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Heat of Formation (H_f): A Predictive Tool For Anti Hiv-5-Phenyl-1-H-Imidazole Derivative

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Abstract: *Quantitative structure activity relationship (QSAR) model of a series of 40 antiHIV-5-phenyl-1-H-imidazole derivative were developed with the help of Quantum chemical descriptors. Molecular modeling and geometry optimization was carried out with CAChe prosoftware .Calculation of descriptors and multilinear regression analysis was done using Project Leader software. Various QSAR model of different combination for each set were developed and five model has been selected on the basis of correlation coefficient .Among them the best model is judged on the basis of values of statistical parameters such as Standard error (SE), Standard error of estimation (SEE), t-value, p- value and Degree of freedom (DOF) that were calculated by Statistica and secondly a direct relationship between heat of formation and observed activity is reported. Heat of formation (H_f) can alone be helpful for searching of antiHIV-5-phenyl-1-H-imidazole derivative of reliable activities before their synthesis.*

Keyword: *QSAR, AntiHIV activity, Heat of formation, Degree of freedom.*

I. Introduction

Acquired immune deficiency syndrome (AIDS) is a disease of the human immune system caused by the human immunodeficiency virus (HIV)[1-3] .The illness interferes with the immune system making people with AIDS much more likely to get infections, including opportunistic infections and tumors that do not affect people with working immune systems. This susceptibility gets worse as the disease continues.

AIDS is the ultimate clinical consequence of infection with HIV, which is a retrovirus that primarily infects vital organs of the human immune system such as $CD4^+$ T cells (a subset of T cells), macrophages and dendritic cells. It directly and indirectly destroys $CD4^+$ T cells[4]. Acquired immune deficiency syndrome is most fatal disorder for which no complete and successful chemotherapy has been developed so far. Recently, QSAR has gained importance in the field of pharmacological sciences [5]. Quantitative structures Activity Relationships (QSAR) are predictive tools for a preliminary evaluation of the activity of chemical compounds by using computer-aided models. The Hohenberg and Khontheorm based DFT[6-8] 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 [9-13]. QSAR techniques increase the probability of success and reduce time and cost involvement in drug discovery process [14-15]. In this article, a Quantitative structure Activity Relationships (QSAR) for forty derivative of anti-HIV 5-phenyl-1-H-imidazole is presented. This study is mainly based on quantum chemical parameter and the quality of the predictions will be adjudged by correlation coefficient and cross validation coefficient. The descriptors or the combination of descriptors providing the best result will be recognized and employed for prediction purpose. This will be helpful in predicting the activity of any new derivative of required activity.

II. Experimental

We have based our QSAR study on a series of 5-phenyl-1-H-imidazole derivatives on the following reactivity indices:

1. Molecular weight (Mw)
2. Heat of formation (H_f)
3. Total energy(TE)
4. HOMO energy(εHOMO)
5. LUMO energy(εLUMO)
6. Absolute hardness(η)
7. Electronegativity(χ)

The evaluation of these parameters is given as below:

In DFT the ground state energy of an atom or a molecule is written in terms of electron density$\rho(r)$, and the external potential $\nu(r)$ in the form (1)

$$E(\rho) = F(\rho) + \int dr\rho(r)\, \nu(r), \qquad 1$$

Where $(\rho) = T(\rho) + V_{ee}(\rho)$,$T(\rho)$ is the electronic kinetic energy functional, and $V_{ee}(\rho)$ is the electron-electron interaction energy functional. The minimization of the total energy is subjected to the condition that the total number of electrons is fixed,

$$N = \int dr\rho(r) \qquad 2$$

It leads to an Euler-Lagrange equation of the form,

$$\mu = (\partial E/\delta\rho(r))_v = \nu(r) + \partial F/\delta\rho(r), \qquad 3$$

Where the Lagrange multiplier μ is the chemical potential. The solution of this equation leads to the ground state density from which one can determine the ground state energy. Parr_ et al define the electronegativity as the negative of chemical potential as,

$$\chi = -\mu = -(\partial E/\partial N)_v \qquad 4$$

Although the Hard & Soft Acids and Bases concept was introduced more than three decades ago by Pearson. The first unambiguous definition of Hardness and Softness was given by Parr and Pearson in early 80s **[16]**, they defined global Hardness η as:

$$\eta = 1/2(\delta\mu/\delta N)_{v(r)}$$
$$= 1/2\,(\delta^2E/\delta^2N)_{v(r)} \qquad 5$$

Where E is the total Energy, N is the number of electrons of the chemical species and $v_{(r)}$ is the external potential.

