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QUANTUM CHEMICAL PARAMETER IS A PREDICTIVE TOOL OF MAXIMAL INHIBITORY CONCENTRATION OF PHENOL DERIVATIVES

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ABSTRACT

The quantitative structure activity relationship models of twenty five phenol derivatives have been made with the help of quantum chemical, topological and geometerical parameters. The molecular modeling and geometry optimization have been carried out with CAChe Pro software. The calculations of topological and quantum chemical parameters have been done by MOPAC2007. The calculations of geometrical parameters have been done by DRAGON-5. The statistical parameters are calculated by STATISTICA and SSP software. This study indicates that the quantum chemical parameters better predict the half maximal inhibitory concentration (IC_{50}) phenol derivatives as indicated by correlation coefficient (0.938037), standard error (0.0747), standard error of estimation (0.1920), p value (0.0000), t value (10.6138), and degree of freedom(0.8231).

Keyword:- phenol, t value, p value.

INTRODUCTION

Phenol was widely used as an antiseptic, especially as Carbolic soap, from the early 1900s through the 1970s. Phenol and its vapors are corrosive to the eyes, the skin, and the respiratory tract.**[1]** Repeated or prolonged skin contact with phenol may cause dermatitis, or even second and third-degree burns due to phenol's caustic and defatting properties.**[2]** Inhalation of phenol vapor may cause lung edema. The substance may cause harmful effects on the central nervous system and heart, resulting in dysrhythmia, seizures, and coma.**[3]** The kidneys may be affected as well. Exposure may result in death and the effects may be

delayed. Long-term or repeated exposure of the substance may have harmful effects on the liver and kidneys."**[4]** There is no evidence to believe that phenol causes cancer in humans.**[5]** Besides its hydrophobic effects, another mechanism for the toxicity of phenol may be the formation of phenoxylradicals.**[6]**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 [7]. 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[8-10] 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 [11-18]. Quantitative structure–activity relationship (QSAR) techniques increase the probability of success and reduce time and cost involvement in drug discovery process [19-20].In this article, a Quantitative structure Activity Relationships (QSAR) of twenty five phenol derivatives is presented. The QSAR study is mainly based on three sets of parameter i. e. quantum chemical, topological and geometrical parameter. The quantum chemical parameter have been evaluated by CAChe prosoftware . The calculations of topological and quantum chemical parameters have been done by MOPAC 2007. The geometrical parameter has been evaluated by DRAGON software.

Experimental

For QSTR study of phenol derivatives, it is necessary to identify a good tool. For this purpose the parameter were divided into three sets:

Quantum chemical parameters (21-28)

In DFT, the electronegativity, commonly known to a chemist, is define as the negative of a partial derivative of energy E of an atomic or molecular system with respect to the number of electrons N with a constant external potential $_{v(r)}$[**21]**

$$\mu=-\chi=-(\delta E/\delta N)_{v(r)} \qquad \textbf{Eq.(1)}$$

In accordance with the earlier work of Iczkowski and Margrave, [2**2]** it should be stated that when assuming a quadratic relationship between E and N and in a finite difference approximation, Eq. 1 may be rewritten as

$$\chi=-\mu=-(IE+EA)/2 \qquad \textbf{Eq. (2)}$$

where IE and EA are the vertical ionization energy and electron affinity, respectively, thereby recovering the electronegativity definition of Mulliken.[2**3]** Moreover, a theoretical justification was provided for Sandersons principle of electronegativity equalization, which states that when two or more atoms come together to form a molecule, their electronegativities become adjusted to the same intermediate value [2**4-26]** The absolute hardness η is define as[2**7]**

$$\eta = (IP-EA)/2 \qquad \text{Eq. (3)}$$

where IP and EA are the ionization potential and electron affinity respectively, of the chemical species. According to the Koopman's theorem, the IP is simply the eigen value of the HOMO with change of sign and the EA is the eigen value of the LUMO with change of sign hence the equations 2 and 3 can be written as

