be clarified through the accurate calculation of topological and electrostatic parameters determined from multipole analysis[6]of charge density distribution of the molecule, which includes the effects of lone pair and p-electron density. So the understanding of charge density distribution is important to determine the molecular properties and to predict the intermolecular interactions[7].

This work explains the theoretical analysis of charge density distribution and some topological parameters of the 3-MDPYP molecule through quantum chemical calculations. In today's scenario, Piperine-4-one compounds play a prime activity in all areas of drug discovery and form important drugs with an essential molecular structures[8-13]. These are reported to possess analgesic[8], anti-inflammatory[9], central nervous system[10], local analgesics[11], anticancer[12] and antibacterial activity[13]. To explore this kind of activity in 3-MDPYP molecule, some theoretical operations with the help of DFT are performed. A clear idea of charge density distribution and topological properties of this molecule has allowed realizing the strength of intermolecular interactions and electrostatic interactions between the drug candidate and receptor which facilitate to examine the interactions of drug-receptor.

The current investigation which explains the charge density distribution of 3-MDPYP molecule from the high-level quantum chemical calculations combined with Bader's theory of Atoms in Molecules (AIM theory)[14]. The arrangement of the atoms in the selected molecule from AIM theory allows extracting the topology of electron density and electrostatic properties of the above molecule. The arrival of ultra-shorter wavelength radiation[15], synchrotron sources and area detectors are made to evaluate the molecular charge density distribution of small molecules to macromolecules[16].

In recent year, charge density analysis becoming an important tool to interpret the molecular structures obtained from crystalline materials[17]. The information obtained from the topological analysis is significant and better than the molecules having classical atomic connectivity. Based on these values, it is confirmed that the 3-MDPYP molecule is apt for the effective candidate for drug-receptor activity.

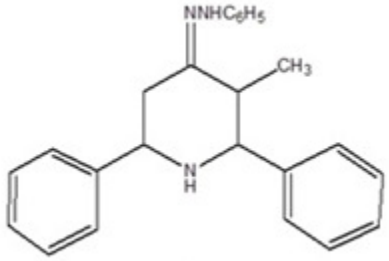

Fig.-1: Chemical structure of 3-MDPYP molecule

EXPERIMENTAL

Computational Details

The 3-MDPYP molecule was obtained from laboratory source and the position of the atom in this molecule was confirmed by Density Functional methods[18] using the Gaussian03 program[19]. A combination of Becke's three parameters exchange and Lee, Yang and Parr gradient-corrected correlation function (B3LYP) is applied for the whole DFT calculation along with 6-311G** basis set, which provided the effective core potential and the detailed description. The position of the atom in the regarding molecule was performed via Berny algorithm in redundant internal co-ordinates[20].

The electron density $\rho_{bcp}(r)$, Laplacian of electron density $\nabla^2\rho_{bcp}(r)$, bond ellipticity ε and the eigen values λ_i were calculated using EXT94b routine incorporated to the AIMPAC software[21]. The Laplacian of charge density and the deformation density maps were plotted using DENPROP and wfn2plots program packages[22].

RESULTS AND DISCUSSION

Structural Aspects

DFT is an effective method to evaluate the geometrical parameters such as bond lengths, bond angles and torsion angles using 6-311G** basis set. The ball and stick model of energy minimized geometry of 3-MDPYP molecule is shown inFig.-2. In-depth investigation of the geometrical parameters and the bond, distances are predicted using DFT method and are shown in this Table-1.

The calculated C–C bond lengths in piperidine ring C1-C6 varied from 1.511 Å to 1.568 Å and similarly the C-C bonds in phenyl rings between 1.389 Å to 1.403 Å. The distance of C5-C17 is 1.534 Å which is similar to the reported structure[23]. Bond lengths of C2-N3 [1.466 Å] and N3-C4 [1.466 Å] are moderately longer than N8-C9 [1.393 Å] and C=N bond distance is 1.185 Å. Nitrogen heteroatoms influence the bond length values of the molecule. Because of C6-N7 [1.393 Å] and N7-N8 [1.348 Å] bonds are comparatively lesser than other C-C bonds. The optimized structure of 3-MDPYP molecule is shown in the Fig. 2 and its atom-numbering scheme is indicated. The C–H bond distances calculated from 1.081 – 1.104 Å. The mean plane calculation of the ring system confirms that the molecule is a non-planar[24].

Charge Density Analysis

The deformation density map shows the arrangement of the electron density of atoms in 3-MDPYP molecule, which is used to visualize the areas of charge accumulation in the bonding regions and

positions of the heteroatoms. This map reveals that the 3-MDPYP having covalent nature of bonds from the continuous region of charge density distribution. A complete spectrum of charge density distribution obtained from the bond topological analysis of 3-MDPYP molecule is presented in the Table-2. Although the N–C and C–C bonds exhibit covalent interaction, its charge density distribution is not similar to the other bonding regions of the molecule; the map clearly differentiates the difference among the charge density distribution of various bonding regions of the molecule.