The corresponding global softness S, which bears an inverse relationship with the global hardness, is defined as in equation **[17]**,

$$S = 1/2\eta = (\partial N/\partial\mu)_{v(r)} \qquad 6$$

The operational definition of global hardness and global softness are obtained by finite differential approximation of eq-1**[18]**

$$\eta = 1/2\,(IP-EA) \qquad 7$$
$$S = 1/(IP-EA) \qquad 8$$

Where IP is the Ionization Potential and EA is the Electron Affinity of the chemical. According to the Koopman's theorem the IP is simply the eigen value of HOMO with change in sign and EA is the eigen value of LUMO with change in sign. **[19]** Thus,

$$\eta = 1/2(\varepsilon\,LUMO - \varepsilon HOMO) \qquad 9$$
$$\Sigma = 1/(\varepsilon\,LUMO - \varepsilon HOMO) \qquad 10$$
$$\chi = 1/2(\varepsilon\,LUMO + \varepsilon HOMO) \qquad 11$$
$$\mu = -1/2(\varepsilon\,LUMO + \varepsilon HOMO) \qquad 12$$

Parr _et.al **[20]** have shown that the electronegativity χ of any chemical species is equal to the negative value of chemical potential μ. Indeed it follows rigorously that.

$$\chi = -\mu = 1/2\,(I + A) \qquad 13$$

Where I and A are ionization potential and electron affinity of molecule. The equation 13 may be written as

$$A = 2\chi - I \qquad 14$$

Density functional theory provides a quantum mechanical justification for electronegativity. A concept used intuitively for a long time and validates Sanderson's postulates **[21]** that when two or more atoms combine to form a molecule, their electronegativity gets equalized and a unique electronegativity exists everywhere in a molecule. Now by putting the value of ionization potential (IP) of an atom in molecule in equation 14 we get electron affinity (EA) of that atom of the molecule as

$$EA = 2\chi - IP \qquad 15$$

According to Koopman's theorem I and A are the eigen value of HOMO and LUMO respectively with change in sign. Therefore from equation 11 and 15 we get

$$EA = (\varepsilon HOMO + \varepsilon LUMO) - (IP) \qquad 16$$

The forty derivatives of anti-HIV 5-phenyl-1-H-imidazole **[22]** used as study material are listed in Table I-II along with their observed biological activity. For QSAR prediction, the molecular modeling and geometry optimization have been carried out with CAChe pro software. The calculation of quantum chemical descriptors has been done by MOPAC2007 using DFT B88-LYP method. For regression analysis, we used the Project program associated with CAChe Pro software of Fujitsu. Various regression equations were developed for prediction of activity.

III. Result And Discussion

The parent skeleton of anti-HIV 5-phenyl-1-H-imidazole is presented in Figure 1.

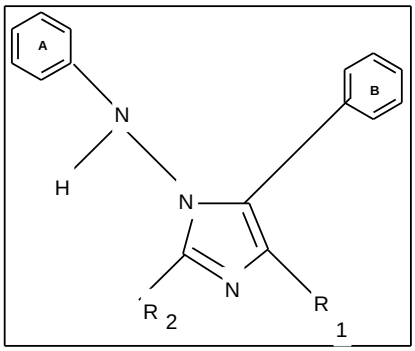

Figure 1. Parent skeleton of Anti-HIV 5-phenyl-1-H-imidazole

Forty derivative of anti-HIV 5-phenyl-1-H-imidazole are divided into two sets, on the basis of structural difference which is based on the nature of substituent. The compounds of the two sets are included in Table I-II, along with their observed activities. The two sets of derivatives contain twenty compounds each. Although a number of quantum chemical descriptors are known, only seven descriptors among them have been used in this work, which provide better results. For QSAR prediction of anti-HIV 5-phenyl-1-H-imidazole we have performed the MLR analysis by using all the quantum chemical parameters. Various QSAR models for each set of compounds using quantum chemical descriptors in different combinations have been developed but only five top models of each set are reported. For the sake of simplicity each set has been discussed separately as below:

First Set: This set contains twenty derivative of anti-HIV 5-phenyl-1-H-imidazole and the value of descriptors has been placed in table III. For QSAR study, regression analysis with the help of quantum chemical descriptors has been made by using different combinations of descriptors. Top five models are selected on the basis of correlation and cross- validation coefficient and their predicted activity are placed in table V. Model number 4 has been recognized as the best model on the basis of other statistical parameters like standard error of estimation, p-value, t-value and degree of freedom as indicated in table VII.

