Supplementary information

Azole-based compounds as antiamoebic agents: A perspective using theoretical calculations

Md. Mushtaque[a*], Shahzaib Ahamad[b], Mariyam Jahan[a], Kakul Hussain[c], Mohd. Shahid Khan[d]

[a*]*School of Physical and Molecular Sciences (Chemistry), Al-Falah University, Dhauj, Faridabad, Haryana, India.*

[b]*Department of Biotechnology, College of Engineering & Technology, IFTM, Lodhipur-Rajput, Delhi Road, Moradabad.*

[c]*Medical Lab Science Department, College of Applied Medical Sciences, Salman bin Abdulaziz University, Wadi Adadawasir, Saudi Arabia.*

[d]*Department of Physics, Jamia Millia Islamia, New Delhi, India.*

Computational Studies Details

The geometry optimization of the amoebicidal heterocyclic compounds was carried out by semi-empirical methods Austin Model 1 (AM1) using Gaussian03 quantum chemical simulation package.[1] The chemical potential, global hardness and electrophilicity, the potency of a molecule can be described as $I = -E_{HOMO}$ represents the ionization energy and $A = -E_{LUMO}$ represents electron affinity. The chemical potential and hardness are derived by mathematical expression; $\mu = -(I+A)/2$ and $\eta = (I-A)/2$. The chemical potential and hardness of the anti-amoebic compounds have been summarized in Table ST2. The stability is represented by negative chemical potential. Marvinsketch calculator plugins[2] were used for structure property prediction and calculation of physico-chemical parameters (log P, Mol. Wt., PSA, rotatable bonds, HBA and HBD). **Table 1** and **Fig. 4** were drawn using Microsoft excel 2010 program[3].

References

1. M. J. Frisch , G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman et al. Gaussian Revision C.02. Wallingford CT: Gaussian Inc.; 2004.

2. Marvin 5.10.0, 2012, ChemAxon (http://www.chemaxon.com).

3. T. J. Ritchie, P. Ertl and R. Lewis, *Drug discovery today*, 2011, **16**, 65-72.

Table ST1: Antiamoebic activity and Lipinski's parameters for standard and reported compounds.

Compounds	IC_{50} (µM)	logP	Mol. Wt	HBA	HBD
1	1.46	-0.46	171.2	4	1
2	0.85[a]	-0.58	247.3	5	0
3	0.36[a]	0.26	219.6	4	1
4	0.05[a]	-0.04	185.2	4	1
5	2.23[b]	4.49	480.6	6	1
6	-	3.69	396.9	2	1
7	-	3.08	328.2	2	0
8	-	-8.31	615.6	19	13
9a	0.02	2.40	321.3	4	0
9b	0.01	0.92	337.3	5	0
9c	0.02	1.03	353.3	6	0
10a	0.96	1.55	301.3	5	1
10b	0.81	0.88	317.3	6	1
11a	0.05	5.48	328.2	2	0
11b	0.09	6.55	400.7	2	0
12a	1.05	7.07	400.4	6	0
12b	1.01	5.73	432.4	8	0
13a	0.05	5.69	455.9	4	0
13b	0.31	4.57	407.5	4	0
13c	0.06	4.42	437.5	5	0
13d	0.29	5.18	441.9	4	0
14a	0.86	4.85	466.5	6	0
14b	1.08	4.18	482.5	7	0
14c	1.16	3.66	468.5	7	0
14d	1.20	4.33	452.5	6	0
15a	0.07	1.44	356.3	7	0
15b	0.08	2.33	362.8	6	0
15c	0.02	-0.61	252.2	6	1
15d	0.008	1.28	299.3	6	0
16a	0.11	5.81	356.5	2	0
16b	0.60	4.40	337.4	3	0
16c	0.44	5.06	396.5	4	0
16d	0.17	5.49	379.5	3	0
16e	0.13	5.32	381.5	4	0
16f	0.64	4.92	382.5	4	1

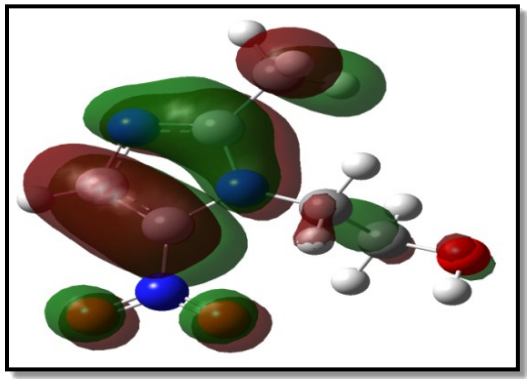
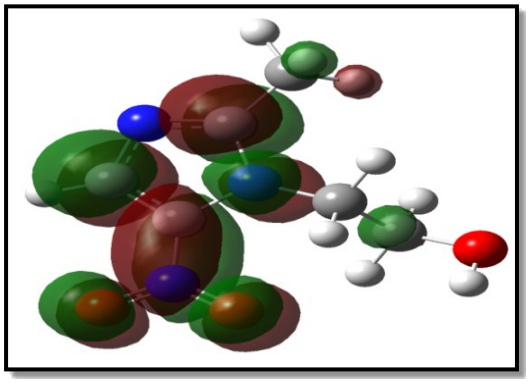
IC_{50} value of the compounds **1** and **9-16** were taken from the references discussed in main the text. [a]B. D. Mata-Cárdenas, J. Vargas-Villarreal, M. T. González-Garza, and S. Said-Fernández, *Pharmacy and Pharmacology Communications*, 1996, **2**, 513-514, [b]S. J. Marshall, P. F. Russell, C. W. Wright, M. M. Anderson, J. D. Phillipson, G. C. Kirby and P. L. Schiff, *Antimicrobial agents and chemotherapy*, 1994, **38**, 96-103.

Table ST2: Calculated chemical potential, hardness, LUMO and HOMO energy of the reported amoebicidal agents.