$$\chi = (\varepsilon LUMO+\varepsilon HOMO/2 \qquad \text{Eq. (4)}$$

$$\eta = (\varepsilon LUMO-\varepsilon HOMO/2 \qquad \text{Eq. (5)}$$

The heat of formation is defined as:

$$\Delta H_f^0 = E_{elect.} + E_{nuc.} - E_{isol.} + E_{atom} \qquad \text{Eq.(6)}$$

where$E_{elect.}$ is the electronic energy, $E_{nuc.}$ is the nuclear-nuclear repulsion energy, E_{isol} is the energy required to strip all the valence electrons of all the atoms in the system, and $E_{atom}$is the total heat of atomization of all the atoms in the system. The total electronic energy of the system is given by [2**8]**

$$E_T = 1/2P(H+F) \qquad \text{Eq.(7)}$$

Where P is the density matrix and H is the one-electron matrix. F is fock matrix.

Topological parameters (29-36)

Kier & Hall molecular connectivity index ($^{\chi}$)

This index, originally defined by Randic´ (1975), and as subsequently refined by Kier and Hall (1976) is a series of numbers designated by "order" and "subgraph type." There are four subgraph types: Path, Cluster, Path/Cluster, and Chain. These types emphasize different aspects of atom connectivity within a molecule; the amount of branching ring structures present and flexibility. Here we refer to these subgraph types as P, C, PC, and CH, respectively.

Molecular connectivity index of order n corresponding to subgraphtype s isdenoted by $^{n}\chi_{s}$. Given an order n and a subgraphtype s, one considers all connected subgraphs of type s consisting of n edges. For each vertex v_i in a subgraph, itsvalence δv_i (with respect to the entire graph) is calculated and the partial index n*P* corresponding to the given subgraph is found according to:

$$^{n}P(subgraph) = \prod_{i=1}^{n} 1/\sqrt{\delta_{v_i}},$$

(*n* = number of subgraph vertices).

Finally, the partial indices are summed over all connected subgraphs of the requested type s (Kier and Hall 1976, 1985):

$$^{n}\chi_{s} = \sum {}^{n}P(subgraph)$$

Order zero χ indices, CHI-0

Let us consider the order zero χ indices first, in the first column (CHI-0), which represent the simplest subdivision or subgraph: the set of vertices. The number of subgraphs of order zero is therefore equal to the number of skeletal atoms or vertices. Each vertex has a property δ, which is the number of its electrons in sigma bonds to skeletal neighbors.

$$\delta = \sigma - h$$

Where:

σ = number of electrons in σ bonds to all neighbors.

h = number of H atoms bonded to atom *i*.

The zerothorder subgraph connectivity weight assigned to each vertex is:

$$c = \delta^{-1/2}$$

The order zero χ index is the sum of all vertex weights in the graph, that is, over all atoms in the skeleton.

$$^{0}\chi = \sum_{i=1}^{\text{Number of atoms}} c_i$$

The zeroorder $^{0}\chi$index holds little structural information. Only the presence of the nearest neighbor to each atom is captured. In the series methane through tetrafluoromethane, we see an increase in CHI-0, which reflects the increasing size of the molecule skeleton.

Kier's shape indices {$^{n}\kappa$ (n = 1, 2, 3)}(29-36)

These indices compare the molecule graph with "minimal" and "maximal" graphs, where the meaning of "minimal" and "maximal" depends on the order n. This is intended to capture different aspects of the molecular shape.

Order 1

The descriptor $^{1}\kappa$ encodes the count of atoms and the presence of cycles relative to the minimal and maximal graphs. For N vertices, the maximal graph includes edges between allvertex pairs. For the minimal graph a linear path of N - 1 edges connecting the vertices is taken.

The shape index of order 1 is then defined as:

$$^{1}\kappa = 2P_{min}P_{max}/P^{2}$$

Where *P* is the number of edges in the graph (edges are paths of length 1, hence the subscript on the $^{1}\kappa$), Pmax is the number of edges in the maximal graph -- namely N(N - 1)/2 -- and Pmin is the number of edges in the minimal graph -- namely N - 1.