Table-1 Geometrical parameters of 3-MDPYP molecule

Bond Lengths (Å)		Bond Angles (º)				Torsion Angles (deg)			
C1-C2	1.546	C2-C1-C6	110.2	C12-C13-C14	121.2	C26-C27-H52	119.6	N8-C9-C10-C11	-179.8
C1-C6	1.511	C2-C1-H28	107.9	C12-C13-H38	119.8	C6-C1-C2-N3	56	N8-C9-C10-H35	0.3
C1-H28	1.096	C2-C1-H29	110.1	C14-C13-H38	118.9	C6-C1-C2-C16	178.5	C14-C9-C10-C11	0.1
C1-H29	1.089	C6-C1-H28	110.7	C9-C14-C13	119.7	C6-C1-C2-H30	-63.7	C14-C9-C10-H35	179.9
C2-N3	1.466	C6-C1-H29	109.3	C9-C14-H39	118.9	H28-C1-C2-N3	-64.9	N8-C9-C14-C13	179.8
C2-C16	1.517	H28-C1-H29	108.5	C13-C14-H39	121.4	H28-C1-C2-C16	57.5	N8-C9-C14-H39	-0.2
C2-H30	1.104	C1-C2-N3	107.9	C4-C15-C23	120.7	H28-C1-C2-H30	175.4	C10-C9-C14-C13	0
N3-C4	1.468	C1-C2-C16	112	C4-C15-C27	120.6	H29-C1-C2-N3	176.6	C10-C9-C14-H39	-179.8
N3-H31	1.015	C1-C2-H30	106.7	C23-C15-C27	118.5	H29-C1-C2-C16	-60.8	C9-C10-C11-C12	-0.03
C4-C5	1.568	N3-C2-C16	110.9	C2-C16-C21	120.1	H29-C1-C2-H30	56.9	C9-C10-C11-H36	179.9
C4-C15	1.518	N3-C2-H30	111.2	C2-C16-C22	121.3	C2-C1-C6-C5	-57.9	H35-C10-C11-C12	-179.8
C4-H32	1.105	C16-C2-H30	107.7	C21-C16-C22	118.6	C2-C1-C6-N7	118.5	H35-C10-C11-H36	0.2
C5-C6	1.528	C2-N3-C4	114.5	C5-C17-H40	112.4	H28-C1-C6-C5	61.3	C10-C11-C12-C13	0.2
C5-C17	1.534	C2-N3-H31	109.8	C5-C17-H41	109.8	H28-C1-C6-N7	-122.1	C10-C11-C12-H37	179.9
C5-H33	1.097	C4-N3-H31	109.2	C5-C17-H42	111.2	H29-C1-C6-C5	-179	H36-C11-C12-C13	-179.9
C6-N7	1.185	N3-C4-C5	109.3	H40-C17-H41	106.5	H29-C1-C6-N7	-2.4	H36-C11-C12-H37	-0.2
N7-N8	1.348	N3-C4-C15	109.1	H40-C17-H42	109.3	C1-C2-N3-C4	-60.3	C11-C12-C13-C14	0.1
N8-C9	1.393	N3-C4-H32	111.6	H41-C17-H42	107.1	C1-C2-N3-H31	176.2	C11-C12-C13-H38	179.9
N8-H34	1.007	C5-C4-C15	112.9	C19-C18-C22	120.2	C16-C2-N3-C4	176.5	H37-C12-C13-C14	-179.9
C9-C10	1.403	C5-C4-H32	106.4	C19-C18-H43	119.9	C16-C2-N3-H31	53	H37-C12-C13-H38	-0.1
C9-C14	1.401	C15-C4-H32	107.7	C22-C18-H43	119.7	H30-C2-N3-C4	56.5	C12-C13-C14-C9	-0.4
C10-C11	1.389	C4-C5-C6	107.4	C18-C19-C20	119.5	H30-C2-N3-H31	-66.3	C12-C13-C14-H39	179.8
C10-H35	1.086	C4-C5-C17	112	C18-C19-H44	120.3	C1-C2-C16-C21	96.6	H38-C13-C14-C9	-179.9
C11-C12	1.393	C4-C5-H33	105.1	C20-C19-H44	120.2	C1-C2-C16-C22	-81.5	H38-C13-C14-H39	-0.2
C11-H36	1.084	C6-C5-C17	118.8	C19-C20-C21	120	N3-C2-C16-C21	-142.6	C4-C15-C23-C24	-179.2
C12-C13	1.394	C6-C5-H33	105.2	C19-C20-H45	120.1	N3-C2-C16-C22	39.1	C4-C15-C23-H48	1.7
C12-H37	1.083	C17-C5-H33	107.1	C21-C20-H45	119.8	H30-C2-C16-C21	-20.5	C27-C15-C23-C24	0.5
C13-C14	1.39	C1-C6-C5	112.2	C16-C21-C20	120.8	H30-C2-C16-C22	161.2	C27-C15-C23-H48	-178.4
C13-H38	1.084	C1-C6-N7	114.9	C16-C21-H46	119.4	C2-N3-C4-C5	61.5	C4-C15-C27-C26	179.2
C14-H39	1.08	C5-C6-N7	132.6	C20-C21-H46	119.7	C2-N3-C4-C15	-174.8	C4-C15-C27-H52	-0.9
C15-C23	1.4	C6-N7-N8	124.5	C16-C22-C18	120.5	C2-N3-C4-H32	-55.8	C23-C15-C27-C26	-0.5
C15-C27	1.397	N7-N8-C9	120.7	C16-C22-H47	119	H31-N3-C4-C5	-174.7	C23-C15-C27-H52	179.1
C16-C21	1.398	N7-N8-H34	121.5	C18-C22-H47	120.3	H31-N3-C4-C15	-50.9	C2-C16-C21-C20	-177.9
C16-C22	1.399	C9-N8-H34	117.7	C15-C23-C24	120.6	H31-N3-C4-H32	68.1	C2-C16-C21-H46	2.1
C17-H40	1.094	N8-C9-C10	118.6	C15-C23-H48	119.2	N3-C4-C5-C6	-56.3	C22-C16-C21-C20	0.2
C17-H41	1.09	N8-C9-C14	122.2	C24-C23-H48	120.1	N3-C4-C5-C17	171.4	C22-C16-C21-H46	-179.5
C17-H42	1.092	C10-C9-C14	119.1	C23-C24-C25	120.2	N3-C4-C5-H33	55.3	C2-C16-C22-C18	178.1
C18-C19	1.393	C9-C10-C11	120.3	C23-C24-H49	119.7	C15-C4-C5-C6	-177.8	C2-C16-C22-H47	-2.5
C18-C22	1.392	C9-C10-H35	119.7	C25-C24-H49	119.9	C15-C4-C5-C17	49.9	C21-C16-C22-C18	-0.01
C18-H43	1.084	C11-C10-H35	119.9	C24-C25-C26	119.5	C15-C4-C5-H33	-66.1	C21-C16-C22-H47	179.2
C19-C20	1.393	C10-C11-C12	120.6	C24-C25-H50	120.2	H32-C4-C5-C6	64.2	C22-C18-C19-C20	0.2
C19-H44	1.084	C10-C11-H36	119.2	C26-C25-H50	120.2	H32-C4-C5-C17	-68	C22-C18-C19-H44	179.9
C20-C21	1.393	C12-C11-H36	120.1	C25-C26-C27	120	H32-C4-C5-H33	175.8	H43-C18-C19-C20	-179.7
C20-H45	1.084	C11-C12-C13	118.9	C25-C26-H51	120.1	N3-C4-C15-C23	-49.8	H43-C18-C19-H44	-0.1
C21-H46	1.085	C11-C12-H37	120.5	C27-C26-H51	119.8	N3-C4-C15-C27	130.3	C19-C18-C22-C16	-0.1
C22-H47	1.083	C13-C12-H37	120.5	C15-C27-C26	120.8	C5-C4-C15-C23	71.6	C19-C18-C22-H47	-179.4