Comp. No.	LUMO (Electron affinity, A) eV	HUMO (Ionisation energy, I) eV	-(I+A)/2 (eV)	(I-A)/2 (eV)
1	-1.07	-9.98	-5.53	-4.46
2	-1.07	-9.94	-5.51	-4.44
3	-1.25	-10.14	-5.69	-4.45
4	-0.729	-9.70	-5.21	-4.48
5	-1.79	-8.02	-4.91	-3.11
6	-0.96	-9.18	-5.07	-4.11
7	-0.65	-9.97	-5.31	-4.46
8	-1.425	-9.59	-5.50	-4.08
9a	-0.91	-8.93	-4.91	-4.01
9b	-1.01	-9.56	-5.28	-4.28
9c	-1.26	-10.01	-5.63	-4.38
10a	-0.96	-9.09	-5.02	-4.06
10b	-0.95	-8.90	-4.97	-3.97
11a	-1.34	-9.11	-5.23	-3.89
11b	-0.90	-9.23	-5.07	-4.16
12a	-1.07	-9.22	-5.15	-4.08
12b	-1.08	-9.22	5.15	-4.07
13a	-0.66	-8.86	-4.76	-4.10
13b	-0.61	8.83	-4.72	-4.11
13c	-0.60	-8.80	-4.70	-4.10
13d	0.64	-8.90	-4.77	-4.13
14a	0.54	-8.95	-4.75	-4.20
14b	-0.64	-9.13	-4.89	-4.23
14c	-0.64	-9.02	-4.83	-4.19
14d	-1.22	-9.20	-5.41	-2.96
15a	-0.91	8.58	-4.59	-3.99
15b	-1.32	-8.57	-4.58	-3.99
15c	-1.27	-8.81	-4.70	-4.11
15d	-1.22	-8.86	-4.76	-4.10
16a	-1.17	-8.40	-4.78	-3.62
16b	-1.15	-8.4	-4.76	-3.62
16c	-1.12	-8.47	-4.79	-3.68
16d	-0.86	-8.09	-4.47	-3.59
16e	-1.83	-8.87	-5.35	-3.52
16f	-1.07	-8.55	-4.81	-3.74

Fig SF1: HOMO-LUMO molecular orbitals of **1-16**.

HOMO **LUMO**

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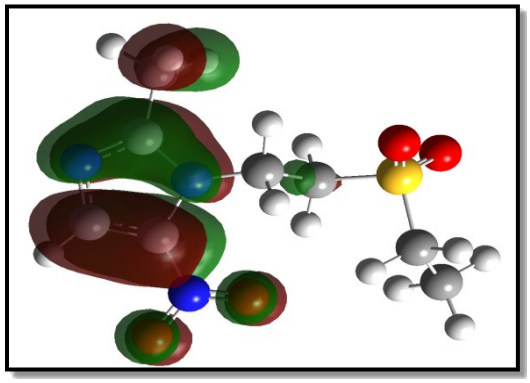
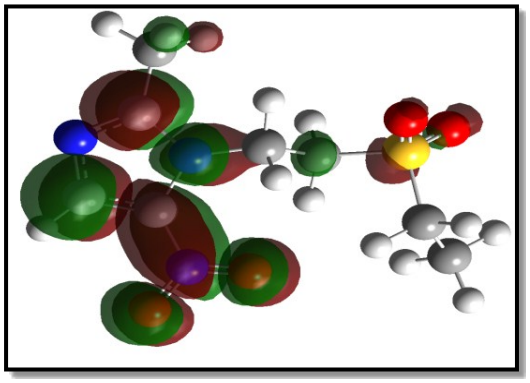

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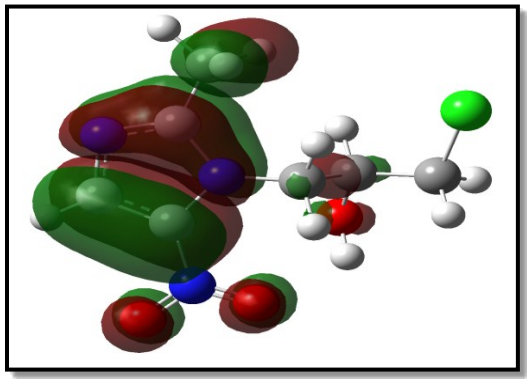
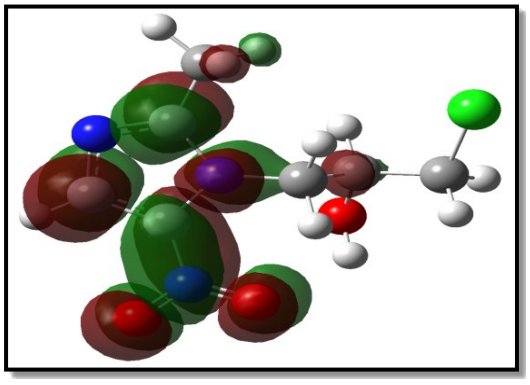

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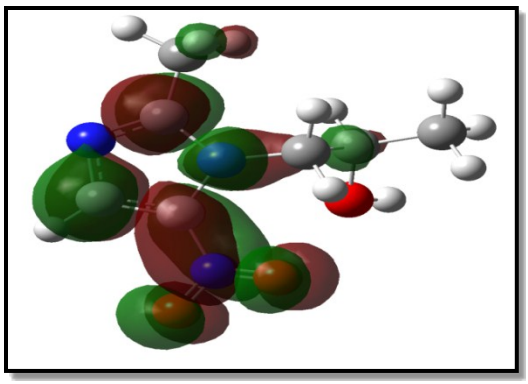
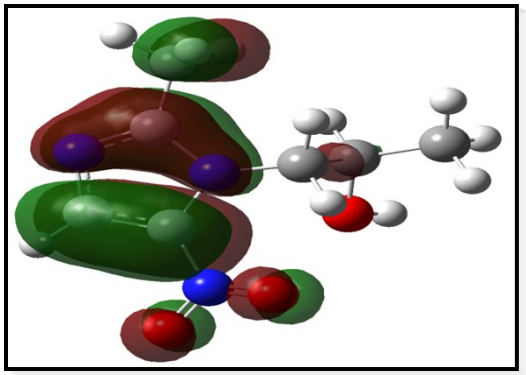

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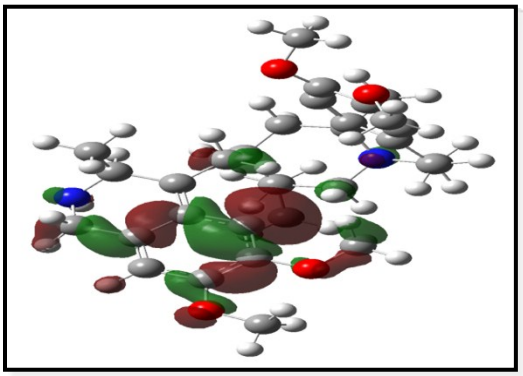
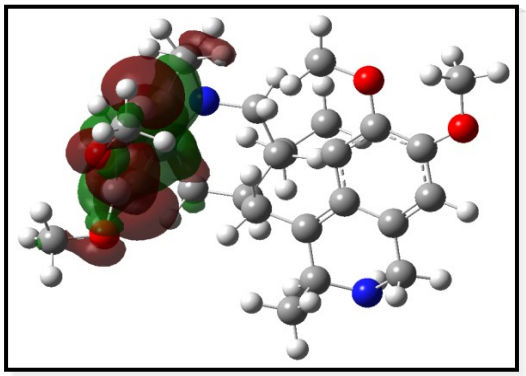

