QSAR study for the prediction of physico-chemical parameter of category barbiturate compounds by using descriptors structure

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Topological indices as molecule indices are used in quantitative studies of structure- properties.

In this study the relationship between the S1K, X0, X0sol, MW, Se, Ms, BAC , BIC2, Xindex, X3A , CSI, S3K, SRW04, IDDE, nSK ,Ss , SMTIV ,GNar , TIC0, X5v , AECC and UNIPcalculated by Dragon to the Polarizability (POL) of 32 barbiturates is represented. The chemical structures of the molecules were optimized using ab initio 6-31G basis sets method and Polak-Ribiere algorithm with conjugated gradient within HyperChem 8.0 environment. The multiple linear regressions (MLR) and Back ward methods (with significant at the 0.05 level) were employed to give the QSAR models.After MLR analysis, we studied the validation of linearity between the molecular descriptors in the best models for used properties. The predictive powers of the models were discussed by using the method of cross-validation. The results have shown that descriptors (S3K, SRW04, and GNar) could be efficiently used for estimating the polarizabilityof respect compounds.

**Key words: ???**

INTRODUCTION

Barbiturates are a group of compounds that are focal nervous system depressants.Barbiturates overdose leads to weakness of the central nervous system, recessional and cardiovascular depression and finally death[1-4]. The first report of Quantitative Structure–Activity Relationship (QSAR) was reported by Crum-Brown and Fraser that studied the relationship between chemical structure and physiological activity [5]. QSAR has been known as a quantum chemical method in connection with the biological activity of compounds of their molecular structure and has been used as a predictive tool in drug design[6]. The medicinal importance of pyrimidine derivatives such as barbituric acid and thiobarbituric acid plays an essential role across different heterocyclic compounds due to theirantineoplastic[7,8], antiviral [9], the antibiotic [10].

and anti-inflammatory [11] activity.Toxicity of the addictive drugs (barbiturates and thiobarbiturates) by using physical and chemical describers have been proposed [12-15].

QSAR studies on the estimation validation approach of chemical mixtureshave been investigated [16]. QSAR studies have been examined using 3D parameters in predicting the biological properties especially molecular toxicity [17-21]. Derivations of barbiturates based on nuclides in a watery environment as a potential anti- cancer agent has been designed [22, 23].

MATERIALS, MATHEMATICAL METHOD,AND GRAPHS

The Polarizability of barbiturates is taken from the quantum mechanics methodology with ab initio 6-31G basis sets method and Polak-Ribiere algorithm with conjugated gradient within HyperChem 8.0 environment. A set of thirty-two essential barbiturates was investigated. Studied barbiturates and their Polarizability are listed in Table 1.

**Table 1.** Barbiturates and their Polarizabilityin the present study.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| POL | No. | Compounds | POL | No. | Compounds |
| 27.55 | 17 | 5-Ethyl-1,3-dimethyl-5-phenylpyrimidine-2,4,6-trione | 11.1 | 1 | Barbituric acid |
| 12.14 | 18 | 5-Methylbarbiturate | 14.22 | 2 | 1,3-Dimethylpyrimidine-2,4,6-trione |
| 13.42 | 19 | 5-Ethyl-barbiturate | 14.77 | 3 | 5,5-Dimethylpyrimidine-2,4,6-trione |
| 16.6 | 20 | Isopropylbarbiturate | 16.6 | 4 | 5-Ethyl-5-methylpyrimidine-2,4,6-trione |
| 18.44 | 21 | 5,5-Diethylbarbiturate | 16.6 | 5 | 5-Ethyl-1-methylpyrimidine-2,4,6-trione |
| 18.24 | 22 | 5-Methyl-5-allylbarbiturate | 23.14 | 6 | 5-Ethyl-5-isopentylpyrimidine-2,4,6-trione |
| 20.27 | 23 | 5-Ethyl-5-propylbarbiturate | 23.94 | 7 | 5-Sec-butyl-5-ethyl-1-methylpyrimidine-2,4,6-trione |
| 22.11 | 24 | 5,5-Dipropylbarbiturate | 23.94 | 8 | 5-Ethyl-5-(pentan-2-yl)pyrimidine-2,4,6-trione |
| 22.11 | 25 | 5,5-Di-i-propylbarbiturate | 22.11 | 9 | 5-Sec-butyl-5-ethylpyrimidine-2,4,6-trione |
| 20.08 | 26 | 5-Ethyl-5-allylbarbiturate | 22.11 | 10 | 5-(Hexan-2-yl)pyrimidine-2,4,6-trione |
| 21.91 | 27 | 5-Methyl-5-(3-methylbut-2-enyl) barbiturate | 29.45 | 11 | 5-Ethyl-5-(Hexan-2-yl)-1,3-dimethylpyrimidine-2,4,6-trione 11 |
| 23.2 | 28 | 5-Ethyl-5-(3-methylbut-2-enyl) barbiturate | 25.58 | 12 | 5-Allyl-5-(pentan-2-yl)pyrimidine-2,4,6-trione |
| 27.61 | 29 | 5-Ethyl-5-heptylbarbiturate | 21.91 | 13 | 5-Sec-butyl-5-allylpyrimidine-2,4,6-trione |
| 23.4 | 30 | 5-Ethyl-5-pentylbarbiturate | 24.01 | 14 | 5-Cyclohexenyl-1,5-dimethylpyrimidine-2,4,6-trione |
| 25.23 | 31 | Hexethal | 24.43 | 15 | 5-Ethyl-5-phenylpyrimidine-2,4,6-trione |
| 25.04 | 32 | 5-i-Propyl-5-(3-methylbut-2-enyl) barbiturate | 26.26 | 16 | 5-Ethyl-1-methyl-5-phenylpyrimidine-2,4,6-trione |

