# ORIGINAL ARTICLE

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# Prediction of toxicity using a novel RBF neural network training methodology

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Abstract A neural network methodology based on the radial basis function (RBF) architecture is introduced in order to establish quantitative structure-toxicity relationship models for the prediction of toxicity. The dataset used consists of 221 phenols and their corresponding toxicity values to *Tetrahymena pyriformis*. Physicochemical parameters and molecular descriptors are used to provide input information to the models. The performance and predictive abilities of the RBF models are compared to standard multiple linear regression (MLR) models. The leave-one-out cross validation procedure and validation through an external test set produce statistically significant  $R^2$  and RMS values for the RBF models, which prove considerably more accurate than the MLR models.

**Keywords** RBF architecture · Neural network · QSTR · Toxicity · *Tetrahymena pyriformis* 

#### Introduction

Toxicology deals with the quantitative assessment of toxic effects to organisms in relation to the level, duration and frequency of exposure. Various segments of the population come in contact with toxic chemicals due to misuse (e.g., accidental poisoning), but also through manufacturing, drug and food consumption. Additionally, people working in various jobs (e.g., painters and applicators of pesticides) are exposed to toxic substances. In general, exposure to toxic substances is to be avoided [1].

G. Melagraki · A. Afantitis · K. Makridima · H. Sarimveis (⊠) O. Igglessi-Markopoulou School of Chemical Engineering, National Technical University of Athens, 9 Heroon Polytechniou Str., Zografou Campus, Athens, 15780 Greece E-mail: hsarimv@central.ntua.gr Tel.: + 30-210-7723237 Fax: + 30-210-7723138 As the experimental determination of toxicological properties is a costly and time-consuming process, it is essential to develop mathematical predictive relationships to theoretically quantify toxicity [2, 3]. Quantitative structure-toxicity relationship (QSTR) studies can provide a useful tool for achieving this goal, given the successful applications of quantitative structure-activity relationships (QSARs) in several scientific areas, such as pharmacology, chemistry and environmental research. Based on a training database containing measured toxicity potencies of compounds and a number of molecular descriptors, QSTRs can be used to predict the toxicity of chemical compounds that are not included in the database [4–6].

For the formal description of relationships between activity measures and structural descriptors of compounds, various statistical techniques can be used. Among them the most frequently used are multiple linear regression (MLR) and partial least squares (PLS). Several other statistical techniques have been used in QSAR, including discriminant analysis, principal component analysis (PCA) and factor analysis, cluster analysis, multivariate analysis, and adaptive least squares [7–9]. Neural network (NN) techniques have also been used successfully in QSAR [10–16]. The NN methodologies are generally used when the relationships cannot be interpreted accurately by linear functions [17].

The goal of the present study is to determine the efficiency of a newly introduced RBF training methodology in predicting the toxicity of compounds. The methodology uses the innovative fuzzy-means clustering technique to determine the number and the locations of the hidden node centres [18]. Compared to traditional training techniques, the method employed in this work is much faster since it does not involve any iterative procedure, utilizes only one tuning parameter and is repetitive, i.e., it does not depend on a random initial selection of centres. The RBF method is applied to a data set of 221 phenols and the results indicate that it can be used as an efficient new technique for predicting toxicity with significant accuracy, using appropriate descriptors as inputs.

## **Materials and methods**

It is essential in order to obtain a successful QSTR that all data used as part of the training and validation procedure are of high quality. High quality data should derive from the same endpoint and protocol and ideally should be measured in the same laboratory [19]. The data set used in this study fulfills this criterion.

## Toxicity data

This data set consists of 221 phenols and their corresponding toxicity data to the ciliate *Tetrahymena pyriformis* in terms of  $log(1/IGC_{50})$  (mmol/L). The toxicity values were taken from the literature [20] and are shown in Table 1. The phenols are structurally heterogeneous and represent a variety of mechanisms of toxic action. The dataset consists of polar narcotics, weak acid respiratory uncouplers, pro-electrophiles and soft electrophiles.

#### Molecular descriptors

The molecular descriptors used to derive the model were taken from the literature [20] and include the logarithm of the octanol/water partition coefficient (log  $K_{ow}$ ), acidity constant ( $pK_a$ ), the energies of the highest occupied and lowest unoccupied molecular orbital ( $E_{HOMO}$  and  $E_{LUMO}$  respectively) and the hydrogen bond donor number ( $N_{hdon}$ ). All these descriptors are related to the toxicity effect of the compounds studied.

#### Statistical analysis (QSAR development)

In this section, we present the basic characteristics of the RBF NN architecture and the training method used to develop the QSAR NN models.

#### RBF network topology and node characteristics

RBF networks consist of three layers: the input layer, the hidden layer and the output layer. The input layer collects the input information and formulates the input vector **x**. The hidden layer consists of *L* hidden nodes, which apply nonlinear transformations to the input vector. The output layer delivers the NN responses to the environment. A typical hidden node *l* in an RBF network is described by a vector  $\hat{x}_l$ , equal in dimension to the input vector and a scalar width  $\sigma_l$ . The activity  $v_l(\mathbf{x})$  of the node is calculated as the Euclidean norm of the difference between the input vector and the node center and is given by

$$v_l(x) = \|x - \hat{x}_l\|$$
(1)

The response of the hidden node is determined by

passing the activity through the radially symmetric Gaussian function:

$$f_l(x) = \exp\left(-\frac{v_l(x)^2}{\sigma_l^2}\right)$$
(2)

Finally, the output values of the network are computed as linear combinations of the hidden layer responses:

$$\hat{y} = g(x) = \sum_{l=1}^{L} f_l(x) w_l$$
 (3)

where  $[w_1, w_2, ..., w_L]$  is the vector of weights, which multiply the hidden node responses in order to calculate the output of the network.

#### RBF network training methodology

Training methodologies for the RBF network architecture are based on a set of input–output training pairs  $(\mathbf{x}(k); \mathbf{y}(k))$  (k=1, 2,...,K). The training procedure used in this work consists of three distinct phases:

(i) Selection of the network structure and calculation of the hidden-node centers using the fuzzy-means clustering algorithm [18]. The algorithm is based on a fuzzy partition of the input space, which is produced by defining a number of triangular fuzzy sets on the domain of each input variable. The centers of these fuzzy sets produce a multidimensional grid on the input space. A rigorous selection algorithm chooses the most appropriate knots of the grid, which are used as hidden node centers in the RBF network model produced. The idea behind the selection algorithm is to place the centers in the multidimensional input space so that there is a minimum distance between the center locations. At the same time, the algorithm assures that for any input example in the training set there is at least one selected hidden node that is close enough according to a distance criterion. It must be emphasized that, in contrast to both the k-means [21] and the c-means clustering [22] algorithms, the fuzzy-means technique does not need the number of clusters to be fixed before the execution of the method. Moreover, due to the fact that it is a one-pass algorithm, it is extremely fast even if a large database of input-output examples is available. Furthermore, the fuzzy-means algorithm needs only one tuning parameter, which is the number of fuzzy sets that are used to partition each input dimension.

(ii) Following the determination of the hidden-node centers, the widths of the Gaussian activation function are calculated using the *P*-nearest neighbor heuristic [23]:

$$\sigma_{l} = \left(\frac{1}{p} \sum_{i=1}^{p} \|\hat{x}_{l} - \hat{x}_{i}\|^{2}\right)^{1/2}$$
(4)

where  $\hat{x}_1, \hat{x}_2, \ldots, \hat{x}_p$  are the *p* nearest-node centers to the hidden node *l*. The parameter *p* is selected so that many

<b>Fable 1</b> Predicted	values	$[\log(1/IGC_{50})]$	for the	training and	the test	set
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A/A	Name	log(1/IGC <sub>50</sub> )	Training set		Validation set		
			RBF $R^2 = 0.9424$	MLR $R^2 = 0.6022$	RBF $R^2 = 0.8824$	MLR $R^2 = 0.7861$	
1	1,3,5-Trihydroxybenzene	-1.26	-1.2577	0.4071			
2	2-(tert)-Butyl-4-methylphenol	1.3	1.1624	1.2334			
3	2,3,5-Trichlorophenol	2.37	2.1688	1.4111			
4 <sup>a</sup>	2,3,5-Trimethylphenol	0.36	0.5460	0.541	0.5785	0.7671	
5	2,3,6-Trimethylphenol	0.28	0.5460	0.7611			
0 7a	2,3-Dichlorophenol	1.28	1.4070	0.8046	0.2007	0.2004	
8	2,5-Dimetryiphenol	0.12	1 8325	1 5046	0.2007	0.3904	
0	2.4.5-Tribromonhenol	2.1	2 3170	1.5040			
10	2.4.6-Tribromoresorcinol	1.06	1 1134	2 5259			
11	2.4.6-Trichlorophenol	1.41	1.3937	1.3193			
12	2,4,6-Trimethylphenol	0.28	0.3515	0.8490			
13	2,4,6-Tris (dimethylaminomethyl) phenol	-0.52	0.5294	0.3641			
14	2,4-Dibromophenol	1.4	1.6666	1.1616			
15	2,4-Dichlorophenol	1.04	1.0157	0.9485			
16	2,4-Difluorophenol	0.6	0.5917	0.4491			
1/	2,4-Dimethylphenol	0.07	0.046/	0.4939	1.1504	0.0715	
18 10 <sup>a</sup>	2,5-Dichlorophenol	1.15			1.1504	0.9715	
20	202 6-Di-( <i>tert</i> )-butyl-4-methylphenol	1.8	1 7939	2 3411	0.0990	0.3404	
21	2.6-Dichloro-4-fluorophenol	0.8	0.9982	1.0697			
22	2.6-Dichlorophenol	0.74	0.6177	0.7097			
23	2,6-Difluorophenol	0.47	0.3470	0.1981			
24	2,6-Dimethoxyphenol	-0.6	0.5510	0.1055			
25	2-Allylphenol	0.33	0.1816	0.3925			
26 <sup>a</sup>	2-Bromo-4-methylphenol	0.6			0.8483	0.8478	
27	2-Bromophenol	0.33	0.5950	0.4488			
28	2-Chloro-4,5-dimethylphenol	0.69	0.6884	1.0551			
29	2-Chloro-5-methylphenol	0.39	0.6920	0.6840			
30 31	2-Chiorophenol	0.18	0.3383	0.3040			
32	2-Cyanophenol	-0.36	0.2517	0.1132			
33 <sup>a</sup>	2-Ethylphenol	0.16	0.1050	0.1740	0.3373	0.3690	
34	2-Fluorophenol	0.19	0.1022	0.0294			
35 <sup>a</sup>	2-Hydroxy-4,5-dimethylacetophenone	0.71			0.5292	0.7995	
36	2-Hydroxy-4-methoxyacetophenone	0.55	0.3823	0.4016			
37	2-Hydroxy-4-methoxybenzophenone	1.42	1.4376	1.7424			
38	2-Hydroxy-5-methylacetophenone	0.31	0.3419	0.7916	0.0010	0.0400	
39ª	2-Hydroxyacetophenone	0.08	0.02(4	0.5205	0.2318	0.3432	
40	2-Hydroxybenzylaiconol 2 Hydroxysthylaaliaylata	-0.95	0.9304	0.5595			
41	2-Hydroxyethylsalicylate 2-Isopropylphenol	-0.08	0.0843	1 2005			
43	2-Methoxy-4-propenvlphenol	0.75	0.7445	1 2005			
44	2-Methoxyphenol	-0.51	0.5486	0.1344			
45	2-Phenylphenol	1.09	1.1577	1.2855			
46	2-(tert)-Butylphenol	1.3	1.3378	0.8191			
47	3,4,5-Trimethylphenol	0.93	0.7390	0.7521			
48	3,4-Dichlorophenol	1.75	1.5232	1.0530			
49	3,4-Dimethylphenol	0.12	0.1552	0.4499			
50	3,5-Dibromosalicylaldehyde	1.64	1.8912	1.5092			
52	3,5-Dichlorosplicy/aldabyda	1.57	1.3014	0.9037			
53	3.5-Dijododsalicylaldehyde	2 34	2 2079	1.5502			
54	3.5-Dimethoxyphenol	-0.09	0.1690	0.1163			
55 <sup>a</sup>	3,5-Dimethylphenol	0.11			0.3133	0.2588	
56	3,5-Di-( <i>tert</i> )-butylphenol	1.64	1.6973	1.8331			
57 <sup>a</sup>	3-Acetamidophenol	-0.16			0.1873	-0.1212	
58 <sup>a</sup>	3-Bromophenol	1.15			0.7477	0.5605	
59	3-Chloro-4-fluorophenol	1.13	1.0300	0.8618			
60	3-Chloro-5-methoxyphenol	0.76	0.7190	0.5070			
01 62	3-Chiorophenol	0.8/	0.7820	0.4292			
63	3-Ethoxy-4-hydroxybenzaldebyde	-0.00	-0.0307	0.1/10			
64	3-Ethoxy-4-methoxyphenol	-0.3	0.2483	0.4874			
65 <sup>a</sup>	3-Ethylphenol	0.23			0.3863	0.3287	
	~ 1						

