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Quantitative Structure Toxicity Relationship Of Phenols With New Set Of Descriptors

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ABSTRACT

Fifty derivatives of phenol whose toxicity is reported have been studied for Quantitative Structure Toxicity Relationship (QSTR). With the help of seven descriptors viz. Core-core repulsion, electronic energy, Log P, dielectric energy, softness, molar refractivity and steric energy. The values of these descriptors have been evaluated with the help of PC MODEL software using the semi empirical PM3 Hamiltonian. 81 multi linear regression models using different combination of descriptors have been developed using the project leader program of CAChe software. The predicted toxicity is close to the observed toxicity and the correlation coefficient in eight models is above 0.80 and, in twenty-nine models above 0.70 and in the remaining thirty have values below 0.5. The values are between 0.50-0.69. 14 models the best QSTR models is obtained by using combinations of descriptors, core-core repulsion, electronic energy, Log P and dielectric energy and the second best by using the combination of descriptors, core-core repulsion, electronic energy, softness and Log P. These models can be treated as very reliable models for predicting the toxicity of phenol derivatives and in helping the preparation of compound of desired toxicity.

KEYWORDS

QSTR;
Phenols;
Quantum chemical descriptors;
Energy descriptors;
Toxicity of phenols.

INTRODUCTION

In our recent communication we have made studies on QSAR of triazine series[1] and on inhibitors of GAO (glycolic acid oxidase)[2]. Besides QSAR studies we have also extended the work to QSTR(quantitative structural toxicity relationship) of phenol derivatives using number of quantum chemical descriptors[3]. Last decade has seen a tremendous advancement in development of several descriptors for QSAR studies[4]. Few important reviews have also come on QSAR and QSTR studies [5-8]. The work on QSTR however appears to have not been studied so extensively. In this paper we present QSTR studies on derivatives of phenol using new descriptors, which have hitherto not been used for such a study.

MATERIAL AND METHOD

Fifty derivatives of phenol whose toxicity is reported have been chosen as study material of this paper [9] and the compounds are listed in TABLE -1. The toxicity of these phenols has been tested against tetrahymena pyriformis. The hazards of the phenols are reported but theoretical methods to predict the hazards are little studied. It is also of interest to find out whether the site of activity in phenols remains confined to hydroxyl group are it changes on change of any substituents having polar properties.

For QSTR predictions the 3-D modeling and geometry optimization of all the derivatives have been done with the help of PC MODEL software using the semiempirical PM3 Hamiltonian[10]. The MOPAC calculations have been performed with Win MOPAC 7.21 software by applying keywords PM3 charge= O Gnorm=0.1 GEO-OK vector density. The descriptors that have been used for QSTR model are: -

Electronic Energy-EE
Dielectric Energy-DE
Steric Energy - SE
Softness. - S
Molar Refractivity -MR
Log P.

The values of these descriptors have been evaluated with the help of following equations using the above software.

1. Electronic energy

The total energy of a molecular system is the sum of the total electronic energy, E_{ee} and the energy of the internuclear repulsion, $E_{nr.}$ The total electronic energy of the system is given by[11].

$$E = 1/2R (H+ F) \quad (1)$$

Where P is density matrix and H is one-electron matrix.

2. Dielectric energy

The dielectric energy is portion of the total energy of a molecule embedded in a dielectric. It is the stabilizing portion that results from screening the charges in the molecule by a dielectric[12].

3. Steric Energy

The steric energy of the molecule is the sum of the molecular mechanics. Potential energy calculated for the bonds, bond angles, dihedral angles, nonbonded atoms and so forth. It is specific to mechanics and depends upon the force field used[13].

4. Softness

The operational definition of absolute hardness and electronegativity is given as: -

$$h = 1/2 (I R - E A \quad (2)$$

Where I P and E A are the ionization potential and electron affinity, respectively, of the chemical species. According to Koopman's theorem, the IP is simply the eigen value of HOMO with change of sign and the E A is the eigen value of the LUMO with change of sign [14]. Hence h and c can be written as: -

$$h=1/2(e_{LUMO}-e_{HOMO}) \quad (3)$$

$$c=m=1/2(e_{LUMO}+e_{HOMO}) \quad (4)$$

Softness is reverse of h [15-16].

$$S=1/2\,h \quad (5)$$

A high value of the absolute hardness indicates high stability and low reactivity. Absolute softness defines the reverse character.

5. Molar Refractivity

$$MR=[(n^2-1)/(n^2+2)]MW/d \quad (6)$$

Where n is the refractive index for the sodium D line, MW is the molecular weight and d is the density of the compound; MR can be used[17] as a steric parameter in the absence of E_s, measures the electronic effects also[17] and may reflect the dipole-dipole interaction at the active site[18].

6. Log P

P is partition coefficient. Log P taken as a measure of the hydrophobicity of the molecule; for measuring P, an octanol-water system preferred[19-20].
Hydrophobic constant

$$\pi = \log P_X - \text{Log } P_H \quad (7)$$

Where R_X is the portion coefficient of the substituted compound and P_H that of unsubstituted compound [20].

RESULT AND DISCUSSION

50 derivatives of phenol having different substituents at different positions on the phenol ring have been studied. The substituents can be divided into three main groups, which are alkyl, phenyl and halogen. The toxicity as reported in TABLE -1. Indicates that there is no significant relation, in the potency of toxicity and substitutions on the phenol ring. Therefore no qualitative explanation of the relation of toxicity with the substitutions has been considered at this stage. The toxicity potency of all the derivatives have been measured only in one unit hence we have drawn QSTR models collectively for all the derivatives of phenol. For QSTR study various descriptors as described in method and material have been used in different combinations. The details of combinations are presented in TABLE -2.

The values of descriptors of all the derivatives of phenol have been evaluated with the help of PC MODEL software using computational technique and the results are presented in TABLE- 3. alongwith reported toxicity. With the help of the values of descriptors 81 MLR equations have been developed using the project leader program of CAChe software. All combinations described in TABLE -2 have been tried. Various MLR equations have also been represented by APA. Out of 81 QSTR models 67 models

TABLE 1: Phenol derivatives and their toxicity against tetrahymena pyriformis[9]

S. No.	Compound	A_{obsd}
1	Phenol	-0.431
2	2, 6-Defluorophenol	0.396
3	2 -Fluorophenol	0.248
4	4 -Fluorophenol	0.017
5	3 -Fluorophenol	0.473
6	4 -Methyphenol	-0.192
7	3 -Methyphenol	-0.062
8	2 -Chlorophenol	0.277
9	2 -Bromophenol	0.504
10	4 -Chlorophenol	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, 5 -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
26	2, 5 - Dichlorophenol	1.128
27	2, 3 - Dichlorophenol	1.271
28	4 - Chloro-2-methylphenol	0.700
29	4 - Chloro-3-methylphenol	0.795
30	2, 4 - Dichlorophenol	1.036
31	3 - tert-Butyphenol	0.730
32	4 - tert - Butyphenol	0.913
33	3, 5 - Dichlorophenol	1.562
34	2 - Phenylphenol	1.094
35	2, 4 - Dibromophenol	1.403
36	2, 3, 6 - Trimethyphenol	0.418
37	3, 4, 5 - Trimethyphenol	0.930
38	2, 4, 6 - Trimethyphenol	1.695
39	4 -Chloro - 3, 5 - dimethylphenol	1.203
40	4 -Bromo - 2, 6 -dichlorophenol	1.779
41	2, 4, 5 -Trichlorophenol	2.100
42	4 -Bromo - 6 chloro - 2-methyphenol	1.277
43	4 -Bromo -2, 6 -dimethyphenol	1.278
44	2, 4, 6 -Tribromophenol	2.050
45	2 - tert - buty -4 -methylphenol	1.297
46	4 -Chloro-2-isopropyl -5methylphenol	1.862
47	6 - tert-Butyl -2, 4 -dimethylphenol	1.245
48	2, 6 - dimethylphenol	2.113
49	2,4 - dibromo-6-phenylphenol	2.207
50	2,6 -Di- tert-butyl -4 -methylphenol	1.788

have correlation coefficient value above 0.50 hence have reliable predictive power. These models are presented below: -

APA1=-0.00217627*CCR-0.00212552*EE-2.34702
rCV^2=0.620815
r^2=0.688866

APA2=0.000151473*CCR+67.3998*Softness-14.8945
rCV^2=0.582225
r^2=0.672468

APA3=-0.000164829*CCR+1.09714*LogP-1.46029
rCV^2=0.626169
r^2=0.668279

APA4=-0.000147897*CCR+0.0841018*MR-1.71038
rCV^2=0.514404
r^2=0.538166

APA5=-0.000143261*EE+64.6681*Softness-14.4792
rCV^2=0.607137
r^2=0.694196

APA6=0.000119775*EE+1.01768*LogP-1.29688
rCV^2=0.586436
r^2=0.638352

APA7=7.30042e-005*EE+0.0691057*MR-1.42897
rCV^2=0.459061
r^2=0.507131

APA8=44.213*Softness+0.534767*LogP-10.4869
rCV^2=0.67338
r^2=0.730833

APA9=51.6865*Softness+0.040396*MR-12.1778
rCV^2=0.651005
r^2=0.688737

APA10=0.689674*LogP-1.0322*DE-1.58363
rCV^2=0.473184
r^2=0.603778

APA11=0.682634*LogP-0.0184903*SE-1.37747
rCV^2=0.534767
r^2=0.605968

APA12=2.20194*LogP-0.130219*MR-0.444436
rCV^2=0.474638
r^2=0.700757

APA13=-0.00138789*CCR-0.00140258*EE+42.0732*Softness-10.8036
rCV^2=0.729899
r^2=0.786532

