DFT Based Electrophilicity Index and QSAR study of Phenols as *Anti Leukaemia Agent*

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Abstract: Density Functional reactivity indices based QSAR study of 49 phenol derivatives is presented in this paper. Two different models to describe the anti leukaemia activity of phenols have been made. First QSAR model includes molecular properties like molecular weight (Mw), hardness (η), chemical potential (μ), total energy, and electrophilicity index (ω). Various regression models have been made and regression quality indicates that these descriptors provides valuable information and have significant role in assessment of activity of phenols. Klopman gave first quantum chemical treatment to describe the reactivity of a chemical system in terms of acidic softness E_n and basic softness E_m at atomic level. In this paper we have derived the partial electrophilicity by the multiplication of global electrophilicity index (given by Parr etal) and the acidic softness En (given by Klopman). This total electrophilicity index has been used as descriptors along with the other atomic properties like highest negative charge (Q_{min}) etc in second QSAR model. This model also provides good results. The DFT calculations have been performed by using B88-PW91 GGA energy functional with the DZVP basis set on Cache pro software and the regression models have been made on project leader software associated with CACHe. These DFT models have high predictive power and have sufficient reliability to describe the Anti leukaemia activity of phenols which is clear from its correlation coefficient r^2 and cross validation coefficient r_{cv}^2.

Key words: DFT, Electrophilicity Index, QSAR, Phenol, Anti Leukaemia

INTRODUCTION

The synthesis of novel pharmacologically active molecules with reduced toxicity is of prime interest. Recently, QSAR has gained importance in the field of pharmacological sciences[1]. Quantitative structure Activity relationships (QSAR) are predictive tools for a preliminary evaluation of the activity of chemical compounds by using computer-aided models. The Hohenberg and Khon theorm based DFT[2-4] provide a major boost to the computational chemistry The performance of DFT method in description of structural, energetic and magnetic molecular properties has been reviewed quite substantially in recent time. DFT methods are in general capable of generating a variety of isolated molecular properties[5-12]. Quantitative structure–activity relationship (QSAR) techniques increase the probability of success and reduce time and cost involvement in drug discovery process[13-14]. In this paper a theoretical technique has been discussed by which the biological activity of hypothetical molecule can be measure prior to their synthesis. This technique shall reduce the drug discovery coast, time and efforts.

THEORY

In DFT the electronegativity commonly known by chemist is defined as negative of partial derivative of energy E of an atomic or molecular system with respect to the number of electron N for a constant external potential v(r)[15]

$$\mu = -\chi = - (\partial E/ \partial N)_{v(r)} \qquad (1)$$

In accordance with the earlier work of Iczkowski and Margrave[16], it should be remarked that when assuming a quadratic relationship between E and N and in a finite difference approximation equation-1 may be rewritten as

$$\chi = -\mu = (IE+EA)/2 \qquad (2)$$

Where IE and EA are the vertical ionization energy and electron affinity respectively, there by recovering the electronegativity definition of Mulliken[17]. More over theoretical justification was provided for Sanderson's

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principle of electronegativity equalization which state that when two or more atoms come together to form molecule, their electronegativities become adjusted to the same intermediate value[18-20]. The absolute hardness η is defined as[21]

$$\eta = 1/2(\delta\mu/\delta N)\nu(r)$$
$$= 1/2 \, (\delta^2 E/\delta N^2)\nu(r) \qquad (3)$$

Where E is the total energy, N the number of electrons of the chemical species and $\nu(r)$ the external potential. The operational definition of absolute hardness and electro negativity is as

$$\eta = 1/2 \, (IP-EA) \qquad (4)$$

Where IP and EA are the ionization potential and electron affinity respectively, of the chemical species. In the matter of QSAR of chemical system the total energy also plays important role. Total energy of a molecular system is the sum of the total electronic energy, E_{ee} and the energy of internuclear repulsion, E_{nr}. The total electronic energy of the system is given by[22]

$$E = 1/2 \, P \, (H + F), \qquad (7)$$

Where P is density matrix and H is one-electron matrix Parr etal have introduced the electrophilicity index[23], in terms of chemical potential and hardness. The electrophilicity index is a reliable property of a chemical system and may be used as quantum chemical descriptor, the operational definition of electrophilicity index may be written as

$$\omega = \mu^2 / 2.\eta \qquad (9)$$

A more general but important property of a molecular system the molecular weight also has been tested as descriptor.
The softness of an atom in a molecule was described by Klopman[24] and modified by Singh et al[25]. The Klopman equation is given below.