TOPOLOGICAL INDICES

A topological index is a numeric amount that is mathematically obtained in a direct and unambiguous method from the structural graph of a molecule. Descriptors of the structure of drugs were computed by standard molecular modeling.Hyperchem 8 for Windows operatingsystem was used. Geometry optimization wasperformed using molecular mechanics ab initio 6-31G force fieldmethod and was followed by quantum chemicalcalculations according to ab initio 6-31Gmethod.In addition, the set of structural descriptors was completed with Dragon 5.5 software.23The list of descriptors is presented in Table (2, 3)

REGRESSION ANALYSES

In the present work, linear regression analyses were performed using SPSS-16 (SPSS Inc., Chicago, IL, USA)) and method Back ward step wise regression routine implemented in SPSS to develop the linear model for the prediction of Polarizability.The Polarizability (POL ) is used as the dependent variable S1K, X0, X0sol,MW, Se,Ms, BAC,BIC2, Xindex, X3A,CSI, S3K, SRW04,IDDE,nSK,Ss,SMTIV,GNar,TIC0, X5v, AECC and UNIPindices as the independent variables. Criteria for selection of the best multiple linear regression models were the statistics: squared multiple correlation coefficients (), adjusted correlation coefficient (), Fisher ratio (F), root mean square error (RMSE), Durbin-Watson value (DW) and significant (Sig).

**Table 2.** Listof structural parameters employed in present study

|  |  |
| --- | --- |
| Abbreviation | Description |
| S1K | 1-path Kier alpha-modified shape index |
| MW | Molecular weight |
| X0sol | solvation connectivity index of order 0 |
| X0 | connectivity index of order 0 |
| Se | sum of atomic Sanderson electronegativities (scaled on Carbon atom) |
| Ms | mean first ionization potential (scaled on Carbon atom) |
| BAC | Balaban centric index |
| BIC2 | Bond Information Content index (neighborhood symmetry of 2-order) |
| Xindex | Balaban X index |
| X3A | average connectivity index of order 3 |
| CSI | eccentric connectivity index |
| S3K | 3-path Kier alpha-modified shape index |
| SRW04 | self-returning walk count of order 4 |
| IDDE | mean information content on the distance degree equality |
| nSK | number of non-H atoms |
| Ss | sum of first ionization potentials (scaled on Carbon atom) |
| SMTIV | Schultz Molecular Topological Index by valence vertex degrees |
| GNar | Narumi geometric topological index |
| TIC0 | Total Information Content index (neighborhood symmetry of 0-order) |
| X5v | valence connectivity index of order 5 |
| AECC | average eccentricity |
| UNIP | unipolarity |