	A/A	Name	log(1/IGC <sub>50</sub> )	Training set		Validation set		
46         5.1 Fluoropherol         0.38         0.3626         0.0624         0.1893         0.2999           68         3.1 Hydroxynesuphenone         -0.38         0.3606         0.2105         0.0073         0.1464           70         3.1 Hydroxynesuphenone         -0.81         0.9606         0.5278         0.0073         0.1464           71         3.1 Hydroxynesuphenol         -1.04         0.2287         0.4854           71         3.1 Hydroxynesuphenol         0.333         0.0317         0.2385           73         3.1 Soprophydrol         0.11         2.2382         1.291         0.9910         0.7758           74         4.4 Mydroxynbenol         0.91         0.9333         0.8211         0.9333         0.8211           74         4.4 Carl-J Marphenol         0.91         0.934         0.9385         0.2407         0.5247           84         4.8 Dycloxybhenol         0.42         0.2407         0.5247         0.4854           74         4.4 Carl-J Marphenol         0.97         0.9034         0.9385         0.2407         0.5247           84         4.8 Dycloxybhenol         0.7         0.77         0.779         1.0973           84         4.8 Dycloxybhe				RBF $R^2 = 0.9424$	MLR $R^2 = 0.6022$	RBF $R^2 = 0.8824$	MLR $R^2 = 0.7861$	
67         3-Hydroxy-4-methoxybenzylakobiol         -0.99         0.1093         0.2009           67         3-Hydroxybenzylakobiol         -0.81         0.9606         0.2105           71         3-Hydroxybenzylakobiol         -1.01         0.9606         0.2287         0.4854           71         3-Hydroxybenzylakobiol         -1.02         0.4854         0.7287         0.4854           71         3-Hydroxybenzylakobiol         -1.03         0.2519         0.7287         0.4854           73         3-Hydroxybenzylakobiol         0.33         0.3613         0.0317         -         0.9910         0.7758           74         4-Kerb/Sutylphenol         0.73         0.9910         0.7758         -         0.2407         0.2407           74         4-Kerb/Sutylphenol         0.17         1.9127         1.9128         -         1.3813           87         4-Kerb/Sutylphenol         1.17         1.217         1.2670         1.3814           87         4-Kerb/Sutylphenol         1.27         1.917         1.2315         1.3466           88         4-Komo-C-Chloro-Z-arcsol         1.28         1.4570         1.333         1.1467           84         4-Komo-S-dimenthylphenol         1.2	66	3-Fluorophenol	0.38	0.3626	0.0624			
68         3-Hydroxyactophenone         -0.38         0.3006         0.2105           71         3-Hydroxybernaldebyde         0.09         0.0073         0.1464           71         3-Hydroxybernaldebyde         1.09         0.5278         0.4854           71         3-Hydroxybernaldebyde         1.01         0.5519         0.7287         0.4854           71         3-Sappropylphenol         0.61         0.5719         0.5519         0.7287         0.4854           73         3-Sappropylphenol         0.73         0.3031         0.3317         0.5217           74         4-Cert-Sutylphenol         0.71         0.9910         0.7758           74         4-Cert-Sutylphenol         0.91         0.9333         0.8211           74         4-Cert-Sutylphenol         1.71         1.3217         1.2670         0.5247           74         4-Marchystrenol         1.72         1.2610         1.7768         1.3813           74         4-Marchystrenol         1.72         1.2610         0.7779         1.0973           74         4-Marchystrenol         1.746         1.7180         0.8554         0.2515         0.5212           74         4-Marchystrenol         1.8	67 <sup>a</sup>	3-Hydroxy-4-methoxybenzylalcohol	-0.99			0.1893	0.2909	
	68	3-Hydroxyacetophenone	-0.38	0.3606	0.2105			
0         -14 Junoy Oetizols add         -0.81         0.9006         0.22/8         0.7287         0.4854           1         34 Junoy Detracial add         -1.62         1.825         0.673         0.7287         0.4854           1         34 Junoy Detracial         -1.61         1.827         0.673         0.7287         0.4854           1         34 Junoy Detracial         -0.61         0.8333         0.811         0.9910         0.7758           1         34 Junoy Detracial         0.91         0.9333         0.8211           1         4 (4cr) Detry Juphenol         0.91         0.9313         0.8211           1         4 (4cr) Detry Juphenol         0.42         0.2407         0.5247           1         4 Renzy Jossyphenol         0.42         0.2407         0.5247           1         4 Renzy Jossyphenol         1.17         1.3517         1.2603           2         4 Ribromo-2.6 defined hyphenol         1.77         1.2768         1.3813           3         4 Bromo-2.5 defined hyphenol         1.85         1.7646         1.7180         1.2638           2         4 Chloro-2sopropy 1-5-methyphenol         0.5         1.2333         1.1467           2         4 Chl	69ª	3-Hydroxybenzaldehyde	0.09	0.0(0)	0.5070	0.0073	0.1464	
17         1.12         1.122         1.125         0.723         0.723         0.723           15         1.5         0.5719         0.5519         0.733         0.9910         0.7758           17         3.5         0.7778         0.9910         0.7758         0.9910         0.7758           17         3.47677.Butylphenol         0.91         0.9333         0.8211           18         4.4767.0507.90         0.91         0.9333         0.8211           18         4.4867.0507.90         0.42         0.2407         0.5247           18         4.8867.0507.90         0.42         0.2407         0.5247           18         4.8867.0507.90         0.42         0.2407         0.5247           18         4.8867.0507.90         1.17         1.3217         1.2670         1.3813           18         4.8807.05.25.00         0.2487         1.3466         1.3466           18         4.8007.05.240107.0779         1.0973         1.0973           19         4.Choro-2-secthylphenol         1.7         1.212         1.233         1.1467           19         4.Choro-2-secthylphenol         0.8         0.737         0.8344         0.977           1	/0 71 <sup>a</sup>	3-HydroxybenZoic acid	-0.81	0.9606	0.5278	0 7297	0 4854	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	72	3-Iodophenol	-1.04	1 1825	0 6973	0.7287	0.4634	
74       3. Methosyphenol       0.33       0.3633       0.0317         78       3. Phenylphenol       1.35       1.2389       1.2931         78       4 (car)-Butylphenol       0.13       0.8211         78       4 (car)-Butylphenol       0.91       0.9333       0.8211         78       4 (car)-Butylphenol       0.42       0.2407       0.5247         78       4 Homo-2.6-dichlorophenol       1.76       1.3813       1.7768       1.3813         74       4 Barzyloxyphenol       1.41       1.0458       1.2864       1.7768       1.3813         84       4 Barzylox-2.6-dichlorophenol       1.77       1.912       1.2013       1.3406         84       4 Barzylox-2.6-dichlorophenol       1.77       1.9473       1.3467       1.3406         87       4 Barzylox-2-disphylphylphenol       1.77       1.9473       1.3467       1.3406         89       4 Chlorox-2-methylphenol       0.8       0.7377       0.8344       0.8775         94       4 Chlorox-3-embylphenol       0.8       0.7377       0.8344       0.3633       1.1423         95       4 Chlorox-3-methylphenol       0.5       0.515       0.5212       0.414414         94	73	3-Isopropylphenol	0.61	0.5719	0.5519			
$  \begin{array}{ccccccccccccccccccccccccccccccccccc$	74	3-Methoxyphenol	-0.33	0.3633	0.0317			
$76^{\circ}$ $3.(ercr)-Bartylphenol       0.73 0.778 74^{\circ} 4.(ercr)-Bartylphenol       0.91 0.9333 0.8211 87^{\circ} 4.(ercr)-Bartylphenol 0.42 0.2407 0.5247 80^{\circ} 4.Alpl_2-methoxyphenol 1.04 1.04858 1.2864 1.7768 1.3813 81^{\circ} 4.Bearcylytyphenol 1.17 1.3217 1.2670 0.7778 1.3813 84^{\circ} 8400^{\circ}. 2.64methylphenol 1.27 1.912 1.2015 1.3813 84^{\circ} 8400^{\circ}. 2.64methylphenol 1.27 1.912 1.2015 3.306 84^{\circ} 8400^{\circ}. 2.64methylphenol 1.27 1.977 0.977 0.9773 84^{\circ} 8400^{\circ}. 2.64methylphenol 1.27 1.9973 0.38504 0.8654 0.8675 0.11233 1.1447 4^{\circ} Albarcylphenol 1.26 1.2688 1.1233 1.1447 1.2681 1.1233 1.1473 1.2681 1.1233 1.1473 1.2681 1.2284 1.2844 1.2844 $	75	3-Phenylphenol	1.35	1.2389	1.2931			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	76 <sup>a</sup>	3-( <i>tert</i> )-Butylphenol	0.73			0.9910	0.7758	
	77	4-( <i>tert</i> )-Octylphenol	2.1	2.0342	1.9128			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	78 <sup>a</sup>	4-(tert)-Butylphenol	0.91	0.0024	0.0205	0.9333	0.8211	
	79 00a	4,6-Dichlororesorcinol	0.97	0.9034	0.9385	0.2407	0.5247	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	80-	4-Allyl-2-methoxyphenol	0.42	1 0459	1 2964	0.2407	0.5247	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	82a	4-Benzyloxyphenol 4-Bromo-2.6-dichlorophenol	1.04	1.0438	1.2804	1 7768	1 3813	
84         4. Horomo-3.5-dimethylphenol         1.27         1.1912         1.2015           85         4. Bromophenol         0.68         0.6965         0.6116           87         4. Battoxyphenol         0.7         0.779         1.0973           84         4. Chloro-2-sinethylphenol         0.7         0.8504         0.8675           94         4. Chloro-2-sinethylphenol         0.7         1.2333         1.1467           97         4. Chloro-3-sethylphenol         0.8         0.7377         0.8344         0.8504         0.8675           97         4. Chloro-3-ethylphenol         0.8         0.7377         0.8344         0.5155         0.5212           94         4. Chlorophenol         0.55         0.5155         0.5212           94         4. Ethylphenol         0.21         0.3014         0.3981           95         4. Ethylphenol         0.02         0.0708         0.2252           94         4. Heylyoxyphenol         1.64         1.5630         1.622           94         4. Heylyoxy-3-methoxybaccophenone         0.12         0.1004         0.3638           104         4. Hydroxy-3-methoxybaccophenone         0.12         0.0004         0.3638 <th< td=""><td>83</td><td>4-Bromo-2 6-dimethylphenol</td><td>1.70</td><td>1 3217</td><td>1 2670</td><td>1.7700</td><td>1.5015</td></th<>	83	4-Bromo-2 6-dimethylphenol	1.70	1 3217	1 2670	1.7700	1.5015	
85         4.9romo-f-chloro-2-cresol         1.28         1.4707         1.3406           84         4.9romophenol         0.7         0.779         1.0973           87"         4.9taxyphenol         0.7         1.7180         0.8504         0.8504           84         C-Chloro-2-methylphenol         1.7         1.233         1.1467           91"         4-Chloro-3-stuphylphenol         1.2         1.233         1.1467           91"         4-Chloro-3-emthylphenol         0.8         0.7377         0.8344         0.974           92"         4-Chloro-3-emthylphenol         0.18         0.55         0.5212         0.5155         0.5212           93"         4-Chloro-3-emthylphenol         0.13         0.5804         0.974         0.5155         0.5212           94         4-Chlororsocrinol         0.11         0.3014         0.3981         -         -           95         4-Stanophenol         0.21         0.3014         0.3981         -         -           96         4-Hetyloxyphenol         2.03         0.21         0.3014         0.392         -           96         4-Hetyloxyphenol         0.20         0.0708         0.2525         1.4144	84	4-Bromo-3.5-dimethylphenol	1.27	1.1912	1.2015			
86       - Bromophenol       0.68       0.6965       0.6116         87       - Batoxyphenol       0.7779       1.0973         88       - CChioro-2-isontrylphenol       0.7       0.8504       0.8675         90*       - CChioro-2-isontrylphenol       0.7       1.2333       1.1467         91*       - CChioro-3-methylphenol       0.8       0.7377       0.8344       1.2658       1.1233         92*       - CChioro-3-methylphenol       0.515       0.5155       0.5212         94       - CChioro-shreathylphenol       0.515       0.5155       0.5212         94       - CChioro-shreathylphenol       0.52       0.3434       0.0974         94       - Echioxyphenol       0.01       0.318       0.5105         95       - Heptyloxyphenol       2.03       2.1227       1.9979         104       - Heptyloxyphenol       1.64       1.5630       1.6922         104       - Heytoxy-2-methylacetophenone       0.12       0.1004       0.3638         104       - Hydroxy-3-methoxybenzylateohol       0.7       0.8639       0.4325         105       - Hydroxy-3-methoxybenzylateohol       0.7       0.8639       0.4326         106       - Hydroxy-3	85	4-Bromo-6-chloro-2-cresol	1.28	1.4570	1.3406			
	86	4-Bromophenol	0.68	0.6965	0.6116			
88         4-Chloro-2-isopropyl-5-methylphenol         1.85         1.7646         1.7180           90*         4-Chloro-3-methylphenol         1.2         1.2333         1.1467           90*         4-Chloro-3-methylphenol         0.8         0.7377         0.8344         1.2658         1.1233           91*         4-Chloro-3-methylphenol         0.55         0.5155         0.5212           94         4-Chloropresorcinol         0.51         0.5155         0.5212           94         4-Chlorophenol         0.01         0.3381         0.5105           95         4-Ethylphenol         0.21         0.3014         0.3981           96         4-Ethylphenol         2.03         2.1227         1.9979           97         4-Hetyloxyphenol         1.64         1.5630         1.6922           101*         4-Hetyloxyphenol         1.64         1.5630         1.6922           101*         4-Hydroxy-3-methylphetone         0.12         0.104         0.3638           102         4-Hydroxy-3-methylphetone         0.12         0.104         0.3638           103         4-Hydroxy-3-methoxybenzylachool         0.7         0.8639         0.4295           104         4-Hydroxybenzylachool </td <td>87<sup>a</sup></td> <td>4-Butoxyphenol</td> <td>0.7</td> <td></td> <td></td> <td>0.7779</td> <td>1.0973</td>	87 <sup>a</sup>	4-Butoxyphenol	0.7			0.7779	1.0973	
89°         4-Chloro-3dimethylphenol         0.7         0.8504         0.8575           91°         4-Chloro-3dimethylphenol         1.08         1.2658         1.1233           91°         4-Chloro-3methylphenol         0.850         0.8544         1.2658         1.1233           92°         4-Chloro-3-methylphenol         0.55         0.5155         0.5212           94         4-Chlororeseorcinol         0.13         0.5804         0.4712         0.5155         0.5212           94         4-Chlororeseorcinol         0.01         -0.1385         0.5105	88	4-Chloro-2-isopropyl-5-methylphenol	1.85	1.7646	1.7180			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	89 <sup>a</sup>	4-Chloro-2-methylphenol	0.7			0.8504	0.8675	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	90 <sup>a</sup>	4-Chloro-3,5-dimethylphenol	1.2			1.2333	1.1467	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	91°	4-Chloro-3-ethylphenol	1.08	0 7277	0.9244	1.2658	1.1233	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	92 02a	4-Chloro-3-methylphenol	0.8	0.7377	0.8344	0.5155	0.5212	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	93 04	4-Chlororesorcinol	0.33	0 5804	0.4712	0.5155	0.3212	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	95	4-Cvanophenol	0.13	0.3434	0.0974			
97       4-Ethylphenol       0.21       0.3014       0.3981         98       4-Fluorophenol       0.02       -0.0708       0.2526         94       Heytjoxyphenol       1.30       2.1227       1.9979         100       4-Hexyloxyphenol       1.64       1.5530       1.6922         101       4-Hexyloxyphenol       1.64       1.5530       1.4144         102       4-Hydroxy-3-methoxybenzonicle       -0.03       0.0216       0.4072         103       4-Hydroxy-3-methoxybenzylacohol       -0.7       0.8639       0.4295         104       4-Hydroxy-3-methoxybenzylacohol       -0.7       0.8639       0.4295         105       4-Hydroxy-3-methoxybenzylamic       -0.97       0.2649       -0.3264         107*       4-Hydroxy-3-methoxybenzylamic       0.97       0.2034       0.1133         108       4-Hydroxybenzallehyde       0.27       -0.0006       0.1058         110       4-Hydroxybenzallehyde       0.27       -0.0006       0.1058         111       4-Hydroxybenzallehyde       0.27       -0.0006       0.3948         112       4-Hydroxybenzallehyde       0.27       -0.0006       0.3948         114       4-Hydroxybenzallehyde	96	4-Ethoxyphenol	0.01	-0.1385	0.5105			
98       4-Fluorophenol       0.02       -0.0708       0.2526         99       4-Heytloxyphenol       2.03       2.1227       1.9979         101       4-Hexyloxyphenol       1.64       1.5630       1.6922         101       4-Hexyloxy-2-methylacetophenone       0.19       0.1939       0.4472         103       4-Hydroxy-3-methoxybenzylatehone       -0.12       0.1004       0.3638         104       4-Hydroxy-3-methoxybenzylatehol       -0.7       0.8639       0.4295         105       4-Hydroxy-3-methoxybenzylatehol       -0.7       0.2649       -0.3264         107       4-Hydroxy-3-methoxybenzylatehol       -0.7       0.8639       0.4295         106       4-Hydroxy-3-methoxybenzylatehol       -0.7       0.8639       0.4295         107       4-Hydroxybenzholehone       -0.3       0.0234       0.1133         108       4-Hydroxybenzholehone       -0.7       0.006       0.158         111       4-Hydroxybenzholehone       -0.7       0.8670       0.3948         112       4-Hydroxybenzholehol       -0.83       0.2107       0.4306         114       4-Hydroxybenzholephenone       0.05       0.3086       0.4059         115       4-H	97	4-Ethylphenol	0.21	0.3014	0.3981			
99       4-Heptyloxyphenol       2.03       2.1227       1.9979         100       4-Hexyloxyphenol       1.64       1.5630       1.6922         101       4-Hexylresorcinol       1.80       1.5525       1.4144         102       4-Hydroxy-3-methoxyacetophenone       0.19       0.1939       0.4472         103       4-Hydroxy-3-methoxybenzonitrile       -0.03       0.0216       0.4072         104       4-Hydroxy-3-methoxybenzonitrile       -0.03       0.0216       0.4072         105       4-Hydroxy-3-methoxybenzylalcohol       -0.7       0.8639       0.4295         106       4-Hydroxy-3-methoxybenzylanine       -0.97       0.2649       -0.3264         107       4-Hydroxy-asymethoxybenzylanine       -0.97       -0.0006       0.1058         110       4-Hydroxybenzylanine       -0.78       0.6438       0.3673         110       4-Hydroxybenzylexnaide       -0.2       1.0913       1.1405         114       4-Hydroxybenzylexnaide       -0.38       0.3997       0.4804         112       4-Hydroxybenzylexnaide       -0.38       0.3997       0.3086       0.4059         113       4-Hydroxybenzylexnia       -0.650       0.4298       0.6119       0.6148<	98	4-Fluorophenol	0.02	-0.0708	0.2526			
	99	4-Heptyloxyphenol	2.03	2.1227	1.9979			
	100	4-Hexyloxyphenol	1.64	1.5630	1.6922	1 5595		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	101"	4-Hexylresorcinol	1.80	0.1020	0 4472	1.5525	1.4144	
	102	4-Hydroxy-2-methylacetophenone	0.19	0.1939	0.4472			
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	105	4-Hydroxy-3-methoxyacetophenone	-0.12	0.1004	0.3038			
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	105	4-Hydroxy-3-methoxybenzylalcohol	-0.7	0.8639	0.4295			
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	106	4-Hydroxy-3-methoxybenzylamine	-0.97	0.2649	-0.3264			
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	107 <sup>a</sup>	4-Hydroxy-3-methoxyphenethylalcohol	-0.18			0.1069	0.1330	
	108	4-Hydroxyacetophenone	-0.3	0.0234	0.1133			
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	109	4-Hydroxybenzaldehyde	0.27	-0.0006	0.1058			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	110	4-Hydroxybenzamide	-0.78	0.6458	0.3673			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	111	4-Hydroxybenzoic acid	-1.02	0.8670	0.3948			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	112	4-Hydroxybenzylevanide	1.02	1.0915	1.1403			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$113 \\ 114^{a}$	4-Hydroxyphenethylalcohol	-0.38	0.3997	0.4804	0.6590	0.4298	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	115	4-Hydroxyphenylacetic acid	-0.85	1.5063	0.2107	0.0570	0.4270	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	116 <sup>a</sup>	4-Hydroxypropiophenone	0.05	110000	012107	0.3086	0.4059	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	117	4-Iodophenol	0.85	0.95	0.7254			
	118 <sup>a</sup>	4-Isopropylphenol	0.47			0.6119	0.6148	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	119	4-Methoxyphenol	-0.14	0.3372	0.1976			
$121^{\circ}$ 4-Propylphenol0.640.71810.7046 $122$ $4 \cdot (sec)$ -Butylphenol0.981.09320.9117 $123$ $4 \cdot (tert)$ -Pentylphenol1.231.33351.1356 $124$ $5 \cdot Bromo-2 \cdot hydroxybenzylalcohol0.340.42470.36081255 \cdot Bromovanillin0.620.60490.72791265 \cdot Fluoro-2 \cdot hydroxyacetophenone0.040.05170.77711275 \cdot Methylresorcinol-0.390.43600.12711285 \cdot Pentylresorcinol1.311.33761.30201296 \cdot (tert) \cdot Butyl-2, 4 \cdot dimethylphenol1.161.18011.5907130a, a, a \cdot Trifluoro - 4 \cdot cresol0.620.68070.5816$	120 <sup>a</sup>	4-Phenylphenol	1.39			1.2357	1.4480	
122 $4-(sec)$ -Bulylphenol $0.98$ $1.0932$ $0.917$ $123$ $4-(tert)$ -Pentylphenol $1.23$ $1.3335$ $1.1356$ $124$ $5$ -Bromo-2-hydroxybenzylalcohol $0.34$ $0.4247$ $0.3608$ $125$ $5$ -Bromovanillin $0.62$ $0.6049$ $0.7279$ $126$ $5$ -Fluoro-2-hydroxyacetophenone $0.04$ $0.0517$ $0.7771$ $127$ $5$ -Methylresorcinol $-0.39$ $0.4360$ $0.1271$ $128$ $5$ -Pentylresorcinol $1.31$ $1.3376$ $1.3020$ $129$ $6-(tert)$ -Butyl-2,4-dimethylphenol $1.16$ $1.1801$ $1.5907$ $130$ $a,a,a$ -Trifluoro-4-cresol $0.62$ $0.6807$ $0.5816$	121"	4-Propylphenol	0.64	1 0022	0.0117	0.7181	0.7046	
125	122	4-(sec)-Bulyiphenol	0.98	1.0952	0.911/ 1.1356			
121       5 Jointo 2-hydroxyoch2ytaconor       0.34       0.4247       0.5006         125       5-Bromovanillin       0.62       0.6049       0.7279         126       5-Fluoro-2-hydroxyacetophenone       0.04       0.0517       0.7771         127       5-Methylresorcinol       -0.39       0.4360       0.1271         128       5-Pentylresorcinol       1.31       1.3376       1.3020         129       6-( <i>tert</i> )-Butyl-2,4-dimethylphenol       1.16       1.1801       1.5907         130       a,a,a-Trifluoro-4-cresol       0.62       0.6807       0.5816	123	5-Bromo-2-hydroxybenzylalcohol	0.34	0 4247	0.3608			
126       5-Fluoro-2-hydroxyacetophenone       0.02       0.0517       0.7771         127       5-Methylresorcinol       -0.39       0.4360       0.1271         128       5-Pentylresorcinol       1.31       1.3376       1.3020         129       6-( <i>tert</i> )-Butyl-2,4-dimethylphenol       1.16       1.1801       1.5907         130       a,a,a-Trifluoro-4-cresol       0.62       0.6807       0.5816	125	5-Bromovanillin	0.62	0.6049	0.7279			
1275-Methylresorcinol-0.390.43600.12711285-Pentylresorcinol1.311.33761.30201296-( <i>tert</i> )-Butyl-2,4-dimethylphenol1.161.18011.5907130a,a,a-Trifluoro-4-cresol0.620.68070.5816	126	5-Fluoro-2-hydroxvacetonhenone	0.04	0.0517	0.7771			
1285-Pentylresorcinol1.311.33761.30201296-( <i>tert</i> )-Butyl-2,4-dimethylphenol1.161.18011.5907130a,a,a-Trifluoro-4-cresol0.620.68070.5816	127	5-Methylresorcinol	-0.39	0.4360	0.1271			
1296-( <i>tert</i> )-Butyl-2,4-dimethylphenol1.161.18011.5907130a,a,a-Trifluoro-4-cresol0.620.68070.5816	128	5-Pentylresorcinol	1.31	1.3376	1.3020			
130 a,a,a-Trifluoro-4-cresol 0.62 0.6807 0.5816	129	6-(tert)-Butyl-2,4-dimethylphenol	1.16	1.1801	1.5907			
	130	a,a,a-Trifluoro-4-cresol	0.62	0.6807	0.5816			