$$E_n^{\ddagger} = IP_n - b^2(IP_n - EA_n) - [\chi_s(C_s^{\,n})^2/R_s](1-1/\in)$$
$$[q_s - 2b^2\chi_s(C_s^{\,n})^2] \qquad (10)$$

Where
$E_n^{\ddagger}$ = Softness of Lewis acid
IP = Ionization potential of an atom in a molecule
EA = Electron affinity of an atom in a Molecule
$\in$ = Dielectric constant of the medium in which reaction is carried out.
R and q = Radius and charge of atom s & r
C = Electron density

χ_r = q - (q-1) $\sqrt{k}$ and k = 0.75
a&b = Variational parameter defined as $a^2 + b^2 = 1$

The ionization potential of an atom in a molecule (IP), electron affinity of an atom in a molecule (EA), charge on atom in a molecule (q) and electron density (C) of an atom in a molecule are essential requirements for the solution of Klopman equations. The method for calculation of ionization potential of an atom in a molecule (IP) has been described by Dewar and Morita [26].The charge and electron density of an atom in a molecule are obtained by DFT [2] calculation on CAche pro software. Water has been chosen for medium hence the value of dielectric constant is taken as 81 [27].

The method for calculation of electron affinity of an atom in a molecule (EA) has been described by us earlier[28].
Since The Local acidic softness En is a measure of electron accepting tendency while the electrophilicity index (ω) of a molecule has been introduced by Parr et al. On the basis of these two important values we may derived a new parameter the partial electrophilicity (ω_p) by multiplying local acidic softness En and elecrtophilicity index (w) as

$$\omega_p = En * \omega \qquad (11)$$

Here this new parameter also has been tested as descriptor in QSAR study.

MATERIAL AND METHODS

The current study has been carried out during sept. to Dec. 2005 at cheminformatics laboratory M. L. K. P. G. college Balrampur and Bareilly college Bareilly India. The 49-substituted Phenol derivatives have been used as study material and are reported under table-1 along with their observed activity ($P_{Obs.}$) against L1210 Leukaemia cells[29].
For first step of QSAR prediction, we employed similar methodology of our earlier work[35] In the second step of QSAR study we have made a modification and derived a new parameter Partial electrophilicity (ω_p). Further we have tested this parameter here as a descriptor along with other descriptors. The values of different descriptors for first and second step of study have been calculated by solving the equations given in theory and the necessary values taken from DFT calculation results. The Project Leader program associated with CAChe pro of Fujitsu, have been used for multiple linear regression (MLR) analysis and various regression equations have been developed for the calculation of activity (A_{Pred}).

RESULTS

The assessment of activity of a hypothetical compound is of prime interest in order to reduce the drug discovery coast. In this paper forty nine phenols

Table 1: The Phenols derivatives and their Observed
Activity against L1210 Leukaemia cells (76)

No.	Substituents	Obs Act
1	4-OCH3	4.48
2	4-OC2H5	4.64
3	4-OC3H7	4.85
4	4-C4H9	5.2
5	4-OC6H13	5.5
6	H	3.27
7	4-NO2	3.45
8	4-Cl	4.29
9	4-I	3.86
10	4-CHO	3.08
11	4-F	3.83
12	4-NH2	5.09
13	4-OH	4.59
14	4-CH3	3.85
15	4-C2H5	3.86
16	4-NHCOCH3	3.73
17	4-CN	3.44
18	4-OC6H5	4.97
19	Bisphenol-A	4.07
20	4-Br	4.2
21	4-C(CH3)3	4.09
22	3-NO2	3.48
23	3-NHCOCH3	2.65
24	3-Cl	3.87
25	3-C(CH3)3	3.88
26	3-CH3	3.54
27	3-OCH3	3.71
28	3-N(CH3)2	4.11
29	3-C2H5	3.71
30	3-Br	3.82
31	3-CN	3.11
32	3-F	3.46
33	3-OH	3.46
34	3-NH2	4.11
35	2-CH3	3.52
36	2-Cl	3.22
37	2-F	3.2
38	2-OCH3	3.78
39	2-C2H5	3.75
40	2-OH	4.92
41	2-OH,4CH3	5.03
42	2-NH2	5.16
43	2-CN	3.3
44	2-NO2	3.34
45	2-Br	3.44
46	2-C(CH3)3	4
47	4-C3H7	4.04
48	4-C4H9	4.33
49	4-C5H11	4.47

Table 2: The Values of DFT based Global descriptors of Phenols and their Predicted Activity (A_{pred}) by equation-12.