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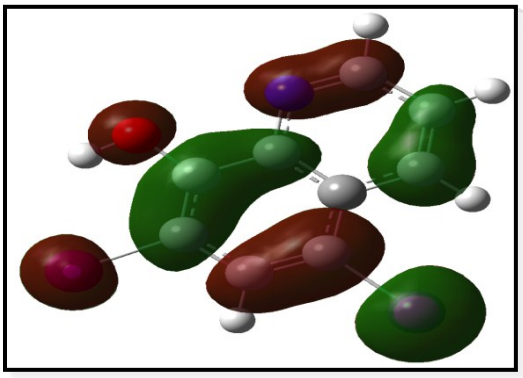
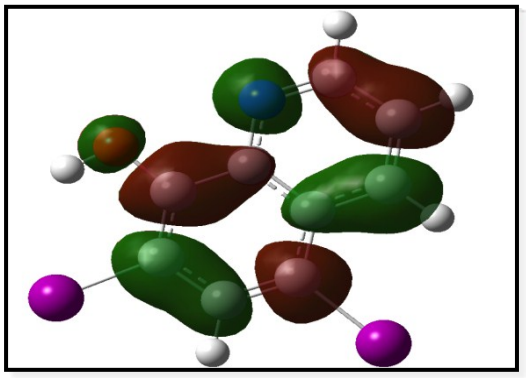

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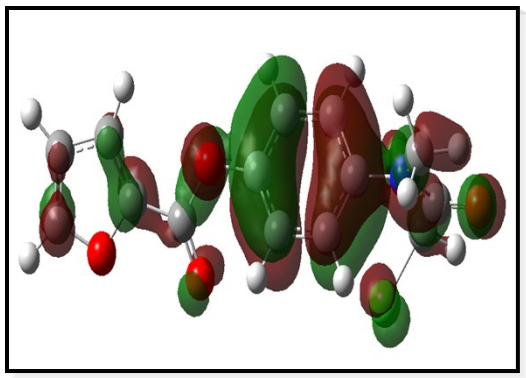
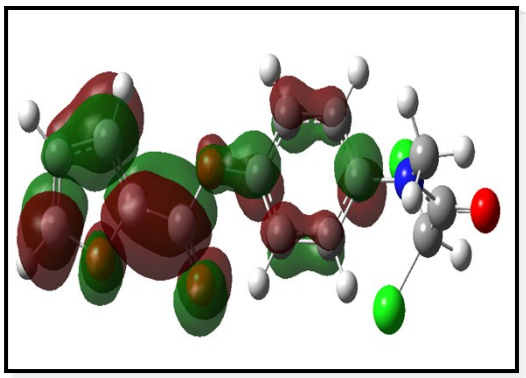

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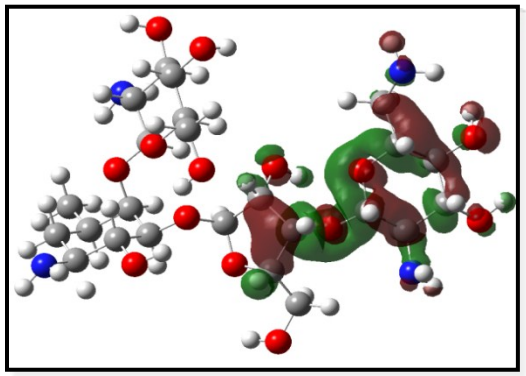
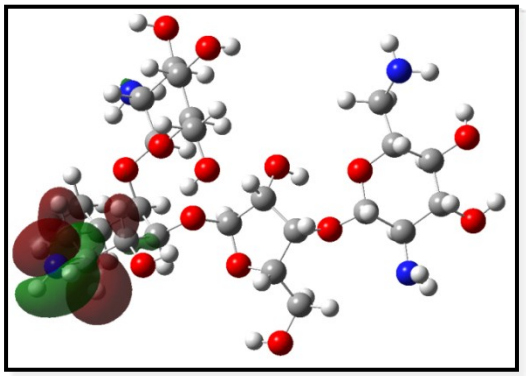

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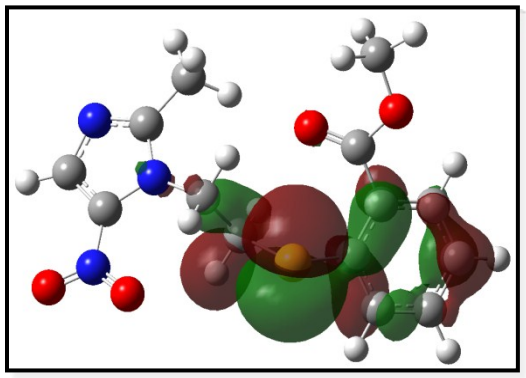
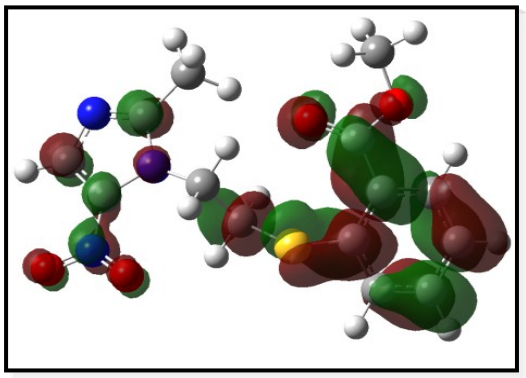

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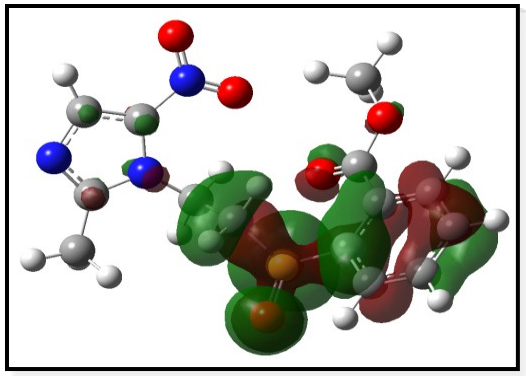
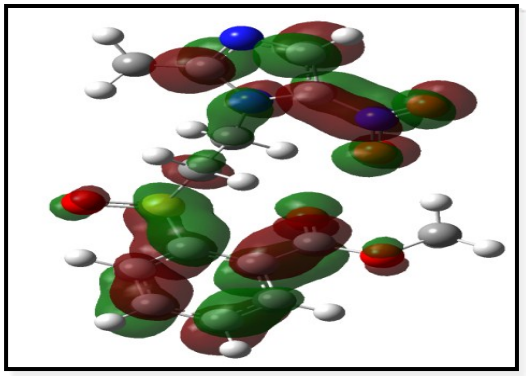