APA14=-0.00172026*CCR-0.0015087*EE+0.745486*LogP-2.59959
rCV^2=0.744728
r^2=0.822723

APA15=-0.002315*CCR-0.00223777*EE+1.41655*DE-1.8883
rCV^2=0.602373
r^2=0.697371

APA16=-0.00216266*CCR-0.00211459*EE-0.00356716*SE-2.37752
rCV^2=0.603424
r^2=0.689138

APA17=-0.00205121*CCR-0.00181269*EE+0.0592699*MR-3.12307
rCV^2=0.726204
r^2=0.794417

APA18=-1.17145e-005*EE+45.6143*Softness+0.496412*LogP-10.7697
rCV^2=0.644572
r^2=0.731086

APA19=- 000148886*EE+63.9927*Softness-0.592*DE-14.5759
rCV^2=0.590227
r^2=0.695878

APA20=-0.000144004*EE+64.4548*Softness-0.00179256*SE-14.4543
rCV^2=0.549404
r^2=0.694265

APA21=-8.42795e-005*EE+58.6859*Softness+0.0179505*MR-13.4452
rCV^2=0.608636
r^2=0.701136

APA22=44.3498*Softness+0.533002*LogP+0.0674595*DE-10.4886
rCV^2=0.642059
r^2=0.730857

APA23=44.5709*Softness+0.532055*LogP+0.00220834*SE-10.5375
rCV^2=0.662152
r^2=0.73094

APA24=33.6192*Softness+1.51834*LogP-0.0808199*MR-7.80439
rCV^2=0.614045
r^2=0.762838

APA25=0.690014*LogP-0.532164*DE-0.0140529*SE-1.54109
rCV^2=0.48135
r^2=0.607076

APA26=2.21157*LogP-0.918019*DE-0.129477*MR-0.81697
rCV^2=0.333153
r^2=0.705443

APA27=0.000121922*EE+1.02161*LogP+0.115742*DE-1.25272
rCV^2=0.55526
r^2=0.638413

APA28=0.000114173*EE+1.00591*LogP-0.00617695*SE-1.36043
rCV^2=0.586793
r^2=0.639169

APA29=3.99197e-005*EE+2.16971*LogP-0.11761*MR-0.557122
rCV^2=0.402743
r^2=0.704291

TABLE 2: Combination of descriptors, for QSTR model

Predicted Activity	First descriptor	Second descriptor	Third descriptor	Fourth descriptor
APA1	Core-Core Repulsion	Electronic Energy	-	-
APA2	Core-Core Repulsion	Softness	-	-
APA3	Core-Core Repulsion	Log P	-	-
APA4	Core-Core Repulsion	Molar Refractivity	-	-
APA5	Electronic Energy	Softness	-	-
APA6	Electronic Energy	Log P	-	-
APA7	Electronic Energy	Molar Refractivity	-	-
APA8	Softness	Log P	-	-
APA9	Softness	Molar Refractivity	-	-
APA10	Log P	Dielectric Energy	-	-
APA11	Log P	Steric Energy	-	-
APA12	Log P	Molar Refractivity	-	-
APA13	Core-Core Repulsion	Electronic Energy	Softness	-
APA14	Core-Core Repulsion	Electronic Energy	Log P	-
APA15	Core-Core Repulsion	Electronic Energy	Dielectric Energy	-
APA16	Core-Core Repulsion	Electronic Energy	Steric Energy	-
APA17	Core-Core Repulsion	Electronic Energy	Molar Refractivity	-
APA18	Electronic Energy	Softness	Log P	-
APA19	Electronic Energy	Softness	Dielectric Energy	-
APA20	Electronic Energy	Softness	Steric Energy	-
APA21	Electronic Energy	Softness	Molar Refractivity	-
APA22	Softness	Log P	Dielectric Energy	-
APA23	Softness	Log P	Steric Energy	-
APA24	Softness	Log P	Molar Refractivity	-
APA25	Log P	Dielectric Energy	Steric Energy	-
APA26	Log P	Dielectric Energy	Molar Refractivity	-
APA27	Electronic Energy	Log P	Dielectric Energy	-
APA28	Electronic Energy	Log P	Steric Energy	-
APA29	Electronic Energy	Log P	Molar Refractivity	-
APA30	Electronic Energy	Dielectric Energy	Molar Refractivity	-
APA31	Electronic Energy	Steric Energy	Molar Refractivity	-
APA32	Softness	Dielectric Energy	Molar Refractivity	-
APA33	Softness	Steric Energy	Molar Refractivity	-
APA34	Core-Core Repulsion	Softness	Log P	-
APA35	Core-Core Repulsion	Softness	Dielectric Energy	-
APA36	Core-Core Repulsion	Softness	Steric Energy	-
APA37	Core-Core Repulsion	Softness	Molar Refractivity	-
APA38	Core-Core Repulsion	Log P	Dielectric Energy	-
APA39	Core-Core Repulsion	Log P	Steric Energy	-
APA40	Core-Core Repulsion	Softness	Log P	Molar Refractivity
APA41	Core-Core Repulsion	Dielectric Energy	Molar Refractivity	-
APA42	Core-Core Repulsion	Steric Energy	Molar Refractivity	-

TABLE 2: Continued

APA43	Log P	Steric Energy	Molar Refractivity	
APA44	Core-Core Repulsion	Electronic Energy	Softness	Log P
APA45	Core-Core Repulsion	Electronic Energy	Softness	Dielectric Energy
APA46	Core-Core Repulsion	Electronic Energy	Softness	Steric Energy
APA47	Core-Core Repulsion	Electronic Energy	Softness	Molar Refractivity
APA48	Core-Core Repulsion	Electronic Energy	Log P	Dielectric Energy
APA49	Core-Core Repulsion	Electronic Energy	Log P	Steric Energy
APA50	Core-Core Repulsion	Electronic Energy	Log P	Molar Refractivity
APA51	Core-Core Repulsion	Electronic Energy	Dielectric Energy	Steric Energy
APA52	Core-Core Repulsion	Electronic Energy	Dielectric Energy	Molar Refractivity
APA53	Core-Core Repulsion	Electronic Energy	Steric Energy	Molar Refractivity
APA54	Electronic Energy	Softness	Log P	Dielectric Energy
APA55	Electronic Energy	Softness	Log P	Steric Energy
APA56	Electronic Energy	Softness	Log P	Molar Refractivity
APA57	Electronic Energy	Softness	Dielectric Energy	Steric Energy
APA58	Electronic Energy	Softness	Dielectric Energy	Molar Refractivity
APA59	Electronic Energy	Softness	Steric Energy	Molar Refractivity
APA60	Electronic Energy	Softness	Dielectric Energy	Steric Energy
APA61	Electronic Energy	Softness	Dielectric Energy	Molar Refractivity
APA62	Softness	Log P	Steric Energy	Molar Refractivity
APA63	Log P	Dielectric Energy	Steric Energy	Molar Refractivity
APA64	Core-Core Repulsion	Softness	Log P	Dielectric Energy
APA65	Core-Core Repulsion	Softness	Log P	Steric Energy
APA66	Core-Core Repulsion	Softness	Dielectric Energy	Steric Energy
APA67	Core-Core Repulsion	Softness	Dielectric Energy	Molar Refractivity

APA30=7.07723e-005*EE-0.0992819*DE+0.0687148*MR-1.46399
rCV^2=0.429336
r^2=0.507175

APA31=8.17552e-005*EE+0.00550212*SE+0.0710751*MR-1.39258
rCV^2=0.446062
r^2=0.507691

APA32=52.3651*Softness+0.404025*DE+0.039583*MR-12.1559
rCV^2=0.628427
r^2=0.689612

APA33=53.6099*Softness+0.0145968*SE+0.0394387*MR-12.4294
rCV^2=0.627925
r^2=0.69362

APA34=-3.32996e-005*CCR+40.0453*Softness+0.633914* LogP-9.66735
rCV^2=0.669866
r^2=0.732525

APA35=0.000158127*CCR+66.8002*Softness-0.611353*DE-15.0113
rCV^2=0.572219
r^2=0.674221

APA36=0.000151933*CCR+67.2891*Softness-0.000991416*SE-14.8819
rCV^2=0.527177
r^2=0.672489

APA37=4.11628e-005*CCR+55.4914*Softness+0.0303809*MR-12.853
rCV^2=0.618029
r^2=0.691019

APA38=-0.000180751*CCR+1.12346*LogP+0.751687*DE-1.18674
rCV^2=0.602979
r^2=0.670765