**Table 3.** List of barbiturates studied and structural parameters.

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Comp. No. | S1K | MW | X0sol | X0 | Se | Ms | BAC | BIC2 | Xindex | X3A | CSI |
| 1 | 6.074 | 128.1 | 6.853 | 6.853 | 14.07 | 3.61 | 10 | 0.733 | 0.817 | 0.201 | 63 |
| 2 | 8.049 | 156.16 | 8.594 | 8.594 | 19.84 | 3.23 | 26 | 0.651 | 0.822 | 0.21 | 89 |
| 3 | 8.049 | 156.16 | 8.646 | 8.646 | 19.84 | 3.3 | 26 | 0.651 | 0.837 | 0.203 | 85 |
| 4 | 9.039 | 170.19 | 9.353 | 9.353 | 22.72 | 3.15 | 27 | 0.711 | 0.819 | 0.197 | 100 |
| 5 | 9.039 | 170.19 | 9.301 | 9.301 | 22.72 | 3.11 | 27 | 0.828 | 0.797 | 0.198 | 104 |
| 6 | 13.015 | 226.31 | 12.345 | 12.35 | 34.25 | 2.76 | 43 | 0.671 | 0.731 | 0.183 | 186 |
| 7 | 13.015 | 226.31 | 12.508 | 12.51 | 34.25 | 2.76 | 55 | 0.721 | 0.807 | 0.181 | 162 |
| 8 | 13.015 | 226.31 | 12.345 | 12.35 | 34.25 | 2.76 | 43 | 0.671 | 0.771 | 0.175 | 182 |
| 9 | 12.046 | 212.28 | 11.422 | 11.42 | 31.37 | 2.63 | 32 | 0.755 | 0.703 | 0.195 | 168 |
| 10 | 12.02 | 212.28 | 11.422 | 11.42 | 31.37 | 2.81 | 30 | 0.726 | 0.689 | 0.189 | 198 |
| 11 | 16.004 | 268.4 | 14.793 | 14.79 | 42.91 | 2.56 | 72 | 0.654 | 0.763 | 0.182 | 252 |
| 12 | 13.752 | 238.32 | 13.052 | 13.05 | 35.25 | 2.77 | 46 | 0.779 | 0.761 | 0.172 | 195 |
| 13 | 11.761 | 210.26 | 11.638 | 11.64 | 29.49 | 2.94 | 42 | 0.761 | 0.794 | 0.17 | 151 |
| 14 | 12.153 | 236.3 | 12.629 | 12.63 | 33.37 | 2.67 | 26 | 0.791 | 0.571 | 0.183 | 212 |
| 15 | 11.648 | 232.26 | 12.466 | 12.47 | 29.6 | 2.79 | 18 | 0.719 | 0.571 | 0.171 | 210 |
| 16 | 12.621 | 246.29 | 13.337 | 13.34 | 32.49 | 2.72 | 27 | 0.758 | 0.575 | 0.174 | 223 |
| 17 | 13.597 | 260.32 | 14.207 | 14.21 | 35.37 | 2.65 | 38 | 0.694 | 0.58 | 0.176 | 236 |
| 18 | 7.06 | 142.13 | 7.724 | 7.724 | 16.95 | 3.43 | 17 | 0.754 | 0.818 | 0.209 | 76 |
| 19 | 8.049 | 156.16 | 8.431 | 8.431 | 19.84 | 3.26 | 18 | 0.778 | 0.789 | 0.193 | 91 |
| 20 | 9.039 | 170.19 | 9.301 | 9.301 | 22.72 | 3.11 | 27 | 0.75 | 0.783 | 0.182 | 102 |
| 21 | 10.032 | 184.22 | 10.06 | 10.06 | 25.6 | 3.02 | 30 | 0.671 | 0.811 | 0.184 | 111 |
| 22 | 9.774 | 182.2 | 10.06 | 10.06 | 23.72 | 3.13 | 28 | 0.798 | 0.784 | 0.19 | 129 |
| 23 | 11.025 | 198.25 | 10.768 | 10.77 | 28.49 | 2.91 | 31 | 0.675 | 0.784 | 0.18 | 140 |
| 24 | 12.02 | 212.28 | 11.475 | 11.48 | 31.37 | 2.82 | 34 | 0.635 | 0.766 | 0.175 | 153 |
| 25 | 12.02 | 212.28 | 11.801 | 11.8 | 31.37 | 2.86 | 54 | 0.574 | 0.823 | 0.163 | 133 |
| 26 | 10.767 | 196.23 | 10.768 | 10.77 | 26.6 | 3.02 | 31 | 0.811 | 0.784 | 0.18 | 140 |
| 27 | 11.761 | 210.26 | 11.638 | 11.64 | 29.49 | 2.89 | 40 | 0.742 | 0.722 | 0.193 | 175 |
| 28 | 12.756 | 224.29 | 12.345 | 12.35 | 32.37 | 2.81 | 43 | 0.76 | 0.731 | 0.183 | 186 |
| 29 | 15.007 | 254.37 | 13.596 | 13.6 | 40.02 | 2.6 | 35 | 0.581 | 0.643 | 0.19 | 299 |
| 30 | 13.015 | 226.31 | 12.182 | 12.18 | 34.25 | 2.73 | 33 | 0.634 | 0.713 | 0.185 | 211 |
| 31 | 14.011 | 240.34 | 12.889 | 12.89 | 37.14 | 2.66 | 34 | 0.607 | 0.677 | 0.188 | 253 |
| 32 | 13.752 | 238.32 | 13.215 | 13.22 | 35.25 | 2.75 | 56 | 0.727 | 0.747 | 0.174 | 197 |