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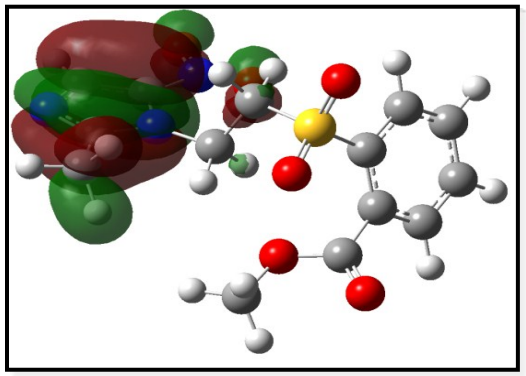
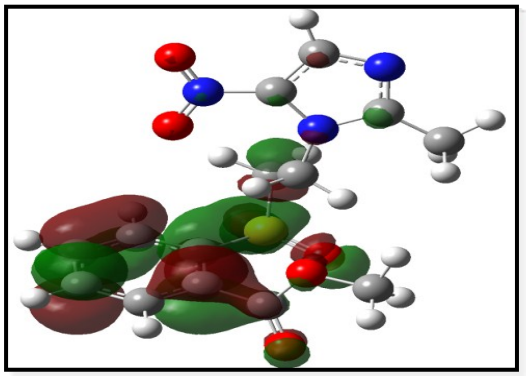

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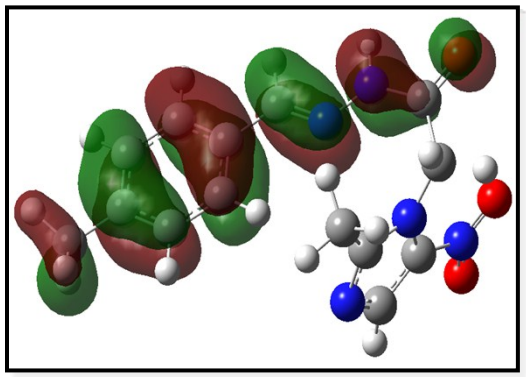
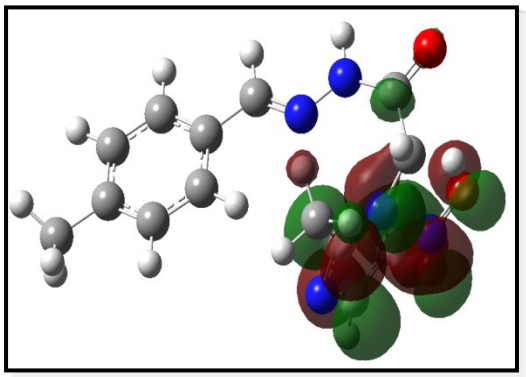

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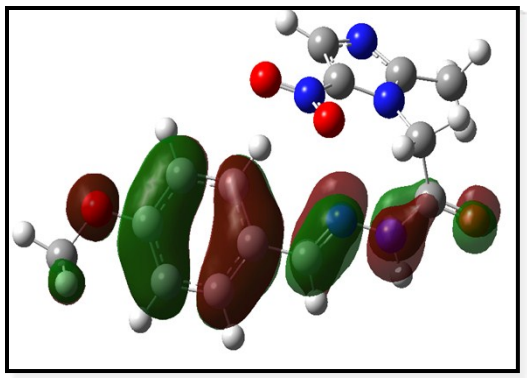
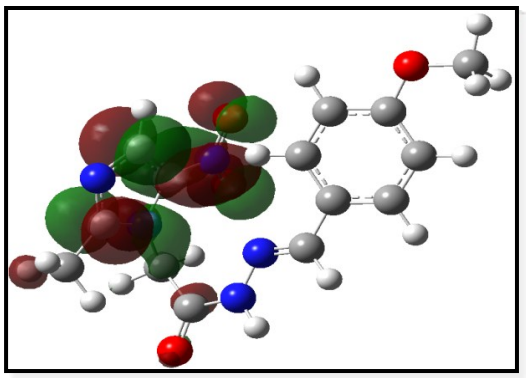

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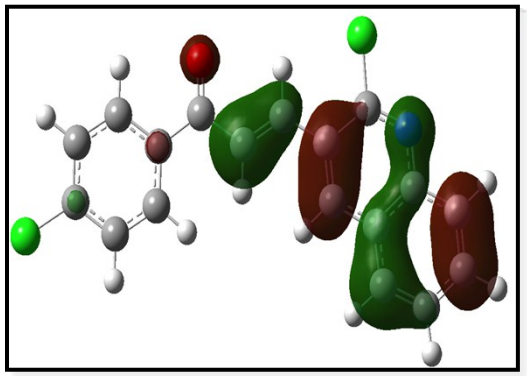
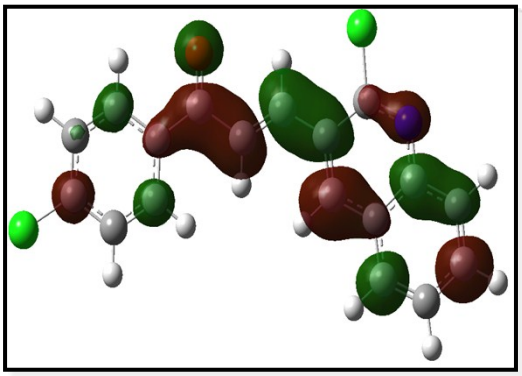

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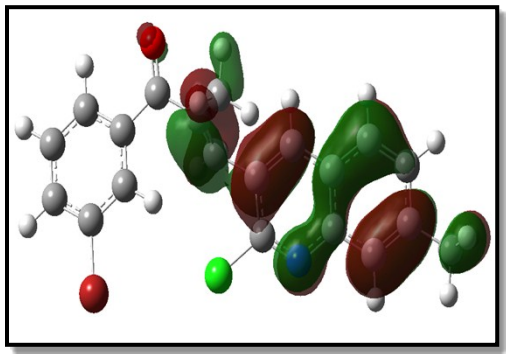
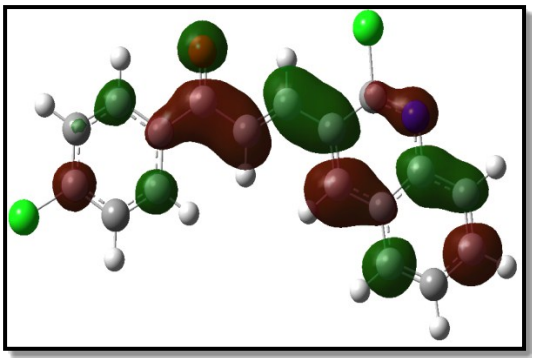