C23-C24	1.392			C15-C27-H52	119.4	C5-C4-C15-C27	-108.2	H43-C18-C22-C16	179.7
C23-H48	1.083					H32-C4-C15-C23	-171.2	H43-C18-C22-H47	0.5
C24-C25	1.394	C4-C5-C17-H41	-62.3	C15-C23-C24-C25	-0.1	H32-C4-C15-C27	8.9	C18-C19-C20-C21	0.3
C24-H49	1.084	C4-C5-C17-H42	179.1	C15-C23-C24-H49	-179.9	C4-C5-C6-C1	56.9	C18-C19-C20-H45	179.6
C25-C26	1.392	C6-C5-C17-H40	-70.2	H48-C23-C24-C25	178.8	C4-C5-C6-N7	-118.7	H44-C19-C20-C21	-179.7
C25-H50	1.084	C6-C5-C17-H41	171.3	H48-C23-C24-H49	-0.9	C17-C5-C6-C1	-174.5	H44-C19-C20-H45	-0.1
C26-C27	1.394	C6-C5-C17-H42	52.8	C23-C24-C25-C26	-0.2	C17-C5-C6-N7	9.7	C19-C20-C21-C16	-0.2
C26-H51	1.084	H33-C5-C17-H40	170.8	C23-C24-C25-H50	-179.8	H33-C5-C6-C1	-54.5	C19-C20-C21-H46	179.5
C27-H52	1.085	H33-C5-C17-H41	52.3	H49-C24-C25-C26	179.6	H33-C5-C6-N7	129.7	H45-C20-C21-C16	-179.8
		H33-C5-C17-H42	-66.1	H49-C24-C25-H50	0	C4-C5-C17-H40	56	H45-C20-C21-H46	-0.2

The charge accumulation of C_{ar}–C_{ar} bond ranges from 1.536 to 2.094 eÅ^{-3}, which is slightly lower than N-atoms attached to C–C bond from 1.782 to 2.434 eÅ^{-3} of the 3-MDPYP molecule. The low $\rho_{bcp}(r)$ of C–C bond is due to the effect of neighboring atoms in the molecule. N–N bond density ranges around 2.447 eÅ^{-3} and N–H bond 2.323 eÅ^{-3} which are comparatively higher than C-C bonds and C-H bonds respectively. Further, the C=N bond density is 2.434 eÅ^{-3}, this implies that the strong bond observed in this molecule. The loan pair region of N-atoms is shown in the Fig.-3. The bond ellipticity, $\varepsilon = (\lambda_1/\lambda_2 - 1)$ is defined as the measure of anisotropy of electron distribution at BCP, where λ_1 and λ_1 are the negative eigenvalues of Hessian matrix [25]. The anisotropy of bond density $\rho_{bcp}(r)$ is confirmed by the high ellipticity values. The ellipticity of C=N bond is found to be higher and the value is 0.326Å The Laplacian of electron density, $\nabla^2\rho_{bcp}(r)$, at the bond critical points of the molecule bears the chemical significance of the bond topological theory [26].