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Comp. No. | S3K | SRW04 | IDDE | nSK | Ss | SMTIV | GNar | TIC0 | X5v | AECC | UNIP |
| 1 | 1.419 | 66 | 1.585 | 9 | 32.5 | 968 | 1.82 | 25.351 | 0.23 | 3.667 | 16 |
| 2 | 1.203 | 86 | 2.732 | 11 | 35.5 | 1330 | 1.76 | 34.446 | 0.438 | 4.273 | 20 |
| 3 | 1.203 | 90 | 2.732 | 11 | 36.25 | 1324 | 1.74 | 34.446 | 0.397 | 4.091 | 19 |
| 4 | 1.321 | 96 | 2.752 | 12 | 37.75 | 1568 | 1.76 | 38.482 | 0.452 | 4.417 | 21 |
| 5 | 1.45 | 92 | 2.918 | 12 | 37.33 | 1582 | 1.77 | 38.482 | 0.562 | 4.583 | 23 |
| 6 | 2.565 | 124 | 2.983 | 16 | 44.08 | 2986 | 1.78 | 53.106 | 1.208 | 6.125 | 34 |
| 7 | 1.738 | 128 | 3.75 | 16 | 44.08 | 2712 | 1.75 | 53.106 | 1.104 | 5.375 | 31 |
| 8 | 2.091 | 124 | 3.078 | 16 | 44.08 | 2858 | 1.78 | 53.106 | 1.007 | 6 | 32 |
| 9 | 2.96 | 110 | 3.64 | 15 | 39.5 | 2624 | 1.82 | 49.606 | 0.689 | 5.867 | 33 |
| 10 | 2.947 | 110 | 3.374 | 15 | 42.17 | 2774 | 1.82 | 49.606 | 1.002 | 6.867 | 34 |
| 11 | 2.373 | 150 | 3.392 | 19 | 48.58 | 4050 | 1.76 | 63.232 | 1.724 | 6.947 | 43 |
| 12 | 2.355 | 130 | 3.41 | 17 | 47.08 | 3397 | 1.79 | 54.692 | 1.2 | 6.059 | 35 |
| 13 | 1.761 | 118 | 3.24 | 15 | 44.08 | 2559 | 1.77 | 47.604 | 0.809 | 5.333 | 28 |
| 14 | 1.757 | 144 | 3.572 | 17 | 45.42 | 3438 | 1.91 | 52.691 | 1.629 | 6.118 | 36 |
| 15 | 1.696 | 140 | 3.146 | 17 | 47.42 | 3724 | 1.95 | 48.087 | 1.149 | 6.059 | 35 |
| 16 | 1.723 | 150 | 3.281 | 18 | 48.92 | 4096 | 1.92 | 51.836 | 1.355 | 6.111 | 38 |
| 17 | 1.742 | 160 | 3.471 | 19 | 50.42 | 4482 | 1.89 | 55.467 | 1.546 | 6.158 | 41 |
| 18 | 1.285 | 76 | 1.895 | 10 | 34.33 | 1142 | 1.78 | 30.126 | 0.324 | 4 | 18 |
| 19 | 1.504 | 82 | 2.914 | 11 | 35.83 | 1376 | 1.8 | 34.446 | 0.387 | 4.364 | 20 |
| 20 | 1.773 | 92 | 2.689 | 12 | 37.33 | 1610 | 1.77 | 38.482 | 0.443 | 4.5 | 22 |
| 21 | 1.408 | 102 | 2.931 | 13 | 39.25 | 1826 | 1.77 | 42.322 | 0.508 | 4.538 | 23 |
| 22 | 1.567 | 102 | 3.085 | 13 | 40.75 | 1981 | 1.77 | 40.068 | 0.546 | 5.231 | 24 |
| 23 | 1.771 | 108 | 3.182 | 14 | 40.75 | 2158 | 1.79 | 46.019 | 0.886 | 5.286 | 26 |
| 24 | 2.137 | 114 | 3.107 | 15 | 42.25 | 2512 | 1.8 | 49.606 | 1.16 | 5.4 | 29 |
| 25 | 1.62 | 122 | 2.84 | 15 | 42.92 | 2372 | 1.74 | 49.606 | 0.59 | 4.733 | 27 |
| 26 | 1.677 | 108 | 3.182 | 14 | 42.25 | 2266 | 1.79 | 43.908 | 0.703 | 5.286 | 26 |
| 27 | 2.378 | 118 | 3.006 | 15 | 43.42 | 2775 | 1.77 | 47.604 | 0.916 | 6.133 | 32 |
| 28 | 2.455 | 124 | 2.983 | 16 | 44.92 | 3104 | 1.78 | 51.191 | 0.984 | 6.125 | 34 |
| 29 | 3.475 | 132 | 3.684 | 18 | 46.75 | 4306 | 1.83 | 59.909 | 1.371 | 8.556 | 48 |
| 30 | 2.565 | 120 | 3.108 | 16 | 43.75 | 3060 | 1.82 | 53.106 | 1.106 | 6.875 | 35 |
| 31 | 2.991 | 126 | 3.735 | 17 | 45.25 | 3638 | 1.83 | 56.537 | 1.246 | 7.706 | 41 |
| 32 | 2.511 | 134 | 3.175 | 17 | 46.75 | 3441 | 1.76 | 54.692 | 1.044 | 6.118 | 36 |