# Table 1 (contd.)

# Table 1 (contd.)

	$\mathbf{A}/\mathbf{A}$	Name	$log(1/IGC_{50})$	Training set		Validation set	
11       Fabyl-1-bydroxy-s-methorypreprotects       0.3       0.389       0.2439         137       Ethyl-1-hydroxy-s-methorypreprotects       0.37       0.6494         138       Ethyl-1-hydroxy-s-methoryset       0.57       0.2235       0.3669         135       32.Cread       0.005       0.2277       0.4489         136       Mathyl-1-hydroxyberzate       0.08       0.2095       0.4817       0.6075       0.6973         139       Nonjlphenol       2.47       2.4674       2.4774       0.4859       0.1592       0.2252         142       4.Cread       0.18       0.1056       0.0954       0.1592       0.2252         143       4.Cyclepentylphenol       1.29       1.2381       0.9981       0.1592       0.2252         144       Phenol       0.21       0.1106       0.3004       0.1592       0.2252         144       Staicyladdwide       0.42       0.4101       0.2386       0.1592       0.2252         145       Saicyladdwide       0.51       0.30758       0.0276       0.3092         145       Saicyladdwide       0.51       0.30752       0.3276       1.55         145       Saicyladdwide       0.51       0.30752 <th></th> <th></th> <th></th> <th>RBF <math>R^2 = 0.9424</math></th> <th>MLR <math>R^2 = 0.6022</math></th> <th>RBF <math>R^2 = 0.8824</math></th> <th>MLR <math>R^2 = 0.7861</math></th>				RBF $R^2 = 0.9424$	MLR $R^2 = 0.6022$	RBF $R^2 = 0.8824$	MLR $R^2 = 0.7861$
12       Ethyl-4-hjdroxyb-nachoxyphenylaectate       0.23       0.0891       0.7127       0.6494         134       Isovanilin       0.14       0.2235       0.3669       0.0257       0.0559         136       Methyl-4-hydroxybenzoate       0.03       0.2478       0.4839       0.4839         137       Methyl-4-hydroxybenzoate       0.03       0.2075       0.6973       0.6973         138       Methyl-4-methoryalicylate       0.62       0.1732       0.6974       0.1732       0.4571         138       Varinita       0.38       0.1732       0.4571       0.1592       0.2252         141       2 Varnitin       0.38       0.1732       0.4571       0.1592       0.2252         143       4 Cyclopentylphenol       1.29       1.2381       0.9981       0.1732       0.4571         144       Phenol       0.21       0.1160       0.304       0.3044       1.48       Nikiyhdrazika       0.42       0.4010       0.2386       0.2254       1.2381       0.3034       1.238       1.2381       0.3034       1.238       1.2381       0.3034       1.238       1.238       1.2381       1.2381       1.2381       1.2381       1.2381       1.2381       1.2381 <t< td=""><td>131</td><td>Ethyl-3-hydroxybenzoate</td><td>0.48</td><td>0.5352</td><td>0.7593</td><td></td><td></td></t<>	131	Ethyl-3-hydroxybenzoate	0.48	0.5352	0.7593		
13*       Edy1-4-bydroxybenzoate       0.71       0.6494         13*       Jax       Lovanilin       0.14       0.2235       0.3669         13*       JACraci       0.0295       0.4817       0.4859         13*       JACraci       0.0295       0.4817       0.4859         13*       Methyl-4-methorysalicylate       0.62       0.6075       0.6973         13*       Methyl-4-methorysalicylate       0.62       0.0752       0.6973         13*       Methyl-4-methorysalicylate       0.62       0.0752       0.6973         140*       2-Cresol       0.18       0.1152       0.4571       0.4571         142*       4-Cyclopentylphenol       1.29       1.2381       0.9981       1.172       0.4571         142       Reacescinol       0.22       0.1610       0.3064       1.182	132	Ethyl-4-hydroxy-3-methoxyphenylacetate	0.23	0.0891	0.2439		
13         Beyannin         0.14         0.233         0.369         0.0257         0.059           137         Melhyl-Hydroxybenzoate         0.06         0.2095         0.4817         0.4859           137         Melhyl-Hydroxybenzoate         0.06         0.2095         0.4817         0.6075         0.6973           138         Melhyl-Hydroxybenzoate         0.62         0.6075         0.6973         0.4771           147         2-Yanilin         0.38         0.1056         0.0954           142         2-Yanilin         0.38         0.192         0.2252           144         Phenol         0.21         0.1106         0.3044           145         Recorscinol         0.65         0.6311         0.2095           143         Acyclopentylphenol         1.29         1.2381         0.9981           144         Salicylhydroxic         0.18         0.1825         0.1927           143         Salicylhydroxic         0.18         0.1825         0.1927           144         Salicylhydroxine cid         0.38         0.3768         0.2226           15         Salicylhydroxine cid         0.316         0.3303         1.317           15         Sal	133 <sup>a</sup>	Ethyl-4-hydroxybenzoate	0.57	0.2225	0.2((0	0.7127	0.6494
167       Methyl-Hydroxybenzoute       0.08       0.2095       0.4817       0.6075       0.6973         138       Methyl-Hydroxybenzoute       0.62       0.0075       0.6973         138       Methyl-Hydroxybenzoute       0.247       2.4674       2.4774       0.0156       0.0954         147       2.Cresol       0.1156       0.0954       0.1572       0.4571         142       2.Cresol       0.18       0.1922       0.2252         144       Phenol       0.21       0.1106       0.3004         145       Resorsinol       0.65       0.6311       0.2099         146       Salicylaldovine       0.25       0.1826       0.1927         147       Salicylaldovine       0.38       0.1825       0.1927         148       Salicylaldovine       0.38       0.1825       0.1927         151       Salicylaldovine       0.17       0.1702       0.2455         153       Salicylaldovine       0.21       0.2683       0.1825         153       Salicylaldovine       0.16       0.5685       0.7841         153       Salicylaldovine       0.17       0.1762       0.3455         153       Salicylaldovine	134 135 <sup>a</sup>	3-Cresol	0.14	0.2235	0.3009	0.0257	0.0559
137       Merhyl-4-hydroxybenzoare       0.08       0.2095       0.4817         138       Merhyl-4-methoxysalicylate       0.62       0.6075       0.6973         149       2/cresol       0.1056       0.0954         141*       2/vanilia       0.38       0.1152       0.2572         142*       4/cresol       0.18       0.192       0.232       0.4571         143       4/cyclopentylphenol       1.29       1.2318       0.9930       0.2252       0.4571         144       Phenol       0.21       0.1060       0.9304       0.2255       0.4571         144       Phenol       0.21       0.4010       0.2986       0.3740       0.3740         145       Salicyludovime       0.23       0.1620       0.3740       0.3740         148       Salicyludovine       0.23       0.1762       0.3455       0.3701         153       Salicyludovine       0.17       0.1762       0.3455       0.3701         153       Salicyludovine       0.21       2.6833       1.8520       0.3701         153       Salicyludovine       0.17       0.1762       0.3455       0.3751       0.3527         153       Salicyludovine	136 <sup>a</sup>	Methyl-3-hydroxybenzoate	0.05			0.2478	0.4859
138*       Methyl-4-methoxysalicylate       0.62       0.6073       0.6973         140*       2-Cresol       0.33       0.1056       0.0954         141*       2-Cresol       0.18       0.1732       0.4571         142*       4-Cresol       0.18       0.1592       0.2252         142*       4-Cresol       0.190       0.3904       0.192       0.2252         144*       4-Cresol       0.190       0.3904       0.192       0.2252         144       Salicyladdryde       0.42       0.4010       0.2906       0.181       0.182         145       Salicyladdrydroxamic acid       0.384       0.0364       0.0554       1.1281	137	Methyl-4-hydroxybenzoate	0.08	0.2095	0.4817		
	138 <sup>a</sup>	Methyl-4-methoxysalicylate	0.62	0.4/74	0.4554	0.6075	0.6973
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	139 140 <sup>a</sup>	Nonylphenol 2-Cresol	2.4/	2.46/4	2.4774	0 1056	0.0954
	141 <sup>a</sup>	2-Vanillin	0.38			0.1732	0.4571
143       4-Cyclopentylphenol       1.29       1.2381       0.9981         144       Phenol       0.65       0.6311       0.2009         145       Sakoylaldehyde       0.42       0.4010       0.2986         147       Salicylaldehyde       0.25       0.1620       0.3740         148       Sakoylande       0.25       0.1620       0.3740         149       Salicylhydroxanic aid       0.38       0.3768       0.2226         151       Salicylhydroxanic aid       0.51       0.5072       0.7902         152       Syringaldehyde       0.17       0.176       0.3455         153       Vanillin       0.03       0.0114       0.3303         154       2.3,5.6-Tetrachlorophenol       2.21       2.2188       1.6755         153       2.3,5.6-Tetrachlorophenol       1.17       1.282       0.6360         153       2.4,6-Tinitrophenol       1.75       1.8195       1.7045         154       2.4,6-Tinitrophenol       1.75       1.8195       1.7045         152       2.6-Ditolotor-4-nitrophenol       1.77       1.7308       1.6515         154       2.6-Ditolotor-4-nitrophenol       1.72       1.3454       1.4416 </td <td>142<sup>a</sup></td> <td>4-Cresol</td> <td>-0.18</td> <td></td> <td></td> <td>0.1592</td> <td>0.2252</td>	142 <sup>a</sup>	4-Cresol	-0.18			0.1592	0.2252
144       Plenol       0.21       0.106       0.3004         145       Resorscinol       0.65       0.6311       0.2009         146       Salicylaldehyde       0.42       0.4010       0.2986         147       Salicylaldoxime       0.25       0.1620       0.3740         148       Salicylhydrazide       0.18       0.1825       0.1927         150       Salicylhydrazide       0.17       0.1762       0.3455         151       Salicylhydroxamic aid       0.38       0.3768       0.2226         152       Syringaldehyde       0.17       0.1762       0.3455         153       Vanillin       0.03       0.0114       0.3303         154       2.3,5.6-Tetrathlorophenol       2.17       2.6883       1.8520         155       2.3,5.6-Tetrathlorophenol       1.17       1.2825       0.6360         158       2.4-Orinitrophenol       0.16       0.1587       0.40631         160       2.4-Dinitrophenol       1.08       0.9775       0.5527         161       2.5-Dinitrophenol       0.63       0.6967       1.1545         162       2.6-Dinitro-f-anitrophenol       0.53       0.60845         163       <	143	4-Cyclopentylphenol	1.29	1.2381	0.9981		
143         Resorscinol         0.03         0.0311         0.2009           145         Salicylaldexine         0.22         0.1620         0.3740           147         Salicylaldexine         0.23         0.1620         0.3740           148         Salicylindrazatic         0.24         0.3046         0.0554           148         Salicylindrazatic         0.38         0.3768         0.2226           151         Salicylindrazatic         0.31         0.3772         0.7902           151         Salicylindrazatic         0.33         0.0114         0.3303           151         2.3,5.6-Tetrachiorophenol         2.21         2.2188         1.6755           152         2.3,5.6-Tetrachiorophenol         2.22         2.1288         1.6755           152         2.3,5.6-Tetrachiorophenol         1.17         1.1895         1.7045           152         2.4,5.7         1.6755         0.4565         0.7661           152         2.4,5.7         1.0176         1.8195         1.7045           152         2.4,5.7         1.0176         1.8195         1.7045           152         2.4,5.7         1.176         1.8195         1.7045           152	144	Phenol	0.21	0.1106	0.3004		
