ISSN: 0974 - 7516 Volume 7 Issue 1

Trade Science Inc.

Organic CHEMISTRY

An Indian Journal

Full Paper

OCAIJ, 7(1), 2011 [41-47]

Hardness based quantitative structure toxicity relationship (QSTR) study on a series of aliphatic alcohol derivatives

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Received: 8th July, 2010 ; Accepted: 18th July, 2010

ABSTRACT

The quantitative structure toxicity relationship of 89 derivatives of alcohol have been studied with the help of total energy, absolute hardness and electronegativity. The alcohols have been divided into four groups. The first group consists of derivatives of amino alcohol, second consists of derivatives of diol, the third and fourth respectively consist of derivatives of halogenated and unsaturated alcohols. A direct relationship between the toxicity of all groups of alcohols and electronegativity has been observed. The QSTR model of all the four sets have been developed. The best QSTR model of first and second set of compounds have correlation coefficient value above 0.94 and 0.7 respectively, which has been derived by combination of all the three descriptors. The best QSTR model of third set and fourth set of compounds have correlation coefficient value above 0.86 and 0.65 respectively, which has been derived by combination of descriptors consisting total energy, absolute hardness and electronegativity. The absolute hardness is one of the most significant descriptor for searching the low toxicity of alcohols.

KEYWORDS

Alcohols;
Toxicity;
QSTR;
Tetrahymena pyriformis;
Absolute hardness.

INTRODUCTION

QSAR study of phenols with the help of quantum mechanical parameter has recently been made by Singh et al[1]. They developed QSAR models having high degree of predicted power with correlation coefficient value above 0.88. QSAR[2-5] has become increasingly helpful in understanding many aspect of chemical biological activity in drug research and pharmacological sciences[6]. QSAR has gained importance in hydroxyl group of alcohols also. Success of QSAR is not limited to development of new drugs, but also in exploring the toxicological and ecotoxicological characterstic of compound. Recently QSTR study of large number of organic molecules were further studied by Singh et al, using different type of descriptors[7]. The models provided correlation coefficient above 0.9.

The hydroxyl group of alcohols has wide range of cellular activities and are important target for study of toxicity. In the present work QSTR study of 89 derivative of alcohol, whose toxicity against tetrahymena pyriformis is reported[8]. has been made. The QSTR study of derivatives of alcohol has been made with the help of quantum mechnical parameter such as, total energy (ET) absolute hardness (η) and electronegativity(χ). The biological toxicity of alcohol derivatives has been reported by four different methods of inhibitory growth concentration[9-12]. The derivatves accordingly have been

studied in four sets and also indicates a relationship between absolute hardness and inhibitory growth concentration.

EXPERIMENTAL

The study materials of this paper are 89 derivatives of aliphatic alcohol, which have been divided in four sets on the basis of different inhibitory growth measurement. For QSTR prediction, the 3D modeling and geometery optimization of all the compounds have been done with the help of PCModel software using PM3 hamiltonian[13]. The MOPAC calculations have been performed with WINMOPAC 7.21 software, by applying keywords PM3 Charge=0 Gnorm=0.1, Bonds, Geo-OK, Vectors density. The four sets of compounds are listed in TABLE 1-4. The values of total energy, absolute hardness and electronegativity have been obtained from this software by solving the equations given below and the results are included in TABLE 1-4.

TABLE 1 : Amino alcohols and their observed toxicity (IGC_{50}) and predicted toxicity against tetrahymena pyriformis