I.QSAR MODELS FOR THE POLARIIZABILITY (POL)

The best linear model for Polarizability contains eight descriptors, namely, Se, Ms, Xindex, S3K, SRW04,GNar, AECC and UNIP indices. The regression parameters of the best eight descriptors correlation model are gathered in equation (1).

Model.I.

POL= -67.609+0.333 Se -5.949Ms +40.940 Xindex +1.806 S3K +0.211 SRW04 +27.225 GNar +0.908 AECC+0.118 UNIP(1) (1)

N=32 R=0.998=0.996 = 0.995 RMSE=9.285 F=818.517 Sig=0.000 DW=2.181

This model produced a root mean square error(RMSE) of 9.285, a squared correlation coefficient of 0.996, and the adjusted correlation coefficient (adjusted r- squared) was calculated as 0.995. The result is therefore very satisfactory.

DISCUSSION

We studied the relationship between descriptorsstructural to the Polarizabilityof 32 barbiturates.In this study, to find the best model for predict the parameters mentioned, we will use the following sections.

MULTICOLLINEARITY

Multiple linear regression is one of the most complex statistical techniques that are usually used for data whose level of their measurement is spatial(distance). Multivariate regression is a method for the collective and individual participation of two or more independent variables in the variations of a dependent variable since the basic task of science is the prediction and explanation of phenomena. The word of collinearity indicates that the two variables are close to a linear combination of each other. When there are more than two variables in the model,the term is changed to "multicollinearity". Test multicollinearity as a basis the variance inflation factor (VIF) value of multicollinearity test results using SPSS. If the VIF value lies between1-10, then there is no multicollinearity, and if the VIF<1 or >10, then there is multicollinearity.

In all our final models, the Multicollinearity has existed, because the values of correlations between independent variables are near to one and VIFs value lies are not use of between 1-10.

VERIFICATION AND VALIDITY OF MODELS

In this section,it emphasizes the validation of regression models on the Durbin-Watson and unstandardized predicted and residual values. The Durbin-Watson is used to evaluate the correlated residuals.The Durbin-Watson statistic is between 0 and 4 that its middle point is 2.

In our model, the value of Durbin-Watson statistic is 2(See eq.1) and hence the errors are uncorrelated.

RESULTS ANDDISCUSSION VALIDATION

Multiple linear regression methodswere used for all QSAR analyses. A good QSARmodel should have both suitable relativity and good predictability. We studied the validation of linearity between the moleculardescriptors in the modelI

We obtained by SPSS the Pearson coefficient correlation and collinearity statistics as follow Tables (4).