QSAR MODEL 1:

$^{Q}RE1=-0.00071984\ H_f + 0.00521657*\ MW - 0.0480385\varepsilon HOMO -2.33504$

$r^{CV2}=0.764644$

$r^2=0.815118$

QSAR MODEL 2:

$^{Q}RE2=-0.000765366\ H_f + 0.00532853\ MW +0.0834568\ \chi -2.28681$

$r^{CV2}=0.743636$

$r^2=0.8204$

QSAR MODEL3:

$^{Q}RE3=-0.000932053\ H_f + 0.00525805\ MW +0.134769\eta -1.29462$

$r^{CV2}=0.778457$

$r^2=0.819805$

QSAR MODEL4:

$^{Q}RE4=0.00534636*\ MW -0.528968*\ H_f\ + 0.0670735*\ \varepsilon\ LUMO -1.9109$

$r^{CV2}=0.744483$

$r^2=0.822225$

QSAR MODEL 5:

$^{Q}RE5=-0.000474403*H_f+0.00532853*MW-0.0909436*E_T+0.0834568*\chi -2.29979$

$r^{CV2}=0.739485$

$r^2=0.819197$

Relationship between heat of formation and observed activity

The first set contains twenty anti-HIV 5-phenyl-1-H-imidazole derivatives with their observed activity which are placed in table I and the values of quantum chemical descriptors is present in table III .A close look of table I indicates that activity increases with the addition of halo group on ring A and B of 5-phenyl-1-H-imidazole derivatives. The relationship between activity and heat of formation is presented in table III. Examination of this table shows that the biological activity is directly proportional to the heat of formation. When the Heat of formation increases, activity also increases, but there is no sequential rise or fall. In order to

provide sequential relationship the table III has been divided into three subgroups: A, B and C. Sub group A contain six compounds and Subgroup B and C contain five and four compounds respectively. Compound 5,10,11,15 and 18 do not follow a sequential trend as in table IX.

Second Set: This set contains other twenty derivatives of anti-HIV 5-phenyl-1-H-imidazole derivatives which are placed in table II. Regression analysis with the help of quantum chemical descriptors has been made by using different combinations of descriptors for the QSAR study .The predicted activities of top five models are placed in tableVI which have been selected on the basis of correlation and cross- validation coefficient. Among top five model model no.2 has been judged as the best model on the basis of other statistical parameters like standard error of estimation, p-value, t-value and degree of freedom as indicated in table VIII.

QSAR MODEL1:

^{Q}RE 1=-0.00361984*MW+0.00800323* H_f+2.3089*ε LUMO -8.5004

r^{CV2}=0.856715

r^2=0.934311

QSAR MODEL2:

^{Q}RE 2=0.0108751* H_f-0.468946*εHOMO +2.07337*ε LUMO -12.2822

r^{CV2}=0.859916

r^2=0.93713

QSAR MODEL 3:

^{Q}RE 3=0.0108751* H_f+1.60442*εHOMO +4.14673*χ-12.2822

r^{CV2}=0.859916

r^2=0.934136

QSAR MODEL 4:

^{Q}RE 4=0.0108751* H_f-2.54231*εHOMO +4.14673*η-12.2822

r^{CV2}=0.859916

r^2=0.932136

QSAR MODEL 5:

^{Q}RE 5=0.0108751* H_f+1.60442*εLUMO +0.937893*χ-12.2822

r^{CV2}=0.859916

r^2=0.935436

Relationship between heat of formation and observed activity

The second set contains other twenty anti-HIV 5-phenyl-1-H-imidazole derivatives with their observed activity which as in table II. A close observation of Table II indicates that activity increases with the addition of halo group on ring A and B of 5-phenyl-1-H-imidazole derivatives. The relationship between activity and heat of formation is given in table IV. Examination of this table shows that the biological activity is directly proportional to the heat of formation. When the Heat of formation increases, activity also increases, but there is no sequential rise or fall. In order to provide sequential relationship the table IV has been divided into three subgroups: A, B C and D. Sub group A contain five compounds and Subgroup B and C contain five compounds in each respectively. Subgroup D contains three compounds. Compound 3 and 16 do not follow a sequential trend as in table X.