127       Silley inducty action       0.75       0.1720       0.3740         148       Silley inducty action       0.24       0.3046       0.0554         148       Silley inducty action       0.18       0.1825       0.1927         151       Silley inducty action       0.18       0.3768       0.2226         151       Silley inducty action       0.17       0.1762       0.3455         152       Syming aldehyde       0.17       0.1762       0.3455         153       Vanillin       0.00114       0.3303       1.8520         154       2.3,3.6-Tetrafilorophenol       2.21       2.138       1.6755         152       2.3,5.6-Tetrafilorophenol       0.16       0.1587       0.4603         158       2.4-Dinitrophenol       0.06       0.9667       1.1545         160       2.4-Dinitrophenol       0.063       0.9697       1.1545         161       2.5-Dinitrophenol       0.63       0.9697       1.1545         162       2.6-Dinitrophenol       1.71       1.3385       0.90451         163       2.6-Dinitrophenol       0.53       0.90357       1.0017         162       2.6-Dinitrophenol       0.54       0.6042       1	145	Resorscinol Salicylaldebyde	0.65	0.6311	0.2009		
148       Salicylamide       0.24       0.3046       0.0554         9       Salicylhydroxanie acid       0.38       0.3768       0.2226         150       Salicylhydroxanie acid       0.38       0.3768       0.2226         151       Salicylhydroxanie acid       0.38       0.3768       0.2226         151       Singingaldehyde       0.17       0.1762       0.3455         151       2.3.4.5-Tetrachlorophenol       2.71       2.6883       1.8520         152       2.3.5.6-Tetrachlorophenol       2.71       2.2883       1.8520         153       2.3.5.6-Tetrachlorophenol       1.17       1.2825       0.6360         157       2.3.5.6-Tetrachlorophenol       1.75       1.8195       1.7045         158       2.4.6-Tinitrophenol       1.75       1.8195       1.7045         159       2.4-Dichloro-4-nitrophenol       1.78       1.8195       1.171         162       2.6-Dinitrophenol       1.71       1.7308       1.6515         162       2.6-Dinitrophenol       0.71       1.545       0.8454         163       2.6-Dinitrophenol       0.72       2.642       2.4724       0.4613         164       2.6-Dinitrophenol       0.266	140	Salicylaldoxime	0.42	0.1620	0.3740		
149       Salicylhydraxide       0.18       0.1825       0.1927         151       Salicylio acid       0.51       0.5072       0.7902         151       Salicylio acid       0.51       0.5072       0.7902         151       Syningladdhyde       0.17       0.1762       0.3455         153       Vanillin       0.03       0.0114       0.3303         154       2.3.4.5 Tetrachlorophenol       2.71       2.6883       1.6755         152       2.3.5.6 Tetrafilorophenol       0.16       0.1587       0.4663         158       2.4.6 Trinitrophenol       0.06       0.585       0.7861         160       2.4-Dinitrophenol       0.63       0.6967       1.154         161       2.5-Dinitrophenol       0.63       0.6967       1.154         162       2.6-Dinitrophenol       1.72       1.8385       0.8045         163       2.4-Dinitrophenol       0.63       0.6967       1.154         164       2.6-Dinitro-d-cresol       1.71       1.7308       1.6515         165       2.6-Dinitro-d-cresol       2.57       2.5622       2.4724         163       4.56-Tetrabromo-2-cresol       2.77       2.5622       2.1188	148	Salicylamide	0.24	0.3046	0.0554		
150       Salicylhydroxamic acid       0.38       0.3768       0.2226         151       Salicylhydrox       0.17       0.1762       0.7902         152       Syringaldehyde       0.17       0.1762       0.3303         154       2.3.4.5-Tetrachlorophenol       2.71       2.6883       1.8520         155       2.3.5.6-Tetrachlorophenol       2.17       2.2883       1.8520         156       2.3.5.6-Tetrachlorophenol       1.17       1.2825       0.6360         158       2.4.5-Drinitrophenol       0.16       0.1587       0.4653         159       2.4-Dinitrophenol       1.07       1.2825       0.6360         150       2.4.5-Drinitrophenol       1.08       0.9775       0.5527         161       2.5-Dnitrophenol       0.63       0.6967       1.1545         162       2.6-Drindor-4-nitrophenol       1.71       1.7308       1.6515         162       2.6-Drindor-4-nitrophenol       0.54       0.6098       0.6845         163       3.4.5.6       1.72       1.8385       0.9805         169       Pentakhorophenol       2.66       2.6674       2.5129         170       Pentakorophenol       2.66       2.6674	149	Salicylhydrazide	0.18	0.1825	0.1927		
131       Sakeylic acid       0.51       0.5072       0.7902         152       Syring aldehyde       0.17       0.1762       0.3435         153       Vanillin       0.03       0.0114       0.3303         154       2.3,4.5-Tetrachlorophenol       2.72       2.2198       1.6755         155       2.3,5.6-Tetrachlorophenol       2.17       1.2683       1.8520         157       2.3-Dinitrophenol       0.46       0.5685       0.7861         158       2.4.6-Tetrafluorophenol       1.17       1.2825       0.6360         159       2.4-Dichloro-6-nitrophenol       1.01       0.518       0.4653         150       2.4-Dichloro-6-nitrophenol       1.08       0.0975       0.5527         161       2.5-Dinitrophenol       0.63       0.6967       1.1545         162       2.6-Dinitro-fuencel       1.71       1.7308       1.6515         164       2.6-Dinitro-fuencel       1.72       1.8385       0.9805         165       2.6-Dinitro-fuencel       2.57       2.5622       2.4724         164       4.6-Dinitro-fuencel       0.27       0.2449       0.6613         168       4.6-Dinitro-fuencel       0.27       0.2479       <	150	Salicylhydroxamic acid	0.38	0.3768	0.2226		
12       Symmatice       0.17       0.1762       0.5433         13       Vanilian       0.03       0.0114       0.3303         154       2.3,4,5-Tetrachlorophenol       2.71       2.6883       1.8520         152       2.3,5,6-Tetrathlorophenol       1.17       1.2825       0.6360         152       2.3,5,6-Tetrathlorophenol       0.16       0.1887       0.4653         158       2.4,6-Trinitrophenol       0.16       0.1887       0.4653         159       2.4-Dichloro-4-nitrophenol       1.75       1.8195       1.7045         160       2.4-Dinitrophenol       0.65       0.9357       0.5527         161       2.5-Dinitrophenol       0.65       0.9067       1.1545         162       2.6-Dichloro-4-nitrophenol       1.71       1.7308       1.6515         162       2.6-Dinitrophenol       0.54       0.6098       0.6845         163       3.6.5       1.835       0.9805       1.66         164       2.6-Dinitrophenol       0.27       0.2449       0.6613         168       4.0-Dinitrophenol       2.05       2.0362       2.1188         170       Pentathorophenol       2.66       2.6674       2.5129 </td <td>151</td> <td>Salicylic acid</td> <td>0.51</td> <td>0.5072</td> <td>0.7902</td> <td></td> <td></td>	151	Salicylic acid	0.51	0.5072	0.7902		
123       Aumin       0.000       0.000         124       2.3,4.5-Tetrachlorophenol       2.22       2.2198       1.6755         125       2.3,5.6-Tetrachlorophenol       2.22       2.2198       1.6755         125       2.3,5.6-Tetrachlorophenol       0.46       0.5685       0.7861         124       2.4.7:rinitrophenol       0.46       0.5685       0.7861         125       2.4.6:rinitrophenol       1.75       1.8195       1.7045         126       2.4.0:hitrophenol       0.86       0.975       0.5527         161       2.5-Dinitrophenol       0.63       0.696       1.1545         162       2.6-Dinitrophenol       1.72       1.9981       1.17         163       2.6-Dinitrophenol       0.54       0.6098       0.6645         164       2.6-Dinitrophenol       0.77       0.2449       0.6613         168       4.6-Dinitrophenol       2.66       2.6674       2.5129         170       Pentachlorophenol       2.05       2.0362       2.1188         171       1.23875       0.9301       1.23-Trihydroxybenzene       0.45         172       2.4-Diaminophenol       1.64       1.525       0.9301	152	Vanillin	0.17	0.1762	0.3455		
155       2.3.5.6-Tetrachlorophenol       2.22       2.2198       1.6755         156       2.3.5.6-Tetrachlorophenol       1.17       1.2825       0.6360         157       2.3.5.6-Tetrachlorophenol       0.46       0.5685       0.7861         158       2.4.0-Entirophenol       0.16       0.1587       0.4653         159       2.4.0-Entirophenol       1.06       0.587       0.5527         160       2.4-Dinitrophenol       0.95       0.9375       0.5527         161       2.5-Dichloro-4-nitrophenol       0.63       0.6967       1.1545         162       2.6-Dichloro-4-nitrophenol       0.71       1.7308       1.6515         164       2.6-Dinitro-4-cresol       1.73       1.0951       1.17         165       2.6-Dinitro-4-cresol       2.77       2.6222       2.4724         167       3.4-Dinitro-2-cresol       2.77       2.632       0.9805         168       4.6-Dinitro-2-cresol       1.72       1.838       0.9805         169       Pentabromophenol       2.66       2.6674       2.519         170       Pentachlorophenol       1.64       1.523       0.9301         171       1.2.3-Trinydroxybenzene       0.44 <t< td=""><td>155</td><td>2.3.4.5-Tetrachlorophenol</td><td>2.71</td><td>2.6883</td><td>1.8520</td><td></td><td></td></t<>	155	2.3.4.5-Tetrachlorophenol	2.71	2.6883	1.8520		
156 $2.3,5,6$ -Tetrafluorophenol       1.17       1.2825       0.6300         157 $2.3.5,6$ -Tetrafluorophenol       0.46       0.5863       0.7861         157 $2.3.5,0$ -Initrophenol       1.05       0.1587       0.4653         159 $2.4.5$ Dichloro-6-nitrophenol       1.05       1.8195       1.7045         161 $2.5$ Dinitrophenol       0.63       0.6967       1.1545         162 $2.6$ Dichloro-4-nitrophenol       1.71       1.7308       1.6615         164 $2.6$ Dinitro-4-cresol       1.23       1.0951       1.17         165 $2.6$ Dinitro-4-cresol       2.57       2.5622       2.4724         166 $3.4,5,6$ -Tetraformo-2-cresol       2.57       2.5622       2.4724         167 $3.4$ Dinitrophenol       0.27       0.2490       0.6613         168 $4.6$ -Dinitro-2-cresol       1.72       1.8385       0.9805         179       Pentachlorophenol       2.65       2.0362       2.1188         171       Pentaflorophenol       0.664       0.4575         173 $1.2,4$ -Trihydroxybenzene       0.840       0.4300         174 $2.3.5$ Diretrhybhydroxybenzene       0.441       0	155	2,3,5,6-Tetrachlorophenol	2.22	2.2198	1.6755		
157       2.3-Dinitrophenol       0.46       0.5685       0.7861         158       2.4-Dichloro-6-nitrophenol       1.75       1.8195       1.7045         160       2.4-Dinitrophenol       0.95       0.9357       0.5527         161       2.5-Dinitrophenol       0.63       0.6967       1.1545         162       2.6-Dichloro-4-nitrophenol       1.71       1.7308       1.6515         163       2.6-Dinitro-4-neophenol       0.71       1.7308       1.6515         164       2.6-Dinitro-4-cressol       1.23       1.0951       1.17         165       2.6-Dinitro-4-cressol       2.57       2.5022       2.4724         166       3.4-5.6-Tetrabromo-2-cressol       2.57       2.5022       2.4724         167       3.4-Dinitrophenol       0.266       2.6674       2.519         170       Pentachorophenol       2.66       2.6674       2.519         171       Pentablorophenol       2.65       2.0362       2.1188         171       Pentablorophenol       2.66       2.6773       2.519         172       1.2.4-Trihydroxybenzene       0.84       0.4386       0.1186         173       1.2.4-Trihydroxybenzene       0.44       0.43	156	2,3,5,6-Tetrafluorophenol	1.17	1.2825	0.6360		