No.	Mw	TE	η	μ	A_{pred}
1	124.139	-421.974	1.895	-2.563	4.571
2	138.166	-461.291	1.889	-2.529	4.772
3	152.193	-500.603	1.89	-2.521	4.934
4	166.219	-539.914	1.889	-2.513	5.1
5	194.273	-618.538	1.8875	-2.5075	5.419
6	94.113	-307.459	2.201	-2.911	3.339
7	139.11	-511.97	1.568	-4.465	3.337
8	128.558	-767.056	2.056	-3.144	3.689
9	220.009	-7226.68	1.8105	-3.4775	3.99
10a	122.123	-420.781	1.585	-3.761	3.854
11	112.103	-406.683	2.0165	-3.0055	3.761
12	109.127	-362.81	1.713	-2.129	5.18
13	110.112	-382.674	1.889	-2.624	4.363
14	108.14	-346.774	2.121	-2.763	3.79
15	122.166	-386.084	2.121	-2.733	3.976
16a	151.165	-515.47	1.9135	-2.7275	4.664
17	119.123	-399.696	1.9665	-3.7685	3.139
18	186.21	-613.709	1.9355	-2.9925	4.739
19a	228.29	-731.648	1.9985	-2.7125	5.384
20	173.009	-2880.52	1.976	-3.377	3.825
21	150.22	-464.705	2.128	-2.733	4.275
22	139.11	-511.968	1.3775	-4.5145	3.623
23a	151.165	-515.47	1.945	-2.975	4.352
24	128.558	-767.057	2.1635	-3.2275	3.412
25	150.22	-464.705	2.171	-2.796	4.133
26	108.14	-346.774	2.1685	-2.8275	3.639
27	124.139	-421.977	2.1785	-2.6555	3.973
28a	137.181	-441.421	1.986	-2.195	4.938
29	122.166	-386.084	2.172	-2.81	3.806
30a	173.009	-0.042	4.648	-4.888	-2.1
31	119.123	-399.694	1.8435	-3.9595	3.159
32	112.103	-406.684	2.2305	-3.0245	3.362
33	110.112	-382.677	2.1835	-2.6845	3.778
34	109.127	-362.815	2.0695	-2.3465	4.322
35	108.14	-346.774	2.202	-2.781	3.628
36	128.558	-767.059	2.1545	-3.2095	3.447
37	112.103	-406.684	2.205	-3.019	3.413
38	124.139	-421.978	2.126	-2.527	4.199
39	122.166	-386.079	2.1295	-2.7355	3.959
40a	110.112	-382.678	2.1195	-2.6105	3.968
41	124.139	-421.994	2.1285	-2.5055	4.217
42	109.127	-362.815	1.9845	-2.2575	4.565
43	119.123	-399.698	1.8425	-3.9725	3.147
44	139.11	-511.98	1.2675	-4.6865	3.639
45	173.009	-2880.52	2.0875	-3.4255	3.577
46	150.22	-464.698	2.127	-2.72	4.29
47	136.193	-425.396	2.1205	-2.7295	4.136
48	150.22	-464.707	2.12	-2.727	4.295
49	164.247	-504.019	2.1215	-2.7225	4.453

MW= molecular weight, η=hardness, μ = chemical potential, APred.= predicted toxicity by eqn. 12. a data points not include in deriving equation

Table 3: The Values of DFT based Electrophilicity Index, Partial electrophilicity and other descriptors of Phenols with their Predicted Activity (A_{Pred}) by equation-13.