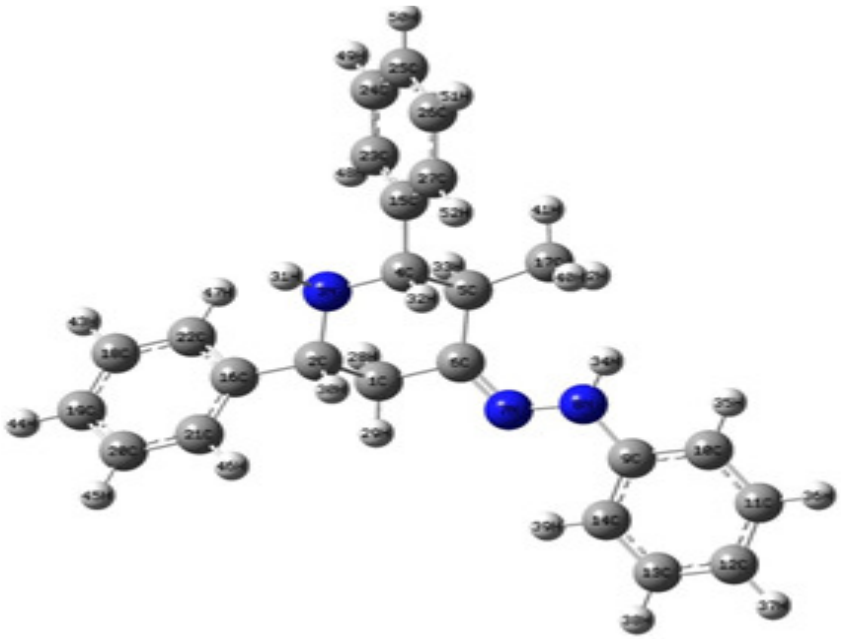

Fig.-2: The optimized structure of 3-MDPYP molecule

The Laplacian of the electron density is negative for all bonds in the molecule and exhibits bond-critical points. As it is noticed in the previous section, the charge accumulation is not same as for all C–C bonds of the aromatic ring. A similar trend can also be seen in the Laplacian of electron density distribution. The Laplacian values for C–C bonds ranges from −11.3 to −20.8 e Å^{-5}, of which the Laplacian values of N-N, C-N, N-H, C=N bonds are -16.71 e Å^{-5}, -16.322 e Å^{-5}, -39.724 e Å^{-5} and -14.357 e Å^{-5} respectively.In Fig.-4 the contour map of Laplacian of electron density derived from the experiment, reveals that the C-C, C-N, N-H and C-H bonds of the 3-MDPYP molecule and confirms the covalent bond character.

Table-2: Bond topological properties of the3-MDPYP molecule at DFT/6-311G** level theory.