APA39=-0.000164385*CCR+1.09632*LogP-0.000441467*SE-1.46448
rCV^2=0.615408
r^2=0.668283

APA40=2.04042e-005*CCR+35.6454*Softness+1.50656*LogP-0.0848439*MR-8.17299
rCV^2=0.528033
r^2=0.763394

TABLE 3: Values of descriptors of fifty derivatives of phenol and their observed toxicity

Compd	Core-Core Repulsion	Electronic Energy	Softness	Log P	Dielectric Energy (kcal/mole)	Steric Energy (kcal/mole)	Molar Refractivity	Activity
1	3250.512	-4347.218	0.211	1.762	-0.357	-10.205	27.752	-0.431
2	5276.761	-7223.134	0.217	2.041	-0.391	-8.894	28.185	0.396
3	4213.156	-5734.727	0.214	1.902	-0.314	-7.858	27.968	0.248
4	4137.182	-5658.771	0.217	1.902	-0.410	-10.416	27.968	0.017
5	4151.000	-5672.608	0.213	1.902	-0.388	-10.442	27.968	0.473
6	4193.104	-5439.517	0.216	2.229	-0.358	-10.752	32.793	-0.192
7	4206.335	-5452.753	0.213	2.229	-0.361	-10.725	32.793	-0.062
8	4155.235	-5553.343	0.218	2.280	-0.286	-8.047	32.557	0.277
9	4107.384	-5542.087	0.221	2.554	-0.318	-8.063	35.375	0.504
10	4078.448	-5476.566	0.221	2.280	-0.369	-10.021	32.557	0.545
11	5228.007	-6623.883	0.213	2.626	-0.363	-8.919	37.394	0.229
12	5354.763	-6750.490	0.215	2.626	-0.305	-4.467	37.394	0.176
13	4039.009	-5473.755	0.215	2.554	-0.420	-9.878	35.375	0.681
14	5370.895	-6766.979	0.216	2.697	-0.342	-9.537	37.835	0.122
15	5300.358	-6696.476	0.218	2.697	-0.335	-10.772	37.835	0.128
16	5300.262	-6696.386	0.217	2.697	-0.336	-10.591	37.835	0.009
17	5294.367	-6690.461	0.217	2.697	-0.365	-8.554	37.835	0.122
18	5253.315	-6649.442	0.214	2.697	-0.365	-11.376	37.835	0.113
19	5139.881	-6962.825	0.223	2.420	-0.407	-6.766	32.773	0.842
20	5190.496	-6738.318	0.220	2.747	-0.289	-8.689	37.598	0.640
21	4005.503	-5375.376	0.237	3.020	-0.398	-10.340	40.160	0.854
22	4016.270	-5386.139	0.234	3.020	-0.385	-10.345	40.160	1.118
23	6617.795	-8163.203	0.214	2.956	-0.280	-6.945	41.943	0.803
24	6439.525	-7984.954	0.213	2.956	-0.354	-8.474	41.943	0.609
25	6403.863	-7949.297	0.214	2.956	-0.348	-8.764	41.943	0.473
26	5077.397	-6776.905	0.225	2.798	-0.288	-7.282	37.362	1.128
27	5155.453	-6854.921	0.220	2.798	-0.290	-4.343	37.362	1.271
28	5186.346	-6734.171	0.223	2.747	-0.339	-9.344	37.598	0.700
29	5183.454	-6731.250	0.222	2.747	-0.366	-9.700	37.598	0.795
30	5076.360	-6775.865	0.226	2.798	-0.288	-10.431	37.362	1.036
31	7809.561	-9504.494	0.213	3.389	-0.355	-5.719	46.418	0.730
32	7761.254	-9456.186	0.214	3.389	-0.354	-5.818	46.418	0.913
33	5025.831	-6725.347	0.219	2.798	-0.356	-12.466	37.362	1.562
34	8573.193	-10441.995	0.224	3.447	-0.351	-20.252	52.888	1.094
35	4983.670	-6756.387	0.225	3.346	-0.369	-9.781	42.998	1.403
36	6556.624	-8102.350	0.218	3.164	-0.303	-10.334	42.876	0.418
37	6491.207	-8036.964	0.218	3.164	-0.375	-7.869	42.876	0.930
38	6497.958	-8043.721	0.220	3.164	-0.298	-11.714	42.876	1.695
39	6390.005	-8087.492	0.223	3.215	-0.360	-10.719	42.639	1.203
40	6120.491	-8157.949	0.227	3.590	-0.341	-11.984	44.985	1.779
41	6157.295	-8158.150	0.232	3.316	-0.290	-6.195	42.166	2.100
42	6230.134	-8115.926	0.225	3.539	-0.396	-8.017	45.221	1.277
43	6339.644	-8073.749	0.219	3.488	-0.353	-9.579	45.457	1.278
44	6027.254	-8137.917	0.228	4.138	-0.426	-11.043	50.621	2.050
45	9283.797	-11128.332	0.218	3.857	-0.284	-4.081	51.459	1.297
46	9031.550	-11028.059	0.224	3.941	-0.276	-6.691	51.789	1.862
47	10721.376	-12715.461	0.219	4.324	-0.233	-5.858	56.500	1.245
49	10990.257	-13534.964	0.227	5.030	-0.432	-16.363	68.134	2.207
50	15648.760	-18091.224	0.220	5.484	-0.180	1.596	70.125	1.788

TABLE 4: Predictive toxicity fifty derivatives of phenol APA1-APA9

Compd	APA1	APA2	APA3	APA4	APA5	APA6	APA7	APA8	APA9
1	-0.181	-0.181	-0.063	0.143	-0.211	-0.024	0.171	-0.216	-0.151
2	1.522	0.531	-0.091	-0.120	0.589	-0.085	-0.009	0.199	0.177
3	0.673	0.167	-0.068	0.019	0.181	-0.048	0.085	-0.008	0.013
4	0.677	0.358	-0.056	0.030	0.364	-0.039	0.091	0.124	0.168
5	0.677	0.090	-0.058	0.028	0.108	-0.041	0.090	-0.053	-0.039
6	0.089	0.299	0.295	0.427	0.268	0.320	0.440	0.255	0.311
7	0.089	0.099	0.292	0.425	0.076	0.319	0.439	0.123	0.156
8	0.414	0.428	0.357	0.413	0.414	0.358	0.415	0.371	0.405
9	0.494	0.623	0.665	0.657	0.606	0.638	0.611	0.650	0.674
10	0.418	0.619	0.369	0.425	0.597	0.368	0.421	0.504	0.560
11	0.355	0.254	0.559	0.661	0.244	0.582	0.672	0.335	0.342
12	0.348	0.408	0.538	0.643	0.391	0.567	0.662	0.423	0.445
13	0.498	0.208	0.676	0.667	0.209	0.647	0.616	0.385	0.364
14	0.348	0.477	0.613	0.677	0.459	0.637	0.692	0.505	0.515
15	0.351	0.602	0.625	0.688	0.578	0.645	0.697	0.594	0.618
16	0.351	0.534	0.625	0.688	0.513	0.645	0.697	0.549	0.567
17	0.352	0.533	0.626	0.689	0.512	0.646	0.697	0.549	0.567
18	0.354	0.325	0.632	0.695	0.312	0.651	0.700	0.417	0.411
19	1.267	0.914	0.347	0.286	0.939	0.332	0.328	0.667	0.672
20	0.679	0.720	0.698	0.684	0.713	0.692	0.677	0.709	0.712
21	0.361	1.686	1.192	1.075	1.617	1.132	0.954	1.606	1.694
22	0.361	1.485	1.191	1.073	1.425	1.131	0.953	1.474	1.539
23	0.602	0.532	0.692	0.838	0.529	0.734	0.874	0.556	0.577
24	0.611	0.437	0.722	0.865	0.439	0.755	0.887	0.511	0.526
25	0.613	0.499	0.728	0.870	0.499	0.759	0.889	0.556	0.577
26	1.008	1.040	0.773	0.681	1.042	0.739	0.658	0.957	0.961
27	1.004	0.714	0.760	0.669	0.730	0.730	0.652	0.736	0.702
28	0.680	0.921	0.699	0.685	0.906	0.692	0.678	0.842	0.867
29	0.680	0.853	0.700	0.685	0.841	0.693	0.678	0.798	0.815
30	1.008	1.107	0.773	0.681	1.106	0.739	0.658	1.002	1.013
31	0.859	0.645	0.971	1.038	0.657	1.014	1.085	0.743	0.707
32	0.862	0.705	0.979	1.046	0.714	1.020	1.088	0.787	0.758
33	1.010	0.627	0.781	0.689	0.647	0.745	0.662	0.692	0.651
34	1.190	1.502	0.908	1.470	1.502	0.960	1.464	1.260	1.536
35	1.168	1.025	1.389	1.169	1.039	1.299	1.049	1.250	1.189
36	0.606	0.792	0.930	0.926	0.779	0.952	0.942	0.843	0.822
37	0.609	0.782	0.941	0.936	0.770	0.960	0.947	0.843	0.822
38	0.609	0.918	0.940	0.935	0.900	0.959	0.947	0.932	0.925
39	0.937	1.104	1.013	0.931	1.100	1.006	0.927	1.092	1.071
40	1.673	1.332	1.470	1.168	1.369	1.379	1.084	1.469	1.372
41	1.593	1.675	1.163	0.925	1.693	1.101	0.889	1.544	1.517
42	1.345	1.214	1.396	1.171	1.234	1.333	1.104	1.354	1.278
43	1.017	0.826	1.322	1.175	0.840	1.286	1.123	1.061	0.978
44	1.833	1.386	2.086	1.655	1.431	1.939	1.475	1.806	1.652
45	1.102	1.205	1.241	1.244	1.213	1.295	1.315	1.214	1.169
46	1.438	1.571	1.375	1.309	1.586	1.393	1.345	1.525	1.492
47	1.347	1.490	1.516	1.456	1.505	1.580	1.547	1.508	1.424
49	2.504	2.070	2.247	2.394	2.139	2.201	2.291	2.239	2.307
50	2.050	2.304	1.977	1.873	2.340	2.117	2.096	2.173	2.026

