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QSAR and QSPR studies with principle eigen value of distance matrix

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ABSTRACT

Principle eigen value of distance matrix for salicylhydroxamic acids derivatives have determined and then correlated with Physicochemical properties namely logP, Molar volume and Parachor values. Excellent results have been obtained while multiple linear graph methods have been used to calculate biological & physico-chemical properties of different derivatives.

Key words: QSAR & QSPR studies, Principle Eigen value, distance matrix.

INTRODUCTION

Transformation of chemical structure into mathematical graph makes it possible to express the chemical structure by a single number, such graph representing the molecular structure are called molecular graph. Each molecular graph can be represented by matrix, a polynomials, a sequence of number or by numerical index.

The advantage of topological index or principle eigen values is that, may be used directly as simple numerical descriptor in Quantity Structure Properties Relationship (QSPR) and Quantity Activity Properties Relationship (QSAR). These relationships are mathematical models that enable the prediction of properties or activity from structural parameters (i.e. Principle eigen values).

Balaban et al made use of eigen values and eigen vectors of a molecular adjacency matrix for correlating the boiling point of alkanes. This proved to be very successful, in this limited domain, giving correlation coefficients greater than 0.98. Yi-qui *et al* used the sum of the absolute value of the eigen values to investigate the boiling points of 149 hydrocarbons which gave correlation coefficient greater than 0.99. Hateroatoms were also introduced by including the electronegativity in the diagonal elements of the adjacency matrix, and valency at the vertex of each bond for the off-diagonal elements. This was tested on 37 alcohols giving a correlation coefficient of 0.98 which proved to be marginally less successful with the use of Randic index connectivity indices. Finally, Yi-qui *et al*[3] tested their indices on the logP values of 25 barbiturates giving a correlation of 0.99.

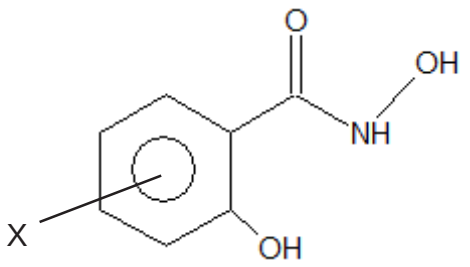

Fig. -1: General molecular structure of SHA

For a distance matrix D with unit matrix I equation $|D-\lambda I| = 0$ is known as characteristic equation are called the proper value or eigen value and it denoted by λ. Principle eigen value is the largest positive eigen value of the distance matrix. The set of eigen value is collectively called the spectra of graph. Eigen value has been often considered and applied as a structure descriptor and topological index.

In the present investigation we have taken a series of salicylhydroxamic acids derivatives. For these derivatives principle eigen values have been determined by molecular graph and its distance matrix*. These principal eigen values than correlated with biological properties logP (partition coefficient of octanol-water system), it is the most widely and frequently used parameter for structure activity studies in bio-chemical system and measure of hydrophobicity (or lipopilicity) of chemicals which in turn is a very important property in medicinal chemistry, toxicology, pharmaceutical and environmental science. In present investigation we have also correlate principle eigen value with Parachor (Pr) and Molar Volume (Mv).

RESULTS AND DISCUSSION

Regression equations shown Table 2 have used for calculated logp, calculated Mv and calculated Pr. These estimated properties have considerable precision. As shown in table -2 correlation coefficient for logp and ev(D) is 0.7319, for Mv and ev(D) is 0.9785 and 0.9801 for Pr and ev(D) which are excellent results. Graphical representation of these results also indicates that principle eigen values can work as molecular descriptors for QSAR and QSPR studies. Graphically the results of correlation of principal eigen value with logP, Pr and Mv are given in Figs. 2-4.

It is worthy mentioning that the studied compounds are nuclear substituted derivatives of salicylhydroxamic acid (SHA) and they differ in the number and the position of various substituents in

Table - 1: Compounds and their principle eigen value with observed and calculated partition coefficient (logP), Parachor (Pr) and Molar Volume(Mv) are listed here