Bonds	Rho(r)	D2r	λ1	λ2	λ3	ε	V(r)	G(r)	H(r)	d1	d2	D	del_d%
C2-C1	1.596	-12.446	-10.677	-10.493	8.724	0.018	-1.609	0.369	-1.24	0.782	0.764	1.546	0.582
C2-N3	1.782	-16.322	-12.673	-11.998	8.49	0.56	-2.599	0.728	-1.871	0.604	0.863	1.467	8.83
N3-C4	1.783	-16.162	-12.763	-12.023	8.624	0.062	-2.546	0.707	-1.839	0.857	0.611	1.468	8.379
C4-C5	1.536	-11.358	-10.206	-9.912	8.76	0.03	-1.496	0.35	-1.146	0.788	0.78	1.568	0.255
C1-C6	1.714	-14.463	-11.914	-11.227	8.678	0.061	-1.831	0.409	-1.422	0.741	0.77	1.511	0.96
C6-C5	1.645	-13.077	-11.207	-10.605	8.735	0.057	-1.702	0.393	-1.309	0.775	0.755	1.529	0.654
C6-N7	2.434	-14.357	-19.549	-14.742	19.933	0.326	-6.546	2.77	-3.776	0.452	0.837	1.289	14.93
C17-H34	0.108	1.505	-0.379	-0.157	2.041	0.407	-0.071	0.088	0.017	1.45	0.879	2.329	12.258
N7-N8	2.447	-16.71	-20.54	-18.574	22.404	0.106	-3.578	1.204	-2.374	0.663	0.686	1.349	0.85
C9-C10	2.057	-20.186	-15.432	-12.61	7.855	0.224	-2.733	0.66	-2.073	0.726	0.678	1.404	1.709
N8-C9	1.991	-19.319	-14.438	-13.247	8.366	0.09	-3.928	1.288	-2.64	0.88	0.514	1.394	13.128
C10-C11	2.091	-20.718	-15.642	-12.77	7.694	0.225	-2.835	0.692	-2.143	0.699	0.691	1.39	0.288
C12-C11	2.082	-20.674	-15.564	-12.88	7.769	0.208	-2.802	0.677	-2.125	0.689	0.705	1.394	0.57
C11-H36	1.899	-23.283	-17.946	-17.657	12.32	0.016	-2.158	0.264	-1.894	0.691	0.379	1.07	14.579
C14-C9	2.057	-20.249	-15.367	-12.653	7.771	0.214	-2.756	0.669	-2.087	0.669	0.733	1.402	2.28
C14-C13	2.091	-20.749	-15.617	-12.831	7.699	0.217	-2.831	0.689	-2.142	0.695	0.696	1.391	0.04
C12-H37	1.896	-23.12	-17.897	-17.446	12.223	0.026	-2.163	0.272	-1.891	0.69	0.379	1.069	14.546
C13-C12	2.082	-20.679	-15.562	-12.901	7.785	0.206	-2.797	0.675	-2.122	0.703	0.692	1.394	0.395
C4-C15	1.695	-14.268	-11.805	-11.237	8.774	0.051	-1.759	0.38	-1.379	0.756	0.762	1.518	0.2
C16-C2	1.698	-14.354	-11.873	-11.256	8.775	0.055	-1.763	0.379	-1.384	0.762	0.755	1.517	0.231
C5-C17	1.607	-12.688	-10.621	-10.572	8.505	0.005	-1.623	0.367	-1.256	0.77	0.764	1.535	0.195
C19-C18	2.089	-20.843	-15.622	-13.015	7.795	0.2	-2.808	0.674	-2.134	0.697	0.697	1.394	0
C22-C16	2.067	-20.275	-15.353	-12.797	7.874	0.2	-2.758	0.669	-2.089	0.695	0.704	1.399	0.32
C19-C20	2.09	-20.871	-15.639	-13.015	7.784	0.202	-2.814	0.677	-2.137	0.696	0.697	1.393	0.04
C21-C16	2.074	-20.412	-15.464	-12.81	7.863	0.207	-2.772	0.672	-2.1	0.697	0.701	1.398	0.14
H44-C19	1.901	-23.305	-17.992	-17.676	12.363	0.018	-2.158	0.263	-1.895	0.378	0.692	1.07	14.67
C20-C21	2.089	-20.825	-15.62	-12.986	7.78	0.203	-2.811	0.677	-2.134	0.696	0.697	1.393	0.04
H30-C2	1.856	-21.835	-17.264	-16.939	12.369	0.019	-2.078	0.274	-1.804	0.388	0.703	1.091	14.44
H45-C20	1.901	-23.32	-17.998	-17.696	12.374	0.017	-2.157	0.262	-1.895	0.378	0.692	1.07	14.67
H43-C18	1.901	-23.309	-17.989	-17.689	12.369	0.017	-2.156	0.262	-1.894	0.378	0.692	1.07	14.67
C18-C22	2.089	-20.82	-15.599	-12.989	7.769	0.201	-2.814	0.678	-2.136	0.697	0.696	1.393	0.036
C15-C23	2.064	-20.213	-15.322	-12.781	7.89	0.199	-2.747	0.666	-2.081	0.704	0.697	1.4	0.25
C24-C25	2.086	-20.804	-15.592	-13.02	7.807	0.198	-2.798	0.671	-2.127	0.697	0.697	1.395	0
C24-H49	1.902	-23.352	-18.029	-17.735	12.412	0.017	-2.156	0.261	-1.895	0.693	0.377	1.07	14.766
C23-C24	2.093	-20.872	-15.631	-13.002	7.76	0.202	-2.823	0.681	-2.142	0.696	0.696	1.392	0
C26-C25	2.094	-20.934	-15.672	-13.035	7.774	0.202	-2.824	0.679	-2.145	0.697	0.695	1.392	0.072
C15-C27	2.076	-20.411	-15.481	-12.788	7.859	0.211	-2.778	0.674	-2.104	0.7	0.697	1.397	0.107