APA41=-0.000171394*CCR+0.878449*DE+0.0879097*MR-1.4246

rCV^2=0.499617

r^2=0.541374

TABLE 5: Predictive toxicity fifty derivatives of phenol APA10-APA18

Compd	APA10	APA11	APA12	APA13	APA14	APA15	APA16	APA17	APA18
1	0.000	0.014	-0.178	-0.340	-0.319	-0.190	-0.178	-0.265	-0.219
2	0.227	0.180	0.380	1.134	0.742	1.506	1.516	0.817	0.226
3	0.052	0.066	0.101	0.396	0.222	0.746	0.666	0.288	0.003
4	0.152	0.113	0.101	0.521	0.238	0.616	0.678	0.306	0.139
5	0.128	0.114	0.101	0.353	0.236	0.647	0.678	0.303	-0.043
6	0.323	0.343	0.194	0.094	0.056	0.070	0.095	0.080	0.253
7	0.326	0.343	0.194	-0.032	0.053	0.065	0.094	0.077	0.117
8	0.284	0.328	0.337	0.390	0.331	0.514	0.408	0.350	0.371
9	0.506	0.515	0.573	0.567	0.600	0.555	0.488	0.595	0.644
10	0.370	0.364	0.337	0.515	0.347	0.402	0.419	0.368	0.507
11	0.601	0.580	0.468	0.193	0.358	0.318	0.355	0.377	0.327
12	0.543	0.498	0.468	0.278	0.331	0.389	0.332	0.346	0.420
13	0.611	0.549	0.573	0.314	0.615	0.416	0.497	0.611	0.369
14	0.629	0.640	0.567	0.321	0.381	0.337	0.350	0.369	0.501
15	0.622	0.662	0.567	0.404	0.396	0.353	0.358	0.386	0.591
16	0.623	0.659	0.567	0.362	0.396	0.351	0.358	0.386	0.546
17	0.653	0.621	0.567	0.362	0.397	0.310	0.351	0.387	0.546
18	0.653	0.674	0.567	0.235	0.406	0.313	0.363	0.397	0.408
19	0.505	0.399	0.616	1.211	0.867	1.218	1.254	0.898	0.685
20	0.609	0.659	0.709	0.700	0.686	0.766	0.677	0.673	0.708
21	0.910	0.875	0.975	1.148	0.871	0.304	0.364	0.785	1.603
22	0.896	0.875	0.975	1.022	0.869	0.322	0.363	0.782	1.466
23	0.744	0.769	0.603	0.465	0.536	0.663	0.597	0.586	0.555
24	0.821	0.797	0.603	0.420	0.573	0.571	0.611	0.628	0.507
25	0.814	0.803	0.603	0.462	0.581	0.583	0.614	0.637	0.552
26	0.643	0.667	0.852	1.121	0.976	1.115	0.998	0.961	0.962
27	0.645	0.613	0.852	0.912	0.960	1.106	0.984	0.942	0.735
28	0.661	0.671	0.709	0.826	0.687	0.695	0.680	0.674	0.845
29	0.689	0.677	0.709	0.784	0.687	0.657	0.681	0.675	0.799
30	0.644	0.726	0.852	1.163	0.977	1.114	1.009	0.961	1.008
31	1.120	1.042	0.974	0.650	0.832	0.799	0.852	0.838	0.740
32	1.119	1.044	0.974	0.691	0.842	0.804	0.854	0.849	0.785
33	0.713	0.763	0.852	0.868	0.987	1.023	1.019	0.973	0.688
34	1.156	1.350	0.258	1.368	0.976	1.135	1.234	1.354	1.281
35	1.105	1.087	1.324	1.222	1.515	1.171	1.166	1.450	1.234
36	0.912	0.973	0.939	0.633	0.704	0.635	0.613	0.656	0.840
37	0.985	0.928	0.939	0.632	0.718	0.539	0.607	0.672	0.839
38	0.906	0.999	0.939	0.716	0.716	0.647	0.621	0.670	0.930
39	1.005	1.015	1.081	1.053	1.006	0.906	0.943	0.957	1.093
40	1.244	1.295	1.603	1.695	1.856	1.716	1.679	1.777	1.462
41	1.002	1.001	1.367	1.854	1.589	1.703	1.580	1.534	1.555
42	1.266	1.187	1.460	1.399	1.566	1.289	1.339	1.490	1.345
43	1.186	1.181	1.317	0.936	1.276	1.003	1.019	1.203	1.046
44	1.709	1.651	2.075	1.838	2.394	1.767	1.835	2.266	1.780
45	1.369	1.331	1.347	1.092	1.094	1.121	1.091	1.056	1.219
46	1.419	1.437	1.490	1.554	1.440	1.492	1.434	1.411	1.534
47	1.639	1.682	1.719	1.365	1.364	1.416	1.345	1.283	1.515
49	2.331	2.359	1.759	2.478	2.665	2.346	2.534	2.907	2.240
50	2.384	2.336	2.499	2.108	1.863	2.114	2.029	1.728	2.200

APA42=-0.000183295*CCR+0.0199161*SE+0.0912767*MR-1.61009
rCV^2=0.510529
r^2=0.545292

APA43=2.61402*LogP-0.0468758*SE-0.162294*MR-0.793333
rCV^2=0.507902
r^2=0.746682

APA44=-0.00147603*CCR-0.00133163*EE+18.7773*Softness+0.569551*LogP-6.31417
rCV^2=0.768045

TABLE 6: Predictive toxicity fifty derivatives of phenol APA19-APA27

Compd	APA19	APA20	APA21	APA22	APA23	APA24	APA25	APA26	APA27
1	-0.215	-0.210	-0.198	-0.216	-0.218	-0.278	0.008	-0.186	-0.024
2	0.617	0.589	0.404	0.197	0.201	0.312	0.200	0.407	-0.093
3	0.159	0.179	0.099	-0.005	-0.005	0.017	0.049	0.056	-0.046
4	0.396	0.366	0.269	0.121	0.123	0.118	0.136	0.144	-0.047
5	0.129	0.110	0.035	-0.055	-0.055	-0.016	0.124	0.123	-0.046
6	0.268	0.271	0.278	0.255	0.252	0.192	0.339	0.196	0.320
7	0.080	0.079	0.103	0.122	0.119	0.091	0.340	0.199	0.318
8	0.371	0.411	0.401	0.376	0.374	0.355	0.298	0.273	0.367
9	0.580	0.603	0.626	0.653	0.654	0.644	0.504	0.543	0.644
10	0.600	0.597	0.570	0.503	0.504	0.456	0.370	0.349	0.366
11	0.255	0.244	0.284	0.333	0.333	0.321	0.589	0.481	0.580
12	0.368	0.384	0.412	0.425	0.432	0.388	0.496	0.429	0.571
13	0.246	0.209	0.269	0.380	0.382	0.443	0.583	0.636	0.641
14	0.457	0.460	0.480	0.505	0.504	0.494	0.636	0.562	0.638
15	0.570	0.581	0.592	0.594	0.590	0.561	0.649	0.555	0.647
16	0.506	0.516	0.533	0.550	0.546	0.528	0.647	0.556	0.647
17	0.523	0.511	0.533	0.548	0.550	0.528	0.634	0.583	0.644
18	0.325	0.317	0.353	0.415	0.410	0.427	0.674	0.583	0.649
19	0.972	0.934	0.817	0.664	0.674	0.718	0.440	0.664	0.323
20	0.677	0.712	0.708	0.713	0.711	0.725	0.630	0.656	0.699
21	1.626	1.614	1.637	1.605	1.610	1.502	0.899	1.026	1.131
22	1.428	1.422	1.462	1.473	1.476	1.402	0.893	1.014	1.131
23	0.499	0.527	0.554	0.559	0.558	0.489	0.745	0.547	0.740
24	0.453	0.440	0.481	0.510	0.510	0.455	0.806	0.616	0.753
25	0.508	0.500	0.536	0.554	0.554	0.489	0.807	0.610	0.758
26	1.002	1.037	1.001	0.962	0.964	0.989	0.645	0.798	0.746
27	0.695	0.721	0.714	0.740	0.747	0.821	0.605	0.800	0.737
28	0.898	0.906	0.884	0.843	0.843	0.825	0.666	0.702	0.694
29	0.849	0.841	0.825	0.797	0.798	0.792	0.686	0.727	0.691
30	1.066	1.107	1.060	1.006	1.001	1.023	0.690	0.799	0.746
31	0.680	0.654	0.689	0.740	0.747	0.751	1.067	0.995	1.010
32	0.736	0.711	0.744	0.785	0.791	0.785	1.068	0.993	1.016
33	0.650	0.652	0.644	0.691	0.685	0.787	0.754	0.860	0.745
34	1.521	1.524	1.530	1.259	1.235	0.685	1.308	0.280	0.955
35	1.047	1.039	1.100	1.248	1.250	1.365	1.101	1.354	1.299
36	0.760	0.782	0.801	0.845	0.839	0.863	0.949	0.907	0.956
37	0.793	0.768	0.795	0.841	0.845	0.863	0.952	0.973	0.956
38	0.876	0.905	0.913	0.935	0.926	0.930	0.965	0.902	0.964
39	1.112	1.103	1.089	1.090	1.089	1.127	1.019	1.102	1.004
40	1.367	1.373	1.372	1.469	1.464	1.642	1.286	1.611	1.381
41	1.657	1.685	1.614	1.549	1.554	1.622	0.988	1.323	1.107
42	1.265	1.231	1.255	1.350	1.356	1.479	1.225	1.519	1.328
43	0.849	0.841	0.903	1.059	1.058	1.181	1.188	1.336	1.286
44	1.478	1.433	1.530	1.800	1.802	2.052	1.696	2.170	1.933
45	1.199	1.207	1.210	1.216	1.222	1.221	1.328	1.310	1.298
46	1.564	1.584	1.559	1.528	1.529	1.525	1.419	1.447	1.397
47	1.469	1.503	1.493	1.513	1.511	1.557	1.649	1.644	1.587
49	2.221	2.155	2.240	2.231	2.220	1.958	2.390	1.882	2.186
50	2.302	2.328	2.249	2.179	2.189	2.251	2.316	2.396	2.123