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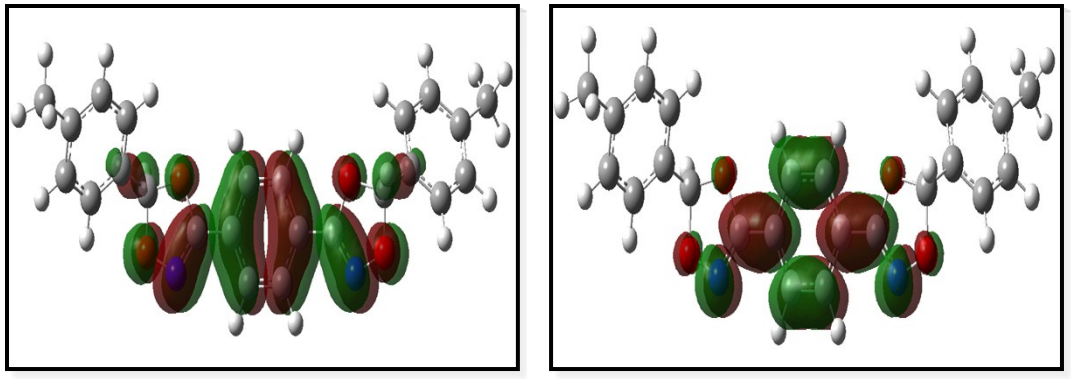

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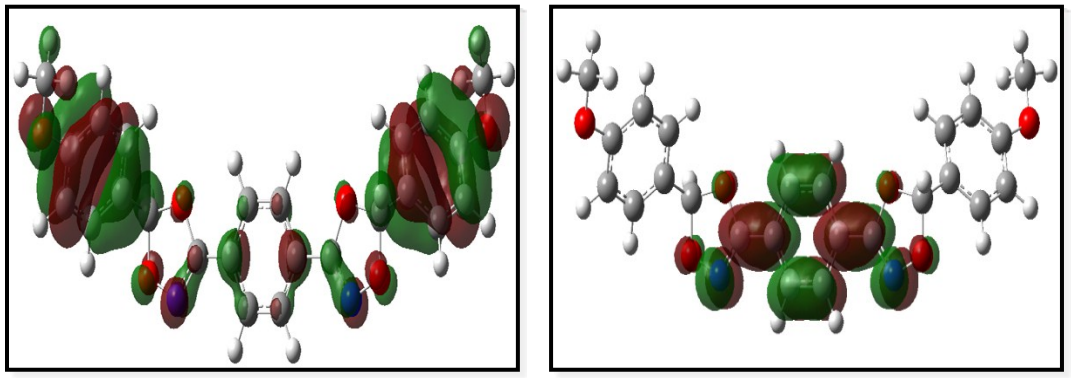

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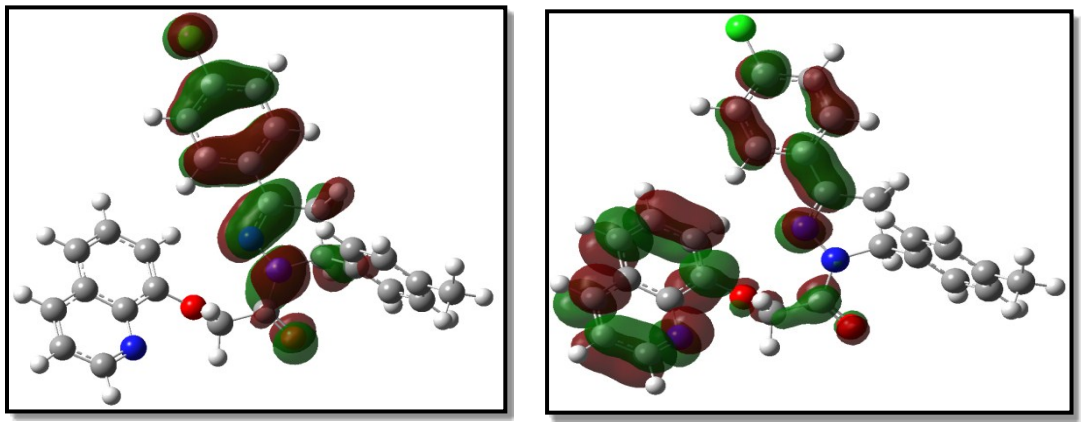

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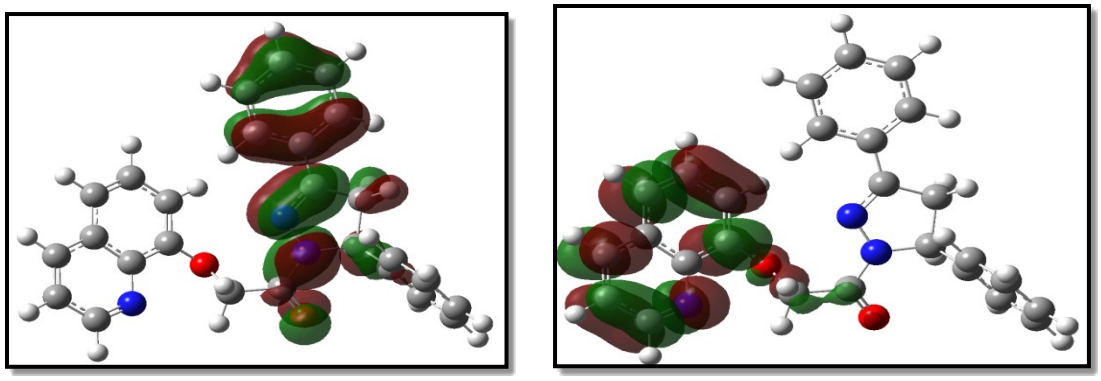

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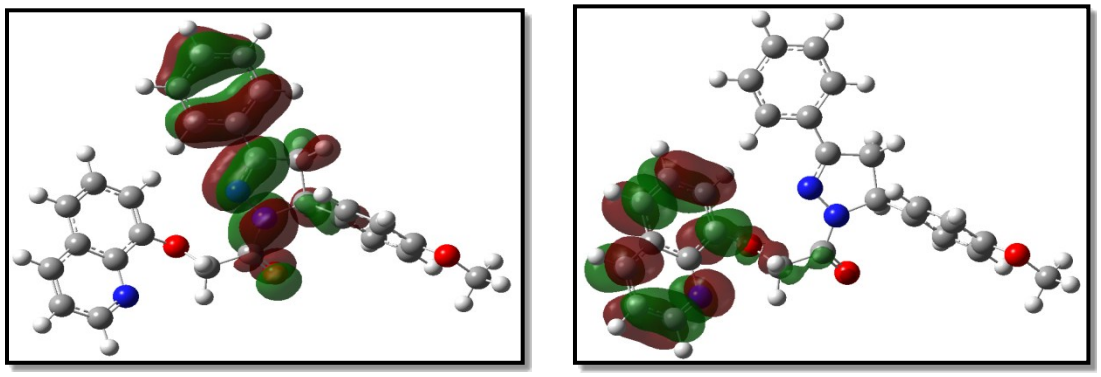