By inserting the formulas for Pmax and Pmin, one obtains the implemented formula:

$$^{1}\kappa = N(N-1)^{2}/P^{2} \qquad (13)$$

Order 2

The descriptor $^{2}\kappa$ encodes the branching. P, Pmin, and Pmax now denote the number of paths of length 2 in the corresponding graphs. The maximal graph is taken to be the star graph in which all atoms are adjacent to a common atom. Thus, Pmax = (N - 1) (N - 2)/2. The linear graph is again taken as the minimal graph, so Pmin = N - 2. Equation (1) thus yields:

$$^{2}\kappa = (N-1)(N-2)^{2}/P^{2} \qquad (14)$$

Order 3

For order 3, the counts of paths of length 3 are considered, and the maximal graph chosen is a twin-star (Kier 1990) with Pmax = (N - 1) (N - 3)/4 for N odd and Pmax = $(N - 2)^2/4$ for N even. The minimal graph is again the linear one with Pmin = N - 3.

The equation is adjusted by another factor of 2 -- in the words of the index designer -- "to bring the values into rough equivalence with the other kappa values" (Kier 1990, Hall and Kier 1991):

$$\kappa_3 = (N-1)(N-3)^2/P^2 \quad \text{for } N \text{ odd}$$

$$\kappa_3 = (N-3)(N-2)^2/P^2 \quad \text{for } N \text{ even}$$

Solvent Accessible surface area

The solvent accessible surface area (SASA) is the surface area of a biomolecule (protein, DNA, etc.) that is accessible to a solvent. Is usually quoted in angstrom square (a standard unit of measurement in molecular biology).SASA was first described by Lee & Richards in 1971 is sometimes called the Lee-Richards molecular surface.

Molar refractivity

The molar refractivity is a constitutive-additive property that is calculated by the Lorenz-Lorentz formula:

$$MR = \frac{n^2 - 1}{n^2 + 2} * \frac{M}{\rho} \qquad (15)$$

Where*M* is the molecular weight, *n* it is the refraction index and *r* the density, and its value depends only of the wave longitude of the light used to measure the refraction index..

Geometrical parameters (37-46)

The following descriptors of this class have been studied: 3D-Winner index (W3D), 3D-Balban index (J3D), 3D-Haray index (H3D), Average geometric distance degPTe (AGDD), D/D index (DDI) and Average distance/distance degPTe (ADDD).

RESULT AND DISCUSSION

Twenty five phenol derivatives have been chosen with their toxicity values **[47]** in terms of IC50 against tetrahymenapyriformis. Experimental determination of toxicological and biochemical end points as well as the human health end points is a difficult task. Hence QSTR modeling of the toxicity of compounds on tetrahymenapyriformis is vital importance

in investigating its toxicity in terms of its (50%) inhibitory concentration. The half maximal inhibitory concentration (IC_{50}) is a measure of the effectiveness of a compound in inhibiting biological or biochemical function. This quantitative measure indicates how much of a particular drug or other substance (inhibitor) is needed to inhibit a given biological process (or component of a process, i.e. an enzyme, cell, cell receptoror microorganism) by half. In other words, it is the half maximal (50%) inhibitory concentration (IC) of a substance (50% IC, or IC_{50}).

In this paper, we have done quantitative structure activity relationship analysis of twenty five phenol derivatives with the help of three sets of parameter i. e. quantum chemical, topological and geometrical parameter. The values of three sets of parameter are included into three tables separately (Table 1-3). Various QSAR models for each set of parameter are given below:

QSAR models of first set of parameters

$^{Q}RE1=0.0111212*\ Hf+2.15069*\varepsilon LUMO\ -8.14435$

$rCV^2=0.848507\ r^2=0.929501$

$^{Q}RE2=-0.0204753*\ T_E\ +2.29742*\varepsilon LUMO\ -8.61339$

$rCV^2=0.878541\ r^2=0.938037$

$^{Q}RE3=-0.0176448*\ T_E\ +3.73144*\ \chi\ -24.6745$

$rCV^2=0.895305\ r^2=0.906387$

$^{Q}RE4=-2.62993*\ \varepsilon HOMO\ +3.65586*\eta-13.5612$

$rCV^2=0.624539\ r^2=0.819063$

$^{Q}RE5=-0.000765366*\ Hf+0.00532853*\ MW\ +0.0834568*\ \chi\ -2.28681$

$rCV^2=0.743636\ r^2=0.8204$

In the above regression models $^{Q}RE2$ is the best model among top five models. The parameter of the model is total energy and LUMO energy, the cross-validation and correlation coefficient are 0.87 and 0.93 respectively, and the predicted activity is presented in Table 1.

QSAR models of second set of parameters

$^{T}RE1=-0.433928*SASA+3.76807*\kappa2+4.49883*\chi1-5.71*\chi2+15.6102$

$rCV^2=0.2789\ r^2=0.745847$

$^{T}RE2=-0.398222*SASA+2.1576*\kappa2+4.01053*\chi1-3.6067*\ MR\ +5.84847$

rCV^2=0.325828 r^2=0.721887

^{T}RE3=-0.547033*SASA+10.7657* MR +5.75132*χ1-6.99964*χ2+20.6758

rCV^2=0.566535 r^2=0.768848

^{T}RE4=-0.489082*SASA+6.09608*κ1+4.83342*χ1-4.19423*χ2+9.03373

rCV^2=0.434941 r^2=0.738932

^{T}RE5=0.106788*κ1+1.96051*κ2+1.36887*χ1-2.42927*χ2-10.3569

rCV^2=0.2993765 r^2=0.667313

In the above regression models ^{T}RE3is the best model among top five models. The parameter of the model is solvent assessable surface area, kier shape index 1 order, molecular connectivity index 1 order and 2 order, the cross-validation and correlation coefficient are 0.56 and 0.76 respectively, and the predicted activity is presented in Table 2.

QSAR models of third set of parameters

^{G}RE1=-0.984387 J3D -0.0904001 J3D -0.177218 AGDD +0.0283245 AGDD +0.82433 ADDD-2.0923

rCV^2=0.496312 r^2=0.890085

^{G}RE2=0.00841297 W3D -1.39253 J3D -0.269004 AGDD -0.0170625 DDI +1.29729 ADDD-2.84314

rCV^2=0.554905 r^2=0.895067

^{G}RE3=0.02738207 W3D -0.244848 H3D -0.149042 AGDD +0.00119957 DDI +0.701745 ADDD-4.12025

rCV^2=0.386082 r^2=0.88077

^{G}RE4=0.00554877 W3D -1.40673 J3D -0.245488 AGDD +1.18339 ADDD-2.21495

rCV^2=0.577145r^2=0.89313

^{G}RE5=0.00823228 J3D -0.988272 W3D -0.0654564 AGDD -0.350971DDI +1.16312

rCV^2=0.575077 r^2=0.896958

In the above regression models^{G}RE5is the best model among top five models. The parameter of the model is 3D-Balban index (J3D),3D-Winner index (W3D),average geometric distance egPTe (AGDD)and D/D index (DDI), the cross-validation and correlation coefficient are 0.57and 0.89respectively, and the predicted activity is presented in Table 3.

The best model of each set of parameters is given below:

^{Q}RE2=-0.0204753* T_E +2.29742*εLUMO -8.61339

rCV^2=0.878541 r^2=0.938037

^{T}RE3=-0.547033*SASA+10.7657* MR +5.75132*χ1-6.99964*χ2+20.6758

rCV^2=0.566535 r^2=0.768848

^{G}RE5=0.00823228 J3D -0.988272 W3D -0.0654564 AGDD -0.350971 DDI +1.16312

rCV^2=0.575077 r^2=0.896958

Table 1: Twenty five Phenol derivatives with observed toxicity against *Tetrahymenapyriformis*