r^2=0.834721

APA45=-0.00150522*CCR-0.00149893*EE+41.3782*Softness+1.06506*DE-10.319

rCV^2=0.707926

r^2=0.791313

APA46=-0.00140024*CCR-0.00141155*EE+42.5161*Softness+0.0054112*SE-10.8464

rCV^2=0.689889

r^2=0.787147

APA47=-0.00162253*CCR-0.0014859*EE+25.1105 *Softness

TABLE 7: Predictive toxicity fifty derivatives of phenol APA28-APA36

Compd	APA28	APA29	APA30	APA31	APA32	APA33	APA34	APA35	APA36
1	-0.021	-0.171	0.171	0.168	-0.152	-0.172	-0.209	-0.184	-0.180
2	-0.077	0.269	0.000	-0.029	0.165	0.186	0.141	0.557	0.530
3	-0.054	0.051	0.083	0.083	0.030	0.031	-0.032	0.142	0.166
4	-0.029	0.054	0.098	0.075	0.149	0.155	0.090	0.389	0.359
5	-0.031	0.053	0.095	0.074	-0.052	-0.060	-0.070	0.110	0.092
6	0.328	0.206	0.440	0.434	0.308	0.287	0.256	0.299	0.300
7	0.326	0.206	0.439	0.433	0.150	0.126	0.135	0.103	0.100
8	0.349	0.340	0.409	0.423	0.433	0.424	0.370	0.383	0.426
9	0.626	0.603	0.606	0.624	0.689	0.696	0.665	0.595	0.621
10	0.370	0.343	0.422	0.419	0.556	0.556	0.492	0.622	0.619
11	0.580	0.478	0.673	0.675	0.332	0.334	0.353	0.265	0.254
12	0.538	0.472	0.658	0.689	0.459	0.506	0.429	0.384	0.403
13	0.645	0.605	0.621	0.620	0.333	0.348	0.427	0.246	0.209
14	0.638	0.574	0.691	0.691	0.514	0.503	0.513	0.476	0.478
15	0.654	0.577	0.695	0.690	0.622	0.592	0.595	0.594	0.603
16	0.653	0.577	0.695	0.691	0.569	0.541	0.555	0.528	0.536
17	0.641	0.577	0.699	0.702	0.557	0.571	0.556	0.545	0.533
18	0.663	0.579	0.701	0.690	0.400	0.369	0.437	0.338	0.327
19	0.320	0.561	0.336	0.330	0.655	0.719	0.625	0.946	0.911
20	0.688	0.713	0.671	0.681	0.736	0.721	0.711	0.682	0.719
21	1.127	1.057	0.955	0.965	1.684	1.709	1.604	1.697	1.684
22	1.126	1.056	0.953	0.965	1.532	1.548	1.484	1.490	1.484
23	0.724	0.598	0.868	0.883	0.598	0.596	0.556	0.501	0.530
24	0.754	0.605	0.888	0.889	0.515	0.520	0.522	0.452	0.437
25	0.760	0.607	0.890	0.890	0.570	0.569	0.563	0.509	0.500
26	0.726	0.850	0.652	0.669	0.989	1.000	0.948	0.998	1.037
27	0.699	0.846	0.647	0.679	0.726	0.775	0.745	0.677	0.709
28	0.692	0.713	0.677	0.678	0.873	0.872	0.832	0.912	0.921
29	0.695	0.713	0.680	0.676	0.810	0.813	0.792	0.862	0.853
30	0.745	0.850	0.652	0.652	1.041	1.008	0.988	1.065	1.107
31	0.999	0.958	1.088	1.098	0.692	0.737	0.751	0.669	0.643
32	1.005	0.960	1.091	1.101	0.745	0.789	0.792	0.727	0.703
33	0.763	0.852	0.663	0.644	0.647	0.603	0.709	0.630	0.630
34	1.039	0.284	1.466	1.401	1.526	1.369	1.202	1.522	1.514
35	1.294	1.376	1.049	1.057	1.179	1.186	1.298	1.032	1.025
36	0.961	0.941	0.939	0.936	0.834	0.798	0.850	0.773	0.794
37	0.953	0.944	0.951	0.954	0.805	0.834	0.852	0.807	0.781
38	0.976	0.944	0.942	0.933	0.941	0.885	0.932	0.894	0.921
39	1.016	1.080	0.929	0.918	1.064	1.051	1.088	1.116	1.105
40	1.393	1.616	1.084	1.072	1.374	1.339	1.495	1.328	1.335
41	1.082	1.353	0.885	0.903	1.545	1.581	1.520	1.637	1.671
42	1.323	1.480	1.108	1.114	1.256	1.299	1.379	1.246	1.213
43	1.286	1.343	1.123	1.126	0.969	0.964	1.103	0.836	0.827
44	1.941	2.142	1.481	1.479	1.615	1.629	1.885	1.432	1.387
45	1.274	1.314	1.313	1.333	1.182	1.227	1.198	1.193	1.202
46	1.387	1.463	1.342	1.350	1.513	1.524	1.501	1.549	1.570
47	1.573	1.672	1.542	1.551	1.455	1.454	1.486	1.456	1.489
49	2.255	1.803	2.303	2.253	2.253	2.188	2.246	2.154	2.079
50	2.080	2.372	2.092	2.121	2.068	2.154	2.098	2.269	2.298

+0.0394372* MR-7.91054
rCV^2=0.751235
r^2=0.817388

APA61=-0.00192014*CCR-0.00165449*EE+0.793456*LogP+ 2.34062*DE-1.85789
rCV^2=0.754212
r^2=0.845389