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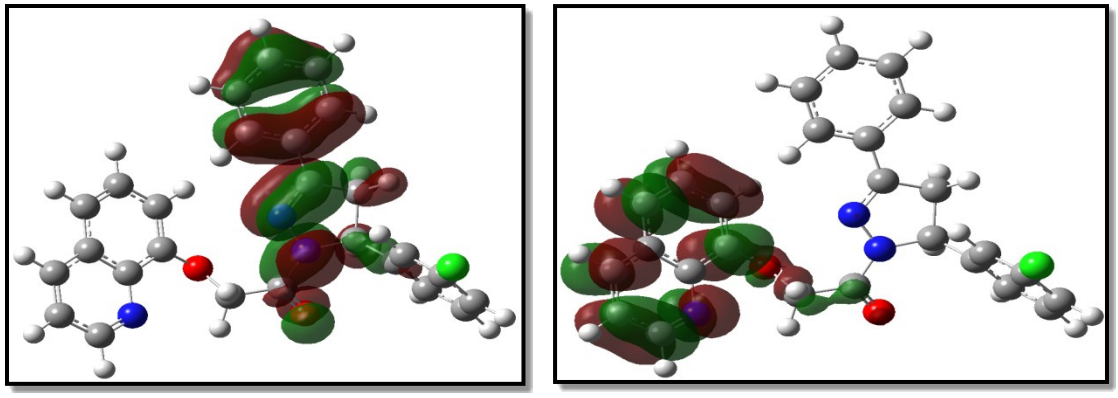

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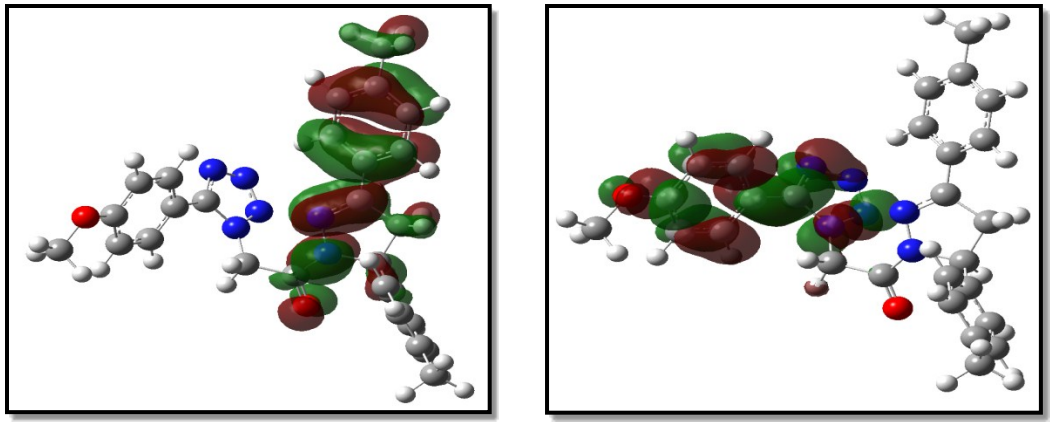

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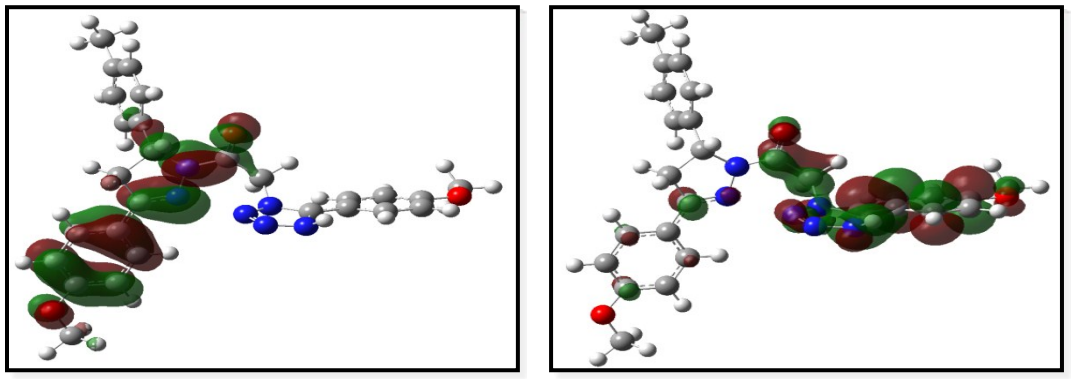

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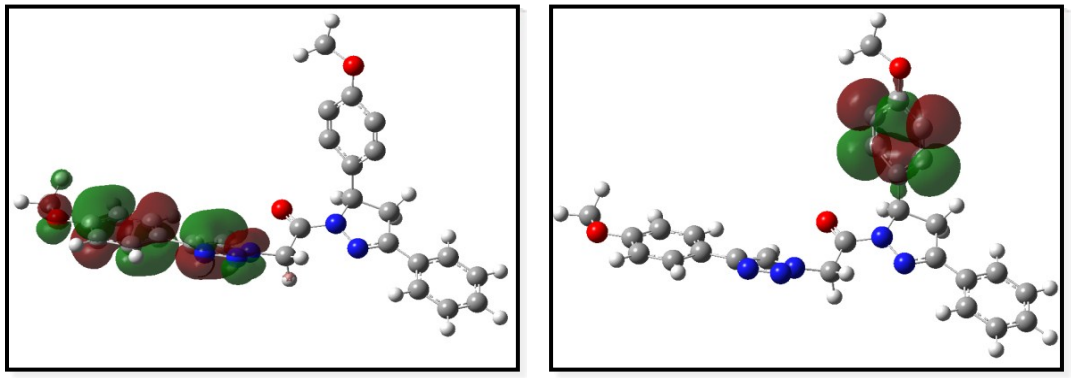

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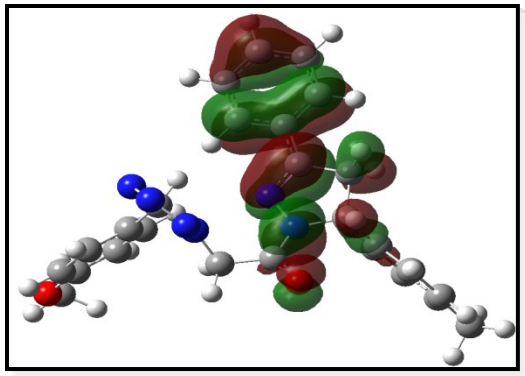
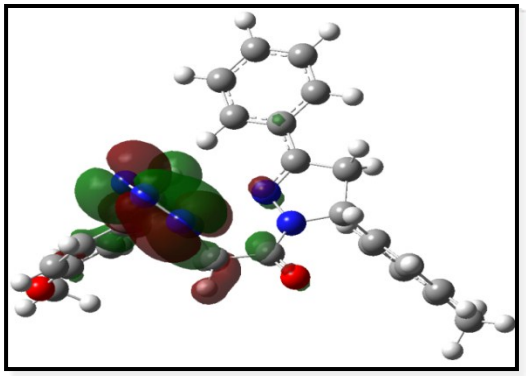