No.	En	εHOMO	εLUMO	ω	ωP	Mw	ET	APred
1	36.8641	-4.458	-0.668	6.224098	229.4458	124.139	-421.974	4.39
2	36.71576	-4.418	-0.64	6.040872	221.7952	138.166	-461.291	4.639
3	36.74446	-4.411	-0.631	6.005892	220.6832	152.193	-500.603	4.856
4	36.70796	-4.402	-0.624	5.964677	218.9511	166.219	-539.914	5.069
5	36.73795	-4.395	-0.62	5.933881	217.9986	194.273	-618.538	5.491
6	38.05268	-5.112	-0.71	9.32555	354.8622	94.113	-307.459	3.183
7a	37.81513	-6.033	-2.897	15.63	591.0505	139.11	-511.97	3.16
8a	37.81567	-5.2	-1.088	10.16151	384.2643	128.558	-767.056	3.651
9	38.08212	-5.288	-1.667	10.94719	416.8924	220.009	-7226.68	3.831
10	37.82559	-5.346	-2.176	11.21001	424.0252	122.123	-420.781	3.291
11	37.82559	-5.022	-0.989	9.107553	344.4986	112.103	-406.683	3.597
12	36.87762	-3.842	-0.416	3.882207	143.1666	109.127	-362.81	5.446
13	37.6554	-4.513	-0.735	6.503238	244.882	110.112	-382.674	4.197
15	37.64331	-4.884	-0.642	8.096036	304.7616	108.14	-346.774	3.593
14	37.79153	-4.854	-0.612	7.921181	299.3535	122.166	-386.084	3.835
16	30.75947	-4.641	-0.814	7.117508	218.9308	151.165	-515.47	3.936
17	37.63149	-5.735	-1.802	13.96372	525.4754	119.123	-399.696	3.498
18	37.50777	-4.928	-1.057	8.666256	325.0519	186.21	-613.709	4.759
19a	37.56671	-4.711	-0.714	7.352138	276.1956	228.29	-731.648	5.577
20	38.13197	-5.353	-1.401	11.26728	429.6436	173.009	-2880.52	3.895
21	37.57694	-4.861	-0.605	7.947323	298.6361	150.22	-464.705	4.213
22a	38.4344	-5.892	-3.137	14.03721	539.5119	139.11	-511.968	2.578
23a	37.48459	-4.92	-1.03	8.607233	322.6386	151.165	-515.47	4.255
24	37.62524	-5.391	-1.064	11.26833	423.9735	128.558	-767.057	3.542
25	37.74151	-4.967	-0.625	8.486022	320.2753	150.22	-464.705	4.101
26	37.62412	-4.996	-0.659	8.668314	326.1377	108.14	-346.774	3.466
27	36.87755	-4.834	-0.477	7.681043	283.258	124.139	-421.977	3.756
28a	36.61466	-4.181	-0.209	4.784299	175.1755	137.181	-441.421	4.954
39	37.58227	-4.982	-0.638	8.575165	322.2742	122.166	-386.084	3.674
30a	46.52332	-9.3607	-0.0743	55.52627	2583.267	173.009	-0.042	7.376
31a	38.0575	-5.803	-2.116	14.45086	549.9638	173.009	-0.042	4.255
32	36.79996	-5.255	-0.794	10.20186	375.4281	119.123	-399.694	3.428
33	37.51956	-4.868	-0.501	7.86774	295.1942	112.103	-406.684	3.596
34	37.45023	-4.416	-0.277	5.697398	213.3689	110.112	-382.677	4.215
35	39.45622	-4.983	-0.579	8.515091	335.9733	109.127	-362.815	3.57
36	37.0561	-5.364	-1.055	11.09663	411.198	108.14	-346.774	3.32
37	38.35446	-5.224	-0.814	10.04858	385.408	128.558	-767.059	3.568
38	37.34109	-4.653	-0.401	6.78803	253.4724	112.103	-406.684	3.853
39	40.01826	-4.865	-0.606	7.967482	318.8448	124.139	-421.978	4.007
40a	38.01605	-4.73	-0.491	7.221889	274.5477	122.166	-386.079	3.987
41a	38.43446	-4.634	-0.377	6.680862	256.7753	110.112	-382.678	3.964
42	38.00736	-4.242	-0.273	5.05681	192.196	124.139	-421.994	4.859
43	38.1965	-5.815	-2.13	14.53802	555.3015	109.127	-362.815	3.222
44	17.28005	-5.954	-3.419	13.91923	240.525	119.123	-399.698	3.381
45	40.64043	-5.513	-1.338	12.24741	497.7402	139.11	-511.98	3.673
46	40.5309	-4.847	-0.593	7.868198	318.9052	173.009	-2880.52	4.374
47	37.57507	-4.85	-0.609	7.899043	296.8071	150.22	-464.698	4.229
48	37.57375	-4.847	-0.607	7.882721	296.1834	136.193	-425.396	4.029
49	37.57147	-4.844	-0.601	7.862286	295.3976	150.22	-464.707	4.234