APA48=-0.00174587*CCR-0.00152503*EE+0.75805*LogP +0.00872653*SE-2.52922
rCV^2=0.725698

TABLE 8: Predictive toxicity fifty derivatives of phenol APA37-APA45

Compd	APA37	APA38	APA39	APA40	APA41	APA42	APA43	APA44	APA45
1	-0.167	-0.063	-0.062	-0.285	0.145	0.124	-0.213	-0.357	-0.345
2	0.262	-0.141	-0.090	0.354	-0.194	-0.182	0.385	0.753	1.128
3	0.045	-0.048	-0.069	0.033	0.036	0.014	0.007	0.205	0.455
4	0.209	-0.107	-0.055	0.139	-0.036	-0.023	0.127	0.272	0.478
5	-0.013	-0.092	-0.057	-0.004	-0.018	-0.026	0.128	0.195	0.336
6	0.302	0.291	0.295	0.188	0.425	0.400	0.216	0.066	0.079
7	0.136	0.286	0.293	0.082	0.420	0.399	0.215	0.008	-0.048
8	0.404	0.409	0.356	0.355	0.474	0.440	0.261	0.340	0.466
9	0.654	0.701	0.664	0.635	0.702	0.705	0.520	0.608	0.612
10	0.568	0.360	0.369	0.461	0.414	0.414	0.353	0.407	0.502
11	0.318	0.546	0.559	0.309	0.648	0.667	0.420	0.285	0.168
12	0.434	0.566	0.536	0.383	0.677	0.733	0.211	0.304	0.310
13	0.319	0.637	0.676	0.420	0.624	0.682	0.605	0.505	0.256
14	0.504	0.615	0.613	0.489	0.680	0.669	0.562	0.361	0.313
15	0.612	0.633	0.625	0.558	0.699	0.657	0.620	0.409	0.404
16	0.556	0.632	0.625	0.523	0.698	0.661	0.612	0.390	0.362
17	0.556	0.611	0.625	0.523	0.673	0.703	0.516	0.391	0.331
18	0.388	0.619	0.633	0.415	0.680	0.654	0.649	0.341	0.207
19	0.729	0.297	0.346	0.746	0.218	0.304	0.530	0.937	1.175
20	0.711	0.745	0.698	0.724	0.738	0.697	0.694	0.693	0.764
21	1.683	1.183	1.192	1.499	1.070	1.115	1.067	1.102	1.092
22	1.517	1.191	1.190	1.392	1.080	1.113	1.067	1.044	0.982
23	0.569	0.728	0.692	0.485	0.883	0.867	0.453	0.490	0.513
24	0.506	0.704	0.722	0.446	0.847	0.869	0.524	0.497	0.393
25	0.560	0.715	0.728	0.481	0.859	0.870	0.538	0.521	0.441
26	0.977	0.823	0.772	0.997	0.737	0.724	0.799	1.034	1.200
27	0.702	0.807	0.758	0.820	0.722	0.769	0.661	0.929	0.990
28	0.877	0.708	0.699	0.831	0.694	0.685	0.725	0.750	0.835
29	0.822	0.688	0.700	0.795	0.671	0.678	0.741	0.732	0.765
30	1.032	0.823	0.773	1.032	0.736	0.662	0.947	1.053	1.241
31	0.698	0.943	0.970	0.747	1.006	1.081	0.801	0.745	0.608
32	0.752	0.952	0.978	0.782	1.015	1.088	0.806	0.771	0.651
33	0.642	0.781	0.783	0.782	0.686	0.631	1.042	0.929	0.880
34	1.537	0.872	0.914	0.692	1.447	1.243	0.582	1.106	1.323
35	1.144	1.394	1.389	1.341	1.177	1.206	1.433	1.457	1.224
36	0.817	0.954	0.931	0.860	0.954	0.896	1.003	0.693	0.654
37	0.814	0.913	0.940	0.859	0.903	0.957	0.887	0.702	0.578
38	0.925	0.969	0.941	0.930	0.969	0.879	1.068	0.739	0.743
39	1.080	0.999	1.014	1.132	0.912	0.897	1.192	1.042	1.029
40	1.362	1.484	1.470	1.635	1.182	1.135	1.852	1.822	1.727
41	1.556	1.208	1.162	1.641	0.972	0.987	1.322	1.706	1.933
42	1.263	1.365	1.395	1.470	1.135	1.216	1.495	1.538	1.356
43	0.942	1.321	1.322	1.161	1.175	1.186	1.397	1.179	0.927
44	1.585	2.052	2.086	2.016	1.619	1.686	2.325	2.264	1.788
45	1.190	1.255	1.239	1.231	1.259	1.304	1.128	1.091	1.106
46	1.522	1.402	1.375	1.540	1.338	1.328	1.418	1.491	1.592
47	1.458	1.558	1.516	1.572	1.500	1.465	1.614	1.368	1.416
49	2.266	2.153	2.251	1.940	2.302	2.269	2.065	2.615	2.359
50	2.130	2.010	1.974	2.300	1.900	1.954	2.086	1.933	2.155

r^2=0.824313

APA49=-0.00160136*CCR-0.00141493*EE+1.03532*LogP-0.0276678*MR-2.33552

rCV^2=0.567682

r^2=0.825491

APA51=-0.00230606*CCR-0.00223095*EE+1.97516*DE-0.0166797*SE-1.85006

rCV^2=0.613547

rv2=0.701997

APA52=-0.00233761*CCR-0.00200488*EE+3.16319*DE+

TABLE 9: Predictive toxicity fifty derivatives of phenol APA46-APA54

Compd	APA46	APA47	APA48	APA49	APA50	APA51	APA52	APA53	APA54
1	-0.346	-0.332	-0.343	-0.328	-0.333	-0.182	-0.302	-0.302	-0.219
2	1.139	0.821	0.666	0.743	0.768	1.473	0.650	0.744	0.228
3	0.405	0.251	0.313	0.234	0.227	0.738	0.378	0.286	0.003
4	0.518	0.337	0.109	0.228	0.241	0.597	0.100	0.232	0.140
5	0.348	0.235	0.159	0.225	0.239	0.642	0.167	0.227	-0.043
6	0.086	0.086	0.022	0.042	0.047	0.088	0.035	0.032	0.253
7	-0.042	0.009	0.011	0.039	0.045	0.081	0.021	0.029	0.117
8	0.399	0.357	0.491	0.344	0.328	0.526	0.563	0.388	0.370
9	0.578	0.605	0.707	0.617	0.594	0.549	0.749	0.666	0.643
10	0.515	0.443	0.317	0.343	0.342	0.401	0.325	0.352	0.507
11	0.191	0.273	0.298	0.358	0.349	0.304	0.299	0.380	0.327
12	0.301	0.305	0.397	0.368	0.325	0.333	0.437	0.476	0.419
13	0.312	0.463	0.488	0.617	0.607	0.384	0.450	0.631	0.370
14	0.317	0.346	0.364	0.375	0.384	0.345	0.348	0.350	0.501
15	0.394	0.406	0.400	0.380	0.397	0.385	0.395	0.334	0.591
16	0.353	0.381	0.398	0.381	0.397	0.380	0.391	0.339	0.545
17	0.364	0.382	0.331	0.400	0.398	0.288	0.300	0.402	0.546
18	0.221	0.312	0.341	0.385	0.406	0.339	0.314	0.330	0.408
19	1.229	0.988	0.761	0.891	0.884	1.140	0.720	0.939	0.686
20	0.704	0.687	0.829	0.692	0.691	0.788	0.865	0.693	0.707
21	1.153	1.113	0.809	0.874	0.871	0.292	0.737	0.840	1.603
22	1.025	1.036	0.837	0.872	0.869	0.317	0.775	0.837	1.466
23	0.471	0.509	0.632	0.546	0.518	0.664	0.719	0.624	0.554
24	0.418	0.509	0.504	0.573	0.551	0.555	0.541	0.630	0.507
25	0.459	0.539	0.529	0.578	0.557	0.576	0.574	0.632	0.553
26	1.137	1.044	1.152	0.999	0.986	1.113	1.192	1.032	0.961
27	0.941	0.908	1.126	1.007	0.971	1.054	1.159	1.097	0.734
28	0.828	0.763	0.713	0.687	0.692	0.701	0.708	0.674	0.845
29	0.783	0.738	0.649	0.685	0.692	0.653	0.622	0.665	0.800
30	1.162	1.070	1.150	0.972	0.986	1.164	1.190	0.938	1.007
31	0.659	0.720	0.730	0.850	0.832	0.739	0.699	0.898	0.740
32	0.701	0.752	0.746	0.860	0.841	0.747	0.719	0.910	0.785
33	0.853	0.901	1.007	0.965	0.996	1.069	0.995	0.892	0.688
34	1.303	1.406	0.870	0.863	0.815	1.320	1.261	1.010	1.282
35	1.225	1.388	1.542	1.525	1.518	1.165	1.509	1.513	1.234
36	0.622	0.655	0.758	0.688	0.719	0.679	0.730	0.606	0.839
37	0.635	0.664	0.608	0.724	0.731	0.502	0.526	0.699	0.839
38	0.699	0.714	0.787	0.689	0.729	0.718	0.768	0.582	0.930
39	1.045	1.020	0.960	0.992	1.023	0.924	0.893	0.907	1.093
40	1.685	1.755	1.938	1.843	1.878	1.763	1.892	1.741	1.462
41	1.878	1.710	1.770	1.622	1.614	1.682	1.769	1.640	1.554
42	1.409	1.474	1.488	1.584	1.584	1.240	1.391	1.563	1.346
43	0.932	1.092	1.269	1.276	1.290	1.006	1.206	1.220	1.046
44	1.835	2.124	2.320	2.399	2.410	1.750	2.197	2.324	1.780
45	1.109	1.065	1.124	1.121	1.113	1.075	1.088	1.142	1.219
46	1.561	1.489	1.528	1.450	1.453	1.493	1.526	1.442	1.533
47	1.369	1.315	1.479	1.371	1.400	1.432	1.425	1.294	1.514
49	2.433	2.756	2.413	2.595	2.539	2.421	2.628	2.728	2.242
50	2.140	1.871	1.956	1.911	1.940	2.042	1.811	1.848	2.199