For modelI the Pearson correlation (Se,Xindex),( Se,Ms),(Xindex,GNar) is near one, and VIF(Se),VIF(Xindex) and VIF (Ms), VIF (GNar)>10, therefore there is a linearity between (Se,Xindex),( Se,Ms) and (Xindex,GNar). After removed Se from this modelsix indices GNar, S3K,Ms,Xindex,AECCand SRW04 remains the Pearson correlation (Xindex,GNar) is near one, and VIF(Xindex),VIF(GNar) )>10,therefore there is a linearity between Xindex and GNar. After removed Xindex from this model, we corrected model Ias follows:

POL= 11.273 +2.098 S3K +0.185 SRW04-8.613GNar (2)

N=32 R=0.991=0.983 = 0.981 RMSE=15.060 F=540.809 Sig=0.000 DW=1.893 Q2=0.933 (2)

Furthermore, we have computed Q2 (Eq.3) by 50% of data, randomly, that is positive and less than one.

Where the notation i|i indicates that the response is predicted by a model estimated when the ith sample was left out from the training set.

**Table 4.** Correlation between the molecular descriptors (modelI)

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| model | Corrected |  |  |  |  |  |  |  | statistical | Collinearity |
| VIF | Tolerance | Se | SRW04 | AECC | Ms | Xindex | S3K | GNar | UNIP |  |
| 82.488 | .012 |  |  |  |  |  |  |  | 1.000 | UNIP |
| 17.323 | .058 |  |  |  |  |  |  | 1.000 | .175 | GNar |
| 15.196 | .066 |  |  |  |  |  | 1.000 | .403 | -.244 | S3K |
| 70.370 | .014 |  |  |  |  | 1.000 | .391 | .869 | .403 | Xindex |
| 41.846 | .024 |  |  |  | 1.000 | -.648 | .048 | -.396 | -.526 | Ms |
| 25.949 | .039 |  |  | 1.000 | -.242 | .360 | .001 | .261 | -.371 | AECC |
| 62.593 | .016 |  | 1.000 | .478 | -.231 | .662 | .768 | .505 | -.161 | SRW04 |
| 179.436 | .006 | 1.000 | -.670 | -.360 | .805 | -.840 | -.338 | -.517 | -.499 | Se |
|  | | | | | | | | | | |

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | model | Corrected |  |  |  |  |  | statistical | Collinearity |
| VIF | VIF | Tolerance | SRW04 | AECC | Xindex | Ms | S3K | GNar |  |
| 1.325 | 12.527 | .080 |  |  |  |  |  | 1.000 | GNar |
| 1.275 | 10.002 | .100 |  |  |  |  | 1.000 | .264 | S3K |
| - | 13.869 | .072 |  |  |  | 1.000 | .540 | .015 | Ms |
| - | 20.701 | .048 |  |  | 1.000 | .083 | .224 | .938 | Xindex |
| - | 12.105 | .083 |  | 1.000 | .125 | -.109 | -.764 | .024 | AECC |
| 1.638 | 14.042 | .071 | 1.000 | -.393 | .347 | .828 | .699 | .257 | SRW04 |

REGULARRESIDUALS

The residual is the difference between the observed and predicted values.Comparisonbetween predicted and observed values of Polarizability,barbiturates show in Table (5). Figures (1) show the linear correlation between theobserved and the predicted Polarizability of barbiturates values obtained using equation (2).