Comp.No.	Compound	Toxicity
1	Phenol	-0.431
2	2,6-Difluorophenol	0.396
3	2-Flurophenol	0.248
4	4-Flurophenol	0.017
5	3-Flurophenol	0.473
6	4-Methylphenol	-0.192
7	3-Methylphenol	-0.062
8	2-Cholorophenol	0.277
9	2-Bromophenol	0.504
10	4-Cholorophenol	0.545
11	3-Ethylphenol	0.229
12	2-Ethylphenol	0.176
13	4-Bromophenol	0.681
14	2,3-Dimethylphenol	0.122
15	2,4-Dimethylphenol	0.128
16	2,4-Dimethylphenol	0.009
17	3,4-Dimethylphenol	0.122
18	3,5-Dimethylphenol	0.113
19	3-Chloro-4-fluorophenol	-0.842
20	2-Chloro-5-methylphenol	0.640
21	4-Iodophenol	0.854
22	3-Iodophenol	1.118
23	2-Isopropylphenol	0.803
24	3-Isopropylphenol	0.609
25	4-Isopropylphenol	0.473

Table 2: Values of quantum chemical parameter of twenty five phenol derivatives

C.N	MW	Hf	T_E	HOMO Energy	LUMO Energy	□	η	Exp.Act.
1	94.113	-21.75	-49.82	-9.174	0.292	-4.441	4.733	-0.431
2	130.094	-106.127	-81.643	-9.618	-0.397	-5.007	4.611	0.396
3	112.103	-64.655	-65.73	-9.397	-0.064	-4.73	4.667	0.248
4	112.103	-65.079	-65.728	-9.273	-0.056	-4.665	4.608	1.203

5	112.103	-65.51	-65.733	-9.433	-0.054	-4.743	4.69	0.473
6	108.14	-31.003	-57.006	-8.954	0.322	-4.316	4.638	-0.192
7	108.14	-31.087	-57.007	-9.092	0.291	-4.401	4.692	-0.062
8	128.558	-28.24	-61.585	-9.21	-0.023	-4.617	4.594	0.277
9	173.009	-13.202	-59.707	-9.368	-0.339	-4.854	4.515	0.506
10	128.558	-28.472	-61.585	-9.009	0.049	-4.48	4.529	0.545
11	122.166	-34.617	-64.163	-9.084	0.304	-4.39	4.694	0.229
12	122.166	-31.174	-64.158	-8.989	0.317	-4.336	4.653	0.176
13	173.009	-14.207	-59.708	-9.312	-0.026	-4.669	4.643	0.681
14	122.166	-39.395	-64.189	-8.991	0.287	-4.352	4.639	0.122
15	122.166	-40.204	-64.191	-8.858	0.302	-4.278	4.58	0.128
16	122.166	-40.338	-64.192	-8.964	0.263	-4.35	4.614	0.009
17	122.166	-39.646	-64.189	-8.874	0.334	-4.27	4.604	0.122
18	122.166	-40.416	-64.195	-9.042	0.295	-4.373	4.669	0.113
19	146.548	-70.493	-77.499	-9.292	-0.311	-4.802	4.491	-0.842
20	142.585	-37.673	-68.773	-9.093	-0.022	-4.557	4.535	0.64
21	220.009	-0.359	-58.632	-9.047	-0.5	-4.773	4.273	0.854
22	220.009	-0.359	-58.632	-9.047	-0.5	-4.773	4.273	1.118
23	136.193	-39.823	-71.327	-9.046	0.296	-4.375	4.671	0.803
24	136.193	-40.37	-71.332	-9.096	0.3	-4.398	4.698	0.609
25	136.193	-40.404	-71.332	-9.016	0.331	-4.342	4.673	0.473

Table 3: Values of predicted activity from PA1 to PA5 calculated by quantum chemical parameter