No.	Compounds	IGC_{50}	E_T	η	χ	$1P_{Toxicity}$	$2P_{Toxicity}$
1	2-(Methylamino)ethanol	-1.8202	-44.455	5.955	-3.338	-1.67	-1.692
2	4-Amino-1-butanol	-0.9752	-51.636	6.134	-3.294	-0.875	-0.992
3	2-(Ethylamino)ethanol	-1.6491	-51.605	5.905	-3.347	-1.729	-1.697
4	2-Propylaminoethanol	-1.6842	-58.766	5.896	-3.364	-1.636	-1.607
5	DL-2-Amino-1-pentanol	-0.6718	-58.793	6.119	-3.237	-0.805	-0.788
6	3-Amino-2,2-dimethyl-1-propanol	-0.9246	-58.811	6.123	-3.329	-0.788	-0.938
7	6-Amino-1-hexanol	-0.958	-65.955	6.137	-3.272	-0.61	-0.656
8	DL-2-Amino-1-hexanol	-0.5848	-65.953	6.113	-3.245	-0.701	-0.675
9	DL-2-Amino-3-methyl-1-butanol	-0.5852	-58.795	6.109	-3.214	-0.842	-0.773
10	2-Amino-3,3-dimethyl-butanol	-0.7178	-65.961	6.1	-3.218	-0.749	-0.661
11	2-Amino-3-methyl-1-pentanol	-0.6594	-65.95	6.115	-3.228	-0.695	-0.641
12	2-Amino-4-methyl-pentanol	-0.6191	-65.953	6.097	-3.234	-0.759	-0.696
13	2-(tert-Butylamino)ethanol	-1.673	-65.923	5.893	-3.38	-1.521	-1.501
14	Diethanolamine	-1.7941	-63.781	5.875	-3.485	-1.627	-1.777
15	1,3-Diamino-2-hydroxy-propane	-1.4275	-53.851	5.953	-3.366	-1.512	-1.559
16	N-Methyldiethanol amine	-1.8338	-70.902	5.753	-3.49	-1.956	-1.97
17	3-(Methylamino)-1,2-propanediol	-1.5341	-63.784	5.854	-3.276	-1.704	-1.464
18	Triethanolamine	-1.7488	-90.224	5.735	-3.572	-1.682	-1.774

IGC_{50} - 50% inhibitory growth concentration, E_T, η, χ are total energy, absolute hardness, electronegativity

In DFT, the electronegativity, commonly known to a chemist, is define as the negative of a partial derivative of energy E of an atomic or molecular system with respect to the number of electrons N with a constant external potential $_{v(r)}$[14].

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

In accordance with the earlier work of Iczkowski and Margrave,[15] it should be stated that when assuming a quadratic relationship between E and N and in a finite difference approximation, Eq. 1 may be rewritten as

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

where IE and EA are the vertical ionization energy and electron affinity, respectively, thereby recovering the electronegativity definition of Mulliken.[16] Moreover, a theoretical justification was provided for Sandersons principle of electronegativity equalization, which states that when two or more atoms come together to form a molecule, their electronegativities become adjusted to the same intermediate value.[17-19] The absolute hardness η is define as[20]

$$\eta = 1/2\ (\delta\mu / \delta N)_{v(r)} = 1/2\ (\delta 2E / \delta N2)_{v(r)} \quad (3)$$

where E is the total enegy, N is the number of electrons of the chemical species, and $_{v(r)}$ is the extenal potential.

TABLE 2 : Acetylenic alcohols and diols & their and toxicity (IGC_{50}) and predicted toxicity against tetrahymena pyriformis

No.	Compounds	IGC_{50}	E_T	η	χ	$3P_{Toxicity}$	$4P_{Toxicity}$
1	3-Butyn-2-ol	-0.4024	-38.564	6.28	-4.513	-1.038	-1.166
2	1-Pentyn-3-ol	-1.1776	-45.723	6.256	-4.669	-0.222	-0.412
3	2-Pentyn-1-ol	-0.5724	-45.779	5.932	-4.27	-1.516	-1.254
4	2-Penten-4-yn-1-ol	-0.5549	-43.915	4.942	-4.621	-0.456	0.132
5	1-Hexyn-3-ol	0.6574	-45.723	6.256	-4.669	-0.222	-0.412
6	1-Heptyn-3-ol	-0.265	-60.043	6.257	-4.679	0.425	0.286
7	4-Heptyn-3-ol	-0.0336	-60.093	6.049	-4.328	-0.713	-0.498
8	2-Octyn-1-ol	0.1944	-67.259	6.007	-4.328	-0.403	-0.136
9	4-Methyl-1-pentyn-3-ol	-0.0267	-52.887	6.228	-4.64	-0.008	-0.133
10	4-Methyl-1-heptyn-3-ol	0.7426	-67.204	6.205	-4.633	0.585	0.536
11	(±)-1,2-Butanediol	-2.0482	-38.564	6.28	-4.513	-1.038	-1.166
12	(±)-1,3-Butanediol	-2.3013	-54.419	6.919	-3.987	-2.063	-2.144
13	1,4-Butanediol	-2.2365	-54.429	6.917	-3.978	-2.093	-2.166
14	1,2-Pentanediol	-1.6269	-61.581	6.92	-4.044	-1.569	-1.659
15	1,5-Pentanediol	-1.9344	-61.589	6.915	-3.973	-1.799	-1.839
16	2-Methyl-2,4-pentanediol	-1.9531	-68.724	6.915	-3.988	-1.443	-1.464
17	(±)-1,2-Hexanediol	-1.2669	-68.741	6.912	-4.051	-1.238	-1.3
18	1,6-Hexanediol	-1.4946	-68.749	6.922	-3.974	-1.489	-1.505