**Table 5.** Comparison between predicted and observed values of models calculated validation of POL respect barbiturates.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Residual | PredictedPOL | Observed  POL | No. | Residual | Predicted  POL | Observed  POL | No. |
| -0.638 | 28.188 | 27.55 | 17 | 0.300 | 10.800 | 11.1 | 1 |
| -0.520 | 12.660 | 12.14 | 18 | -0.357 | 14.577 | 14.22 | 2 |
| -0.653 | 14.073 | 13.42 | 19 | -0.710 | 15.480 | 14.77 | 3 |
| -0.118 | 16.718 | 16.6 | 20 | -0.056 | 16.656 | 16.6 | 4 |
| 0.639 | 17.801 | 18.44 | 21 | 0.559 | 16.041 | 16.6 | 5 |
| 0.106 | 18.134 | 18.24 | 22 | -1.086 | 24.226 | 23.14 | 6 |
| 0.736 | 19.534 | 20.27 | 23 | 0.443 | 23.497 | 23.94 | 7 |
| 0.811 | 21.299 | 22.11 | 24 | 0.709 | 23.231 | 23.94 | 8 |
| -0.168 | 22.278 | 22.11 | 25 | -0.056 | 22.166 | 22.11 | 9 |
| 0.744 | 19.336 | 20.08 | 26 | -0.028 | 22.138 | 22.11 | 10 |
| -0.926 | 22.836 | 21.91 | 27 | 0.641 | 28.809 | 29.45 | 11 |
| -0.795 | 23.995 | 23.2 | 28 | 0.789 | 24.791 | 25.58 | 12 |
| 0.444 | 27.166 | 27.61 | 29 | 0.368 | 21.542 | 21.91 | 13 |
| 0.198 | 23.202 | 23.4 | 30 | -1.080 | 25.090 | 24.01 | 14 |
| 0.111 | 25.119 | 25.23 | 31 | 0.491 | 23.939 | 24.43 | 15 |
| -1.076 | 26.116 | 25.04 | 32 | 0.175 | 26.085 | 26.26 | 16 |

**Fig .1.** Comparison between the predicted and observed of models calculated validationof Polarizability by MLR method.

QSAR STUDIES AND PREDICTIONS

OF PROPERTIES BASED ON IT:

As mentioned in the second part,it can investigate the Quantitative Structure-Activity Relationship (QSAR) using the graph theory and obtain the appropriate index that correlates with the desired properties. In this section of the research, it is possible to predict properties using the findings of the first part of the study and determine the appropriate indicators of each property by applying the index to the desired state. So, for this purpose, choose ten combinations of barbiturates such as (5-t-Butyl-5-(3-methylbut-2-enyl) barbiturate, 5-Ethyl-5-octylbarbiturate,5-Ethyl-5-nonylbarbiturate, Cyclopropane-spirobarbiturate, Cyclobutane- Spiro barbiturate, Cyclopentane- Spiro barbiturate,Cyclohexane- Spiro barbiturate, Cycloheptane-spirobarbiturate,5-Allyl-5-phenylbarbiturate,and 5,5-Diphenylbarbiturate )and then was found a suitable index using the obtained results(Equation2) for molecular, computational and Physico-chemical properties. Thus,the S3K,SRW04 and GNarindicesare considered to the Polarizabilityand the results are shown in the Table(6).

**Table 6.** Comparison between predicted and HyperChem values of models calculated validation of POL for ten compounds of Barbiturates.

|  |  |  |  |
| --- | --- | --- | --- |
| Δ[POL(Hyper) –POL( Pre)] | POL(Pre) | POL(Hyper) | compounds No. |
| S3K, SRW04,GNar | S3K, SRW04,GNar |  |  |
| -2.28 | 29.15 | 26.87 | 1 5-t-Butyl-5-(3-methylbut-2-enyl) barbiturate |
| -0.32 | 29.22 | 28.9 | 2 5-Ethyl-5-octylbarbiturate |
| -0.65 | 31.39 | 30.74 | 3 5-Ethyl-5-nonylbarbiturate |
| -1.08 | 14.53 | 13.45 | 4 Cyclopropane-spirobarbiturate |
| -1.93 | 17.21 | 15.28 | 5 Cyclobutane-spirobarbiturate |
| -1.11 | 18.23 | 17.12 | 6 Cyclopentane-spirobarbiturate |
| -0.11 | 19.06 | 18.95 | 7 Cyclohexane-spirobarbiturate |
| -0.02 | 20.81 | 20.79 | 8 Cycloheptane-spirobarbiturate |
| -0.03 | 25.55 | 25.52 | 9 5-Allyl-5-phenylbarbiturate |
| -0.76 | 30.63 | 29.87 | 10 5,5-Diphenylbarbiturate |

CONCLUSIONS

In the present study, a set of 22 descriptors is adopted to build a model to describe Polarizability of 32 barbiturates. Results show that MLR model based on selected molecular descriptors showed a high degree of correlation between Polarizability observed and calculated.Cross-validation as the evaluation technique has been designed to evaluate the quality and predictive ability of the MLR model. The obtained results showed that (S3K, SRW04, and GNar) indicesare the good descriptorsstructuralfor predicting POL.

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