C.N.	PA1	PA2	PA3	PA4	PA5	Exp.Act.
1	-0.323	-0.367	-0.888	-4.684	-0.535	-0.431
2	0.323	0.263	0.609	0.261	0.391	0.396
3	0.289	0.298	0.239	1.723	0.256	0.248
4	1.689	1.878	1.2	1.662	1.343	1.203
5	0.689	0.583	0.258	0.773	0.479	0.473
6	-0.189	-0.176	-0.15	-0.939	-0.131	-0.192
7	-0.035	-0.837	-0.042	-0.667	-0.0315	-0.062
8	0.323	0.257	0.507	0.686	0.239	0.277
9	0.323	0.71	0.329	0.755	0.381	0.506
10	0.689	0.63	0.397	0.669	0.53	0.545
11	0.507	0.604	0.383	0.648	0.549	0.229
12	0.507	0.044	0.326	0.108	0.161	0.176
13	0.871	0.845	0.791	0.583	0.483	0.681
14	0.169	0.156	0.185	0.245	0.146	0.122
15	0.116	0.145	0.141	0.13	0.164	0.128
16	0.117	0.292	0.223	0.089	0.083	0.009
17	0.343	1.088	0.021	0.195	0.616	0.122
18	0.107	0.208	0.146	0.104	0.134	0.113
19	-0.233	-1.314	-1.322	-0.774	-0.925	-0.842

20	0.116	0.503	0.661	0.582	0.472	0.64
21	0.787	0.42	0.329	0.551	0.308	0.854
22	1.982	1.164	1.054	1.849	1.975	1.118
23	0.786	0.788	0.643	0.466	0.747	0.803
24	0.458	0.895	0.509	0.501	0.44	0.609
25	0.996	0.171	0.081	0.22	0.974	0.473

Table 4: Correlation summary of predicted activity from PA1 to PA5 calculated by quantum chemical parameter

PA	rCV^2	r^2	SE	SEE	t-Value	p-Value	DOF
1	0.848507	0.929501	0.0921	0.2440	7.8079	0.0000	0.7142
2	0.878541	0.938037	0.0747	0.1920	10.6138	0.0000	0.8231
3	0.895305	0.906387	0.0783	0.2455	7.7447	0.0000	0.7108
4	0.624539	0.819063	0.0567	0.3396	4.5131	0.0001	0.4466
5	0.743636	0.82040	0.0828	0.2255	8.6824	0.0000	0.7561

Table 5: Values of topological parameter of twenty five phenol derivatives

Chemical Sample	VCI-1	VCI-2	MR	Sh.I-1	Sh.I-2	SASA	Experimental Toxicity
1	5.113	3.394	27.752	5.143	2.344	115.04	-0.431
2	6.853	4.215	28.185	7.111	2.722	114.59	0.396
3	5.983	3.805	27.968	6.125	2.52	119.17	0.248
4	5.983	3.788	27.968	6.125	2.52	120.69	1.203
5	5.983	3.788	27.968	6.125	2.52	117.99	0.473
6	5.983	3.788	32.793	6.125	2.52	116.28	-0.192
7	5.983	3.788	32.793	6.125	2.52	111.23	-0.062
8	5.983	3.805	32.557	6.125	2.52	113.18	0.277
9	5.983	3.805	35.375	6.125	2.52	114.56	0.506
10	5.983	3.788	32.557	6.125	2.52	118.15	0.545
11	6.69	4.326	37.394	7.111	3.24	137.41	0.229
12	6.69	4.343	37.394	7.111	3.24	120.23	0.176
13	5.983	3.788	35.375	6.125	2.52	125.64	0.681
14	6.853	4.215	37.835	7.111	2.722	139.64	0.122
15	6.853	4.198	37.835	7.111	2.722	146.01	0.128
16	6.853	4.198	37.835	7.111	2.722	150.75	0.009
17	6.853	4.198	37.835	7.111	2.722	129.08	0.122
18	6.853	4.182	37.835	7.111	2.722	146.82	0.113
19	6.853	4.198	32.773	7.111	2.722	139.29	-0.842
20	6.853	4.198	37.598	7.111	2.722	143.28	0.64
21	5.983	3.788	40.16	6.125	2.52	137.46	0.854
22	5.983	3.788	40.16	6.125	2.52	128.88	1.118
23	7.56	4.715	41.943	8.1	3.408	118.15	0.803
24	7.56	4.698	41.943	8.1	3.408	137.41	0.609
25	7.56	4.698	41.943	8.1	3.408	120.23	0.473