S. No.	Name of compounds	ev(D)*	logp (obs)	logp (cal)	Mv (obs)	Mv (cal)	Pr (obs)	Pr (cal)
1	Salicylhydroxamic acid (SHA)	44.2304	0.313	0.1166	109.2	109.8493	312.3	313.2851
2	4- Methoxy SHA	57.2018	0.121	0.9816	133.2	141.0391	369.0	387.0142
3	5- Methoxy SHA	56.1404	0.121	0.9108	133.2	138.487	369.0	380.9813
4	4,5- Methoxy SHA	68.027	0.155	1.7034	157.2	167.0684	425.7	448.5444
5	4- Methyl SHA	50.0858	0.732	0.5071	125.4	123.9287	350.0	346.5671
6	5- Methyl SHA	49.478	0.732	0.4665	125.4	122.4672	350.0	343.1123
7	4,5- Methyl SHA	54.9659	1.151	0.8325	141.7	135.6629	387.6	374.3054
8	4- Ethyl SHA	57.2018	1.251	0.9816	142.0	141.0391	388.9	387.0142
9	5- Ethyl SHA	56.1404	1.251	0.9108	142.0	138.487	388.9	380.9813
10	4,5- Ethyl SHA	68.027	2.189	1.7033	174.8	167.0684	465.5	448.5444
11	4-Propyl SHA	65.666	1.787	1.5459	158.5	161.3914	428.7	435.1246
12	5- Propyl SHA	64.055	1.787	1.4385	158.5	157.5177	428.7	425.9677
13	4,5- Propyl SHA	83.7578	3.261	2.7523	207.8	204.8933	545.1	537.9579

Table -2: Correlation Expressions

S. No.	Correlation paramters	Regression Equations	Correlation coefficient
1	ev(D) and logP	logp = 0.066679 × ev(D) - 2.83261	0.731998
2	ev(D) and Mv	Mv = 2.404509 × ev(D) + 3.496905	0.978536
3	ev(D) and Pr	Pr = (5.683977) × ev(D) +61.88055	0.980107

* ev(D) = Principle eigen value for distance matrix
logP(cal) = Calculated logrithmic partition coefficient
Mv(cal) = Calculated Molar Volume
Pr(cal) = Calculated Parachor
logP(obs) = Observed logrithmic partition coefficient
Mv(obs) = Observed Molar Volume
Pr(obs) = Observed Parachor

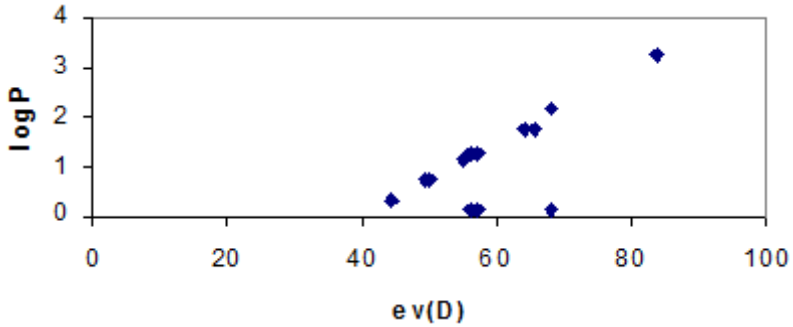

Fig. -2: Correlation graph of principle eigen value ev(D) and logP

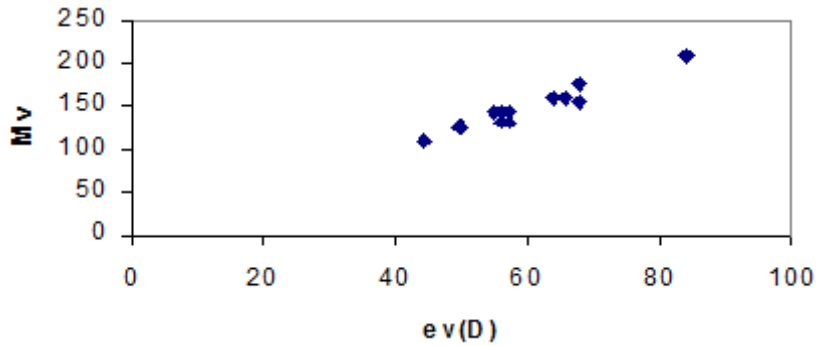

Fig. -3: Correlation graph of principle eigen value ev(D) and volume Mv

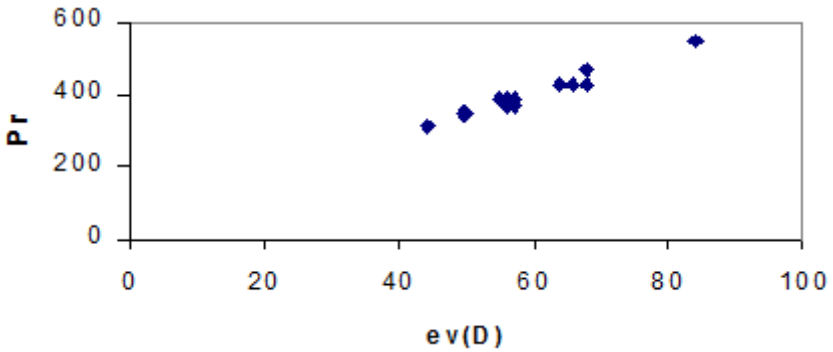

Fig. -4: Correlation graph of principle eigen value ev(D) and parachore Pr

the aromatic skeleton of SHA moiety. Therefore changes in the property as well as changes in principle eigen values may be attributed.

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