138       2,4,0-1 rnitrophenol       -0.16       0.158/       0.4953         159       2,4-Dichloro-6-nitrophenol       1.08       0.9775       0.5527         160       2,4-Dinitrophenol       0.95       0.9357       1.0017         162       2,6-Dinitrophenol       0.63       0.6967       1.1545         163       2,6-Dinitro-4-nitrophenol       1.71       1.7308       1.6515         164       2,6-Dinitro-4-resol       1.23       1.0951       1.17         165       2,6-Dinitro-d-resol       2.57       2.5622       2.4724         167       3,4-Dinitro-2-cresol       2.57       2.5622       2.4724         168       4,6-Dinitro-2-cresol       2.72       0.2449       0.6613         168       4,6-Dinitro-2-cresol       2.72       0.2459       0.6613         170       Pentabromophenol       2.66       2.6674       2.5129         170       Pentabromophenol       1.64       1.5253       0.9301         171       1.2.3-Trihydroxybenzene       0.85       0.3641       -0.4755         173       1.2.4-Trihydroxybenzene       0.44       0.4386       0.1186         174       2.3-Dimethylhydroquinone       1.41       2.	157	2,3-Dinitrophenol	0.46	0.5685	0.7861		
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	158	2,4,6-Trinitrophenol	-0.16	0.1587	0.4653		
100       2.4* Dimitrophenol       1.03       0.9357       1.0017         162       2.6* Dichloro-4-nitrophenol       0.63       0.6967       1.1545         162       2.6* Dinitrophenol       1.71       1.7308       1.6515         164       2.6* Dinitrophenol       0.54       0.6098       0.6845         165       2.6* Dinitro-2-cresol       2.57       2.5622       2.4724         167       3.4* Dinitro-2-cresol       1.72       1.8385       0.9805         168       4.6* Dinitro-2-cresol       1.72       1.8385       0.9805         169       Pentabromophenol       2.05       2.0362       2.1188         171       Pentachlorophenol       1.64       1.5253       0.9301         172       1.2.3*Trihydroxybenzene       0.85       0.3641       -0.4575         173       1.2.4*Trihydroxybenzene       0.84       0.4380       0.1186         174       2.3*Dimethylhydroquinone       1.41       2.1983       0.4201         175       2.4*Diaminophenol       0.37       0.3471       1.0426         177       2.4*mino-4(tert)-butylphenol       0.37       0.3471       1.0426         177       2.4*mino-phenol       0.28 <td< td=""><td>160</td><td>2,4-Dichloro-6-Introphenol</td><td>1.75</td><td>0.9775</td><td>1.7043</td><td></td><td></td></td<>	160	2,4-Dichloro-6-Introphenol	1.75	0.9775	1.7043		
162       2.6-Dichloro-4-nitrophenol       0.63       0.6967       1.1545         163       2.6-Diixdo-4-nitrophenol       1.71       1.7308       1.6515         164       2.6-Dinitro-4-recsol       1.23       1.0951       1.17         165       2.6-Dinitro-d-recsol       2.57       2.5622       2.4724         166       3.4,5.6-Tetrabromo-2-cresol       2.57       2.5622       2.4724         167       3.4-Dinitro-2-cresol       1.72       1.8385       0.9805         168       4.6-Dinitro-2-cresol       1.72       1.8385       0.9805         170       Pentachlorophenol       2.66       2.6674       2.5129         171       Pentafluorophenol       1.64       1.5253       0.9301         172       1.2,3-Trihydroxybenzene       0.44       0.4386       0.1186         173       1.2,4-Trihydroxybenzene       0.44       0.4386       0.1186         174       2.3-Dimethylhydroquinone       1.41       2.1983       0.4201         175       2.4-Diaminophenol       0.37       0.3471       1.0426         2-A-minophenol       0.94       1.0797       0.0342         178       3.5-Di-(terr)-butylcatechol       0.28       0.3889 <td>161</td> <td>2.5-Dinitrophenol</td> <td>0.95</td> <td>0.9357</td> <td>1.0017</td> <td></td> <td></td>	161	2.5-Dinitrophenol	0.95	0.9357	1.0017		
163       2,6-Diidod-4-nitrophenol       1.71       1.7308       1.6515         164       2,6-Dinitro-4-cresol       1.23       1.0951       1.17         165       2,6-Dinitrophenol       0.54       0.6088       0.6845         166       3,4.5,6-Tetrabromo-2-cresol       2.57       2.5622       2.4724         167       3,4-Dinitrophenol       0.27       0.2449       0.6613         168       4,6-Dinitro-2-cresol       1.72       1.8385       0.9805         169       Pentabromophenol       2.06       2.6674       2.5129         170       Pentachlorophenol       2.05       2.0362       2.1188         171       Pentafluorophenol       0.44       0.4386       0.1186         172       1,2,3-Trihydroxybenzene       0.84       0.4386       0.1186         174       2,3-Dimethylhydroquinone       1.41       2.1983       0.4201         175       2,4-Diaminophenol       0.37       0.3471       1.0426         176       2-Aminophenol       0.94       1.0797       0.0342         178       3,5-Di-(tert)-butylactohol       2.12       2.1321	162	2,6-Dichloro-4-nitrophenol	0.63	0.6967	1.1545		
164       2.6-Dinitro-4-cresol       1.23       1.0951       1.17         165       2.6-Dinitrophenol       0.54       0.6098       0.6845         167       3.4-Dinitrophenol       0.27       0.2449       0.6613         168       4.6-Dinitro-2-cresol       1.72       1.8385       0.9805         169       Pentabromophenol       2.66       2.6674       2.5129         170       Pentachlorophenol       1.64       1.5253       0.9301         172       1.2.3-Trihydroxybenzene       0.85       0.3641       -0.4575         173       1.2.4-Trihydroxybenzene       0.85       0.3641       -0.4575         173       1.2.4-Trihydroxybenzene       0.84       0.4386       0.1186         174       2.3-Dimethylhydroquinone       1.41       2.1983       0.4201         175       2.4-Diaminophenol       0.37       0.3471       1.0426         177       2-Aminophenol       0.28       0.3889       0.2381         184       4-Acetamidophenol       -0.52       0.6763       0.4105         180       3-Methylcatechol       0.28       0.8889       0.2381         181       4-Acetamidophenol       -0.08       0.0292       0.0	163	2,6-Diiodo-4-nitrophenol	1.71	1.7308	1.6515		
165       2,6-Dimitrophenol       0.54       0.6098       0.6845         163       3,4-Dinitrophenol       2.57       2.5622       2.4724         167       3,4-Dinitrophenol       0.27       0.2449       0.6613         168       4,6-Dinitro-2-cresol       1.72       1.8385       0.9805         169       Pentabromophenol       2.66       2.6674       2.5129         170       Pentachlorophenol       2.05       2.0362       2.1188         171       Pentafluorophenol       1.64       1.5233       0.9301         172       1.2,3-Trihydroxybenzene       0.44       0.4386       0.1186         174       2,3-Dimethylhydroquinone       1.41       2.1983       0.4201         175       2.4-Diaminophenol       0.37       0.3471       1.0426         177       2-Amino-4(tert)-butylphenol       0.37       0.3471       1.0426         177       2-Aminophenol       0.94       1.0797       0.0342         178       3.5-Di-(tert)-butylcatechol       2.11       2.1321       -         179       3-Aminophenol       -0.52       0.6763       0.4105         180       3-Methylcatechol       0.28       0.3889       0.2381 </td <td>164</td> <td>2,6-Dinitro-4-cresol</td> <td>1.23</td> <td>1.0951</td> <td>1.17</td> <td></td> <td></td>	164	2,6-Dinitro-4-cresol	1.23	1.0951	1.17		
1005.4.3.6 retration2.372.30222.47241633.4.5.0 retration0.270.24490.66131684.6-Dinitro-2-cresol1.721.83850.9805169Pentabromophenol2.662.66742.5129170Pentachlorophenol1.641.52530.93011711.2.3-Trihydroxybenzene0.850.3641-0.45751721.2.3-Trihydroxybenzene0.440.43860.11861742.3-Dimethylhydroquinone1.412.19830.42011752.4-Diaminophenol0.370.34711.04261762-Amino-4-(tert)-butylphenol0.370.34711.04261772-Aminophenol0.941.07970.03421783.5-Dir( <i>ert</i> )-butylcatechol2.112.10322.13211793-Aminophenol-0.520.67630.41051803-Methylcatechol0.280.38890.23811814-Acetamidophenol-0.820.18540.04241824-Amino-2,3-dimethylphenol1.441.39200.06181834-Amino-2,-resol1.311.29520.23621844-Amino-2,-resol1.311.29520.23621854-Chlorocatechol0.370.74501864-Methylcatechol0.370.74501864-Chlorocatechol0.780.78090.74501864-Chlorocatechol0.750.2268-0.09381864-Chlorocatechol0	165	2,6-Dinitrophenol	0.54	0.6098	0.6845		
10111111211211211211644,6-Dinitro-2-cresol1.721.8350.98051179Pentabromophenol2.662.66742.51291170Pentadhorophenol1.641.52330.930111711.2,3-Trihydroxybenzene0.850.3641-0.457511731,2,4-Trihydroxybenzene0.440.43860.118611722,3-Dimethylhydroquinone1.412.19830.420111752,4-Diaminophenol0.130.1296-0.1773122,4-Diaminophenol0.370.34711.042611722.Amino-4-(tert)-butylphenol0.370.34711.042611733,5-Di-( <i>tert</i> )-butylcatechol2.112.10322.13211184-Acetamidophenol-0.520.67630.41051193-Aminophenol-0.520.67630.41051193-Aminophenol-0.820.18540.04241184-Acetamidophenol-0.820.18540.04241184-Acetamidophenol-0.080.02920.08451184-Amino-2-cresol1.311.29520.23621184-Aminophenol-0.080.02920.08451184-Aminophenol0.450.4527-0.14561184-Amino-2-methoxyphenol0.450.4527-0.14561185-Chloro-2-hydroxyaniline0.780.78090.7450119G-Amino-2-4imethylphenol0.470.3551-0.0659<	167	3 4-Dinitrophenol	0.27	0.2449	0.6613		
169Pentabhorophenol2.662.66742.5129170Pentachlorophenol2.052.03622.1188171Pentafluorophenol1.641.52530.93011721,2,3-Trihydroxybenzene0.850.3641-0.45751731,2,4-Trihydroxybenzene0.440.43860.11861742,3-Dimethylhydroquinone1.412.19830.42011752,4-Diaminophenol0.130.1296-0.17731762-Amino-4-(tert)-butylphenol0.370.34711.04261772-Aminophenol0.941.07970.03421783,5-Di-( <i>tert</i> )-butylcatechol2.112.10322.13211793-Aminophenol-0.520.67630.41051803-Methylcatechol0.280.38890.23811814-Acetamidophenol-0.820.18540.04241834-Amino-2,-dimethylphenol1.441.39200.06181834-Amino-2-cresol1.311.29520.23621844-Aminophenol-0.080.02920.08451854-Choloroatechol0.660.86530.70611864-Methylcatechol0.370.78090.74501875-Amino-2-methoxyphenol0.450.4527-0.14561885-Chloro-2-hydroxyaniline0.750.2268-0.0938191aCatechol0.750.2268-0.0938191aCatechol0.750.2268-0.0938191a	168	4,6-Dinitro-2-cresol	1.72	1.8385	0.9805		
170Pentachlorophenol2.052.03622.1188171Pentafluorophenol1.641.52530.93011721.2,3-Trihydroxybenzene0.850.3641-0.45751731,2,4-Trihydroxybenzene0.440.43860.11861742,3-Dimethylhydroquinone1.412.19830.42011752,4-Diaminophenol0.130.1296-0.17731762-Amino-4.(tert)-butylphenol0.370.34711.04261772-Aminophenol0.941.07970.03421783,5-Di-( <i>tert</i> )-butylcatechol2.112.10322.13211793-Aminophenol-0.520.67630.41051803-Methylcatechol0.280.38890.23811814-Acetamidophenol-0.820.18540.04241834-Amino-2dimethylphenol1.441.39200.06181834-Amino-2dimethylphenol1.311.29520.23621844-Amino-2dimethylphenol0.450.45230.7061186 <sup>a</sup> 4-Methylcatechol0.370.66420.27571875-Amino-2methoxyphenol0.450.4527-0.14561885-Chloro-2-hydroxyaniline0.780.78090.74501861.74390.80860.2268-0.0938191 <sup>a</sup> Catechol0.750.2268-0.0938192Chlorohydroquinone1.681.74390.8086191 <sup>a</sup> Catechol0.750.2268-0.0938 </td <td>169</td> <td>Pentabromophenol</td> <td>2.66</td> <td>2.6674</td> <td>2.5129</td> <td></td> <td></td>	169	Pentabromophenol	2.66	2.6674	2.5129		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	170	Pentachlorophenol	2.05	2.0362	2.1188		