Table 6: Values of predicted activity from PA1 to PA5 calculated by topological parameter

	PT1	PT2	PT3	PT4	PT5	Exp. Toxi.
1	-0.434	-0335	-0.211	-0.495	-0.369	-0.431
2	0.448	0.312	0.842	0.249	0.357	0.396
3	0.373	0.244	0.386	0.149	0.257	0.248
4	0.973	0.241	0.516	1.209	1.425	1.203
5	0.548	0.241	0.393	0.471	0.393	0.473
6	-0.168	-0.179	-0.578	-0.199	-0.479	-0.192
7	0.068	-0.0920	-0.785	-0.061	-0.194	-0.062
8	0.668	0.241	0.661	0.259	-0.066	0.277
9	0.668	0.832	0.712	0.514	0.278	0.506
10	0.668	0.549	0.485	0.543	0.509	0.545
11	0.368	0.353	0.993	0.212	0.543	0.229
12	0.168	0.175	0.675	0.181	0.227	0.176
13	0.668	0.715	0.828	0.659	0.179	0.681
14	0.548	0.845	1.445	0.137	0.683	0.122
15	0.548	0.345	1.445	0.124	0.129	0.128
16	1.073	0.052	0.478	0.011	0.129	0.009
17	1.073	0.125	0.389	0.122	0.006	0.122
18	1.073	0.171	0.481	0.121	0.125	0.113
19	-0.668	-0.91	-1.025	-0.854	-0.844	-0.842
20	0.668	0.623	0.746	0.71	0.67	0.64
21	0.668	1.067	1.014	0.859	0.855	0.854
22	0.668	1.031	0.95	1.115	1.119	1.118
23	1.708	1.047	1.759	0.809	0.801	0.803
24	0.548	0.443	0.46	0.622	0.607	0.609
25	0.668	0.463	1.122	0.475	0.477	0.473

Table 7: Correlation summary of predicted activity from PA1 to PA5 calculated by topological parameter

PA	rCV^2	r^2	SE	SEE	t-Value	p-Value	DOF
1	0.2789	0.745847	0.1425	0.3453	4.3517	0.0001	0.4277
2	0.325828	0.721887	0.0013	0.4366	1.7988	0.0426	0.0852
3	0.566535	0.768848	0.1127	0.3640	3.8403	0.0004	0.3642
4	0.434941	0.738932	0.0792	0.0399	5.5829	0.0000	0.6924
5	0.4993765	0.867313	0.0175	0.1932	10.5315	0.0000	0.7208

Table 8: Values of Geometrical parameter of twenty five phenol derivatives

Name	W3D	J3D	H3D	AGDD	DDI	ADDD	G1
1	228.54	2.596	16.655	35.16	83.884	12.905	6.832
2	234.11	2.542	15.739	36.017	86.002	13.231	10.797
3	231.45	2.567	16.164	35.608	84.997	13.076	8.737
4	231.42	2.569	16.184	35.603	84.966	13.072	8.577

5	231.34	2.57	16.186	35.591	84.946	13.069	8.603
6	393.01	2.807	22.316	49.126	126.578	15.822	8.108
7	389.24	2.83	22.347	48.655	126.461	15.808	8.123
8	234.41	2.541	15.856	36.063	86.165	13.256	9.598
9	236.2	2.526	15.724	36.338	86.838	13.36	12.47
10	234.85	2.541	15.833	36.131	86.251	13.269	9.293
11	601.33	3.053	28.55	63.298	176.374	18.566	9.372
12	585.26	3.125	29.253	61.606	174.704	18.39	9.586
13	236.39	2.529	15.761	36.368	86.814	13.356	11.872
14	575.64	3.186	29.208	60.594	174.812	18.401	9.662
15	600.6	3.06	28.634	63.221	177.342	18.668	9.566
16	607.69	3.028	28.569	63.967	177.52	18.686	9.561
17	587.6	3.13	28.866	61.853	175.995	18.526	9.541
18	606.57	3.037	28.28	63.849	178.516	18.791	9.469
19	237.44	2.516	15.393	36.529	87.26	13.425	11.577
20	399.03	2.775	21.514	49.879	129.381	16.173	10.98
21	237.52	2.518	15.671	36.542	87.279	13.427	14.424
22	237.52	2.518	15.671	36.542	87.279	13.427	14.424
23	810.42	3.499	36.355	73.675	229.91	20.901	11.117
24	836.61	3.398	35.423	76.055	232.92	21.175	10.828
25	845	3.369	35.35	76.818	232.935	21.176	10.797