MW= molecular weight, TE = total energy of system, ω= Electrophilicity Index, En is local softness given by Klopman, $ε_{HOMO}$ is energy of HOMO, $ε_{LUMO}$ is energy of LUMO, $ω_P$ is Partial electrophilicity, A_{Pred}.= predicted toxicity by eqn. 13. [a] data points not include in deriving equation

derivatives have been taken with their activity from literature[29] and are reported in table-1.The predictive model of QSAR study has been buildup with the help of following important descriptors

Molecular Weight	(M_W)
HOMO Energy (eV)	(ε_{HOMO})
LUMO Energy (eV)	(ε_{LUMO})
Hardness	(η)
Chemical Potential	(μ)
Electrophilicity Index	(ω)
Total Energy (Hartree)	(T_E)
Partial electrophilicity	(ω_p)

The values of these descriptors for all the fourty nine derivatives have been calculated with the help of DFT method. In the formation of first QSAR model we have generated various equations by employing all the variables and the best-fitted equation of this class is equation-12.

$$PA=0.0114432*Mw+0.00012912*T_E-1.77179*\eta+1.03748*\mu+9.22152 \qquad (12)$$
$$r^2_{CV}=0.713606 \quad r^2=0.821269$$

This model includes the molecular weight, total energy, hardness and chemical potential. All these values are molecular property and we already have tested these values as a molecular descriptor in our previous communication[30-35]. The predicted activity (A_{Pred}) from equation-12 is reported in table-2. On the basis of statistical quality of result it is clear that one can use this equation to predict the antileukemia activity of a hypothetical compound of similar series. However in search of a more significant model and to recognized the Partial electrophilicity (ω_p) as a QSAR descriptor we have performed the study at atomic level and proceed to second step of QSAR study.

The second QSAR model has been formed with the help of newly derived descriptor the Partial electrophilicity (ω_p) along with Molecular Weight (M_W), HOMO Energy (eV) (ε_{HOMO}), LUMO Energy (eV) (ε_{LUMO}), Electrophilicity Index (ω) and Total Energy (Hartree) (T_E). In this model we have generated various equations by employing all the variables and the only best fitted equation-13 is reported here.

$$A_{Pred}=0.272295*En+4.65224*\varepsilon_{HOMO}+0.344202*\varepsilon_{LUMO}+1.63431*\omega-0.0248194*\omega_P+0.0149739*Mw+0.000174617*E_T+9.05945 \qquad -13$$
$$r^2_{CV}=0.21454 \quad r^2=0.895067$$

The predicted activity (A_{Pred}) from equation-13 is reported in table-3. On the basis of this model we can

also justify the validity of newly derived descriptor Partial electrophilicity (ω_p)

CONCLUSION

The first model involves all the descriptors which are basically energy related values and they are capable to describe the activity successfully however the second model includes energy values along with the electron accepting tendency of a molecule. Here we have derived a new parameter the Partial electrophilicity (ω_p) and tested it as a QSAR descriptor. The good result suggests us to realize the validity of newly derived descriptor electronic exchange in biochemical interaction with in the body. This study results a framework by which one can calculate the activity of any hypothetical compound of the series prior than their synthesis. The study is also helpful in the determination of effect of any particular phenol derivatives of this series over Leukaemia cells.