IGC_{50} - 50% inhibitory growth concentration, E_T, η, χ are total energy, absolute hardness, electronegativity

TABLE 3 : Halogenated and saturated alcohols and their observed toxicity (IGC_{50}) & predicted toxicity against tetrahymena pyriformis

No.	Compounds	IGC_{50}	E_T	η	χ	$5P_{Toxicity}$	$6P_{Toxicity}$
1	2-Bromoethanol	-0.3538	-37.783	5.375	-5.677	-1.342	-0.575
2	2-Chloroethanol	-1.5343	-39.654	5.804	-4.706	-1.327	-1.489
3	1-Chloro-2-propanol	-1.2446	-46.808	5.799	-4.675	-1.033	-1.2
4	3-Chloro-1-propanol	-1.1622	-46.816	5.809	-4.639	-1.034	-1.242
5	4-Chloro-1-butanol	-0.5329	-53.976	5.817	-4.633	-0.743	-0.905
6	3-Chloro-2,2-dimethyl-1-propanol	-0.8568	-61.151	5.793	-4.563	-0.446	-0.689
7	6-Chloro-1-hexanol	-0.353	-68.296	5.819	-4.613	-0.157	-0.255
8	8-Chloro-1-octanol	-0.1879	-82.616	5.82	-4.606	0.429	0.412
9	6-Bromo-1-hexanol	0.5721	-66.426	5.383	-5.563	-0.171	0.622
10	2,3-Dibromopropanol	-0.9264	-56.975	4.639	-5.251	-0.452	-0.967
11	Methyl alcohol	-2.6656	-20.788	7.323	-3.815	-2.316	-2.253
12	Ethyl alcohol	-1.9912	-27.933	7.116	-3.782	-1.994	-2.155
13	1-Propanol	-1.7464	-35.093	7.056	-3.827	-1.692	-1.808
14	2-Propanol	-1.8819	-35.088	7.157	-3.881	-1.707	-1.637
15	1-Butanol	-1.4306	-42.253	7.023	-3.864	-1.395	-1.447
16	(±)-2-Butanol	-1.542	-42.243	7.106	-3.906	-1.407	-1.31
17	2-Methyl-1-propanol	-1.3724	-42.259	7.063	-3.85	-1.4	-1.431
18	2-Pentanol	-1.1596	-49.405	7.076	-3.922	-1.11	-0.977
19	3-Pentanol	-1.2437	-49.402	7.025	-3.897	-1.102	-1.059
20	3-Methyl-2-butanol	-0.9959	-49.407	7.082	-3.915	-1.11	-0.981
21	tert-Amylalcohol	-1.1729	-49.432	7.051	-3.855	-1.105	-1.095
22	2-Methyl-1-butanol	-0.9528	-49.415	7.033	-3.875	-1.103	-1.085
23	3-Methyl-1-butanol	-1.0359	-49.417	6.968	-3.814	-1.094	-1.232
24	2,2-Dimethyl-1-propanol	-0.8702	-49.432	7.051	-3.855	-1.105	-1.095
25	2-Methyl-2-propanol	-1.7911	-42.259	7.063	-3.85	-1.4	-1.431
26	1-Hexanol	-0.3789	-56.573	6.987	-3.903	-0.804	-0.748
27	3,3-Dimethyl-1-butanol	-0.7368	-56.587	6.927	-3.791	-0.794	-0.965
28	4-Methyl-1-pentanol	-0.6372	-56.578	6.982	-3.869	-0.803	-0.803
29	1-Heptanol	0.105	-63.733	6.977	-3.915	-0.509	-0.402
30	2,4-Dimethyl-3-pentanol	-0.7052	-63.726	6.905	-3.877	-0.499	-0.524