C25-H50	1.902	-23.35	-18.03	-17.724	12.405	0.017	-2.157	0.261	-1.896	0.692	0.377	1.07	14.72
C27-C26	2.085	-20.764	-15.583	-12.977	7.796	0.201	-2.8	0.673	-2.127	0.698	0.696	1.394	0.072
H51-C26	1.902	-23.341	-18.021	-17.72	12.4	0.017	-2.157	0.261	-1.896	0.377	0.693	1.07	14.77
C1-H28	1.848	-21.772	-16.967	-16.876	12.071	0.005	-2.096	0.286	-1.81	0.697	0.385	1.083	14.404
H29-C1	1.887	-22.758	-17.691	-17.616	12.549	0.004	-2.136	0.271	-1.865	0.378	0.698	1.076	14.87
H31-N3	2.291	-36.205	-29.934	-28.435	22.165	0.053	-3.352	0.409	-2.943	0.261	0.736	0.997	23.82
H32-C4	1.852	-21.718	-17.171	-16.898	12.351	0.016	-2.071	0.275	-1.796	0.388	0.703	1.092	14.42
H52-C27	1.895	-23.125	-17.893	-17.553	12.321	0.019	-2.151	0.266	-1.885	0.379	0.692	1.071	14.61
C5-H33	1.863	-22.02	-17.239	-17.089	12.309	0.009	-2.115	0.287	-1.828	0.7	0.384	1.084	14.576
N8-H34	2.323	-39.724	-31.721	-29.728	21.726	0.067	-3.548	0.384	-3.164	0.74	0.248	0.988	24.899
C10-H35	1.876	-22.584	-17.508	-17.029	11.952	0.028	-2.147	0.283	-1.864	0.689	0.383	1.072	14.272
H38-C13	1.9	-23.312	-17.969	-17.696	12.353	0.015	-2.156	0.262	-1.894	0.378	0.692	1.07	14.67
C14-H39	1.92	-23.674	-18.495	-18.041	12.863	0.025	-2.175	0.259	-1.916	0.696	0.37	1.066	15.291
H40-C17	1.837	-21.512	-16.654	-16.449	11.591	0.012	-2.113	0.304	-1.809	0.391	0.69	1.081	13.83
C17-H41	1.87	-22.295	-17.399	-17.27	12.374	0.007	-2.129	0.284	-1.845	0.697	0.38	1.077	14.717
C17-H42	1.853	-21.885	-16.95	-16.768	11.834	0.011	-2.127	0.297	-1.83	0.692	0.387	1.079	14.133
C22-H47	1.913	-23.545	-18.297	-17.968	12.719	0.018	-2.163	0.257	-1.906	0.696	0.373	1.069	15.108
C21-H46	1.895	-23.116	-17.885	-17.55	12.318	0.019	-2.15	0.266	-1.884	0.693	0.379	1.071	14.659
H48-C23	1.912	-23.523	-18.271	-17.953	12.701	0.018	-2.16	0.257	-1.903	0.373	0.696	1.069	15.11

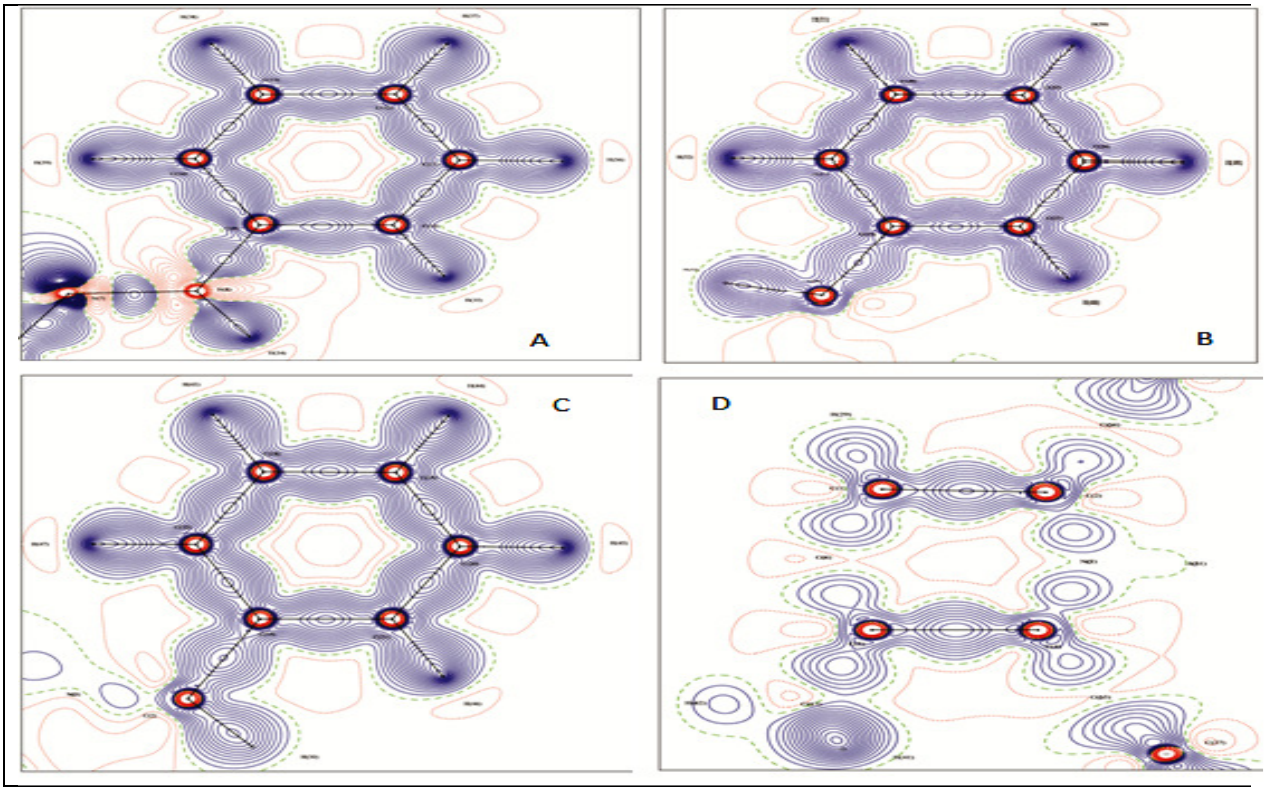

Fig.-3: Deformation density maps of 3-MDPYP molecule drawn at (A) 2-Phenyl ring (B) 4-Ylidine Phenyl ring (C) 6-Phenyl ring and (D) Piperidine ring. Contours are drawn at 0.05 e $Å^{-3}$ intervals. The solid lines (blue) are positive, dashed (red) are negative and dotted lines are zero contours. Contour intervals are drawn at 0.05 $eÅ^{-3}$