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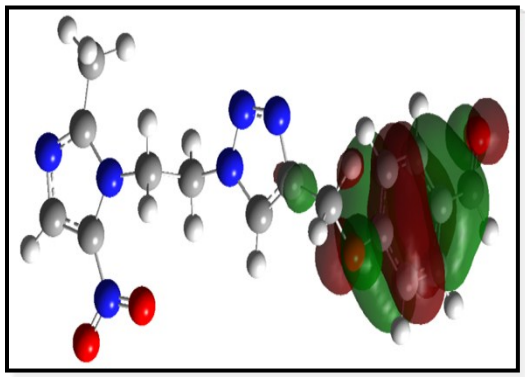
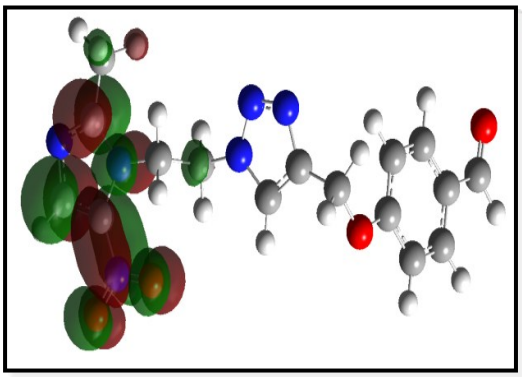

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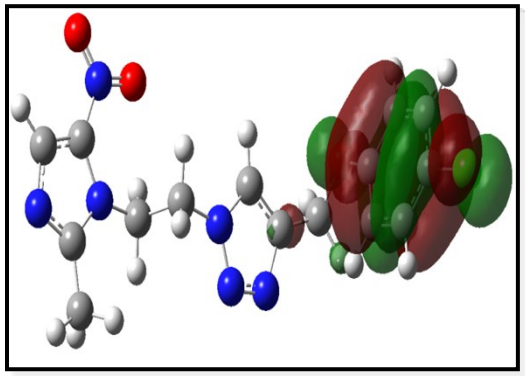
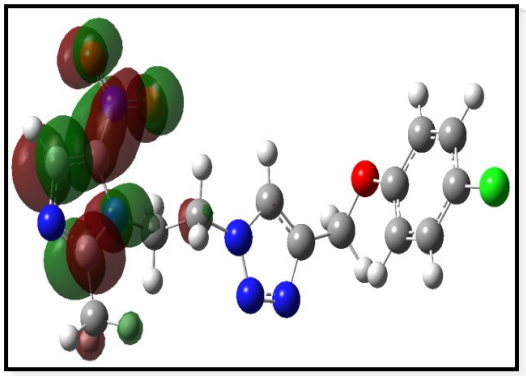

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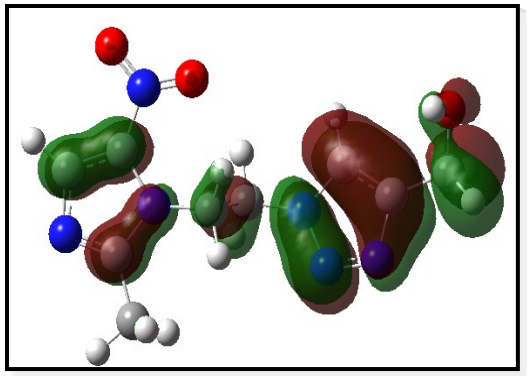
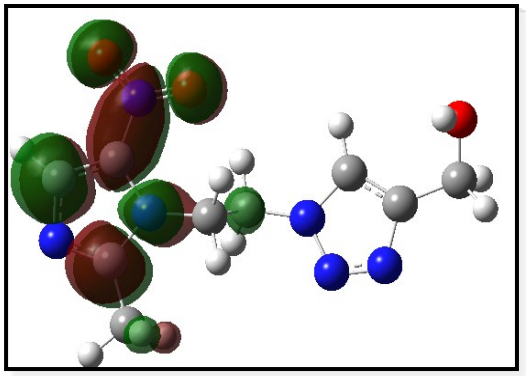

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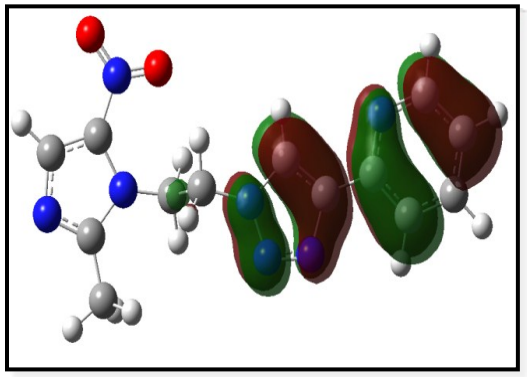
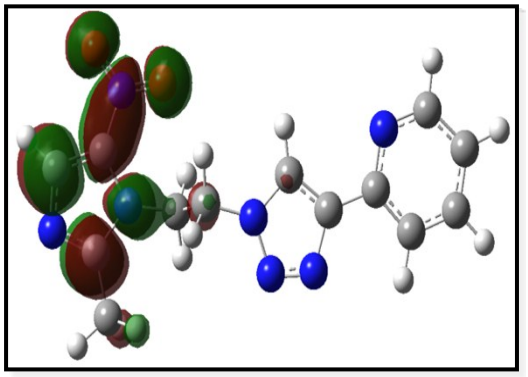

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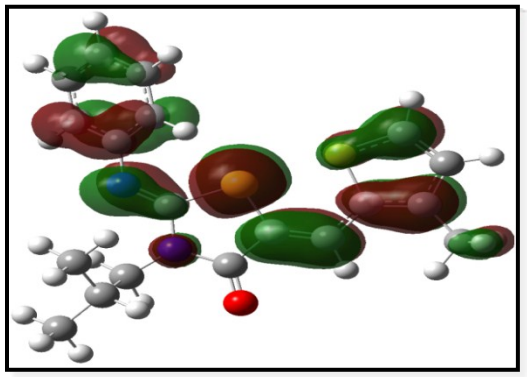
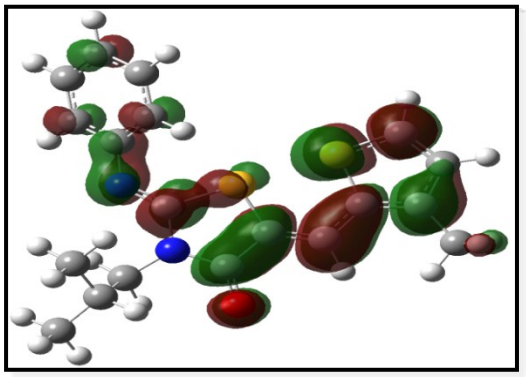