IV. Conclusion

The QSAR models developed by quantum chemical descriptors for the first and second set of anti-HIV5-phenyl-1-H-imidazole derivatives provide higher values of correlation coefficients(r^2).The best model between two set have been selected on the basis of values of correlation coefficient followed by other regression quality parameters calculated by statistical software. which are indicated in Fig.2 and Fig.3 respectively.

Set no.	SE	SEE	t-value	p-value	DOF	VC	VU	r^2
1	0.0690	0.1023	14.2421	0.0000	0.9684	3	MW, H_f ,εLUMO	0.822225
2	0.0361	0.1001	15.4579	0.0000	0.9861	3	H_f, εHOMO, εLUMO	0.937130

The structural analysis of various derivatives has shown that halo group substitution at A & B generally increases the observed activity. Secondly it has also been reported that there is a direct relationship between reported biological activity and heat of formation (H_f).Thus, heat of formation alone can be helpful for searching out of anti-HIV 5-phenyl-1-H-imidazole derivatives of reliable activities before their synthesis.

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Table I: Structural Features and Observed Activity Data of First Set of Anti-HIV5-phenyl-1-H-imidazole derivatives

S. No.	A	B	R1	R2	Obs. Act.
1	3-Cl	H	3-CH_3	SH	1.176
2	2-Cl	H	3-CH_3	SH	0.791
3	4-F	H	3-CH_3	SH	0.657
4	3-Cl	H	3-CH_3	SH	0.872
5	3-Cl	3-Br	3-CH_3	SH	1.357
6	3-Cl	4-Br	3-CH_3	SH	1.478
7	3-Cl	3-Cl	3-CH_3	SH	1.509
8	3-Cl	4-Cl	3-CH_3	SH	1.389
9	3-Cl	4-OCH_3	3-CH_3	SH	1.412
10	H	H	3-CH_3	SH	0.718
11	3-Br	H	3-CH_3	SH	1.354
12	2,5-Cl	H	3-CH_3	SH	0.832
13	3-NO_2	H	3-CH_3	SH	1.316
14	3-F	H	3-CH_3	SH	0.966
15	3-CH_3	H	3-CH_3	SH	1.054
16	3-CH_3	H	$(CH_3)_2CH$	SH	1.370
17	3-Cl	H	C_2H_5	SH	1.409
18	3-CH_3	H	C_2H_5	SH	1.271
19	3-Cl	H	C_6H_5	SH	1.440
20	3-OCH_3	H	3-CH_3	SH	1.420

Table II: Structural Features and Observed Activity Data of Second Set of Anti-HIV5-phenyl-1-H-imidazole derivatives

S. No.	A	B	R1	R2	Obs. Act.
1	3-Cl	3-CN	3-CH_3	SH	1.003
2	3-CH_3	3-CN	3-CH_3	SH	1.341
3	3-Cl	3$COCH_3$	3-CH_3	SH	1.172

4	3-Cl	3-COOH	3-CH_3	SH	0.921
5	3-CH_3	3-COOH	3-CH_3	SH	0.728
6	4-C_2H_5	H	3-CH_3	SH	1.463
7	4-CH_3S	H	3-CH_3	SH	1.275
8	3-Cl	H	3-CH_3	H	1.757
9	3-Cl	3-Br	3-CH_3	H	1.785
10	3-Cl	3-Cl	3-CH_3	H	1.923
11	H	H	3-CH_3	H	1.282
12	3-CH_3	H	3-CH_3	H	1.568
13	4-F	H	3-CH_3	H	1.511
14	4-CH_3	H	3-CH_3	H	1.555
15	3,5CH_3	H	3-CH_3	H	1.690
16	3-OCH_3	H	3-CH_3	H	1.463
17	3-Cl	3-CN	3-CH_3	H	1.434
18	3-CH_3	3-CN	3-CH_3	H	1.350
19	3-Cl	3-$CONH_2$	3-CH_3	H	0.584
20	3-CH_3	3-$CONH_2$	3-CH_3	H	0.790

Table III: Values of Quantum Chemical Descriptors of First Set of Anti-HIV5-phenyl-1-H-imidazole derivatives.