0.0703487*MR-2.24381
rCV^2=0.781497
r^2=0.833139

APA53=-0.00214385*CCR-0.0018502*EE+0.0299671*SE+0.0695519*MR-3.00141
rCV^2=0.746348
r^2=0.810443

APA54=-1.19846e-005*EE+45.6184*Softness+0.495892*LogP-0.0139227*DE-10.7759
rCV^2=0.614388

TABLE 10: Predictive toxicity fifty derivatives of phenol APA55-APA63

Compd	APA55	APA56	APA57	APA58	APA59	APA60	APA61	APA62	APA63
1	-0.221	-0.303	-0.219	-0.201	-0.201	-0.218	-0.278	-0.273	-0.211
2	0.225	0.450	0.623	0.430	0.384	0.201	0.317	0.331	0.352
3	0.004	0.071	0.159	0.093	0.097	-0.005	0.011	-0.015	0.042
4	0.137	0.183	0.399	0.290	0.253	0.124	0.124	0.128	0.077
5	-0.046	0.029	0.128	0.050	0.020	-0.055	-0.012	0.027	0.106
6	0.251	0.176	0.264	0.277	0.272	0.252	0.192	0.205	0.219
7	0.114	0.060	0.075	0.103	0.097	0.119	0.093	0.127	0.214
8	0.374	0.355	0.368	0.381	0.408	0.374	0.346	0.309	0.325
9	0.647	0.616	0.582	0.613	0.639	0.654	0.639	0.598	0.546
10	0.507	0.467	0.601	0.574	0.568	0.504	0.457	0.437	0.341
11	0.327	0.286	0.257	0.287	0.287	0.334	0.324	0.330	0.390
12	0.427	0.370	0.379	0.400	0.438	0.432	0.383	0.265	0.199
13	0.369	0.379	0.251	0.282	0.272	0.383	0.453	0.492	0.530
14	0.500	0.473	0.454	0.478	0.480	0.503	0.494	0.509	0.567
15	0.589	0.547	0.563	0.587	0.585	0.590	0.560	0.592	0.648
16	0.543	0.508	0.500	0.529	0.527	0.546	0.526	0.562	0.636
17	0.547	0.508	0.527	0.536	0.538	0.550	0.530	0.509	0.482
18	0.404	0.389	0.318	0.356	0.343	0.410	0.430	0.506	0.647
19	0.689	0.807	0.988	0.840	0.820	0.675	0.724	0.646	0.446
20	0.709	0.722	0.672	0.692	0.712	0.710	0.717	0.712	0.760
21	1.605	1.474	1.634	1.640	1.649	1.610	1.505	1.426	1.022
22	1.468	1.359	1.433	1.461	1.473	1.476	1.403	1.350	1.038
23	0.557	0.478	0.498	0.539	0.564	0.558	0.482	0.433	0.489
24	0.507	0.430	0.455	0.485	0.483	0.510	0.458	0.447	0.489
25	0.552	0.467	0.508	0.538	0.538	0.554	0.491	0.480	0.513
26	0.966	1.013	1.004	0.985	1.011	0.963	0.980	0.927	0.856
27	0.743	0.823	0.705	0.699	0.740	0.747	0.814	0.723	0.682
28	0.846	0.838	0.897	0.881	0.884	0.843	0.823	0.806	0.738
29	0.799	0.799	0.851	0.830	0.823	0.798	0.794	0.790	0.726
30	1.007	1.052	1.058	1.043	1.053	1.001	1.013	1.034	1.039
31	0.743	0.738	0.690	0.698	0.702	0.747	0.756	0.709	0.732
32	0.788	0.775	0.746	0.752	0.757	0.792	0.789	0.737	0.740
33	0.683	0.778	0.640	0.646	0.627	0.685	0.789	0.908	1.078
34	1.261	0.715	1.484	1.537	1.468	1.235	0.684	0.762	0.633
35	1.235	1.302	1.049	1.100	1.108	1.250	1.369	1.415	1.420
36	0.837	0.848	0.751	0.791	0.794	0.839	0.859	0.917	1.060
37	0.840	0.845	0.800	0.805	0.802	0.845	0.869	0.853	0.831
38	0.926	0.923	0.862	0.901	0.899	0.925	0.925	1.004	1.148
39	1.090	1.136	1.109	1.095	1.079	1.089	1.130	1.178	1.192
40	1.459	1.631	1.358	1.370	1.359	1.464	1.643	1.771	1.903
41	1.561	1.680	1.664	1.602	1.628	1.553	1.614	1.536	1.368
42	1.348	1.456	1.276	1.268	1.265	1.357	1.487	1.494	1.427
43	1.045	1.126	0.848	0.904	0.906	1.059	1.185	1.258	1.392
44	1.779	1.959	1.483	1.546	1.534	1.802	2.066	2.196	2.262
45	1.224	1.245	1.208	1.204	1.228	1.222	1.217	1.130	1.122
46	1.536	1.566	1.564	1.550	1.564	1.528	1.518	1.477	1.457
47	1.517	1.595	1.466	1.477	1.497	1.511	1.547	1.538	1.687
49	2.226	1.930	2.206	2.272	2.203	2.221	1.974	2.080	1.980
50	2.209	2.382	2.317	2.238	2.274	2.189	2.238	2.082	2.118

r^2=0.731087

APA55=-1.06359e-005*EE+45.7457*Softness+0.49797*LogP+ 0.00160688*SE-10.7805

rCV^2=0.607731

r^2=0.731141

APA56=-5.3096e-005*EE+38.7634*Softness+1.45661*LogP-0.0900323*MR-8.78068

rCV^2=0.570572

r^2=0.767636

APA57=-0.000148534*EE+64.2702*Softness-0.703179*

Full Paper

TABLE 11: Predictive toxicity fifty derivatives of phenol APA64-APA67

Compd	APA64	APA65	APA66	APA67
1	-0.207	-0.213	-0.189	-0.166
2	0.114	0.138	0.565	0.252
3	-0.023	-0.028	0.143	0.047
4	0.064	0.085	0.393	0.200
5	-0.087	-0.077	0.109	-0.019
6	0.255	0.250	0.294	0.302
7	0.134	0.129	0.097	0.136
8	0.395	0.376	0.380	0.412
9	0.683	0.674	0.598	0.660
10	0.487	0.492	0.623	0.566
11	0.348	0.352	0.267	0.317
12	0.443	0.447	0.398	0.439
13	0.410	0.427	0.253	0.314
14	0.515	0.511	0.473	0.505
15	0.600	0.589	0.585	0.613
16	0.560	0.549	0.519	0.558
17	0.549	0.558	0.550	0.554
18	0.432	0.427	0.329	0.387
19	0.598	0.636	0.968	0.719
20	0.734	0.715	0.676	0.718
21	1.595	1.610	1.707	1.681
22	1.481	1.489	1.497	1.517
23	0.575	0.561	0.499	0.575
24	0.515	0.521	0.454	0.505
25	0.559	0.561	0.509	0.559
26	0.970	0.959	1.000	0.983
27	0.768	0.767	0.691	0.709
28	0.835	0.833	0.912	0.878
29	0.785	0.791	0.864	0.820
30	1.010	0.986	1.053	1.038
31	0.739	0.759	0.683	0.695
32	0.781	0.801	0.741	0.749
33	0.710	0.697	0.617	0.641
34	1.182	1.149	1.473	1.534
35	1.301	1.301	1.036	1.145
36	0.863	0.843	0.761	0.821
37	0.839	0.856	0.816	0.810
38	0.946	0.920	0.875	0.930
39	1.080	1.081	1.112	1.077
40	1.502	1.487	1.318	1.364
41	1.539	1.537	1.647	1.560
42	1.364	1.387	1.261	1.258
43	1.105	1.102	0.835	0.942
44	1.871	1.884	1.439	1.580
45	1.205	1.212	1.204	1.192
46	1.512	1.506	1.549	1.525
47	1.507	1.490	1.451	1.463
49	2.200	2.209	2.135	2.254
50	2.113	2.123	2.289	2.133

DE+0.00339796*SE-14.6414
rCV^2=0.547634
r^2=0.696064

APA58=-9.07403e-005*EE+58.7533*Softness-0.279372* DE+0.0167921*MR-13.5576
rCV^2=0.5803
r^2=0.701481

APA59=-7.56408e-005*EE+58.6837*Softness+0.00542773*SE+0.0198953*MR-13.4089
rCV^2=0.527445
r^2=0.701681

APA60=44.565*Softness+0.532187*LogP-0.00808249*DE+0.00227299*SE-10.5387
rCV^2=0.638706
r^2=0.73094

APA61=33.2979*Softness+1.52628*LogP-0.134983*DE-0.0811829*MR-7.78882
rCV^2=0.493328
r^2=0.762933

APA62=25.5245*Softness+1.91114*LogP-0.0259593*SE-0.110477*MR-6.22551
rCV^2=0.568233
r^2=0.773323

APA63=2.70282*LogP+1.19691*DE-0.0584051*SE-0.17115*MR-0.393438
rCV^2=0.436292
r^2=0.751869

APA64=-4.24139e-005*CCR+39.6541*Softness+0.65138*LogP+0.369624*DE-9.45266
rCV^2=0.647354
r^2=0.733121

APA65=-3.67233e-005*CCR+40.3073*Softness+0.638875*LogP+0.0042604*SE-9.68066
rCV^2=0.652514
r^2=0.732906

APA66=0.000157641*CCR+67.1598*Softness-0.759272*DE+0.0045165*SE-15.0971
rCV^2=0.528298
r^2=0.67455

APA67=3.76813e-005*CCR+55.3601*Softness+ 0.113433*DE+0.0309997*MR-12.7897
rCV^2=0.599329
r^2=0.691072

The predicted toxicity as obtained from the above mentioned equations are presented because the placement of 67 models in one table is difficult. In nine TABLES (4-11) each table includes the predicted toxicity of nine models the predicted toxicity and the observed toxicity are very close to each other.