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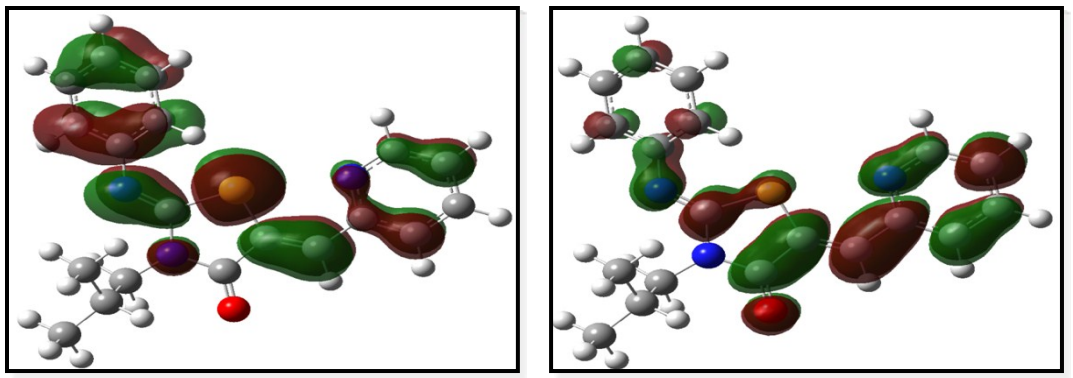

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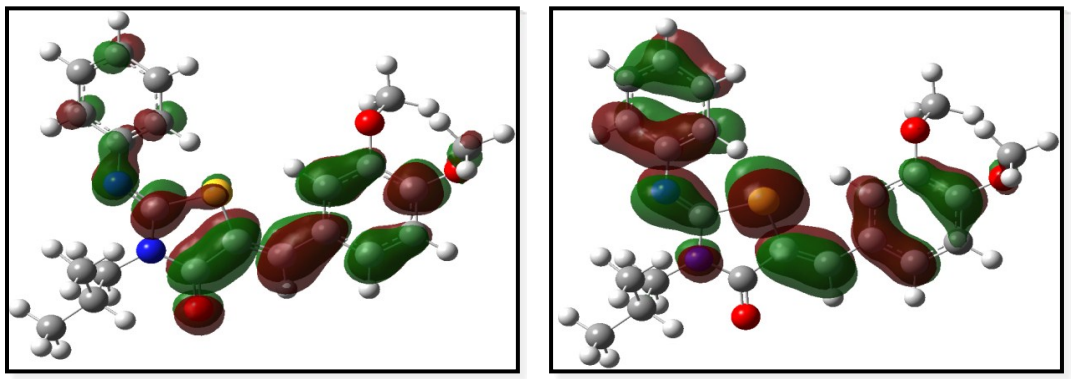

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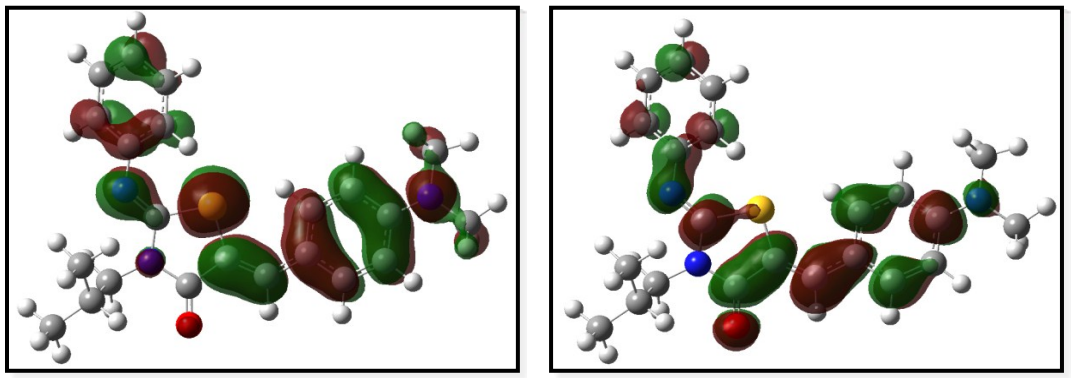

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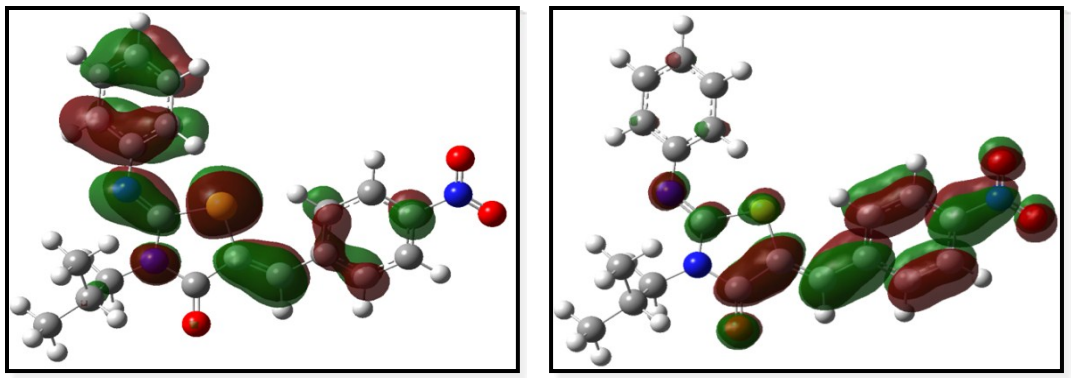

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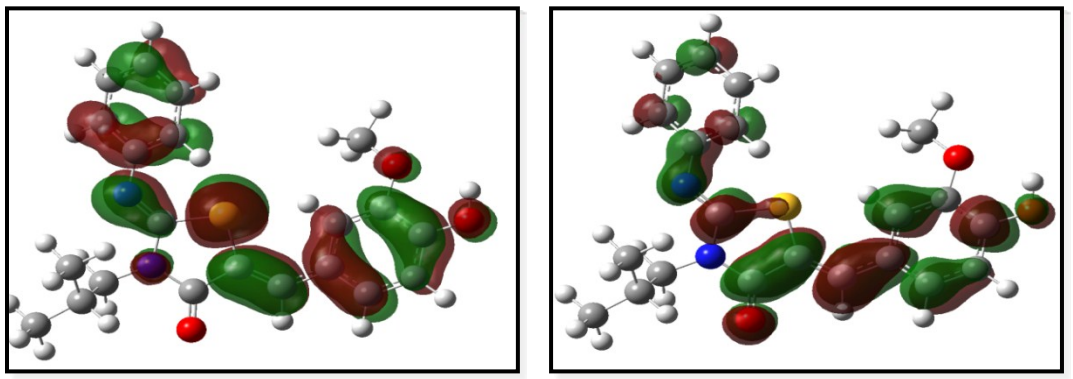

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