1721,2,3-111000Xybenzele0.830.3641-0.43731731,2,4-Trihydroxybenzele0.440.43860.11861742,3-Dimethylhydroquinone1.412.19830.42011752,4-Diaminophenol0.130.1296-0.17731762-Aminophenol0.941.07970.03421783,5-Di-( <i>tert</i> )-butylcatechol2.112.10322.13211793-Aminophenol-0.520.67630.41051803-Methylcatechol0.280.38890.23811814-Acetamidophenol-0.820.18540.04241824-Amino-2,3-dimethylphenol1.441.39200.06181834-Amino-2-cresol1.311.29520.23621844-Amino-2-cresol1.311.29520.23621854-Chlorocatechol0.0370.66420.27571875-Amino-2-methoxyphenol0.450.4527-0.14561885-Chloro-2-hydroxyaniline0.780.78090.74501896-Amino-2,4-dimethylphenol0.890.96030.4623190Bromohydroquinone1.681.74390.8086191 <sup>4</sup> Catechol0.750.2268-0.0938192Chlorohydroquinone1.260.81430.3379193Hydroquinone0.470.3551-0.0659194Methoxyhydroquinone1.861.56770.2166	171	Pentafluorophenol	1.64	1.5253	0.9301		
1742.3-Dimethyllydroquinone0.440.4300.42011752,4-Diaminophenol0.130.1296-0.17731762-Aminop-4-(tert)-butylphenol0.370.34711.04261772-Aminophenol0.941.07970.03421783,5-Di-(tert)-butylcatechol2.112.10322.13211793-Aminophenol-0.520.67630.41051803-Methylcatechol0.280.38890.23811814-Acetamidophenol-0.820.18540.04241824-Amino-2,3-dimethylphenol1.441.39200.06181834-Amino-2,-cresol1.311.29520.23621844-Aminophenol-0.080.02920.08451854-Chlorocatechol1.060.86530.7061186*4-Methylcatechol0.370.66420.27571755-Amino-2,-methoxyphenol0.450.4527-0.14561885-Chloro-2-hydroxyaniline0.780.78090.74501896-Amino-2,4-dimethylphenol0.890.96030.4623190Bromohydroquinone1.681.7390.8086191*Catechol0.750.2268-0.0938192Chlorohydroquinone1.260.81430.3379193Hydroquinone0.470.3551-0.0659194Methoxyhydroquinone1.861.56270.2166	173	1,2,3-1 rinydroxybenzene	0.85	0.3041	-0.45/5		
1752.4-Diaminophenol0.130.126-0.17731762-Aminophenol0.370.34711.04261772-Aminophenol0.941.07970.03421783,5-Di-( <i>tert</i> )-butylcatechol2.112.10322.13211793-Aminophenol-0.520.67630.41051803-Methylcatechol0.280.38890.23811814-Acetamidophenol-0.820.18540.04241824-Amino-2,3-dimethylphenol1.441.39200.06181834-Aminophenol-0.080.02920.23621844-Aminophenol-0.080.02920.08451854-Chlorocatechol1.060.86530.7061186 <sup>a</sup> 4-Methylcatechol0.370.66420.27571875-Amino-2-methoxyphenol0.450.4527-0.14561885-Chloro-2-hydroxyaniline0.780.78090.74501896-Amino-2,4-dimethylphenol0.890.96030.4623190Bromohydroquinone1.681.74390.8086191 <sup>a</sup> Catechol0.750.2268-0.0938192Chlorohydroquinone1.260.81430.3379193Hydroquinone0.4770.3551-0.0659194Methoxyhydroquinone1.260.8448-0.0157195Methylkydroquinone1.861.56770.2166	174	2.3-Dimethylhydroguinone	1.41	2.1983	0.4201		
1762-Amino-4-(tert)-butylphenol $0.37$ $0.3471$ $1.0426$ 1772-Aminophenol $0.94$ $1.0797$ $0.0342$ 1783,5-Di-(tert)-butylcatechol $2.11$ $2.1032$ $2.1321$ 1793-Aminophenol $-0.52$ $0.6763$ $0.4105$ 1803-Methylcatechol $0.28$ $0.3889$ $0.2381$ 1814-Acetamidophenol $-0.82$ $0.1854$ $0.0424$ 1824-Amino-2,3-dimethylphenol $1.44$ $1.3920$ $0.0618$ 1834-Aminophenol $-0.08$ $0.0292$ $0.0845$ 1844-Aminophenol $0.08$ $0.0292$ $0.0845$ 1854-Chlorocatechol $1.06$ $0.8653$ $0.7061$ 186 <sup>a</sup> 4-Methylcatechol $0.37$ $0.6642$ $0.2757$ 1875-Amino-2-methoxyphenol $0.45$ $0.4527$ $-0.1456$ 1885-Chloro-2-hydroxyaniline $0.78$ $0.7809$ $0.7450$ 1896-Amino-2,4-dimethylphenol $0.89$ $0.9603$ $0.4623$ 190Bromohydroquinone $1.68$ $1.7439$ $0.8086$ 191 <sup>a</sup> Catechol $0.75$ $0.2268$ $-0.0938$ 192Chlorohydroquinone $1.26$ $0.8143$ $0.3379$ 193Hydroquinone $0.47$ $0.3551$ $-0.0659$ 194Methoxyhydroquinone $1.26$ $0.8448$ $-0.0157$ 195Methylydroquinone $1.86$ $1.5677$ $0.2166$	175	2,4-Diaminophenol	0.13	0.1296	-0.1773		
1772-Aminophenol0.941.07970.03421783,5-Di-(tert)-butylcatechol2.112.10322.13211793-Aminophenol-0.520.67630.41051803-Methylcatechol0.280.38890.23811814-Acetamidophenol-0.820.18540.04241824-Amino-2,3-dimethylphenol1.441.39200.06181834-Aminophenol-0.080.02920.08451844-Aminophenol-0.080.02920.08451854-Chlorocatechol1.060.86530.7061186 <sup>a</sup> 4-Methylcatechol0.370.66420.27571875-Amino-2-methoxyphenol0.450.4527-0.14561885-Chloro-2-hydroxyaniline0.780.78090.7450190Bromohydroquinone1.681.74390.8086191 <sup>a</sup> Catechol0.750.2268-0.0938192Chlorohydroquinone1.260.81430.3379193Hydroquinone0.470.3551-0.0659194Methoxyhydroquinone2.200.8448-0.0157195Methoxyhydroquinone1.861.56270.2166	176	2-Amino-4-(tert)-butylphenol	0.37	0.3471	1.0426		
$178$ 3,5-Di-( <i>tert</i> )-butylcatechol2.112.10322.1321 $179$ 3-Aminophenol-0.520.67630.4105 $180$ 3-Methylcatechol0.280.38890.2381 $181$ 4-Acetamidophenol-0.820.18540.0424 $182$ 4-Amino-2,3-dimethylphenol1.441.39200.0618 $183$ 4-Aminophenol-0.080.02920.0845 $184$ 4-Aminophenol-0.080.02920.0845 $185$ 4-Chlorocatechol1.060.86530.7061 $186^a$ 4-Methylcatechol0.370.66420.2757 $187$ 5-Amino-2-methoxyphenol0.450.4527-0.1456 $188$ 5-Chloro-2-hydroxyaniline0.780.78090.7450 $190$ Bromohydroquinone1.681.74390.8086 $191^a$ Catechol0.750.2268-0.0938 $192$ Chlorohydroquinone1.260.81430.3379 $193$ Hydroquinone0.470.3551-0.0659 $194$ Methoxyhydroquinone2.200.8448-0.0157 $195$ Methylydroquinone1.861.56270.2166	177	2-Aminophenol	0.94	1.0797	0.0342		
1795-Animophenol $-0.32$ $0.3705$ $0.4103$ 1803-Methylcatechol $0.28$ $0.3889$ $0.2381$ 1814-Acetamidophenol $-0.82$ $0.1854$ $0.0424$ 1824-Amino-2,3-dimethylphenol $1.44$ $1.3920$ $0.0618$ 1834-Amino-2-cresol $1.31$ $1.2952$ $0.2362$ 1844-Aminophenol $-0.08$ $0.0292$ $0.0845$ 1854-Chlorocatechol $1.06$ $0.8653$ $0.7061$ 186 <sup>a</sup> 4-Methylcatechol $0.37$ $0.6642$ $0.2757$ 1875-Amino-2-methoxyphenol $0.45$ $0.4527$ $-0.1456$ 1885-Chloro-2-hydroxyaniline $0.78$ $0.7809$ $0.7450$ 1896-Amino-2,4-dimethylphenol $0.89$ $0.9603$ $0.4623$ 190Bromohydroquinone $1.68$ $1.7439$ $0.8086$ 191 <sup>a</sup> Catechol $0.75$ $0.2268$ $-0.0938$ 192Chlorohydroquinone $0.47$ $0.3551$ $-0.0659$ 193Hydroquinone $0.47$ $0.3551$ $-0.0659$ 194Methoxyhydroquinone $2.20$ $0.8448$ $-0.0157$ 195Methylhydroquinone $1.86$ $1.5627$ $0.2166$	178	3,5-Di-( <i>tert</i> )-butylcatechol	2.11	2.1032	2.1321		
1003 Acctamidophenol0.1200.18030.12041814-Acctamidophenol $-0.82$ $0.1854$ $0.0424$ 1824-Amino-2,3-dimethylphenol $1.44$ $1.3920$ $0.0618$ 1834-Aminophenol $-0.08$ $0.0292$ $0.2362$ 1844-Aminophenol $-0.08$ $0.0292$ $0.0845$ 1854-Chlorocatechol $1.06$ $0.8653$ $0.7061$ 186 <sup>a</sup> 4-Methylcatechol $0.37$ $0.6642$ $0.2757$ 1875-Amino-2-methoxyphenol $0.45$ $0.4527$ $-0.1456$ 1885-Chloro-2-hydroxyaniline $0.78$ $0.7809$ $0.7450$ 1896-Amino-2,4-dimethylphenol $0.89$ $0.9603$ $0.4623$ 190Bromohydroquinone $1.68$ $1.7439$ $0.8086$ 191 <sup>a</sup> Catechol $0.75$ $0.2268$ $-0.0938$ 192Chlorohydroquinone $0.47$ $0.3551$ $-0.0659$ 193Hydroquinone $0.47$ $0.3551$ $-0.0659$ 194Methoxyhydroquinone $2.20$ $0.8448$ $-0.0157$ 195Methylhydroquinone $1.86$ $1.5627$ $0.2166$	180	3-Methylcatechol	0.32	0.3889	0.4103		
1824-Amino-2,3-dimethylphenol1.441.39200.06181834-Amino-2-cresol1.311.29520.23621844-Aminophenol-0.080.02920.08451854-Chlorocatechol1.060.86530.7061186 <sup>a</sup> 4-Methylcatechol0.370.66420.27571875-Amino-2-methoxyphenol0.450.4527-0.14561885-Chloro-2-hydroxyaniline0.780.78090.74501896-Amino-2,4-dimethylphenol0.890.96030.4623190Bromohydroquinone1.681.74390.8086191 <sup>a</sup> Catechol0.750.2268-0.0938192Chlorohydroquinone1.260.81430.3379193Hydroquinone0.470.3551-0.0659194Methoxyhydroquinone2.200.8448-0.0157195Methylydroquinone1.861.56270.2166	181	4-Acetamidophenol	-0.82	0.1854	0.0424		
1834-Amino-2-cresol1.311.29520.23621844-Aminophenol-0.080.02920.08451854-Chlorocatechol1.060.86530.7061186a4-Methylcatechol0.370.66420.27571875-Amino-2-methoxyphenol0.450.4527-0.14561885-Chloro-2-hydroxyaniline0.780.78090.74501896-Amino-2,4-dimethylphenol0.890.96030.4623190Bromohydroquinone1.681.74390.8086191aCatechol0.750.2268-0.0938192Chlorohydroquinone1.260.81430.3379193Hydroquinone0.470.3551-0.0659194Methoxyhydroquinone2.200.8448-0.0157195Methylydroquinone1.861.56270.2166	182	4-Amino-2,3-dimethylphenol	1.44	1.3920	0.0618		
1844-Aminophenol-0.080.02920.08451854-Chlorocatechol1.060.86530.70611864-Methylcatechol0.370.66420.27571875-Amino-2-methoxyphenol0.450.4527-0.14561885-Chloro-2-hydroxyaniline0.780.78090.74501896-Amino-2,4-dimethylphenol0.890.96030.4623190Bromohydroquinone1.681.74390.8086191aCatechol0.750.2268-0.0938192Chlorohydroquinone1.260.81430.3379193Hydroquinone0.470.3551-0.0659194Methoxyhydroquinone2.200.8448-0.0157195Methylkydroquinone1.861.56270.2166	183	4-Amino-2-cresol	1.31	1.2952	0.2362		
1854-Chlorocatechol1.06 $0.8653$ $0.7061$ 186°4-Methylcatechol $0.37$ $0.6642$ $0.2757$ 1875-Amino-2-methoxyphenol $0.45$ $0.4527$ $-0.1456$ 1885-Chloro-2-hydroxyaniline $0.78$ $0.7809$ $0.7450$ 1896-Amino-2,4-dimethylphenol $0.89$ $0.9603$ $0.4623$ 190Bromohydroquinone $1.68$ $1.7439$ $0.8086$ 191°Catechol $0.75$ $0.2268$ $-0.0938$ 192Chlorohydroquinone $1.26$ $0.8143$ $0.3379$ 193Hydroquinone $0.47$ $0.3551$ $-0.0659$ 194Methoxyhydroquinone $2.20$ $0.8448$ $-0.0157$ 195Methylhydroquinone $1.86$ $1.5627$ $0.2166$	184	4-Aminophenol	-0.08	0.0292	0.0845		
1804-Methyladechol $0.37$ $0.2757$ 1875-Amino-2-methoxyphenol $0.45$ $0.4527$ $-0.1456$ 1885-Chloro-2-hydroxyaniline $0.78$ $0.7809$ $0.7450$ 1896-Amino-2,4-dimethylphenol $0.89$ $0.9603$ $0.4623$ 190Bromohydroquinone $1.68$ $1.7439$ $0.8086$ 191 <sup>a</sup> Catechol $0.75$ $0.2268$ $-0.0938$ 192Chlorohydroquinone $1.26$ $0.8143$ $0.3379$ 193Hydroquinone $0.47$ $0.3551$ $-0.0659$ 194Methoxyhydroquinone $1.26$ $1.5627$ $0.2166$	185 196 <sup>a</sup>	4-Chlorocatechol	1.06	0.8653	0./061	0.6642	0 2757
1885-Chloro-2-hydroxyaniline0.780.78090.74501896-Amino-2,4-dimethylphenol0.890.96030.4623190Bromohydroquinone1.681.74390.8086191aCatechol0.750.2268-0.0938192Chlorohydroquinone1.260.81430.3379193Hydroquinone0.470.3551-0.0659194Methoxyhydroquinone1.861.56270.2166	187	5-Amino-2-methoxyphenol	0.45	0.4527	-0.1456	0.0042	0.2737
$      \begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$	188	5-Chloro-2-hydroxyaniline	0.78	0.7809	0.7450		
190Bromohydroquinone $1.68$ $1.7439$ $0.8086$ 191aCatechol $0.75$ $0.2268$ $-0.0938$ 192Chlorohydroquinone $1.26$ $0.8143$ $0.3379$ 193Hydroquinone $0.47$ $0.3551$ $-0.0659$ 194Methoxyhydroquinone $2.20$ $0.8448$ $-0.0157$ 195Methylhydroquinone $1.86$ $1.5627$ $0.2166$	189	6-Amino-2,4-dimethylphenol	0.89	0.9603	0.4623		
191" Catechol       0.75       0.2268       -0.0938         192 Chlorohydroquinone       1.26       0.8143       0.3379         193 Hydroquinone       0.47       0.3551       -0.0659         194 Methoxyhydroquinone       2.20       0.8448       -0.0157         195 Methylhydroquinone       1.86       1.5627       0.2166	190	Bromohydroquinone	1.68	1.7439	0.8086	0.00.00	0.0000
192       Chloronydroquinone       1.20       0.8143       0.3579         193       Hydroquinone       0.47       0.3551       -0.0659         194       Methoxyhydroquinone       2.20       0.8448       -0.0157         195       Methylhydroquinone       1.86       1.5627       0.2166	191 <sup>a</sup>	Catechol	0.75	0.9142	0 2270	0.2268	-0.0938
194         Methoxyhydroquinone         2.20         0.8448         -0.0157           195         Methylhydroquinone         1.86         1.5627         0.2166	192 103	Unoronyaroquinone Hydroquinone	1.20	0.8143	0.3379		
195 Methylhydroguinone 1.86 1.5627 0.2166	194	Methoxyhydroquinone	2.20	0.8448	-0.0157		
	195	Methylhydroquinone	1.86	1.5627	0.2166		