REFERENCES

1. Smeyers, Y. G., L. Bouniam, N. J. Smeyers, A. Ezzamarty, A. Hernandez-Laguna,A., and C. I. Sainz-Diaz, 1998 *Eur.J. Med. Chem.*,33 ,103
2. Parr R. G., and W. Yang, 1989, *Density Functional Theory of Atoms and Molecules,* Oxford University Press, New York
3. Kohn, W., A. D. Becke, and R. G. Parr, 1996 *J. Phys. Chem.*, 100: 12974.
4. Hohenberg, P., and W. Kohn, 1964, *Phys. Rev.* B, 136: 864.
5. Chattaraj, P. K., A. Cedillo, and R. G. Parr, 1991, *J. Phys. Chem.*, 103: 7645.
6. Ayers, P. W., and R. G. Parr, 2000, *J Am Chem Soc*, 122: 2010, 2000.
7. De Proft, F., J. M. L. Martin, and P. Geerlings, 1996, *Chem. Phys Let.,* 250: 393.
8. Geerlings, P., F. De Proft, and J. M. L. Martin, *In Theoretical and Computational Chemistry;* Seminario, J., Ed.; Elsveir; Amsterdam. 1996; Vol-4 (Recent Developments in Density Functional Theory), p773
9. De Proft, F. , J. M. L. Martin, and P. Geerlings, 1996, *Chem. Phys Let.,* 256: 400
10. De Proft, F., and P. Geerlings, 1997, *J Chem Phy*s, 106: 3270
11. Geerlings, P., F. De Proft, and W. Langenaeker, 1996, *Adv. Quantum Chem.*33: 303
12. Parr, R. G., R. A. Donnelly, M. Levy, and W. E. Palke, 1978, *J. Chem. Phys.,* 68: 3801

13. Hansch, C., P. G. Sammes, and J. B. Taylor,Computers and the medicinal chemist; in: Comprehensive Medicinal Chemistry, vol. 4, Eds. Pergamon Press, Oxford, 1990, pp. 33–58

14. R. Franke, Theoretical Drug Design Methods, Elsevier, Amsterdam, 1984.

15. Parr, R. G., R. A. Donnelly, M. Levy, and W. E. Palke, 1978, *J. Chem. Phys.,* 68:3801

16. Iczkowski, R. P., and J. L.Margrave, 1961, *J Am Chem Soc*, 83: 3547

17. Mulliken, R. S., 1934, *J. Chem. Phys.* 2: 782.

18. Sanderson, R. T., 1955, *Science*, 121: 207.

19. Sanderson, R. T., 1976, *Chemical Bonds and Bond Energ*y, (Academic, New York), 1976.

20. Sanderson, R. T., 1983, *Polar Covalence; Academic Press; New York .*

21. Parr, R. G., and R. G. Pearson, 1983, *J Am Chem Soc* 105: 7512.

22. Clare, B. W., 1995, Structure-Activity Correlations for Psychotomimetics .3. Tryptamines, Aust*. J. Chem.*, 48, 1385.

23. Parr, R. G., L. V. Szentpaly, and S. Liu, 1999, *J. Am. Chem. Soc.*, 121: 1922.

24. Klopman, G., 1968, *J. Am. Chem. Soc,* 90: 223.

25. Singh, P. P., S. K. Srivastava, and A. K. Srivastava, 1980, *J Inor Nucl Chem*, 42: 521.

26. Dewar, M. J. S., and T. F. Morita, 1969, *J. Am. Chem. Soc.*, 91: 796.

27. Daniels, D. J., *Surface-penetrating radar-IEE Radar, Sonar, Navigation and Avionics*, Series 6: London, The Institute of Electrical Engineers, 1996, p.320.

28. Singh, P. P. , F. A. Pasha, and H. K. Srivastava, 2003, *QSAR & Combi. Sci.*, 22: 841.

29. Selassie, C. D., A. J. Shusterman, S. Kapur, R. P. Verma, L. Zhang, and C. Hansch, 1999, *J. Chem. Soc. Perkin Trans* 2: 2729.

30. Singh, P. P., H. K. Srivastava, and F. A. Pasha, 2004, *Bioorg. Med. Chem.*, 12 (1): 171.

31. Pasha, F. A., H. K. Srivastava, A. Srivastava and P. P. Singh, 2006, *QSAR & Comb. Sci.*, in press.

32. Srivastava, H. K., F. A. Pasha, and P. P. Singh, 2005, *Int. J. Quantum. Chem.*, 103 (3): 237.

33. Pasha, F. A., H. K. Srivastava, and P. P. Singh, 2005, *Molecular Diversity*, 9(1-3): 215.

34. Pasha, F. A., H. K. Srivastava, and P. P. Singh, 2005, *Int. J. Quantum. Chem.*, 104 (1): 87.

35. Pasha, F. A., H. K. Srivastava, and P. P. Singh, 2005, *Bioorg. Med. Chem.*, 13(24): 6823.