Table 9: Values of predicted activity from PA1 to PA5 calculated by Geometerical parameter

Comp. No.	PT1	PT2	PT3	PT4	PT5	Exp. Toxi.
1	-0.396	-0.430	-0.423	0.299	-0.469	-0.431
2	0.423	0.389	0.455	0.902	0.357	0.396
3	0.252	0.251	0.282	0.465	0.257	0.248
4	1.652	1.210	0.982	0.641	1.425	1.203
5	0.556	0.479	0.455	0.381	0.393	0.473
6	-0.973	-0.194	-0.982	0.669	-0.479	-0.192
7	0.073	-0.066	0.082	0.921	-0.194	-0.062
8	0.373	0.278	0.682	0.751	-0.066	0.277
9	0.673	0.509	0.682	0.852	0.278	0.506
10	0.573	0.543	0587	0.559	0.509	0.545
11	0.433	0.227	0.382	0.74	0.543	0.229
12	0.116	0.179	0.182	0.185	0.227	0.176
13	0.661	0.683	0.682	0.815	0.179	0.681
14	0.783	0.129	0.455	1.445	0.683	0.122
15	0.783	0.129	0.455	1.445	0.129	0.128
16	0.067	0.006	0.908	0.552	0.129	0.009
17	0.817	0.125	0.908	0.445	0.006	0.122
18	0.967	0.119	0.908	0.571	0.125	0.113
19	-0.65	-0.841	-0.682	0.91	-0.844	-0.842
20	0.65	0.69	0.682	0.613	0.67	0.64

21	0.661	0.851	0.682	1.067	0.855	0.854
22	0.661	1.120	0.682	1.011	1.119	1.118
23	1.384	0.802	1.241	1.877	0.801	0.803
24	0.206	0.605	0.455	0.253	0.607	0.609
25	0.65	0.471	0.682	1.063	0.477	0.473

Table 10: Correlation summary of predicted activity from PA1 to PA5 calculated by Geometerical parameter

PA	rCV^2	r^2	SE	SEE	t-Value	p-Value	DOF
1	0.577145	0.79313	0.3093	0.1116	5.408	0.0000	0.5407
2	0.554905	0.795067	0.1106	0.1047	0.8148	0.0000	0.4995
3	0.386082	0.78077	0.4638	0.1428	0.4925	0.1250	0.1020
4	0.496312	0.790085	0.4792	0.1528	0.8430	0.1435	0.1140
5	0.345077	0.896958	0.0932	0.0492	8.5315	0.0000	0.7208

CONCLUSION

The best model is provided by the quantum chemical parameters. The parameter is total energy and LUMO energy. The best model has been selected on the basis of values of correlation coefficient (r^2) fallowed by other regression quality parameter such as standard error, standard error of estimation, t-value, p-value and degree of freedom as shown below:

SET	$_r$CV2	r^2	SE	SEE	t-Value	p-Value	DOF
^{Q}RE2	0.878541	0.938037	0.0747	0.1920	10.6138	0.0000	0.8231
^{T}RE3	0.566535	0.768848	0.1127	0.3640	3.8403	0.0004	0.3642
^{G}RE5	0.4993765	0.867313	0.0175	0.1932	10.5315	0.0000	0.7208

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