IGC_{50} - 50% inhibitory growth concentration, E_T, η, χ are total energy, absolute hardness, electronegativity

The operational definition of absolute hardness and electronegativity is given as

$$\eta = 1/2(IE - EA) \quad (4)$$

$$\chi = -\mu = -(IE + EA)/2 \quad (5)$$

where IE and EA are the ionization energy and electron affinity, respectively, of the chemical species. According to Koopman's theorem, the IP is simply the eigenvalue of HOMO with change of sign and EA is eigenvalue of LUMO with change of sign; hence Eqs. 3 and 4 may be written as

$$\eta = 1/2(\varepsilon LUMO - \varepsilon HOMO) \quad (6)$$

$$\chi = -\mu = 1/2(\varepsilon LUMO + \varepsilon HOMO) \quad (7)$$

With regard to QSTR of a chemical system, the total energy also played an important role. The total energy of a molecular system is sum of the total electronic energy (E_{ee}) and the energy energy of the internuclear repulsion (E_{nr}).The total electronic energy of the system is given by[21]

$$TE = 1/2\ P(H+F) \quad (8)$$

where P is the density matrix and H is the one-electron matrix.

RESULT AND DISCUSSION

The biological toxicity of alcohol derivatives has been reported by four different parameters. The alcohol derivatives are accordingly divided in four different sets, which is along with their reported biological toxicity are

TABLE 4 : Unsaturated alcohols and their observed toxicity (IGC_{50}) and predicted toxicity against tetrahymena pyriformis

No.	Compounds	IGC_{50}	E_T	η	χ	$7P_{Toxicity}$	$8P_{Toxicity}$
1	2-Methyl-3-buten-2-ol	-1.3889	-47.57	5.731	-4.538	-1.271	-1.274
2	4-Pentyn-1-ol	-1.4204	-45.736	6.321	-4.488	-1.505	-1.502
3	2-Methyl-3-butyn-2-ol	-1.3114	-45.731	6.388	-4.59	-1.52	-1.521
4	trans-3-Hexen-1-ol	-0.7772	-54.754	5.335	-4.281	-0.775	-0.772
5	5-Hexyn-1-ol	-1.2948	-52.896	6.315	-4.477	-1.097	-1.095
6	3-Methyl-1-pentyn-3-ol	-1.3226	-52.886	6.374	-4.729	-1.11	-1.119
7	4-Hexen-1-ol	-0.754	-54.754	5.353	-4.293	-0.779	-0.777
8	5-Hexen-1-ol	-0.8411	-54.734	5.602	-4.462	-0.835	-0.838
9	4-Pentyn-2-ol	-1.6324	-45.729	6.298	-4.512	-1.5	-1.498
10	5-Hexyn-3-ol	-1.4043	-52.884	6.332	-4.397	-1.101	-1.096
11	3-Heptyn-1-ol	-0.3231	-60.107	5.971	-4.293	-0.611	-0.606
12	4-Heptyn-2-ol	-0.616	-60.1	6.006	-4.298	-0.619	-0.614
13	3-Octyn-1-ol	0.017	-67.267	5.97	-4.296	-0.204	-0.201
14	2-Propen-1-ol	-1.9178	-33.253	5.571	-4.499	-2.049	-2.048
15	2-Buten-1-ol	-1.4719	-40.433	5.336	-4.328	-1.589	-1.585
16	(±)-3-Buten-2-ol	-1.0529	-40.409	5.673	-4.6	-1.665	-1.669
17	cis-2-Buten-1,4-diol	-2.1495	-52.608	5.307	-4.377	-0.891	-0.892
18	cis-2-Penten-1-ol	-1.1052	-47.593	5.324	-4.3	-1.18	-1.176
19	3-Penten-2-ol	-1.401	-47.592	5.424	-4.399	-1.202	-1.201
22	trans-2-Hexen-1-ol	-0.4718	-54.753	5.323	-4.301	-0.772	-0.771
21	1-Hexen-3-ol	-0.8113	-54.728	5.7	-4.849	-0.857	-0.876
22	cis-2-Hexen-1-ol	-0.7767	-54.753	5.323	-4.301	-0.772	-0.771
23	trans-2-Octen-1-ol	0.3654	-69.073	5.322	-4.306	0.042	0.039