A/A	Name	log(1/IGC <sub>50</sub> )	g(1/IGC <sub>50</sub> ) Training set		Validation set		
			RBF $R^2 = 0.9424$	MLR $R^2 = 0.6022$	RBF $R^2 = 0.8824$	MLR $R^2 = 0.786$	
196	Phenylhydroquinone	2.01	2.0494	1.4188			
197	Tetrachlorocatechol	1.700	1.6398	2.3871			
198	Trimethylhydroquinone	1.34	1.0404	0.7284			
199	2,6-Dibromo-4-nitrophenol	1.36	1.2960	1.3558			
200	2-Amino-4-chloro-5-nitrophenol	1.17	1.1656	1.3096			
201	2-Amino-4-nitrophenol	0.48	0.5334	1.0231			
202	2-Chloro-4-nitrophenol	1.59	1.4875	0.8898			
203	2-Chloromethyl-4-nitrophenol	0.75	1.0330	0.7947			
204	2-Nitrophenol	0.67	0.8831	0.6586			
205	2-Nitroresorcinol	0.66	0.6898	1.1367			
206 <sup>a</sup>	3-Fluoro-4-nitrophenol	0.94	0.3165		0.9997	0.4381	
207	3-Hydroxy-4-nitrobenzaldehyde	0.27	0.3165	0.6154			
208	3-Methyl-4-nitrophenol	1.73	1.3591	0.6877			
209	3-Nitrophenol	0.51	0.4308	0.6024			
210	4-Amino-2-nitrophenol	0.88	0.8491	1.0359			
211	4-Chloro-2-nitrophenol	2.05	2.0047	1.3347			
212	4-Chloro-6-nitro-3-cresol	1.64	1.5944	1.6378			
213	4-Hydroxy-3-nitrobenzaldehyde	0.61	0.6226	0.4118			
214	4-Methyl-2-nitrophenol	0.57	0.6544	1.1031			
215	4-Methyl-3-nitrophenol	0.74	0.7122	1.0180			
216	4-Nitro-3-(trifluoromethyl)-phenol	1.65	1.5893	1.0526			
217	4-Nitrocatechol	1.17	1.1431	0.9175			
218	4-Nitrophenol	1.42	1.4467	0.4263			
219	4-Nitrosophenol	0.65	0.5828	0.3104			
220	5-Fluoro-2-nitrophenol	1.13	1.2294	0.7792			
221	5-Hydroxy-2-nitrobenzaldehyde	0.33	0.1427	0.5858			