MLR equations also provide the values of cross-validation coefficient and correlation coefficient. The correlation coefficient indicates the quality of the QSTR model or the regression model. If the value of correlation coefficient is above 0.5, it is said to have

TABLE 12: Predicted activity in decreasing order of regression coefficient

Predicted Activity	rCV^2	r^2	Descriptors Used in MLR Analysis
APA48	0.754212	0.845389	Core-Core Repulsion, Electronic Energy, Log P, Dielectric Energy
APA44	0.768045	0.834721	Core-Core Repulsion, Electronic Energy, Softness, Log P
APA52	0.781497	0.833139	Core-Core Repulsion, Electronic Energy, Dielectric Energy, Molar Refractivity
APA50	0.567682	0.825491	Core-Core Repulsion, Electronic Energy, log P, Molar Refractivity
APA49	0.725698	0.824313	Core-Core Repulsion, Electronic Energy, log P, Steric Energy
APA14	0.744728	0.822723	Core-Core Repulsion, Electronic Energy, log P
APA47	0.751235	0.817388	Core-Core Repulsion, Electronic Energy, Softness, Molar Refractivity
APA53	0.746348	0.810443	Core-Core Repulsion, Electronic Energy, Steric Energy, Molar Refractivity
APA17	0.726204	0.794417	Core-Core Repulsion, Electronic Energy, Molar Refractivity
APA45	0.707926	0.791313	Core-Core Repulsion, Electronic Energy, Softness, Dielectric Energy
APA46	0.689889	0.787147	Softness, Dielectric Energy, Molar Refractivity
APA13	0.729899	0.786532	Core-Core Repulsion, Electronic Energy, Softness
APA62	0.568233	0.773323	Softness, Log P, Steric Energy, Molar Refractivity
APA56	0.570572	0.767636	Electronic Energy, Softness, log P, Molar Refractivity
APA40	0.528033	0.763394	Core-Core Repulsion, Softness, log P, Molar Refractivity
APA61	0.493328	0.762933	Electronic Energy, Softness, Dielectric Energy, Molar Refractivity
APA24	0.614045	0.762838	Softness, log P, Molar Refractivity
APA63	0.436292	0.751869	Log P, Dielectric Energy, Steric Energy, Molar Refractivity
APA43	0.507902	0.746682	Log P, Steric Energy, Molar Refractivity
APA64	0.647354	0.733121	Core-Core Repulsion, Softness, log P, Dielectric Energy
APA65	0.652514	0.732906	Core-Core Repulsion, Softness, log P, Steric Energy
APA34	0.669866	0.732525	Core-Core Repulsion, Softness, log P
APA55	0.607731	0.731141	Electronic Energy, Softness, log P, Steric Energy
APA54	0.614388	0.731087	Electronic Energy, Softness, log P, Dielectric Energy
APA18	0.644572	0.731086	Electronic Energy, Softness, log P
APA23	0.662152	0.73094	Softness, log P, Steric Energy
APA60	0.638706	0.73094	Electronic Energy, Softness, Dielectric Energy, Steric Energy
APA22	0.642059	0.730857	Softness, log P, Dielectric Energy
APA8	0.67338	0.730833	Softness, log P
APA26	0.333153	0.705443	Log P, Dielectric Energy, Molar Refractivity
APA29	0.402743	0.704291	Electronic Energy, Log P, Molar Refractivity
APA51	0.613547	0.701997	Core-Core Repulsion, Electronic Energy, Dielectric Energy, Steric Energy
APA59	0.527445	0.701681	Electronic Energy, Softness, Steric Energy, Molar Refractivity
APA58	0.5803	0.701481	Electronic Energy, Softness, Dielectric Energy, Molar Refractivity
APA21	0.608636	0.701136	Electronic Energy, Softness, Molar Refractivity
APA12	0.474638	0.700757	Log P, Molar Refractivity
APA15	0.602373	0.697371	Core-Core Repulsion, Electronic Energy, Dielectric Energy
APA57	0.547634	0.696064	Electronic Energy, Softness, Dielectric Energy, Steric Energy
APA19	0.590227	0.695878	Electronic Energy, Softness, Dielectric Energy
APA20	0.549404	0.694265	Electronic Energy, Softness, Steric Energy
APA5	0.607137	0.694196	Electronic Energy, Softness

TABLE 12 Continued

APA33	0.627925	0.69362	Softness, Steric Energy, Molar Refractivity
APA67	0.599329	0.691072	Core-Core Repulsion, Softness, Dielectric Energy, Molar Refractivity
APA37	0.618029	0.691019	Core-Core Repulsion, Softness, Molar Refractivity
APA32	0.628427	0.689612	Softness, Dielectric Energy, Molar Refractivity
APA16	0.603424	0.689138	Core-Core Repulsion, Electronic Energy, Steric Energy
APA1	0.620815	0.688866	Core-Core Repulsion, Electronic Energy
APA9	0.651005	0.688737	Softness, Molar Refractivity
APA66	0.528298	0.67455	Core-Core Repulsion, Softness, Dielectric Energy, Steric Energy
APA35	0.572219	0.674221	Core-Core Repulsion, Softness, Dielectric Energy
APA36	0.527177	0.672489	Core-Core Repulsion, Softness, Steric Energy
APA2	0.582225	0.672468	Core-Core Repulsion, Softness
APA38	0.602979	0.670765	Core-Core Repulsion, log P, Dielectric Energy
APA39	0.615408	0.668283	Core-Core Repulsion, log P, Steric Energy
APA3	0.626169	0.668279	Core-Core Repulsion, log P
APA28	0.586793	0.639169	Electronic Energy, log P, Steric Energy
APA27	0.55526	0.638413	Electronic Energy, log P, Dielectric Energy
APA6	0.586436	0.638352	Electronic Energy, log P
APA25	0.48135	0.607076	log P, Dielectric Energy, Steric Energy
APA11	0.534767	0.605968	log P, Steric Energy
APA10	0.473184	0.603778	log P, Dielectric Energy
APA42	0.510529	0.545292	Core-Core Repulsion, Steric Energy, Molar Refractivity
APA41	0.499617	0.541374	Core-Core Repulsion, Dielectric Energy, Molar Refractivity
APA4	0.514404	0.538166	Core-Core Repulsion, Molar Refractivity
APA31	0.446062	0.507691	Electronic Energy, Steric Energy, Molar Refractivity
APA30	0.429336	0.507175	Electronic Energy, Dielectric Energy, Molar Refractivity
APA7	0.459061	0.507131	Electronic Energy, Molar Refractivity

good predictive power. The cross-validation coefficient above 0.2 is said to be a successful model. The values of correlation coefficient are included in decreasing order in TABLE 13. All the correlation coefficients are above 0.5 and the highest is 0.84.Those having lower values have been omitted from the TABLE 12. The cross-validation coefficient values are more than 0.33 and the highest is 0.78. There is no negative value. On the basis of correlation coefficient and cross-validation coefficient, the models can be treated as reliable predictive models.

A reference to TABLE 12 shows that eight models have correlation coefficient values above 0.80. They can be treated as first quality model. Twenty-nine models have correlation coefficients above 0.70. They can be considered as second quality models. Rest can be placed as a third quality model. The descriptors used for first, second and third quality models of MLR analysis are also shown in the same table.

CONCLUSION

(1) The QSTR study of fifty derivatives of phenol having different type of substituents at phenol ring have been collectively studied without giving any significance to substituents. 81 models have been drawn out of which 67, have correlation coefficients above 0.5.

(2) Eight QSTR models have correlation coefficients values above 0.845. They have been considered as first quality models. The first out of them is APA 61, which has been drawn by using the combinations of descriptors:-

(I)Core-core Repulsion

(II)Electronic Energy

(III)Log P

(IV)Dielectric Energy.

This model can therefore be used as a high quality predictive tool.

(3) The second best model is APA 57, which has correlation coefficient 0.834 and has been developed by using the combinations of descriptors:-

(I)Core-core Repulsion

(II)Electronic Energy

(III)Softness

(IV) Log P.

The predictive capacity of the models described above is quite high, hence they can provide a model, which can help in preparing compounds of desired toxicity and also can be helpful in predicting the toxicity of any unknown compound. Such a technique saves the cost and time of preparing compounds of choice.

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