C. No.	MW	H_f	TE	εHOMO	ε LUMO	χ	η	Obs. Act.
1	314.812	134.099	-145.576	-5.732	-0.724	-3.228	2.504	1.176
2	314.812	47.036	-145.746	-6.39	-1.943	-4.166	2.224	0.791
3	298.357	97.519	-149.72	-5.735	-0.856	-3.296	2.439	0.657
4	314.812	117.618	-145.753	-5.494	-0.956	-3.225	2.269	0.872
5	393.708	122.941	-155.648	-5.566	-1.134	-3.35	2.216	1.357
6	393.708	98.683	-155.658	-6.706	-3.055	-4.881	1.826	1.478
7	349.257	109.644	-157.524	-5.538	-1.096	-3.317	2.221	1.509
8	349.257	98.178	-157.407	-6.637	-2.926	-4.782	1.856	1.389
9	344.838	71.36	-164.955	-5.624	-1.706	-3.665	1.959	1.412
10	280.367	140.638	-133.808	-5.643	-0.766	-3.205	2.438	0.718
11	359.263	139.929	-143.927	-5.709	-1.108	-3.409	2.3	1.354
12	349.257	67.709	-157.389	-4.303	-1.523	-2.913	1.39	0.832
13	327.38	164.678	-167.317	-5.719	-1.248	-3.483	2.236	1.316
14	298.357	97.635	-149.72	-5.786	-0.781	-3.284	2.502	0.966
15	294.394	227.73	-141.27	-5.762	-0.955	-3.359	2.403	1.054
16	322.447	219.657	-155.318	-5.728	-1.069	-3.399	2.33	1.37
17	328.839	112.745	-152.912	-5.501	-0.954	-3.227	2.273	1.409
18	308.42	225.241	-148.288	-5.62	-1.234	-3.427	2.193	1.271
19	376.883	152.444	-174.781	-5.546	-0.981	-3.264	2.282	1.44
20	310.393	95.891	-153.358	-5.593	-0.92	-3.256	2.337	1.42

Table IV: Values of Quantum Chemical Descriptors of Second Set of Anti-HIV5-phenyl-1-H-imidazole derivatives

C. No.	MW	H_f	TE	εHOMO	εLUMO	χ	η	Obs. Act.
1	339.822	154.53	-158.542	-5.679	-1.442	-3.56	2.119	1.003
2	339.822	154.53	-158.543	-5.68	-1.442	-3.561	2.119	1.341
3	374.864	37.797	-184.487	-5.462	-0.853	-3.157	2.305	1.172
4	358.822	29.878	-175.479	-5.606	-1.35	-3.478	2.128	0.921
5	352.43	131.625	-178.33	-5.885	-1.442	-3.664	2.221	0.728
6	308.42	126.28	-148.156	-5.643	-0.609	-3.126	2.517	1.463
7	326.454	142.207	-150.159	-5.661	-0.784	-3.222	2.439	1.275
8	283.76	95.461	-137.265	-8.958	-0.495	-4.727	4.232	1.757
9	362.656	103.222	-147.156	-9.028	-0.59	-4.809	4.219	1.785
10	318.205	176.1	-149.032	-6.763	-4.209	-5.486	1.277	1.923
11	249.315	188.008	-125.497	-6.6	-4.04	-5.32	1.28	1.282
12	263.341	178.655	-132.684	-6.557	-4.039	-5.298	1.259	1.568
13	267.305	144.37	-141.41	-6.664	-4.169	-5.416	1.248	1.511
14	263.341	178.647	-132.685	-6.557	-4.04	-5.299	1.258	1.555
15	277.368	168.131	-139.879	-6.564	-4.01	-5.287	1.277	1.69
16	279.341	151.48	-144.875	-6.58	-3.994	-5.287	1.293	1.463
17	308.77	217.639	-150.055	-6.908	-4.352	-5.63	1.278	1.434
18	288.351	212.093	-145.473	-6.832	-4.305	-5.569	1.263	1.35
19	326.785	70.825	-163.927	-9.204	-1.012	-5.108	4.096	0.584
20	306.366	52.891	-159.615	-9.05	-0.648	-4.849	4.201	0.79

Table V: Predicted Activity of First Set of Anti-HIV5-phenyl-1-H-imidazole derivatives