IGC_{50} - 50% inhibitory growth concentration, E_T, η, χ are total energy, absolute hardness, electronegativity

presented in TABLE 1-4. Each table is divided into subgroups in order to demonstrate better and sequential relationship between the biological toxicity and reactivity parameters. The observed biological toxicity in each table has been arranged in increasing order. The reactivity indices such as total energy (ET) absolute hardness(η) and electronegativity(χ) of the corresponding alcohol derivatives are also presented in the table. The discussion has been made under two captions:-

1. Relationship with reactivity indices
2. QSTR model

Relationship with reactivity indices

First set

The first set contain 18 amino alcohol derivatives and their biological toxicity has been measured in terms of 50% inhibitory growth concentration.The reactivity indices along with biological toxicity of this set of compounds are placed in TABLE 1. A close look of this table indicates that toxicity increases by increasing the carbon chain in homologous series and decreases by the addition of alkyl amino group (R-NH_2). (R= CH_3 or C_2H_5 or C_3H_7). Except with absolute hardness where there is direct relatively, there appears no relationship of toxicity with other reactivity indices. Since there is direct relationship of toxicity with absolute hardness, the values have been separately tabulated in TABLE 5 and for sequential representation the table have been divided in three subgroups A, B and C. Compound **(5)**, **(6)** and **(13)** do not follow the sequential trend.

Second set

The second set contain 18 acetylenic alcohol and diol derivatives and their reported biological toxicity has been reported in terms of 50% inhibitory growth concentration. The reactivity indices along with biological toxicity of this set of compounds are placed in TABLE 2. A close look of this table indicates that the toxicity decreases when two hydroxyl (-OH) group are attached at one carbon atom i.e. diol derivatives and toxicity increases by the addition of double/triple bond. Only the absolute hardness shows direct relationship, the other reactivity indices show no relationship. There is a inverse relationship between absolute hardness and ob-

TABLE 5 : Relationship between absolute hardness and toxicity of first set

Compd. No	η	T
SUBGROUP-A		
16	5.753	-1.8338
14	5.875	-1.7941
4	5.896	-1.6842
3	5.905	-1.6491
15	5.953	-1.4275
12	6.097	-0.6191
9	6.109	-0.5852
8	6.113	-0.5848
SUBGROUP-B		
18	5.735	-1.7488
17	5.854	-1.5341
10	6.100	-0.7178
11	6.115	-0.6594
SUBGROUP-C		
1	5.955	-1.8202
2	6.134	-0.9752
7	6.137	-0.958

η is absolute hardness and T is reported toxicity in tems of 50% inhibitory growth concentration for tetrahymena pyriformis

TABLE 6 : Relationship between absolute hardness and toxicity of second set

Compd. No	η	T
SUBGROUP-A		
12	6.919	-2.3013
13	6.917	-2.2365
16	6.915	-1.9531
17	6.912	-1.2669
1	6.280	-0.4024
6	6.257	-0.265
9	6.228	-0.0267
10	6.205	0.7426
SUBGROUP-B		
11	6.280	-2.0482
2	6.256	-1.1776
7	6.049	-0.0336
8	6.007	0.1944
SUBGROUP-C		
15	6.915	-1.9344
3	5.932	-0.5724
4	4.942	-0.5549

η is absolute hardness and T is reported toxicity in tems of 50% inhibitory growth concentration for tetrahymena pyriformis

served toxicity. In order to demonstrate the relationship, the values of absolute hardness and toxicity are placed in TABLE 6, and for sequential representation the table has been further divided into three subgroups- A, B and C. Compounds **(5)**, **(14)** and **(18)** do not follow this trend.