<sup>a</sup>Compounds used in the validation set

nodes are activated when an input vector is presented to the NN model.

(iii) The connection weights are determined using linear regression between the hidden-layer responses and the corresponding output training set.

# **Results**

In order to evaluate and compare the performance of the **RBF** training methodology presented in this work, the data set was initially split into a training and a validation set in a ratio of approximately 80:20% (180 and 41 compounds, respectively). For that, the Kennard and Stones algorithm [24] was used. The Kennard–Stones algorithm has gained increasing popularity for splitting data sets into two subsets. The algorithm starts by finding two samples that are the farthest apart from each other on the basis of the input variables in terms of some metric, e.g., the Euclidean distance. These two samples are removed from the original data set and put into the calibration data set. The procedure described is repeated until the desired number of samples has been reached in the calibration set. The advantages of this algorithm are that the calibration samples map the measured region of the variable space completely with respect to the induced metric and that the test samples all fall inside the measured region. The training and validation compounds are clearly indicated in Table 1. Both RBF network and MLR models were developed based on exactly the same training set. The validation set was not involved in any way during the training phase. The results are shown in Table 1, where the predictions of the two models are shown for both the training and the external examples. The same results are shown in a graphical format in Figs. 1, 2, 3 and 4, where the experimental toxicity is plotted against the predictions of the RBF network and the MLR model. In each figure the corresponding coefficients of determination ( $R^2$ -value) are presented, which indicate a much higher correlation between experimental and predicted values using the RBF network methodology. The full linear equation for the prediction of toxicity is the following:

$$\begin{split} log1/IGC_{50} = & 0.5617 logK_{ow} + 0.0026 pK_{a} - 0.8792 E_{LUMO} \\ & + 0.7995 E_{HUMO} + 0.2734 N_{hdon} + 6.2044, \\ & n = & 180, R^{2} = & 0.6022, RMS = & 0.5352. \end{split}$$

. .....

To compare the performance of the modeling schemes further, their predictive ability was also evaluated by the leave-one-out (LOO) cross-validation procedure. A number of modified data sets were created by deleting in each case one object from the data. An RBF network and an MLR model were developed in each case based on the remaining data and were validated using the object that had been deleted. Consequently, 221 RBF networks and MLR models were built, by deleting each time one compound from the training set.

# Table 1 (contd.)



**Fig. 1** Experimental versus predicted toxicity using the RBF methodology for the training set (180 compounds)

Figures 5 and 6 show the experimental toxicity versus the predictions produced by the RBF NN models and the multiple regression technique, using the LOO cross validation procedure. The corresponding coefficients of determination  $R_{CV}^2$  indicate again that the models derived from the RBF methodology have a higher predictive potential. The comparison between the RBF and the MLR methods is summarized in Table 2. In all cases, the RBF models proved to be remarkably more accurate than the MLR models. The predictive abilities of both modeling techniques can be improved if different models are developed for each one of the several different mechanisms of action, but in this paper we concentrated on building a single model for each methodology that can predict toxicity for the variety of mechanisms that are included in the data set.



Fig. 3 Experimental versus predicted toxicity using the RBF methodology for the test set (41 compounds)



Fig. 2 Experimental versus predicted toxicity using the MLR methodology for the training set (180 compounds)

It should finally be noted that the MATLAB programming language was used to implement all the training and testing procedures. The computational time required to build the NN models in a Pentium IV 3 GHz processor was always less than 0.2 s. It should also be emphasized that the RBF training method has been developed in-house, so no commercial packages were used to develop the NN models. The complete QSTR models can be made available to the interested readers.

#### **Discussion and conclusions**

In this work, we presented a novel QSTR methodology based on the RBF NN architecture. The method was illustrated using a data set of 221 phenols and compared



Fig. 4 Experimental versus predicted toxicity using the MLR methodology for the test set (41 compounds)

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 Table 2 Summary of the results

 produced by the different

 methods

Method	Training set	Validation set	$R^2_{\text{train}}$	$R^2_{\rm pred}$	RMS	RMS <sub>pred</sub>	Figure
RBF	180	41	0.9424		0.2037		1
MLR	180	41	0.6022		0.5352		2
RBF	180	41		0.8824		0.2398	3
MLR	180	41		0.7861		0.3197	4
RBF LOO	221- <i>i</i>	221– <i>i</i>		0.7203		0.4350	5
MLR LOO	221- <i>i</i>	221 <i>—i</i>		0.6010		0.5194	6



**Fig. 5** Experimental versus predicted toxicity with cross validation (RBF methodology)



Fig. 6 Experimental versus predicted toxicity with cross validation (MLR methodology)

with standard MLR. Validation of the different QSTR methodologies was based on two evaluation procedures. In the first method the data were split into a training and a validation set and the model generated using the training set was used to predict toxicity in the validation set. The second method was the standard LOO cross-

validation procedure. The modeling procedures used in this work illustrated the accuracy of the models produced, not only by calculating their fitness on sets of training data but also by testing the predicting abilities of the models.

The RBF NN models were produced based on the fuzzy-means training method, which is fast and repetitive, in contrast to most traditional training techniques. The model generated for the data set required five descriptors. In terms of the  $R^2$ ,  $R_{cv}^2$  and RMS values, the RBF models proved to have a significant predictive potential. The results obtained illustrated that the RBF NN architecture can be used to derive QSTRs, which are more accurate and have better generalization capabilities compared to linear regression models at the expense of the increased complexity of the model compared to a simple structure of a linear model. The method proposed could be a substitute to costly and time-consuming experiments for determining toxicity.

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