C. No.	PA1	PA2	PA3	PA4	PA5	O. Activity
1	0.985	1.145	1.258	1.234	1.098	1.176
2	0.871	0.745	0.745	0.897	0.465	0.791
3	0.589	0.642	0.652	0.599	0.637	0.657
4	0.798	0.789	0.826	0.845	0.489	0.872
5	1.258	1.236	1.235	1.574	0.985	1.357
6	1.389	1.365	0.981	1.347	1.357	1.478
7	1.476	1.457	1.64	1.324	1.556	1.509
8	1.375	1.345	1.235	1.389	1.69	1.389
9	1.364	1.345	1.356	1.456	1.684	1.412
10	0.689	0.568	0.687	0.786	0.687	0.718
11	0.975	1.347	1.324	1.324	1.324	1.354
12	0.824	0.984	0.875	0.852	0.875	0.832
13	0.956	1.342	1.1235	1.324	1.1235	1.316
14	0.8974	0.9831	0.897	0.897	0.897	0.966
15	1.045	1.12	1.23	1.024	1.23	1.054
16	1.27	1.156	1.59	1.235	1.256	1.37
17	1.35	1.258	1.32	1.326	1.389	1.409
18	1.125	1.257	1.258	1.257	1.542	1.271
19	1.232	1.325	1.357	1.239	1.232	1.44
20	1.356	1.37	1.45	1.349	0.987	1.42

Table VI: Predicted Activity of Second Set of Anti-HIV5-phenyl-1-H-imidazole derivatives

C. No.	PA1	PA2	PA3	PA4	PA5	O.A.
1	1.002	1.003	1.008	1.008	1.005	1.003
2	1.587	1.593	1.594	1.194	1.594	1.568
3	1.562	1.777	1.592	1.572	1.552	1.555
4	1.676	1.935	1.558	1.552	1.556	1.69
5	1.429	1.611	1.578	1.478	1.378	1.463
6	1.425	1.337	1.482	1.354	1.482	1.434
7	1.351	1.421	1.364	1.461	1.262	1.35
8	0.567	0.546	0.47	0.47	0.57	0.584
9	0.72	0.864	0.758	0.753	0.655	0.79
10	1.467	1.5	1.428	1.456	1.425	1.341
11	1.147	1.158	1.142	1.122	1.132	1.172
12	0.911	0.852	0.719	0.813	0.819	0.921
13	0.435	0.631	0.724	0.629	0.726	0.728
14	1.511	1.552	1.519	1.519	1.519	1.463
15	1.274	1.247	1.276	1.279	1.295	1.275
16	1.733	1.715	1.791	1.681	1.751	1.757
17	1.78	1.705	1.776	1.756	1.766	1.785
18	1.982	1.88	1.904	1.804	1.905	1.923
19	1.124	1.109	1.243	1.273	1.283	1.282
20	1.516	1.567	1.547	1.529	1.533	1.511

Table VII: Statistical Summary of Best 5 model of set A

PA	SE	SEE	t-value	p-value	DOF	VC	VU	r^2
1	0.1011	0.1159	9.7230	0.0000	0.8312	3	H_f, MW, εHOMO	0.815118
2	0.0735	0.0853	13.7792	0.0000	0.9086	3	H_f, MW, χ	0.8204
3	0.1153	0.1464	7.2463	0.0000	0.7305	3	H_f, MW, η	0.819805
4	0.0690	0.1023	14.2421	0.0000	0.9684	3	MW, H_f ,εLUMO	0.822225
5	0.1040	0.1682	5.9487	0.0000	0.6441	4	H_f, TE ,MW, χ	0.819197

Table VIII: Statistical Summary of Best 5 model of set B

PA	SE	SEE	t-value	p-value	DOF	VC	VU	r^2
1	0.0377	0.0679	23.2244	0.0000	0.9659	3	H_f, MW, εLUMO	0.934311
2	0.0361	0.1001	15.4579	0.0000	0.9861	3	H_f, εHOMO, εLUMO	0.937130
3	0.0371	0.0650	14.2941	0.0000	0.9688	3	H_f, χ,εHOMO	0.934136
4	0.0640	0.1058	14.5491	0.0000	0.9173	3	H_f, εHOMO, η	0.932136
5	0.0366	0.0594	26.6651	0.0000	0.9739	3	H_f, εLUMO, η	0.935436

Table IX: Relationship between Heat of formation of First set of anti-HIV5-phenyl-1-H-imidazole derivatives