Third set

Third set of derivatives contains 30 halogenated alcohol and saturated alcohol derivatives and their reported biological toxicity is shown in terms of 50% inhibitory growth concentration. The relationship between reported biological toxicity and electronegativity of this set are shown in TABLE 3. A close look at this table indicates that the toxicity increases by the addition of halo group (-Cl or -Br) and toxicity decreases by the decrease in the carbon chain of homologous series. In order to examin the relationship between reported biological toxicity and absolute hardness the values, are placed in TABLE 7. A reference to this table indicates that there is direct relationship between absolute hardness and reported biological toxicity. However, no sequential relationship is seen by the values presented in TABLE 7. In order to provide sequential relationship the table has been divided into four subgroups- A, B, C, D, E and F. Compound **(1)**, **(9)**, **(13)**, **(17)**, **(25)** and **(26)** do not follow sequential relationship.

TABLE 7 : Relationship between absolute hardness and toxicity of third set

Compd. No	η	T
SUBGROUP-A		
11	7.323	-2.6656
12	7.116	-1.9912
25	7.063	-1.7911
13	7.056	-1.7464
15	7.023	-1.4306
23	6.968	-1.0359
27	6.927	-0.7368
30	6.905	-0.7052
5	5.817	-0.5329
1	5.375	-0.3538
SUBGROUP-B		
14	7.157	-1.8819
16	7.106	-1.542
18	7.076	-1.1596
24	7.051	-0.8702
28	6.982	-0.6372
29	6.977	0.1050
9	5.383	0.5721
SUBGROUP-C		
17	7.063	-1.3724
21	7.051	-1.1729
22	7.033	-0.9528
26	6.987	-0.3789
8	5.820	-0.1879
SUBGROUP-D		
2	5.804	-1.5343
3	5.799	-1.2446
6	5.793	-0.8568

η is absolute hardness and T is reported toxicity in tems of 50% inhibitory growth concentration for tetrahymena pyriformis

Fourth set

Fourth set of derivatives contains 23 unsaturated alcohol derivatives and their reported biological toxic-

TABLE 8 : Relationship between absolute hardness and toxicity of fourth set

Compd. No	η	T
SUBGROUP-A		
10	6.332	-1.4043
1	5.731	-1.3889
16	5.673	-1.0529
8	5.602	-0.8411
7	5.353	-0.754
20	5.323	-0.4718
23	5.322	0.3654
SUBGROUP-B		
2	6.321	-1.4204
5	6.315	-1.2948
21	5.700	-0.8113
4	5.335	-0.7772
22	5.323	-0.7767
SUBGROUP-C		
9	6.298	-1.6324
12	6.006	-0.6160
11	5.971	-0.3231
13	5.970	0.0170
SUBGROUP-D		
14	5.571	-1.9178
15	5.336	-1.4719
19	5.424	-1.4010
18	5.324	-1.1052

η is absolute hardness and T is reported toxicity in tems of 50% inhibitory growth concentration for tetrahymena pyriformis

ity is in terms of 50% inhibitory growth concentration. The reported biological toxicity along with reactivity indices are given in TABLE 4. A close look at this table indicates that the toxicity increases by the addition of double/triple bond and the examination of this table also indicates that cis form of the compound show less toxicity. In order to examin the relationship between reported biological toxicity and absolute hardness the value are placed in TABLE 8. A close look at this table indicates that there is direct relationship between absolute hardness and reported biological toxicity. However, no sequential relationship is seen by the values presented in TABLE 8. In order to provide sequential relationship the table has been divided into four subgroups- A, B, C and D. Compound **(3)**, **(6)** and **(17)** do not follow sequential relationship.