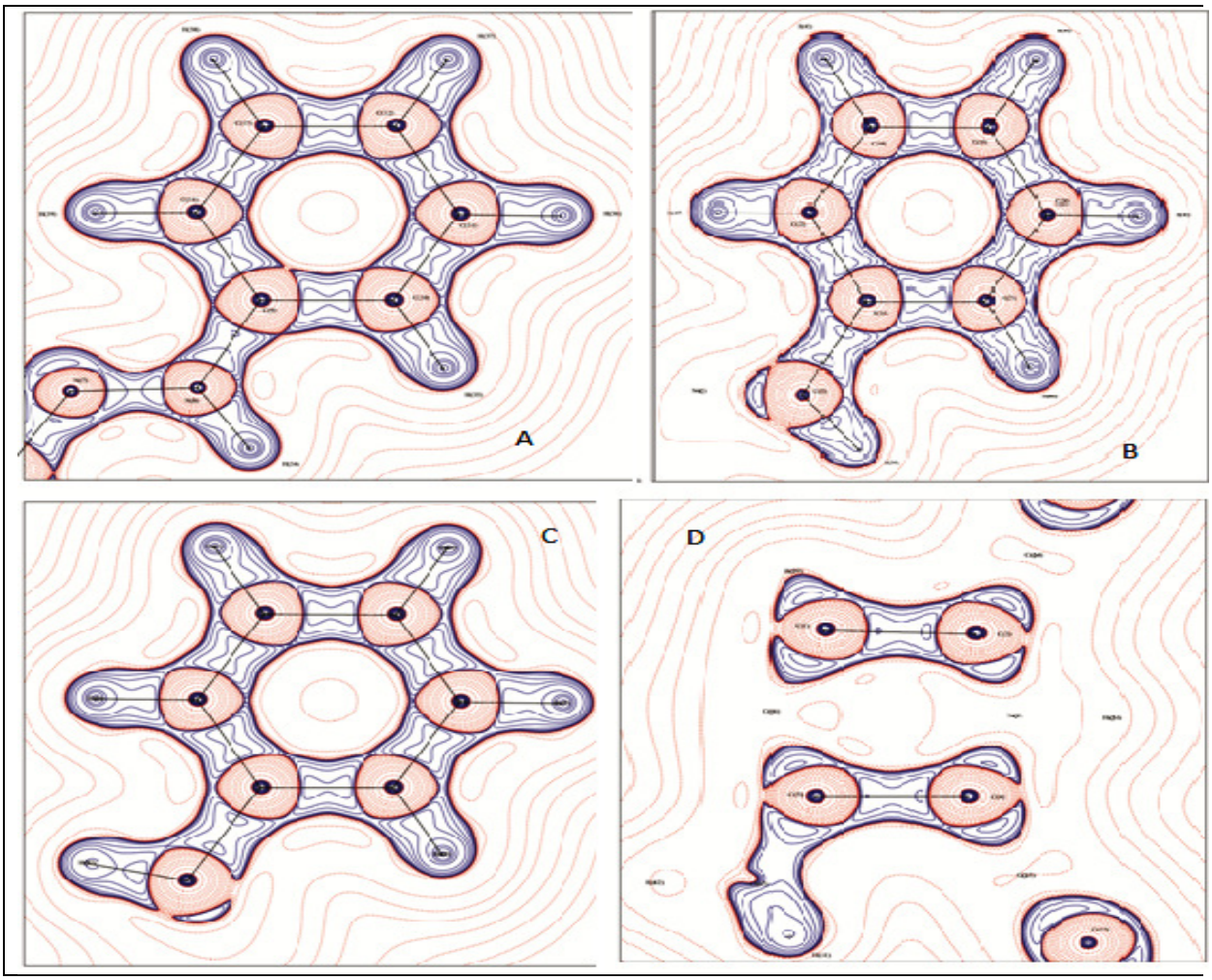

Fig.-4: Laplacian of electron density maps of the 3-MDPYP molecule shown at (A) 2-Phenyl ring (B) 4-Ylidine Phenyl ring (C) 6-Phenyl ring and (D) Piperidine ring. Solid lines indicate positive contours, and dashed lines are negative contours eÅ^{-5}.