Subgroup A		
C. No.	O.A	H_f
2	0.791	47.036
12	0.832	67.709
14	0.966	97.635
8	1.389	98.178
17	1.409	112.745
19	1.44	152.444
Subgroup B		
C. No.	O.A	H_f
3	0.657	97.519
4	0.872	117.618
1	1.176	134.099
13	1.316	164.678
16	1.37	219.657
Subgroup C		
C. No.	O.A	H_f
9	1.412	71.36
20	1.42	95.891
6	1.478	98.683
7	1.509	109.644

Table X: Relationship between Heat of formation of second set of anti-HIV5-phenyl-1-H-imidazole derivatives

Subgroup **A**		
C. No.	O.A	H_f
5	0.728	131.625
1	1.003	154.53
11	1.282	188.008
18	1.35	212.093
17	1.434	217.639
Subgroup B		
19	0.584	70.825
7	1.275	142.207
2	1.341	154.53
14	1.555	178.647
12	1.568	178.655
Subgroup **C**		
4	0.921	29.878
6	1.463	126.28
13	1.511	144.37
15	1.69	168.131
10	1.923	176.1
Subgroup D		
20	0.79	52.891
8	1.757	95.461
9	1.785	103.222

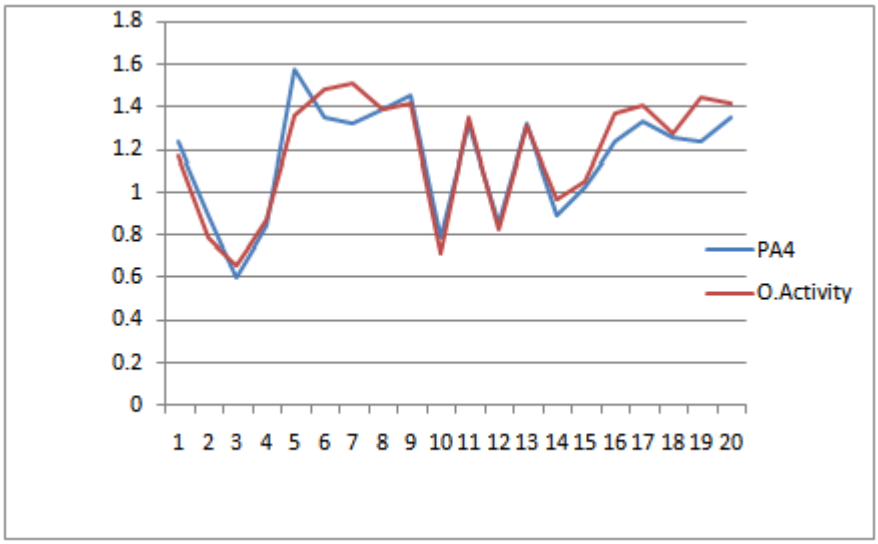

Fig2. Graphical presentation of Best Model (PA4) of set A

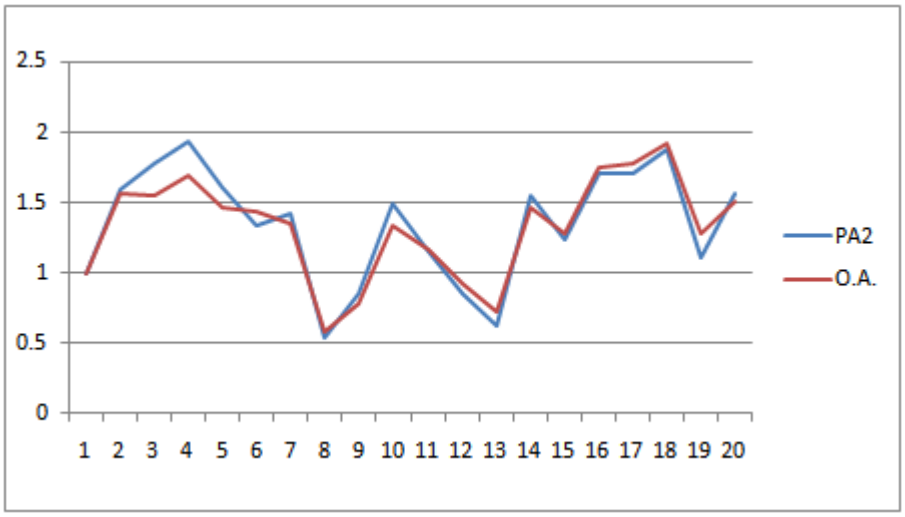

Fig3. Graphical presentation of Best Model (PA2) of set B