QSTR models

The QSTR models of four groups of alcohol, have been developed separately in four sets. The quantitative values of descriptors (E_T, η, and χ) of all the sets of compounds have been evaluated with the help of PC Model software, using PM3 Hamiltonian and the results are included in TABLE 1-4 for the four sets, alongwith their reported values of toxicity. The QSTR study of each set is presented below:

First set

This set consists of eighteen derivatives of amino alcohol. The values of various descriptors of these compounds, in different combinations have been used for MLR analysis. The MLR analysis has been done by Project leader. The following four MLR equations providing high quality predictive toxicity are the following models:

RE1=-0.0176448 E_T +3.73144η-24.6745
r CV^2=0.895305 r^2=0.906387 (9)

RE2=-0.0200482 E_T +2.6751η+1.76358χ-12.6263
rC^2=0.891749 r^2=0.94147 (10)

The equ. 10 (RE2) provides best result (rC^2=0.891749 r^2=0.94147) and is treated as best QSTR model. This model includes total energy as first descriptor, absolute hardness as second and electronegativity as third descriptor.

Second set

This set consists of eighteen derivatives of acetylenic alcohol and diol derivatives. The values of various descriptors of these compounds, in different combinations have been used for MLR analysis. The following two MLR equations providing high quality predictive toxicity are the following models:

RE3=-0.0430362 E_T -3.24659χ-17.3497
rCV^2=0.48888 r^2=0.666245 (11)

RE4=-0.0470833 E_T -0.57337 η -2.58083χ-11.0288
rCV^2=0.314847 r^2=0.707338 (12)

The equ. 12 (RE4) provides best result (rCV^2=0.314847 r^2=0.707338) and is treated as best QSTR model. This model includes total energy as first descriptor, absolute hardness as second and electronegativity as third descriptor.

Third set

This set consists of thirty derivatives of halogenated alcohol and saturated alcohol. The values of various descriptors of these compounds, in different combinations have been used for MLR analysis. The following three MLR equations providing high quality predictive toxicity are the following models:

RE5=-0.0409116 E_T -0.142859 η -2.11995
rCV^2=0.610654 r^2=0.721792 (13)

RE6=-0.0472426 E_T +0.930021 η -1.44334 χ-15.552
rCV^2=0.790504 r^2=0.863758 (14)

The equ. 14 (RE6) provides best result (r^2=0.790504 r^2=0.863758) and treated as best QSTR model. This model also includes total energy as first descriptor, absolute hardness as second and electronegativity as third descriptor.

Fourth set

This set consists of twenty three derivatives of unsaturated alcohol. The values of various descriptors of these compounds, in different combinations have been used for MLR analysis. The following three MLR equations providing high quality predictive toxicity are the following models:

RE7=-0.0568369 E_T -0.220659η-2.70974
rCV^2=0.529661 r^2=0.659909 (15)

RE8=-0.0565628 E_T -0.213777η+0.0424689χ-2.54696
rCV^2=0.51909 r^2=0.659993 (16)

In the above regression equations, the equ. 16 (RE8) provides best result (rCV^2=0.51909 r^2=0.659993) and treated as best QSTR model. This model also includes total energy as first descriptor, absolute hardness as second and electronegativity as third descriptor.

CONCLUSION

1. There is direct relationship between reported biological toxicity and absolute hardness of all the four sets of alcohol .viz 1, 2, 3 and 4. The absolute hardness can alone be helpful for searching alcohol of desired toxicity.
2. Total energy, absolute hardness and electronegativity are important parameter for QSTR study. The above combination of these descriptors provides best QSTR models as is indicated below.

RE2=-0.0200482 E_T +2.6751η+1.76358χ-12.6263
rC^2=0.891749 r^2=0.94147 (10)

RE4=-0.0470833 E_T -0.57337 η -2.58083χ-11.0288
rCV^2=0.314847 r^2=0.707338 (12)

RE6=-0.0472426 E_T +0.930021 η -1.44334 χ-15.552
rCV^2=0.790504 r^2=0.863758 (14)

RE8=-0.0565628 E_T -0.213777η+0.0424689χ-2.54696
rCV^2=0.51909 r^2=0.659993 (16)

On the basis of statistical quality of results it is clear that one can use these equations to demonstrate the relative toxicity of compounds of similar series.

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