CONCLUSION

The bond topological and electrostatic properties of the energetic 3-MDPYP molecule are carefully evaluated by ab initio (DFT) calculation. The optimized geometric parameters obtained from the DFT/6-311G**basis set is excellent in agreement with the similar type experimental data. For the calculation of C=N and N-H bonds have low charge accumulation at the bond critical point, which indicates the charge depletion of the molecule. This analysis gives effective results for the molecule by using AIM theory. From the bond topological properties and the energy density distribution, it confirms that C-N and N-H bonds are the weakest bonds in the molecule. In the case of aromatic C_{ar}-C_{ar} bonds, reveals that these bonds are also considerably weak. Further, the C_{ar}-C_{ar} and C-N bonds are more sensitive than the other bonds in the molecule. Molecular docking study of this 3-MDPYP molecule and its results also found to be least when compared with the DHFR protein[27]. Two prominent hydrogen bonds are observed between the drug molecules and binding site residues such as Thr56, Ser59 with the bond distance of 2.10 Å, 2.40 Å respectively and it is confirmed that these two bonds are the weakest bonds in the molecule. Thus, it can be concluded that the present study reveals the fine details of structural, charge density distribution and the electrostatic properties which are very convenient one for designing the new piperidone-based drugs for cancer therapeutics.

REFERENCES

1. A. David Stephen, P. Srinivasan, K. Poomani, *Central European Journal of Energetic Materials*, **9(3)**, 201(2012).
2. S. Ali Muhammad, A. Thangamani, S. Ravi, DOI 10.1007/s11164-017-2953-0.
3. G.A. Jeffrey and J.F. Piniella, The Application of Charge Density Research to Chemistry and Drug Design, Plenum Press, New York and London, (1991).
4. N. Muzet, B. Guillot, C. Jelsch, E. Howard, C. Lecomte, *Proc. Natl. Acad. Sci,* **100**, 8742(2003).
5. P. Poltizer, J.S. Murray, *Trans. Am. Crystallogr. Asso.,* **26**, 23(1993).
6. N.K. Hansen, P. Coppens, *Acta Crystallogr. A*, **34**, 909(1978).
7. M.V. Fernadez-serra, J. Junquera, C. Jelsch, C. Lecomte, E. Artacho, *Solid State Commun,* **116**, 395(2000).
8. G. Richardo, B.C. Juan, R.A. Mario, M. Roldan, C.R. Peinado, *Fernando Spen*, **47**, 166-172(1979).
9. B.R. Jerom, K.H. Spencer, *Eur. Pat. Appl.,* EP 277794 (1988).
10. R.V. Perumal, M. Adiraj, P. Shanmugapandian, *Indian Drugs,* **38**, 156(2001).
11. C.R. Ganellin, R.G. Spickett, *J. Med. Chem.,* **8(5)**, 619(1965).
12. B. Ilena, V. Dobre, I. Niculescu-Duvaz, *J. Prakt. Chem.,* **327(4)**, 667(1985).
13. I.G. Mobio, A.T. Soldatenkov, V.O. Fedrov, E.A. Ageev, N.D. Sergeeva, S. Lin, E.E. Stashenku, N.S. Prostakov, E.L. Andreeva, *Khim. Farm,* **23(4)**, 421(1989).
14. R.F.W. Bader, Atoms in Molecules – A Quantum Theory, Clarendon Press,Oxford, (1990).
15. A. David Stephen, R. Venkatesh, K. Poomani, *Cryst. Growth De,* **12**, 4357(2012).
16. B. Zarychta, V. Pichon-Pesme, B. Guillot, C. Lecomte, C. Jelsch, *Acta Crystallogr. A*, **63**, 108(2007).
17. M.A. Davis, S.J. Teague, *Angew. Chem. Int. Ed,* **38**, 736(1999).
18. J.P. Perdew, *Phys. Rev,* **B33**, 8822(1986).
19. M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, Gaussian Inc Pittsburgh P A, (2003).
20. K. Selvaraju, M. Jothi, P. Kumaradhas, *J. Comput.Theo. Chem,***1-10**, 1(2012).
21. F.W. Beiger-Kring, R.F.W. Bader, T. Ting-han, *J. Comput. Chem.,* **3**, 317(1982).
22. T. Koritsanszky, P. Macchi, C. Gatti, L.J. Farrugia, P.R. Mallinson, A. Volkov, T. Ritcher, XD-2006, A Computer Program Package for Multipole Refinement and Topological Analysis of Charge Densties and Evaluation of Intermolecular Energies from Experimental and Theoretical Structure Factore, Version 5.33, (2007).
23. A. David Stephen, R.B. Pawar, P. Kumaradhas, *Theochem.,* **55***,* 959(2010).
24. F.H. Allen, O. Kennard, D.G. Watson, L. Brammer, O. Guy, R. Taylor, Tables of Bond Length Determined by X-Ray and Neutron Diffraction, Part 1 Bond Lengths in Organic Compounds. *J. Chem. Soc., Perkin Trans,* S1(1987).
25. G.M. Sheldrick, SHELX97, Programs for Crystal Structure Refinement (Release 97-2); Institut fur Anorganische Chemie der Universitat, Gottingen, Germany, (1998).
26. R.G. Parr, W. Yang, Density Functional Theory of Atoms; Oxford University Press: London,(1989).
27. P. Rajesh, M. Dinesh Kumar, R. Jamunarani, J. Manigandan, *Asian Journal of Chemistry*, **27 (11)**, 3969(2015).

[RJC-1820/2017]